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### Section 8: Clinical Data

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ISTA Integrated Summary of Efficacy

Table 1: Summary of Patient Disposition by Randomized Group
(Phase III: VIT-02-08961X and VIT-03-08961X, All Patients)

| Number of Patients: | Saline Control | 55 IU Vitrase | 75 IU Vitrase | Overall |
|---|---|---|---|---|
| RANDOMIZED | 385 | 368 | 383 | 1136 |
| SCREENED | 383 | 365 | 377 | 1125 |
| INTENT-TO-TREAT POPULATION | 383 | 365 | 377 | 1125 |
| RECEIVED STUDY INJECTION | 378 | 359 | 374 | 1111 |
| COMPLETED VISIT: | | | | |
| 1 DAY POST TREATMENT | 373 ( 96.9%) | 354 ( 96.2%) | 369 ( 96.3%) | 1096 ( 96.5%) |
| WEEK 1 | 364 ( 94.5%) | 341 ( 92.7%) | 359 ( 93.7%) | 1064 ( 93.7%) |
| MONTH 1 | 327 ( 84.9%) | 294 ( 79.9%) | 321 ( 83.8%) | 942 ( 82.9%) |
| MONTH 2 | 334 ( 86.8%) | 315 ( 85.6%) | 330 ( 86.2%) | 979 ( 86.2%) |
| MONTH 3 | 348 ( 90.4%) | 320 ( 87.0%) | 342 ( 89.3%) | 1010 ( 88.9%) |
| MONTH 6 | 239 ( 62.1%) | 239 ( 64.9%) | 250 ( 65.3%) | 728 ( 64.1%) |
| MONTH 12 | 156 ( 40.5%) | 148 ( 40.2%) | 148 ( 38.6%) | 452 ( 39.8%) |
| REASON FOR DISCONTINUATION BEFORE 3 MONTHS | | | | |
| PATIENT WITHDREW CONSENT | 9 ( 2.3%) | 7 ( 1.9%) | 4 ( 1.0%) | 20 ( 1.8%) |
| LOST TO FOLLOW-UP | 0 ( 0.0%) | 5 ( 1.4%) | 3 ( 0.8%) | 8 ( 0.7%) |
| NON-COMPLIANCE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.1%) |
| (SERIOUS) ADVERSE EVENT | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 4 ( 0.4%) |
| DEATH | 2 ( 0.5%) | 9 ( 2.4%) | 6 ( 1.6%) | 17 ( 1.5%) |
| OTHER | 3 ( 0.8%) | 6 ( 1.6%) | 2 ( 0.5%) | 11 ( 1.0%) |
| REASON FOR DISCONTINUATION BEFORE 12 MONTHS | | | | |
| PATIENT WITHDREW CONSENT | 20 ( 5.2%) | 12 ( 3.3%) | 12 ( 3.1%) | 44 ( 3.9%) |
| LOST TO FOLLOW-UP | 12 ( 3.1%) | 5 ( 1.4%) | 14 ( 3.7%) | 31 ( 2.7%) |
| NON-COMPLIANCE | 1 ( 0.3%) | 3 ( 0.8%) | 2 ( 0.5%) | 6 ( 0.5%) |
| (SERIOUS) ADVERSE EVENT | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.0%) | 6 ( 0.5%) |
| DEATH | 14 ( 3.6%) | 15 ( 4.1%) | 19 ( 5.0%) | 48 ( 4.2%) |
| OTHER | 4 ( 1.0%) | 7 ( 1.9%) | 6 ( 1.6%) | 17 ( 1.5%) |
| REASON FOR DISCONTINUATION AFTER 12 MONTHS | | | | |
| PATIENT WITHDREW CONSENT | 3 ( 0.8%) | 6 ( 1.6%) | 7 ( 1.8%) | 16 ( 1.4%) |
| LOST TO FOLLOW-UP | 5 ( 1.3%) | 3 ( 0.8%) | 5 ( 1.3%) | 13 ( 1.1%) |
| NON-COMPLIANCE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.1%) |
| (SERIOUS) ADVERSE EVENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.1%) |
| DEATH | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 6 ( 0.5%) |
| OTHER | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) | 5 ( 0.4%) |

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Percentages (%) based on the number of patients randomized.
Patients in the watchful waiting controlled population are not included in this table.

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ISTA Integrated Summary of Efficacy

Table 2: Summary of Patient Disposition by Randomized Group
(Phase IIb: ACS202-HYA-001A (US) and ACS203-HYA-001MEX, All Patients)

| Number of Patients: | 7.5 IU Vitrase | 37.5 IU Vitrase | 75 IU Vitrase | Overall |
|---|---|---|---|---|
| SCREENED | 129 | 124 | 125 | 378 |
| RANDOMIZED | 129 | 124 | 125 | 378 |
| RECEIVED STUDY INJECTION | 129 | 124 | 125 | 378 |
| COMPLETED VISIT: | | | | |
| 1 DAY POST TREATMENT | 129 (100.0%) | 124 (100.0%) | 125 (100.0%) | 378 (100.0%) |
| WEEK 1 (DAY 7) | 125 ( 96.9%) | 118 ( 95.2%) | 124 ( 99.2%) | 367 ( 97.1%) |
| MONTH 1 (DAY 28) | 82 ( 63.6%) | 92 ( 74.2%) | 93 ( 74.4%) | 267 ( 70.6%) |
| MONTH 2 (DAY 56) | 66 ( 51.2%) | 68 ( 54.8%) | 54 ( 43.2%) | 188 ( 49.7%) |
| FOLLOW-UP MONTH 3 | 13 ( 10.1%) | 17 ( 13.7%) | 17 ( 13.6%) | 47 ( 12.4%) |
| FOLLOW-UP MONTH 6 | 11 ( 8.5%) | 8 ( 6.5%) | 10 ( 8.0%) | 29 ( 7.7%) |
| FOLLOW-UP 1 YEAR | 52 ( 40.3%) | 53 ( 42.7%) | 61 ( 48.8%) | 166 ( 43.9%) |
| REASON FOR DISCONTINUATION | | | | |
| ADVERSE EXPERIENCE | 1 ( 0.8%) | 2 ( 1.6%) | 1 ( 0.8%) | 4 ( 1.1%) |
| SUBJECT'S REQUEST TO END PARTICIPATION | 0 ( 0.0%) | 2 ( 1.6%) | 0 ( 0.0%) | 2 ( 0.5%) |
| NONCOMPLIANCE | 4 ( 3.1%) | 5 ( 4.0%) | 2 ( 1.6%) | 11 ( 2.9%) |
| LOST TO FOLLOW-UP | 5 ( 3.9%) | 3 ( 2.4%) | 5 ( 4.0%) | 13 ( 3.4%) |
| OTHER | 2 ( 1.6%) | 4 ( 3.2%) | 1 ( 0.8%) | 7 ( 1.9%) |

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Percentages (%) based on the number of patients randomized.

ISTA Integrated Summary of Efficacy

Table 3: Summary of Baseline Patient Characteristics
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| Variable | Value | Saline Control | 55 IU Vitrase | 75 IU Vitrase | Overall |
|---|---|---|---|---|---|
| GENDER | MALE | 185 ( 48.3%) | 185 ( 50.7%) | 211 ( 56.0%) | 581 ( 51.6%) |
| | FEMALE | 198 ( 51.7%) | 179 ( 49.0%) | 165 ( 43.8%) | 542 ( 48.2%) |
| | | 0.0940 (a) | | | |
| AGE (YRS) | 18-30 | 4 ( 1.0%) | 5 ( 1.4%) | 4 ( 1.1%) | 13 ( 1.2%) |
| | 31-50 | 51 ( 13.3%) | 58 ( 15.9%) | 55 ( 14.6%) | 164 ( 14.6%) |
| | 51-70 | 230 ( 60.1%) | 211 ( 57.8%) | 214 ( 56.8%) | 655 ( 58.2%) |
| | >70 | 95 ( 24.8%) | 89 ( 24.4%) | 104 ( 27.6%) | 288 ( 25.6%) |
| | Mean (N) | 62.0 ( 380) | 61.5 ( 363) | 62.6 ( 377) | 62.0 (1120) |
| | SD | 12.7 | 12.2 | 12.5 | 12.4 |
| | Min-Max | 26 - 93 | 23 - 90 | 23 - 91 | 23 - 93 |
| | | 0.5313 (b) | | | |
| ETHNICITY | CAUCASIAN | 259 ( 67.6%) | 244 ( 66.8%) | 257 ( 68.2%) | 760 ( 67.6%) |
| | BLACK | 32 ( 8.4%) | 24 ( 6.6%) | 31 ( 8.2%) | 87 ( 7.7%) |
| | ASIAN | 14 ( 3.7%) | 15 ( 4.1%) | 10 ( 2.7%) | 39 ( 3.5%) |
| | OTHER | 78 ( 20.4%) | 81 ( 22.2%) | 79 ( 21.0%) | 238 ( 21.2%) |
| | | 0.7647 (c) | | | |
| DIABETIC STATUS | NON-DIABETIC | 88 ( 23.0%) | 102 ( 27.9%) | 77 ( 20.4%) | 267 ( 23.7%) |
| | DIABETIC | 295 ( 77.0%) | 263 ( 72.1%) | 300 ( 79.6%) | 858 ( 76.3%) |
| | TYPE I | 171 ( 44.6%) | 161 ( 44.1%) | 178 ( 47.2%) | 510 ( 45.3%) |
| | TYPE II (NON-INSULIN DEPENDENT) | 124 ( 32.4%) | 102 ( 27.9%) | 122 ( 32.4%) | 348 ( 30.9%) |
| | | 0.1881 (d) | | | |

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Note: Patients 168-4629 (Vit-02, Saline Control), 334-6502 (Vit-03, Saline Control), 348-6540 (Vit-03, Saline Control), and 351-8117 (Vit-03,55 IU Vitrase) had calculated ages resolving to zero due to incorrect birth years recorded on the Demographics Case Report Form. Patient 146-3559 (Vit-02, 55 IU Vitrase) has no birth date value. These observations are not in the age calculations. Misrandomized Patient 146-3559 (Vit-02, 55 IU Vitrase) and Patient 361-9623 (Vit-03, 75 IU Vitrase) have no gender values. Misrandomized Patient 146-3559 (Vit-02, 55 IU Vitrase) has no ethnicity value.

(a) Cochran-Mantel-Haenszel('row mean scores differ') test, stratified by study
(b) two-way ANOVA(effects for study and treatment)
(c) Cochran-Mantel-Haenszel('general association') test, stratified by study
(d) Cochran-Mantel-Haenszel('general association') test, stratified by study(non-diabetic vs. Type I vs. Type II)

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ISTA Integrated Summary of Efficacy

Table 4: Summary of Baseline Patient Characteristics
(Phase IIb: ACS202-HYA-001A (US) and ACS203-HYA-001MEX, All Patients)

| Variable | Value | 7.5 IU Vitrase | 37.5 IU Vitrase | 75 IU Vitrase | Overall |
|---|---|---|---|---|---|
| GENDER | MALE | 59 ( 45.7%) | 59 ( 47.6%) | 59 ( 47.2%) | 177 ( 46.8%) |
| | FEMALE | 70 ( 54.3%) | 65 ( 52.4%) | 66 ( 52.8%) | 201 ( 53.2%) |
| | | | 0.9488 (a) | | |
| AGE (YRS) | 18-30 | 2 ( 1.6%) | 0 ( 0.0%) | 1 ( 0.8%) | 3 ( 0.8%) |
| | 31-50 | 22 ( 17.1%) | 19 ( 15.3%) | 23 ( 18.4%) | 64 ( 16.9%) |
| | 51-70 | 83 ( 64.3%) | 87 ( 70.2%) | 83 ( 66.4%) | 253 ( 66.9%) |
| | >70 | 22 ( 17.1%) | 18 ( 14.5%) | 18 ( 14.4%) | 58 ( 15.3%) |
| | Mean (N) | 60.0 ( 129) | 59.6 ( 124) | 59.6 ( 125) | 59.7 ( 378) |
| | SD | 11.8 | 9.9 | 11.2 | 11.0 |
| | Min-Max | 29 - 83 | 36 - 88 | 27 - 89 | 27 - 89 |
| | | | 0.9591 (b) | | |
| ETHNICITY | CAUCASIAN | 32 ( 24.8%) | 25 ( 20.2%) | 29 ( 23.2%) | 86 ( 22.8%) |
| | BLACK | 10 ( 7.8%) | 7 ( 5.6%) | 11 ( 8.8%) | 28 ( 7.4%) |
| | ASIAN | 2 ( 1.6%) | 0 ( 0.0%) | 1 ( 0.8%) | 3 ( 0.8%) |
| | OTHER | 85 ( 65.9%) | 92 ( 74.2%) | 84 ( 67.2%) | 261 ( 69.0%) |
| | | | 0.4024 (c) | | |
| DIABETIC STATUS | NON-DIABETIC | 15 ( 11.6%) | 19 ( 15.3%) | 13 ( 10.4%) | 47 ( 12.4%) |
| | DIABETIC | 113 ( 87.6%) | 105 ( 84.7%) | 112 ( 89.6%) | 330 ( 87.3%) |
| | | | 0.4754 (a) | | |

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NOTE: MEX patient 1-117 (7.5 IU VITRASE) had 'Unknown' check for Diabetes at baseline and therefore excluded from the calculations under 'Diabetic Status'.
(a) Cochran-Mantel-Haenszel('row mean scores differ') test, stratified by study
(b) two-way ANOVA(effects for study and treatment)
(c) Cochran-Mantel-Haenszel ('general association') test, stratified by study

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ISTA Integrated Summary of Efficacy

Table 5: Summary of History of Vitreous Hemorrhage (Study Eye)
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| Measurement | | Saline Control | 55 IU Vitrase | 75 IU Vitrase | Overall |
|---|---|---|---|---|---|
| | NUMBER OF PATIENTS | 383 | 365 | 377 | 1125 |
| VITREOUS HEMORRHAGE | | | | | |
| PROBABLE CAUSE | PROLIFERATIVE DIABETIC RETINOPATHY | 278 ( 72.6%) | 250 ( 68.5%) | 281 ( 74.5%) | 809 ( 71.9%) |
| | CENTRAL RETINAL VEIN OCCLUSION | 20 ( 5.2%) | 17 ( 4.7%) | 17 ( 4.5%) | 54 ( 4.8%) |
| | BRANCH RETINAL VEIN OCCLUSION | 18 ( 4.7%) | 25 ( 6.8%) | 10 ( 2.7%) | 53 ( 4.7%) |
| | EXUDATIVE MACULAR DEGENERATION WITH CHOROIDAL NEOVASCULAR MEMBRANE | 20 ( 5.2%) | 14 ( 3.8%) | 15 ( 4.0%) | 49 ( 4.4%) |
| | MACROANEURYSM | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 4 ( 0.4%) |
| | HEMORRHAGIC POSTERIOR VITREOUS DETACHMENT | 6 ( 1.6%) | 11 ( 3.0%) | 8 ( 2.1%) | 25 ( 2.2%) |
| | OTHER | 6 ( 1.6%) | 10 ( 2.7%) | 11 ( 2.9%) | 27 ( 2.4%) |
| | missing or NA | 34 ( 8.9%) | 36 ( 9.9%) | 34 ( 9.0%) | 104 ( 9.2%) |
| | | --------- p-Value = 0.3817 (a) --------- | | | |
| DURATION (DAYS) AT ENTRY | <= 28 | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 0.4%) |
| | 29 - 90 | 195 ( 50.9%) | 193 ( 52.9%) | 182 ( 48.3%) | 570 ( 50.7%) |
| | > 90 | 179 ( 46.7%) | 168 ( 46.0%) | 187 ( 49.6%) | 534 ( 47.5%) |
| | missing or NA | 7 ( 1.8%) | 4 ( 1.1%) | 6 ( 1.6%) | 17 ( 1.5%) |
| | Mean (N) | 119.1 ( 376) | 117.7 ( 361) | 124.3 ( 371) | 120.4 (1108) |
| | SD | 115.0 | 102.2 | 112.4 | 110.0 |
| | Min-Max | 15 - 1383 | 29 - 695 | 6 - 997 | 6 - 1383 |
| | | --------- p-Value = 0.6650 (b) --------- | | | |

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(a) Cochran-Mantel-Haenszel('general association') test, stratified by study(excluding 'missing or NA')
(b) two-way ANOVA(effects for study and treatment)
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ISTA Integrated Summary of Efficacy

Table 6: Summary of History of Vitreous Hemorrhage (Study Eye)
(Phase IIb: ACS202-HYA-001A (US) and ACS203-HYA-001MEX, All Patients)

| Measurement | | 7.5 IU Vitrase | 37.5 IU Vitrase | 75 IU Vitrase | Overall |
|---|---|---|---|---|---|
| | NUMBER OF PATIENTS | 129 | 124 | 125 | 378 |
| VITREOUS HEMORRHAGE | | | | | |
| PROBABLE CAUSE | DIABETIC RETINOPATHY | 111 ( 86.0%) | 106 ( 85.5%) | 108 ( 86.4%) | 325 ( 86.0%) |
| | OTHER ETIOLOGY | 17 ( 13.2%) | 15 ( 12.1%) | 11 ( 8.8%) | 43 ( 11.4%) |
| | both YES (a) | 1 ( 0.8%) | 0 ( 0.0%) | 2 ( 1.6%) | 3 ( 0.8%) |
| | missing or NA (b) | 0 ( 0.0%) | 3 ( 2.4%) | 4 ( 3.2%) | 7 ( 1.9%) |
| | | ---------- p-Value = 0.5877 (c) ---------- | | | |
| DURATION (MONTHS) AT ENTRY | < 1 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0 0%) |
| | 1 - 3 | 77 ( 59.7%) | 70 ( 56.5%) | 66 ( 52.8%) | 213 ( 56.3%) |
| | > 3 | 52 ( 40.3%) | 54 ( 43.5%) | 59 ( 47.2%) | 165 ( 43.7%) |
| | missing or NA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | Mean (N) | 3.9 (129) | 3.9 (124) | 4.2 (125) | 4.0 (378) |
| | SD | 3.3 | 3.4 | 3.5 | 3.4 |
| | Min-Max | 1 - 25 | 1 - 24 | 1 - 24 | 1 - 25 |
| | | ---------- p-Value = 0.7732 (d) ---------- | | | |



(a) US Patients 19-13 (7.5 IU VITRASE), 11-1 (75 IU VITRASE) and 19-1 (75 IU VITRASE)
(b) MEX Patients 1-65 (37.5 IU VITRASE), 2-35 (37.5 IU VITRASE), 1-75 (75 IU VITRASE), 2-87 (75 IU VITRASE), 2-99 (75 IU VITRASE), 2-102 (75 IU VITRASE), and US Patient 26-2 (37.5 IU VITRASE)
(c) Cochran-Mantel-Haenszel('row mean scores differ') test, stratified by study (excluding 'both YES' and 'missing or NA')
(d) two-way ANOVA(effects for study and treatment)
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ISTA Integrated Summary of Efficacy

Table 7: Proportion of Patients with Efficacy Outcome by Month 2 based on Monthly Assessment (1, 2, 3)
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| | Saline Control | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|
| NUMBER OF PATIENTS | 383 | 365 | 377 |
| NO. (%) OF PATIENTS WITH OUTCOME OF EFFICACY 'SUCCESS' | 106 ( 27.7%) | 143 ( 39.2%) | 144 ( 38.2%) |
| p-Values FOR PAIRWISE COMPARISONS WITH SALINE (a) | -- | 0.0008 | 0.0023 |
| Homogeneity p-value (b) | -- | 0.9443 | 0.7398 |
| NO. (%) OF PATIENTS WITH OUTCOME OF EFFICACY 'FAILURE' | 277 ( 72.3%) | 222 ( 60.8%) | 233 ( 61.8%) |
| p-Values FOR PAIRWISE COMPARISONS WITH SALINE (c) | -- | 0.0008 | 0.0023 |
| Homogeneity p-value (b) | -- | 0.9443 | 0.7398 |

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'Success' indicates investigator marked box 1, 2, or 3 on the efficacy CRF page at any visit on or prior to 2 months post-treatment. A patient that does not meet this criteria is considered an efficacy 'Failure'.
Pairwise comparison p-Values are based on the Cochran-Mantel-Haenszel (CMH) test, stratified by study (active dose vs. saline control) with no multiplicity adjustments.
(a) Cochran-Mantel-Haenszel test on the binary outcome of 'efficacy success' or 'non-success'. 'Non-success' includes 'treatment failure' and 'indeterminate'
(b) Breslow-Day test of homogeneity across studies
(c) Cochran-Mantel-Haenszel test on the binary outcome of 'efficacy failure' or 'non-failure'. 'Non-failure' includes 'treatment success' and 'indeterminate'
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ISTA Integrated Summary of Efficacy

Table 8: Endpoint Evaluation: Incidence of Hemorrhage Clearance on or Prior to Week 8
(Phase IIb: ACS202-HYA-001A (US) and ACS203-HYA-001MEX, All Patients)

| Posttreatment Visit | 7.5 IU Vitrase | 37.5 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|
| ALL PATIENTS | | | |
| NUMBER OF PATIENTS | 129 | 124 | 125 |
| NO. (%) OF PATIENTS WITH OUTCOME OF EFFICACY 'SUCCESS' | 60 ( 46.5%) | 49 ( 39.5%) | 69 ( 55.2%) |
| | | p-Value = 0.0465 (a) | |
| PATIENTS WITH MILD OR MODERATE HEMORRHAGE | | | |
| NUMBER OF PATIENTS | 34 | 25 | 26 |
| NO. (%) OF PATIENTS WITH OUTCOME OF EFFICACY 'SUCCESS' | 25 ( 73.5%) | 15 ( 60.0%) | 14 ( 53.8%) |
| | | p-Value = 0.2712 (a) | |
| PATIENTS WITH SEVERE HEMORRHAGE | | | |
| NUMBER OF PATIENTS | 95 | 99 | 99 |
| NO. (%) OF PATIENTS WITH OUTCOME OF EFFICACY 'SUCCESS' | 35 ( 36.8%) | 34 ( 34.3%) | 55 ( 55.6%) |
| | | p-Value = 0.0051 (a) | |

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'Success' indicates investigator marked box 1 on the Study Exit CRF page on or prior to 8 weeks post-treatment. A patient that does not meet this criteria is considered an efficacy 'Failure'.
(a) Cochran-Mantel-Haenszel('row mean scores differ') test on the binary outcome of efficacy 'success' or 'failure', stratified by study.

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ISTA Integrated Summary of Efficacy

Table 9: Summary of 'Improvement' Rates in Hemorrhage Density from Baseline on or Prior to Month 2 (Study Eye)
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| Hemorrhage Density on or Prior to Month 2 | | Saline Control | 55 IU Vitrase | 75 IU Vitrase | p-Value |
|---|---|---|---|---|---|
| NUMBER OF PATIENTS | | 383 | 365 | 377 | |
| "MARKED IMPROVEMENT" | | | | | |
| NO. OF CLOCK HOURS WITH GRADE 0 OR 1: | | | | | |
| YES | >= 6 | 80 (20.9%) | 119 (32.6%) | 114 (30.2%) | 0.0007 |
| NO | < 6 | 297 (77.5%) | 240 (65.8%) | 260 (69.0%) | |
| "IMPROVEMENT" | | | | | |
| NO. OF CLOCK HOURS WITH GRADE 0, 1, OR 2: | | | | | |
| YES | >= 6 | 137 (35.8%) | 176 (48.2%) | 169 (44.8%) | 0.0016 |
| NO | < 6 | 240 (62.7%) | 183 (50.1%) | 205 (54.4%) | |



p-Values for '>=6' vs. '<6' based on Cochran-Mantel-Haenszel('row mean scores differ') test, stratified by study

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ISTA Integrated Summary of Efficacy

Table 10: Cumulative Percentage of Reduction in Vitreous Hemorrhage Density
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| Posttreatment Visit | | Saline Control | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|
| | NUMBER OF PATIENTS | 383 | 365 | 377 |
| MONTH 1 | NO. (%) OF PATIENTS WITH HEMORRHAGE DENSITY IMPROVEMENT | 42 ( 11.0%) | 74 ( 20.3%) | 72 ( 19.1%) |
| | p-Value(a) | -- | 0.0004 | 0.0019 |
| | Homogeneity p-Value(b) | -- | 0.9213 | 0.1274 |
| MONTH 2 | NO. (%) OF PATIENTS WITH HEMORRHAGE DENSITY IMPROVEMENT | 82 ( 21.4%) | 120 ( 32.9%) | 114 ( 30.2%) |
| | p-Value(a) | -- | 0.0004 | 0.0061 |
| | Homogeneity p-Value(b) | -- | 0.9461 | 0.2935 |
| MONTH 3 | NO. (%) OF PATIENTS WITH HEMORRHAGE DENSITY IMPROVEMENT | 109 ( 28.5%) | 141 ( 38.6%) | 144 ( 38.2%) |
| | p-Value(a) | -- | 0.0030 | 0.0049 |
| | Homogeneity p-Value(b) | -- | 0.6677 | 0.7883 |



Reduction of Hemorrhage Density is defined as at least 6 clock hours with density grades 0-1 (or at least 3 hours with grades 0-1 for patients that have BRVO recorded as causative condition for study hemorrhage) at a given posttreatment visit (prior to vitrectomy or recurrent vitreous hemorrhage).
(a) Cochran-Mantel-Haenszel test, stratified by study (active dose vs. saline control) with no multiplicity adjustments
(b) Breslow-Day test of homogeneity across studies
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ISTA Integrated Summary of Efficacy

Table 11: Life Table Analysis: Time to BCVA Improvement (a) on or Prior to Month 3
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| | Saline Control | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|
| NUMBER OF PATIENTS | 383 | 365 | 377 |
| SURVIVAL FUNCTION FOR TIME TO BCVA IMPROVEMENT ON OR PRIOR TO MONTH 3 (b) | ---------- p-Value = 0.0167 (c) ---------- | | |

012

Note: Survival Function is defined as the probability that a patient improves prior to the given time point

(a) Time to BCVA Improvement is defined as first evidence of post-Vitrase BCVA improvement from baseline of at least 0.3 LogMAR
(b) Patients that do not show BCVA improvement are censored at the days to first Vitrectomy surgery or Recurrent Vitreous Hemorrhage. Patients that do not show BCVA improvement with no Vitrectomy or Recurrent Hemorrhage are censored at 123 days (92 days +/- 31 days) for the Month 3 analysis.

(c) p-Value for time to BCVA Improvement is based on log rank test stratified by study

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ISTA Integrated Summary of Efficacy

Table 12: Cumulative Percentages of BCVA Improvement (a)
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| Posttreatment Visit | | Saline Control | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|
| | NUMBER OF PATIENTS | 383 | 365 | 377 |
| MONTH 1 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 77 ( 20.1%) | 112 ( 30.7%) | 105 ( 27.9%) |
| | | ---------- | p-value=0.0029 (b) | ---------- |
| MONTH 2 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 105 ( 27.4%) | 150 ( 41.1%) | 144 ( 38.2%) |
| | | ---------- | p-value=0.0002 (b) | ---------- |
| MONTH 3 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 132 ( 34.5%) | 164 ( 44.9%) | 164 ( 43.5%) |
| | | ---------- | p-value=0.0065 (b) | ---------- |



Note: Cell entries represent the number (%) of patients achieving BCVA improvement on or before the indicated visit
(a) BCVA Improvement is defined as first evidence of post-Vitrase BCVA improvement at Months 1, 2, and 3 from baseline of at least 0.3 LogMAR (prior to vitrectomy or recurrent vitreous hemorrhage). Count fingers to any letters read is one line improvement, to 20/800 is a second line of improvement.
(b) Cochran-Mantel-Haenszel('row mean scores differ') test, stratified by study

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ISTA Integrated Summary of Efficacy

Table 13: Cumulative Percentages of BCVA Improvement (a)
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| Posttreatment Visit | | Saline Control | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|
| | NUMBER OF PATIENTS | 383 | 365 | 377 |
| MONTH 1 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 77 ( 20.1%) | 112 ( 30.7%) | 105 ( 27.9%) |
| | p-Value (b) | -- | 0.0009 | 0.0127 |
| | Homogeneity p-Value (c) | -- | 0.8642 | 0.0445 |
| MONTH 2 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 105 ( 27.4%) | 150 ( 41.1%) | 144 ( 38 2%) |
| | p-Value (b) | -- | 0.0001 | 0.0016 |
| | Homogeneity p-Value (c) | -- | 0.8452 | 0.3883 |
| MONTH 3 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 132 ( 34.5%) | 164 ( 44.9%) | 164 ( 43.5%) |
| | p-Value (b) | -- | 0.0035 | 0.0113 |
| | Homogeneity p-Value (c) | -- | 0.3720 | 0.9515 |



Note: Cell entries represent the number (%) of patients achieving BCVA improvement on or before the indicated visit
(a) BCVA Improvement is defined as first evidence of post-Vitrase BCVA improvement at Months 1, 2, and 3 from baseline of at least 0.3 LogMAR (prior to vitrectomy or recurrent vitreous hemorrhage). Count fingers to any letters read is one line improvement, to 20/800 is a second line of improvement.
(b) Cochran-Mantel-Haenszel test, stratified by study (active dose vs. saline control) with no multiplicity adjustments
(c) Breslow-Day test of homogeneity across studies

ISTA Integrated Summary of Efficacy

Table 14: Cumulative Percentages of BCVA Improvement (a)
(Phase IIb: ACS202-HYA-001A (US) and ACS203-HYA-001MEX, All Patients)

| Posttreatment Visit | | 7.5 IU Vitrase | 37.5 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|
| | NUMBER OF PATIENTS | 129 | 124 | 125 |
| MONTH 1 (DAY 28) | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 40 ( 31.0%) | 30 ( 24.2%) | 29 ( 23.2%) |
| | | ---------- | p-Value = 0.3106 (b) | ---------- |
| MONTH 2 (DAY 56) | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 49 ( 38.0%) | 38 ( 30.6%) | 36 ( 28.8%) |
| | | ---------- | p-Value = 0.2600 (b) | ---------- |

0153

Note: Cell entries represent the number (%) of patients achieving BCVA improvement on or before the indicated visit
(a) Time to BCVA Improvement is defined as first evidence of post-Vitrase BCVA improvement from baseline of at least 0.3 LogMAR (prior to vitrectomy). Count fingers to any letters read is one line improvement, to 20/800 is a second line of improvement.
(b) Cochran-Mantel-Haenszel('row mean scores differ') test, stratified by study

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ISTA Integrated Summary of Efficacy

Table 15: Cumulative Percentages of BCVA Improvement (a)
Read Letters As Is
(Phase III: VIT-02-08961X and VIT-03-08961X, Intent-to-Treat Population)

| Posttreatment Visit | | Saline Control | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|
| | NUMBER OF PATIENTS | 383 | 365 | 377 |
| MONTH 1 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 78 ( 20.4%) | 112 ( 30.7%) | 105 ( 27.9%) |
| | p-Value (b) | -- | 0.0013 | 0.0163 |
| | Homogeneity p-Value (c) | -- | 0.9455 | 0.0557 |
| MONTH 2 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 106 ( 27.7%) | 150 ( 41.1%) | 144 ( 38.2%) |
| | p-Value (b) | -- | 0.0001 | 0.0021 |
| | Homogeneity p-Value (c) | -- | 0.7792 | 0.4358 |
| MONTH 3 | NO. (%) OF PATIENTS WITH BCVA IMPROVEMENT | 131 ( 34.2%) | 164 ( 44.9%) | 164 ( 43.5%) |
| | p-Value (b) | -- | 0.0027 | 0.0091 |
| | Homogeneity p-Value (c) | -- | 0.4137 | 0.9887 |

016

Note: Cell entries represent the number (%) of patients achieving BCVA improvement on or before the indicated visit
(a) Time to BCVA Improvement is defined as first evidence of post-Vitrase BCVA improvement from baseline of at least 0.3 LogMAR (prior to vitrectomy or recurrent vitreous hemorrhage). When determining improvement, LogMAR records worse than 1.6 (20/800) are left as is.
(b) Cochran-Mantel-Haenszel test, stratified by study (active dose vs. saline control) with no multiplicity adjustments
(c) *Breslow-Day test of homogeneity across studies*

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# 10.0 SAFETY TABLES REFERRED TO BUT NOT INCLUDED IN THE TEXT

| Table No. | Title |
|---|---|
| 1 | Enrollment Status<br>All Studies |
| 2 | Summary of Enrollment Status and Completion Status by Treatment<br>All Studies |
| 3.1 | Summary of Extent of Exposure and Follow-up Duration<br>All Studies by Treatment |
| 3.2 | Summary of Extent of Exposure and Follow-up Duration<br>All Studies by Study for Vitrase Groups Only |
| 3.3 | Summary of Extent of Exposure and Follow-up Duration<br>Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 3.4 | Summary of Extent of Exposure and Follow-up Duration<br>PVD Study (PVD-01-08961x) by Treatment |
| 4.1 | Summary of Demographics and Baseline Characteristics<br>All Studies by Treatment |
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| 5.1 | Incidence of Serious Adverse Events by System Organ Class<br>All Studies by Treatment |
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| 5.3 | Incidence of Serious Adverse Events by System Organ Class<br>Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 5.4 | Incidence of Serious Adverse Events by System Organ Class<br>PVD Study (PVD-01-08961X) by Treatment |
| 6 | Incidence of Serious Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset |
| 7.1 | Incidence of Adverse Events by System Organ Class<br>All Studies by Treatment |
| 7.2 | Incidence of Adverse Events by System Organ Class<br>All Studies by Study for Vitrase Groups Only |
| 7.3 | Incidence of Adverse Events by System Organ Class<br>Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 7.4 | Incidence of Adverse Events by System Organ Class<br>PVD Study (PVD-01-08961X) by Treatment |
| 8 | Incidence of Related Adverse Events by System Organ Class<br>Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |

| Table No. | Title |
|---|---|
| 9 | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 9.a | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class for Saline and 55 IU and 75 IU Vitrase Combined – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 10 | Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 11 | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset |
| 12 | Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset |
| 13 | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present |
| 14 | Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present |
| 15 | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity |
| 16 | Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity |
| 17 | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex |
| 18 | Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex |
| 19 | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age |
| 20 | Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age |
| 21 | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race |
| 22 | Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race |
| 23 | Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status |
| 24 | Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status |
| 25 | Analysis of Selected Ocular Adverse Events Affecting the Study Eye by System Organ Class – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
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| Table No. | Title |
|---|---|
| 27 | Duration of Selected Ocular Adverse Events Affecting the Study Eye – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 28 | Duration of Related Selected Ocular Adverse Events Affecting the Study Eye Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 29 | Duration of Selected Ocular Adverse Events Affecting the Study Eye that Required Medication – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 30 | Duration of Related Selected Ocular Adverse Events Affecting the Study Eye that Required Medication – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 31 | Incidence of Cataract Affecting the Study Eye – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset |
| 32.1 | Summary of Ocular Symptoms Post-Treatment All Studies by Treatment |
| 32.2 | Summary of Ocular Symptoms Post-Treatment All Studies by Study for Vitrase Groups Only |
| 32.3 | Summary of Ocular Symptoms Post-Treatment – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 32.4 | Summary of Ocular Symptoms Post-Treatment PVD Study (PVD-01-08961X) by Treatment |
| 33 | Summary of Ocular Symptoms Maximum Severity Post-Treatment Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 34 | Summary of Ocular Symptoms Maximum Severity Post-Treatment, Stratified by Baseline Severity – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 35 | Summary of Ocular Symptoms Change from Baseline at Specified Visits Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 36.1 | Summary of Anterior Chamber Signs Post-Treatment All Studies by Treatment |
| 36.2 | Summary of Anterior Chamber Signs Post-Treatment All Studies by Study for Vitrase Groups Only |
| 36.3 | Summary of Anterior Chamber Signs Post-Treatment Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 36.4 | Summary of Anterior Chamber Signs Post-Treatment PVD Study (PVD-01-08961X) by Treatment |
| 37 | Summary of Anterior Chamber Signs Maximum Severity Post-Treatment Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 38 | Summary of Anterior Chamber Signs Maximum Severity Post-Treatment Stratified by Baseline Severity – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 39 | Summary of Anterior Chamber Signs Change from Baseline at Specified Visits – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 40.1 | Summary of Minimum and Maximum Intraocular Pressure Post-Treatment All Studies by Treatment |
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| 40.3 | Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 40.4 | Summary of Minimum and Maximum Intraocular Pressure Post-Treatment PVD Study (PVD-01-08961X) by Treatment |

| Table No. | Title |
|---|---|
| 41.1 | Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Change from Baseline – All Studies by Treatment |
| 41.2 | Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Change from Baseline – All Studies by Study for Vitrase Groups Only |
| 41.3 | Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Change from Baseline – Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 41.4 | Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Change from Baseline – All Studies by Treatment |
| 42 | Summary of Intraocular Pressure at Specified Visits Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 43 | Summary of Intraocular Pressure Change from baseline at Specified Visits Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment |
| 44 | Summary of Intraocular Pressure at Specified Visits – Study V-01-VIT-08961X by Treatment |
| 45 | Summary of Intraocular Pressure Change from Baseline at Specified Visits Study V-01-VIT-08961X by Treatment |
| 46 | Incidence of Deaths All Studies |
| 47 | Incidence of Deaths by Treatment Primary Phase III Studies: VIT-02-08961X and VIT-03-08961X |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 1
Enrollment Status
All Studies

| Study | Indication | Treatment Regimen | ITT [1] | Safety [2] |
|---|---|---|---|---|
| ACS201-HYA-001A | CLEARANCE OF VITREOUS HEMORRHAGE | SALINE, VITRASE: 37.5 IU, 75 IU | 14 | 14 |
| ACS201-HYA-002A | CLEARANCE OF VITREOUS HEMORRHAGE | SALINE, 75 IU VITRASE | 28 | 28 |
| PROBE STUDY | CLEARANCE OF VITREOUS HEMORRHAGE | 75 IU VITRASE | 34 | 34 |
| V-01-VIT-08961X | CLEARANCE OF VITREOUS HEMORRHAGE | SALINE, 75 IU VITRASE | 61 | 61 |
| ACS202-HYA-001US | CLEARANCE OF VITREOUS HEMORRHAGE | VITRASE: 7.5 IU, 37.5 IU, 75 IU | 153 | 153 |
| ACS203-HYA-001MEX | CLEARANCE OF VITREOUS HEMORRHAGE | VITRASE: 7.5 IU, 37.5 IU, 75 IU | 225 | 225 |
| VIT-02-08961X (WW) | CLEARANCE OF VITREOUS HEMORRHAGE | CONTROL, VITRASE: 7.5 IU, 55 IU, 75 IU | 71 | 71 |
| VIT-02-08961X | CLEARANCE OF VITREOUS HEMORRHAGE | SALINE, VITRASE: 7.5 IU, 55 IU, 75 IU | 750 | 740 |
| VIT-03-08961X | CLEARANCE OF VITREOUS HEMORRHAGE | SALINE, VITRASE: 55 IU, 75 IU | 556 | 551 |
| PVD-01-08961X | INDUCING POSTERIOR VITREOUS DETACHMENT | SALINE, 75 IU VITRASE, SF6, 75 IU VITRASE + SF6 | 60 | 60 |
| COR-01-08961X | CORRECTION OF MYOPIA | 50 IU VITRASE + ACS-101C, 500 IU VITRASE + ACS-101C, ACS-101C | 41 | 41 |
| COP-01-08961X | CLEARANCE OF CORNEAL OPACITIES | SALINE, VITRASE: 50 IU, 100 IU, 200 IU, 400 IU, 500 IU | 30 | 30 |



[1] For studies VIT-02-08961X and VIT-03-08961X, the Intent-to-Treat Population consists of all patients randomized to receive treatment and have a screening visit. For all other studies, Intent-to-Treat population consists of all patients randomized to receive treatment with any available data in the individual databases.
[2] Safety population consists of all patients randomized to receive treatment and had at least one post-treatment assessment.

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ISTA Pharmaceuticals, Inc.
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Table 2
Summary of Enrollment Status and Completion Status by Treatment
All Studies

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| | WW | Saline [4] | 7.5 IU | 37.5 IU | 55 IU | 75 IU [5] | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| TOTAL ITT POPULATION | 18 | 422 | 328 | 130 | 383 | 612 | 1453 | 84 | 21 | 70 |
| TOTAL SAFETY POPULATION | 18 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| NUMBER COMPLETED [2] | 5 (27.8%) | 59 (14.1%) | 153 (46.8%) | 114 (87.7%) | 34 ( 9.0%) | 193 (31.7%) | 494 (34.2%) | 75 (89.3%) | 20 (95.2%) | 56 (80.0%) |
| NUMBER DISCONTINUED DUE TO ADVERSE EVENT [3] | 0 ( 0.0%) | 1 ( 0.2%) | 3 ( 0.9%) | 2 ( 1.5%) | 2 ( 0.5%) | 8 ( 1.3%) | 15 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NUMBER DISCONTINUED DUE TO DEATH | 6 (33.3%) | 17 ( 4.1%) | 8 ( 2.4%) | 0 ( 0.0%) | 17 ( 4.5%) | 23 ( 3.8%) | 48 ( 3.3%) | 0 ( 0.0%) | 1 ( 4.8%) | 0 ( 0.0%) |

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Percents are based on the number of patients in the Safety Population.
Note: One patient in the study ACS201-HYA-002A received byth 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve Patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.

[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). 44 patients who received both Vitrase and another active study treatment are included in both groups.
[2] Studies ACS201-HYA-002A and the Probe Study did not have a termination page or sufficient visit information to determine whether a patient completed the study. Patients in study ACS-201-HYA-001A where considered to have completed the study if they completed the Day 56 Visit.
[3] Patients in studies VIT-02-08961X and VIT-03-08961X were only considered discontinued if due to a Serious Adverse Event.
[4] Patient 01-024 (Study V-01-VIT-08961X, Saline Control) did not have a reason for discontinuation recorded. However, this patient was noted as dying 284 days post-treatment (See Listing of Deaths).
[5] Patient 149-3702 (Study VIT-02-08961X , 75.0 IU Vitrase) died 450 days after discontinuing due to Lost to Follow-up. This patient is not included here.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 3.1
Summary of Extent of Exposure and Follow-up Duration
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU [2] | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [3] |
| NUMBER OF PATIENTS RECEIVING TREATMENT | 0 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| DURATION OF FOLLOW-UP (DAYS) [1] | | | | | | | | | | |
| n | 18 | 417 | 327 | 130 | 377 | 605 | 1439 | 84 | 21 | 70 |
| Mean (SD) | 469.6 (259) | 312.0 (193) | 361.3 (255) | 380.3 (288) | 327.4 (215) | 316.7 (227) | 335.4 (238) | 286.5 (134) | 386.3 (147) | 294.7 (138) |
| Median | 373.0 | 346.0 | 364.0 | 455.5 | 352.0 | 343.0 | 358.0 | 243.0 | 483.0 | 252.5 |
| Range | 34 - 966 | 5 - 784 | 1 - 964 | 2 - 811 | 7 - 972 | 6 - 1412 | 1 - 1412 | 21 - 511 | 81 - 511 | 0 - 511 |
| NUMBER AND PERCENT OF PATIENTS WITH FOLLOW-UP DATA THROUGH: | | | | | | | | | | |
| MONTH 6 | 16 (88.9%) | 313 (75.1%) | 237 (72.5%) | 83 (63.8%) | 285 (75.6%) | 421 (69.1%) | 1026 (71.1%) | 78 (92.9%) | 20 (95.2%) | 61 (87.1%) |
| MONTH 12 | 15 (83.3%) | 218 (52.3%) | 187 (57.2%) | 77 (59.2%) | 205 (54.4%) | 316 (51.9%) | 785 (54.4%) | 25 (29.8%) | 15 (71.4%) | 23 (32.9%) |

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Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
"Watchful Waiting - Control" patients did not receive study injection.
[1] Follow-up is defined as days from treatment to last visit completed for each patient.
[2] Treatment date for 4 patients from study ACS201-HYA-002A could not be determined. Duration of follow-up could not be calculated.
[3] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 3.2
Summary of Extent of Exposure and Follow-up Duration
All Studies by Study for Vitrase Groups Only
Safety Population

| | Phase I [2] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [3] |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS RECEIVING TREATMENT | 68 | 31 | 153 | 225 | 602 | 364 | 84 |
| DURATION OF FOLLOW-UP (DAYS) [1] | | | | | | | |
| n | 64 | 31 | 153 | 225 | 602 | 364 | 84 |
| Mean (SD) | 200.9 (278.6) | 362.0 ( 37.4) | 97.2 (110.8) | 530.6 (215.2) | 355.3 (229.5) | 303.4 (191.2) | 286.5 (134.2) |
| Median | 85.0 | 365.0 | 56.0 | 584.0 | 363.0 | 343.0 | 243.0 |
| Range | 28 - 1412 | 190 - 470 | 1 - 470 | 6 - 829 | 7 - 972 | 7 - 790 | 21 - 511 |
| NUMBER AND PERCENT OF PATIENTS WITH: | | | | | | | |
| MONTH 6 FOLLOW-UP DATA | 18 (26.5%) | 31 ( 100%) | 34 (22.2%) | 201 (89.3%) | 474 (78.7%) | 268 (73.6%) | 78 (92.9%) |
| MONTH 12 FOLLOW-UP DATA | 11 (16.2%) | 30 (96.8%) | 18 (11.8%) | 191 (84.9%) | 347 (57.6%) | 188 (51.6%) | 25 (29.8%) |



Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Follow-up is defined as days from treatment to last visit completed for each patient.
[2] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
Note: Treatment date for 4 patients from study ACS201-HYA-002A could not be determined. Duration of follow-up could not be calculated.
[3] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 3.3
Summary of Extent of Exposure and Follow-up Duration
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| | Control | | | | |
|---|---|---|---|---|---|
| | WW | Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
| NUMBER OF PATIENTS RECEIVING TREATMENT | 0 | 378 | 198 | 377 | 391 |
| DURATION OF FOLLOW-UP (DAYS) [1] | | | | | |
| n | 18 | 378 | 198 | 377 | 391 |
| Mean (SD) | 469.6 (258.9) | 307.0 (196.3) | 372.4 (232.5) | 327.4 (215.5) | 325.2 (209.5) |
| Median | 373.0 | 319.5 | 365.0 | 352.0 | 343.0 |
| Range | 34 - 966 | 5 - 784 | 8 - 964 | 7 - 972 | 7 - 965 |
| NUMBER AND PERCENT OF PATIENTS WITH: | | | | | |
| MONTH 6 FOLLOW-UP DATA | 16 (88.9%) | 278 (73.5%) | 159 (80.3%) | 285 (75.6%) | 298 (76.2%) |
| MONTH 12 FOLLOW-UP DATA | 15 (83.3%) | 187 (49.5%) | 121 (61.1%) | 205 (54.4%) | 209 (53.5%) |



"Watchful Waiting - Control" patients did not receive study injection.
[1] Follow-up is defined as days from treatment to last visit completed for each patient.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 3.4
Summary of Extent of Exposure and Follow-up Duration
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| NUMBER OF PATIENTS RECEIVING TREATMENT | 15 | 15 | 14 | 16 |
| DURATION OF FOLLOW-UP (DAYS) [1] | | | | |
| n | 15 | 15 | 14 | 16 |
| Mean (SD) | 452.5 (109) | 392.7 (151) | 401.0 (147) | 449.3 (105) |
| Median | 483.0 | 483.0 | 483.0 | 483.0 |
| Range | 84 - 511 | 112 - 511 | 84 - 511 | 81 - 511 |
| NUMBER AND PERCENT OF PATIENTS WITH: | | | | |
| MONTH 6 FOLLOW-UP DATA | 14 (93.3%) | 12 (80.0%) | 12 (85.7%) | 15 (93.8%) |
| MONTH 12 FOLLOW-UP DATA | 14 (93.3%) | 12 (80.0%) | 11 (78.6%) | 15 (93.8%) |

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[1] Follow-up is defined as days from treatment to last visit completed for each patient.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 4.1
Summary of Demographics and Baseline Characteristics
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| NUMBER OF PATIENTS | 18 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| GENDER | | | | | | | | | | |
| MALE | 13 (72.2%) | 198 (47.5%) | 159 (48.6%) | 61 (46.9%) | 193 (51.2%) | 323 (53.0%) | 736 (51.0%) | 39 (46.4%) | 14 (66.7%) | 29 (41.4%) |
| FEMALE | 5 (27.8%) | 219 (52.5%) | 168 (51.4%) | 69 (53.1%) | 184 (48.8%) | 285 (46.8%) | 706 (48.9%) | 45 (53.6%) | 7 (33.3%) | 41 (58.6%) |
| MISSING OR N/A | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RACE | | | | | | | | | | |
| CAUCASIAN | 7 (38.9%) | 255 (61.2%) | 129 (39.4%) | 25 (19.2%) | 250 (66.3%) | 294 (48.3%) | 698 (48.4%) | 1 ( 1.2%) | 0 ( 0.0%) | 1 ( 1.4%) |
| HISPANIC | 5 (27.8%) | 65 (15.6%) | 131 (40.1%) | 60 (46.2%) | 73 (19.4%) | 158 (25.9%) | 422 (29.2%) | 83 (98.8%) | 21 ( 100%) | 69 (98.6%) |
| BLACK | 3 (16.7%) | 31 ( 7.4%) | 21 ( 6.4%) | 7 ( 5.4%) | 26 ( 6.9%) | 43 ( 7.1%) | 97 ( 6.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OTHER | 3 (16.7%) | 57 (13.7%) | 46 (14.1%) | 32 (24.6%) | 28 ( 7.4%) | 85 (14.0%) | 191 (13.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MISSING OR N/A | 0 ( 0.0%) | 9 ( 2.2%) | 0 ( 0.0%) | 6 ( 4.6%) | 0 ( 0.0%) | 29 ( 4.8%) | 35 ( 2.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| AGE (YEARS) | | | | | | | | | | |
| n | 18 | 406 | 327 | 130 | 376 | 601 | 1434 | 84 | 21 | 70 |
| Mean (SD) | 66.2 ( 9.3) | 61.5 (12.9) | 60.1 (12.9) | 59.6 (10.5) | 61.6 (12.2) | 60.9 (12.7) | 60.8 (12.4) | 39.7 (16.1) | 50.5 ( 9.6) | 39.6 (15.3) |
| Median | 67.5 | 62.0 | 61.0 | 58.0 | 62.0 | 61.0 | 61.0 | 35.0 | 51.0 | 36.0 |
| Range | 48 - 81 | 18 - 93 | 25 - 97 | 36 - 91 | 23 - 90 | 7 - 91 | 7 - 97 | 18 - 77 | 33 - 66 | 18 - 68 |
| STUDY EYE | | | | | | | | | | |
| OD | 9 (50.0%) | 214 (51.3%) | 178 (54.4%) | 69 (53.1%) | 184 (48.8%) | 295 (48.4%) | 726 (50.3%) | 47 (56.0%) | 11 (52.4%) | 36 (51.4%) |
| OS | 9 (50.0%) | 202 (48.4%) | 149 (45.6%) | 61 (46.9%) | 193 (51.2%) | 310 (50.9%) | 713 (49.4%) | 37 (44.0%) | 10 (47.6%) | 34 (48.6%) |
| OU | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 2 ( 0.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MISSING OR N/A | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 2 ( 0.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
One patient in study VIT-02-08961X (Saline) and three patients (two Saline and one 55 IU) in study VIT-03-08961X had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 4.2
Summary of Demographics and Baseline Characteristics
All Studies by Study for Vitrase Groups Only
Safety Population

| | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 68 | 31 | 153 | 225 | 602 | 364 | 84 |
| GENDER | | | | | | | |
| MALE | 32 (47.1%) | 19 (61.3%) | 79 (51.6%) | 98 (43.6%) | 313 (52.0%) | 195 (53.6%) | 39 (46.4%) |
| FEMALE | 36 (52.9%) | 12 (38.7%) | 74 (48.4%) | 127 (56.4%) | 289 (48.0%) | 168 (46.2%) | 45 (53.6%) |
| MISSING OR N/A | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RACE | | | | | | | |
| CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 76 (49.7%) | 10 ( 4.4%) | 307 (51.0%) | 305 (83.8%) | 1 ( 1.2%) |
| HISPANIC | 33 (48.5%) | 0 ( 0.0%) | 36 (23.5%) | 136 (60.4%) | 217 (36.0%) | 0 ( 0.0%) | 83 (98.8%) |
| BLACK | 0 ( 0.0%) | 0 ( 0.0%) | 28 (18.3%) | 0 ( 0.0%) | 35 ( 5.8%) | 34 ( 9.3%) | 0 ( 0.0%) |
| OTHER | 0 ( 0.0%) | 31 ( 100%) | 13 ( 8.5%) | 79 (35.1%) | 43 ( 7.1%) | 25 ( 6.9%) | 0 ( 0.0%) |
| MISSING OR N/A | 35 (51.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| AGE (YEARS) | | | | | | | |
| n | 65 | 26 | 153 | 225 | 602 | 363 | 84 |
| Mean (SD) | 56.3 (14.5) | 54.0 (11.0) | 61.8 (12.9) | 58.3 ( 9.2) | 61.3 (13.2) | 62.3 (11.9) | 39.7 (16.1) |
| Median | 58.0 | 56.0 | 63.0 | 58.0 | 61.0 | 64.0 | 35.0 |
| Range | 7 - 91 | 22 - 71 | 29 - 88 | 27 - 89 | 25 - 97 | 23 - 91 | 18 - 77 |
| STUDY EYE | | | | | | | |
| OD | 32 (47.1%) | 16 (51.6%) | 75 (49.0%) | 126 (56.0%) | 307 (51.0%) | 170 (46.7%) | 47 (56.0%) |
| OS | 32 (47.1%) | 15 (48.4%) | 78 (51.0%) | 99 (44.0%) | 295 (49.0%) | 194 (53.3%) | 37 (44.0%) |
| OU | 2 ( 2.9%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MISSING OR N/A | 2 ( 2.9%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: One patient in study VIT-03-08961X (55 IU) had a calculated age resolving to zero. This record is not included in the age calculation.
In addition, patients with a missing DOB were not included in the age calculation.
[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 4.3
Summary of Demographics and Baseline Characteristics
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| | Control | | | | |
|---|---|---|---|---|---|
| | WW | Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| GENDER | | | | | |
| MALE | 13 (72.2%) | 183 (48.4%) | 100 (50.5%) | 193 (51.2%) | 215 (55.0%) |
| FEMALE | 5 (27.8%) | 195 (51.6%) | 98 (49.5%) | 184 (48.8%) | 175 (44.8%) |
| MISSING OR N/A | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RACE | | | | | |
| CAUCASIAN | 7 (38.9%) | 255 (67.5%) | 97 (49.0%) | 250 (66.3%) | 265 (67.8%) |
| HISPANIC | 5 (27.8%) | 65 (17.2%) | 74 (37.4%) | 73 (19.4%) | 70 (17.9%) |
| BLACK | 3 (16.7%) | 31 ( 8.2%) | 11 ( 5.6%) | 26 ( 6.9%) | 32 ( 8.2%) |
| OTHER | 3 (16.7%) | 27 ( 7.1%) | 16 ( 8.1%) | 28 ( 7.4%) | 24 ( 6.1%) |
| AGE (YEARS) | | | | | |
| n | 18 | 375 | 198 | 376 | 391 |
| Mean (SD) | 66.2 ( 9.3) | 62.0 (12.7) | 60.2 (13.7) | 61.6 (12.2) | 62.5 (12.7) |
| Median | 67.5 | 63.0 | 60.0 | 62.0 | 63.0 |
| Range | 48 - 81 | 26 - 93 | 25 - 97 | 23 - 90 | 23 - 91 |
| STUDY EYE | | | | | |
| OD | 9 (50.0%) | 194 (51.3%) | 104 (52.5%) | 184 (48.8%) | 189 (48.3%) |
| OS | 9 (50.0%) | 184 (48.7%) | 94 (47.5%) | 193 (51.2%) | 202 (51.7%) |
| DIABETIC STATUS [1] | | | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| TYPE I DIABETES | 5 (27.8%) | 169 (44.7%) | 106 (53.5%) | 164 (43.5%) | 187 (47.8%) |
| TYPE II DIABETES | 11 (61.1%) | 123 (32.5%) | 67 (33.8%) | 109 (28.9%) | 124 (31.7%) |
| NON-DIABETIC | 2 (11.1%) | 86 (22.8%) | 25 (12.6%) | 104 (27.6%) | 80 (20.5%) |

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Note: One patient in study VIT-02-08961X (Saline) and three patients (two Saline and one 55 IU) in study VIT-03-08961X had calculated ages resolving to zero due to incorrect birth dates recorded. This record is not included in the age calculation.
In addition, patients with a missing DOB were not included in the age calculation.
[1] Diabetic status is only summarized for studies VIT-02-08961X and VIT-03-08961X. Percents are based on total number of patients in those studies. Type I diabetes includes all insulin-dependent diabetics.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 4.4
Summary of Demographics and Baseline Characteristics
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| NUMBER OF PATIENTS | 15 | 15 | 14 | 16 |
| GENDER | | | | |
| MALE | 8 (53.3%) | 5 (33.3%) | 11 (78.6%) | 10 (62.5%) |
| FEMALE | 7 (46.7%) | 10 (66.7%) | 3 (21.4%) | 6 (37.5%) |
| RACE | | | | |
| HISPANIC | 15 ( 100%) | 15 ( 100%) | 14 ( 100%) | 16 ( 100%) |
| AGE (YEARS) | | | | |
| n | 15 | 15 | 14 | 16 |
| Mean (SD) | 53.7 ( 8.6) | 53.3 (11.1) | 55.3 ( 8.5) | 54.3 ( 7.5) |
| Median | 54.0 | 57.0 | 53.0 | 53.5 |
| Range | 40 - 65 | 32 - 68 | 44 - 68 | 39 - 66 |
| STUDY EYE | | | | |
| OD | 12 (80.0%) | 8 (53.3%) | 12 (85.7%) | 11 (68.8%) |
| OS | 3 (20.0%) | 7 (46.7%) | 2 (14.3%) | 5 (31.3%) |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| NUMBER OF PATIENTS | 18 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 12 ( 67%) | 159 ( 38%) | 114 ( 35%) | 11 ( 8%) | 158 ( 42%) | 199 ( 33%) | 482 ( 33%) | 27 ( 32%) | 15 ( 71%) | 16 ( 23%) |
| EYE DISORDERS | 7 ( 39%) | 102 ( 24%) | 82 ( 25%) | 9 ( 7%) | 119 ( 32%) | 141 ( 23%) | 351 ( 24%) | 26 ( 31%) | 14 ( 67%) | 16 ( 23%) |
| VITREOUS HEMORRHAGE | 2 ( 11%) | 54 ( 13%) | 50 ( 15%) | 0 ( 0%) | 67 ( 18%) | 71 ( 12%) | 188 ( 13%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL DETACHMENT | 3 ( 17%) | 26 ( 6%) | 17 ( 5%) | 5 ( 4%) | 30 ( 8%) | 38 ( 6%) | 90 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RUBEOSIS IRIDIS | 1 ( 6%) | 15 ( 4%) | 13 ( 4%) | 0 ( 0%) | 13 ( 3%) | 12 ( 2%) | 38 ( 3%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CATARACT SUBCAPSULAR | 1 ( 6%) | 5 ( 1%) | 6 ( 2%) | 0 ( 0%) | 12 ( 3%) | 14 ( 2%) | 32 ( 2%) | 5 ( 6%) | 4 ( 19%) | 3 ( 4%) |
| VISUAL ACUITY REDUCED | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 5 ( <1%) | 11 ( 13%) | 6 ( 29%) | 7 ( 10%) |
| BLINDNESS NEC | 1 ( 6%) | 6 ( 1%) | 5 ( 2%) | 0 ( 0%) | 6 ( 2%) | 8 ( 1%) | 19 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIS ADHESIONS | 2 ( 11%) | 4 ( 1%) | 5 ( 2%) | 0 ( 0%) | 5 ( 1%) | 9 ( 1%) | 19 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CATARACT NUCLEAR | 0 ( 0%) | 2 ( <1%) | 5 ( 2%) | 0 ( 0%) | 6 ( 2%) | 7 ( 1%) | 18 ( 1%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| CATARACT CORTICAL | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 1 ( 1%) | 7 ( 2%) | 5 ( 1%) | 15 ( 1%) | 2 ( 2%) | 0 ( 0%) | 3 ( 4%) |
| GLAUCOMA NOS | 0 ( 0%) | 5 ( 1%) | 4 ( 1%) | 0 ( 0%) | 4 ( 1%) | 5 ( 1%) | 13 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CATARACT NEC | 0 ( 0%) | 5 ( 1%) | 1 ( <1%) | 0 ( 0%) | 4 ( 1%) | 5 ( 1%) | 10 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| VITREOUS FLOATERS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 4 ( 5%) | 5 ( 24%) | 2 ( 3%) |
| VITREOUS HAEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 4 ( 3%) | 0 ( 0%) | 3 ( <1%) | 8 ( 1%) | 3 ( 4%) | 3 ( 14%) | 1 ( 1%) |
| VITREOUS DETACHMENT | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 4 ( 1%) | 3 ( <1%) | 8 ( 1%) | 1 ( 1%) | 0 ( 0%) | 3 ( 4%) |
| EYE PAIN | 1 ( 6%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 5%) | 3 ( 14%) | 1 ( 1%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 1 ( <1%) | 5 ( 2%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 9 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPHEMA | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 2 ( <1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CATARACT NOS AGGRAVATED | 1 ( 6%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MACULAR EDEMA | 1 ( 6%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 4 ( 1%) | 2 ( <1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 3 ( <1%) | 6 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| IRITIS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 3 ( <1%) | 2 ( 2%) | 0 ( 0%) | 1 ( 1%) |
| MACULAR OEDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 3 ( 4%) | 3 ( 14%) | 2 ( 3%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MACULOPATHY | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 4%) | 3 ( 14%) | 0 ( 0%) |
| RETINOPATHY DIABETIC | 1 ( 6%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PSEUDOPHAKIA | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PHOTOPSIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 1 ( 5%) | 1 ( 1%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 5%) | 0 ( 0%) | 1 ( 1%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 10%) | 0 ( 0%) |
| CORNEAL EDEMA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE IRRITATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 4%) | 0 ( 0%) | 0 ( 0%) |
| HYPOTONY OF EYE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.

[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| LACRIMATION INCREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 10%) | 0 ( 0%) |
| OCULAR HYPERAEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 4%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL HEMORRHAGE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ISCHEMIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITREOUS DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL DETACHMENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL OEDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| PHOTOPHOBIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 5%) | 0 ( 0%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL DEGENERATION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ACCOMMODATION DISORDER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONJUNCTIVAL EDEMA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORECTOPIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL EROSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL GRAFT REJECTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL INFILTRATES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL ULCER NEC | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE DISCHARGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIS VASCULAR DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| KERATITIS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| OCULAR HYPEREMIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC ATROPHY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL DISORDER NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL NEOVASCULARIZATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISION BLURRED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC DISORDERS | 7 ( 39%) | 21 ( 5%) | 19 ( 6%) | 0 ( 0%) | 21 ( 6%) | 35 ( 6%) | 75 ( 5%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| MYOCARDIAL INFARCTION | 3 ( 17%) | 5 ( 1%) | 7 ( 2%) | 0 ( 0%) | 3 ( 1%) | 12 ( 2%) | 22 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC FAILURE CONGESTIVE | 2 ( 11%) | 4 ( 1%) | 5 ( 2%) | 0 ( 0%) | 5 ( 1%) | 6 ( 1%) | 16 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC ARREST | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 5 ( 1%) | 2 ( <1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANGINA UNSTABLE | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( 1%) | 3 ( <1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORONARY ARTERY OCCLUSION | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANGINA PECTORIS | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARRHYTHMIA NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ATRIAL FIBRILLATION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC FAILURE NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIOVASCULAR DISORDER NOS | 1 ( 6%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY EDEMA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORONARY ARTERY DISEASE NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LEFT VENTRICULAR FAILURE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AORTIC VALVE STENOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIO-RESPIRATORY ARREST | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MYOCARDIAL ISCHEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ATRIOVENTRICULAR BLOCK NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BRADYCARDIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIOGENIC SHOCK | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIOMYOPATHY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNEA PAROXYSMAL NOCTURNAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNOEA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERTROPHIC CARDIOMYOPATHY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ISCHEMIC CARDIOMYOPATHY | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PALPITATIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY CONGESTION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VENTRICULAR TACHYCARDIA | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INVESTIGATIONS | 1 ( 6%) | 13 ( 3%) | 23 ( 7%) | 0 ( 0%) | 19 ( 5%) | 23 ( 4%) | 65 ( 5%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 13 ( 3%) | 23 ( 7%) | 0 ( 0%) | 17 ( 5%) | 22 ( 4%) | 62 ( 4%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD GLUCOSE FLUCTUATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD GLUCOSE INCREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMATOCRIT DECREASED | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WEIGHT DECREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INFECTIONS AND INFESTATIONS | 1 ( 6%) | 11 ( 3%) | 8 ( 2%) | 0 ( 0%) | 14 ( 4%) | 14 ( 2%) | 36 ( 2%) | 2 ( 2%) | 1 ( 5%) | 0 ( 0%) |
| PNEUMONIA NOS | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 4 ( 1%) | 3 ( <1%) | 9 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.

[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| CELLULITIS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 4 ( 1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OSTEOMYELITIS NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 3 ( 1%) | 2 ( <1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LOCALISED INFECTION | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SEPSIS NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BRONCHITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INFECTED SKIN ULCER | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PYELONEPHRITIS NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| STAPHYLOCOCCAL INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AMERICAN TRYPANOSOMIASIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BACTERIAL INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLEPHARITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 5%) | 0 ( 0%) |
| BRONCHITIS ACUTE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BRONCHOPNEUMONIA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CELLULITIS STAPHYLOCOCCAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INFLUENZA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATITIS HERPETIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| KIDNEY INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| LUNG INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OSTEOMYELITIS CHRONIC NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY TUBERCULOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SEPTIC ARTHRITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SEPTICEMIA STAPHYLOCOCCAL | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| URINARY TRACT INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UROSEPSIS | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 6%) | 15 ( 4%) | 11 ( 3%) | 0 ( 0%) | 11 ( 3%) | 11 ( 2%) | 33 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITRECTOMY | 0 ( 0%) | 7 ( 2%) | 2 ( 1%) | 0 ( 0%) | 3 ( 1%) | 3 ( <1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 3 ( 1%) | 2 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORONARY ARTERY SURGERY | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOOT AMPUTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LEG AMPUTATION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TOE AMPUTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTERIAL BYPASS OPERATION (EXC CORONARY ARTERY) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD PRODUCT TRANSFUSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC OPERATION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.



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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| CARDIAC PACEMAKER INSERTION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CAROTID ENDARTERECTOMY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CRYOTHERAPY NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEVICE FAILURE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOOT OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HIP ARTHROPLASTY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HOSPITALIZATION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KNEE ARTHROPLASTY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LIMB OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| METATARSAL EXCISION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST PROCEDURAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WOUND DEBRIDEMENT | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 6%) | 8 ( 2%) | 8 ( 2%) | 1 ( 1%) | 8 ( 2%) | 12 ( 2%) | 29 ( 2%) | 3 ( 4%) | 0 ( 0%) | 1 ( 1%) |
| CEREBROVASCULAR ACCIDENT NOS | 1 ( 6%) | 5 ( 1%) | 4 ( 1%) | 0 ( 0%) | 5 ( 1%) | 7 ( 1%) | 16 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SYNCOPE | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEADACHE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| DIZZINESS (EXC VERTIGO) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMORRHAGIC STROKE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COMA NEC | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONVULSIONS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEPRESSED LEVEL OF CONSCIOUSNESS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMIPARESIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOAESTHESIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IIIRD NERVE PARALYSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| LACUNAR INFARCTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PUPILLARY DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL AND URINARY DISORDERS | 4 ( 22%) | 13 ( 3%) | 7 ( 2%) | 1 ( 1%) | 6 ( 2%) | 8 ( 1%) | 22 ( 2%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE NOS | 1 ( 6%) | 5 ( 1%) | 4 ( 1%) | 1 ( 1%) | 3 ( 1%) | 5 ( 1%) | 13 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE ACUTE | 3 ( 17%) | 3 ( 1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 2 ( <1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE CHRONIC | 1 ( 6%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL ARTERY STENOSIS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CALCULUS RENAL NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CALCULUS URINARY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GLOMERULONEPHRITIS CHRONIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE CHRONIC AGGRAVATED | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL IMPAIRMENT NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL VASCULAR DISORDER NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| VASCULAR DISORDERS | 0 ( 0%) | 15 ( 4%) | 7 ( 2%) | 0 ( 0%) | 8 ( 2%) | 8 ( 1%) | 23 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GANGRENE NOS | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERTENSION NOS | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIPHERAL VASCULAR DISEASE NOS | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TRANSIENT ISCHEMIC ATTACK | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERTENSION AGGRAVATED | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOTENSION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| THROMBOEMBOLISM NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTERIAL ANEURYSM NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTERIAL OCCLUSION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CEREBRAL INFARCTION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CEREBRAL ISCHEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CEREBROVASCULAR ACCIDENT NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COLLAPSE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMATOMA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ISCHEMIC FOOT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POSTURAL HYPOTENSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY EMBOLISM | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY HYPERTENSION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SUBARACHNOID HEMORRHAGE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VENOUS THROMBOSIS DEEP LIMB | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| METABOLISM AND NUTRITION DISORDERS | 2 ( 11%) | 8 ( 2%) | 3 ( 1%) | 0 ( 0%) | 4 ( 1%) | 11 ( 2%) | 18 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| HYPOGLYCAEMIA NOS | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 5 ( 1%) | 5 ( <1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| HYPERGLYCEMIA NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEHYDRATION | 1 ( 6%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC COMA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERKALEMIA | 1 ( 6%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC COMPLICATION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC NEUROPATHY NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETES MELLITUS AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC AMYOTROPHY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC EYE DISEASE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC KETOACIDOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOGLYCAEMIC COMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NONKETOTIC HYPERGLYCEMIC-HYPEROSMOLAR COMA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINOPATHY DIABETIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

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Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| GASTROINTESTINAL DISORDERS | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 0 ( 0%) | 9 ( 2%) | 7 ( 1%) | 17 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTROINTESTINAL HEMORRHAGE NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 3 ( 1%) | 2 ( <1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIARRHEA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABDOMINAL PAIN UPPER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DUODENITIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ESOPHAGITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABDOMINAL PAIN NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIVERTICULUM INTESTINAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DUODENAL ULCER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTRIC ULCER | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTRITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INGUINAL HERNIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PEPTIC ULCER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PEPTIC ULCER HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERITONEAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERITONITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RECTAL PROLAPSE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VOLVULUS OF BOWEL | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VOMITING NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 0 ( 0%) | 3 ( 1%) | 4 ( 1%) | 0 ( 0%) | 6 ( 2%) | 4 ( 1%) | 14 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNEA NOS | 0 ( 0%) | 1 ( <1%) | 4 ( 1%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHRONIC OBSTRUCTIVE AIRWAYS DISEASE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ASTHMA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNEA EXACERBATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EMPHYSEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EPISTAXIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PLEURAL EFFUSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PNEUMONIA VIRAL NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY CONGESTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RESPIRATORY FAILURE (EXC NEONATAL) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 1 ( 6%) | 5 ( 1%) | 2 ( 1%) | 1 ( 1%) | 1 ( <1%) | 6 ( 1%) | 10 ( 1%) | 0 ( 0%) | 1 ( 5%) | 0 ( 0%) |
| CHEST PAIN NEC | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEATH NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 1 ( 5%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.



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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| MULTI-ORGAN FAILURE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FALL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MASS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PYREXIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RIGORS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SENSATION OF PRESSURE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WEAKNESS | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJURY AND POISONING | 0 ( 0%) | 4 ( 1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 8 ( 1%) | 12 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HIP FRACTURE | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FEMUR FRACTURE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LACERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ACCIDENTAL OVERDOSE (THERAPEUTIC AGENT) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOOT FRACTURE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJURY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LEG FRACTURE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MEDICATION ERROR | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TIBIA FRACTURE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 4 ( 1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BREAST CANCER FEMALE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHRONIC LEUKEMIA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COLON CANCER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| METASTASES TO LUNG | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MYELODYSPLASTIC SYNDROME NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NONHODGKIN'S LYMPHOMA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PROSTATE CANCER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RESPIRATORY TRACT NEOPLASM NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN NEOPLASM NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ENDOCRINE DISORDERS | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETES MELLITUS INADEQUATE CONTROL | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 4 ( 1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| ANEMIA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANAEMIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANEMIA NOS AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DISSEMINATED INTRAVASCULAR COAGULATION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 1 ( 1%) | 1 ( 5%) | 1 ( 1%) |
| DERMATITIS ALLERGIC | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC FOOT ULCER | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ECCHYMOSIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 5%) | 0 ( 0%) |
| FOOT ULCER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| SKIN LESION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| URTICARIA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS | 0 ( 0%) | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PAIN IN LIMB | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTHRALGIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ROTATOR CUFF SYNDROME | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PSYCHIATRIC DISORDERS | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONFUSION | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DELIRIUM | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEPRESSION NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DISORIENTATION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HALLUCINATION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCHIZOPHRENIA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AXILLARY MASS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LOWER EXTREMITY MASS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WEAKNESS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEPATO-BILIARY DISORDERS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOLELITHIASIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEPATITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.1
Incidence of Serious Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PYREXIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KIDNEY TRANSPLANT REJECTION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| REPRODUCTIVE AND BREAST DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PROSTATITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| REPRODUCTIVE SYSTEM AND BREAST DISORDERS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PROSTATITIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.2
Incidence of Serious Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 68 | 31 | 153 | 225 | 602 | 364 | 84 |
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 0 ( 0.0%) | 10 (32.3%) | 30 (19.6%) | 1 ( 0.4%) | 322 (53.5%) | 119 (32.7%) | 27 (32.1%) |
| EYE DISORDERS | 0 ( 0.0%) | 2 ( 6.5%) | 17 (11.1%) | 1 ( 0.4%) | 240 (39.9%) | 91 (25.0%) | 26 (31.0%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 143 (23.8%) | 45 (12.4%) | 0 ( 0.0%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 2 ( 6.5%) | 7 ( 4.6%) | 1 ( 0.4%) | 53 ( 8.8%) | 27 ( 7.4%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 35 ( 5.8%) | 3 ( 0.8%) | 1 ( 1.2%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 26 ( 4.3%) | 6 ( 1.6%) | 5 ( 6.0%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 16 ( 2.7%) | 2 ( 0.5%) | 2 ( 2.4%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 13 ( 2.2%) | 6 ( 1.6%) | 1 ( 1.2%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 15 ( 2.5%) | 4 ( 1.1%) | 0 ( 0.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 9 ( 1.5%) | 5 ( 1.4%) | 2 ( 2.4%) |
| VISUAL ACUITY REDUCED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 2 ( 0.5%) | 11 (13 1%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 10 ( 1.7%) | 3 ( 0.8%) | 0 ( 0.0%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 4 ( 0.7%) | 5 ( 1.4%) | 1 ( 1.2%) |
| VITREOUS HAEMORRHAGE | 0 ( 0.0%) | 1 ( 3.2%) | 7 ( 4.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 8 ( 1.3%) | 0 ( 0.0%) | 1 ( 1.2%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 1 ( 0.3%) | 1 ( 1.2%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPHEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VITREOUS FLOATERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 4 ( 4.8%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IRITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 2 ( 2.4%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| EYE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 4.8%) |
| MACULAR OEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 4.8%) |
| CORNEAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| OCULAR HYPERAEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL OEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHOTOPSIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.2
Incidence of Serious Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| ACCOMMODATION DISORDER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORECTOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL EROSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL GRAFT REJECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL INFILTRATES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ULCER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE DISCHARGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS VASCULAR DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| LACRIMATION INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHOTOPHOBIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL NEOVASCULARIZATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC DISORDERS | 0 ( 0.0%) | 2 ( 6.5%) | 7 ( 4.6%) | 0 ( 0.0%) | 55 ( 9.1%) | 11 ( 3.0%) | 0 ( 0.0%) |
| MYOCARDIAL INFARCTION | 0 ( 0.0%) | 2 ( 6.5%) | 3 ( 2.0%) | 0 ( 0.0%) | 14 ( 2.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| CARDIAC FAILURE CONGESTIVE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 13 ( 2.2%) | 3 ( 0.8%) | 0 ( 0.0%) |
| ANGINA UNSTABLE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 8 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC ARREST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIAC FAILURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ARRHYTHMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ATRIAL FIBRILLATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CORONARY ARTERY OCCLUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY EDEMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 2 ( 0.5%) | 0 ( 0.0%) |
| AORTIC VALVE STENOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

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[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.2
Incidence of Serious Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| CORONARY ARTERY DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEFT VENTRICULAR FAILURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ANGINA PECTORIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ATRIOVENTRICULAR BLOCK NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BRADYCARDIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIO-RESPIRATORY ARREST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIOGENIC SHOCK | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIOMYOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIOVASCULAR DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPNEA PAROXYSMAL NOCTURNAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPNOEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYOCARDIAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PALPITATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 56 ( 9.3%) | 9 ( 2.5%) | 1 ( 1.2%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 54 ( 9.0%) | 8 ( 2.2%) | 1 ( 1.2%) |
| BLOOD GLUCOSE FLUCTUATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOOD GLUCOSE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| WEIGHT DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 27 ( 4.5%) | 8 ( 2.2%) | 2 ( 2.4%) |
| PNEUMONIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 7 ( 1.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CELLULITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OSTEOMYELITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LOCALISED INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SEPSIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) |
| BRONCHITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STAPHYLOCOCCAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| AMERICAN TRYPANOSOMIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BACTERIAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BRONCHITIS ACUTE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CELLULITIS STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATITIS HERPETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| KIDNEY INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| LUNG INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OSTEOMYELITIS CHRONIC NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY TUBERCULOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SEPTIC ARTHRITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SEPTICEMIA STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| URINARY TRACT INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.2
Incidence of Serious Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| SURGICAL AND MEDICAL PROCEDURES | 0 ( 0.0%) | 2 ( 6.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 31 ( 5.1%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 2 ( 6.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORONARY ARTERY SURGERY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOOT AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOE AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTERIAL BYPASS OPERATION (EXC CORONARY ARTERY) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD PRODUCT TRANSFUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC PACEMAKER INSERTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CAROTID ENDARTERECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOOT OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HIP ARTHROPLASTY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KNEE ARTHROPLASTY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEG AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LIMB OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST PROCEDURAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.3%) | 0 ( 0.0%) | 21 ( 3.5%) | 6 ( 1.6%) | 3 ( 3.6%) |
| CEREBROVASCULAR ACCIDENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 9 ( 1.5%) | 6 ( 1.6%) | 0 ( 0.0%) |
| SYNCOPE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEADACHE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| DIZZINESS (EXC VERTIGO) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONVULSIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMIPARESIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMORRHAGIC STROKE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOAESTHESIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IIIRD NERVE PARALYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| LACUNAR INFARCTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL AND URINARY DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 15 ( 2.5%) | 6 ( 1.6%) | 1 ( 1.2%) |
| RENAL FAILURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 11 ( 1.8%) | 1 ( 0.3%) | 1 ( 1.2%) |
| RENAL FAILURE ACUTE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 4 ( 1.1%) | 0 ( 0.0%) |
| CALCULUS RENAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLOMERULONEPHRITIS CHRONIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RENAL ARTERY STENOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL IMPAIRMENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 17 ( 2.8%) | 5 ( 1.4%) | 0 ( 0.0%) |
| GANGRENE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.2
Incidence of Serious Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| HYPERTENSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| HYPOTENSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TRANSIENT ISCHEMIC ATTACK | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTERIAL ANEURYSM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTERIAL OCCLUSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CEREBROVASCULAR ACCIDENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLLAPSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMATOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERTENSION AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ISCHEMIC FOOT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL VASCULAR DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTURAL HYPOTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PULMONARY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY HYPERTENSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THROMBOEMBOLISM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VENOUS THROMBOSIS DEEP LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| METABOLISM AND NUTRITION DISORDERS | 0 ( 0.0%) | 1 ( 3.2%) | 1 ( 0.7%) | 0 ( 0.0%) | 11 ( 1.8%) | 5 ( 1.4%) | 1 ( 1.2%) |
| HYPOGLYCAEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 0 ( 0.0%) | 1 ( 1.2%) |
| DIABETIC COMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPERGLYCEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC NEUROPATHY NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| DIABETES MELLITUS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC AMYOTROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC COMPLICATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETIC EYE DISEASE NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC KETOACIDOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERKALEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPOGLYCAEMIC COMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTROINTESTINAL DISORDERS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 13 ( 2.2%) | 3 ( 0.8%) | 0 ( 0.0%) |
| GASTROINTESTINAL HEMORRHAGE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIARRHEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ABDOMINAL PAIN UPPER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ESOPHAGITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ABDOMINAL PAIN NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIVERTICULUM INTESTINAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DUODENAL ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DUODENITIS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTRITIS NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INGUINAL HERNIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PEPTIC ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X



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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.2
Incidence of Serious Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| PEPTIC ULCER HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERITONEAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERITONITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RECTAL PROLAPSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VOMITING NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 13 ( 2.2%) | 1 ( 0.3%) | 1 ( 1.2%) |
| DYSPNEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHRONIC OBSTRUCTIVE AIRWAYS DISEASE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPNEA EXACERBATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EMPHYSEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EPISTAXIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PLEURAL EFFUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY CONGESTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| RESPIRATORY FAILURE (EXC NEONATAL) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | 0 ( 0.0%) | 1 ( 3.2%) | 2 ( 1.3%) | 0 ( 0.0%) | 5 ( 0.8%) | 4 ( 1.1%) | 0 ( 0.0%) |
| HIP FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LACERATION | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ACCIDENTAL OVERDOSE (THERAPEUTIC AGENT) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FEMUR FRACTURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOOT FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEG FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| TIBIA FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0.0%) | 2 ( 6.5%) | 1 ( 0.7%) | 0 ( 0.0%) | 7 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEST PAIN NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEATH NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FALL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MASS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MULTI-ORGAN FAILURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PYREXIA | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RIGORS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SENSATION OF PRESSURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CHRONIC LEUKEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLON CANCER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X



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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.2
Incidence of Serious Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| METASTASES TO LUNG | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYELODYSPLASTIC SYNDROME NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROSTATE CANCER NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RESPIRATORY TRACT NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SKIN NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 5 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANAEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANEMIA NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DISSEMINATED INTRAVASCULAR COAGULATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAIN IN LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTHRALGIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ROTATOR CUFF SYNDROME | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ENDOCRINE DISORDERS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETES MELLITUS INADEQUATE CONTROL | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0 3%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| AXILLARY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LOWER EXTREMITY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| WEAKNESS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 1 ( 1.2%) |
| DIABETIC FOOT ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOOT ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| SKIN LESION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSYCHIATRIC DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DELIRIUM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEPRESSION NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PYREXIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEPATO-BILIARY DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEPATITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0:0%) | 1 ( 0.3%) | 0 ( 0.0%) |

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[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.2
Incidence of Serious Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| IMMUNE SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KIDNEY TRANSPLANT REJECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| REPRODUCTIVE AND BREAST DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROSTATITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

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[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 5.3
Incidence of Serious Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 12 (66.7%) | 151 (39.9%) | 105 (53.0%) | 158 (41.9%) | 178 (45.5%) |
| EYE DISORDERS | 7 (38.9%) | 100 (26.5%) | 79 (39.9%) | 119 (31.6%) | 133 (34.0%) |
| VITREOUS HEMORRHAGE | 2 (11.1%) | 54 (14.3%) | 50 (25.3%) | 67 (17.8%) | 71 (18.2%) |
| RETINAL DETACHMENT | 3 (16.7%) | 24 ( 6.3%) | 16 ( 8.1%) | 30 ( 8.0%) | 34 ( 8.7%) |
| RUBEOSIS IRIDIS | 1 ( 5.6%) | 15 ( 4.0%) | 13 ( 6.6%) | 13 ( 3.4%) | 12 ( 3.1%) |
| CATARACT SUBCAPSULAR | 1 ( 5.6%) | 5 ( 1.3%) | 6 ( 3.0%) | 12 ( 3.2%) | 14 ( 3.6%) |
| BLINDNESS NEC | 1 ( 5.6%) | 6 ( 1.6%) | 5 ( 2.5%) | 6 ( 1.6%) | 8 ( 2.0%) |
| IRIS ADHESIONS | 2 (11.1%) | 4 ( 1.1%) | 5 ( 2.5%) | 5 ( 1.3%) | 9 ( 2.3%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 2 ( 0.5%) | 5 ( 2.5%) | 6 ( 1.6%) | 7 ( 1.8%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 2.0%) | 4 ( 1.1%) | 5 ( 1.3%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 7 ( 1.9%) | 5 ( 1.3%) |
| CATARACT NEC | 0 ( 0.0%) | 5 ( 1.3%) | 1 ( 0.5%) | 4 ( 1.1%) | 4 ( 1.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 2.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| HYPHEMA | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| MACULAR EDEMA | 1 ( 5.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| VISUAL ACUITY REDUCED | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 4 ( 1.1%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 4 ( 1.1%) | 3 ( 0.8%) |
| CATARACT NOS AGGRAVATED | 1 ( 5.6%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 3 ( 0.8%) | 0 ( 0.0%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 0.8%) |
| MACULOPATHY | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINOPATHY DIABETIC | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| IRITIS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CORNEAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| EYE PAIN | 1 ( 5.6%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| VITREOUS FLOATERS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL ULCER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 5.3
Incidence of Serious Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL NEOVASCULARIZATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC DISORDERS | 7 (38.9%) | 19 ( 5.0%) | 16 ( 8.1%) | 21 ( 5.6%) | 29 ( 7.4%) |
| MYOCARDIAL INFARCTION | 3 (16.7%) | 5 ( 1.3%) | 5 ( 2.5%) | 3 ( 0.8%) | 9 ( 2.3%) |
| CARDIAC FAILURE CONGESTIVE | 2 (11.1%) | 3 ( 0.8%) | 5 ( 2.5%) | 5 ( 1.3%) | 6 ( 1.5%) |
| CARDIAC ARREST | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 5 ( 1.3%) | 2 ( 0.5%) |
| ANGINA UNSTABLE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 3 ( 0.8%) | 3 ( 0.8%) |
| CORONARY ARTERY OCCLUSION | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ANGINA PECTORIS | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ARRHYTHMIA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ATRIAL FIBRILLATION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| PULMONARY EDEMA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| CARDIAC FAILURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CARDIOVASCULAR DISORDER NOS | 1 ( 5.6%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEFT VENTRICULAR FAILURE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CARDIO-RESPIRATORY ARREST | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORONARY ARTERY DISEASE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MYOCARDIAL ISCHEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| AORTIC VALVE STENOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ATRIOVENTRICULAR BLOCK NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BRADYCARDIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIAC DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIOGENIC SHOCK | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIOMYOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DYSPNEA PAROXYSMAL NOCTURNAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPERTROPHIC CARDIOMYOPATHY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ISCHEMIC CARDIOMYOPATHY | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PALPITATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VENTRICULAR TACHYCARDIA | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 1 ( 5.6%) | 13 ( 3.4%) | 23 (11.6%) | 19 ( 5.0%) | 23 ( 5.9%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 13 ( 3.4%) | 23 (11.6%) | 17 ( 4.5%) | 22 ( 5.6%) |
| BLOOD GLUCOSE FLUCTUATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLOOD GLUCOSE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEMATOCRIT DECREASED | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| WEIGHT DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

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Table 5.3
Incidence of Serious Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| INFECTIONS AND INFESTATIONS | 1 ( 5.6%) | 10 ( 2.6%) | 8 ( 4.0%) | 14 ( 3.7%) | 13 ( 3.3%) |
| PNEUMONIA NOS | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| CELLULITIS | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| OSTEOMYELITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| LOCALISED INFECTION | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| SEPSIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| BRONCHITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| INFECTED SKIN ULCER | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STAPHYLOCOCCAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| AMERICAN TRYPANOSOMIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BACTERIAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BRONCHITIS ACUTE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BRONCHOPNEUMONIA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CELLULITIS STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INFLUENZA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LUNG INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OSTEOMYELITIS CHRONIC NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY TUBERCULOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PYELONEPHRITIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SEPTIC ARTHRITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SEPTICEMIA STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| URINARY TRACT INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UROSEPSIS | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 5.6%) | 13 ( 3.4%) | 11 ( 5.6%) | 11 ( 2.9%) | 9 ( 2.3%) |
| VITRECTOMY | 0 ( 0.0%) | 6 ( 1.6%) | 2 ( 1.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CORONARY ARTERY SURGERY | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| FOOT AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| TOE AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ARTERIAL BYPASS OPERATION (EXC CORONARY ARTERY) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD PRODUCT TRANSFUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CARDIAC OPERATION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC PACEMAKER INSERTION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CAROTID ENDARTERECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEVICE FAILURE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOOT OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HIP ARTHROPLASTY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HOSPITALIZATION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KNEE ARTHROPLASTY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEG AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LIMB OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| METATARSAL EXCISION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST PROCEDURAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 5.3
Incidence of Serious Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| WOUND DEBRIDEMENT | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL AND URINARY DISORDERS | 4 (22.2%) | 12 ( 3.2%) | 7 ( 3.5%) | 6 ( 1.6%) | 8 ( 2.0%) |
| RENAL FAILURE NOS | 1 ( 5.6%) | 5 ( 1.3%) | 4 ( 2.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| RENAL FAILURE ACUTE | 3 (16.7%) | 3 ( 0.8%) | 2 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| RENAL FAILURE CHRONIC | 1 ( 5.6%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL ARTERY STENOSIS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CALCULUS RENAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| GLOMERULONEPHRITIS CHRONIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RENAL FAILURE CHRONIC AGGRAVATED | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL IMPAIRMENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RENAL VASCULAR DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 14 ( 3.7%) | 6 ( 3.0%) | 8 ( 2.1%) | 8 ( 2.0%) |
| HYPERTENSION NOS | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| GANGRENE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PERIPHERAL VASCULAR DISEASE NOS | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| TRANSIENT ISCHEMIC ATTACK | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| HYPERTENSION AGGRAVATED | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPOTENSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ARTERIAL ANEURYSM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTERIAL OCCLUSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CEREBRAL INFARCTION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CEREBRAL ISCHEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CEREBROVASCULAR ACCIDENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| COLLAPSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HEMATOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ISCHEMIC FOOT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POSTURAL HYPOTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PULMONARY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY HYPERTENSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUBARACHNOID HEMORRHAGE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THROMBOEMBOLISM NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VENOUS THROMBOSIS DEEP LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 5.6%) | 7 ( 1.9%) | 7 ( 3.5%) | 8 ( 2.1%) | 12 ( 3.1%) |
| CEREBROVASCULAR ACCIDENT NOS | 1 ( 5.6%) | 4 ( 1.1%) | 3 ( 1.5%) | 5 ( 1.3%) | 7 ( 1.8%) |
| SYNCOPE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| DIZZINESS (EXC VERTIGO) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEMORRHAGIC STROKE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| COMA NEC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONVULSIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DEPRESSED LEVEL OF CONSCIOUSNESS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMIPARESIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOAESTHESIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACUNAR INFARCTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 5.3
Incidence of Serious Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| METABOLISM AND NUTRITION DISORDERS | 2 (11.1%) | 7 ( 1.9%) | 3 ( 1.5%) | 4 ( 1.1%) | 9 ( 2.3%) |
| HYPOGLYCAEMIA NOS | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) |
| HYPERGLYCEMIA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| DEHYDRATION | 1 ( 5.6%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC COMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| HYPERKALEMIA | 1 ( 5.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETIC COMPLICATION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DIABETIC NEUROPATHY NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| DIABETES MELLITUS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETIC AMYOTROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC KETOACIDOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPOGLYCAEMIC COMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| NONKETOTIC HYPERGLYCEMIC-HYPEROSMOLAR COMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTROINTESTINAL DISORDERS | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 9 ( 2.4%) | 6 ( 1.5%) |
| GASTROINTESTINAL HEMORRHAGE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| DIARRHEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| ABDOMINAL PAIN UPPER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ESOPHAGITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ABDOMINAL PAIN NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DIVERTICULUM INTESTINAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DUODENAL ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DUODENITIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTRIC ULCER | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INGUINAL HERNIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PEPTIC ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PEPTIC ULCER HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERITONEAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERITONITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RECTAL PROLAPSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VOLVULUS OF BOWEL | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VOMITING NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 2.0%) | 6 ( 1.6%) | 4 ( 1.0%) |
| DYSPNEA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CHRONIC OBSTRUCTIVE AIRWAYS DISEASE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ASTHMA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPNEA EXACERBATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EMPHYSEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EPISTAXIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PLEURAL EFFUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PNEUMONIA VIRAL NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RESPIRATORY FAILURE (EXC NEONATAL) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 5.3
Incidence of Serious Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 1 ( 5.6%) | 4 ( 1.1%) | 2 ( 1.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| CHEST PAIN NEC | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| MULTI-ORGAN FAILURE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DEATH NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FALL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MASS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| WEAKNESS | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 2 ( 0.5%) | 7 ( 1.8%) |
| HIP FRACTURE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| FEMUR FRACTURE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOOT FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| LACERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| LEG FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEDICATION ERROR | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TIBIA FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| CHRONIC LEUKEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLON CANCER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| METASTASES TO LUNG | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYELODYSPLASTIC SYNDROME NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NONHODGKIN'S LYMPHOMA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RESPIRATORY TRACT NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SKIN NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ENDOCRINE DISORDERS | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| DIABETES MELLITUS INADEQUATE CONTROL | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| ANEMIA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| ANEMIA NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DISSEMINATED INTRAVASCULAR COAGULATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 2.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PAIN IN LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ARTHRALGIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ROTATOR CUFF SYNDROME | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSYCHIATRIC DISORDERS | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONFUSION | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DELIRIUM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DEPRESSION NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DISORIENTATION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 5.3
Incidence of Serious Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| HALLUCINATION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCHIZOPHRENIA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| AXILLARY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LOWER EXTREMITY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| WEAKNESS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETIC FOOT ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN LESION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| URTICARIA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEPATO-BILIARY DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOLELITHIASIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEPATITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PYREXIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KIDNEY TRANSPLANT REJECTION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| REPRODUCTIVE AND BREAST DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PROSTATITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| REPRODUCTIVE SYSTEM AND BREAST DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROSTATITIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 5.4
Incidence of Serious Adverse Events by System Organ Class
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| System Organ Class / Preferred Term | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| NUMBER OF PATIENTS | 15 | 15 | 14 | 16 |
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 9 ( 60%) | 7 ( 47%) | 9 ( 64%) | 14 ( 88%) |
| EYE DISORDERS | 9 ( 60%) | 7 ( 47%) | 9 ( 64%) | 13 ( 81%) |
| VISUAL ACUITY REDUCED | 6 ( 40%) | 3 ( 20%) | 4 ( 29%) | 6 ( 38%) |
| VITREOUS FLOATERS | 4 ( 27%) | 2 ( 13%) | 0 ( 0%) | 5 ( 31%) |
| CATARACT SUBCAPSULAR | 2 ( 13%) | 1 ( 7%) | 2 ( 14%) | 4 ( 25%) |
| EYE PAIN | 2 ( 13%) | 0 ( 0%) | 1 ( 7%) | 3 ( 19%) |
| MACULAR OEDEMA | 1 ( 7%) | 0 ( 0%) | 2 ( 14%) | 3 ( 19%) |
| PHOTOPHOBIA AGGRAVATED | 3 ( 20%) | 0 ( 0%) | 0 ( 0%) | 3 ( 19%) |
| VITREOUS HAEMORRHAGE | 2 ( 13%) | 0 ( 0%) | 1 ( 7%) | 3 ( 19%) |
| PHOTOPSIA | 2 ( 13%) | 1 ( 7%) | 0 ( 0%) | 1 ( 6%) |
| PUPILLARY REFLEX IMPAIRED | 3 ( 20%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| VITREOUS DETACHMENT | 1 ( 7%) | 3 ( 20%) | 0 ( 0%) | 0 ( 0%) |
| ABNORMAL SENSATION IN EYE | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 2 ( 13%) |
| CATARACT CORTICAL | 0 ( 0%) | 1 ( 7%) | 2 ( 14%) | 0 ( 0%) |
| LACRIMATION INCREASED | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 2 ( 13%) |
| CATARACT NUCLEAR | 2 ( 13%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRITIS | 1 ( 7%) | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) |
| EYE IRRITATION | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIS VASCULAR DISORDER NOS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RUBEOSIS IRIDIS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITREOUS DISORDER NOS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INFECTIONS AND INFESTATIONS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| BLEPHARITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| KIDNEY INFECTION NOS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 1 ( 6%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| FOOT ULCER | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| DEATH NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| METABOLISM AND NUTRITION DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| HYPOGLYCAEMIA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| IIIRD NERVE PARALYSIS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |

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Table 5.4
Incidence of Serious Adverse Events by System Organ Class
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| System Organ Class / Preferred Term | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| RENAL AND URINARY DISORDERS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE NOS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

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Table 6
Incidence of Serious Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: WW Control (n = 18)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 2 (11.1%) | 1 ( 5.6%) | 4 (22.2%) | 2 (11.1%) |
| EYE DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 2 (11.1%) | 1 ( 5.6%) | 4 (22.2%) | 2 (11.1%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 (16.7%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 5.6%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Events are included in the period in which they began.

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Table 6
Incidence of Serious Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 5 ( 1.3%) | 3 ( 0.8%) | 5 ( 1.3%) | 8 ( 2.1%) | 20 ( 5.3%) | 32 ( 8.5%) | 40 (10.6%) |
| EYE DISORDERS | 2 ( 0.5%) | 1 ( 0.3%) | 4 ( 1.1%) | 7 ( 1.9%) | 18 ( 4.8%) | 24 ( 6.3%) | 39 (10.3%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 1.3%) | 9 ( 2.4%) | 14 ( 3.7%) | 10 ( 2.6%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.1%) | 4 ( 1.1%) | 9 ( 2.4%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) | 1 ( 0.3%) | 6 ( 1.6%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.1%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.1%) |
| HYPHEMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| VISUAL ACUITY REDUCED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| EYE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CONJUNCTIVAL HEMORRHAGE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IRITIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 5 ( 1.3%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE INCREASED | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 5 ( 1.3%) | 1 ( 0.3%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 1.3%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

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Events are included in the period in which they began.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 6
Incidence of Serious Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 6 ( 3.0%) | 5 ( 2.5%) | 13 ( 6.6%) | 18 ( 9.1%) | 15 ( 7.6%) | 35 (17.7%) | 34 (17.2%) |
| EYE DISORDERS | 1 ( 0.5%) | 3 ( 1.5%) | 9 ( 4.5%) | 14 ( 7.1%) | 15 ( 7.6%) | 31 (15.7%) | 33 (16.7%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.5%) | 5 ( 2.5%) | 7 ( 3.5%) | 6 ( 3.0%) | 16 ( 8.1%) | 16 ( 8.1%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 4 ( 2.0%) | 4 ( 2.0%) | 6 ( 3.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 3 ( 1.5%) | 1 ( 0.5%) | 6 ( 3.0%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 4 ( 2.0%) | 1 ( 0.5%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 1.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 2.0%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 1 ( 0.5%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) |
| HYPHEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CATARACT NOS AGGRAVATED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORNEAL ULCER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| RETINAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL ACUITY REDUCED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| VITREOUS FLOATERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 3 ( 1.5%) | 2 ( 1.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 1 ( 0.5%) | 8 ( 4.0%) | 5 ( 2.5%) |
| INTRAOCULAR PRESSURE INCREASED | 3 ( 1.5%) | 2 ( 1.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 1 ( 0.5%) | 8 ( 4.0%) | 5 ( 2.5%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 6
Incidence of Serious Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Events are included in the period in which they began.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 6
Incidence of Serious Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 7 ( 1.9%) | 7 ( 1.9%) | 14 ( 3.7%) | 18 ( 4.8%) | 21 ( 5.6%) | 39 (10.3%) | 38 (10.1%) |
| EYE DISORDERS | 5 ( 1.3%) | 7 ( 1.9%) | 13 ( 3.4%) | 16 ( 4.2%) | 21 ( 5.6%) | 35 ( 9.3%) | 34 ( 9.0%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) | 8 ( 2.1%) | 13 ( 3.4%) | 17 ( 4.5%) | 12 ( 3.2%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 1.1%) | 3 ( 0.8%) | 5 ( 1.3%) | 9 ( 2.4%) | 8 ( 2.1%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| RUBEOSIS IRIDIS | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 4 ( 1.1%) |
| CATARACT CORTICAL | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.1%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) |
| IRIS ADHESIONS | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |
| VISUAL ACUITY REDUCED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| HYPOPYON | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| HYPHEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 6 ( 1.6%) | 6 ( 1.6%) |
| INTRAOCULAR PRESSURE INCREASED | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 6 ( 1.6%) | 6 ( 1.6%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 6
Incidence of Serious Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE SERIOUS ADVERSE EVENT | 14 ( 3.6%) | 7 ( 1.8%) | 13 ( 3.3%) | 16 ( 4.1%) | 21 ( 5.4%) | 50 (12.8%) | 51 (13.0%) |
| EYE DISORDERS | 8 ( 2.0%) | 6 ( 1.5%) | 10 ( 2.6%) | 16 ( 4.1%) | 20 ( 5.1%) | 47 (12.0%) | 50 (12.8%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 4 ( 1.0%) | 5 ( 1.3%) | 24 ( 6.1%) | 30 ( 7.7%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.0%) | 6 ( 1.5%) | 17 ( 4.3%) | 8 ( 2.0%) |
| CATARACT SUBCAPSULAR | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 6 ( 1.5%) |
| IRIS ADHESIONS | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 5 ( 1.3%) |
| RUBEOSIS IRIDIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.0%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) | 0 ( 0.0%) |
| GLAUCOMA NOS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPOPYON | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| HYPHEMA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| IRITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EDEMA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 6 ( 1.5%) | 1 ( 0.3%) | 3 ( 0.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 8 ( 2.0%) | 5 ( 1.3%) |
| INTRAOCULAR PRESSURE INCREASED | 6 ( 1.5%) | 1 ( 0.3%) | 3 ( 0.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 8 ( 2.0%) | 5 ( 1.3%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| NUMBER OF PATIENTS | 18 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 18 (100%) | 347 ( 83%) | 221 ( 68%) | 60 ( 46%) | 331 ( 88%) | 458 ( 75%) | 1070 ( 74%) | 75 ( 89%) | 19 ( 90%) | 51 ( 73%) |
| EYE DISORDERS | 17 ( 94%) | 334 ( 80%) | 212 ( 65%) | 53 ( 41%) | 323 ( 86%) | 455 ( 75%) | 1043 ( 72%) | 73 ( 87%) | 18 ( 86%) | 48 ( 69%) |
| IRITIS | 4 ( 22%) | 151 ( 36%) | 124 ( 38%) | 3 ( 2%) | 223 ( 59%) | 274 ( 45%) | 624 ( 43%) | 11 ( 13%) | 1 ( 5%) | 5 ( 7%) |
| OCULAR HYPEREMIA | 4 ( 22%) | 142 ( 34%) | 113 ( 35%) | 0 ( 0%) | 204 ( 54%) | 215 ( 35%) | 532 ( 37%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE PAIN | 3 ( 17%) | 86 ( 21%) | 76 ( 23%) | 3 ( 2%) | 140 ( 37%) | 168 ( 28%) | 387 ( 27%) | 15 ( 18%) | 6 ( 29%) | 2 ( 3%) |
| EYE IRRITATION | 10 ( 56%) | 123 ( 29%) | 91 ( 28%) | 0 ( 0%) | 132 ( 35%) | 159 ( 26%) | 382 ( 26%) | 15 ( 18%) | 4 ( 19%) | 0 ( 0%) |
| LACRIMATION INCREASED | 4 ( 22%) | 103 ( 25%) | 66 ( 20%) | 0 ( 0%) | 124 ( 33%) | 166 ( 27%) | 356 ( 25%) | 9 ( 11%) | 3 ( 14%) | 0 ( 0%) |
| VITREOUS HEMORRHAGE | 3 ( 17%) | 99 ( 24%) | 86 ( 26%) | 0 ( 0%) | 111 ( 29%) | 104 ( 17%) | 301 ( 21%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABNORMAL SENSATION IN EYE | 2 ( 11%) | 72 ( 17%) | 62 ( 19%) | 2 ( 2%) | 101 ( 27%) | 123 ( 20%) | 288 ( 20%) | 10 ( 12%) | 5 ( 24%) | 0 ( 0%) |
| VISUAL ACUITY REDUCED | 4 ( 22%) | 76 ( 18%) | 79 ( 24%) | 0 ( 0%) | 105 ( 28%) | 102 ( 17%) | 286 ( 20%) | 15 ( 18%) | 6 ( 29%) | 7 ( 10%) |
| VITREOUS FLOATERS | 6 ( 33%) | 70 ( 17%) | 66 ( 20%) | 1 ( 1%) | 91 ( 24%) | 105 ( 17%) | 263 ( 18%) | 6 ( 7%) | 5 ( 24%) | 2 ( 3%) |
| PHOTOPHOBIA | 6 ( 33%) | 63 ( 15%) | 60 ( 18%) | 0 ( 0%) | 87 ( 23%) | 108 ( 18%) | 255 ( 18%) | 6 ( 7%) | 3 ( 14%) | 0 ( 0%) |
| CONJUNCTIVAL EDEMA | 1 ( 6%) | 59 ( 14%) | 48 ( 15%) | 0 ( 0%) | 96 ( 25%) | 89 ( 15%) | 233 ( 16%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 42 ( 32%) | 6 ( 2%) | 80 ( 13%) | 131 ( 9%) | 2 ( 2%) | 0 ( 0%) | 1 ( 1%) |
| RETINAL DETACHMENT | 3 ( 17%) | 35 ( 8%) | 26 ( 8%) | 5 ( 4%) | 38 ( 10%) | 51 ( 8%) | 120 ( 8%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PHOTOPSIA | 0 ( 0%) | 23 ( 6%) | 24 ( 7%) | 0 ( 0%) | 45 ( 12%) | 44 ( 7%) | 113 ( 8%) | 3 ( 4%) | 2 ( 10%) | 1 ( 1%) |
| CATARACT SUBCAPSULAR | 2 ( 11%) | 27 ( 6%) | 34 ( 10%) | 1 ( 1%) | 29 ( 8%) | 43 ( 7%) | 107 ( 7%) | 8 ( 10%) | 4 ( 19%) | 5 ( 7%) |
| CATARACT NUCLEAR | 5 ( 28%) | 36 ( 9%) | 29 ( 9%) | 2 ( 2%) | 37 ( 10%) | 34 ( 6%) | 102 ( 7%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| EYE DISCHARGE | 0 ( 0%) | 31 ( 7%) | 12 ( 4%) | 1 ( 1%) | 23 ( 6%) | 48 ( 8%) | 84 ( 6%) | 10 ( 12%) | 2 ( 10%) | 4 ( 6%) |
| CATARACT CORTICAL | 5 ( 28%) | 27 ( 6%) | 14 ( 4%) | 1 ( 1%) | 30 ( 8%) | 31 ( 5%) | 76 ( 5%) | 3 ( 4%) | 0 ( 0%) | 4 ( 6%) |
| CORNEAL EDEMA | 1 ( 6%) | 12 ( 3%) | 18 ( 6%) | 0 ( 0%) | 22 ( 6%) | 26 ( 4%) | 66 ( 5%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RUBEOSIS IRIDIS | 1 ( 6%) | 21 ( 5%) | 17 ( 5%) | 1 ( 1%) | 21 ( 6%) | 25 ( 4%) | 64 ( 4%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| MACULAR EDEMA | 1 ( 6%) | 12 ( 3%) | 22 ( 7%) | 0 ( 0%) | 16 ( 4%) | 24 ( 4%) | 62 ( 4%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIS ADHESIONS | 2 ( 11%) | 14 ( 3%) | 10 ( 3%) | 3 ( 2%) | 13 ( 3%) | 31 ( 5%) | 57 ( 4%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL EROSION | 1 ( 6%) | 24 ( 6%) | 10 ( 3%) | 0 ( 0%) | 25 ( 7%) | 17 ( 3%) | 52 ( 4%) | 6 ( 7%) | 0 ( 0%) | 1 ( 1%) |
| CORNEAL DISORDER NOS | 0 ( 0%) | 8 ( 2%) | 6 ( 2%) | 0 ( 0%) | 18 ( 5%) | 26 ( 4%) | 50 ( 3%) | 26 ( 31%) | 0 ( 0%) | 22 ( 31%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0%) | 26 ( 6%) | 12 ( 4%) | 0 ( 0%) | 17 ( 5%) | 18 ( 3%) | 47 ( 3%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPHEMA | 0 ( 0%) | 6 ( 1%) | 9 ( 3%) | 0 ( 0%) | 14 ( 4%) | 16 ( 3%) | 39 ( 3%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CATARACT NEC | 0 ( 0%) | 17 ( 4%) | 3 ( 1%) | 0 ( 0%) | 11 ( 3%) | 21 ( 3%) | 35 ( 2%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| VITREOUS HAEMORRHAGE | 0 ( 0%) | 6 ( 1%) | 9 ( 3%) | 6 ( 5%) | 0 ( 0%) | 18 ( 3%) | 33 ( 2%) | 3 ( 4%) | 3 ( 14%) | 2 ( 3%) |
| CONJUNCTIVAL OEDEMA | 0 ( 0%) | 17 ( 4%) | 0 ( 0%) | 3 ( 2%) | 0 ( 0%) | 28 ( 5%) | 31 ( 2%) | 9 ( 11%) | 0 ( 0%) | 8 ( 11%) |
| RETINOPATHY DIABETIC | 1 ( 6%) | 11 ( 3%) | 7 ( 2%) | 1 ( 1%) | 6 ( 2%) | 14 ( 2%) | 28 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLINDNESS NEC | 1 ( 6%) | 6 ( 1%) | 9 ( 3%) | 0 ( 0%) | 7 ( 2%) | 9 ( 1%) | 25 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DRY EYE NEC | 0 ( 0%) | 7 ( 2%) | 7 ( 2%) | 0 ( 0%) | 5 ( 1%) | 12 ( 2%) | 24 ( 2%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| GLAUCOMA NOS | 0 ( 0%) | 6 ( 1%) | 6 ( 2%) | 0 ( 0%) | 6 ( 2%) | 12 ( 2%) | 24 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISION BLURRED | 0 ( 0%) | 8 ( 2%) | 11 ( 3%) | 0 ( 0%) | 7 ( 2%) | 5 ( 1%) | 23 ( 2%) | 2 ( 2%) | 2 ( 10%) | 0 ( 0%) |
| UVEITIS NOS | 1 ( 6%) | 2 ( <1%) | 4 ( 1%) | 3 ( 2%) | 8 ( 2%) | 7 ( 1%) | 22 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITREOUS DETACHMENT | 1 ( 6%) | 3 ( 1%) | 4 ( 1%) | 0 ( 0%) | 10 ( 3%) | 7 ( 1%) | 21 ( 1%) | 1 ( 1%) | 0 ( 0%) | 3 ( 4%) |
| RED EYE | 0 ( 0%) | 14 ( 3%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 19 ( 3%) | 20 ( 1%) | 3 ( 4%) | 3 ( 14%) | 0 ( 0%) |
| KERATITIS NEC | 0 ( 0%) | 4 ( 1%) | 4 ( 1%) | 2 ( 2%) | 4 ( 1%) | 9 ( 1%) | 19 ( 1%) | 17 ( 20%) | 0 ( 0%) | 17 ( 24%) |
| MACULOPATHY | 0 ( 0%) | 5 ( 1%) | 6 ( 2%) | 0 ( 0%) | 6 ( 2%) | 6 ( 1%) | 18 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLEPHARITIS | 0 ( 0%) | 2 ( <1%) | 5 ( 2%) | 0 ( 0%) | 3 ( 1%) | 8 ( 1%) | 16 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYELID OEDEMA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 15 ( 2%) | 16 ( 1%) | 3 ( 4%) | 0 ( 0%) | 3 ( 4%) |
| OCULAR HYPERAEMIA | 0 ( 0%) | 10 ( 2%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 15 ( 2%) | 16 ( 1%) | 22 ( 26%) | 5 ( 24%) | 0 ( 0%) |
| CATARACT NOS AGGRAVATED | 1 ( 6%) | 8 ( 2%) | 6 ( 2%) | 0 ( 0%) | 5 ( 1%) | 4 ( 1%) | 15 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 3 ( 1%) | 6 ( 2%) | 0 ( 0%) | 3 ( 1%) | 6 ( 1%) | 15 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL HEMORRHAGE | 0 ( 0%) | 7 ( 2%) | 6 ( 2%) | 0 ( 0%) | 6 ( 2%) | 3 ( <1%) | 15 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) | 0 ( 0%) | 7 ( 2%) | 5 ( 1%) | 14 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL ABRASION | 0 ( 0%) | 2 ( <1%) | 4 ( 1%) | 0 ( 0%) | 5 ( 1%) | 2 ( <1%) | 11 ( 1%) | 6 ( 7%) | 0 ( 0%) | 7 ( 10%) |
| CORNEAL EPITHELIUM DEFECT | 1 ( 6%) | 2 ( <1%) | 3 ( 1%) | 0 ( 0%) | 5 ( 1%) | 2 ( <1%) | 10 ( 1%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| DIPLOPIA | 0 ( 0%) | 2 ( <1%) | 3 ( 1%) | 0 ( 0%) | 5 ( 1%) | 2 ( <1%) | 10 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOTONY OF EYE | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 6 ( 1%) | 10 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ISCHEMIA | 0 ( 0%) | 1 ( <1%) | 4 ( 1%) | 0 ( 0%) | 4 ( 1%) | 2 ( <1%) | 10 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONJUNCTIVITIS NEC | 0 ( 0%) | 2 ( <1%) | 4 ( 1%) | 0 ( 0%) | 1 ( <1%) | 4 ( 1%) | 9 ( 1%) | 14 ( 17%) | 0 ( 0%) | 12 ( 17%) |
| IRIS DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( 2%) | 0 ( 0%) | 4 ( 1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 6 ( 2%) | 2 ( <1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE PAIN | 1 ( 6%) | 10 ( 2%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 5 ( 1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0%) | 1 ( <1%) | 4 ( 1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MYDRIASIS | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 4 ( 1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL OEDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 3 ( <1%) | 5 ( <1%) | 50 ( 60%) | 3 ( 14%) | 27 ( 39%) |
| OCULAR HYPERTENSION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 2 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 5 ( <1%) | 3 ( 4%) | 3 ( 14%) | 0 ( 0%) |
| RETINAL NEOVASCULARIZATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( <1%) | 3 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITREOUS DISORDER NOS | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 2 ( <1%) | 5 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( 1%) | 1 ( <1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE ALLERGY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYELID PTOSIS | 0 ( 0%) | 1 ( <1%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPHAEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 1 ( 1%) | 1 ( <1%) | 1 ( <1%) | 4 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| MACULAR DEGENERATION | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC ATROPHY | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| CORTICAL OPACITY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIDOCYCLITIS | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PAINFUL RED EYES | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| PSEUDOPHAKIA | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL DISORDER NOS | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL MICROANEURYSMS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL SCAR | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| APHAKIA | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLINDNESS TRANSIENT | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CATARACT UNILATERAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHEMOSIS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL DETACHMENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONJUNCTIVITIS VIRAL NOS | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL OPACITY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 3 ( 4%) | 0 ( 0%) | 2 ( 3%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFLAMMATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYALOSIS ASTEROID | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOPATHY BAND | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOPATHY NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MACULAR OEDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 4 ( 5%) | 3 ( 14%) | 2 ( 3%) |
| MEIBOMIAN CYST | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIORBITAL HEMATOMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL DEGENERATION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL DEPIGMENTATION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| STRABISMUS NEC | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITREOUS OPACITIES | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANISEIKONIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANTERIOR CHAMBER DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARCUS SENILIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| BLINDNESS NIGHT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOODSHOT EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHALAZION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHORIORETINAL ATROPHY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COLOUR BLINDNESS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONJUNCTIVAL CYST | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL SCAR | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL ULCER NEC | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| EYE HAEMORRHAGE NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION STAPHYLOCOCCAL | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INJURY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYELID DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GLAUCOMA AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIS VASCULAR DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LENTICULAR OPACITIES | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC NEUROPATHY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PAPILLEDEMA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PINGUECULA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ARTERY THROMBOSIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL VASCULITIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCLERITIS NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| STYE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TIRED EYES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UVEITIS DIABETIC | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISION ABNORMAL NEC | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| ACCOMMODATION DISORDER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 1 ( 5%) | 0 ( 0%) |
| CHORIORETINAL SCAR | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONJUNCTIVAL HAEMORRHAGE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 5%) | 0 ( 0%) |
| CONJUNCTIVITIS PAPILLARY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| CORECTOPIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 5%) | 0 ( 0%) |
| CORNEAL DEPOSITS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 5 ( 6%) | 0 ( 0%) | 3 ( 4%) |
| CORNEAL DYSTROPHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| CORNEAL EPITHELIUM DISORDER | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL GRAFT REJECTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL INFILTRATES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 5 ( 6%) | 0 ( 0%) | 3 ( 4%) |
| CORNEAL LESION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| CORNEAL NEOVASCULARIZATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| EXOPHTHALMOS ENDOCRINE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE HEMORRHAGE NEC | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIS NEVUS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LENTICULAR PIGMENTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC NERVE INJURY NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 5%) | 0 ( 0%) | 1 ( 1%) |
| RETINAL EXUDATES | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL VASCULAR DISORDER NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SUBEPITHELIAL OPACITIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 3 ( 4%) |
| INVESTIGATIONS | 6 ( 33%) | 53 ( 13%) | 57 ( 17%) | 5 ( 4%) | 59 ( 16%) | 63 ( 10%) | 184 ( 13%) | 3 ( 4%) | 1 ( 5%) | 3 ( 4%) |
| INTRAOCULAR PRESSURE INCREASED | 3 ( 17%) | 43 ( 10%) | 46 ( 14%) | 3 ( 2%) | 45 ( 12%) | 46 ( 8%) | 140 ( 10%) | 1 ( 1%) | 1 ( 5%) | 1 ( 1%) |
| CORNEAL STAINING | 0 ( 0%) | 7 ( 2%) | 8 ( 2%) | 2 ( 2%) | 9 ( 2%) | 12 ( 2%) | 31 ( 2%) | 2 ( 2%) | 0 ( 0%) | 2 ( 3%) |
| BLOOD GLUCOSE INCREASED | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD CREATININE INCREASED | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD PRESSURE INCREASED | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD CHOLESTEROL INCREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMATURIA PRESENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BIOPSY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD GLUCOSE ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD GLUCOSE DECREASED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD GLUCOSE FLUCTUATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD PHOSPHATE DECREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD SODIUM DECREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| BLOOD TRIGLYCERIDES INCREASED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD UREA INCREASED | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CANDIDURIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COAGULATION FACTOR DECREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ELECTROCARDIOGRAM ABNORMAL NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ENLARGED PROSTATE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LIVER FUNCTION TESTS NOS ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PROTEINURIA PRESENT | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PROTHROMBIN TIME PROLONGED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RED BLOOD CELL SEDIMENTATION RATE INCREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WEIGHT DECREASED | 1 ( 6%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC ENZYMES INCREASED | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMATOCRIT DECREASED | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMOGLOBIN DECREASED | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL ACUITY TESTS DISTANCE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 2 ( 11%) | 38 ( 9%) | 27 ( 8%) | 1 ( 1%) | 50 ( 13%) | 61 ( 10%) | 139 ( 10%) | 8 ( 10%) | 2 ( 10%) | 3 ( 4%) |
| EYELID EDEMA | 0 ( 0%) | 15 ( 4%) | 13 ( 4%) | 0 ( 0%) | 29 ( 8%) | 25 ( 4%) | 67 ( 5%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ERYTHEMA NEC | 0 ( 0%) | 17 ( 4%) | 8 ( 2%) | 0 ( 0%) | 21 ( 6%) | 30 ( 5%) | 59 ( 4%) | 5 ( 6%) | 2 ( 10%) | 0 ( 0%) |
| PRURITUS NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 2 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DERMATITIS NOS | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOOT ULCER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 4 ( <1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| SKIN ULCER NOS | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONTUSION | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CUTIS LAXA | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DERMATITIS ALLERGIC | 1 ( 6%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FACE EDEMA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OCULAR HYPEREMIA | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIORBITAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PSORIASIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN IRRITATION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN LESION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ALOPECIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC FOOT ULCER | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DRY SKIN | 1 ( 6%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ECCHYMOSIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| EYELID OEDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( 2%) | 0 ( 0%) | 2 ( 3%) |
| LEG ULCER (EXC VARICOSE) | 1 ( 6%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PALMAR ERYTHEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN NECROSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN NODULE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN ULCER HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| STASIS ULCER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SWEATING INCREASED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TELANGIECTASIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INTERTRIGO | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PRURIGO | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| URTICARIA NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 6%) | 31 ( 7%) | 30 ( 9%) | 3 ( 2%) | 40 ( 11%) | 50 ( 8%) | 123 ( 9%) | 18 ( 21%) | 4 ( 19%) | 1 ( 1%) |
| HEADACHE NOS | 0 ( 0%) | 16 ( 4%) | 13 ( 4%) | 3 ( 2%) | 20 ( 5%) | 25 ( 4%) | 61 ( 4%) | 15 ( 18%) | 3 ( 14%) | 0 ( 0%) |
| CEREBROVASCULAR ACCIDENT NOS | 1 ( 6%) | 5 ( 1%) | 4 ( 1%) | 0 ( 0%) | 5 ( 1%) | 8 ( 1%) | 17 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIZZINESS (EXC VERTIGO) | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 4 ( 1%) | 6 ( 1%) | 11 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| INSOMNIA NEC | 0 ( 0%) | 2 ( <1%) | 3 ( 1%) | 0 ( 0%) | 3 ( 1%) | 4 ( 1%) | 10 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PUPILLARY DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 4 ( 1%) | 3 ( <1%) | 10 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SYNCOPE | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 4 ( 1%) | 7 ( <1%) | 0 ( 0%) | 1 ( 5%) | 0 ( 0%) |
| DEMENTIA NOS | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOESTHESIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BALANCE IMPAIRED NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONVULSIONS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FACIAL PALSY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MOVEMENT DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NEUROPATHY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TREMOR NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BURNING SENSATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSARTHRIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMIPARESIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMORRHAGIC STROKE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOAESTHESIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LACUNAR INFARCTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MIGRAINE NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OBSTRUCTIVE SLEEP APNEA SYNDROME | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PARKINSON'S DISEASE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SPEECH DISORDER NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL PATHWAY DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITH NERVE PARALYSIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AMNESIA NEC | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COMA NEC | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEMENTIA OF THE ALZHEIMER'S TYPE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEPRESSED LEVEL OF CONSCIOUSNESS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IIIRD NERVE PARALYSIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 1 ( 1%) |
| VOCAL CORD PARALYSIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INFECTIONS AND INFESTATIONS | 2 ( 11%) | 40 ( 10%) | 29 ( 9%) | 0 ( 0%) | 40 ( 11%) | 41 ( 7%) | 110 ( 8%) | 6 ( 7%) | 3 ( 14%) | 0 ( 0%) |
| NASOPHARYNGITIS | 0 ( 0%) | 3 ( 1%) | 4 ( 1%) | 0 ( 0%) | 5 ( 1%) | 7 ( 1%) | 16 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PNEUMONIA NOS | 0 ( 0%) | 5 ( 1%) | 5 ( 2%) | 0 ( 0%) | 6 ( 2%) | 4 ( 1%) | 15 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| URINARY TRACT INFECTION NOS | 1 ( 6%) | 6 ( 1%) | 3 ( 1%) | 0 ( 0%) | 3 ( 1%) | 6 ( 1%) | 12 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INFLUENZA | 1 ( 6%) | 3 ( 1%) | 4 ( 1%) | 0 ( 0%) | 4 ( 1%) | 1 ( <1%) | 9 ( 1%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| CELLULITIS | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 5 ( 1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BRONCHITIS NOS | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 4 ( 1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LOCALISED INFECTION | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 3 ( 1%) | 2 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OSTEOMYELITIS NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 4 ( 1%) | 2 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SINUSITIS NOS | 0 ( 0%) | 2 ( <1%) | 3 ( 1%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SEPSIS NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UPPER RESPIRATORY TRACT INFECTION NOS | 1 ( 6%) | 1 ( <1%) | 3 ( 1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HERPES ZOSTER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PHARYNGITIS NOS | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BRONCHITIS ACUTE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FUNGAL INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ORAL CANDIDIASIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RESPIRATORY TRACT INFECTION NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN CANDIDA NOS | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| STAPHYLOCOCCAL INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TOOTH INFECTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AMERICAN TRYPANOSOMIASIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTHROPOD BITE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BACTERIAL INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here. Ocular Events include events reported for study eye and non-study eye.

[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| BLADDER INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CANDIDAL INFECTION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CELLULITIS STAPHYLOCOCCAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CYSTITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJECTION SITE INFECTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LARYNGITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LOWER RESPIRATORY TRACT INFECTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LUNG INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NAIL TINEA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OSTEOMYELITIS CHRONIC NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PHARYNGITIS STREPTOCOCCAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PNEUMONIA HAEMOPHILUS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY TUBERCULOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ROUNDWORM INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SEPTIC ARTHRITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SEPTICEMIA STAPHYLOCOCCAL | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VAGINOSIS FUNGAL NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WOUND INFECTION NEC | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLEPHARITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 5%) | 0 ( 0%) |
| BRONCHOPNEUMONIA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CANDIDA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EAR INFECTION NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTROINTESTINAL INFECTION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INFECTED SKIN ULCER | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATITIS HERPETIC | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| KIDNEY INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| MYCOBACTERIAL INFECTION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PNEUMONIA MYCOPLASMAL | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PYELONEPHRITIS NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN & SUBCUTANEOUS TISSUE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABSCESS | | | | | | | | | | |
| SORE THROAT NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 1 ( 5%) | 0 ( 0%) |
| TONSILLITIS ACUTE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 5%) | 0 ( 0%) |
| TUBERCULOSIS NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UROSEPSIS | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC DISORDERS | 8 ( 44%) | 26 ( 6%) | 23 ( 7%) | 0 ( 0%) | 27 ( 7%) | 43 ( 7%) | 93 ( 6%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| MYOCARDIAL INFARCTION | 3 ( 17%) | 5 ( 1%) | 7 ( 2%) | 0 ( 0%) | 3 ( 1%) | 12 ( 2%) | 22 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC FAILURE CONGESTIVE | 2 ( 11%) | 6 ( 1%) | 6 ( 2%) | 0 ( 0%) | 6 ( 2%) | 7 ( 1%) | 19 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANGINA UNSTABLE | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( 1%) | 3 ( <1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC ARREST | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 5 ( 1%) | 2 ( <1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ATRIAL FIBRILLATION | 1 ( 6%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 5 ( 1%) | 2 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC FAILURE NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EDEMA LOWER LIMB | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 2 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY EDEMA NOS | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 2 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARRHYTHMIA NOS | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIOMEGALY NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIOVASCULAR DISORDER NOS | 1 ( 6%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORONARY ARTERY DISEASE NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORONARY ARTERY OCCLUSION | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANGINA PECTORIS | 1 ( 6%) | 5 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AORTIC VALVE STENOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ATRIOVENTRICULAR BLOCK NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC MURMUR NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EDEMA PERIPHERAL | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LEFT VENTRICULAR FAILURE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MYOCARDIAL ISCHEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PALPITATIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AORTIC VALVE DISEASE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ATRIAL FLUTTER | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BRADYCARDIA NOS | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC FAILURE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIO-RESPIRATORY ARREST | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIOGENIC SHOCK | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIOMYOPATHY NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNEA PAROXYSMAL NOCTURNAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNOEA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EDEMA UPPER LIMB | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ISCHEMIC CARDIOMYOPATHY | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MYOCARDITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VENTRICULAR EXTRASYSTOLES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VENTRICULAR TACHYCARDIA | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERTROPHIC CARDIOMYOPATHY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OEDEMA PERIPHERAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| ORTHOPNEA | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY CONGESTION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VENTRICULAR HYPOKINESIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTROINTESTINAL DISORDERS | 3 ( 17%) | 26 ( 6%) | 14 ( 4%) | 1 ( 1%) | 35 ( 9%) | 32 ( 5%) | 82 ( 6%) | 3 ( 4%) | 0 ( 0%) | 1 ( 1%) |
| NAUSEA | 1 ( 6%) | 10 ( 2%) | 5 ( 2%) | 0 ( 0%) | 13 ( 3%) | 11 ( 2%) | 29 ( 2%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| VOMITING NOS | 1 ( 6%) | 6 ( 1%) | 2 ( 1%) | 0 ( 0%) | 7 ( 2%) | 5 ( 1%) | 14 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIARRHEA NOS | 0 ( 0%) | 6 ( 1%) | 3 ( 1%) | 0 ( 0%) | 7 ( 2%) | 3 ( <1%) | 13 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONSTIPATION | 0 ( 0%) | 6 ( 1%) | 1 ( <1%) | 0 ( 0%) | 3 ( 1%) | 8 ( 1%) | 12 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTROINTESTINAL HEMORRHAGE NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 3 ( 1%) | 3 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABDOMINAL PAIN NOS | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 2 ( <1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPEPSIA | 1 ( 6%) | 3 ( 1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ESOPHAGITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTRITIS NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SORE THROAT NOS | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABDOMINAL PAIN UPPER | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTRO-ESOPHAGEAL REFLUX DISEASE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIVERTICULUM INTESTINAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ESOPHAGEAL REFLUX | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTRIC ULCER | 1 ( 6%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTROINTESTINAL UPSET | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABDOMINAL PAIN AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABDOMINAL TENDERNESS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ASCITES | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DUODENAL ULCER | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DUODENITIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPHAGIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTRIC EROSIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTRIC IRRITATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTROENTERITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GASTROINTESTINAL DISORDER NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMATEMESIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMORRHOIDS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IMPAIRED GASTRIC EMPTYING | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INGUINAL HERNIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PEPTIC ULCER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PEPTIC ULCER HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIODONTAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | Vitrase | Saline | Other |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | 50-500 IU | Control | Active [1] |
| PERITONEAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERITONEAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERITONITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RECTAL BLEEDING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RECTAL PROLAPSE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TOOTHACHE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABDOMINAL DISTENSION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIARRHOEA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| VOLVULUS OF BOWEL | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| METABOLISM AND NUTRITION DISORDERS | 4 ( 22%) | 21 ( 5%) | 23 ( 7%) | 0 ( 0%) | 23 ( 6%) | 28 ( 5%) | 74 ( 5%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| HYPERCHOLESTEROLEMIA | 1 ( 6%) | 5 ( 1%) | 8 ( 2%) | 0 ( 0%) | 5 ( 1%) | 5 ( 1%) | 18 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOGLYCAEMIA NOS | 0 ( 0%) | 6 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 9 ( 1%) | 11 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| HYPERGLYCEMIA NOS | 0 ( 0%) | 2 ( <1%) | 3 ( 1%) | 0 ( 0%) | 4 ( 1%) | 1 ( <1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEHYDRATION | 2 ( 11%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 4 ( 1%) | 2 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERLIPIDEMIA NOS | 0 ( 0%) | 2 ( <1%) | 3 ( 1%) | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| APPETITE DECREASED NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 4 ( 1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERKALEMIA | 1 ( 6%) | 4 ( 1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 5 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC NEUROPATHY NEC | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC COMA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETES MELLITUS AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETES MELLITUS INSULIN-DEPENDENT | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GOUT | 1 ( 6%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GOUT AGGRAVATED | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOCALCEMIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOKALEMIA | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OBESITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETES MELLITUS NON INSULIN-DEPENDENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC AMYOTROPHY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC COMPLICATION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC EYE DISEASE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC KETOACIDOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ELECTROLYTE IMBALANCE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GLUCOSE TOLERANCE IMPAIRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERLIPIDAEMIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERPHOSPHATEMIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| HYPERVOLEMIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOGLYCAEMIC COMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPONATREMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOVOLEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INSULIN RESISTANCE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| METABOLIC ACIDOSIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POLYDIPSIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINOPATHY DIABETIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CALCIUM DEFICIENCY | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FLUID RETENTION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOLATE DEFICIENCY | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERURICEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NONKETOTIC HYPERGLYCEMIC-HYPEROSMOLAR COMA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 3 ( 17%) | 31 ( 7%) | 12 ( 4%) | 5 ( 4%) | 8 ( 2%) | 48 ( 8%) | 73 ( 5%) | 8 ( 10%) | 3 ( 14%) | 1 ( 1%) |
| PAIN NOS | 0 ( 0%) | 16 ( 4%) | 1 ( <1%) | 1 ( 1%) | 0 ( 0%) | 28 ( 5%) | 30 ( 2%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| CHEST PAIN NEC | 1 ( 6%) | 5 ( 1%) | 6 ( 2%) | 1 ( 1%) | 2 ( 1%) | 5 ( 1%) | 14 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FALL | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FATIGUE | 1 ( 6%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PAIN IN FACE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SENSATION OF FOREIGN BODY NOS | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WEAKNESS | 1 ( 6%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EDEMA LOWER LIMB | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PYREXIA | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 3 ( <1%) | 1 ( 1%) | 1 ( 5%) | 0 ( 0%) |
| DIFFICULTY IN WALKING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EDEMA PERIPHERAL | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| APPLICATION SITE BLEEDING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| APPLICATION SITE ERYTHEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEATH NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 1 ( 5%) | 0 ( 0%) |
| GROIN PAIN | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HERNIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IMPAIRED HEALING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LOWER EXTREMITY MASS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MASS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| MULTI-ORGAN FAILURE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RIGORS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SENSATION OF PRESSURE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMORRHAGE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJECTION SITE EXTRAVASATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 4%) | 0 ( 0%) | 0 ( 0%) |
| INJECTION SITE PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| INJECTION SITE REACTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 1 ( 5%) | 0 ( 0%) |
| MALAISE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MENTAL STATUS CHANGES | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIPHERAL SWELLING | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 11%) | 25 ( 6%) | 15 ( 5%) | 0 ( 0%) | 27 ( 7%) | 21 ( 3%) | 63 ( 4%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| POST-OPERATIVE COMPLICATIONS NOS | 1 ( 6%) | 10 ( 2%) | 5 ( 2%) | 0 ( 0%) | 8 ( 2%) | 6 ( 1%) | 19 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITRECTOMY | 0 ( 0%) | 7 ( 2%) | 2 ( 1%) | 0 ( 0%) | 4 ( 1%) | 4 ( 1%) | 10 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 4 ( 1%) | 2 ( <1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORONARY ARTERY SURGERY | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOOT AMPUTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NAUSEA POST-OPERATIVE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TOE AMPUTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TOOTH EXTRACTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTERIAL BYPASS OPERATION (EXC CORONARY ARTERY) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTERIO-VENOUS FISTULA OPERATION | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD PRODUCT TRANSFUSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CARDIAC PACEMAKER INSERTION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CAROTID ENDARTERECTOMY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHEMOTHERAPY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE IRRITATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FLUID REPLACEMENT PARENTERAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOOT OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HIP ARTHROPLASTY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJECTION SITE OEDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KNEE ARTHROPLASTY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LEG AMPUTATION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LENS IMPLANT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.

[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| LIMB OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST PROCEDURAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST PROCEDURAL PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCLERAL OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SHUNT OCCLUSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN CYST EXCISION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SUTURE LINE PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VOMITING POST-OPERATIVE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| APPLICATION SITE REACTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| CARDIAC OPERATION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CRYOTHERAPY NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEVICE FAILURE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HOSPITALIZATION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| METATARSAL EXCISION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WOUND DEBRIDEMENT | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VASCULAR DISORDERS | 0 ( 0%) | 28 ( 7%) | 15 ( 5%) | 0 ( 0%) | 24 ( 6%) | 24 ( 4%) | 63 ( 4%) | 3 ( 4%) | 0 ( 0%) | 0 ( 0%) |
| HYPERTENSION NOS | 0 ( 0%) | 9 ( 2%) | 6 ( 2%) | 0 ( 0%) | 13 ( 3%) | 12 ( 2%) | 31 ( 2%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| HYPERTENSION AGGRAVATED | 0 ( 0%) | 6 ( 1%) | 1 ( <1%) | 0 ( 0%) | 6 ( 2%) | 2 ( <1%) | 9 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GANGRENE NOS | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOTENSION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TRANSIENT ISCHEMIC ATTACK | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIPHERAL VASCULAR DISEASE NOS | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POSTURAL HYPOTENSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VENOUS THROMBOSIS DEEP LIMB | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTERIAL ANEURYSM NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTERIAL OCCLUSION NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD PRESSURE FLUCTUATION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD PRESSURE INADEQUATELY CONTROLLED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CAROTID ARTERY DISEASE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CAROTID ARTERY STENOSIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CEREBROVASCULAR ACCIDENT NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COLLAPSE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMATOMA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HOT FLUSHES NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ISCHEMIC FOOT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

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Ocular Events include events reported for study eye and non-study eye.
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Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POOR PERIPHERAL CIRCULATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY EMBOLISM | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY HYPERTENSION NOS | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| THROMBOEMBOLISM NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CEREBRAL INFARCTION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CEREBRAL ISCHEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FLUSHING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| HYPERTENSIVE ENCEPHALOPATHY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LABILE HYPERTENSION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIPHERAL CIRCULATORY FAILURE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SUBARACHNOID HEMORRHAGE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 5 ( 28%) | 12 ( 3%) | 17 ( 5%) | 0 ( 0%) | 19 ( 5%) | 15 ( 2%) | 51 ( 4%) | 7 ( 8%) | 2 ( 10%) | 0 ( 0%) |
| DYSPNEA NOS | 2 ( 11%) | 3 ( 1%) | 7 ( 2%) | 0 ( 0%) | 6 ( 2%) | 4 ( 1%) | 17 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COUGH | 0 ( 0%) | 1 ( <1%) | 3 ( 1%) | 0 ( 0%) | 6 ( 2%) | 3 ( <1%) | 12 ( 1%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| CHRONIC OBSTRUCTIVE AIRWAYS DISEASE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PLEURAL EFFUSION | 1 ( 6%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RHINORRHEA | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EPISTAXIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LUNG INFILTRATION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SNEEZING | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ASTHMA AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ASTHMA NOS | 2 ( 11%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ATELECTASIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNEA EXACERBATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNEA EXERTIONAL | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNOEA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EMPHYSEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEMOPTYSIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOXIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INTERSTITIAL LUNG DISEASE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NASAL CONGESTION | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY FIBROSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RESPIRATORY FAILURE (EXC NEONATAL) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.



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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| RHINITIS SEASONAL | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SINUS PAIN | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DYSPNEA PAROXYSMAL NOCTURNAL | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NASOPHARYNGITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| PNEUMONIA VIRAL NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PULMONARY CONGESTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RHINORRHOEA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| SORE THROAT NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 2 ( 10%) | 0 ( 0%) |
| RENAL AND URINARY DISORDERS | 4 ( 22%) | 19 ( 5%) | 10 ( 3%) | 1 ( 1%) | 15 ( 4%) | 19 ( 3%) | 45 ( 3%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE NOS | 1 ( 6%) | 6 ( 1%) | 4 ( 1%) | 1 ( 1%) | 6 ( 2%) | 6 ( 1%) | 17 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RENAL IMPAIRMENT NOS | 1 ( 6%) | 2 ( <1%) | 2 ( 1%) | 0 ( 0%) | 5 ( 1%) | 2 ( <1%) | 9 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE ACUTE | 3 ( 17%) | 4 ( 1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 4 ( 1%) | 8 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE CHRONIC | 1 ( 6%) | 3 ( 1%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| URINARY RETENTION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CALCULUS RENAL NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLADDER PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FLUID RETENTION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GLOMERULONEPHRITIS CHRONIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GLOMERULONEPHRITIS MINIMAL LESION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LOIN PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POLYURIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL ARTERY STENOSIS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE CHRONIC AGGRAVATED | 1 ( 6%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| URINE DISCOLOURATION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLADDER PROLAPSE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CALCULUS URINARY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETIC NEPHROPATHY NOS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MICROALBUMINURIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL CYST NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL VASCULAR DISORDER NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJURY AND POISONING | 0 ( 0%) | 11 ( 3%) | 9 ( 3%) | 3 ( 2%) | 9 ( 2%) | 23 ( 4%) | 44 ( 3%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LACERATION | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 5 ( 1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOOT FRACTURE | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HIP FRACTURE | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL EROSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| DRUG TOXICITY NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ABRASION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BURNS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FRACTURE NOS | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LEG FRACTURE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ACCIDENT NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ACCIDENTAL OVERDOSE (THERAPEUTIC AGENT) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANKLE FRACTURE | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BACK INJURY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLISTER | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHEMICAL BURNS OF EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL ABRASION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FEMUR FRACTURE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOREARM FRACTURE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOTHERMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJURY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| JOINT SPRAIN | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LOCALISED INFECTION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PHANTOM LIMB PAIN | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RIB FRACTURE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SUNBURN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| THERAPEUTIC AGENT TOXICITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TIBIA FRACTURE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UPPER LIMB FRACTURE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WHIPLASH INJURY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEAD INJURY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MEDICATION ERROR | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS | 0 ( 0%) | 12 ( 3%) | 11 ( 3%) | 2 ( 2%) | 10 ( 3%) | 11 ( 2%) | 34 ( 2%) | 3 ( 4%) | 1 ( 5%) | 0 ( 0%) |
| PAIN IN LIMB | 0 ( 0%) | 4 ( 1%) | 5 ( 2%) | 0 ( 0%) | 3 ( 1%) | 1 ( <1%) | 9 ( 1%) | 2 ( 2%) | 1 ( 5%) | 0 ( 0%) |
| BACK PAIN | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 2 ( 1%) | 3 ( <1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTHRALGIA | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NECK PAIN | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 1 ( 1%) | 0 ( 0%) | 2 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARTHRITIS NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MYALGIA | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 2 ( <1%) | 3 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| TENDONITIS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| BACK PAIN AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BUTTOCK PAIN | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COSTAL PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| JAW DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MUSCLE CRAMPS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MUSCLE SPASMS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OSTEOARTHRITIS NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OSTEOPOROSIS NOS | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ROTATOR CUFF SYNDROME | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TENDONITIS EXACERBATED | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BURSITIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| JOINT STIFFNESS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCIATICA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PSYCHIATRIC DISORDERS | 3 ( 17%) | 7 ( 2%) | 5 ( 2%) | 0 ( 0%) | 13 ( 3%) | 10 ( 2%) | 28 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEPRESSION NEC | 2 ( 11%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 4 ( 1%) | 7 ( 1%) | 13 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANXIETY NEC | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 5 ( 1%) | 4 ( 1%) | 11 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DELIRIUM | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ALCOHOLIC WITHDRAWAL SYMPTOMS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CONFUSION | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DEPRESSION AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DISORIENTATION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NEUROSIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| STRESS SYMPTOMS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AGITATION | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HALLUCINATION NOS | 1 ( 6%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCHIZOPHRENIA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 1 ( 6%) | 10 ( 2%) | 3 ( 1%) | 0 ( 0%) | 12 ( 3%) | 11 ( 2%) | 26 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANEMIA NOS | 1 ( 6%) | 4 ( 1%) | 2 ( 1%) | 0 ( 0%) | 12 ( 3%) | 7 ( 1%) | 21 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANAEMIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANEMIA NOS AGGRAVATED | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COAGULATION DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DISSEMINATED INTRAVASCULAR COAGULATION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRON DEFICIENCY ANEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SECONDARY ANAEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| LEUCOCYTOSIS NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NORMOCHROMIC NORMOCYTIC ANEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SECONDARY ANEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| THROMBOCYTHEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| THROMBOCYTOPENIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0%) | 4 ( 1%) | 5 ( 2%) | 0 ( 0%) | 3 ( 1%) | 7 ( 1%) | 15 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BASAL CELL CARCINOMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BENIGN BREAST NEOPLASM NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BENIGN SKIN NEOPLASM NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLADDER NEOPLASM NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHRONIC LEUKEMIA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COLON CANCER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MALIGNANT MELANOMA OF SKIN STAGE UNSPECIFIED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| METASTASES TO LUNG | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MYELODYSPLASTIC SYNDROME NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PROSTATE CANCER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RESPIRATORY TRACT NEOPLASM NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN CARCINOMA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN NEOPLASM NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| THYROID NEOPLASM NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BREAST CANCER FEMALE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LIPOMA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NONHODGKIN'S LYMPHOMA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ENDOCRINE DISORDERS | 0 ( 0%) | 7 ( 2%) | 2 ( 1%) | 1 ( 1%) | 2 ( 1%) | 5 ( 1%) | 10 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| DIABETES MELLITUS INADEQUATE CONTROL | 0 ( 0%) | 5 ( 1%) | 1 ( <1%) | 1 ( 1%) | 1 ( <1%) | 4 ( 1%) | 7 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ADRENAL INSUFFICIENCY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GOITRE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOTHYROIDISM | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| THYROTOXICOSIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IMMUNE SYSTEM DISORDERS | 1 ( 6%) | 2 ( <1%) | 3 ( 1%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 6 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.

[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| DRUG HYPERSENSITIVITY | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERSENSITIVITY NOS | 1 ( 6%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KIDNEY TRANSPLANT REJECTION | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MULTIPLE ALLERGIES | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 2 ( 1%) | 1 ( <1%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| AXILLARY MASS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EDEMA LOWER LIMB | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LOWER EXTREMITY MASS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| WEAKNESS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEPATO-BILIARY DISORDERS | 0 ( 0%) | 3 ( 1%) | 3 ( 1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 4 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOLECYSTITIS ACUTE NOS | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOLELITHIASIS | 0 ( 0%) | 2 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEPATITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEPATOMEGALY | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GALLBLADDER DISEASE NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEPATOSPLENOMEGALY NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPROTEINEMIA | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EAR AND LABYRINTH DISORDERS | 0 ( 0%) | 1 ( <1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EARACHE | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SUDDEN HEARING LOSS NOS | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VERTIGO NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LABYRINTHITIS NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITION | 0 ( 0%) | 6 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 2 ( <1%) | 3 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PYREXIA | 0 ( 0%) | 4 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| THIRST | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FISTULA NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PAIN IN FACE | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| REPRODUCTIVE SYSTEM AND BREAST DISORDERS | 0 ( 0%) | 2 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( <1%) | 2 ( <1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| BENIGN PROSTATIC HYPERPLASIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MENOPAUSE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.1
Incidence of Adverse Events by System Organ Class
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| System Organ Class / Preferred Term | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| PROSTATIC DISORDER NOS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PROSTATITIS | 0 ( 0%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VAGINAL HAEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CONGENITAL AND FAMILIAL/GENETIC DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CUTIS LAXA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| REPRODUCTIVE AND BREAST DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PROSTATITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( <1%) | 1 ( <1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| PREGNANCY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |

Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
Ocular Events include events reported for study eye and non-study eye.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.



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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 68 | 31 | 153 | 225 | 602 | 364 | 84 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 1 ( 1.5%) | 31 ( 100%) | 93 (60.8%) | 70 (31.1%) | 593 (98.5%) | 282 (77.5%) | 75 (89.3%) |
| EYE DISORDERS | 1 ( 1.5%) | 31 ( 100%) | 77 (50.3%) | 69 (30.7%) | 590 (98.0%) | 275 (75.5%) | 73 (86.9%) |
| IRITIS | 0 ( 0.0%) | 31 ( 100%) | 3 ( 2.0%) | 0 ( 0.0%) | 438 (72.8%) | 152 (41.8%) | 11 (13.1%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 393 (65.3%) | 139 (38.2%) | 0 ( 0.0%) |
| EYE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 9 ( 5.9%) | 0 ( 0.0%) | 286 (47.5%) | 92 (25.3%) | 15 (17.9%) |
| EYE IRRITATION | 0 ( 0.0%) | 15 (48.4%) | 4 ( 2.6%) | 0 ( 0.0%) | 294 (48.8%) | 69 (19.0%) | 15 (17.9%) |
| LACRIMATION INCREASED | 0 ( 0.0%) | 26 (83.9%) | 1 ( 0.7%) | 0 ( 0.0%) | 261 (43.4%) | 68 (18.7%) | 9 (10.7%) |
| VISUAL ACUITY REDUCED | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 238 (39.5%) | 47 (12.9%) | 15 (17.9%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 230 (38.2%) | 71 (19.5%) | 0 ( 0 0%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0.0%) | 7 (22.6%) | 2 ( 1.3%) | 0 ( 0.0%) | 227 (37.7%) | 52 (14.3%) | 10 (11.9%) |
| VITREOUS FLOATERS | 0 ( 0.0%) | 1 ( 3.2%) | 5 ( 3.3%) | 0 ( 0.0%) | 207 (34.4%) | 50 (13.7%) | 6 ( 7.1%) |
| PHOTOPHOBIA | 0 ( 0.0%) | 6 (19.4%) | 1 ( 0.7%) | 0 ( 0.0%) | 197 (32.7%) | 51 (14.0%) | 6 ( 7.1%) |
| CONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 172 (28.6%) | 61 (16.8%) | 0 ( 0.0%) |
| HYPOPYON | 1 ( 1.5%) | 0 ( 0.0%) | 46 (30.1%) | 56 (24.9%) | 19 ( 3.2%) | 9 ( 2.5%) | 2 ( 2.4%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 2 ( 6.5%) | 8 ( 5.2%) | 1 ( 0.4%) | 77 (12.8%) | 32 ( 8.8%) | 0 ( 0.0%) |
| PHOTOPSIA | 0 ( 0.0%) | 4 (12.9%) | 3 ( 2.0%) | 0 ( 0.0%) | 87 (14.5%) | 19 ( 5.2%) | 3 ( 3.6%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 1 ( 3.2%) | 2 ( 1.3%) | 2 ( 0.9%) | 86 (14.3%) | 16 ( 4.4%) | 8 ( 9.5%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 3 ( 9.7%) | 2 ( 1.3%) | 0 ( 0.0%) | 83 (13.8%) | 14 ( 3.8%) | 2 ( 2.4%) |
| EYE DISCHARGE | 0 ( 0.0%) | 27 (87.1%) | 2 ( 1.3%) | 0 ( 0.0%) | 45 ( 7.5%) | 10 ( 2.7%) | 10 (11.9%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 57 ( 9.5%) | 18 ( 4.9%) | 3 ( 3.6%) |
| CORNEAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 29 ( 4.8%) | 21 ( 5.8%) | 26 (31.0%) |
| CORNEAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 54 ( 9.0%) | 12 ( 3.3%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.3%) | 0 ( 0.0%) | 52 ( 8.6%) | 10 ( 2.7%) | 1 ( 1.2%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 56 ( 9.3%) | 6 ( 1.6%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 3.3%) | 2 ( 0.9%) | 32 ( 5.3%) | 18 ( 4.9%) | 2 ( 2.4%) |
| CORNEAL EROSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 43 ( 7.1%) | 9 ( 2.5%) | 6 ( 7.1%) |
| CORNEAL OEDEMA | 0 ( 0.0%) | 3 ( 9.7%) | 2 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 50 (59.5%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 42 ( 7.0%) | 5 ( 1.4%) | 0 ( 0.0%) |
| CONJUNCTIVAL OEDEMA | 0 ( 0.0%) | 28 (90.3%) | 3 ( 2.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 9 (10.7%) |
| HYPHEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 37 ( 6.1%) | 2 ( 0.5%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | 0 ( 0.0%) | 14 (45.2%) | 1 ( 0.7%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 22 (26.2%) |
| CATARACT NEC | 0 ( 0.0%) | 6 (19.4%) | 2 ( 1.3%) | 0 ( 0.0%) | 14 ( 2.3%) | 13 ( 3.6%) | 2 ( 2.4%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 2.0%) | 0 ( 0.0%) | 15 ( 2.5%) | 1 ( 0.3%) | 17 (20.2%) |
| VITREOUS HAEMORRHAGE | 0 ( 0.0%) | 12 (38.7%) | 19 (12.4%) | 2 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 19 ( 3.2%) | 8 ( 2.2%) | 0 ( 0.0%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 23 ( 3.8%) | 0 ( 0.0%) | 2 ( 2.4%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 21 ( 3.5%) | 4 ( 1.1%) | 0 ( 0.0%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 21 ( 3.5%) | 2 ( 0.5%) | 2 ( 2.4%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 18 ( 3.0%) | 6 ( 1.6%) | 0 ( 0.0%) |

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[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 1 ( 3.2%) | 1 ( 0.7%) | 0 ( 0.0%) | 4 ( 0.7%) | 3 ( 0.8%) | 14 (16.7%) |
| RED EYE | 0 ( 0.0%) | 19 (61.3%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| UVEITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 8 ( 3.6%) | 5 ( 0.8%) | 9 ( 2.5%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 21 ( 3.5%) | 0 ( 0.0%) | 1 ( 1.2%) |
| EYELID OEDEMA | 0 ( 0.0%) | 15 (48.4%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 17 ( 2.8%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 10 ( 1.7%) | 0 ( 0.0%) | 6 ( 7.1%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.3%) | 0 ( 0.0%) | 13 ( 2.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 13 ( 2.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 12 ( 2.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 14 ( 2.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 11 ( 1.8%) | 3 ( 0.8%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 9 ( 1.5%) | 1 ( 0.3%) | 2 ( 2.4%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 10 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 9 ( 1.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 10 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 2.0%) | 5 ( 2.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 3 ( 3.6%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR OEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 4.8%) |
| MYDRIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL DEPOSITS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 6.0%) |
| CORNEAL INFILTRATES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 6.0%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 3 ( 3.6%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 1 ( 1.2%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 2 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) |
| RETINAL NEOVASCULARIZATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPHAEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 3 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 1 ( 1.2%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 4.8%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE HAEMORRHAGE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 2 ( 0.5%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.3%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ACCOMMODATION DISORDER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CATARACT UNILATERAL | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CORNEAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL NEOVASCULARIZATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 1 ( 1.2%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYALOSIS ASTEROID | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS VASCULAR DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| KERATOPATHY BAND | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 1 ( 1.2%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL HEMATOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUBEPITHELIAL OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANISEIKONIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANTERIOR CHAMBER DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARCUS SENILIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHALAZION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVAL CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVAL HAEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CONJUNCTIVITIS PAPILLARY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORECTOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL DYSTROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL GRAFT REJECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL LESION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| CORNEAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ULCER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLAUCOMA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENTICULAR PIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| OPTIC NEUROPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAPILLEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ARTERY THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VASCULITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCLERITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TIRED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION ABNORMAL NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 0 ( 0.0%) | 7 (22.6%) | 8 ( 5.2%) | 2 ( 0.9%) | 139 (23.1%) | 28 ( 7.7%) | 3 ( 3.6%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 3 ( 9.7%) | 6 ( 3.9%) | 2 ( 0.9%) | 107 (17.8%) | 22 ( 6.0%) | 1 ( 1.2%) |
| CORNEAL STAINING | 0 ( 0.0%) | 4 (12.9%) | 2 ( 1.3%) | 0 ( 0.0%) | 20 ( 3.3%) | 5 ( 1.4%) | 2 ( 2.4%) |
| BLOOD GLUCOSE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD CREATININE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| BLOOD CHOLESTEROL INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMATURIA PRESENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BIOPSY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD GLUCOSE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD GLUCOSE DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD GLUCOSE FLUCTUATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOOD PHOSPHATE DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD SODIUM DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD TRIGLYCERIDES INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD UREA INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CANDIDURIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COAGULATION FACTOR DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ELECTROCARDIOGRAM ABNORMAL NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ENLARGED PROSTATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LIVER FUNCTION TESTS NOS ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROTEINURIA PRESENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROTHROMBIN TIME PROLONGED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RED BLOOD CELL SEDIMENTATION RATE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| WEIGHT DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0.0%) | 10 (32.3%) | 1 ( 0.7%) | 0 ( 0.0%) | 106 (17.6%) | 22 ( 6.0%) | 8 ( 9.5%) |
| EYELID EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 50 ( 8.3%) | 17 ( 4.7%) | 0 ( 0.0%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 10 (32.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 37 ( 6.1%) | 12 ( 3.3%) | 5 ( 6.0%) |
| FOOT ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 1 ( 1.2%) |
| PRURITUS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DERMATITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID OEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| SKIN ULCER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONTUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DERMATITIS ALLERGIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FACE EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSORIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN LESION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ALOPECIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETIC FOOT ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRY SKIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

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[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| LEG ULCER (EXC VARICOSE) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PALMAR ERYTHEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN NECROSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SKIN NODULE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN ULCER HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STASIS ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SWEATING INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TELANGIECTASIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0.0%) | 1 ( 3.2%) | 6 ( 3.9%) | 0 ( 0.0%) | 94 (15.6%) | 22 ( 6.0%) | 18 (21.4%) |
| HEADACHE NOS | 0 ( 0.0%) | 1 ( 3.2%) | 5 ( 3.3%) | 0 ( 0.0%) | 46 ( 7.6%) | 9 ( 2.5%) | 15 (17.9%) |
| CEREBROVASCULAR ACCIDENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 10 ( 1.7%) | 6 ( 1.6%) | 0 ( 0.0%) |
| DIZZINESS (EXC VERTIGO) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 10 ( 1.7%) | 1 ( 0.3%) | 1 ( 1.2%) |
| INSOMNIA NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 9 ( 1.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 3 ( 0.8%) | 0 ( 0.0%) |
| SYNCOPE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEMENTIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOESTHESIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BALANCE IMPAIRED NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONVULSIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FACIAL PALSY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IIIRD NERVE PARALYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| MOVEMENT DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEUROPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TREMOR NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BURNING SENSATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSARTHRIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMIPARESIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMORRHAGIC STROKE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOAESTHESIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACUNAR INFARCTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MIGRAINE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OBSTRUCTIVE SLEEP APNEA SYNDROME | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PARKINSON'S DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SPEECH DISORDER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL PATHWAY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITH NERVE PARALYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 2.0%) | 0 ( 0.0%) | 93 (15.4%) | 14 ( 3.8%) | 6 ( 7.1%) |
| NASOPHARYNGITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 16 ( 2.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PNEUMONIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.3%) | 0 ( 0.0%) | 12 ( 2.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

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[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| URINARY TRACT INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 12 ( 2.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFLUENZA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 6 ( 1.0%) | 2 ( 0.5%) | 2 ( 2.4%) |
| CELLULITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BRONCHITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LOCALISED INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OSTEOMYELITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SINUSITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SEPSIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| UPPER RESPIRATORY TRACT INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HERPES ZOSTER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHARYNGITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BRONCHITIS ACUTE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FUNGAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATITIS HERPETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| ORAL CANDIDIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RESPIRATORY TRACT INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SKIN CANDIDA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SORE THROAT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| STAPHYLOCOCCAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOOTH INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| AMERICAN TRYPANOSOMIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ARTHROPOD BITE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BACTERIAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLADDER INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CANDIDAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CELLULITIS STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYSTITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJECTION SITE INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KIDNEY INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| LARYNGITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LOWER RESPIRATORY TRACT INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LUNG INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| NAIL TINEA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OSTEOMYELITIS CHRONIC NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHARYNGITIS STREPTOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PNEUMONIA HAEMOPHILUS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY TUBERCULOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ROUNDWORM INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SEPTIC ARTHRITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SEPTICEMIA STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VAGINOSIS FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| WOUND INFECTION NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X



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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| CARDIAC DISORDERS | 0 ( 0.0%) | 2 ( 6.5%) | 8 ( 5.2%) | 0 ( 0.0%) | 68 (11.3%) | 15 ( 4.1%) | 1 ( 1.2%) |
| MYOCARDIAL INFARCTION | 0 ( 0.0%) | 2 ( 6.5%) | 3 ( 2.0%) | 0 ( 0.0%) | 14 ( 2.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| CARDIAC FAILURE CONGESTIVE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 16 ( 2.7%) | 3 ( 0.8%) | 0 ( 0.0%) |
| ANGINA UNSTABLE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 8 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC ARREST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ATRIAL FIBRILLATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CARDIAC FAILURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EDEMA LOWER LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| PULMONARY EDEMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ARRHYTHMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIOMEGALY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIOVASCULAR DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORONARY ARTERY DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORONARY ARTERY OCCLUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANGINA PECTORIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| AORTIC VALVE STENOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ATRIOVENTRICULAR BLOCK NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIAC DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC MURMUR NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EDEMA PERIPHERAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEFT VENTRICULAR FAILURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MYOCARDIAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PALPITATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| AORTIC VALVE DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ATRIAL FLUTTER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BRADYCARDIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC FAILURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIO-RESPIRATORY ARREST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIOGENIC SHOCK | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIOMYOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPNEA PAROXYSMAL NOCTURNAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPNOEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EDEMA UPPER LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0 0%) | 0 ( 0.0%) |
| ISCHEMIC CARDIOMYOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYOCARDITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OEDEMA PERIPHERAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| VENTRICULAR EXTRASYSTOLES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VENTRICULAR TACHYCARDIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTROINTESTINAL DISORDERS | 0 ( 0.0%) | 1 ( 3.2%) | 2 ( 1.3%) | 0 ( 0.0%) | 69 (11.5%) | 10 ( 2.7%) | 3 ( 3.6%) |
| NAUSEA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 28 ( 4.7%) | 1 ( 0.3%) | 2 ( 2.4%) |
| VOMITING NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 8 ( 1.3%) | 5 ( 1.4%) | 0 ( 0.0%) |
| DIARRHEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 10 ( 1.7%) | 3 ( 0.8%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X



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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| CONSTIPATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 9 ( 1.5%) | 3 ( 0.8%) | 0 ( 0.0%) |
| GASTROINTESTINAL HEMORRHAGE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ABDOMINAL PAIN NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPEPSIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ESOPHAGITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GASTRITIS NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 2 ( 0.5%) | 0 ( 0.0%) |
| SORE THROAT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ABDOMINAL PAIN UPPER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GASTRO-ESOPHAGEAL REFLUX DISEASE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIVERTICULUM INTESTINAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ESOPHAGEAL REFLUX | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTRIC ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTROINTESTINAL UPSET | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ABDOMINAL PAIN AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ABDOMINAL TENDERNESS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ASCITES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIARRHOEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| DUODENAL ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DUODENITIS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPHAGIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTRIC EROSIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTRIC IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTROENTERITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTROINTESTINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMATEMESIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMORRHOIDS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IMPAIRED GASTRIC EMPTYING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INGUINAL HERNIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PEPTIC ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PEPTIC ULCER HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIODONTAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERITONEAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERITONEAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERITONITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RECTAL BLEEDING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RECTAL PROLAPSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOOTHACHE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0.0%) | 26 (83.9%) | 6 ( 3.9%) | 0 ( 0.0%) | 41 ( 6.8%) | 0 ( 0.0%) | 8 ( 9.5%) |
| PAIN NOS | 0 ( 0.0%) | 25 (80.6%) | 2 ( 1.3%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 2 ( 2.4%) |
| CHEST PAIN NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 13 ( 2.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FALL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| FATIGUE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAIN IN FACE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PYREXIA | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 1 ( 1.2%) |
| SENSATION OF FOREIGN BODY NOS | 0 ( 0.0%) | 4 (12.9%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| WEAKNESS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EDEMA LOWER LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJECTION SITE EXTRAVASATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.6%) |
| DIFFICULTY IN WALKING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EDEMA PERIPHERAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJECTION SITE REACTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| APPLICATION SITE BLEEDING | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| APPLICATION SITE ERYTHEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEATH NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GROIN PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HERNIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IMPAIRED HEALING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LOWER EXTREMITY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MASS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MULTI-ORGAN FAILURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RIGORS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SENSATION OF PRESSURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| METABOLISM AND NUTRITION DISORDERS | 0 ( 0.0%) | 2 ( 6.5%) | 2 ( 1.3%) | 0 ( 0.0%) | 61 (10.1%) | 9 ( 2.5%) | 1 ( 1.2%) |
| HYPERCHOLESTEROLEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 16 ( 2.7%) | 2 ( 0.5%) | 0 ( 0.0%) |
| HYPOGLYCAEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 11 ( 1.8%) | 0 ( 0.0%) | 1 ( 1.2%) |
| HYPERGLYCEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 8 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEHYDRATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERLIPIDEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 2 ( 0.5%) | 0 ( 0.0%) |
| APPETITE DECREASED NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERKALEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| DIABETIC NEUROPATHY NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) |
| DIABETIC COMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETES MELLITUS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETES MELLITUS INSULIN-DEPENDENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GOUT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GOUT AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOCALCEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOKALEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OBESITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETES MELLITUS NON INSULIN-DEPENDENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| DIABETIC AMYOTROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC COMPLICATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETIC EYE DISEASE NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC KETOACIDOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ELECTROLYTE IMBALANCE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLUCOSE TOLERANCE IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERLIPIDAEMIA NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERPHOSPHATEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERVOLEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOGLYCAEMIC COMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPONATREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOVOLEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INSULIN RESISTANCE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| METABOLIC ACIDOSIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POLYDIPSIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 1 ( 3.2%) | 1 ( 0.7%) | 0 ( 0.0%) | 50 ( 8.3%) | 11 ( 3.0%) | 3 ( 3.6%) |
| HYPERTENSION NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 25 ( 4.2%) | 5 ( 1.4%) | 2 ( 2.4%) |
| HYPERTENSION AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 2 ( 0.5%) | 0 ( 0.0%) |
| GANGRENE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPOTENSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TRANSIENT ISCHEMIC ATTACK | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL VASCULAR DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTURAL HYPOTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VENOUS THROMBOSIS DEEP LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ARTERIAL ANEURYSM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTERIAL OCCLUSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOOD PRESSURE FLUCTUATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD PRESSURE INADEQUATELY CONTROLLED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CAROTID ARTERY DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CAROTID ARTERY STENOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CEREBROVASCULAR ACCIDENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLLAPSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| FLUSHING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMATOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HOT FLUSHES NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ISCHEMIC FOOT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POOR PERIPHERAL CIRCULATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY HYPERTENSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THROMBOEMBOLISM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| SURGICAL AND MEDICAL PROCEDURES | 0 ( 0.0%) | 2 ( 6.5%) | 1 ( 0.7%) | 0 ( 0.0%) | 53 ( 8.8%) | 7 ( 1.9%) | 1 ( 1.2%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 15 ( 2.5%) | 4 ( 1.1%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 2 ( 6.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 8 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORONARY ARTERY SURGERY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOOT AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NAUSEA POST-OPERATIVE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| TOE AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOOTH EXTRACTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| APPLICATION SITE REACTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| ARTERIAL BYPASS OPERATION (EXC CORONARY ARTERY) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTERIO-VENOUS FISTULA OPERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD PRODUCT TRANSFUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC PACEMAKER INSERTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CAROTID ENDARTERECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEMOTHERAPY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FLUID REPLACEMENT PARENTERAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOOT OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HIP ARTHROPLASTY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJECTION SITE OEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KNEE ARTHROPLASTY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEG AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENS IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LIMB OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST PROCEDURAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST PROCEDURAL PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SHUNT OCCLUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN CYST EXCISION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUTURE LINE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VOMITING POST-OPERATIVE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 45 ( 7.5%) | 5 ( 1.4%) | 7 ( 8.3%) |
| DYSPNEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 17 ( 2.8%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COUGH | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 10 ( 1.7%) | 2 ( 0.5%) | 2 ( 2.4%) |
| CHRONIC OBSTRUCTIVE AIRWAYS DISEASE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PLEURAL EFFUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| RHINORRHEA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EPISTAXIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LUNG INFILTRATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SNEEZING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SORE THROAT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.4%) |
| ASTHMA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ASTHMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ATELECTASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DYSPNEA EXACERBATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPNEA EXERTIONAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPNOEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EMPHYSEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEMOPTYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOXIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTERSTITIAL LUNG DISEASE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NASAL CONGESTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NASOPHARYNGITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| PULMONARY CONGESTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| PULMONARY FIBROSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RESPIRATORY FAILURE (EXC NEONATAL) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RHINITIS SEASONAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RHINORRHOEA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |
| SINUS PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL AND URINARY DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 35 ( 5.8%) | 9 ( 2.5%) | 1 ( 1.2%) |
| RENAL FAILURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 14 ( 2.3%) | 2 ( 0.5%) | 1 ( 1.2%) |
| RENAL IMPAIRMENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 9 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL FAILURE ACUTE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 4 ( 1.1%) | 0 ( 0.0%) |
| RENAL FAILURE AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL FAILURE CHRONIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| URINARY RETENTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CALCULUS RENAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLADDER PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FLUID RETENTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLOMERULONEPHRITIS CHRONIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GLOMERULONEPHRITIS MINIMAL LESION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LOIN PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POLYURIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL ARTERY STENOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL FAILURE CHRONIC AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| URINE DISCOLOURATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | 0 ( 0.0%) | 4 (12.9%) | 5 ( 3.3%) | 0 ( 0.0%) | 29 ( 4.8%) | 6 ( 1.6%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
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Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| LACERATION | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOOT FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HIP FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 2 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL EROSION | 0 ( 0.0%) | 3 ( 9.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRUG TOXICITY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ABRASION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BURNS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FRACTURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEG FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ACCIDENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ACCIDENTAL OVERDOSE (THERAPEUTIC AGENT) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANKLE FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BACK INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLISTER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEMICAL BURNS OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FEMUR FRACTURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOREARM FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTHERMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| JOINT SPRAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LOCALISED INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHANTOM LIMB PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RIB FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUNBURN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THERAPEUTIC AGENT TOXICITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TIBIA FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| UPPER LIMB FRACTURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| WHIPLASH INJURY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.3%) | 0 ( 0.0%) | 27 ( 4.5%) | 5 ( 1.4%) | 3 ( 3.6%) |
| PAIN IN LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 9 ( 1.5%) | 0 ( 0.0%) | 2 ( 2.4%) |
| BACK PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ARTHRALGIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYALGIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 1.2%) |
| NECK PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTHRITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TENDONITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BACK PAIN AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BUTTOCK PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COSTAL PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| JAW DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MUSCLE CRAMPS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MUSCLE SPASMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OSTEOARTHRITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OSTEOPOROSIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ROTATOR CUFF SYNDROME | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TENDONITIS EXACERBATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSYCHIATRIC DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 26 ( 4.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DEPRESSION NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 13 ( 2.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANXIETY NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 11 ( 1.8%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DELIRIUM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ALCOHOLIC WITHDRAWAL SYMPTOMS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONFUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEPRESSION AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DISORIENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEUROSIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| STRESS SYMPTOMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 24 ( 4.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ANEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 20 ( 3.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ANAEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANEMIA NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COAGULATION DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DISSEMINATED INTRAVASCULAR COAGULATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRON DEFICIENCY ANEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SECONDARY ANAEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 11 ( 1.8%) | 3 ( 0.8%) | 0 ( 0.0%) |
| BASAL CELL CARCINOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BENIGN BREAST NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BENIGN SKIN NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLADDER NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHRONIC LEUKEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0 0%) |
| COLON CANCER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MALIGNANT MELANOMA OF SKIN STAGE UNSPECIFIED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| METASTASES TO LUNG | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYELODYSPLASTIC SYNDROME NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROSTATE CANCER NOS | 0 ( 0.0%) | 1 ( 3.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RESPIRATORY TRACT NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
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Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| SKIN CARCINOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| THYROID NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ENDOCRINE DISORDERS | 0 ( 0.0%) | 1 ( 3.2%) | 1 ( 0.7%) | 0 ( 0.0%) | 7 ( 1.2%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETES MELLITUS INADEQUATE CONTROL | 0 ( 0.0%) | 1 ( 3.2%) | 1 ( 0.7%) | 0 ( 0.0%) | 4 ( 0.7%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ADRENAL INSUFFICIENCY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GOITRE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTHYROIDISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRUG HYPERSENSITIVITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERSENSITIVITY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KIDNEY TRANSPLANT REJECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MULTIPLE ALLERGIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| AXILLARY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EDEMA LOWER LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LOWER EXTREMITY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| WEAKNESS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEPATO-BILIARY DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOLECYSTITIS ACUTE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOLELITHIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEPATITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEPATOMEGALY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EAR AND LABYRINTH DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EARACHE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUDDEN HEARING LOSS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VERTIGO NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PYREXIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THIRST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| REPRODUCTIVE SYSTEM AND BREAST DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 1 ( 1.2%) |
| BENIGN PROSTATIC HYPERPLASIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MENOPAUSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VAGINAL HAEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.2%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

ISTA Pharmaceuticals, Inc.
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Table 7.2
Incidence of Adverse Events by System Organ Class
All Studies by Study for Vitrase Groups Only
Safety Population

| System Organ Class / Preferred Term | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| CONGENITAL AND FAMILIAL/GENETIC DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| REPRODUCTIVE AND BREAST DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROSTATITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.2%) | 0 ( 0.0%) | 0 ( 0.0%) |

[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 18 ( 100%) | 317 (83.9%) | 194 (98.0%) | 331 (87.8%) | 350 (89.5%) |
| EYE DISORDERS | 17 (94.4%) | 306 (81.0%) | 193 (97.5%) | 323 (85.7%) | 349 (89.3%) |
| IRITIS | 4 (22.2%) | 128 (33.9%) | 124 (62.6%) | 223 (59.2%) | 243 (62.1%) |
| OCULAR HYPEREMIA | 4 (22.2%) | 142 (37.6%) | 113 (57.1%) | 204 (54.1%) | 215 (55.0%) |
| EYE IRRITATION | 10 (55.6%) | 112 (29.6%) | 90 (45.5%) | 132 (35.0%) | 141 (36.1%) |
| EYE PAIN | 3 (16.7%) | 86 (22.8%) | 74 (37.4%) | 140 (37.1%) | 164 (41.9%) |
| LACRIMATION INCREASED | 4 (22.2%) | 87 (23.0%) | 65 (32.8%) | 124 (32.9%) | 140 (35.8%) |
| VITREOUS HEMORRHAGE | 3 (16.7%) | 99 (26.2%) | 86 (43.4%) | 111 (29.4%) | 104 (26.6%) |
| VISUAL ACUITY REDUCED | 4 (22.2%) | 76 (20.1%) | 79 (39.9%) | 105 (27.9%) | 101 (25.8%) |
| ABNORMAL SENSATION IN EYE | 2 (11.1%) | 68 (18.0%) | 62 (31.3%) | 101 (26.8%) | 116 (29.7%) |
| VITREOUS FLOATERS | 6 (33.3%) | 70 (18.5%) | 65 (32.8%) | 91 (24.1%) | 101 (25.8%) |
| PHOTOPHOBIA | 6 (33.3%) | 61 (16.1%) | 59 (29.8%) | 87 (23.1%) | 102 (26.1%) |
| CONJUNCTIVAL EDEMA | 1 ( 5.6%) | 59 (15.6%) | 48 (24.2%) | 96 (25.5%) | 89 (22.8%) |
| RETINAL DETACHMENT | 3 (16.7%) | 32 ( 8.5%) | 24 (12.1%) | 38 (10.1%) | 47 (12.0%) |
| CATARACT NUCLEAR | 5 (27.8%) | 36 ( 9.5%) | 29 (14.6%) | 37 ( 9.8%) | 31 ( 7.9%) |
| CATARACT SUBCAPSULAR | 2 (11.1%) | 27 ( 7.1%) | 34 (17.2%) | 29 ( 7.7%) | 39 (10.0%) |
| PHOTOPSIA | 0 ( 0.0%) | 22 ( 5.8%) | 23 (11.6%) | 45 (11.9%) | 38 ( 9.7%) |
| CATARACT CORTICAL | 5 (27.8%) | 27 ( 7.1%) | 14 ( 7.1%) | 30 ( 8.0%) | 31 ( 7.9%) |
| RUBEOSIS IRIDIS | 1 ( 5.6%) | 21 ( 5.6%) | 17 ( 8.6%) | 21 ( 5.6%) | 24 ( 6.1%) |
| CORNEAL EDEMA | 1 ( 5.6%) | 12 ( 3.2%) | 18 ( 9.1%) | 22 ( 5.8%) | 26 ( 6.6%) |
| CORNEAL EROSION | 1 ( 5.6%) | 24 ( 6.3%) | 10 ( 5.1%) | 25 ( 6.6%) | 17 ( 4.3%) |
| MACULAR EDEMA | 1 ( 5.6%) | 12 ( 3.2%) | 22 (11.1%) | 16 ( 4.2%) | 24 ( 6.1%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0.0%) | 26 ( 6.9%) | 12 ( 6.1%) | 17 ( 4.5%) | 18 ( 4.6%) |
| EYE DISCHARGE | 0 ( 0.0%) | 18 ( 4.8%) | 11 ( 5.6%) | 23 ( 6.1%) | 21 ( 5.4%) |
| IRIS ADHESIONS | 2 (11.1%) | 14 ( 3.7%) | 9 ( 4.5%) | 13 ( 3.4%) | 28 ( 7.2%) |
| CORNEAL DISORDER NOS | 0 ( 0.0%) | 8 ( 2.1%) | 6 ( 3.0%) | 18 ( 4.8%) | 26 ( 6.6%) |
| HYPHEMA | 0 ( 0.0%) | 6 ( 1.6%) | 9 ( 4.5%) | 14 ( 3.7%) | 16 ( 4.1%) |
| CATARACT NEC | 0 ( 0.0%) | 12 ( 3.2%) | 3 ( 1.5%) | 11 ( 2.9%) | 13 ( 3.3%) |
| RETINOPATHY DIABETIC | 1 ( 5.6%) | 11 ( 2.9%) | 7 ( 3.5%) | 6 ( 1.6%) | 14 ( 3.6%) |
| BLINDNESS NEC | 1 ( 5.6%) | 6 ( 1.6%) | 9 ( 4.5%) | 7 ( 1.9%) | 9 ( 2.3%) |
| VISION BLURRED | 0 ( 0.0%) | 8 ( 2.1%) | 11 ( 5.6%) | 7 ( 1.9%) | 5 ( 1.3%) |
| DRY EYE NEC | 0 ( 0.0%) | 7 ( 1.9%) | 7 ( 3.5%) | 5 ( 1.3%) | 11 ( 2.8%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 6 ( 1.6%) | 6 ( 3.0%) | 6 ( 1.6%) | 12 ( 3.1%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 6 ( 1.6%) | 21 ( 5.4%) |
| VITREOUS DETACHMENT | 1 ( 5.6%) | 3 ( 0.8%) | 4 ( 2.0%) | 10 ( 2.7%) | 7 ( 1.8%) |
| CATARACT NOS AGGRAVATED | 1 ( 5.6%) | 8 ( 2.1%) | 5 ( 2.5%) | 5 ( 1.3%) | 4 ( 1.0%) |
| MACULOPATHY | 0 ( 0.0%) | 5 ( 1.3%) | 6 ( 3.0%) | 6 ( 1.6%) | 6 ( 1.5%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 7 ( 1.9%) | 6 ( 3.0%) | 6 ( 1.6%) | 3 ( 0.8%) |
| KERATITIS NEC | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 2.0%) | 4 ( 1.1%) | 8 ( 2.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 3 ( 0.8%) | 6 ( 3.0%) | 3 ( 0.8%) | 6 ( 1.5%) |
| POST-OPERATIVE PAIN | 1 ( 5.6%) | 10 ( 2.6%) | 0 ( 0.0%) | 2 ( 0.5%) | 5 ( 1.3%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 7 ( 1.9%) | 5 ( 1.3%) |
| UVEITIS NOS | 1 ( 5.6%) | 2 ( 0.5%) | 2 ( 1.0%) | 8 ( 2.1%) | 4 ( 1.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| BLEPHARITIS | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 2.0%) | 3 ( 0.8%) | 7 ( 1.8%) |
| CORNEAL EPITHELIUM DEFECT | 1 ( 5.6%) | 2 ( 0.5%) | 3 ( 1.5%) | 5 ( 1.3%) | 2 ( 0.5%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 5 ( 1.3%) | 2 ( 0.5%) |
| DIPLOPIA | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 5 ( 1.3%) | 2 ( 0.5%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 2 ( 0.5%) | 6 ( 1.5%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| MYDRIASIS | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 0 ( 0.0%) | 4 ( 1.0%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 6 ( 1.6%) | 2 ( 0.5%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 0 ( 0.0%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| APHAKIA | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE ALLERGY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| RETINAL NEOVASCULARIZATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| CHEMOSIS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONJUNCTIVITIS VIRAL NOS | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| HYALOSIS ASTEROID | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| KERATOPATHY BAND | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| PERIORBITAL HEMATOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ANISEIKONIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ARCUS SENILIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHALAZION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL SCAR | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVAL CYST | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DISORDER | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ULCER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EXOPHTHALMOS ENDOCRINE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE HEMORRHAGE NEC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFECTION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GLAUCOMA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| IRIS NEVUS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPTIC NERVE INJURY NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAPILLEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL EXUDATES | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VASCULAR DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| RETINAL VASCULITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCLERITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STYE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION ABNORMAL NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INVESTIGATIONS | 6 (33.3%) | 51 (13.5%) | 53 (26.8%) | 59 (15.6%) | 55 (14.1%) |
| INTRAOCULAR PRESSURE INCREASED | 3 (16.7%) | 42 (11.1%) | 42 (21.2%) | 45 (11.9%) | 42 (10.7%) |
| CORNEAL STAINING | 0 ( 0.0%) | 7 ( 1.9%) | 8 ( 4.0%) | 9 ( 2.4%) | 8 ( 2.0%) |
| BLOOD GLUCOSE INCREASED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| BLOOD PRESSURE INCREASED | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| BLOOD CREATININE INCREASED | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| WEIGHT DECREASED | 1 ( 5.6%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOOD CHOLESTEROL INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| BLOOD UREA INCREASED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HEMATURIA PRESENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BIOPSY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLOOD GLUCOSE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOOD GLUCOSE DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD GLUCOSE FLUCTUATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLOOD PHOSPHATE DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLOOD SODIUM DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLOOD TRIGLYCERIDES INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CANDIDURIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIAC ENZYMES INCREASED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COAGULATION FACTOR DECREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ENLARGED PROSTATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMATOCRIT DECREASED | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEMOGLOBIN DECREASED | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LIVER FUNCTION TESTS NOS ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PROTEINURIA PRESENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROTHROMBIN TIME PROLONGED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RED BLOOD CELL SEDIMENTATION RATE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 2 (11.1%) | 35 ( 9.3%) | 27 (13.6%) | 50 (13.3%) | 51 (13.0%) |
| EYELID EDEMA | 0 ( 0.0%) | 15 ( 4.0%) | 13 ( 6.6%) | 29 ( 7.7%) | 25 ( 6.4%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 16 ( 4.2%) | 8 ( 4.0%) | 21 ( 5.6%) | 20 ( 5.1%) |
| DERMATITIS NOS | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| PRURITUS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| FOOT ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONTUSION | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DERMATITIS ALLERGIC | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| DRY SKIN | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FACE EDEMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| LEG ULCER (EXC VARICOSE) | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN IRRITATION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SKIN ULCER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PSORIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| SKIN LESION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| URTICARIA NOS | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ALOPECIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETIC FOOT ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INTERTRIGO | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PALMAR ERYTHEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PRURIGO | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN NECROSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SKIN NODULE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN ULCER HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| STASIS ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SWEATING INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TELANGIECTASIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | 2 (11.1%) | 39 (10.3%) | 28 (14.1%) | 40 (10.6%) | 39 (10.0%) |
| NASOPHARYNGITIS | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 2.0%) | 5 ( 1.3%) | 7 ( 1.8%) |
| URINARY TRACT INFECTION NOS | 1 ( 5.6%) | 6 ( 1.6%) | 3 ( 1.5%) | 3 ( 0.8%) | 6 ( 1.5%) |
| PNEUMONIA NOS | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 2.0%) | 6 ( 1.6%) | 3 ( 0.8%) |
| CELLULITIS | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| INFLUENZA | 1 ( 5.6%) | 3 ( 0.8%) | 4 ( 2.0%) | 4 ( 1.1%) | 0 ( 0.0%) |
| BRONCHITIS NOS | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.0%) |
| LOCALISED INFECTION | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| SINUSITIS NOS | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| OSTEOMYELITIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 4 ( 1.1%) | 2 ( 0.5%) |
| UPPER RESPIRATORY TRACT INFECTION NOS | 1 ( 5.6%) | 1 ( 0.3%) | 3 ( 1.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SEPSIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| PHARYNGITIS NOS | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RESPIRATORY TRACT INFECTION NOS | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| SKIN INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HERPES ZOSTER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| BRONCHITIS ACUTE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CANDIDAL INFECTION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EAR INFECTION NOS | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FUNGAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| INFECTED SKIN ULCER | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ORAL CANDIDIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SKIN CANDIDA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| STAPHYLOCOCCAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| TOOTH INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VAGINOSIS FUNGAL NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| WOUND INFECTION NEC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| AMERICAN TRYPANOSOMIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ARTHROPOD BITE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BACTERIAL INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLADDER INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BRONCHOPNEUMONIA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CANDIDA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CELLULITIS STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CYSTITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| GASTROINTESTINAL INFECTION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJECTION SITE INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| KERATITIS HERPETIC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LARYNGITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LOWER RESPIRATORY TRACT INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LUNG INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MYCOBACTERIAL INFECTION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NAIL TINEA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OSTEOMYELITIS CHRONIC NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHARYNGITIS STREPTOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PNEUMONIA HAEMOPHILUS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PNEUMONIA MYCOPLASMAL | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY TUBERCULOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PYELONEPHRITIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ROUNDWORM INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SEPTIC ARTHRITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SEPTICEMIA STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE ABSCESS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TUBERCULOSIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UROSEPSIS | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 5.6%) | 30 ( 7.9%) | 28 (14.1%) | 40 (10.6%) | 48 (12.3%) |
| HEADACHE NOS | 0 ( 0.0%) | 16 ( 4.2%) | 12 ( 6.1%) | 20 ( 5.3%) | 23 ( 5.9%) |
| CEREBROVASCULAR ACCIDENT NOS | 1 ( 5.6%) | 4 ( 1.1%) | 3 ( 1.5%) | 5 ( 1.3%) | 8 ( 2.0%) |
| DIZZINESS (EXC VERTIGO) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 4 ( 1.1%) | 6 ( 1.5%) |
| INSOMNIA NEC | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 3 ( 0.8%) | 4 ( 1.0%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 4 ( 1.1%) | 3 ( 0.8%) |
| SYNCOPE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| DEMENTIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPOESTHESIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BALANCE IMPAIRED NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONVULSIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| FACIAL PALSY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| HEMORRHAGIC STROKE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MOVEMENT DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| NEUROPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| TREMOR NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| AMNESIA NEC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BURNING SENSATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| COMA NEC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEMENTIA OF THE ALZHEIMER'S TYPE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEPRESSED LEVEL OF CONSCIOUSNESS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSARTHRIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HEMIPARESIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOAESTHESIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IIIRD NERVE PARALYSIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACUNAR INFARCTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MIGRAINE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OBSTRUCTIVE SLEEP APNEA SYNDROME | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PARKINSON'S DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SPEECH DISORDER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VISUAL PATHWAY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITH NERVE PARALYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VOCAL CORD PARALYSIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC DISORDERS | 8 (44.4%) | 24 ( 6.3%) | 20 (10.1%) | 27 ( 7.2%) | 36 ( 9.2%) |
| CARDIAC FAILURE CONGESTIVE | 2 (11.1%) | 5 ( 1.3%) | 6 ( 3.0%) | 6 ( 1.6%) | 7 ( 1.8%) |
| MYOCARDIAL INFARCTION | 3 (16.7%) | 5 ( 1.3%) | 5 ( 2.5%) | 3 ( 0.8%) | 9 ( 2.3%) |
| CARDIAC ARREST | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 5 ( 1.3%) | 2 ( 0.5%) |
| ATRIAL FIBRILLATION | 1 ( 5.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 5 ( 1.3%) | 2 ( 0.5%) |
| PULMONARY EDEMA NOS | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| ANGINA PECTORIS | 1 ( 5.6%) | 5 ( 1.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ANGINA UNSTABLE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 3 ( 0.8%) | 3 ( 0.8%) |
| EDEMA LOWER LIMB | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| CARDIOVASCULAR DISORDER NOS | 1 ( 5.6%) | 3 ( 0.8%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ARRHYTHMIA NOS | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CORONARY ARTERY OCCLUSION | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIAC FAILURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CARDIOMEGALY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CORONARY ARTERY DISEASE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EDEMA PERIPHERAL | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEFT VENTRICULAR FAILURE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| MYOCARDIAL ISCHEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ATRIOVENTRICULAR BLOCK NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| BRADYCARDIA NOS | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIAC MURMUR NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIO-RESPIRATORY ARREST | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| CARDIOMYOPATHY NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ISCHEMIC CARDIOMYOPATHY | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ORTHOPNEA | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PALPITATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VENTRICULAR TACHYCARDIA | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| AORTIC VALVE DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| AORTIC VALVE STENOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ATRIAL FLUTTER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC FAILURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CARDIOGENIC SHOCK | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DYSPNEA PAROXYSMAL NOCTURNAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EDEMA UPPER LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPERTROPHIC CARDIOMYOPATHY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYOCARDITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VENTRICULAR EXTRASYSTOLES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VENTRICULAR HYPOKINESIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GASTROINTESTINAL DISORDERS | 3 (16.7%) | 26 ( 6.9%) | 14 ( 7.1%) | 35 ( 9.3%) | 30 ( 7.7%) |
| NAUSEA | 1 ( 5.6%) | 10 ( 2.6%) | 5 ( 2.5%) | 13 ( 3.4%) | 11 ( 2.8%) |
| VOMITING NOS | 1 ( 5.6%) | 6 ( 1.6%) | 2 ( 1.0%) | 7 ( 1.9%) | 4 ( 1.0%) |
| DIARRHEA NOS | 0 ( 0.0%) | 6 ( 1.6%) | 3 ( 1.5%) | 7 ( 1.9%) | 3 ( 0.8%) |
| CONSTIPATION | 0 ( 0.0%) | 6 ( 1.6%) | 1 ( 0.5%) | 3 ( 0.8%) | 8 ( 2.0%) |
| DYSPEPSIA | 1 ( 5.6%) | 3 ( 0.8%) | 2 ( 1.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| GASTROINTESTINAL HEMORRHAGE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 3 ( 0.8%) |
| ABDOMINAL PAIN NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| SORE THROAT NOS | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| ABDOMINAL PAIN UPPER | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| GASTRITIS NOS | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| ESOPHAGITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| GASTRIC ULCER | 1 ( 5.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| GASTRO-ESOPHAGEAL REFLUX DISEASE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| GASTROINTESTINAL UPSET | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| DIVERTICULUM INTESTINAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| DUODENAL ULCER | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ESOPHAGEAL REFLUX | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| GASTROINTESTINAL DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ABDOMINAL DISTENSION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ABDOMINAL PAIN AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ABDOMINAL TENDERNESS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ASCITES | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DUODENITIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DYSPHAGIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GASTRIC EROSIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GASTRIC IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEMATEMESIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| HEMORRHOIDS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IMPAIRED GASTRIC EMPTYING | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INGUINAL HERNIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PEPTIC ULCER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PEPTIC ULCER HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERIODONTAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERITONEAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERITONEAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERITONITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RECTAL BLEEDING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RECTAL PROLAPSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| TOOTHACHE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VOLVULUS OF BOWEL | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| METABOLISM AND NUTRITION DISORDERS | 4 (22.2%) | 20 ( 5.3%) | 22 (11.1%) | 23 ( 6.1%) | 25 ( 6.4%) |
| HYPERCHOLESTEROLEMIA | 1 ( 5.6%) | 5 ( 1.3%) | 8 ( 4.0%) | 5 ( 1.3%) | 5 ( 1.3%) |
| HYPOGLYCAEMIA NOS | 0 ( 0.0%) | 5 ( 1.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 9 ( 2.3%) |
| DEHYDRATION | 2 (11.1%) | 2 ( 0.5%) | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| HYPERGLYCEMIA NOS | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 4 ( 1.1%) | 1 ( 0.3%) |
| HYPERKALEMIA | 1 ( 5.6%) | 4 ( 1.1%) | 2 ( 1.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| HYPERLIPIDEMIA NOS | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 4 ( 1.1%) | 0 ( 0.0%) |
| APPETITE DECREASED NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 4 ( 1.0%) |
| GOUT | 1 ( 5.6%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPOKALEMIA | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| DIABETIC NEUROPATHY NEC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| DIABETIC COMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| GOUT AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DIABETES MELLITUS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETES MELLITUS INSULIN-DEPENDENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIABETIC COMPLICATION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPOCALCEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OBESITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CALCIUM DEFICIENCY | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETES MELLITUS NON INSULIN-DEPENDENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DIABETIC AMYOTROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIABETIC KETOACIDOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ELECTROLYTE IMBALANCE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FLUID RETENTION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOLATE DEFICIENCY | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLUCOSE TOLERANCE IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPERPHOSPHATEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERURICEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERVOLEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOGLYCAEMIC COMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPONATREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPOVOLEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| INSULIN RESISTANCE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| METABOLIC ACIDOSIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NONKETOTIC HYPERGLYCEMIC-HYPEROSMOLAR COMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POLYDIPSIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 27 ( 7.1%) | 14 ( 7.1%) | 24 ( 6.4%) | 23 ( 5.9%) |
| HYPERTENSION NOS | 0 ( 0.0%) | 9 ( 2.4%) | 6 ( 3.0%) | 13 ( 3.4%) | 11 ( 2.8%) |
| HYPERTENSION AGGRAVATED | 0 ( 0.0%) | 6 ( 1.6%) | 1 ( 0.5%) | 6 ( 1.6%) | 2 ( 0.5%) |
| TRANSIENT ISCHEMIC ATTACK | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| GANGRENE NOS | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PERIPHERAL VASCULAR DISEASE NOS | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| HYPOTENSION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| PULMONARY HYPERTENSION NOS | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARTERIAL OCCLUSION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CAROTID ARTERY STENOSIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POSTURAL HYPOTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| VENOUS THROMBOSIS DEEP LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| ARTERIAL ANEURYSM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD PRESSURE FLUCTUATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD PRESSURE INADEQUATELY CONTROLLED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CAROTID ARTERY DISEASE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CEREBRAL INFARCTION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CEREBRAL ISCHEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CEREBROVASCULAR ACCIDENT NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| COLLAPSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HEMATOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HOT FLUSHES NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERTENSIVE ENCEPHALOPATHY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ISCHEMIC FOOT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LABILE HYPERTENSION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL CIRCULATORY FAILURE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POOR PERIPHERAL CIRCULATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PULMONARY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUBARACHNOID HEMORRHAGE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THROMBOEMBOLISM NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 (11.1%) | 23 ( 6.1%) | 15 ( 7.6%) | 27 ( 7.2%) | 18 ( 4.6%) |
| POST-OPERATIVE COMPLICATIONS NOS | 1 ( 5.6%) | 10 ( 2.6%) | 5 ( 2.5%) | 8 ( 2.1%) | 6 ( 1.5%) |
| VITRECTOMY | 0 ( 0.0%) | 6 ( 1.6%) | 2 ( 1.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| CORONARY ARTERY SURGERY | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| NAUSEA POST-OPERATIVE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| ARTERIO-VENOUS FISTULA OPERATION | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOOT AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| TOE AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| TOOTH EXTRACTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ARTERIAL BYPASS OPERATION (EXC CORONARY ARTERY) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOOD PRODUCT TRANSFUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CARDIAC OPERATION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CARDIAC PACEMAKER INSERTION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CAROTID ENDARTERECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEMOTHERAPY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DEVICE FAILURE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FLUID REPLACEMENT PARENTERAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOOT OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HIP ARTHROPLASTY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HOSPITALIZATION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KNEE ARTHROPLASTY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEG AMPUTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENS IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| LIMB OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| METATARSAL EXCISION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST PROCEDURAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POST PROCEDURAL PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SHUNT OCCLUSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SKIN CYST EXCISION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SUTURE LINE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VOMITING POST-OPERATIVE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| WOUND DEBRIDEMENT | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS | 5 (27.8%) | 12 ( 3.2%) | 16 ( 8.1%) | 19 ( 5.0%) | 15 ( 3.8%) |
| DYSPNEA NOS | 2 (11.1%) | 3 ( 0.8%) | 7 ( 3.5%) | 6 ( 1.6%) | 4 ( 1.0%) |
| COUGH | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 6 ( 1.6%) | 3 ( 0.8%) |
| PLEURAL EFFUSION | 1 ( 5.6%) | 2 ( 0.5%) | 2 ( 1.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| RHINORRHEA | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) |
| ASTHMA NOS | 2 (11.1%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHRONIC OBSTRUCTIVE AIRWAYS DISEASE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| EPISTAXIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| DYSPNEA EXERTIONAL | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LUNG INFILTRATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| NASAL CONGESTION | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SNEEZING | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ASTHMA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ATELECTASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DYSPNEA EXACERBATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DYSPNEA PAROXYSMAL NOCTURNAL | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EMPHYSEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| HEMOPTYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOXIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INTERSTITIAL LUNG DISEASE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PNEUMONIA VIRAL NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PULMONARY FIBROSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RESPIRATORY FAILURE (EXC NEONATAL) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RHINITIS SEASONAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SINUS PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL AND URINARY DISORDERS | 4 (22.2%) | 18 ( 4.8%) | 10 ( 5.1%) | 15 ( 4.0%) | 19 ( 4.9%) |
| RENAL FAILURE NOS | 1 ( 5.6%) | 6 ( 1.6%) | 4 ( 2.0%) | 6 ( 1.6%) | 6 ( 1.5%) |
| RENAL FAILURE ACUTE | 3 (16.7%) | 4 ( 1.1%) | 2 ( 1.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| RENAL IMPAIRMENT NOS | 1 ( 5.6%) | 2 ( 0.5%) | 2 ( 1.0%) | 5 ( 1.3%) | 2 ( 0.5%) |
| RENAL FAILURE CHRONIC | 1 ( 5.6%) | 3 ( 0.8%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RENAL FAILURE AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| URINARY RETENTION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CALCULUS RENAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DIABETIC NEPHROPATHY NOS | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FLUID RETENTION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RENAL ARTERY STENOSIS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL FAILURE CHRONIC AGGRAVATED | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLADDER PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLADDER PROLAPSE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLOMERULONEPHRITIS CHRONIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GLOMERULONEPHRITIS MINIMAL LESION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LOIN PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MICROALBUMINURIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POLYURIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RENAL CYST NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL VASCULAR DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| URINE DISCOLOURATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 3 (16.7%) | 13 ( 3.4%) | 12 ( 6.1%) | 8 ( 2.1%) | 21 ( 5.4%) |
| CHEST PAIN NEC | 1 ( 5.6%) | 5 ( 1.3%) | 6 ( 3.0%) | 2 ( 0.5%) | 5 ( 1.3%) |
| FALL | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) |
| WEAKNESS | 1 ( 5.6%) | 1 ( 0.3%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| FATIGUE | 1 ( 5.6%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EDEMA LOWER LIMB | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| PAIN IN FACE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.0%) |
| PAIN NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| DIFFICULTY IN WALKING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| EDEMA PERIPHERAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MULTI-ORGAN FAILURE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PYREXIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DEATH NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GROIN PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| HEMORRHAGE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HERNIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| IMPAIRED HEALING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LOWER EXTREMITY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MALAISE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MASS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MENTAL STATUS CHANGES | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL SWELLING | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INJURY AND POISONING | 0 ( 0.0%) | 10 ( 2.6%) | 7 ( 3.5%) | 9 ( 2.4%) | 19 ( 4.9%) |
| LACERATION | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| FOOT FRACTURE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| DRUG TOXICITY NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| HIP FRACTURE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| ANKLE FRACTURE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BURNS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| FEMUR FRACTURE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FRACTURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| JOINT SPRAIN | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LEG FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ABRASION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BACK INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLISTER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHEMICAL BURNS OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOREARM FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTHERMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| LOCALISED INFECTION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEDICATION ERROR | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHANTOM LIMB PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RIB FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SUNBURN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| THERAPEUTIC AGENT TOXICITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| TIBIA FRACTURE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UPPER LIMB FRACTURE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| WHIPLASH INJURY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MUSCULOSKELETAL, CONNECTIVE TISSUE AND BONE DISORDERS | 0 ( 0.0%) | 12 ( 3.2%) | 11 ( 5.6%) | 10 ( 2.7%) | 11 ( 2.8%) |
| PAIN IN LIMB | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 2.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| BACK PAIN | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| ARTHRALGIA | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| ARTHRITIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| MYALGIA | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NECK PAIN | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| TENDONITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| MUSCLE CRAMPS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OSTEOPOROSIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BACK PAIN AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BURSITIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BUTTOCK PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COSTAL PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| JAW DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| JOINT STIFFNESS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MUSCLE SPASMS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OSTEOARTHRITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ROTATOR CUFF SYNDROME | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCIATICA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TENDONITIS EXACERBATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSYCHIATRIC DISORDERS | 3 (16.7%) | 7 ( 1.9%) | 4 ( 2.0%) | 13 ( 3.4%) | 10 ( 2.6%) |
| DEPRESSION NEC | 2 (11.1%) | 1 ( 0.3%) | 2 ( 1.0%) | 4 ( 1.1%) | 7 ( 1.8%) |
| ANXIETY NEC | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 5 ( 1.3%) | 4 ( 1.0%) |
| CONFUSION | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DELIRIUM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| DISORIENTATION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HALLUCINATION NOS | 1 ( 5.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| AGITATION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEPRESSION AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| NEUROSIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SCHIZOPHRENIA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STRESS SYMPTOMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 1 ( 5.6%) | 10 ( 2.6%) | 3 ( 1.5%) | 12 ( 3.2%) | 10 ( 2.6%) |
| ANEMIA NOS | 1 ( 5.6%) | 4 ( 1.1%) | 2 ( 1.0%) | 12 ( 3.2%) | 7 ( 1.8%) |
| ANEMIA NOS AGGRAVATED | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| COAGULATION DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DISSEMINATED INTRAVASCULAR COAGULATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRON DEFICIENCY ANEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| LEUCOCYTOSIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NORMOCHROMIC NORMOCYTIC ANEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SECONDARY ANAEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SECONDARY ANEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THROMBOCYTHEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THROMBOCYTOPENIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 2.5%) | 3 ( 0.8%) | 6 ( 1.5%) |
| BASAL CELL CARCINOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BENIGN BREAST NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| BENIGN SKIN NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLADDER NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHRONIC LEUKEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLON CANCER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| LIPOMA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MALIGNANT MELANOMA OF SKIN STAGE UNSPECIFIED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| METASTASES TO LUNG | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYELODYSPLASTIC SYNDROME NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NONHODGKIN'S LYMPHOMA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RESPIRATORY TRACT NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SKIN CARCINOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SKIN NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| THYROID NEOPLASM NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ENDOCRINE DISORDERS | 0 ( 0.0%) | 7 ( 1.9%) | 2 ( 1.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| *DIABETES MELLITUS INADEQUATE CONTROL* | 0 ( 0.0%) | 5 ( 1.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| HYPOTHYROIDISM | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ADRENAL INSUFFICIENCY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| GOITRE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THYROTOXICOSIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITION | 0 ( 0.0%) | 6 ( 1.6%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| PYREXIA | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| FISTULA NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAIN IN FACE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| THIRST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IMMUNE SYSTEM DISORDERS | 1 ( 5.6%) | 2 ( 0.5%) | 3 ( 1.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| DRUG HYPERSENSITIVITY | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| HYPERSENSITIVITY NOS | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| KIDNEY TRANSPLANT REJECTION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MULTIPLE ALLERGIES | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEPATO-BILIARY DISORDERS | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 1.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOLELITHIASIS | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOLECYSTITIS ACUTE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GALLBLADDER DISEASE NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEPATITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEPATOMEGALY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEPATOSPLENOMEGALY NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPROTEINEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATIVE SITE CONDITIONS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| AXILLARY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EDEMA LOWER LIMB | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 7.3
Incidence of Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| LOWER EXTREMITY MASS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| WEAKNESS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| REPRODUCTIVE SYSTEM AND BREAST DISORDERS | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| BENIGN PROSTATIC HYPERPLASIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MENOPAUSE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PROSTATIC DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PROSTATITIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EAR AND LABYRINTH DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EARACHE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LABYRINTHITIS NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUDDEN HEARING LOSS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| REPRODUCTIVE AND BREAST DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PROSTATITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 7.4
Incidence of Adverse Events by System Organ Class
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| System Organ Class / Preferred Term | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| NUMBER OF PATIENTS | 15 | 15 | 14 | 16 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 11 ( 73%) | 8 ( 53%) | 10 ( 71%) | 14 ( 88%) |
| EYE DISORDERS | 10 ( 67%) | 7 ( 47%) | 9 ( 64%) | 13 ( 81%) |
| VISUAL ACUITY REDUCED | 6 ( 40%) | 3 ( 20%) | 4 ( 29%) | 6 ( 38%) |
| VITREOUS FLOATERS | 4 ( 27%) | 2 ( 13%) | 0 ( 0%) | 5 ( 31%) |
| CATARACT SUBCAPSULAR | 2 ( 13%) | 1 ( 7%) | 3 ( 21%) | 4 ( 25%) |
| MACULAR OEDEMA | 2 ( 13%) | 0 ( 0%) | 2 ( 14%) | 3 ( 19%) |
| VITREOUS HAEMORRHAGE | 2 ( 13%) | 1 ( 7%) | 1 ( 7%) | 3 ( 19%) |
| EYE PAIN | 2 ( 13%) | 0 ( 0%) | 1 ( 7%) | 3 ( 19%) |
| PHOTOPHOBIA AGGRAVATED | 3 ( 20%) | 0 ( 0%) | 0 ( 0%) | 3 ( 19%) |
| PHOTOPSIA | 2 ( 13%) | 1 ( 7%) | 0 ( 0%) | 2 ( 13%) |
| PUPILLARY REFLEX IMPAIRED | 3 ( 20%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| VITREOUS DETACHMENT | 1 ( 7%) | 3 ( 20%) | 0 ( 0%) | 0 ( 0%) |
| ABNORMAL SENSATION IN EYE | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 2 ( 13%) |
| CATARACT CORTICAL | 0 ( 0%) | 1 ( 7%) | 2 ( 14%) | 0 ( 0%) |
| LACRIMATION INCREASED | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 2 ( 13%) |
| CATARACT NUCLEAR | 2 ( 13%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRITIS | 1 ( 7%) | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) |
| EYE IRRITATION | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIS VASCULAR DISORDER NOS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RUBEOSIS IRIDIS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VITREOUS DISORDER NOS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 7%) | 0 ( 0%) | 1 ( 7%) | 1 ( 6%) |
| *IIIRD NERVE PARALYSIS* | 1 ( 7%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| SYNCOPE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) | 1 ( 6%) |
| DEATH NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| INJECTION SITE PAIN | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) |
| INFECTIONS AND INFESTATIONS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| BLEPHARITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| KIDNEY INFECTION NOS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 1 ( 6%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 6%) |
| FOOT ULCER | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| GASTROINTESTINAL DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| DIARRHOEA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |



NOTE: Ocular Events include events reported for study eye and non-study eye.

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Table 7.4
Incidence of Adverse Events by System Organ Class
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| System Organ Class / Preferred Term | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| INVESTIGATIONS | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) |
| METABOLISM AND NUTRITION DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| HYPOGLYCAEMIA NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) |
| RENAL AND URINARY DISORDERS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RENAL FAILURE NOS | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |



NOTE: Ocular Events include events reported for study eye and non-study eye.

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Table 8
Incidence of Related Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 11 (61.1%) | 244 (64.6%) | 168 (84.8%) | 290 (76.9%) | 326 (83.4%) |
| EYE DISORDERS | 11 (61.1%) | 243 (64.3%) | 168 (84.8%) | 288 (76.4%) | 326 (83.4%) |
| IRITIS | 1 ( 5.6%) | 106 (28.0%) | 100 (50.5%) | 202 (53.6%) | 231 (59.1%) |
| OCULAR HYPEREMIA | 1 ( 5.6%) | 113 (29.9%) | 85 (42.9%) | 158 (41.9%) | 183 (46.8%) |
| EYE PAIN | 1 ( 5.6%) | 57 (15.1%) | 48 (24.2%) | 113 (30.0%) | 128 (32.7%) |
| EYE IRRITATION | 5 (27.8%) | 79 (20.9%) | 61 (30.8%) | 96 (25.5%) | 103 (26.3%) |
| LACRIMATION INCREASED | 1 ( 5.6%) | 56 (14.8%) | 45 (22.7%) | 94 (24.9%) | 103 (26.3%) |
| ABNORMAL SENSATION IN EYE | 1 ( 5.6%) | 50 (13.2%) | 43 (21.7%) | 78 (20.7%) | 92 (23.5%) |
| PHOTOPHOBIA | 3 (16.7%) | 42 (11.1%) | 41 (20.7%) | 63 (16.7%) | 85 (21.7%) |
| CONJUNCTIVAL EDEMA | 1 ( 5.6%) | 49 (13.0%) | 30 (15.2%) | 74 (19.6%) | 77 (19.7%) |
| VITREOUS FLOATERS | 3 (16.7%) | 42 (11.1%) | 40 (20.2%) | 58 (15.4%) | 74 (18.9%) |
| VISUAL ACUITY REDUCED | 2 (11.1%) | 43 (11.4%) | 47 (23.7%) | 66 (17.5%) | 58 (14.8%) |
| VITREOUS HEMORRHAGE | 1 ( 5.6%) | 25 ( 6.6%) | 32 (16.2%) | 37 ( 9.8%) | 29 ( 7.4%) |
| PHOTOPSIA | 0 ( 0.0%) | 14 ( 3.7%) | 18 ( 9.1%) | 25 ( 6.6%) | 28 ( 7.2%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 11 ( 2.9%) | 20 (10.1%) | 20 ( 5.3%) | 18 ( 4.6%) |
| RETINAL DETACHMENT | 1 ( 5.6%) | 10 ( 2.6%) | 12 ( 6.1%) | 18 ( 4.8%) | 22 ( 5.6%) |
| CATARACT NUCLEAR | 1 ( 5.6%) | 16 ( 4.2%) | 12 ( 6.1%) | 22 ( 5.8%) | 10 ( 2.6%) |
| CATARACT CORTICAL | 1 ( 5.6%) | 16 ( 4.2%) | 3 ( 1.5%) | 19 ( 5.0%) | 19 ( 4.9%) |
| CORNEAL EROSION | 0 ( 0.0%) | 16 ( 4.2%) | 6 ( 3.0%) | 14 ( 3.7%) | 11 ( 2.8%) |
| CORNEAL DISORDER NOS | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 2.0%) | 14 ( 3.7%) | 21 ( 5.4%) |
| EYE DISCHARGE | 0 ( 0.0%) | 13 ( 3.4%) | 3 ( 1.5%) | 12 ( 3.2%) | 14 ( 3.6%) |
| IRIS ADHESIONS | 2 (11.1%) | 3 ( 0.8%) | 4 ( 2.0%) | 10 ( 2.7%) | 18 ( 4.6%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0.0%) | 14 ( 3.7%) | 6 ( 3.0%) | 6 ( 1.6%) | 8 ( 2.0%) |
| CORNEAL EDEMA | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 2.0%) | 8 ( 2.1%) | 17 ( 4.3%) |
| RUBEOSIS IRIDIS | 1 ( 5.6%) | 5 ( 1.3%) | 8 ( 4.0%) | 6 ( 1.6%) | 9 ( 2.3%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 6 ( 1.6%) | 21 ( 5.4%) |
| HYPHEMA | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 1.5%) | 5 ( 1.3%) | 6 ( 1.5%) |
| MACULAR EDEMA | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 1.5%) | 3 ( 0.8%) | 8 ( 2.0%) |
| UVEITIS NOS | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 5 ( 1.3%) | 4 ( 1.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 6 ( 1.6%) | 3 ( 0.8%) |
| MACULOPATHY | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) |
| KERATITIS NEC | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| CATARACT NEC | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| CATARACT NOS AGGRAVATED | 1 ( 5.6%) | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| DRY EYE NEC | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| DIPLOPIA | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 5 ( 1.3%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| BLINDNESS NEC | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| MYDRIASIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |

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Table 8
Incidence of Related Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CORNEAL EPITHELIUM DEFECT | 1 ( 5.6%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| APHAKIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE ALLERGY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INFLAMMATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 8
Incidence of Related Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INVESTIGATIONS | 0 ( 0.0%) | 24 ( 6.3%) | 21 (10.6%) | 24 ( 6.4%) | 20 ( 5.1%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 20 ( 5.3%) | 16 ( 8.1%) | 18 ( 4.8%) | 16 ( 4.1%) |
| CORNEAL STAINING | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 2.5%) | 6 ( 1.6%) | 4 ( 1.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0.0%) | 15 ( 4.0%) | 10 ( 5.1%) | 29 ( 7.7%) | 25 ( 6.4%) |
| EYELID EDEMA | 0 ( 0.0%) | 6 ( 1.6%) | 6 ( 3.0%) | 22 ( 5.8%) | 19 ( 4.9%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 9 ( 2.4%) | 3 ( 1.5%) | 14 ( 3.7%) | 12 ( 3.1%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| FACE EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SWEATING INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 2.0%) | 7 ( 1.9%) | 14 ( 3.6%) |
| HEADACHE NOS | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 5 ( 1.3%) | 8 ( 2.0%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INSOMNIA NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| IIIRD NERVE PARALYSIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SYNCOPE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 5 ( 1.3%) | 4 ( 1.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| GASTROINTESTINAL DISORDERS | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| NAUSEA | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 8
Incidence of Related Adverse Events by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| *VOMITING NOS* | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CONSTIPATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DIARRHEA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIAC DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ANGINA PECTORIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CARDIAC FAILURE CONGESTIVE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PNEUMONIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRUG TOXICITY NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSYCHIATRIC DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ANXIETY NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DEPRESSION NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| HYPERTENSION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLOOD AND LYMPHATIC SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ANEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| THIRST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PAIN IN FACE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| METABOLISM AND NUTRITION DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERCHOLESTEROLEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL AND URINARY DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RENAL FAILURE CHRONIC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 9
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 17 (94.4%) | 298 (78.8%) | 193 (97.5%) | 323 (85.7%) | 349 (89.3%) |
| EYE DISORDERS | 17 (94.4%) | 297 (78.6%) | 192 (97.0%) | 322 (85.4%) | 349 (89.3%) |
| IRITIS | 4 (22.2%) | 126 (33.3%) | 123 (62.1%) | 222 (58.9%) | 243 (62.1%) |
| OCULAR HYPEREMIA | 4 (22.2%) | 140 (37.0%) | 113 (57.1%) | 202 (53.6%) | 215 (55.0%) |
| EYE IRRITATION | 10 (55.6%) | 111 (29.4%) | 90 (45.5%) | 132 (35.0%) | 139 (35.5%) |
| EYE PAIN | 2 (11.1%) | 84 (22.2%) | 72 (36.4%) | 139 (36.9%) | 161 (41.2%) |
| LACRIMATION INCREASED | 4 (22.2%) | 87 (23.0%) | 65 (32.8%) | 124 (32.9%) | 139 (35.5%) |
| VISUAL ACUITY REDUCED | 4 (22.2%) | 74 (19.6%) | 77 (38.9%) | 101 (26.8%) | 98 (25.1%) |
| ABNORMAL SENSATION IN EYE | 2 (11.1%) | 68 (18.0%) | 62 (31.3%) | 101 (26.8%) | 114 (29.2%) |
| VITREOUS FLOATERS | 6 (33.3%) | 67 (17.7%) | 63 (31.8%) | 88 (23.3%) | 100 (25.6%) |
| VITREOUS HEMORRHAGE | 2 (11.1%) | 66 (17.5%) | 70 (35.4%) | 91 (24.1%) | 90 (23.0%) |
| PHOTOPHOBIA | 6 (33.3%) | 60 (15.9%) | 59 (29.8%) | 86 (22.8%) | 102 (26.1%) |
| CONJUNCTIVAL EDEMA | 1 ( 5.6%) | 59 (15.6%) | 48 (24.2%) | 96 (25.5%) | 89 (22.8%) |
| CATARACT NUCLEAR | 5 (27.8%) | 34 ( 9.0%) | 27 (13.6%) | 37 ( 9.8%) | 29 ( 7.4%) |
| RETINAL DETACHMENT | 3 (16.7%) | 26 ( 6.9%) | 22 (11.1%) | 35 ( 9.3%) | 45 (11.5%) |
| CATARACT SUBCAPSULAR | 2 (11.1%) | 26 ( 6.9%) | 33 (16.7%) | 29 ( 7.7%) | 38 ( 9.7%) |
| PHOTOPSIA | 0 ( 0.0%) | 22 ( 5.8%) | 22 (11.1%) | 45 (11.9%) | 38 ( 9.7%) |
| CATARACT CORTICAL | 5 (27.8%) | 27 ( 7.1%) | 14 ( 7.1%) | 30 ( 8.0%) | 31 ( 7.9%) |
| CORNEAL EROSION | 1 ( 5.6%) | 24 ( 6.3%) | 10 ( 5.1%) | 25 ( 6.6%) | 17 ( 4.3%) |
| CORNEAL EDEMA | 1 ( 5.6%) | 12 ( 3.2%) | 17 ( 8.6%) | 20 ( 5.3%) | 24 ( 6.1%) |
| RUBEOSIS IRIDIS | 1 ( 5.6%) | 19 ( 5.0%) | 16 ( 8.1%) | 17 ( 4.5%) | 19 ( 4.9%) |
| EYE DISCHARGE | 0 ( 0.0%) | 18 ( 4.8%) | 10 ( 5.1%) | 23 ( 6.1%) | 20 ( 5.1%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0.0%) | 25 ( 6.6%) | 11 ( 5.6%) | 14 ( 3.7%) | 18 ( 4.6%) |
| IRIS ADHESIONS | 2 (11.1%) | 13 ( 3.4%) | 9 ( 4.5%) | 13 ( 3.4%) | 27 ( 6.9%) |
| MACULAR EDEMA | 1 ( 5.6%) | 11 ( 2.9%) | 16 ( 8.1%) | 11 ( 2.9%) | 19 ( 4.9%) |
| CORNEAL DISORDER NOS | 0 ( 0.0%) | 8 ( 2.1%) | 6 ( 3.0%) | 17 ( 4.5%) | 25 ( 6.4%) |
| HYPHEMA | 0 ( 0.0%) | 6 ( 1.6%) | 8 ( 4.0%) | 12 ( 3.2%) | 15 ( 3.8%) |
| CATARACT NEC | 0 ( 0.0%) | 10 ( 2.6%) | 1 ( 0.5%) | 10 ( 2.7%) | 9 ( 2.3%) |
| BLINDNESS NEC | 1 ( 5.6%) | 4 ( 1.1%) | 9 ( 4.5%) | 6 ( 1.6%) | 9 ( 2.3%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 6 ( 1.6%) | 21 ( 5.4%) |
| DRY EYE NEC | 0 ( 0.0%) | 6 ( 1.6%) | 7 ( 3.5%) | 5 ( 1.3%) | 9 ( 2.3%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 5 ( 1.3%) | 5 ( 2.5%) | 3 ( 0.8%) | 12 ( 3.1%) |
| VISION BLURRED | 0 ( 0.0%) | 5 ( 1.3%) | 10 ( 5.1%) | 5 ( 1.3%) | 4 ( 1.0%) |
| CATARACT NOS AGGRAVATED | 1 ( 5.6%) | 8 ( 2.1%) | 4 ( 2.0%) | 5 ( 1.3%) | 3 ( 0.8%) |
| KERATITIS NEC | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 2.0%) | 4 ( 1.1%) | 8 ( 2.0%) |
| VITREOUS DETACHMENT | 1 ( 5.6%) | 2 ( 0.5%) | 3 ( 1.5%) | 9 ( 2.4%) | 5 ( 1.3%) |
| MACULOPATHY | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 2.0%) | 5 ( 1.3%) | 5 ( 1.3%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 3 ( 0.8%) | 6 ( 3.0%) | 3 ( 0.8%) | 6 ( 1.5%) |
| UVEITIS NOS | 1 ( 5.6%) | 2 ( 0.5%) | 2 ( 1.0%) | 7 ( 1.9%) | 4 ( 1.0%) |
| POST-OPERATIVE PAIN | 1 ( 5.6%) | 7 ( 1.9%) | 0 ( 0.0%) | 2 ( 0.5%) | 5 ( 1.3%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 6 ( 1.6%) | 5 ( 1.3%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 4 ( 1.1%) | 1 ( 0.5%) | 3 ( 0.8%) | 6 ( 1.5%) |
| BLEPHARITIS | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 3 ( 0.8%) | 5 ( 1.3%) |

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Table 9
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| HYPOTONY OF EYE | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 2 ( 0.5%) | 6 ( 1.5%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 5 ( 1.3%) | 2 ( 1.0%) | 5 ( 1.3%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | 1 ( 5.6%) | 1 ( 0.3%) | 3 ( 1.5%) | 4 ( 1.1%) | 2 ( 0.5%) |
| DIPLOPIA | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 4 ( 1.1%) | 2 ( 0.5%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 4 ( 1.1%) | 2 ( 0.5%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| MYDRIASIS | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 0 ( 0.0%) | 4 ( 1.0%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 5 ( 1.3%) | 2 ( 0.5%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| APHAKIA | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE ALLERGY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CHEMOSIS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS VIRAL NOS | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| KERATOPATHY BAND | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PERIORBITAL HEMATOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 9
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ANISEIKONIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ARCUS SENILIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHALAZION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORNEAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ULCER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EXOPHTHALMOS ENDOCRINE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE HEMORRHAGE NEC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFECTION NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INFLAMMATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| IRIS NEVUS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC NERVE INJURY NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAPILLEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL EXUDATES | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VASCULITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SCLERITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION ABNORMAL NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INVESTIGATIONS | 3 (16.7%) | 44 (11.6%) | 48 (24.2%) | 50 (13.3%) | 46 (11.8%) |

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Table 9
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| INTRAOCULAR PRESSURE INCREASED | 3 (16.7%) | 39 (10.3%) | 40 (20.2%) | 42 (11.1%) | 40 (10.2%) |
| CORNEAL STAINING | 0 ( 0.0%) | 6 ( 1.6%) | 8 ( 4.0%) | 9 ( 2.4%) | 8 ( 2.0%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0.0%) | 26 ( 6.9%) | 19 ( 9.6%) | 39 (10.3%) | 38 ( 9.7%) |
| EYELID EDEMA | 0 ( 0.0%) | 15 ( 4.0%) | 12 ( 6.1%) | 29 ( 7.7%) | 25 ( 6.4%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 15 ( 4.0%) | 8 ( 4.0%) | 21 ( 5.6%) | 20 ( 5.1%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| DERMATITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ECCHYMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PRURITUS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 5.6%) | 14 ( 3.7%) | 7 ( 3.5%) | 13 ( 3.4%) | 8 ( 2.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 1 ( 5.6%) | 8 ( 2.1%) | 4 ( 2.0%) | 5 ( 1.3%) | 4 ( 1.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| VITRECTOMY | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EYE IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENS IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SUTURE LINE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 2.5%) | 4 ( 1.1%) | 7 ( 1.8%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 4 ( 1.1%) | 3 ( 0.8%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| FACIAL PALSY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HEADACHE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITH NERVE PARALYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPERSENSITIVITY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MULTIPLE ALLERGIES | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHEMICAL BURNS OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEAD INJURY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 9
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 9.a
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Saline | 55 IU Vitrase & 75 IU Vitrase |
|---|---|---|
| NUMBER OF PATIENTS | 378 | 768 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 298 (78.8%) | 672 (87.5%) |
| EYE DISORDERS | 297 (78.6%) | 671 (87.4%) |
| IRITIS | 126 (33.3%) | 465 (60.5%) |
| OCULAR HYPEREMIA | 140 (37.0%) | 417 (54.3%) |
| EYE PAIN | 84 (22.2%) | 300 (39.1%) |
| EYE IRRITATION | 111 (29.4%) | 271 (35.3%) |
| LACRIMATION INCREASED | 87 (23.0%) | 263 (34.2%) |
| ABNORMAL SENSATION IN EYE | 68 (18.0%) | 215 (28.0%) |
| VISUAL ACUITY REDUCED | 74 (19.6%) | 199 (25.9%) |
| VITREOUS FLOATERS | 67 (17.7%) | 188 (24.5%) |
| PHOTOPHOBIA | 60 (15.9%) | 188 (24.5%) |
| VITREOUS HEMORRHAGE | 66 (17.5%) | 181 (23.6%) |
| CONJUNCTIVAL EDEMA | 59 (15.6%) | 185 (24.1%) |
| RETINAL DETACHMENT | 26 ( 6.9%) | 80 (10.4%) |
| PHOTOPSIA | 22 ( 5.8%) | 83 (10.8%) |
| CATARACT NUCLEAR | 34 ( 9.0%) | 66 ( 8.6%) |
| CATARACT SUBCAPSULAR | 26 ( 6.9%) | 67 ( 8.7%) |
| CATARACT CORTICAL | 27 ( 7.1%) | 61 ( 7.9%) |
| CORNEAL EROSION | 24 ( 6.3%) | 42 ( 5.5%) |
| EYE DISCHARGE | 18 ( 4.8%) | 43 ( 5.6%) |
| CONJUNCTIVAL HEMORRHAGE | 25 ( 6.6%) | 32 ( 4.2%) |
| CORNEAL EDEMA | 12 ( 3.2%) | 44 ( 5.7%) |
| RUBEOSIS IRIDIS | 19 ( 5.0%) | 36 ( 4.7%) |
| IRIS ADHESIONS | 13 ( 3.4%) | 40 ( 5.2%) |
| CORNEAL DISORDER NOS | 8 ( 2.1%) | 42 ( 5.5%) |
| MACULAR EDEMA | 11 ( 2.9%) | 30 ( 3.9%) |
| HYPHEMA | 6 ( 1.6%) | 27 ( 3.5%) |
| CATARACT NEC | 10 ( 2.6%) | 19 ( 2.5%) |
| HYPOPYON | 0 ( 0.0%) | 27 ( 3.5%) |
| DRY EYE NEC | 6 ( 1.6%) | 14 ( 1.8%) |
| GLAUCOMA NOS | 5 ( 1.3%) | 15 ( 2.0%) |
| BLINDNESS NEC | 4 ( 1.1%) | 15 ( 2.0%) |
| CATARACT NOS AGGRAVATED | 8 ( 2.1%) | 8 ( 1.0%) |
| KERATITIS NEC | 4 ( 1.1%) | 12 ( 1.6%) |
| VITREOUS DETACHMENT | 2 ( 0.5%) | 14 ( 1.8%) |
| MACULOPATHY | 5 ( 1.3%) | 10 ( 1.3%) |
| POST-OPERATIVE PAIN | 7 ( 1.9%) | 7 ( 0.9%) |
| POSTERIOR CAPSULE OPACIFICATION | 3 ( 0.8%) | 11 ( 1.4%) |
| VISION BLURRED | 5 ( 1.3%) | 9 ( 1.2%) |
| RETINOPATHY DIABETIC | 4 ( 1.1%) | 9 ( 1.2%) |
| UVEITIS NOS | 2 ( 0.5%) | 11 ( 1.4%) |
| INTRAOCULAR PRESSURE INCREASED | 3 ( 0.8%) | 9 ( 1.2%) |
| HYPOTONY OF EYE | 2 ( 0.5%) | 8 ( 1.0%) |

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Table 9.a
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Saline | 55 IU Vitrase & 75 IU Vitrase |
|---|---|---|
| RETINAL HEMORRHAGE | 5 ( 1.3%) | 5 ( 0.7%) |
| BLEPHARITIS | 1 ( 0.3%) | 8 ( 1.0%) |
| DIPLOPIA | 2 ( 0.5%) | 6 ( 0.8%) |
| RETINAL TEAR (EXC DETACHMENT) | 1 ( 0.3%) | 7 ( 0.9%) |
| CORNEAL EPITHELIUM DEFECT | 1 ( 0.3%) | 6 ( 0.8%) |
| MYDRIASIS | 3 ( 0.8%) | 4 ( 0.5%) |
| RETINAL ISCHEMIA | 1 ( 0.3%) | 6 ( 0.8%) |
| CORNEAL ABRASION | 1 ( 0.3%) | 5 ( 0.7%) |
| PSEUDOPHAKIA | 3 ( 0.8%) | 3 ( 0.4%) |
| CONJUNCTIVITIS NEC | 2 ( 0.5%) | 3 ( 0.4%) |
| PHOTOPHOBIA AGGRAVATED | 1 ( 0.3%) | 4 ( 0.5%) |
| EYE ALLERGY | 0 ( 0.0%) | 4 ( 0.5%) |
| OCULAR HYPERTENSION | 1 ( 0.3%) | 3 ( 0.4%) |
| OPTIC ATROPHY | 1 ( 0.3%) | 3 ( 0.4%) |
| PAINFUL RED EYES | 1 ( 0.3%) | 3 ( 0.4%) |
| VITREOUS DISORDER NOS | 2 ( 0.5%) | 2 ( 0.3%) |
| APHAKIA | 2 ( 0.5%) | 1 ( 0.1%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 3 ( 0.4%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 2 ( 0.3%) |
| INTRAOCULAR PRESSURE DECREASED | 3 ( 0.8%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 1 ( 0.3%) | 2 ( 0.3%) |
| LENTICULAR OPACITIES | 2 ( 0.5%) | 1 ( 0.1%) |
| RETINAL SCAR | 0 ( 0.0%) | 3 ( 0.4%) |
| CHEMOSIS | 1 ( 0.3%) | 1 ( 0.1%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 2 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 2 ( 0.3%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 2 ( 0.3%) |
| EYELID PTOSIS | 1 ( 0.3%) | 1 ( 0.1%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 2 ( 0.3%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 2 ( 0.3%) |
| PERIORBITAL HEMATOMA | 0 ( 0.0%) | 2 ( 0.3%) |
| RETINAL DISORDER NOS | 1 ( 0.3%) | 1 ( 0.1%) |
| RETINAL MICROANEURYSMS | 1 ( 0.3%) | 1 ( 0.1%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 1 ( 0.3%) | 1 ( 0.1%) |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0.0%) | 1 ( 0.1%) |
| ANISEIKONIA | 0 ( 0.0%) | 1 ( 0.1%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0.0%) | 1 ( 0.1%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 1 ( 0.1%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 1 ( 0.1%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 1 ( 0.1%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0.0%) | 1 ( 0.1%) |
| CHALAZION | 0 ( 0.0%) | 1 ( 0.1%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.1%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 1 ( 0.1%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0.0%) | 1 ( 0.1%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 1 ( 0.1%) |

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Table 9.a
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Saline | 55 IU Vitrase & 75 IU Vitrase |
|---|---|---|
| CORNEAL DEGENERATION | 0 ( 0.0%) | 1 ( 0.1%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 1 ( 0.1%) |
| CYCLITIS | 0 ( 0.0%) | 1 ( 0.1%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 1 ( 0.1%) |
| EXOPHTHALMOS ENDOCRINE | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE HEMORRHAGE NEC | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| EYE INFECTION NOS | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 1 ( 0.1%) |
| EYE INFLAMMATION NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| EYELID DISORDER NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| EYELID EDEMA | 0 ( 0.0%) | 1 ( 0.1%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0.0%) | 1 ( 0.1%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 1 ( 0.1%) |
| IRIS NEVUS | 1 ( 0.3%) | 0 ( 0.0%) |
| KERATOPATHY BAND | 0 ( 0.0%) | 1 ( 0.1%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 1 ( 0.1%) |
| OCULAR HYPERAEMIA | 0 ( 0.0%) | 1 ( 0.1%) |
| OPTIC NERVE INJURY NOS | 1 ( 0.3%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 1 ( 0.1%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 1 ( 0.1%) |
| RETINAL EXUDATES | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 1 ( 0.1%) |
| STRABISMUS NEC | 0 ( 0.0%) | 1 ( 0.1%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 1 ( 0.1%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 1 ( 0.1%) |
| INVESTIGATIONS | 44 (11.6%) | 96 (12.5%) |
| INTRAOCULAR PRESSURE INCREASED | 39 (10.3%) | 82 (10.7%) |
| CORNEAL STAINING | 6 ( 1.6%) | 17 ( 2.2%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 26 ( 6.9%) | 77 (10.0%) |
| EYELID EDEMA | 15 ( 4.0%) | 54 ( 7.0%) |
| ERYTHEMA NEC | 15 ( 4.0%) | 41 ( 5.3%) |
| OCULAR HYPEREMIA | 2 ( 0.5%) | 1 ( 0.1%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 2 ( 0.3%) |
| DERMATITIS NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| ECCHYMOSIS | 0 ( 0.0%) | 1 ( 0.1%) |
| PRURITUS NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| SURGICAL AND MEDICAL PROCEDURES | 14 ( 3.7%) | 21 ( 2.7%) |
| POST-OPERATIVE COMPLICATIONS NOS | 8 ( 2.1%) | 9 ( 1.2%) |

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Table 9.a
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Saline | 55 IU Vitrase & 75 IU Vitrase |
|---|---|---|
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 0.5%) | 6 ( 0.8%) |
| VITRECTOMY | 4 ( 1.1%) | 2 ( 0.3%) |
| EYE IRRITATION | 0 ( 0.0%) | 1 ( 0.1%) |
| LENS IMPLANT | 0 ( 0.0%) | 1 ( 0.1%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.1%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| SUTURE LINE PAIN | 0 ( 0.0%) | 1 ( 0.1%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.3%) | 11 ( 1.4%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 7 ( 0.9%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 1 ( 0.1%) |
| FACIAL PALSY | 0 ( 0.0%) | 1 ( 0.1%) |
| HEADACHE NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 1 ( 0.1%) |
| INJURY AND POISONING | 1 ( 0.3%) | 1 ( 0.1%) |
| CHEMICAL BURNS OF EYE | 0 ( 0.0%) | 1 ( 0.1%) |
| HEAD INJURY | 1 ( 0.3%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 1 ( 0.3%) | 1 ( 0.1%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0.0%) | 1 ( 0.1%) |
| RADIOACTIVE IODINE THERAPY | 1 ( 0.3%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0.0%) | 1 ( 0.1%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0.0%) | 1 ( 0.1%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0.0%) | 1 ( 0.1%) |
| HYPERSENSITIVITY NOS | 0 ( 0.0%) | 1 ( 0.1%) |
| INFECTIONS AND INFESTATIONS | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPOPYON | 1 ( 0.3%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 1 ( 0.1%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 1 ( 0.1%) |

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Table 10
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 11 (61.1%) | 244 (64.6%) | 168 (84.8%) | 290 (76.9%) | 326 (83.4%) |
| EYE DISORDERS | 11 (61.1%) | 243 (64.3%) | 168 (84.8%) | 288 (76.4%) | 326 (83.4%) |
| IRITIS | 1 ( 5.6%) | 106 (28.0%) | 100 (50.5%) | 202 (53.6%) | 231 (59.1%) |
| OCULAR HYPEREMIA | 1 ( 5.6%) | 113 (29.9%) | 85 (42.9%) | 158 (41.9%) | 183 (46.8%) |
| EYE PAIN | 1 ( 5.6%) | 57 (15.1%) | 48 (24.2%) | 113 (30.0%) | 128 (32.7%) |
| EYE IRRITATION | 5 (27.8%) | 79 (20.9%) | 61 (30.8%) | 96 (25.5%) | 103 (26.3%) |
| LACRIMATION INCREASED | 1 ( 5.6%) | 56 (14.8%) | 45 (22.7%) | 94 (24.9%) | 103 (26.3%) |
| ABNORMAL SENSATION IN EYE | 1 ( 5.6%) | 50 (13.2%) | 43 (21.7%) | 78 (20.7%) | 92 (23.5%) |
| PHOTOPHOBIA | 3 (16.7%) | 42 (11.1%) | 41 (20.7%) | 63 (16.7%) | 85 (21.7%) |
| CONJUNCTIVAL EDEMA | 1 ( 5.6%) | 49 (13.0%) | 30 (15.2%) | 74 (19.6%) | 77 (19.7%) |
| VITREOUS FLOATERS | 3 (16.7%) | 42 (11.1%) | 40 (20.2%) | 58 (15.4%) | 74 (18.9%) |
| VISUAL ACUITY REDUCED | 2 (11.1%) | 43 (11.4%) | 47 (23.7%) | 66 (17.5%) | 58 (14.8%) |
| VITREOUS HEMORRHAGE | 1 ( 5.6%) | 25 ( 6.6%) | 32 (16.2%) | 37 ( 9.8%) | 29 ( 7.4%) |
| PHOTOPSIA | 0 ( 0.0%) | 14 ( 3.7%) | 18 ( 9.1%) | 25 ( 6.6%) | 28 ( 7.2%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 11 ( 2.9%) | 20 (10.1%) | 20 ( 5.3%) | 17 ( 4.3%) |
| RETINAL DETACHMENT | 1 ( 5.6%) | 10 ( 2.6%) | 12 ( 6.1%) | 18 ( 4.8%) | 22 ( 5.6%) |
| CATARACT NUCLEAR | 1 ( 5.6%) | 16 ( 4.2%) | 12 ( 6.1%) | 22 ( 5.8%) | 10 ( 2.6%) |
| CATARACT CORTICAL | 1 ( 5.6%) | 16 ( 4.2%) | 3 ( 1.5%) | 19 ( 5.0%) | 19 ( 4.9%) |
| CORNEAL EROSION | 0 ( 0.0%) | 16 ( 4.2%) | 6 ( 3.0%) | 14 ( 3.7%) | 11 ( 2.8%) |
| CORNEAL DISORDER NOS | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 2.0%) | 14 ( 3.7%) | 21 ( 5.4%) |
| EYE DISCHARGE | 0 ( 0.0%) | 13 ( 3.4%) | 3 ( 1.5%) | 12 ( 3.2%) | 14 ( 3.6%) |
| IRIS ADHESIONS | 2 (11.1%) | 3 ( 0.8%) | 4 ( 2.0%) | 10 ( 2.7%) | 18 ( 4.6%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0.0%) | 14 ( 3.7%) | 6 ( 3.0%) | 6 ( 1.6%) | 8 ( 2.0%) |
| CORNEAL EDEMA | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 2.0%) | 8 ( 2.1%) | 17 ( 4.3%) |
| RUBEOSIS IRIDIS | 1 ( 5.6%) | 5 ( 1.3%) | 8 ( 4.0%) | 6 ( 1.6%) | 9 ( 2.3%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 6 ( 1.6%) | 21 ( 5.4%) |
| HYPHEMA | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 1.5%) | 5 ( 1.3%) | 6 ( 1.5%) |
| MACULAR EDEMA | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 1.5%) | 3 ( 0.8%) | 8 ( 2.0%) |
| UVEITIS NOS | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 5 ( 1.3%) | 4 ( 1.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 6 ( 1.6%) | 3 ( 0.8%) |
| MACULOPATHY | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) |
| KERATITIS NEC | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| CATARACT NEC | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| CATARACT NOS AGGRAVATED | 1 ( 5.6%) | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| DRY EYE NEC | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| DIPLOPIA | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 5 ( 1.3%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| BLINDNESS NEC | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| MYDRIASIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |

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Table 10
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CORNEAL EPITHELIUM DEFECT | 1 ( 5.6%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| APHAKIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE ALLERGY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INFLAMMATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 10
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INVESTIGATIONS | 0 ( 0.0%) | 24 ( 6.3%) | 21 (10.6%) | 24 ( 6.4%) | 20 ( 5.1%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 20 ( 5.3%) | 16 ( 8.1%) | 18 ( 4.8%) | 16 ( 4.1%) |
| CORNEAL STAINING | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 2.5%) | 6 ( 1.6%) | 4 ( 1.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0.0%) | 15 ( 4.0%) | 9 ( 4.5%) | 29 ( 7.7%) | 24 ( 6.1%) |
| EYELID EDEMA | 0 ( 0.0%) | 6 ( 1.6%) | 6 ( 3.0%) | 22 ( 5.8%) | 19 ( 4.9%) |
| ERYTHEMA NEC | 0 ( 0.0%) | 9 ( 2.4%) | 3 ( 1.5%) | 14 ( 3.7%) | 12 ( 3.1%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 5 ( 1.3%) | 4 ( 1.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 6 ( 1.5%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HEADACHE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0 0%) | 1 ( 0.3%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 10
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: WW Control (n = 18)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 5 (27.8%) | 2 (11.1%) | 6 (33.3%) | 11 (61.1%) | 8 (44.4%) | 9 (50.0%) | 7 (38.9%) |
| EYE DISORDERS | 5 (27.8%) | 2 (11.1%) | 6 (33.3%) | 11 (61.1%) | 8 (44.4%) | 8 (44.4%) | 7 (38.9%) |
| EYE IRRITATION | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 0 ( 0.0%) | 3 (16.7%) | 5 (27.8%) | 0 ( 0.0%) |
| PHOTOPHOBIA | 3 (16.7%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| VITREOUS FLOATERS | 1 ( 5.6%) | 0 ( 0.0%) | 2 (11.1%) | 4 (22.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 3 (16.7%) |
| LACRIMATION INCREASED | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) |
| IRITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 (16.7%) | 0 ( 0.0%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0.0%) | 0 ( 0.0%) | 2 (11.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 5.6%) |
| VISUAL ACUITY REDUCED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 (11.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS HEMORRHAGE | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| CORNEAL EROSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| INVESTIGATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 2 (11.1%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 2 (11.1%) |
| SURGICAL AND MEDICAL PROCEDURES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |



Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
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Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 235 (62.2%) | 63 (16.7%) | 74 (19.6%) | 62 (16.4%) | 84 (22.2%) | 115 (30.4%) | 113 (29.9%) |
| EYE DISORDERS | 233 (61.6%) | 63 (16.7%) | 74 (19.6%) | 58 (15.3%) | 84 (22.2%) | 106 (28.0%) | 112 (29.6%) |
| OCULAR HYPEREMIA | 123 (32.5%) | 6 ( 1.6%) | 5 ( 1.3%) | 0 ( 0.0%) | 8 ( 2.1%) | 9 ( 2.4%) | 10 ( 2.6%) |
| IRITIS | 89 (23.5%) | 17 ( 4.5%) | 11 ( 2.9%) | 3 ( 0.8%) | 10 ( 2.6%) | 17 ( 4.5%) | 11 ( 2.9%) |
| EYE IRRITATION | 61 (16.1%) | 9 ( 2.4%) | 15 ( 4.0%) | 9 ( 2.4%) | 19 ( 5.0%) | 14 ( 3.7%) | 15 ( 4.0%) |
| LACRIMATION INCREASED | 39 (10.3%) | 8 ( 2.1%) | 14 ( 3.7%) | 11 ( 2.9%) | 10 ( 2.6%) | 10 ( 2.6%) | 10 ( 2.6%) |
| EYE PAIN | 52 (13.8%) | 6 ( 1.6%) | 5 ( 1.3%) | 3 ( 0.8%) | 11 ( 2.9%) | 21 ( 5.6%) | 13 ( 3.4%) |
| VISUAL ACUITY REDUCED | 9 ( 2.4%) | 7 ( 1.9%) | 11 ( 2.9%) | 12 ( 3.2%) | 20 ( 5.3%) | 10 ( 2.6%) | 18 ( 4.8%) |
| ABNORMAL SENSATION IN EYE | 44 (11.6%) | 4 ( 1.1%) | 7 ( 1.9%) | 7 ( 1.9%) | 4 ( 1.1%) | 10 ( 2.6%) | 7 ( 1.9%) |
| VITREOUS FLOATERS | 9 ( 2.4%) | 17 ( 4.5%) | 8 ( 2.1%) | 11 ( 2.9%) | 17 ( 4.5%) | 14 ( 3.7%) | 12 ( 3.2%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 8 ( 2.1%) | 14 ( 3.7%) | 22 ( 5.8%) | 26 ( 6.9%) |
| PHOTOPHOBIA | 18 ( 4.8%) | 9 ( 2.4%) | 9 ( 2.4%) | 10 ( 2.6%) | 8 ( 2.1%) | 11 ( 2.9%) | 13 ( 3.4%) |
| CONJUNCTIVAL EDEMA | 48 (12.7%) | 3 ( 0.8%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.1%) |
| CATARACT NUCLEAR | 1 ( 0.3%) | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 0.8%) | 2 ( 0.5%) | 6 ( 1.6%) | 19 ( 5.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.1%) | 1 ( 0.3%) | 1 ( 0.3%) | 8 ( 2.1%) | 13 ( 3.4%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 15 ( 4.0%) |
| CONJUNCTIVAL HEMORRHAGE | 19 ( 5.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 2 ( 0.5%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) | 5 ( 1.3%) | 5 ( 1.3%) | 10 ( 2.6%) |
| CORNEAL EROSION | 14 ( 3.7%) | 5 ( 1.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| PHOTOPSIA | 2 ( 0.5%) | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 1.1%) | 1 ( 0.3%) | 3 ( 0.8%) | 8 ( 2.1%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) | 2 ( 0.5%) | 11 ( 2.9%) |
| EYE DISCHARGE | 13 ( 3.4%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 7 ( 1.9%) |
| CORNEAL EDEMA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 1.3%) | 4 ( 1.1%) |
| MACULAR EDEMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 8 ( 2.1%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 1.1%) |
| CORNEAL DISORDER NOS | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) |
| DRY EYE NEC | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) |
| HYPHEMA | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.1%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.1%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| KERATITIS NEC | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| MYDRIASIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
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Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| UVEITIS NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEMOSIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EXOPHTHALMOS ENDOCRINE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE HEMORRHAGE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS NEVUS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPTIC NERVE INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL EXUDATES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INVESTIGATIONS | 15 ( 4.0%) | 4 ( 1.1%) | 1 ( 0.3%) | 5 ( 1.3%) | 1 ( 0.3%) | 12 ( 3.2%) | 11 ( 2.9%) |
| INTRAOCULAR PRESSURE INCREASED | 12 ( 3.2%) | 3 ( 0.8%) | 1 ( 0.3%) | 4 ( 1.1%) | 1 ( 0.3%) | 11 ( 2.9%) | 11 ( 2.9%) |
| CORNEAL STAINING | 3 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 14 ( 3.7%) | 2 ( 0.5%) | 3 ( 0.8%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) | 3 ( 0.8%) |
| ERYTHEMA NEC | 9 ( 2.4%) | 1 ( 0.3%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EYELID EDEMA | 7 ( 1.9%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| OCULAR HYPEREMIA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 8 ( 2.1%) | 2 ( 0.5%) |
| POST-OPERATIVE COMPLICATIONS NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) | 2 ( 0.5%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Events are included in the period in which they began.

ISTA Pharmaceuticals, Inc.
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Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INJURY AND POISONING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Events are included in the period in which they began.

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Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 166 (83.8%) | 55 (27.8%) | 58 (29.3%) | 67 (33.8%) | 64 (32.3%) | 102 (51.5%) | 98 (49.5%) |
| EYE DISORDERS | 165 (83.3%) | 52 (26.3%) | 55 (27.8%) | 64 (32.3%) | 62 (31.3%) | 97 (49.0%) | 98 (49.5%) |
| IRITIS | 85 (42.9%) | 11 ( 5.6%) | 10 ( 5.1%) | 7 ( 3.5%) | 10 ( 5.1%) | 21 (10.6%) | 21 (10.6%) |
| OCULAR HYPEREMIA | 99 (50.0%) | 3 ( 1.5%) | 4 ( 2.0%) | 6 ( 3.0%) | 4 ( 2.0%) | 15 ( 7.6%) | 17 ( 8.6%) |
| EYE IRRITATION | 45 (22.7%) | 9 ( 4.5%) | 13 ( 6.6%) | 14 ( 7.1%) | 13 ( 6.6%) | 15 ( 7.6%) | 19 ( 9.6%) |
| VISUAL ACUITY REDUCED | 23 (11.6%) | 6 ( 3.0%) | 10 ( 5.1%) | 13 ( 6.6%) | 13 ( 6.6%) | 16 ( 8.1%) | 16 ( 8.1%) |
| EYE PAIN | 33 (16.7%) | 7 ( 3.5%) | 3 ( 1.5%) | 6 ( 3.0%) | 12 ( 6.1%) | 20 (10.1%) | 12 ( 6.1%) |
| VITREOUS HEMORRHAGE | 1 ( 0.5%) | 4 ( 2.0%) | 6 ( 3.0%) | 9 ( 4.5%) | 14 ( 7.1%) | 23 (11.6%) | 25 (12.6%) |
| LACRIMATION INCREASED | 26 (13.1%) | 4 ( 2.0%) | 13 ( 6.6%) | 7 ( 3.5%) | 9 ( 4.5%) | 11 ( 5.6%) | 14 ( 7.1%) |
| VITREOUS FLOATERS | 17 ( 8.6%) | 12 ( 6.1%) | 14 ( 7.1%) | 13 ( 6.6%) | 10 ( 5.1%) | 10 ( 5.1%) | 10 ( 5.1%) |
| ABNORMAL SENSATION IN EYE | 33 (16.7%) | 2 ( 1.0%) | 6 ( 3.0%) | 5 ( 2.5%) | 9 ( 4.5%) | 11 ( 5.6%) | 10 ( 5.1%) |
| PHOTOPHOBIA | 14 ( 7.1%) | 6 ( 3.0%) | 11 ( 5.6%) | 10 ( 5.1%) | 9 ( 4.5%) | 12 ( 6.1%) | 17 ( 8.6%) |
| CONJUNCTIVAL EDEMA | 30 (15.2%) | 2 ( 1.0%) | 3 ( 1.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 4 ( 2.0%) | 11 ( 5.6%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 3 ( 1.5%) | 4 ( 2.0%) | 10 ( 5.1%) | 14 ( 7.1%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 6 ( 3.0%) | 2 ( 1.0%) | 6 ( 3.0%) | 15 ( 7.6%) |
| PHOTOPSIA | 3 ( 1.5%) | 4 ( 2.0%) | 1 ( 0.5%) | 4 ( 2.0%) | 5 ( 2.5%) | 5 ( 2.5%) | 6 ( 3.0%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 4 ( 2.0%) | 8 ( 4.0%) | 8 ( 4.0%) |
| CORNEAL EDEMA | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 6 ( 3.0%) | 9 ( 4.5%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 11 ( 5.6%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 3 ( 1.5%) | 2 ( 1.0%) | 8 ( 4.0%) |
| CATARACT CORTICAL | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) | 3 ( 1.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 5 ( 2.5%) |
| CONJUNCTIVAL HEMORRHAGE | 6 ( 3.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) |
| CORNEAL EROSION | 5 ( 2.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) |
| EYE DISCHARGE | 4 ( 2.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) |
| VISION BLURRED | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 1.0%) | 4 ( 2.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 4 ( 2.0%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 5 ( 2.5%) |
| HYPHEMA | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 2.0%) | 4 ( 2.0%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 5 ( 2.5%) |
| CORNEAL DISORDER NOS | 4 ( 2.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) |
| INTRAOCULAR PRESSURE INCREASED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 1.0%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 2 ( 1.0%) |
| CATARACT NOS AGGRAVATED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 1.0%) |
| KERATITIS NEC | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.5%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| CORNEAL ABRASION | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| INTRAOCULAR PRESSURE DECREASED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| UVEITIS NOS | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| ARCUS SENILIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CHEMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CORNEAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORNEAL ULCER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| EYE INFECTION STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| KERATOPATHY BAND | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| MYDRIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| PAPILLEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL VASCULITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| SCLERITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| STRABISMUS NEC | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION ABNORMAL NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| INVESTIGATIONS | 10 ( 5.1%) | 3 ( 1.5%) | 3 ( 1.5%) | 5 ( 2.5%) | 3 ( 1.5%) | 18 ( 9.1%) | 16 ( 8.1%) |
| INTRAOCULAR PRESSURE INCREASED | 6 ( 3.0%) | 2 ( 1.0%) | 3 ( 1.5%) | 5 ( 2.5%) | 2 ( 1.0%) | 16 ( 8.1%) | 13 ( 6.6%) |
| CORNEAL STAINING | 4 ( 2.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 8 ( 4.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 3 ( 1.5%) | 4 ( 2.0%) | 6 ( 3.0%) | 2 ( 1.0%) |
| EYELID EDEMA | 6 ( 3.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 3 ( 1.5%) | 4 ( 2.0%) | 1 ( 0.5%) |
| ERYTHEMA NEC | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 1 ( 0.5%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| OCULAR HYPEREMIA | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 3 ( 1.5%) | 1 ( 0.5%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 1 ( 0.5%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITH NERVE PARALYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |



Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 277 (73.5%) | 77 (20.4%) | 99 (26.3%) | 88 (23.3%) | 104 (27.6%) | 107 (28.4%) | 122 (32.4%) |
| EYE DISORDERS | 275 (72.9%) | 76 (20.2%) | 99 (26.3%) | 85 (22.5%) | 100 (26.5%) | 102 (27.1%) | 118 (31.3%) |
| IRITIS | 198 (52.5%) | 21 ( 5.6%) | 15 ( 4.0%) | 6 ( 1.6%) | 10 ( 2.7%) | 14 ( 3.7%) | 16 ( 4.2%) |
| OCULAR HYPEREMIA | 182 (48.3%) | 9 ( 2.4%) | 7 ( 1.9%) | 8 ( 2.1%) | 7 ( 1.9%) | 13 ( 3.4%) | 15 ( 4.0%) |
| EYE PAIN | 109 (28.9%) | 7 ( 1.9%) | 11 ( 2.9%) | 8 ( 2.1%) | 12 ( 3.2%) | 17 ( 4.5%) | 13 ( 3.4%) |
| EYE IRRITATION | 76 (20.2%) | 13 ( 3.4%) | 29 ( 7.7%) | 14 ( 3.7%) | 18 ( 4.8%) | 18 ( 4.8%) | 18 ( 4.8%) |
| LACRIMATION INCREASED | 81 (21.5%) | 6 ( 1.6%) | 16 ( 4.2%) | 20 ( 5.3%) | 8 ( 2.1%) | 10 ( 2.7%) | 14 ( 3.7%) |
| ABNORMAL SENSATION IN EYE | 70 (18.6%) | 5 ( 1.3%) | 13 ( 3.4%) | 10 ( 2.7%) | 9 ( 2.4%) | 11 ( 2.9%) | 9 ( 2.4%) |
| VISUAL ACUITY REDUCED | 27 ( 7.2%) | 8 ( 2.1%) | 13 ( 3.4%) | 13 ( 3.4%) | 27 ( 7.2%) | 24 ( 6.4%) | 17 ( 4.5%) |
| CONJUNCTIVAL EDEMA | 85 (22.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 5 ( 1.3%) | 5 ( 1.3%) |
| VITREOUS HEMORRHAGE | 1 ( 0.3%) | 1 ( 0.3%) | 7 ( 1.9%) | 13 ( 3.4%) | 23 ( 6.1%) | 25 ( 6.6%) | 29 ( 7.7%) |
| PHOTOPHOBIA | 42 (11.1%) | 13 ( 3.4%) | 13 ( 3.4%) | 10 ( 2.7%) | 10 ( 2.7%) | 7 ( 1.9%) | 18 ( 4.8%) |
| VITREOUS FLOATERS | 23 ( 6.1%) | 13 ( 3.4%) | 21 ( 5.6%) | 13 ( 3.4%) | 15 ( 4.0%) | 12 ( 3.2%) | 13 ( 3.4%) |
| PHOTOPSIA | 7 ( 1.9%) | 6 ( 1.6%) | 13 ( 3.4%) | 8 ( 2.1%) | 4 ( 1.1%) | 6 ( 1.6%) | 11 ( 2.9%) |
| CATARACT NUCLEAR | 2 ( 0.5%) | 1 ( 0.3%) | 7 ( 1.9%) | 1 ( 0.3%) | 9 ( 2.4%) | 5 ( 1.3%) | 15 ( 4.0%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 1.1%) | 3 ( 0.8%) | 6 ( 1.6%) | 11 ( 2.9%) | 11 ( 2.9%) |
| CATARACT CORTICAL | 3 ( 0.8%) | 0 ( 0.0%) | 4 ( 1.1%) | 1 ( 0.3%) | 6 ( 1.6%) | 5 ( 1.3%) | 14 ( 3.7%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 0.8%) | 5 ( 1.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 12 ( 3.2%) |
| CORNEAL EROSION | 16 ( 4.2%) | 3 ( 0.8%) | 1 ( 0.3%) | 4 ( 1.1%) | 2 ( 0.5%) | 0 ( 0.0%) | 5 ( 1.3%) |
| EYE DISCHARGE | 12 ( 3.2%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 4 ( 1.1%) | 1 ( 0.3%) |
| CORNEAL EDEMA | 4 ( 1.1%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 7 ( 1.9%) |
| CORNEAL DISORDER NOS | 12 ( 3.2%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| RUBEOSIS IRIDIS | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.1%) | 1 ( 0.3%) | 2 ( 0.5%) | 7 ( 1.9%) |
| CONJUNCTIVAL HEMORRHAGE | 9 ( 2.4%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 4 ( 1.1%) | 3 ( 0.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 1.3%) |
| HYPHEMA | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 6 ( 1.6%) |
| MACULAR EDEMA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 6 ( 1.6%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 5 ( 1.3%) |
| UVEITIS NOS | 6 ( 1.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | 4 ( 1.1%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 0.8%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 1 ( 0.3%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| CORNEAL ABRASION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| DIPLOPIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EYE ALLERGY | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OCULAR HYPERTENSION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| PERIORBITAL HEMATOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANISEIKONIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYELID EDEMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INVESTIGATIONS | 10 ( 2.7%) | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) | 5 ( 1.3%) | 16 ( 4.2%) | 16 ( 4.2%) |
| INTRAOCULAR PRESSURE INCREASED | 4 ( 1.1%) | 1 ( 0.3%) | 3 ( 0.8%) | 2 ( 0.5%) | 5 ( 1.3%) | 16 ( 4.2%) | 15 ( 4.0%) |
| CORNEAL STAINING | 6 ( 1.6%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 26 ( 6.9%) | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) | 1 ( 0.3%) | 7 ( 1.9%) | 3 ( 0.8%) |
| EYELID EDEMA | 22 ( 5.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) | 2 ( 0.5%) |
| ERYTHEMA NEC | 11 ( 2.9%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 7 ( 1.9%) | 2 ( 0.5%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PRURITUS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 5 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE IRRITATION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUTURE LINE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PUPILLARY DISORDER NOS | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPERSENSITIVITY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INJURY AND POISONING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEMICAL BURNS OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |



Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 314 (80.3%) | 77 (19.7%) | 102 (26.1%) | 92 (23.5%) | 106 (27.1%) | 129 (33.0%) | 131 (33.5%) |
| EYE DISORDERS | 314 (80.3%) | 75 (19.2%) | 98 (25.1%) | 92 (23.5%) | 104 (26.6%) | 127 (32.5%) | 129 (33.0%) |
| IRITIS | 231 (59.1%) | 24 ( 6.1%) | 13 ( 3.3%) | 7 ( 1.8%) | 9 ( 2.3%) | 17 ( 4.3%) | 14 ( 3.6%) |
| OCULAR HYPEREMIA | 198 (50.6%) | 6 ( 1.5%) | 9 ( 2.3%) | 7 ( 1.8%) | 12 ( 3.1%) | 8 ( 2.0%) | 11 ( 2.8%) |
| EYE PAIN | 111 (28.4%) | 15 ( 3.8%) | 10 ( 2.6%) | 8 ( 2.0%) | 8 ( 2.0%) | 23 ( 5.9%) | 20 ( 5.1%) |
| LACRIMATION INCREASED | 76 (19.4%) | 10 ( 2.6%) | 22 ( 5.6%) | 14 ( 3.6%) | 15 ( 3.8%) | 14 ( 3.6%) | 15 ( 3.8%) |
| EYE IRRITATION | 69 (17.6%) | 20 ( 5.1%) | 24 ( 6.1%) | 20 ( 5.1%) | 17 ( 4.3%) | 17 ( 4.3%) | 21 ( 5.4%) |
| ABNORMAL SENSATION IN EYE | 76 (19.4%) | 14 ( 3.6%) | 13 ( 3.3%) | 9 ( 2.3%) | 10 ( 2.6%) | 15 ( 3.8%) | 10 ( 2.6%) |
| PHOTOPHOBIA | 52 (13.3%) | 13 ( 3.3%) | 10 ( 2.6%) | 11 ( 2.8%) | 16 ( 4.1%) | 11 ( 2.8%) | 15 ( 3.8%) |
| VITREOUS FLOATERS | 28 ( 7.2%) | 13 ( 3.3%) | 27 ( 6.9%) | 18 ( 4.6%) | 17 ( 4.3%) | 21 ( 5.4%) | 19 ( 4.9%) |
| VISUAL ACUITY REDUCED | 31 ( 7.9%) | 12 ( 3.1%) | 11 ( 2.8%) | 13 ( 3.3%) | 24 ( 6.1%) | 18 ( 4.6%) | 23 ( 5.9%) |
| CONJUNCTIVAL EDEMA | 81 (20.7%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 5 ( 1.3%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 2 ( 0.5%) | 6 ( 1.5%) | 8 ( 2.0%) | 10 ( 2.6%) | 32 ( 8.2%) | 40 (10.2%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 5 ( 1.3%) | 9 ( 2.3%) | 19 ( 4.9%) | 16 ( 4.1%) |
| CATARACT SUBCAPSULAR | 4 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 6 ( 1.5%) | 4 ( 1.0%) | 5 ( 1.3%) | 17 ( 4.3%) |
| PHOTOPSIA | 8 ( 2.0%) | 3 ( 0.8%) | 9 ( 2.3%) | 6 ( 1.5%) | 3 ( 0.8%) | 3 ( 0.8%) | 11 ( 2.8%) |
| CATARACT CORTICAL | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 4 ( 1.0%) | 10 ( 2.6%) | 7 ( 1.8%) |
| CATARACT NUCLEAR | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 2 ( 0.5%) | 5 ( 1.3%) | 7 ( 1.8%) | 10 ( 2.6%) |
| IRIS ADHESIONS | 6 ( 1.5%) | 1 ( 0.3%) | 4 ( 1.0%) | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) | 11 ( 2.8%) |
| CORNEAL DISORDER NOS | 17 ( 4.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 1.3%) | 4 ( 1.0%) |
| CORNEAL EDEMA | 19 ( 4.9%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) | 7 ( 1.8%) |
| HYPOPYON | 18 ( 4.6%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE DISCHARGE | 13 ( 3.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) | 9 ( 2.3%) |
| RUBEOSIS IRIDIS | 4 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) | 9 ( 2.3%) |
| CONJUNCTIVAL HEMORRHAGE | 11 ( 2.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| CORNEAL EROSION | 11 ( 2.8%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 0.5%) | 2 ( 0.5%) |
| HYPHEMA | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 6 ( 1.5%) | 5 ( 1.3%) |
| GLAUCOMA NOS | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 6 ( 1.5%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 1.0%) |
| DRY EYE NEC | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 6 ( 1.5%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| HYPOTONY OF EYE | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) | 1 ( 0.3%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 1 ( 0.3%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 4 ( 1.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MYDRIASIS | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UVEITIS NOS | 4 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CONJUNCTIVITIS NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHALAZION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHEMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY BAND | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
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Table 11
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INVESTIGATIONS | 15 ( 3.8%) | 4 ( 1.0%) | 6 ( 1.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 19 ( 4.9%) | 13 ( 3.3%) |
| INTRAOCULAR PRESSURE INCREASED | 12 ( 3.1%) | 2 ( 0.5%) | 4 ( 1.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 18 ( 4.6%) | 12 ( 3.1%) |
| CORNEAL STAINING | 4 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 25 ( 6.4%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) | 3 ( 0.8%) |
| EYELID EDEMA | 17 ( 4.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 2 ( 0.5%) |
| ERYTHEMA NEC | 12 ( 3.1%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| DERMATITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ECCHYMOSIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENS IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NERVOUS SYSTEM DISORDERS | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FACIAL PALSY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEADACHE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Events are included in the period in which they began.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: WW Control (n = 18)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 3 (16.7%) | 2 (11.1%) | 2 (11.1%) | 6 (33.3%) | 3 (16.7%) | 3 (16.7%) | 2 (11.1%) |
| EYE DISORDERS | 3 (16.7%) | 2 (11.1%) | 2 (11.1%) | 6 (33.3%) | 3 (16.7%) | 3 (16.7%) | 2 (11.1%) |
| EYE IRRITATION | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) | 2 (11.1%) | 1 ( 5.6%) | 0 ( 0.0%) |
| PHOTOPHOBIA | 2 (11.1%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS FLOATERS | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 5.6%) | 2 (11.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 5.6%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| LACRIMATION INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL ACUITY REDUCED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS HEMORRHAGE | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Events are included in the period in which they began.

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Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 202 (53.4%) | 49 (13.0%) | 53 (14.0%) | 37 ( 9.8%) | 39 (10.3%) | 50 (13.2%) | 49 (13.0%) |
| EYE DISORDERS | 200 (52.9%) | 49 (13.0%) | 53 (14.0%) | 33 ( 8.7%) | 39 (10.3%) | 48 (12.7%) | 48 (12.7%) |
| OCULAR HYPEREMIA | 106 (28.0%) | 6 ( 1.6%) | 4 ( 1.1%) | 0 ( 0.0%) | 4 ( 1.1%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IRITIS | 83 (22.0%) | 15 ( 4.0%) | 11 ( 2.9%) | 2 ( 0.5%) | 2 ( 0.5%) | 5 ( 1.3%) | 1 ( 0.3%) |
| EYE IRRITATION | 51 (13.5%) | 8 ( 2.1%) | 10 ( 2.6%) | 7 ( 1.9%) | 12 ( 3.2%) | 3 ( 0.8%) | 6 ( 1.6%) |
| EYE PAIN | 45 (11.9%) | 4 ( 1.1%) | 2 ( 0.5%) | 1 ( 0.3%) | 4 ( 1.1%) | 1 ( 0.3%) | 3 ( 0.8%) |
| LACRIMATION INCREASED | 32 ( 8.5%) | 6 ( 1.6%) | 10 ( 2.6%) | 5 ( 1.3%) | 5 ( 1.3%) | 4 ( 1.1%) | 2 ( 0.5%) |
| ABNORMAL SENSATION IN EYE | 37 ( 9.8%) | 3 ( 0.8%) | 4 ( 1.1%) | 5 ( 1.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| CONJUNCTIVAL EDEMA | 45 (11.9%) | 3 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL ACUITY REDUCED | 7 ( 1.9%) | 6 ( 1.6%) | 8 ( 2.1%) | 7 ( 1.9%) | 7 ( 1.9%) | 5 ( 1.3%) | 8 ( 2.1%) |
| PHOTOPHOBIA | 15 ( 4.0%) | 7 ( 1.9%) | 8 ( 2.1%) | 6 ( 1.6%) | 3 ( 0.8%) | 6 ( 1.6%) | 4 ( 1.1%) |
| VITREOUS FLOATERS | 5 ( 1.3%) | 14 ( 3.7%) | 6 ( 1.6%) | 8 ( 2.1%) | 7 ( 1.9%) | 7 ( 1.9%) | 3 ( 0.8%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 4 ( 1.1%) | 11 ( 2.9%) | 7 ( 1.9%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.6%) | 7 ( 1.9%) |
| CATARACT NUCLEAR | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 9 ( 2.4%) |
| CORNEAL EROSION | 11 ( 2.9%) | 3 ( 0.8%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CONJUNCTIVAL HEMORRHAGE | 12 ( 3.2%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PHOTOPSIA | 2 ( 0.5%) | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 0.8%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) |
| EYE DISCHARGE | 11 ( 2.9%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 6 ( 1.6%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CORNEAL EDEMA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| CORNEAL DISORDER NOS | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPHEMA | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRY EYE NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATITIS NEC | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYDRIASIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| PHOTOPHOBIA AGGRAVATED | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UVEITIS NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 12 ( 3.2%) | 4 ( 1.1%) | 1 ( 0.3%) | 5 ( 1.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| INTRAOCULAR PRESSURE INCREASED | 10 ( 2.6%) | 3 ( 0.8%) | 1 ( 0.3%) | 4 ( 1.1%) | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| CORNEAL STAINING | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 12 ( 3.2%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | 7 ( 1.9%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | 5 ( 1.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INJURY AND POISONING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
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Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 147 (74.2%) | 41 (20.7%) | 42 (21.2%) | 48 (24.2%) | 38 (19.2%) | 44 (22.2%) | 40 (20.2%) |
| EYE DISORDERS | 146 (73.7%) | 38 (19.2%) | 39 (19.7%) | 46 (23.2%) | 38 (19.2%) | 42 (21.2%) | 40 (20.2%) |
| IRITIS | 80 (40.4%) | 10 ( 5.1%) | 8 ( 4.0%) | 5 ( 2.5%) | 6 ( 3.0%) | 3 ( 1.5%) | 6 ( 3.0%) |
| OCULAR HYPEREMIA | 78 (39.4%) | 2 ( 1.0%) | 2 ( 1.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 2 ( 1.0%) | 2 ( 1.0%) |
| EYE IRRITATION | 40 (20.2%) | 6 ( 3.0%) | 8 ( 4.0%) | 8 ( 4.0%) | 7 ( 3.5%) | 4 ( 2.0%) | 5 ( 2.5%) |
| EYE PAIN | 29 (14.6%) | 5 ( 2.5%) | 3 ( 1.5%) | 3 ( 1.5%) | 5 ( 2.5%) | 5 ( 2.5%) | 4 ( 2.0%) |
| VISUAL ACUITY REDUCED | 20 (10.1%) | 4 ( 2.0%) | 6 ( 3.0%) | 4 ( 2.0%) | 9 ( 4.5%) | 7 ( 3.5%) | 6 ( 3.0%) |
| LACRIMATION INCREASED | 23 (11.6%) | 3 ( 1.5%) | 9 ( 4.5%) | 7 ( 3.5%) | 6 ( 3.0%) | 4 ( 2.0%) | 4 ( 2.0%) |
| ABNORMAL SENSATION IN EYE | 27 (13.6%) | 0 ( 0.0%) | 3 ( 1.5%) | 4 ( 2.0%) | 5 ( 2.5%) | 5 ( 2.5%) | 5 ( 2.5%) |
| PHOTOPHOBIA | 11 ( 5.6%) | 3 ( 1.5%) | 9 ( 4.5%) | 9 ( 4.5%) | 6 ( 3.0%) | 5 ( 2.5%) | 4 ( 2.0%) |
| VITREOUS FLOATERS | 12 ( 6.1%) | 7 ( 3.5%) | 7 ( 3.5%) | 12 ( 6.1%) | 4 ( 2.0%) | 5 ( 2.5%) | 2 ( 1.0%) |
| VITREOUS HEMORRHAGE | 1 ( 0.5%) | 1 ( 0.5%) | 4 ( 2.0%) | 7 ( 3.5%) | 7 ( 3.5%) | 10 ( 5.1%) | 7 ( 3.5%) |
| CONJUNCTIVAL EDEMA | 25 (12.6%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 6 ( 3.0%) | 9 ( 4.5%) |
| PHOTOPSIA | 3 ( 1.5%) | 4 ( 2.0%) | 1 ( 0.5%) | 4 ( 2.0%) | 4 ( 2.0%) | 3 ( 1.5%) | 3 ( 1.5%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 3 ( 1.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 4 ( 2.0%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 1.0%) | 5 ( 2.5%) | 4 ( 2.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 3 ( 1.5%) |
| CONJUNCTIVAL HEMORRHAGE | 5 ( 2.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EROSION | 4 ( 2.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL DISORDER NOS | 3 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORNEAL EDEMA | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| EYE DISCHARGE | 3 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPHEMA | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.5%) |
| KERATITIS NEC | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| INTRAOCULAR PRESSURE DECREASED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORNEAL ABRASION | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |



Events are included in the period in which they began.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| STRABISMUS NEC | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS NOS | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION BLURRED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| INVESTIGATIONS | 8 ( 4.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 3 ( 1.5%) | 0 ( 0.0%) | 4 ( 2.0%) | 3 ( 1.5%) |
| INTRAOCULAR PRESSURE INCREASED | 5 ( 2.5%) | 2 ( 1.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 0 ( 0.0%) | 4 ( 2.0%) | 2 ( 1.0%) |
| CORNEAL STAINING | 3 ( 1.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 6 ( 3.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| EYELID EDEMA | 5 ( 2.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| ERYTHEMA NEC | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
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Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 259 (68.7%) | 66 (17.5%) | 75 (19.9%) | 60 (15.9%) | 70 (18.6%) | 53 (14.1%) | 52 (13.8%) |
| EYE DISORDERS | 256 (67.9%) | 65 (17.2%) | 75 (19.9%) | 59 (15.6%) | 68 (18.0%) | 52 (13.8%) | 52 (13.8%) |
| IRITIS | 184 (48.8%) | 19 ( 5.0%) | 13 ( 3.4%) | 4 ( 1.1%) | 6 ( 1.6%) | 5 ( 1.3%) | 4 ( 1.1%) |
| OCULAR HYPEREMIA | 150 (39.8%) | 8 ( 2.1%) | 3 ( 0.8%) | 4 ( 1.1%) | 4 ( 1.1%) | 2 ( 0.5%) | 2 ( 0.5%) |
| EYE PAIN | 96 (25.5%) | 6 ( 1.6%) | 8 ( 2.1%) | 5 ( 1.3%) | 9 ( 2.4%) | 7 ( 1.9%) | 3 ( 0.8%) |
| EYE IRRITATION | 64 (17.0%) | 10 ( 2.7%) | 15 ( 4.0%) | 9 ( 2.4%) | 11 ( 2.9%) | 4 ( 1.1%) | 3 ( 0.8%) |
| LACRIMATION INCREASED | 66 (17.5%) | 5 ( 1.3%) | 12 ( 3.2%) | 17 ( 4.5%) | 5 ( 1.3%) | 4 ( 1.1%) | 3 ( 0.8%) |
| ABNORMAL SENSATION IN EYE | 59 (15.6%) | 4 ( 1.1%) | 9 ( 2.4%) | 8 ( 2.1%) | 2 ( 0.5%) | 4 ( 1.1%) | 1 ( 0.3%) |
| CONJUNCTIVAL EDEMA | 69 (18.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) |
| VISUAL ACUITY REDUCED | 23 ( 6.1%) | 5 ( 1.3%) | 13 ( 3.4%) | 8 ( 2.1%) | 16 ( 4.2%) | 12 ( 3.2%) | 6 ( 1.6%) |
| PHOTOPHOBIA | 34 ( 9.0%) | 12 ( 3.2%) | 8 ( 2.1%) | 6 ( 1.6%) | 6 ( 1.6%) | 4 ( 1.1%) | 5 ( 1.3%) |
| VITREOUS FLOATERS | 18 ( 4.8%) | 8 ( 2.1%) | 12 ( 3.2%) | 7 ( 1.9%) | 13 ( 3.4%) | 8 ( 2.1%) | 4 ( 1.1%) |
| VITREOUS HEMORRHAGE | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) | 6 ( 1.6%) | 13 ( 3.4%) | 8 ( 2.1%) | 10 ( 2.7%) |
| PHOTOPSIA | 6 ( 1.6%) | 3 ( 0.8%) | 8 ( 2.1%) | 5 ( 1.3%) | 3 ( 0.8%) | 4 ( 1.1%) | 3 ( 0.8%) |
| CATARACT NUCLEAR | 2 ( 0.5%) | 1 ( 0.3%) | 5 ( 1.3%) | 1 ( 0.3%) | 4 ( 1.1%) | 4 ( 1.1%) | 6 ( 1.6%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 0.5%) | 4 ( 1.1%) | 1 ( 0.3%) | 2 ( 0.5%) | 8 ( 2.1%) |
| CATARACT CORTICAL | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 7 ( 1.9%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 1.1%) | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 1.3%) | 5 ( 1.3%) |
| CORNEAL DISORDER NOS | 11 ( 2.9%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EROSION | 12 ( 3.2%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE DISCHARGE | 10 ( 2.7%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 4 ( 1.1%) | 3 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CORNEAL EDEMA | 3 ( 0.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) |
| CONJUNCTIVAL HEMORRHAGE | 5 ( 1.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | 4 ( 1.1%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPHEMA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| UVEITIS NOS | 4 ( 1.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| DIPLOPIA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

Events are included in the period in which they began.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID EDEMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OCULAR HYPERTENSION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 22 ( 5.8%) | 2 ( 0.5%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| EYELID EDEMA | 18 ( 4.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ERYTHEMA NEC | 10 ( 2.7%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 9 ( 2.4%) | 3 ( 0.8%) | 2 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) | 5 ( 1.3%) | 3 ( 0.8%) |
| INTRAOCULAR PRESSURE INCREASED | 4 ( 1.1%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) | 5 ( 1.3%) | 3 ( 0.8%) |
| CORNEAL STAINING | 5 ( 1.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 5 ( 1.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 302 (77.2%) | 66 (16.9%) | 75 (19.2%) | 63 (16.1%) | 56 (14.3%) | 60 (15.3%) | 49 (12.5%) |
| EYE DISORDERS | 302 (77.2%) | 65 (16.6%) | 73 (18.7%) | 63 (16.1%) | 55 (14.1%) | 58 (14.8%) | 48 (12.3%) |
| IRITIS | 223 (57.0%) | 24 ( 6.1%) | 12 ( 3.1%) | 5 ( 1.3%) | 3 ( 0.8%) | 4 ( 1.0%) | 5 ( 1.3%) |
| OCULAR HYPEREMIA | 174 (44.5%) | 4 ( 1.0%) | 5 ( 1.3%) | 4 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| EYE PAIN | 101 (25.8%) | 13 ( 3.3%) | 7 ( 1.8%) | 2 ( 0.5%) | 4 ( 1.0%) | 7 ( 1.8%) | 3 ( 0.8%) |
| EYE IRRITATION | 61 (15.6%) | 17 ( 4.3%) | 16 ( 4.1%) | 12 ( 3.1%) | 6 ( 1.5%) | 7 ( 1.8%) | 9 ( 2.3%) |
| LACRIMATION INCREASED | 64 (16.4%) | 8 ( 2.0%) | 11 ( 2.8%) | 8 ( 2.0%) | 8 ( 2.0%) | 5 ( 1.3%) | 8 ( 2.0%) |
| ABNORMAL SENSATION IN EYE | 71 (18.2%) | 8 ( 2.0%) | 8 ( 2.0%) | 7 ( 1.8%) | 3 ( 0.8%) | 4 ( 1.0%) | 2 ( 0.5%) |
| PHOTOPHOBIA | 45 (11.5%) | 9 ( 2.3%) | 8 ( 2.0%) | 11 ( 2.8%) | 13 ( 3.3%) | 5 ( 1.3%) | 6 ( 1.5%) |
| CONJUNCTIVAL EDEMA | 74 (18.9%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS FLOATERS | 21 ( 5.4%) | 11 ( 2.8%) | 21 ( 5.4%) | 14 ( 3.6%) | 11 ( 2.8%) | 11 ( 2.8%) | 6 ( 1.5%) |
| VISUAL ACUITY REDUCED | 27 ( 6.9%) | 9 ( 2.3%) | 9 ( 2.3%) | 7 ( 1.8%) | 10 ( 2.6%) | 8 ( 2.0%) | 5 ( 1.3%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 4 ( 1.0%) | 12 ( 3.1%) | 10 ( 2.6%) |
| PHOTOPSIA | 8 ( 2.0%) | 3 ( 0.8%) | 7 ( 1.8%) | 5 ( 1.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 4 ( 1.0%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 1.3%) | 9 ( 2.3%) | 7 ( 1.8%) |
| CORNEAL DISORDER NOS | 17 ( 4.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| HYPOPYON | 18 ( 4.6%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 10 ( 2.6%) | 3 ( 0.8%) |
| IRIS ADHESIONS | 6 ( 1.5%) | 1 ( 0.3%) | 4 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.0%) |
| CATARACT SUBCAPSULAR | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 4 ( 1.0%) | 3 ( 0.8%) | 3 ( 0.8%) | 4 ( 1.0%) |
| CORNEAL EDEMA | 17 ( 4.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE DISCHARGE | 9 ( 2.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORNEAL EROSION | 8 ( 2.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT NUCLEAR | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| RUBEOSIS IRIDIS | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CONJUNCTIVAL HEMORRHAGE | 7 ( 1.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.0%) |
| HYPHEMA | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| GLAUCOMA NOS | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| HYPOTONY OF EYE | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| MYDRIASIS | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UVEITIS NOS | 4 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OCULAR HYPERAEMIA | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 20 ( 5.1%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) |
| EYELID EDEMA | 15 ( 3.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) |
| ERYTHEMA NEC | 10 ( 2.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ECCHYMOSIS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 12 ( 3.1%) | 3 ( 0.8%) | 4 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE INCREASED | 10 ( 2.6%) | 2 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) | 1 ( 0.3%) |
| CORNEAL STAINING | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEADACHE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Events are included in the period in which they began.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 12
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |



Events are included in the period in which they began.

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Integrated Summary of Safety

Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: WW Control (n = 18)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 6 (33.3%) | 7 (38.9%) | 9 (50.0%) | 14 (77.8%) | 16 (88.9%) | 13 (72.2%) | 14 (77.8%) |
| EYE DISORDERS | 6 (33.3%) | 7 (38.9%) | 9 (50.0%) | 14 (77.8%) | 16 (88.9%) | 13 (72.2%) | 13 (72.2%) |
| EYE IRRITATION | 1 ( 5.6%) | 1 ( 5.6%) | 3 (16.7%) | 3 (16.7%) | 4 (22.2%) | 9 (50.0%) | 7 (38.9%) |
| PHOTOPHOBIA | 3 (16.7%) | 3 (16.7%) | 4 (22.2%) | 3 (16.7%) | 2 (11.1%) | 3 (16.7%) | 1 ( 5.6%) |
| VITREOUS FLOATERS | 1 ( 5.6%) | 1 ( 5.6%) | 3 (16.7%) | 6 (33.3%) | 6 (33.3%) | 2 (11.1%) | 1 ( 5.6%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 2 (11.1%) | 3 (16.7%) | 3 (16.7%) | 4 (22.2%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 5 (27.8%) |
| IRITIS | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 3 (16.7%) | 3 (16.7%) | 3 (16.7%) | 2 (11.1%) |
| LACRIMATION INCREASED | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 3 (16.7%) | 3 (16.7%) | 2 (11.1%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 2 (11.1%) | 1 ( 5.6%) | 2 (11.1%) | 2 (11.1%) |
| VISUAL ACUITY REDUCED | 2 (11.1%) | 2 (11.1%) | 2 (11.1%) | 4 (22.2%) | 4 (22.2%) | 3 (16.7%) | 2 (11.1%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 (16.7%) | 0 ( 0.0%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0.0%) | 0 ( 0.0%) | 2 (11.1%) | 2 (11.1%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) |
| EYE PAIN | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) |
| VITREOUS HEMORRHAGE | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| CONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| CORNEAL EROSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| UVEITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| INVESTIGATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 3 (16.7%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 3 (16.7%) |
| SURGICAL AND MEDICAL PROCEDURES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |

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Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 240 (63.5%) | 248 (65.6%) | 206 (54.5%) | 162 (42.9%) | 163 (43.1%) | 181 (47.9%) | 162 (42.9%) |
| EYE DISORDERS | 237 (62.7%) | 245 (64.8%) | 204 (54.0%) | 160 (42.3%) | 162 (42.9%) | 177 (46.8%) | 161 (42.6%) |
| OCULAR HYPEREMIA | 123 (32.5%) | 127 (33.6%) | 72 (19.0%) | 22 ( 5.8%) | 13 ( 3.4%) | 20 ( 5.3%) | 22 ( 5.8%) |
| IRITIS | 89 (23.5%) | 104 (27.5%) | 72 (19.0%) | 31 ( 8.2%) | 23 ( 6.1%) | 32 ( 8.5%) | 22 ( 5.8%) |
| EYE IRRITATION | 63 (16.7%) | 67 (17.7%) | 53 (14.0%) | 38 (10.1%) | 43 (11.4%) | 50 (13.2%) | 37 ( 9.8%) |
| LACRIMATION INCREASED | 39 (10.3%) | 45 (11.9%) | 34 ( 9.0%) | 31 ( 8.2%) | 30 ( 7.9%) | 32 ( 8.5%) | 22 ( 5.8%) |
| EYE PAIN | 52 (13.8%) | 56 (14.8%) | 31 ( 8.2%) | 12 ( 3.2%) | 18 ( 4.8%) | 32 ( 8.5%) | 24 ( 6.3%) |
| VISUAL ACUITY REDUCED | 9 ( 2.4%) | 16 ( 4.2%) | 21 ( 5.6%) | 25 ( 6.6%) | 39 (10.3%) | 38 (10.1%) | 37 ( 9.8%) |
| ABNORMAL SENSATION IN EYE | 45 (11.9%) | 46 (12.2%) | 28 ( 7.4%) | 17 ( 4.5%) | 14 ( 3.7%) | 19 ( 5.0%) | 18 ( 4.8%) |
| VITREOUS FLOATERS | 9 ( 2.4%) | 25 ( 6.6%) | 30 ( 7.9%) | 31 ( 8.2%) | 38 (10.1%) | 42 (11.1%) | 33 ( 8.7%) |
| VITREOUS HEMORRHAGE | 2 ( 0.5%) | 3 ( 0.8%) | 6 ( 1.6%) | 14 ( 3.7%) | 25 ( 6.6%) | 39 (10.3%) | 41 (10.8%) |
| PHOTOPHOBIA | 18 ( 4.8%) | 26 ( 6.9%) | 29 ( 7.7%) | 30 ( 7.9%) | 30 ( 7.9%) | 34 ( 9.0%) | 32 ( 8.5%) |
| CONJUNCTIVAL EDEMA | 48 (12.7%) | 51 (13.5%) | 23 ( 6.1%) | 9 ( 2.4%) | 5 ( 1.3%) | 6 ( 1.6%) | 8 ( 2.1%) |
| CATARACT NUCLEAR | 1 ( 0.3%) | 1 ( 0.3%) | 5 ( 1.3%) | 8 ( 2.1%) | 10 ( 2.6%) | 16 ( 4.2%) | 30 ( 7.9%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 1.3%) | 6 ( 1.6%) | 7 ( 1.9%) | 15 ( 4.0%) | 21 ( 5.6%) |
| CATARACT SUBCAPSULAR | 1 ( 0.3%) | 2 ( 0.5%) | 4 ( 1.1%) | 6 ( 1.6%) | 8 ( 2.1%) | 10 ( 2.6%) | 23 ( 6.1%) |
| RETINAL DETACHMENT | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 6 ( 1.6%) | 10 ( 2.6%) | 11 ( 2.9%) | 15 ( 4.0%) |
| CONJUNCTIVAL HEMORRHAGE | 19 ( 5.0%) | 20 ( 5.3%) | 15 ( 4.0%) | 6 ( 1.6%) | 1 ( 0.3%) | 3 ( 0.8%) | 2 ( 0.5%) |
| CORNEAL EROSION | 14 ( 3.7%) | 18 ( 4.8%) | 10 ( 2.6%) | 6 ( 1.6%) | 3 ( 0.8%) | 5 ( 1.3%) | 5 ( 1.3%) |
| PHOTOPSIA | 2 ( 0.5%) | 2 ( 0.5%) | 6 ( 1.6%) | 8 ( 2.1%) | 7 ( 1.9%) | 9 ( 2.4%) | 13 ( 3.4%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 5 ( 1.3%) | 14 ( 3.7%) |
| EYE DISCHARGE | 13 ( 3.4%) | 14 ( 3.7%) | 5 ( 1.3%) | 3 ( 0.8%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| CATARACT NEC | 4 ( 1.1%) | 4 ( 1.1%) | 5 ( 1.3%) | 5 ( 1.3%) | 6 ( 1.6%) | 7 ( 1.9%) | 9 ( 2.4%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 12 ( 3.2%) |
| CORNEAL EDEMA | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 6 ( 1.6%) | 6 ( 1.6%) |
| MACULAR EDEMA | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) | 11 ( 2.9%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 5 ( 1.3%) | 5 ( 1.3%) |
| CORNEAL DISORDER NOS | 1 ( 0.3%) | 3 ( 0.8%) | 4 ( 1.1%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) |
| DRY EYE NEC | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) | 3 ( 0.8%) |
| HYPHEMA | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.1%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 5 ( 1.3%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 5 ( 1.3%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| KERATITIS NEC | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 2 ( 0.5%) |
| INTRAOCULAR PRESSURE DECREASED | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| MYDRIASIS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) |
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| UVEITIS NOS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CHEMOSIS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EXOPHTHALMOS ENDOCRINE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EYE HEMORRHAGE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INFECTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| IRIS NEVUS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| KERATOCONJUNCTIVITIS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPTIC NERVE INJURY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL EXUDATES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INVESTIGATIONS | 15 ( 4.0%) | 14 ( 3.7%) | 10 ( 2.6%) | 10 ( 2.6%) | 8 ( 2.1%) | 18 ( 4.8%) | 17 ( 4.5%) |
| INTRAOCULAR PRESSURE INCREASED | 12 ( 3.2%) | 10 ( 2.6%) | 9 ( 2.4%) | 8 ( 2.1%) | 7 ( 1.9%) | 16 ( 4.2%) | 17 ( 4.5%) |
| CORNEAL STAINING | 3 ( 0.8%) | 4 ( 1.1%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 14 ( 3.7%) | 16 ( 4.2%) | 10 ( 2.6%) | 5 ( 1.3%) | 3 ( 0.8%) | 5 ( 1.3%) | 4 ( 1.1%) |
| ERYTHEMA NEC | 9 ( 2.4%) | 10 ( 2.6%) | 6 ( 1.6%) | 5 ( 1.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EYELID EDEMA | 7 ( 1.9%) | 9 ( 2.4%) | 6 ( 1.6%) | 2 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.1%) | 4 ( 1.1%) |
| OCULAR HYPEREMIA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SURGICAL AND MEDICAL PROCEDURES | 3 ( 0.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 8 ( 2.1%) | 3 ( 0.8%) |
| POST-OPERATIVE COMPLICATIONS NOS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) | 3 ( 0.8%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INJURY AND POISONING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| INTRAOCULAR MELANOMA NOS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 168 (84.8%) | 174 (87.9%) | 153 (77.3%) | 141 (71.2%) | 140 (70.7%) | 151 (76.3%) | 124 (62.6%) |
| EYE DISORDERS | 167 (84.3%) | 173 (87.4%) | 152 (76.8%) | 138 (69.7%) | 136 (68.7%) | 148 (74.7%) | 122 (61.6%) |
| IRITIS | 85 (42.9%) | 93 (47.0%) | 67 (33.8%) | 33 (16.7%) | 27 (13.6%) | 38 (19.2%) | 32 (16.2%) |
| OCULAR HYPEREMIA | 99 (50.0%) | 97 (49.0%) | 61 (30.8%) | 20 (10.1%) | 12 ( 6.1%) | 20 (10.1%) | 22 (11.1%) |
| EYE IRRITATION | 46 (23.2%) | 48 (24.2%) | 44 (22.2%) | 35 (17.7%) | 36 (18.2%) | 40 (20.2%) | 36 (18.2%) |
| VISUAL ACUITY REDUCED | 23 (11.6%) | 29 (14.6%) | 30 (15.2%) | 34 (17.2%) | 41 (20.7%) | 49 (24.7%) | 33 (16.7%) |
| EYE PAIN | 33 (16.7%) | 36 (18.2%) | 26 (13.1%) | 15 ( 7.6%) | 20 (10.1%) | 32 (16.2%) | 21 (10.6%) |
| VITREOUS HEMORRHAGE | 2 ( 1.0%) | 5 ( 2.5%) | 11 ( 5.6%) | 19 ( 9.6%) | 30 (15.2%) | 48 (24.2%) | 39 (19.7%) |
| LACRIMATION INCREASED | 26 (13.1%) | 27 (13.6%) | 28 (14.1%) | 25 (12.6%) | 24 (12.1%) | 26 (13.1%) | 22 (11.1%) |
| VITREOUS FLOATERS | 18 ( 9.1%) | 29 (14.6%) | 40 (20.2%) | 47 (23.7%) | 42 (21.2%) | 35 (17.7%) | 32 (16.2%) |
| ABNORMAL SENSATION IN EYE | 33 (16.7%) | 30 (15.2%) | 21 (10.6%) | 13 ( 6.6%) | 17 ( 8.6%) | 23 (11.6%) | 23 (11.6%) |
| PHOTOPHOBIA | 14 ( 7.1%) | 18 ( 9.1%) | 25 (12.6%) | 28 (14.1%) | 31 (15.7%) | 36 (18.2%) | 36 (18.2%) |
| CONJUNCTIVAL EDEMA | 30 (15.2%) | 30 (15.2%) | 13 ( 6.6%) | 4 ( 2.0%) | 5 ( 2.5%) | 7 ( 3.5%) | 12 ( 6.1%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 6 ( 3.0%) | 9 ( 4.5%) | 19 ( 9.6%) | 28 (14.1%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 9 ( 4.5%) | 11 ( 5.6%) | 16 ( 8.1%) | 23 (11.6%) |
| PHOTOPSIA | 3 ( 1.5%) | 7 ( 3.5%) | 7 ( 3.5%) | 7 ( 3.5%) | 11 ( 5.6%) | 14 ( 7.1%) | 13 ( 6.6%) |
| RETINAL DETACHMENT | 1 ( 0.5%) | 1 ( 0.5%) | 3 ( 1.5%) | 3 ( 1.5%) | 5 ( 2.5%) | 12 ( 6.1%) | 13 ( 6.6%) |
| CORNEAL EDEMA | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 9 ( 4.5%) | 10 ( 5.1%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 3 ( 1.5%) | 6 ( 3.0%) | 16 ( 8.1%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 6 ( 3.0%) | 7 ( 3.5%) | 9 ( 4.5%) | 14 ( 7.1%) |
| CATARACT CORTICAL | 1 ( 0.5%) | 2 ( 1.0%) | 4 ( 2.0%) | 7 ( 3.5%) | 7 ( 3.5%) | 8 ( 4.0%) | 9 ( 4.5%) |
| CONJUNCTIVAL HEMORRHAGE | 6 ( 3.0%) | 6 ( 3.0%) | 3 ( 1.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 3 ( 1.5%) | 2 ( 1.0%) |
| CORNEAL EROSION | 5 ( 2.5%) | 5 ( 2.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 3 ( 1.5%) |
| EYE DISCHARGE | 4 ( 2.0%) | 5 ( 2.5%) | 3 ( 1.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) | 4 ( 2.0%) |
| VISION BLURRED | 1 ( 0.5%) | 2 ( 1.0%) | 3 ( 1.5%) | 3 ( 1.5%) | 3 ( 1.5%) | 2 ( 1.0%) | 6 ( 3.0%) |
| BLINDNESS NEC | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 8 ( 4.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 4 ( 2.0%) | 3 ( 1.5%) | 4 ( 2.0%) | 7 ( 3.5%) |
| HYPHEMA | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 4 ( 2.0%) | 6 ( 3.0%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 6 ( 3.0%) |
| CORNEAL DISORDER NOS | 4 ( 2.0%) | 4 ( 2.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 3 ( 1.5%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 3 ( 1.5%) |
| INTRAOCULAR PRESSURE INCREASED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 4 ( 2.0%) | 3 ( 1.5%) |
| CATARACT NOS AGGRAVATED | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 4 ( 2.0%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.5%) | 2 ( 1.0%) |
| KERATITIS NEC | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 4 ( 2.0%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| DIPLOPIA | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 3 ( 1.5%) | 2 ( 1.0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 1 ( 0.5%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 2 ( 1.0%) |
| CORNEAL ABRASION | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| INTRAOCULAR PRESSURE DECREASED | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) |
| UVEITIS NOS | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| ARCUS SENILIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CHEMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CORNEAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORNEAL ULCER NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| EYE INFECTION STAPHYLOCOCCAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| KERATOCONJUNCTIVITIS | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| KERATOPATHY BAND | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| MYDRIASIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| PAPILLEDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| PSEUDOPHAKIA | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL VASCULITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| SCLERITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| STRABISMUS NEC | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION ABNORMAL NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| INVESTIGATIONS | 10 ( 5.1%) | 10 ( 5.1%) | 9 ( 4.5%) | 12 ( 6.1%) | 10 ( 5.1%) | 24 (12.1%) | 24 (12.1%) |
| INTRAOCULAR PRESSURE INCREASED | 6 ( 3.0%) | 5 ( 2.5%) | 6 ( 3.0%) | 11 ( 5.6%) | 8 ( 4.0%) | 21 (10.6%) | 20 (10.1%) |
| CORNEAL STAINING | 4 ( 2.0%) | 5 ( 2.5%) | 3 ( 1.5%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 3 ( 1.5%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 8 ( 4.0%) | 8 ( 4.0%) | 7 ( 3.5%) | 4 ( 2.0%) | 7 ( 3.5%) | 9 ( 4.5%) | 7 ( 3.5%) |
| EYELID EDEMA | 6 ( 3.0%) | 5 ( 2.5%) | 4 ( 2.0%) | 3 ( 1.5%) | 5 ( 2.5%) | 6 ( 3.0%) | 2 ( 1.0%) |
| ERYTHEMA NEC | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 5 ( 2.5%) | 4 ( 2.0%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) |
| OCULAR HYPEREMIA | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 3 ( 1.5%) | 2 ( 1.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 2 ( 1.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 3 ( 1.5%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITH NERVE PARALYSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| IMMUNE SYSTEM DISORDERS | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) |
| HYPERSENSITIVITY NOS | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| MULTIPLE ALLERGIES | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |



Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 283 (75.1%) | 289 (76.7%) | 251 (66.6%) | 215 (57.0%) | 209 (55.4%) | 208 (55.2%) | 171 (45.4%) |
| EYE DISORDERS | 281 (74.5%) | 287 (76.1%) | 251 (66.6%) | 214 (56.8%) | 207 (54.9%) | 206 (54.6%) | 169 (44.8%) |
| IRITIS | 198 (52.5%) | 208 (55.2%) | 140 (37.1%) | 59 (15.6%) | 35 ( 9.3%) | 32 ( 8.5%) | 27 ( 7.2%) |
| OCULAR HYPEREMIA | 182 (48.3%) | 187 (49.6%) | 100 (26.5%) | 39 (10.3%) | 22 ( 5.8%) | 25 ( 6.6%) | 23 ( 6.1%) |
| EYE PAIN | 110 (29.2%) | 108 (28.6%) | 65 (17.2%) | 30 ( 8.0%) | 25 ( 6.6%) | 29 ( 7.7%) | 26 ( 6.9%) |
| EYE IRRITATION | 78 (20.7%) | 84 (22.3%) | 80 (21.2%) | 59 (15.6%) | 48 (12.7%) | 47 (12.5%) | 36 ( 9.5%) |
| LACRIMATION INCREASED | 83 (22.0%) | 85 (22.5%) | 63 (16.7%) | 48 (12.7%) | 45 (11.9%) | 36 ( 9.5%) | 33 ( 8.8%) |
| VISUAL ACUITY REDUCED | 29 ( 7.7%) | 36 ( 9.5%) | 35 ( 9.3%) | 38 (10.1%) | 52 (13.8%) | 61 (16.2%) | 48 (12.7%) |
| ABNORMAL SENSATION IN EYE | 71 (18.8%) | 74 (19.6%) | 50 (13.3%) | 33 ( 8.8%) | 28 ( 7.4%) | 33 ( 8.8%) | 23 ( 6.1%) |
| CONJUNCTIVAL EDEMA | 85 (22.5%) | 87 (23.1%) | 37 ( 9.8%) | 9 ( 2.4%) | 9 ( 2.4%) | 8 ( 2.1%) | 9 ( 2.4%) |
| VITREOUS HEMORRHAGE | 5 ( 1.3%) | 6 ( 1.6%) | 12 ( 3.2%) | 24 ( 6.4%) | 43 (11.4%) | 59 (15.6%) | 52 (13.8%) |
| VITREOUS FLOATERS | 26 ( 6.9%) | 37 ( 9.8%) | 49 (13.0%) | 52 (13.8%) | 55 (14.6%) | 49 (13.0%) | 41 (10.9%) |
| PHOTOPHOBIA | 43 (11.4%) | 53 (14.1%) | 48 (12.7%) | 43 (11.4%) | 37 ( 9.8%) | 34 ( 9.0%) | 37 ( 9.8%) |
| PHOTOPSIA | 8 ( 2.1%) | 14 ( 3.7%) | 24 ( 6.4%) | 25 ( 6.6%) | 21 ( 5.6%) | 21 ( 5.6%) | 22 ( 5.8%) |
| CATARACT NUCLEAR | 2 ( 0.5%) | 3 ( 0.8%) | 9 ( 2.4%) | 10 ( 2.7%) | 19 ( 5.0%) | 20 ( 5.3%) | 25 ( 6.6%) |
| RETINAL DETACHMENT | 1 ( 0.3%) | 4 ( 1.1%) | 8 ( 2.1%) | 7 ( 1.9%) | 10 ( 2.7%) | 18 ( 4.8%) | 15 ( 4.0%) |
| CATARACT CORTICAL | 4 ( 1.1%) | 4 ( 1.1%) | 8 ( 2.1%) | 9 ( 2.4%) | 12 ( 3.2%) | 16 ( 4.2%) | 22 ( 5.8%) |
| CATARACT SUBCAPSULAR | 1 ( 0.3%) | 5 ( 1.3%) | 8 ( 2.1%) | 13 ( 3.4%) | 13 ( 3.4%) | 15 ( 4.0%) | 24 ( 6.4%) |
| CORNEAL EROSION | 16 ( 4.2%) | 18 ( 4.8%) | 12 ( 3.2%) | 11 ( 2.9%) | 7 ( 1.9%) | 2 ( 0.5%) | 6 ( 1.6%) |
| EYE DISCHARGE | 13 ( 3.4%) | 14 ( 3.7%) | 4 ( 1.1%) | 3 ( 0.8%) | 5 ( 1.3%) | 8 ( 2.1%) | 5 ( 1.3%) |
| CORNEAL EDEMA | 4 ( 1.1%) | 5 ( 1.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 4 ( 1.1%) | 7 ( 1.9%) | 10 ( 2.7%) |
| CORNEAL DISORDER NOS | 12 ( 3.2%) | 15 ( 4.0%) | 7 ( 1.9%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| RUBEOSIS IRIDIS | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 7 ( 1.9%) | 7 ( 1.9%) | 6 ( 1.6%) | 12 ( 3.2%) |
| CONJUNCTIVAL HEMORRHAGE | 9 ( 2.4%) | 10 ( 2.7%) | 10 ( 2.7%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 4 ( 1.1%) | 7 ( 1.9%) | 4 ( 1.1%) | 4 ( 1.1%) | 3 ( 0.8%) | 4 ( 1.1%) | 6 ( 1.6%) |
| HYPHEMA | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 8 ( 2.1%) |
| MACULAR EDEMA | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 6 ( 1.6%) | 11 ( 2.9%) |
| CATARACT NEC | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) | 4 ( 1.1%) | 3 ( 0.8%) | 8 ( 2.1%) |
| VITREOUS DETACHMENT | 1 ( 0.3%) | 2 ( 0.5%) | 4 ( 1.1%) | 5 ( 1.3%) | 7 ( 1.9%) | 6 ( 1.6%) | 7 ( 1.9%) |
| CATARACT NOS AGGRAVATED | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.1%) | 6 ( 1.6%) |
| UVEITIS NOS | 6 ( 1.6%) | 6 ( 1.6%) | 3 ( 0.8%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLINDNESS NEC | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 5 ( 1.3%) |
| DRY EYE NEC | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 2 ( 0.5%) | 3 ( 0.8%) | 5 ( 1.3%) |
| HYPOPYON | 4 ( 1.1%) | 6 ( 1.6%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| RETINAL HEMORRHAGE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) |
| RETINAL TEAR (EXC DETACHMENT) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 0 ( 0.0%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 1.1%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) |
| DIPLOPIA | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |



Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| EYE ALLERGY | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| OPTIC ATROPHY | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| HYPOTONY OF EYE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| OCULAR HYPERTENSION | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERIORBITAL HEMATOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANISEIKONIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ERYTHEMA NEC | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYELID EDEMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| INVESTIGATIONS | 11 ( 2.9%) | 12 ( 3.2%) | 11 ( 2.9%) | 10 ( 2.7%) | 9 ( 2.4%) | 22 ( 5.8%) | 26 ( 6.9%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| INTRAOCULAR PRESSURE INCREASED | 5 ( 1.3%) | 5 ( 1.3%) | 7 ( 1.9%) | 7 ( 1.9%) | 8 ( 2.1%) | 21 ( 5.6%) | 25 ( 6.6%) |
| CORNEAL STAINING | 6 ( 1.6%) | 7 ( 1.9%) | 4 ( 1.1%) | 4 ( 1.1%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 26 ( 6.9%) | 28 ( 7.4%) | 15 ( 4.0%) | 5 ( 1.3%) | 3 ( 0.8%) | 9 ( 2.4%) | 8 ( 2.1%) |
| EYELID EDEMA | 22 ( 5.8%) | 23 ( 6.1%) | 8 ( 2.1%) | 2 ( 0.5%) | 2 ( 0.5%) | 6 ( 1.6%) | 7 ( 1.9%) |
| ERYTHEMA NEC | 11 ( 2.9%) | 12 ( 3.2%) | 6 ( 1.6%) | 2 ( 0.5%) | 1 ( 0.3%) | 7 ( 1.9%) | 6 ( 1.6%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PRURITUS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 5 ( 1.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 5 ( 1.3%) | 3 ( 0.8%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) | 2 ( 0.5%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 3 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE IRRITATION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUTURE LINE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |
| PUPILLARY DISORDER NOS | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPERSENSITIVITY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INJURY AND POISONING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHEMICAL BURNS OF EYE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |

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Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 319 (81.6%) | 329 (84.1%) | 265 (67.8%) | 212 (54.2%) | 224 (57.3%) | 219 (56.0%) | 201 (51.4%) |
| EYE DISORDERS | 319 (81.6%) | 328 (83.9%) | 263 (67.3%) | 209 (53.5%) | 220 (56.3%) | 218 (55.8%) | 199 (50.9%) |
| IRITIS | 232 (59.3%) | 235 (60.1%) | 147 (37.6%) | 55 (14.1%) | 30 ( 7.7%) | 30 ( 7.7%) | 28 ( 7.2%) |
| OCULAR HYPEREMIA | 199 (50.9%) | 200 (51.2%) | 97 (24.8%) | 36 ( 9.2%) | 21 ( 5.4%) | 21 ( 5.4%) | 26 ( 6.6%) |
| EYE PAIN | 114 (29.2%) | 116 (29.7%) | 66 (16.9%) | 38 ( 9.7%) | 31 ( 7.9%) | 43 (11.0%) | 33 ( 8.4%) |
| LACRIMATION INCREASED | 78 (19.9%) | 81 (20.7%) | 62 (15.9%) | 51 (13.0%) | 48 (12.3%) | 48 (12.3%) | 36 ( 9.2%) |
| EYE IRRITATION | 71 (18.2%) | 85 (21.7%) | 67 (17.1%) | 59 (15.1%) | 56 (14.3%) | 53 (13.6%) | 43 (11.0%) |
| ABNORMAL SENSATION IN EYE | 76 (19.4%) | 80 (20.5%) | 59 (15.1%) | 38 ( 9.7%) | 28 ( 7.2%) | 36 ( 9.2%) | 31 ( 7.9%) |
| PHOTOPHOBIA | 53 (13.6%) | 63 (16.1%) | 49 (12.5%) | 35 ( 9.0%) | 42 (10.7%) | 39 (10.0%) | 33 ( 8.4%) |
| VITREOUS FLOATERS | 30 ( 7.7%) | 43 (11.0%) | 56 (14.3%) | 54 (13.8%) | 51 (13.0%) | 55 (14.1%) | 46 (11.8%) |
| VISUAL ACUITY REDUCED | 34 ( 8.7%) | 42 (10.7%) | 40 (10.2%) | 41 (10.5%) | 52 (13.3%) | 57 (14.6%) | 46 (11.8%) |
| VITREOUS HEMORRHAGE | 5 ( 1.3%) | 7 ( 1.8%) | 12 ( 3.1%) | 19 ( 4.9%) | 26 ( 6.6%) | 55 (14.1%) | 62 (15.9%) |
| CONJUNCTIVAL EDEMA | 81 (20.7%) | 83 (21.2%) | 32 ( 8.2%) | 6 ( 1.5%) | 3 ( 0.8%) | 6 ( 1.5%) | 11 ( 2.8%) |
| RETINAL DETACHMENT | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 8 ( 2.0%) | 15 ( 3.8%) | 28 ( 7.2%) | 26 ( 6.6%) |
| CATARACT SUBCAPSULAR | 4 ( 1.0%) | 5 ( 1.3%) | 6 ( 1.5%) | 11 ( 2.8%) | 15 ( 3.8%) | 19 ( 4.9%) | 29 ( 7.4%) |
| PHOTOPSIA | 8 ( 2.0%) | 8 ( 2.0%) | 12 ( 3.1%) | 14 ( 3.6%) | 15 ( 3.8%) | 16 ( 4.1%) | 21 ( 5.4%) |
| CATARACT CORTICAL | 3 ( 0.8%) | 4 ( 1.0%) | 6 ( 1.5%) | 11 ( 2.8%) | 15 ( 3.8%) | 23 ( 5.9%) | 25 ( 6.4%) |
| CATARACT NUCLEAR | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 6 ( 1.5%) | 11 ( 2.8%) | 16 ( 4.1%) | 23 ( 5.9%) |
| IRIS ADHESIONS | 6 ( 1.5%) | 7 ( 1.8%) | 9 ( 2.3%) | 11 ( 2.8%) | 11 ( 2.8%) | 12 ( 3.1%) | 16 ( 4.1%) |
| CORNEAL DISORDER NOS | 18 ( 4.6%) | 18 ( 4.6%) | 8 ( 2.0%) | 4 ( 1.0%) | 3 ( 0.8%) | 6 ( 1.5%) | 8 ( 2.0%) |
| CORNEAL EDEMA | 20 ( 5.1%) | 20 ( 5.1%) | 3 ( 0.8%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 9 ( 2.3%) |
| HYPOPYON | 18 ( 4.6%) | 20 ( 5.1%) | 4 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE DISCHARGE | 13 ( 3.3%) | 15 ( 3.8%) | 9 ( 2.3%) | 4 ( 1.0%) | 4 ( 1.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 1.3%) | 8 ( 2.0%) | 11 ( 2.8%) | 15 ( 3.8%) |
| RUBEOSIS IRIDIS | 4 ( 1.0%) | 4 ( 1.0%) | 4 ( 1.0%) | 5 ( 1.3%) | 7 ( 1.8%) | 5 ( 1.3%) | 11 ( 2.8%) |
| CONJUNCTIVAL HEMORRHAGE | 11 ( 2.8%) | 10 ( 2.6%) | 6 ( 1.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 4 ( 1.0%) | 2 ( 0.5%) |
| CORNEAL EROSION | 11 ( 2.8%) | 12 ( 3.1%) | 10 ( 2.6%) | 3 ( 0.8%) | 6 ( 1.5%) | 6 ( 1.5%) | 5 ( 1.3%) |
| HYPHEMA | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 8 ( 2.0%) | 9 ( 2.3%) |
| GLAUCOMA NOS | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 1 ( 0.3%) | 4 ( 1.0%) | 7 ( 1.8%) | 6 ( 1.5%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 9 ( 2.3%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) | 6 ( 1.5%) |
| DRY EYE NEC | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 8 ( 2.0%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 6 ( 1.5%) |
| HYPOTONY OF EYE | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 4 ( 1.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 1.3%) | 3 ( 0.8%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 4 ( 1.0%) |
| CATARACT NOS AGGRAVATED | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) | 4 ( 1.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 4 ( 1.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) | 3 ( 0.8%) | 4 ( 1.0%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| MYDRIASIS | 2 ( 0.5%) | 3 ( 0.8%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UVEITIS NOS | 4 ( 1.0%) | 4 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.0%) |
| CONJUNCTIVITIS NEC | 2 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHALAZION | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHEMOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY BAND | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| OCULAR HYPERAEMIA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |



Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 13
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| INVESTIGATIONS | 16 ( 4.1%) | 15 ( 3.8%) | 13 ( 3.3%) | 9 ( 2.3%) | 8 ( 2.0%) | 22 ( 5.6%) | 24 ( 6.1%) |
| INTRAOCULAR PRESSURE INCREASED | 13 ( 3.3%) | 10 ( 2.6%) | 8 ( 2.0%) | 7 ( 1.8%) | 7 ( 1.8%) | 21 ( 5.4%) | 24 ( 6.1%) |
| CORNEAL STAINING | 4 ( 1.0%) | 6 ( 1.5%) | 5 ( 1.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 25 ( 6.4%) | 25 ( 6.4%) | 12 ( 3.1%) | 5 ( 1.3%) | 5 ( 1.3%) | 6 ( 1.5%) | 6 ( 1.5%) |
| EYELID EDEMA | 17 ( 4.3%) | 16 ( 4.1%) | 5 ( 1.3%) | 2 ( 0.5%) | 4 ( 1.0%) | 5 ( 1.3%) | 5 ( 1.3%) |
| ERYTHEMA NEC | 12 ( 3.1%) | 13 ( 3.3%) | 7 ( 1.8%) | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) |
| DERMATITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| ECCHYMOSIS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 4 ( 1.0%) | 3 ( 0.8%) | 3 ( 0.8%) |
| PUPILLARY DISORDER NOS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| FACIAL PALSY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| HEADACHE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| LENS IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: WW Control (n = 18)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 3 (16.7%) | 4 (22.2%) | 5 (27.8%) | 7 (38.9%) | 9 (50.0%) | 10 (55.6%) | 7 (38.9%) |
| EYE DISORDERS | 3 (16.7%) | 4 (22.2%) | 5 (27.8%) | 7 (38.9%) | 9 (50.0%) | 10 (55.6%) | 7 (38.9%) |
| EYE IRRITATION | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 2 (11.1%) | 3 (16.7%) | 4 (22.2%) | 3 (16.7%) |
| PHOTOPHOBIA | 2 (11.1%) | 2 (11.1%) | 3 (16.7%) | 3 (16.7%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| VITREOUS FLOATERS | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 3 (16.7%) | 3 (16.7%) | 2 (11.1%) | 1 ( 5.6%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) |
| VISUAL ACUITY REDUCED | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 2 (11.1%) | 2 (11.1%) | 2 (11.1%) | 1 ( 5.6%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) |
| CONJUNCTIVAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| EYE PAIN | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRITIS | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) |
| LACRIMATION INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) |
| OCULAR HYPEREMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| UVEITIS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) |
| VITREOUS HEMORRHAGE | 1 ( 5.6%) | 1 ( 5.6%) | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 203 (53.7%) | 209 (55.3%) | 165 (43.7%) | 122 (32.3%) | 104 (27.5%) | 105 (27.8%) | 92 (24.3%) |
| EYE DISORDERS | 201 (53.2%) | 207 (54.8%) | 163 (43.1%) | 119 (31.5%) | 103 (27.2%) | 105 (27.8%) | 91 (24.1%) |
| OCULAR HYPEREMIA | 106 (28.0%) | 110 (29.1%) | 66 (17.5%) | 19 ( 5.0%) | 7 ( 1.9%) | 7 ( 1.9%) | 4 ( 1.1%) |
| IRITIS | 83 (22.0%) | 96 (25.4%) | 67 (17.7%) | 27 ( 7.1%) | 14 ( 3.7%) | 12 ( 3.2%) | 6 ( 1.6%) |
| EYE IRRITATION | 53 (14.0%) | 56 (14.8%) | 42 (11.1%) | 30 ( 7.9%) | 32 ( 8.5%) | 29 ( 7.7%) | 20 ( 5.3%) |
| EYE PAIN | 45 (11.9%) | 48 (12.7%) | 22 ( 5.8%) | 8 ( 2.1%) | 8 ( 2.1%) | 7 ( 1.9%) | 5 ( 1.3%) |
| LACRIMATION INCREASED | 32 ( 8.5%) | 36 ( 9.5%) | 27 ( 7.1%) | 19 ( 5.0%) | 14 ( 3.7%) | 15 ( 4.0%) | 9 ( 2.4%) |
| ABNORMAL SENSATION IN EYE | 37 ( 9.8%) | 37 ( 9.8%) | 20 ( 5.3%) | 11 ( 2.9%) | 9 ( 2.4%) | 8 ( 2.1%) | 8 ( 2.1%) |
| CONJUNCTIVAL EDEMA | 45 (11.9%) | 48 (12.7%) | 21 ( 5.6%) | 7 ( 1.9%) | 3 ( 0.8%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VISUAL ACUITY REDUCED | 7 ( 1.9%) | 13 ( 3.4%) | 17 ( 4.5%) | 17 ( 4.5%) | 20 ( 5.3%) | 20 ( 5.3%) | 20 ( 5.3%) |
| PHOTOPHOBIA | 15 ( 4.0%) | 22 ( 5.8%) | 24 ( 6.3%) | 23 ( 6.1%) | 18 ( 4.8%) | 19 ( 5.0%) | 14 ( 3.7%) |
| VITREOUS FLOATERS | 5 ( 1.3%) | 19 ( 5.0%) | 23 ( 6.1%) | 22 ( 5.8%) | 22 ( 5.8%) | 23 ( 6.1%) | 16 ( 4.2%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 8 ( 2.1%) | 10 ( 2.6%) | 16 ( 4.2%) | 15 ( 4.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) | 9 ( 2.4%) | 12 ( 3.2%) |
| CATARACT NUCLEAR | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 5 ( 1.3%) | 6 ( 1.6%) | 7 ( 1.9%) | 15 ( 4.0%) |
| CORNEAL EROSION | 11 ( 2.9%) | 14 ( 3.7%) | 7 ( 1.9%) | 5 ( 1.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CONJUNCTIVAL HEMORRHAGE | 12 ( 3.2%) | 13 ( 3.4%) | 10 ( 2.6%) | 4 ( 1.1%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PHOTOPSIA | 2 ( 0.5%) | 2 ( 0.5%) | 5 ( 1.3%) | 7 ( 1.9%) | 6 ( 1.6%) | 8 ( 2.1%) | 7 ( 1.9%) |
| EYE DISCHARGE | 11 ( 2.9%) | 11 ( 2.9%) | 3 ( 0.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.1%) | 5 ( 1.3%) | 10 ( 2.6%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.1%) | 5 ( 1.3%) | 5 ( 1.3%) | 4 ( 1.1%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.1%) |
| CORNEAL EDEMA | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CATARACT NEC | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 3 ( 0.8%) | 2 ( 0.5%) |
| CORNEAL DISORDER NOS | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HYPHEMA | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| DRY EYE NEC | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| APHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE DECREASED | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATITIS NEC | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYDRIASIS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: Saline Control (n = 378)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| PAINFUL RED EYES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UVEITIS NOS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| INVESTIGATIONS | 12 ( 3.2%) | 12 ( 3.2%) | 9 ( 2.4%) | 9 ( 2.4%) | 6 ( 1.6%) | 7 ( 1.9%) | 5 ( 1.3%) |
| INTRAOCULAR PRESSURE INCREASED | 10 ( 2.6%) | 9 ( 2.4%) | 8 ( 2.1%) | 7 ( 1.9%) | 5 ( 1.3%) | 6 ( 1.6%) | 5 ( 1.3%) |
| CORNEAL STAINING | 2 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 12 ( 3.2%) | 13 ( 3.4%) | 7 ( 1.9%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | 7 ( 1.9%) | 7 ( 1.9%) | 3 ( 0.8%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | 5 ( 1.3%) | 6 ( 1.6%) | 4 ( 1.1%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INJURY AND POISONING | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 147 (74.2%) | 150 (75.8%) | 125 (63.1%) | 107 (54.0%) | 103 (52.0%) | 98 (49.5%) | 77 (38.9%) |
| EYE DISORDERS | 146 (73.7%) | 149 (75.3%) | 125 (63.1%) | 105 (53.0%) | 100 (50.5%) | 96 (48.5%) | 74 (37.4%) |
| IRITIS | 80 (40.4%) | 88 (44.4%) | 62 (31.3%) | 29 (14.6%) | 20 (10.1%) | 16 ( 8.1%) | 13 ( 6.6%) |
| OCULAR HYPEREMIA | 78 (39.4%) | 76 (38.4%) | 44 (22.2%) | 12 ( 6.1%) | 7 ( 3.5%) | 7 ( 3.5%) | 6 ( 3.0%) |
| EYE IRRITATION | 40 (20.2%) | 40 (20.2%) | 31 (15.7%) | 22 (11.1%) | 22 (11.1%) | 19 ( 9.6%) | 15 ( 7.6%) |
| EYE PAIN | 29 (14.6%) | 31 (15.7%) | 23 (11.6%) | 12 ( 6.1%) | 10 ( 5.1%) | 12 ( 6.1%) | 6 ( 3.0%) |
| VISUAL ACUITY REDUCED | 20 (10.1%) | 24 (12.1%) | 22 (11.1%) | 19 ( 9.6%) | 23 (11.6%) | 24 (12.1%) | 11 ( 5.6%) |
| LACRIMATION INCREASED | 23 (11.6%) | 23 (11.6%) | 21 (10.6%) | 19 ( 9.6%) | 20 (10.1%) | 18 ( 9.1%) | 10 ( 5.1%) |
| ABNORMAL SENSATION IN EYE | 27 (13.6%) | 23 (11.6%) | 13 ( 6.6%) | 10 ( 5.1%) | 12 ( 6.1%) | 14 ( 7.1%) | 16 ( 8.1%) |
| PHOTOPHOBIA | 11 ( 5.6%) | 13 ( 6.6%) | 19 ( 9.6%) | 23 (11.6%) | 23 (11.6%) | 21 (10.6%) | 17 ( 8.6%) |
| VITREOUS FLOATERS | 12 ( 6.1%) | 18 ( 9.1%) | 24 (12.1%) | 31 (15.7%) | 28 (14.1%) | 22 (11.1%) | 16 ( 8.1%) |
| VITREOUS HEMORRHAGE | 1 ( 0.5%) | 2 ( 1.0%) | 6 ( 3.0%) | 13 ( 6.6%) | 18 ( 9.1%) | 24 (12.1%) | 10 ( 5.1%) |
| CONJUNCTIVAL EDEMA | 25 (12.6%) | 25 (12.6%) | 9 ( 4.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) |
| CATARACT SUBCAPSULAR | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 5 ( 2.5%) | 5 ( 2.5%) | 11 ( 5.6%) | 17 ( 8.6%) |
| PHOTOPSIA | 3 ( 1.5%) | 7 ( 3.5%) | 7 ( 3.5%) | 7 ( 3.5%) | 10 ( 5.1%) | 11 ( 5.6%) | 9 ( 4.5%) |
| CATARACT NUCLEAR | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 5 ( 2.5%) | 7 ( 3.5%) | 8 ( 4.0%) | 10 ( 5.1%) |
| RETINAL DETACHMENT | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 8 ( 4.0%) | 7 ( 3.5%) |
| RUBEOSIS IRIDIS | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 4 ( 2.0%) | 5 ( 2.5%) | 5 ( 2.5%) | 6 ( 3.0%) |
| CONJUNCTIVAL HEMORRHAGE | 5 ( 2.5%) | 5 ( 2.5%) | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CORNEAL EROSION | 4 ( 2.0%) | 4 ( 2.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL DISORDER NOS | 3 ( 1.5%) | 3 ( 1.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) |
| CORNEAL EDEMA | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 2 ( 1.0%) | 3 ( 1.5%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 1.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 3 ( 1.5%) |
| EYE DISCHARGE | 3 ( 1.5%) | 3 ( 1.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPHEMA | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 1.0%) |
| KERATITIS NEC | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 3 ( 1.5%) |
| CONJUNCTIVITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) |
| INTRAOCULAR PRESSURE DECREASED | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CHORIORETINAL ATROPHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| CORNEAL ABRASION | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 7.5 IU Vitrase (n = 198)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| EYELID PTOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| GLAUCOMA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| INTRAOCULAR PRESSURE INCREASED | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL DEPIGMENTATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL HEMORRHAGE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| RETINAL MICROANEURYSMS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| STRABISMUS NEC | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS NOS | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION BLURRED | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.5%) |
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0 5%) |
| INVESTIGATIONS | 8 ( 4.0%) | 8 ( 4.0%) | 7 ( 3.5%) | 8 ( 4.0%) | 4 ( 2.0%) | 6 ( 3.0%) | 6 ( 3.0%) |
| INTRAOCULAR PRESSURE INCREASED | 5 ( 2.5%) | 4 ( 2.0%) | 5 ( 2.5%) | 8 ( 4.0%) | 4 ( 2.0%) | 6 ( 3.0%) | 5 ( 2.5%) |
| CORNEAL STAINING | 3 ( 1.5%) | 4 ( 2.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 6 ( 3.0%) | 6 ( 3.0%) | 4 ( 2.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| EYELID EDEMA | 5 ( 2.5%) | 4 ( 2.0%) | 2 ( 1.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| ERYTHEMA NEC | 1 ( 0.5%) | 2 ( 1.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) |
| CUTIS LAXA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| PUPILLARY DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITRECTOMY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 261 (69.2%) | 268 (71.1%) | 223 (59.2%) | 178 (47.2%) | 164 (43.5%) | 154 (40.8%) | 109 (28.9%) |
| EYE DISORDERS | 258 (68.4%) | 265 (70.3%) | 222 (58.9%) | 178 (47.2%) | 162 (43.0%) | 150 (39.8%) | 109 (28.9%) |
| IRITIS | 184 (48.8%) | 194 (51.5%) | 131 (34.7%) | 56 (14.9%) | 30 ( 8.0%) | 22 ( 5.8%) | 13 ( 3.4%) |
| OCULAR HYPEREMIA | 150 (39.8%) | 155 (41.1%) | 82 (21.8%) | 31 ( 8.2%) | 14 ( 3.7%) | 9 ( 2.4%) | 2 ( 0.5%) |
| EYE PAIN | 96 (25.5%) | 94 (24.9%) | 54 (14.3%) | 22 ( 5.8%) | 17 ( 4.5%) | 16 ( 4.2%) | 12 ( 3.2%) |
| EYE IRRITATION | 65 (17.2%) | 69 (18.3%) | 57 (15.1%) | 39 (10.3%) | 34 ( 9.0%) | 26 ( 6.9%) | 12 ( 3.2%) |
| LACRIMATION INCREASED | 67 (17.8%) | 68 (18.0%) | 47 (12.5%) | 36 ( 9.5%) | 36 ( 9.5%) | 25 ( 6.6%) | 16 ( 4.2%) |
| ABNORMAL SENSATION IN EYE | 60 (15.9%) | 63 (16.7%) | 41 (10.9%) | 26 ( 6.9%) | 16 ( 4.2%) | 17 ( 4.5%) | 6 ( 1.6%) |
| CONJUNCTIVAL EDEMA | 69 (18.3%) | 71 (18.8%) | 30 ( 8.0%) | 6 ( 1.6%) | 6 ( 1.6%) | 4 ( 1.1%) | 3 ( 0.8%) |
| VISUAL ACUITY REDUCED | 24 ( 6.4%) | 29 ( 7.7%) | 31 ( 8.2%) | 32 ( 8.5%) | 35 ( 9.3%) | 37 ( 9.8%) | 22 ( 5.8%) |
| PHOTOPHOBIA | 35 ( 9.3%) | 45 (11.9%) | 39 (10.3%) | 34 ( 9.0%) | 27 ( 7.2%) | 23 ( 6.1%) | 20 ( 5.3%) |
| VITREOUS FLOATERS | 19 ( 5.0%) | 25 ( 6.6%) | 30 ( 8.0%) | 32 ( 8.5%) | 37 ( 9.8%) | 32 ( 8.5%) | 22 ( 5.8%) |
| VITREOUS HEMORRHAGE | 1 ( 0.3%) | 2 ( 0.5%) | 5 ( 1.3%) | 10 ( 2.7%) | 20 ( 5.3%) | 24 ( 6.4%) | 19 ( 5.0%) |
| PHOTOPSIA | 6 ( 1.6%) | 9 ( 2.4%) | 16 ( 4.2%) | 15 ( 4.0%) | 13 ( 3.4%) | 14 ( 3.7%) | 12 ( 3.2%) |
| CATARACT NUCLEAR | 2 ( 0.5%) | 3 ( 0.8%) | 7 ( 1.9%) | 8 ( 2.1%) | 12 ( 3.2%) | 13 ( 3.4%) | 14 ( 3.7%) |
| CATARACT SUBCAPSULAR | 1 ( 0.3%) | 5 ( 1.3%) | 7 ( 1.9%) | 11 ( 2.9%) | 10 ( 2.7%) | 10 ( 2.7%) | 16 ( 4.2%) |
| CATARACT CORTICAL | 4 ( 1.1%) | 4 ( 1.1%) | 7 ( 1.9%) | 8 ( 2.1%) | 7 ( 1.9%) | 12 ( 3.2%) | 13 ( 3.4%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 3 ( 0.8%) | 7 ( 1.9%) | 3 ( 0.8%) | 6 ( 1.6%) | 10 ( 2.7%) | 6 ( 1.6%) |
| CORNEAL DISORDER NOS | 11 ( 2.9%) | 14 ( 3.7%) | 6 ( 1.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EROSION | 12 ( 3.2%) | 14 ( 3.7%) | 9 ( 2.4%) | 6 ( 1.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE DISCHARGE | 10 ( 2.7%) | 11 ( 2.9%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS ADHESIONS | 4 ( 1.1%) | 7 ( 1.9%) | 3 ( 0.8%) | 3 ( 0.8%) | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| CORNEAL EDEMA | 3 ( 0.8%) | 4 ( 1.1%) | 3 ( 0.8%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| CONJUNCTIVAL HEMORRHAGE | 5 ( 1.3%) | 6 ( 1.6%) | 6 ( 1.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | 4 ( 1.1%) | 6 ( 1.6%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 4 ( 1.1%) | 5 ( 1.3%) | 3 ( 0.8%) | 3 ( 0.8%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 5 ( 1.3%) | 4 ( 1.1%) | 4 ( 1.1%) |
| HYPHEMA | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 0.8%) |
| UVEITIS NOS | 4 ( 1.1%) | 4 ( 1.1%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL TEAR (EXC DETACHMENT) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| DIPLOPIA | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |
| DRY EYE NEC | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| BLEPHARITIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| CATARACT NEC | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| POSTERIOR CAPSULE OPACIFICATION | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |



Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 55 IU Vitrase (n = 377)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ERYTHEMA NEC | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| EYELID EDEMA | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| HYPOTONY OF EYE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MACULAR DEGENERATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MEIBOMIAN CYST | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OCULAR HYPERTENSION | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PSEUDOPHAKIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| RETINAL HEMORRHAGE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 22 ( 5.8%) | 24 ( 6.4%) | 12 ( 3.2%) | 4 ( 1.1%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) |
| EYELID EDEMA | 18 ( 4.8%) | 19 ( 5.0%) | 6 ( 1.6%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ERYTHEMA NEC | 10 ( 2.7%) | 11 ( 2.9%) | 5 ( 1.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 1 ( 0.3%) |
| PERIORBITAL EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 9 ( 2.4%) | 10 ( 2.7%) | 9 ( 2.4%) | 7 ( 1.9%) | 4 ( 1.1%) | 8 ( 2.1%) | 4 ( 1.1%) |
| INTRAOCULAR PRESSURE INCREASED | 4 ( 1.1%) | 4 ( 1.1%) | 5 ( 1.3%) | 4 ( 1.1%) | 4 ( 1.1%) | 8 ( 2.1%) | 4 ( 1.1%) |
| CORNEAL STAINING | 5 ( 1.3%) | 6 ( 1.6%) | 4 ( 1.1%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 5 ( 1.3%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 3 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PUPILLARY DISORDER NOS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |

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Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 304 (77.7%) | 312 (79.8%) | 240 (61.4%) | 173 (44.2%) | 158 (40.4%) | 147 (37.6%) | 126 (32.2%) |
| EYE DISORDERS | 304 (77.7%) | 311 (79.5%) | 239 (61.1%) | 171 (43.7%) | 156 (39.9%) | 145 (37.1%) | 123 (31.5%) |
| IRITIS | 224 (57.3%) | 228 (58.3%) | 141 (36.1%) | 50 (12.8%) | 22 ( 5.6%) | 11 ( 2.8%) | 12 ( 3.1%) |
| OCULAR HYPEREMIA | 175 (44.8%) | 176 (45.0%) | 85 (21.7%) | 29 ( 7.4%) | 11 ( 2.8%) | 8 ( 2.0%) | 8 ( 2.0%) |
| EYE PAIN | 103 (26.3%) | 103 (26.3%) | 59 (15.1%) | 29 ( 7.4%) | 20 ( 5.1%) | 22 ( 5.6%) | 13 ( 3.3%) |
| LACRIMATION INCREASED | 65 (16.6%) | 67 (17.1%) | 49 (12.5%) | 33 ( 8.4%) | 30 ( 7.7%) | 27 ( 6.9%) | 20 ( 5.1%) |
| EYE IRRITATION | 62 (15.9%) | 73 (18.7%) | 56 (14.3%) | 43 (11.0%) | 34 ( 8.7%) | 26 ( 6.6%) | 20 ( 5.1%) |
| ABNORMAL SENSATION IN EYE | 71 (18.2%) | 71 (18.2%) | 47 (12.0%) | 28 ( 7.2%) | 16 ( 4.1%) | 18 ( 4.6%) | 13 ( 3.3%) |
| PHOTOPHOBIA | 46 (11.8%) | 53 (13.6%) | 39 (10.0%) | 29 ( 7.4%) | 36 ( 9.2%) | 30 ( 7.7%) | 19 ( 4.9%) |
| CONJUNCTIVAL EDEMA | 74 (18.9%) | 76 (19.4%) | 29 ( 7.4%) | 5 ( 1.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| VITREOUS FLOATERS | 22 ( 5.6%) | 33 ( 8.4%) | 47 (12.0%) | 45 (11.5%) | 39 (10.0%) | 35 ( 9.0%) | 21 ( 5.4%) |
| VISUAL ACUITY REDUCED | 29 ( 7.4%) | 34 ( 8.7%) | 31 ( 7.9%) | 28 ( 7.2%) | 29 ( 7.4%) | 30 ( 7.7%) | 15 ( 3.8%) |
| VITREOUS HEMORRHAGE | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) | 7 ( 1.8%) | 10 ( 2.6%) | 20 ( 5.1%) | 16 ( 4.1%) |
| PHOTOPSIA | 8 ( 2.0%) | 8 ( 2.0%) | 10 ( 2.6%) | 12 ( 3.1%) | 12 ( 3.1%) | 12 ( 3.1%) | 11 ( 2.8%) |
| CORNEAL DISORDER NOS | 18 ( 4.6%) | 18 ( 4.6%) | 8 ( 2.0%) | 4 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) | 3 ( 0.8%) |
| RETINAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 7 ( 1.8%) | 13 ( 3.3%) | 16 ( 4.1%) |
| HYPOPYON | 18 ( 4.6%) | 20 ( 5.1%) | 4 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CATARACT CORTICAL | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 4 ( 1.0%) | 7 ( 1.8%) | 16 ( 4.1%) | 15 ( 3.8%) |
| CORNEAL EDEMA | 18 ( 4.6%) | 18 ( 4.6%) | 3 ( 0.8%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |
| IRIS ADHESIONS | 6 ( 1.5%) | 7 ( 1.8%) | 9 ( 2.3%) | 11 ( 2.8%) | 10 ( 2.6%) | 10 ( 2.6%) | 8 ( 2.0%) |
| CATARACT SUBCAPSULAR | 2 ( 0.5%) | 3 ( 0.8%) | 3 ( 0.8%) | 6 ( 1.5%) | 9 ( 2.3%) | 11 ( 2.8%) | 12 ( 3.1%) |
| EYE DISCHARGE | 9 ( 2.3%) | 11 ( 2.8%) | 8 ( 2.0%) | 3 ( 0.8%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CORNEAL EROSION | 8 ( 2.0%) | 9 ( 2.3%) | 7 ( 1.8%) | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CATARACT NUCLEAR | 1 ( 0.3%) | 2 ( 0.5%) | 4 ( 1.0%) | 4 ( 1.0%) | 6 ( 1.5%) | 7 ( 1.8%) | 8 ( 2.0%) |
| RUBEOSIS IRIDIS | 3 ( 0.8%) | 3 ( 0.8%) | 3 ( 0.8%) | 4 ( 1.0%) | 5 ( 1.3%) | 4 ( 1.0%) | 4 ( 1.0%) |
| CONJUNCTIVAL HEMORRHAGE | 7 ( 1.8%) | 6 ( 1.5%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| MACULAR EDEMA | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) | 8 ( 2.0%) |
| HYPHEMA | 2 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |
| GLAUCOMA NOS | 1 ( 0.3%) | 3 ( 0.8%) | 3 ( 0.8%) | 1 ( 0.3%) | 2 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| CATARACT NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| HYPOTONY OF EYE | 2 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| MACULOPATHY | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) | 3 ( 0.8%) |
| MYDRIASIS | 2 ( 0.5%) | 3 ( 0.8%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UVEITIS NOS | 4 ( 1.0%) | 4 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRY EYE NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| KERATITIS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| VITREOUS DETACHMENT | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) |
| CONJUNCTIVITIS NEC | 2 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| VISION BLURRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| VITREOUS DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CYCLITIS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIPLOPIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OCULAR HYPERAEMIA | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL ISCHEMIA | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL SCAR | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| STRABISMUS NEC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VISUAL DISTURBANCE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS OPACITIES | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 20 ( 5.1%) | 19 ( 4.9%) | 10 ( 2.6%) | 2 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |
| EYELID EDEMA | 15 ( 3.8%) | 14 ( 3.6%) | 5 ( 1.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 2 ( 0.5%) | 2 ( 0.5%) |
| ERYTHEMA NEC | 10 ( 2.6%) | 10 ( 2.6%) | 5 ( 1.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) |
| ECCHYMOSIS | 1 ( 0.3%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | 12 ( 3.1%) | 11 ( 2.8%) | 8 ( 2.0%) | 5 ( 1.3%) | 3 ( 0.8%) | 6 ( 1.5%) | 4 ( 1.0%) |
| INTRAOCULAR PRESSURE INCREASED | 10 ( 2.6%) | 8 ( 2.0%) | 5 ( 1.3%) | 3 ( 0.8%) | 2 ( 0.5%) | 6 ( 1.5%) | 4 ( 1.0%) |
| CORNEAL STAINING | 2 ( 0.5%) | 3 ( 0.8%) | 3 ( 0.8%) | 2 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | 2 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 0.5%) | 2 ( 0.5%) |
| PUPILLARY DISORDER NOS | 1 ( 0.3%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| HEADACHE NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
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Table 14
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period During Which Event was Present
Safety Population
Treatment: 75 IU Vitrase (n = 391)

| System Organ Class / Preferred Term | Day 0-Day 1 | Day 2-Day 7 | Day 8-Day 30 | Day 31-Day 60 | Day 61-Day 90 | Day 90-Day 180 | > Day 180 |
|---|---|---|---|---|---|---|---|
| PUPILLARY REFLEX IMPAIRED | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |



Note: Events are included in all periods in which they are present.
The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing or 'Ongoing' is marked.

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ISTA Pharmaceuticals, Inc.
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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| NUMBER OF PATIENTS | | 18 | 378 | 198 | 377 | 391 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | MILD | 3 (16.7%) | 110 (29.1%) | 46 (23.2%) | 70 (18.6%) | 79 (20.2%) |
| | MODERATE | 5 (27.8%) | 107 (28.3%) | 57 (28.8%) | 114 (30.2%) | 111 (28.4%) |
| | SEVERE | 9 (50.0%) | 81 (21.4%) | 90 (45.5%) | 139 (36.9%) | 159 (40.7%) |
| EYE DISORDERS | MILD | 3 (16.7%) | 116 (30.7%) | 48 (24.2%) | 73 (19.4%) | 80 (20.5%) |
| | MODERATE | 5 (27.8%) | 103 (27.2%) | 60 (30.3%) | 113 (30.0%) | 115 (29.4%) |
| | SEVERE | 9 (50.0%) | 78 (20.6%) | 84 (42.4%) | 136 (36.1%) | 154 (39.4%) |
| IRITIS | MILD | 4 (22.2%) | 96 (25.4%) | 83 (41.9%) | 95 (25.2%) | 88 (22.5%) |
| | MODERATE | 0 ( 0.0%) | 23 ( 6.1%) | 31 (15.7%) | 83 (22.0%) | 102 (26.1%) |
| | SEVERE | 0 ( 0.0%) | 7 ( 1.9%) | 9 ( 4.5%) | 44 (11.7%) | 53 (13.6%) |
| OCULAR HYPEREMIA | MILD | 4 (22.2%) | 99 (26.2%) | 72 (36.4%) | 126 (33.4%) | 144 (36.8%) |
| | MODERATE | 0 ( 0.0%) | 37 ( 9.8%) | 32 (16.2%) | 62 (16.4%) | 60 (15.3%) |
| | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 9 ( 4.5%) | 14 ( 3.7%) | 11 ( 2.8%) |
| EYE IRRITATION | MILD | 9 (50.0%) | 92 (24.3%) | 74 (37.4%) | 91 (24.1%) | 95 (24.3%) |
| | MODERATE | 0 ( 0.0%) | 16 ( 4.2%) | 12 ( 6.1%) | 29 ( 7.7%) | 31 ( 7.9%) |
| | SEVERE | 1 ( 5.6%) | 3 ( 0.8%) | 4 ( 2.0%) | 12 ( 3.2%) | 13 ( 3.3%) |
| EYE PAIN | MILD | 1 ( 5.6%) | 60 (15.9%) | 54 (27.3%) | 83 (22.0%) | 95 (24.3%) |
| | MODERATE | 1 ( 5.6%) | 20 ( 5.3%) | 13 ( 6.6%) | 42 (11.1%) | 48 (12.3%) |
| | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 2.5%) | 14 ( 3.7%) | 18 ( 4.6%) |
| LACRIMATION INCREASED | MILD | 1 ( 5.6%) | 67 (17.7%) | 41 (20.7%) | 71 (18.8%) | 78 (19.9%) |
| | MODERATE | 3 (16.7%) | 14 ( 3.7%) | 16 ( 8.1%) | 39 (10.3%) | 41 (10.5%) |
| | SEVERE | 0 ( 0.0%) | 6 ( 1.6%) | 8 ( 4.0%) | 14 ( 3.7%) | 20 ( 5.1%) |
| VISUAL ACUITY REDUCED | MILD | 3 (16.7%) | 49 (13.0%) | 37 (18.7%) | 58 (15.4%) | 53 (13.6%) |
| | MODERATE | 1 ( 5.6%) | 20 ( 5.3%) | 24 (12.1%) | 33 ( 8.8%) | 23 ( 5.9%) |
| | SEVERE | 0 ( 0.0%) | 5 ( 1.3%) | 16 ( 8.1%) | 10 ( 2.7%) | 22 ( 5.6%) |
| ABNORMAL SENSATION IN EYE | MILD | 2 (11.1%) | 55 (14.6%) | 38 (19.2%) | 67 (17.8%) | 79 (20.2%) |
| | MODERATE | 0 ( 0.0%) | 11 ( 2.9%) | 19 ( 9.6%) | 31 ( 8.2%) | 24 ( 6.1%) |
| | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 5 ( 2.5%) | 3 ( 0.8%) | 11 ( 2.8%) |
| VITREOUS FLOATERS | MILD | 1 ( 5.6%) | 37 ( 9.8%) | 28 (14.1%) | 52 (13.8%) | 56 (14.3%) |
| | MODERATE | 1 ( 5.6%) | 16 ( 4.2%) | 22 (11.1%) | 19 ( 5.0%) | 24 ( 6.1%) |
| | SEVERE | 4 (22.2%) | 14 ( 3.7%) | 13 ( 6.6%) | 17 ( 4.5%) | 20 ( 5.1%) |
| VITREOUS HEMORRHAGE | MILD | 1 ( 5.6%) | 19 ( 5.0%) | 16 ( 8.1%) | 20 ( 5.3%) | 24 ( 6.1%) |

Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VITREOUS HEMORRHAGE | MODERATE | 0 ( 0.0%) | 29 ( 7.7%) | 28 (14.1%) | 42 (11.1%) | 30 ( 7.7%) |
| | SEVERE | 1 ( 5.6%) | 18 ( 4.8%) | 26 (13.1%) | 29 ( 7.7%) | 36 ( 9.2%) |
| PHOTOPHOBIA | MILD | 3 (16.7%) | 35 ( 9.3%) | 30 (15.2%) | 33 ( 8.8%) | 48 (12.3%) |
| | MODERATE | 2 (11.1%) | 15 ( 4.0%) | 15 ( 7.6%) | 38 (10.1%) | 34 ( 8.7%) |
| | SEVERE | 1 ( 5.6%) | 10 ( 2.6%) | 14 ( 7.1%) | 15 ( 4.0%) | 20 ( 5.1%) |
| CONJUNCTIVAL EDEMA | MILD | 1 ( 5.6%) | 49 (13.0%) | 36 (18.2%) | 70 (18.6%) | 70 (17.9%) |
| | MODERATE | 0 ( 0.0%) | 9 ( 2.4%) | 10 ( 5.1%) | 21 ( 5.6%) | 18 ( 4.6%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 5 ( 1.3%) | 1 ( 0.3%) |
| CATARACT NUCLEAR | MILD | 1 ( 5.6%) | 10 ( 2.6%) | 4 ( 2.0%) | 12 ( 3.2%) | 9 ( 2.3%) |
| | MODERATE | 4 (22.2%) | 16 ( 4.2%) | 12 ( 6.1%) | 16 ( 4.2%) | 13 ( 3.3%) |
| | SEVERE | 0 ( 0.0%) | 8 ( 2.1%) | 11 ( 5.6%) | 9 ( 2.4%) | 7 ( 1.8%) |
| RETINAL DETACHMENT | MILD | 0 ( 0.0%) | 6 ( 1.6%) | 0 ( 0.0%) | 8 ( 2.1%) | 11 ( 2.8%) |
| | MODERATE | 1 ( 5.6%) | 8 ( 2.1%) | 9 ( 4.5%) | 10 ( 2.7%) | 11 ( 2.8%) |
| | SEVERE | 2 (11.1%) | 12 ( 3.2%) | 13 ( 6.6%) | 17 ( 4.5%) | 23 ( 5.9%) |
| CATARACT SUBCAPSULAR | MILD | 1 ( 5.6%) | 18 ( 4.8%) | 20 (10.1%) | 16 ( 4.2%) | 24 ( 6.1%) |
| | MODERATE | 0 ( 0.0%) | 7 ( 1.9%) | 9 ( 4.5%) | 12 ( 3.2%) | 12 ( 3.1%) |
| | SEVERE | 1 ( 5.6%) | 1 ( 0.3%) | 4 ( 2.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| PHOTOPSIA | MILD | 0 ( 0.0%) | 12 ( 3.2%) | 14 ( 7.1%) | 31 ( 8.2%) | 17 ( 4.3%) |
| | MODERATE | 0 ( 0.0%) | 6 ( 1.6%) | 6 ( 3.0%) | 12 ( 3.2%) | 17 ( 4.3%) |
| | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 1.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| CATARACT CORTICAL | MILD | 5 (27.8%) | 17 ( 4.5%) | 8 ( 4.0%) | 12 ( 3.2%) | 19 ( 4.9%) |
| | MODERATE | 0 ( 0.0%) | 8 ( 2.1%) | 3 ( 1.5%) | 13 ( 3.4%) | 9 ( 2.3%) |
| | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 5 ( 1.3%) | 3 ( 0.8%) |
| CORNEAL EROSION | MILD | 1 ( 5.6%) | 19 ( 5.0%) | 8 ( 4.0%) | 19 ( 5.0%) | 15 ( 3.8%) |
| | MODERATE | 0 ( 0.0%) | 5 ( 1.3%) | 0 ( 0.0%) | 5 ( 1.3%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CORNEAL EDEMA | MILD | 1 ( 5.6%) | 10 ( 2.6%) | 7 ( 3.5%) | 12 ( 3.2%) | 16 ( 4.1%) |
| | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 8 ( 4.0%) | 6 ( 1.6%) | 6 ( 1.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| RUBEOSIS IRIDIS | MILD | 1 ( 5.6%) | 6 ( 1.6%) | 7 ( 3.5%) | 8 ( 2.1%) | 7 ( 1.8%) |
| | MODERATE | 0 ( 0.0%) | 9 ( 2.4%) | 2 ( 1.0%) | 6 ( 1.6%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 7 ( 3.5%) | 3 ( 0.8%) | 8 ( 2.0%) |



Note: Events are counted once per patient as most severe reported.

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Integrated Summary of Safety

Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| EYE DISCHARGE | MILD | 0 ( 0.0%) | 17 ( 4.5%) | 8 ( 4.0%) | 20 ( 5.3%) | 17 ( 4.3%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 3 ( 0.8%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVAL HEMORRHAGE | MILD | 0 ( 0.0%) | 19 ( 5.0%) | 8 ( 4.0%) | 10 ( 2.7%) | 14 ( 3.6%) |
| | MODERATE | 0 ( 0.0%) | 5 ( 1.3%) | 3 ( 1.5%) | 4 ( 1.1%) | 3 ( 0.8%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| IRIS ADHESIONS | MILD | 2 (11.1%) | 8 ( 2.1%) | 3 ( 1.5%) | 7 ( 1.9%) | 14 ( 3.6%) |
| | MODERATE | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 2.0%) | 5 ( 1.3%) | 7 ( 1.8%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 6 ( 1.5%) |
| MACULAR EDEMA | MILD | 0 ( 0.0%) | 5 ( 1.3%) | 10 ( 5.1%) | 5 ( 1.3%) | 13 ( 3.3%) |
| | MODERATE | 1 ( 5.6%) | 6 ( 1.6%) | 5 ( 2.5%) | 5 ( 1.3%) | 5 ( 1.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CORNEAL DISORDER NOS | MILD | 0 ( 0.0%) | 8 ( 2.1%) | 3 ( 1.5%) | 11 ( 2.9%) | 16 ( 4.1%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 4 ( 1.1%) | 7 ( 1.8%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| HYPHEMA | MILD | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 2.5%) | 7 ( 1.9%) | 6 ( 1.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 5 ( 1.3%) | 3 ( 0.8%) |
| | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 6 ( 1.5%) |
| CATARACT NEC | MILD | 0 ( 0.0%) | 6 ( 1.6%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 5 ( 1.3%) | 7 ( 1.8%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| BLINDNESS NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 8 ( 4.0%) | 4 ( 1.1%) | 8 ( 2.0%) |
| HYPOPYON | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 10 ( 2.6%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 6 ( 1.5%) |
| DRY EYE NEC | MILD | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 2.0%) | 3 ( 0.8%) | 9 ( 2.3%) |
| | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLAUCOMA NOS | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 3 ( 0.8%) | 6 ( 1.5%) |

Note: Events are counted once per patient as most severe reported.

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ISTA Pharmaceuticals, Inc.
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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISION BLURRED | MILD | 0 ( 0.0%) | 5 ( 1.3%) | 8 ( 4.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| CATARACT NOS AGGRAVATED | MILD | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 4 ( 1.1%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 1.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| KERATITIS NEC | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 1.5%) | 3 ( 0.8%) | 5 ( 1.3%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | MILD | 1 ( 5.6%) | 2 ( 0.5%) | 2 ( 1.0%) | 6 ( 1.6%) | 3 ( 0.8%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MACULOPATHY | MILD | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| INTRAOCULAR PRESSURE INCREASED | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| UVEITIS NOS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 5 ( 1.3%) | 3 ( 0.8%) |
| | MODERATE | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| POST-OPERATIVE PAIN | MILD | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| | MODERATE | 1 ( 5.6%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) |
| | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| BLEPHARITIS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 5 ( 1.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| HYPOTONY OF EYE | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| RETINAL HEMORRHAGE | MILD | 0 ( 0.0%) | 5 ( 1.3%) | 2 ( 1.0%) | 5 ( 1.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | MILD | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| DIPLOPIA | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 4 ( 1.1%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| CONJUNCTIVITIS NEC | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MYDRIASIS | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL TEAR (EXC DETACHMENT) | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 4 ( 1.1%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| FOREIGN BODY RETAINED IN EYE | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 2 ( 0.5%) | 1 ( 0.3%) |



Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| PSEUDOPHAKIA | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| APHAKIA | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| OCULAR HYPERTENSION | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAINFUL RED EYES | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CHEMOSIS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL SCAR | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLINDNESS TRANSIENT | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CONJUNCTIVITIS (INFECTIVE) NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS ALLERGIC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL OPACITY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| KERATOPATHY BAND | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MEIBOMIAN CYST | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL HEMATOMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ARTERY EMBOLISM | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEPIGMENTATION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STRABISMUS NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISUAL ACUITY REDUCED TRANSIENTLY | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS OPACITIES | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANGLE CLOSURE GLAUCOMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANISEIKONIA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARCUS SENILIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHAROCONJUNCTIVITIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHALAZION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL ATROPHY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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ISTA Pharmaceuticals, Inc.
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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CHORIORETINAL DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| COLOUR BLINDNESS NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL DEGENERATION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL SCAR | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ULCER NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EXOPHTHALMOS ENDOCRINE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE HEMORRHAGE NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| EYE INFECTION NOS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION STAPHYLOCOCCAL | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HERPES SIMPLEX OPHTHALMIC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS NEVUS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC DISC HEMORRHAGE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| OPTIC NERVE INJURY NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAPILLEDEMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEGENERATION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL EXUDATES | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VASCULITIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCLERITIS NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISION ABNORMAL NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | MILD | 2 (11.1%) | 22 ( 5.8%) | 19 ( 9.6%) | 23 ( 6.1%) | 20 ( 5.1%) |
| | MODERATE | 1 ( 5.6%) | 17 ( 4.5%) | 20 (10.1%) | 22 ( 5.8%) | 15 ( 3.8%) |
| | SEVERE | 0 ( 0.0%) | 5 ( 1.3%) | 9 ( 4.5%) | 5 ( 1.3%) | 11 ( 2.8%) |
| INTRAOCULAR PRESSURE INCREASED | MILD | 2 (11.1%) | 18 ( 4.8%) | 13 ( 6.6%) | 17 ( 4.5%) | 16 ( 4.1%) |
| | MODERATE | 1 ( 5.6%) | 16 ( 4.2%) | 18 ( 9.1%) | 20 ( 5.3%) | 13 ( 3.3%) |
| | SEVERE | 0 ( 0.0%) | 5 ( 1.3%) | 9 ( 4.5%) | 5 ( 1.3%) | 11 ( 2.8%) |
| CORNEAL STAINING | MILD | 0 ( 0.0%) | 5 ( 1.3%) | 6 ( 3.0%) | 7 ( 1.9%) | 6 ( 1.5%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE ABNORMAL | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | MILD | 0 ( 0.0%) | 23 ( 6.1%) | 13 ( 6.6%) | 32 ( 8.5%) | 31 ( 7.9%) |
| | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 2.5%) | 6 ( 1.6%) | 7 ( 1.8%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| EYELID EDEMA | MILD | 0 ( 0.0%) | 12 ( 3.2%) | 10 ( 5.1%) | 22 ( 5.8%) | 19 ( 4.9%) |
| | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 6 ( 1.6%) | 6 ( 1.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| ERYTHEMA NEC | MILD | 0 ( 0.0%) | 14 ( 3.7%) | 5 ( 2.5%) | 17 ( 4.5%) | 18 ( 4.6%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CUTIS LAXA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| PERIORBITAL EDEMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DERMATITIS NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PRURITUS NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | MILD | 0 ( 0.0%) | 6 ( 1.6%) | 2 ( 1.0%) | 4 ( 1.1%) | 3 ( 0.8%) |
| | MODERATE | 1 ( 5.6%) | 7 ( 1.9%) | 1 ( 0.5%) | 5 ( 1.3%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 4 ( 1.1%) | 1 ( 0.3%) |
| POST-OPERATIVE COMPLICATIONS NOS | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 1 ( 0 3%) | 2 ( 0.5%) |
| | MODERATE | 1 ( 5.6%) | 5 ( 1.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| VITRECTOMY | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENS IMPLANT | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Events are counted once per patient as most severe reported.

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| SCLERAL OPERATION NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUTURE LINE PAIN | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 3 ( 0.8%) | 5 ( 1.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL FIELD DEFECT NOS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FACIAL PALSY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEADACHE NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY REFLEX IMPAIRED | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITH NERVE PARALYSIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IMMUNE SYSTEM DISORDERS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERSENSITIVITY NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



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Table 15
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Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| MULTIPLE ALLERGIES | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CHEMICAL BURNS OF EYE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| HEAD INJURY | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BENIGN NEOPLASM OF CHOROID | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RADIOACTIVE IODINE THERAPY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MECHANICAL COMPLICATION OF IMPLANT | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



*Note: Events are counted once per patient as most severe reported.*

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Table 15
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VASCULAR DISORDERS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| *PERIPHERAL ISCHEMIA NOS* | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| NUMBER OF PATIENTS | | 18 | 378 | 198 | 377 | 391 |
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | MILD | 4 (22.2%) | 117 (31.0%) | 59 (29.8%) | 80 (21.2%) | 93 (23.8%) |
| | MODERATE | 3 (16.7%) | 84 (22.2%) | 48 (24.2%) | 109 (28.9%) | 117 (29.9%) |
| | SEVERE | 4 (22.2%) | 43 (11.4%) | 61 (30.8%) | 101 (26.8%) | 116 (29 7%) |
| EYE DISORDERS | MILD | 4 (22.2%) | 118 (31.2%) | 62 (31.3%) | 80 (21.2%) | 94 (24.0%) |
| | MODERATE | 3 (16.7%) | 84 (22.2%) | 51 (25.8%) | 109 (28.9%) | 118 (30.2%) |
| | SEVERE | 4 (22.2%) | 41 (10.8%) | 55 (27.8%) | 99 (26.3%) | 114 (29.2%) |
| IRITIS | MILD | 1 ( 5.6%) | 81 (21.4%) | 70 (35.4%) | 91 (24.1%) | 84 (21.5%) |
| | MODERATE | 0 ( 0.0%) | 20 ( 5.3%) | 24 (12.1%) | 70 (18.6%) | 98 (25.1%) |
| | SEVERE | 0 ( 0.0%) | 5 ( 1.3%) | 6 ( 3.0%) | 41 (10.9%) | 49 (12.5%) |
| OCULAR HYPEREMIA | MILD | 1 ( 5.6%) | 79 (20.9%) | 59 (29.8%) | 100 (26.5%) | 120 (30.7%) |
| | MODERATE | 0 ( 0.0%) | 30 ( 7.9%) | 20 (10.1%) | 50 (13.3%) | 54 (13.8%) |
| | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 6 ( 3.0%) | 8 ( 2.1%) | 9 ( 2.3%) |
| EYE PAIN | MILD | 1 ( 5.6%) | 49 (13.0%) | 38 (19.2%) | 71 (18.8%) | 79 (20.2%) |
| | MODERATE | 0 ( 0.0%) | 7 ( 1.9%) | 7 ( 3.5%) | 31 ( 8.2%) | 34 ( 8.7%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 11 ( 2.9%) | 15 ( 3.8%) |
| EYE IRRITATION | MILD | 4 (22.2%) | 64 (16.9%) | 52 (26.3%) | 69 (18.3%) | 71 (18.2%) |
| | MODERATE | 0 ( 0.0%) | 12 ( 3.2%) | 6 ( 3.0%) | 19 ( 5.0%) | 24 ( 6.1%) |
| | SEVERE | 1 ( 5.6%) | 3 ( 0.8%) | 3 ( 1.5%) | 8 ( 2.1%) | 8 ( 2.0%) |
| LACRIMATION INCREASED | MILD | 0 ( 0.0%) | 42 (11.1%) | 29 (14.6%) | 54 (14.3%) | 58 (14.8%) |
| | MODERATE | 1 ( 5.6%) | 12 ( 3.2%) | 12 ( 6.1%) | 29 ( 7.7%) | 29 ( 7.4%) |
| | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 2.0%) | 11 ( 2.9%) | 16 ( 4.1%) |
| ABNORMAL SENSATION IN EYE | MILD | 1 ( 5.6%) | 40 (10.6%) | 28 (14.1%) | 54 (14.3%) | 62 (15.9%) |
| | MODERATE | 0 ( 0.0%) | 9 ( 2.4%) | 10 ( 5.1%) | 21 ( 5.6%) | 21 ( 5.4%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 2.5%) | 3 ( 0.8%) | 9 ( 2.3%) |
| PHOTOPHOBIA | MILD | 0 ( 0.0%) | 25 ( 6.6%) | 24 (12.1%) | 28 ( 7.4%) | 43 (11.0%) |
| | MODERATE | 2 (11.1%) | 10 ( 2.6%) | 6 ( 3.0%) | 25 ( 6.6%) | 27 ( 6.9%) |
| | SEVERE | 1 ( 5.6%) | 7 ( 1.9%) | 11 ( 5.6%) | 10 ( 2.7%) | 15 ( 3.8%) |
| CONJUNCTIVAL EDEMA | MILD | 1 ( 5.6%) | 42 (11.1%) | 27 (13.6%) | 55 (14.6%) | 59 (15.1%) |
| | MODERATE | 0 ( 0.0%) | 6 ( 1.6%) | 3 ( 1.5%) | 15 ( 4.0%) | 17 ( 4.3%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 4 ( 1.1%) | 1 ( 0.3%) |
| VITREOUS FLOATERS | MILD | 1 ( 5.6%) | 25 ( 6.6%) | 18 ( 9.1%) | 33 ( 8.8%) | 44 (11.3%) |

Note: Events are counted once per patient as most severe reported.

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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VITREOUS FLOATERS | MODERATE | 1 ( 5.6%) | 9 ( 2.4%) | 14 ( 7.1%) | 13 ( 3.4%) | 17 ( 4.3%) |
| | SEVERE | 1 ( 5.6%) | 8 ( 2.1%) | 8 ( 4.0%) | 12 ( 3.2%) | 13 ( 3.3%) |
| VISUAL ACUITY REDUCED | MILD | 2 (11.1%) | 30 ( 7.9%) | 30 (15.2%) | 40 (10.6%) | 32 ( 8.2%) |
| | MODERATE | 0 ( 0.0%) | 11 ( 2.9%) | 9 ( 4.5%) | 18 ( 4.8%) | 16 ( 4.1%) |
| | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 8 ( 4.0%) | 8 ( 2.1%) | 10 ( 2.6%) |
| VITREOUS HEMORRHAGE | MILD | 1 ( 5.6%) | 5 ( 1.3%) | 9 ( 4.5%) | 7 ( 1.9%) | 10 ( 2.6%) |
| | MODERATE | 0 ( 0.0%) | 12 ( 3.2%) | 11 ( 5.6%) | 14 ( 3.7%) | 10 ( 2.6%) |
| | SEVERE | 0 ( 0.0%) | 8 ( 2.1%) | 12 ( 6.1%) | 16 ( 4.2%) | 9 ( 2.3%) |
| PHOTOPSIA | MILD | 0 ( 0.0%) | 7 ( 1.9%) | 14 ( 7.1%) | 17 ( 4.5%) | 12 ( 3.1%) |
| | MODERATE | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 1.0%) | 6 ( 1.6%) | 12 ( 3.1%) |
| | SEVERE | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| CATARACT SUBCAPSULAR | MILD | 0 ( 0.0%) | 6 ( 1.6%) | 13 ( 6.6%) | 12 ( 3.2%) | 13 ( 3.3%) |
| | MODERATE | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 2.0%) | 7 ( 1.9%) | 3 ( 0.8%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL DETACHMENT | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| | MODERATE | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 2.0%) | 5 ( 1.3%) | 3 ( 0.8%) |
| | SEVERE | 1 ( 5.6%) | 5 ( 1.3%) | 8 ( 4.0%) | 10 ( 2.7%) | 14 ( 3.6%) |
| CATARACT NUCLEAR | MILD | 0 ( 0.0%) | 5 ( 1.3%) | 2 ( 1.0%) | 11 ( 2.9%) | 4 ( 1.0%) |
| | MODERATE | 1 ( 5.6%) | 10 ( 2.6%) | 6 ( 3.0%) | 7 ( 1.9%) | 6 ( 1.5%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 4 ( 1.1%) | 0 ( 0.0%) |
| CATARACT CORTICAL | MILD | 1 ( 5.6%) | 12 ( 3.2%) | 1 ( 0.5%) | 12 ( 3.2%) | 12 ( 3.1%) |
| | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 6 ( 1.6%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| CORNEAL EROSION | MILD | 0 ( 0.0%) | 13 ( 3.4%) | 5 ( 2.5%) | 11 ( 2.9%) | 10 ( 2.6%) |
| | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL DISORDER NOS | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 9 ( 2.4%) | 13 ( 3.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 0.8%) | 7 ( 1.8%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| EYE DISCHARGE | MILD | 0 ( 0.0%) | 13 ( 3.4%) | 3 ( 1.5%) | 9 ( 2.4%) | 11 ( 2 8%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 0.8%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Events are counted once per patient as most severe reported.

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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| IRIS ADHESIONS | MILD | 2 (11.1%) | 1 ( 0.3%) | 1 ( 0.5%) | 6 ( 1.6%) | 9 ( 2.3%) |
| | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 4 ( 1.1%) | 5 ( 1.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.0%) |
| CONJUNCTIVAL HEMORRHAGE | MILD | 0 ( 0.0%) | 12 ( 3.2%) | 6 ( 3.0%) | 4 ( 1.1%) | 6 ( 1.5%) |
| | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| CORNEAL EDEMA | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 1.5%) | 5 ( 1.3%) | 13 ( 3.3%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| RUBEOSIS IRIDIS | MILD | 1 ( 5.6%) | 1 ( 0.3%) | 6 ( 3.0%) | 3 ( 0.8%) | 4 ( 1.0%) |
| | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| HYPOPYON | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 10 ( 2.6%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 6 ( 1.5%) |
| HYPHEMA | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) |
| MACULAR EDEMA | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 5 ( 1.3%) |
| | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| UVEITIS NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 0.8%) |
| | MODERATE | 1 ( 5.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| VITREOUS DETACHMENT | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULOPATHY | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| KERATITIS NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CATARACT NEC | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | MILD | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| DRY EYE NEC | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIPLOPIA | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLAUCOMA NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) |
| POSTERIOR CAPSULE OPACIFICATION | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION BLURRED | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| HYPOTONY OF EYE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| MYDRIASIS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CONJUNCTIVITIS NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | MILD | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| RETINAL TEAR (EXC DETACHMENT) | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| RETINAL HEMORRHAGE | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHARITIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSEUDOPHAKIA | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STRABISMUS NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS OPACITIES | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Events are counted once per patient as most severe reported.

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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| APHAKIA | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS TRANSIENT | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| BLOODSHOT EYE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL ATROPHY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL OPACITY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Events are counted once per patient as most severe reported.

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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| ERYTHEMA NEC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MEIBOMIAN CYST | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

ISTA Pharmaceuticals, Inc.
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Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| OCULAR HYPERAEMIA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAINFUL RED EYES | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEPIGMENTATION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL SCAR | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Events are counted once per patient as most severe reported.

Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| TOPOGRAPHY CORNEAL ABNORMAL | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | MILD | 0 ( 0.0%) | 10 ( 2.6%) | 8 ( 4.0%) | 9 ( 2.4%) | 9 ( 2.3%) |
| | MODERATE | 0 ( 0.0%) | 12 ( 3.2%) | 9 ( 4.5%) | 12 ( 3.2%) | 6 ( 1.5%) |
| | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 2.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| INTRAOCULAR PRESSURE INCREASED | MILD | 0 ( 0.0%) | 7 ( 1.9%) | 4 ( 2.0%) | 5 ( 1.3%) | 6 ( 1.5%) |
| | MODERATE | 0 ( 0.0%) | 11 ( 2.9%) | 8 ( 4.0%) | 10 ( 2.7%) | 5 ( 1.3%) |
| | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 2.0%) | 3 ( 0.8%) | 5 ( 1.3%) |
| CORNEAL STAINING | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 2.0%) | 4 ( 1.1%) | 3 ( 0.8%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | MILD | 0 ( 0.0%) | 15 ( 4.0%) | 6 ( 3.0%) | 23 ( 6.1%) | 20 ( 5.1%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 6 ( 1.6%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | MILD | 0 ( 0.0%) | 6 ( 1.6%) | 5 ( 2.5%) | 16 ( 4.2%) | 15 ( 3.8%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 6 ( 1.6%) | 4 ( 1.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | MILD | 0 ( 0.0%) | 9 ( 2.4%) | 2 ( 1.0%) | 11 ( 2.9%) | 11 ( 2.8%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CUTIS LAXA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Events are counted once per patient as most severe reported.

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Integrated Summary of Safety

Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| OCULAR HYPEREMIA | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| VITRECTOMY | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY DISORDER NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

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Integrated Summary of Safety

Table 16
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Severity
Safety Population

| System Organ Class / Preferred Term | Severity | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISUAL FIELD DEFECT NOS | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEADACHE NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PUPILLARY REFLEX IMPAIRED | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL ISCHEMIA NOS | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Events are counted once per patient as most severe reported.

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 17
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| NUMBER OF PATIENTS | 13 | 5 | 183 | 195 | 100 | 98 | 193 | 184 | 215 | 175 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 12 ( 92%) | 5 (100%) | 151 ( 83%) | 147 ( 75%) | 100 (100%) | 93 ( 95%) | 163 ( 84%) | 160 ( 87%) | 192 ( 89%) | 156 ( 89%) |
| EYE DISORDERS | 12 ( 92%) | 5 (100%) | 151 ( 83%) | 146 ( 75%) | 99 ( 99%) | 93 ( 95%) | 162 ( 84%) | 160 ( 87%) | 192 ( 89%) | 156 ( 89%) |
| IRITIS | 2 ( 15%) | 2 ( 40%) | 64 ( 35%) | 62 ( 32%) | 66 ( 66%) | 57 ( 58%) | 115 ( 60%) | 107 ( 58%) | 141 ( 66%) | 102 ( 58%) |
| OCULAR HYPEREMIA | 2 ( 15%) | 2 ( 40%) | 69 ( 38%) | 71 ( 36%) | 65 ( 65%) | 48 ( 49%) | 96 ( 50%) | 106 ( 58%) | 120 ( 56%) | 95 ( 54%) |
| EYE IRRITATION | 8 ( 62%) | 2 ( 40%) | 51 ( 28%) | 60 ( 31%) | 42 ( 42%) | 48 ( 49%) | 60 ( 31%) | 72 ( 39%) | 74 ( 34%) | 65 ( 37%) |
| EYE PAIN | 1 ( 8%) | 1 ( 20%) | 44 ( 24%) | 40 ( 21%) | 36 ( 36%) | 36 ( 37%) | 62 ( 32%) | 77 ( 42%) | 84 ( 39%) | 77 ( 44%) |
| LACRIMATION INCREASED | 2 ( 15%) | 2 ( 40%) | 44 ( 24%) | 43 ( 22%) | 37 ( 37%) | 28 ( 29%) | 55 ( 28%) | 69 ( 38%) | 80 ( 37%) | 59 ( 34%) |
| VISUAL ACUITY REDUCED | 3 ( 23%) | 1 ( 20%) | 38 ( 21%) | 36 ( 18%) | 36 ( 36%) | 41 ( 42%) | 55 ( 28%) | 46 ( 25%) | 59 ( 27%) | 39 ( 22%) |
| ABNORMAL SENSATION IN EYE | 2 ( 15%) | 0 ( 0%) | 36 ( 20%) | 32 ( 16%) | 31 ( 31%) | 31 ( 32%) | 44 ( 23%) | 57 ( 31%) | 63 ( 29%) | 51 ( 29%) |
| VITREOUS FLOATERS | 4 ( 31%) | 2 ( 40%) | 37 ( 20%) | 30 ( 15%) | 31 ( 31%) | 32 ( 33%) | 39 ( 20%) | 49 ( 27%) | 56 ( 26%) | 44 ( 25%) |
| VITREOUS HEMORRHAGE | 2 ( 15%) | 0 ( 0%) | 36 ( 20%) | 30 ( 15%) | 30 ( 30%) | 40 ( 41%) | 47 ( 24%) | 44 ( 24%) | 47 ( 22%) | 43 ( 25%) |
| PHOTOPHOBIA | 4 ( 31%) | 2 ( 40%) | 36 ( 20%) | 24 ( 12%) | 28 ( 28%) | 31 ( 32%) | 39 ( 20%) | 47 ( 26%) | 58 ( 27%) | 44 ( 25%) |
| CONJUNCTIVAL EDEMA | 1 ( 8%) | 0 ( 0%) | 33 ( 18%) | 26 ( 13%) | 24 ( 24%) | 24 ( 24%) | 45 ( 23%) | 51 ( 28%) | 55 ( 26%) | 34 ( 19%) |
| CATARACT NUCLEAR | 3 ( 23%) | 2 ( 40%) | 21 ( 11%) | 13 ( 7%) | 15 ( 15%) | 12 ( 12%) | 22 ( 11%) | 15 ( 8%) | 17 ( 8%) | 12 ( 7%) |
| RETINAL DETACHMENT | 3 ( 23%) | 0 ( 0%) | 15 ( 8%) | 11 ( 6%) | 16 ( 16%) | 6 ( 6%) | 17 ( 9%) | 18 ( 10%) | 30 ( 14%) | 15 ( 9%) |
| CATARACT SUBCAPSULAR | 1 ( 8%) | 1 ( 20%) | 10 ( 5%) | 16 ( 8%) | 16 ( 16%) | 17 ( 17%) | 15 ( 8%) | 14 ( 8%) | 17 ( 8%) | 20 ( 11%) |
| PHOTOPSIA | 0 ( 0%) | 0 ( 0%) | 12 ( 7%) | 10 ( 5%) | 6 ( 6%) | 16 ( 16%) | 19 ( 10%) | 26 ( 14%) | 23 ( 11%) | 15 ( 9%) |
| CATARACT CORTICAL | 3 ( 23%) | 2 ( 40%) | 12 ( 7%) | 15 ( 8%) | 9 ( 9%) | 5 ( 5%) | 15 ( 8%) | 15 ( 8%) | 18 ( 8%) | 13 ( 7%) |
| CORNEAL EROSION | 0 ( 0%) | 1 ( 20%) | 8 ( 4%) | 16 ( 8%) | 5 ( 5%) | 5 ( 5%) | 12 ( 6%) | 13 ( 7%) | 9 ( 4%) | 8 ( 5%) |
| CORNEAL EDEMA | 1 ( 8%) | 0 ( 0%) | 7 ( 4%) | 5 ( 3%) | 13 ( 13%) | 4 ( 4%) | 12 ( 6%) | 8 ( 4%) | 16 ( 7%) | 8 ( 5%) |
| RUBEOSIS IRIDIS | 0 ( 0%) | 1 ( 20%) | 11 ( 6%) | 8 ( 4%) | 8 ( 8%) | 8 ( 8%) | 6 ( 3%) | 11 ( 6%) | 13 ( 6%) | 6 ( 3%) |
| EYE DISCHARGE | 0 ( 0%) | 0 ( 0%) | 10 ( 5%) | 8 ( 4%) | 7 ( 7%) | 3 ( 3%) | 11 ( 6%) | 12 ( 7%) | 10 ( 5%) | 10 ( 6%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 13 ( 7%) | 12 ( 6%) | 7 ( 7%) | 4 ( 4%) | 6 ( 3%) | 8 ( 4%) | 7 ( 3%) | 11 ( 6%) |
| IRIS ADHESIONS | 2 ( 15%) | 0 ( 0%) | 6 ( 3%) | 7 ( 4%) | 5 ( 5%) | 4 ( 4%) | 8 ( 4%) | 5 ( 3%) | 16 ( 7%) | 11 ( 6%) |
| MACULAR EDEMA | 0 ( 0%) | 1 ( 20%) | 6 ( 3%) | 5 ( 3%) | 6 ( 6%) | 10 ( 10%) | 8 ( 4%) | 3 ( 2%) | 12 ( 6%) | 7 ( 4%) |
| CORNEAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 7 ( 4%) | 4 ( 4%) | 2 ( 2%) | 8 ( 4%) | 9 ( 5%) | 16 ( 7%) | 9 ( 5%) |
| HYPHEMA | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 4 ( 2%) | 4 ( 4%) | 4 ( 4%) | 4 ( 2%) | 8 ( 4%) | 7 ( 3%) | 8 ( 5%) |
| CATARACT NEC | 0 ( 0%) | 0 ( 0%) | 6 ( 3%) | 4 ( 2%) | 0 ( 0%) | 1 ( 1%) | 3 ( 2%) | 7 ( 4%) | 6 ( 3%) | 3 ( 2%) |
| BLINDNESS NEC | 1 ( 8%) | 0 ( 0%) | 3 ( 2%) | 1 ( 1%) | 8 ( 8%) | 1 ( 1%) | 3 ( 2%) | 3 ( 2%) | 5 ( 2%) | 4 ( 2%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 2 ( 1%) | 4 ( 2%) | 13 ( 6%) | 8 ( 5%) |
| DRY EYE NEC | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 4 ( 2%) | 3 ( 3%) | 4 ( 4%) | 3 ( 2%) | 2 ( 1%) | 3 ( 1%) | 6 ( 3%) |
| GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 4 ( 2%) | 1 ( 1%) | 1 ( 1%) | 4 ( 4%) | 2 ( 1%) | 1 ( 1%) | 9 ( 4%) | 3 ( 2%) |
| VISION BLURRED | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 4 ( 2%) | 5 ( 5%) | 5 ( 5%) | 3 ( 2%) | 2 ( 1%) | 2 ( 1%) | 2 ( 1%) |
| CATARACT NOS AGGRAVATED | 1 ( 8%) | 0 ( 0%) | 2 ( 1%) | 6 ( 3%) | 2 ( 2%) | 2 ( 2%) | 1 ( 1%) | 4 ( 2%) | 1 ( 0%) | 2 ( 1%) |
| KERATITIS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 2%) | 1 ( 1%) | 3 ( 3%) | 1 ( 1%) | 3 ( 2%) | 4 ( 2%) | 4 ( 2%) |
| VITREOUS DETACHMENT | 1 ( 8%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 2 ( 2%) | 6 ( 3%) | 3 ( 2%) | 2 ( 1%) | 3 ( 2%) |
| MACULOPATHY | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 3 ( 2%) | 1 ( 1%) | 3 ( 3%) | 3 ( 2%) | 2 ( 1%) | 2 ( 1%) | 3 ( 2%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 4 ( 4%) | 2 ( 2%) | 2 ( 1%) | 1 ( 1%) | 2 ( 1%) | 4 ( 2%) |
| UVEITIS NOS | 1 ( 8%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 3 ( 2%) | 4 ( 2%) | 0 ( 0%) | 4 ( 2%) |
| POST-OPERATIVE PAIN | 1 ( 8%) | 0 ( 0%) | 2 ( 1%) | 5 ( 3%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 2 ( 1%) | 4 ( 2%) | 4 ( 2%) | 1 ( 1%) |



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Table 17
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| RETINOPATHY DIABETIC | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 2 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 3 ( 1%) | 3 ( 2%) |
| BLEPHARITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 2 ( 2%) | 3 ( 2%) | 0 ( 0%) | 0 ( 0%) | 5 ( 3%) |
| HYPOTONY OF EYE | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 5 ( 2%) | 1 ( 1%) |
| RETINAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 3 ( 2%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 4 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL EPITHELIUM DEFECT | 1 ( 8%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 2 ( 2%) | 4 ( 2%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) |
| DIPLOPIA | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 1 ( 1%) | 2 ( 2%) | 0 ( 0%) | 4 ( 2%) | 1 ( 0%) | 1 ( 1%) |
| RETINAL ISCHEMIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 2 ( 2%) | 2 ( 1%) | 2 ( 1%) | 1 ( 0%) | 1 ( 1%) |
| CORNEAL ABRASION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 2 ( 1%) | 1 ( 0%) | 1 ( 1%) |
| MYDRIASIS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 1 ( 1%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 5 ( 3%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) |
| CONJUNCTIVITIS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 2 ( 2%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 3 ( 3%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 3%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) |
| PSEUDOPHAKIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| EYELID PTOSIS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 3%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC ATROPHY | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 3 ( 2%) | 0 ( 0%) | 0 ( 0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| VITREOUS DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) |
| APHAKIA | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| EYE ALLERGY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 1 ( 0%) | 0 ( 0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) |
| OCULAR HYPERTENSION | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) |
| PAINFUL RED EYES | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) |
| CHEMOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| CORTICAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| IRIDOCYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LENTICULAR OPACITIES | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| MACULAR DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) |
| RETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| RETINAL MICROANEURYSMS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL SCAR | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) |
| BLINDNESS TRANSIENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL DETACHMENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0%) | 1 ( 20%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| CORNEAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOPATHY BAND | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| KERATOPATHY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| MEIBOMIAN CYST | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| PERIORBITAL HEMATOMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| RETINAL DEPIGMENTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |



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Table 17
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| STRABISMUS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| VITREOUS OPACITIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANISEIKONIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| ARCUS SENILIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLINDNESS NIGHT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| BLOODSHOT EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| CHALAZION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| CHORIORETINAL ATROPHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| COLOUR BLINDNESS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| CORNEAL DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL SCAR | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL ULCER NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EXOPHTHALMOS ENDOCRINE | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE HEMORRHAGE NEC | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION STAPHYLOCOCCAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| EYE INFLAMMATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| EYELID DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| IRIS NEVUS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| OCULAR HYPERAEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| OPTIC DISC HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC NERVE INJURY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PAPILLEDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PINGUECULA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| RETINAL DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL EXUDATES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL VASCULITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| SCLERITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UVEITIS DIABETIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

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Table 17
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| VISION ABNORMAL NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| INVESTIGATIONS | 3 ( 23%) | 0 ( 0%) | 22 ( 12%) | 22 ( 11%) | 25 ( 25%) | 23 ( 23%) | 30 ( 16%) | 20 ( 11%) | 24 ( 11%) | 22 ( 13%) |
| INTRAOCULAR PRESSURE INCREASED | 3 ( 23%) | 0 ( 0%) | 20 ( 11%) | 19 ( 10%) | 23 ( 23%) | 17 ( 17%) | 27 ( 14%) | 15 ( 8%) | 22 ( 10%) | 18 ( 10%) |
| CORNEAL STAINING | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 3 ( 2%) | 2 ( 2%) | 6 ( 6%) | 3 ( 2%) | 6 ( 3%) | 3 ( 1%) | 5 ( 3%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0%) | 0 ( 0%) | 12 ( 7%) | 14 ( 7%) | 10 ( 10%) | 9 ( 9%) | 17 ( 9%) | 22 ( 12%) | 24 ( 11%) | 14 ( 8%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 7 ( 4%) | 8 ( 4%) | 8 ( 8%) | 4 ( 4%) | 12 ( 6%) | 17 ( 9%) | 17 ( 8%) | 8 ( 5%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 7 ( 4%) | 8 ( 4%) | 4 ( 4%) | 4 ( 4%) | 8 ( 4%) | 13 ( 7%) | 14 ( 7%) | 6 ( 3%) |
| OCULAR HYPEREMIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| CUTIS LAXA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIORBITAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) |
| DERMATITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| ECCHYMOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| PRURITUS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 8%) | 0 ( 0%) | 8 ( 4%) | 6 ( 3%) | 5 ( 5%) | 2 ( 2%) | 8 ( 4%) | 5 ( 3%) | 4 ( 2%) | 4 ( 2%) |
| POST-OPERATIVE COMPLICATIONS NOS | 1 ( 8%) | 0 ( 0%) | 4 ( 2%) | 4 ( 2%) | 3 ( 3%) | 1 ( 1%) | 2 ( 1%) | 3 ( 2%) | 2 ( 1%) | 2 ( 1%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 2 ( 2%) | 0 ( 0%) | 2 ( 1%) | 2 ( 1%) | 1 ( 0%) | 1 ( 1%) |
| VITRECTOMY | 0 ( 0%) | 0 ( 0%) | 4 ( 2%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| EYE IRRITATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LENS IMPLANT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCLERAL OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| SUTURE LINE PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 4 ( 4%) | 1 ( 1%) | 1 ( 1%) | 3 ( 2%) | 6 ( 3%) | 1 ( 1%) |
| PUPILLARY DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 3%) | 0 ( 0%) | 1 ( 1%) | 3 ( 2%) | 3 ( 1%) | 0 ( 0%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| FACIAL PALSY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| HEADACHE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| VITH NERVE PARALYSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| HYPERSENSITIVITY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| MULTIPLE ALLERGIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJURY AND POISONING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHEMICAL BURNS OF EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEAD INJURY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |

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Table 17
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VASCULAR DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |

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Integrated Summary of Safety

Table 18
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| System Organ Class / Preferred Term | Control: WW Male | Control: WW Female | Control: Saline Male | Control: Saline Female | 7.5 IU Vitrase Male | 7.5 IU Vitrase Female | 55 IU Vitrase Male | 55 IU Vitrase Female | 75 IU Vitrase Male | 75 IU Vitrase Female |
|---|---|---|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 13 | 5 | 183 | 195 | 100 | 98 | 193 | 184 | 215 | 175 |
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 10 ( 77%) | 1 ( 20%) | 116 ( 63%) | 128 ( 66%) | 85 ( 85%) | 83 ( 85%) | 145 ( 75%) | 145 ( 79%) | 182 ( 85%) | 143 ( 82%) |
| EYE DISORDERS | 10 ( 77%) | 1 ( 20%) | 116 ( 63%) | 127 ( 65%) | 85 ( 85%) | 83 ( 85%) | 143 ( 74%) | 145 ( 79%) | 182 ( 85%) | 143 ( 82%) |
| IRITIS | 1 ( 8%) | 0 ( 0%) | 50 ( 27%) | 56 ( 29%) | 53 ( 53%) | 47 ( 48%) | 102 ( 53%) | 100 ( 54%) | 134 ( 62%) | 97 ( 55%) |
| OCULAR HYPEREMIA | 1 ( 8%) | 0 ( 0%) | 52 ( 28%) | 61 ( 31%) | 50 ( 50%) | 35 ( 36%) | 76 ( 39%) | 82 ( 45%) | 104 ( 48%) | 79 ( 45%) |
| EYE PAIN | 1 ( 8%) | 0 ( 0%) | 29 ( 16%) | 28 ( 14%) | 23 ( 23%) | 25 ( 26%) | 53 ( 27%) | 60 ( 33%) | 68 ( 32%) | 60 ( 34%) |
| EYE IRRITATION | 5 ( 38%) | 0 ( 0%) | 37 ( 20%) | 42 ( 22%) | 30 ( 30%) | 31 ( 32%) | 48 ( 25%) | 48 ( 26%) | 51 ( 24%) | 52 ( 30%) |
| LACRIMATION INCREASED | 1 ( 8%) | 0 ( 0%) | 28 ( 15%) | 28 ( 14%) | 26 ( 26%) | 19 ( 19%) | 43 ( 22%) | 51 ( 28%) | 55 ( 26%) | 48 ( 27%) |
| ABNORMAL SENSATION IN EYE | 1 ( 8%) | 0 ( 0%) | 26 ( 14%) | 24 ( 12%) | 21 ( 21%) | 22 ( 22%) | 34 ( 18%) | 44 ( 24%) | 52 ( 24%) | 40 ( 23%) |
| PHOTOPHOBIA | 3 ( 23%) | 0 ( 0%) | 26 ( 14%) | 16 ( 8%) | 20 ( 20%) | 21 ( 21%) | 28 ( 15%) | 35 ( 19%) | 47 ( 22%) | 38 ( 22%) |
| CONJUNCTIVAL EDEMA | 1 ( 8%) | 0 ( 0%) | 26 ( 14%) | 23 ( 12%) | 15 ( 15%) | 15 ( 15%) | 39 ( 20%) | 35 ( 19%) | 48 ( 22%) | 29 ( 17%) |
| VITREOUS FLOATERS | 3 ( 23%) | 0 ( 0%) | 22 ( 12%) | 20 ( 10%) | 19 ( 19%) | 21 ( 21%) | 26 ( 13%) | 32 ( 17%) | 39 ( 18%) | 35 ( 20%) |
| VISUAL ACUITY REDUCED | 2 ( 15%) | 0 ( 0%) | 18 ( 10%) | 25 ( 13%) | 21 ( 21%) | 26 ( 27%) | 38 ( 20%) | 28 ( 15%) | 36 ( 17%) | 22 ( 13%) |
| VITREOUS HEMORRHAGE | 1 ( 8%) | 0 ( 0%) | 15 ( 8%) | 10 ( 5%) | 17 ( 17%) | 15 ( 15%) | 17 ( 9%) | 20 ( 11%) | 16 ( 7%) | 13 ( 7%) |
| PHOTOPSIA | 0 ( 0%) | 0 ( 0%) | 10 ( 5%) | 4 ( 2%) | 3 ( 3%) | 15 ( 15%) | 12 ( 6%) | 13 ( 7%) | 18 ( 8%) | 10 ( 6%) |
| CATARACT SUBCAPSULAR | 0 ( 0%) | 0 ( 0%) | 4 ( 2%) | 7 ( 4%) | 9 ( 9%) | 11 ( 11%) | 8 ( 4%) | 12 ( 7%) | 9 ( 4%) | 7 ( 4%) |
| RETINAL DETACHMENT | 1 ( 8%) | 0 ( 0%) | 7 ( 4%) | 3 ( 2%) | 9 ( 9%) | 3 ( 3%) | 8 ( 4%) | 10 ( 5%) | 13 ( 6%) | 9 ( 5%) |
| CATARACT NUCLEAR | 1 ( 8%) | 0 ( 0%) | 10 ( 5%) | 6 ( 3%) | 6 ( 6%) | 6 ( 6%) | 16 ( 8%) | 6 ( 3%) | 5 ( 2%) | 5 ( 3%) |
| CATARACT CORTICAL | 1 ( 8%) | 0 ( 0%) | 8 ( 4%) | 8 ( 4%) | 2 ( 2%) | 1 ( 1%) | 8 ( 4%) | 11 ( 6%) | 11 ( 5%) | 8 ( 5%) |
| CORNEAL EROSION | 0 ( 0%) | 0 ( 0%) | 5 ( 3%) | 11 ( 6%) | 2 ( 2%) | 4 ( 4%) | 7 ( 4%) | 7 ( 4%) | 7 ( 3%) | 4 ( 2%) |
| CORNEAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 2 ( 2%) | 2 ( 2%) | 7 ( 4%) | 7 ( 4%) | 13 ( 6%) | 8 ( 5%) |
| EYE DISCHARGE | 0 ( 0%) | 0 ( 0%) | 7 ( 4%) | 6 ( 3%) | 2 ( 2%) | 1 ( 1%) | 8 ( 4%) | 4 ( 2%) | 7 ( 3%) | 7 ( 4%) |
| IRIS ADHESIONS | 2 ( 15%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 3 ( 3%) | 1 ( 1%) | 6 ( 3%) | 4 ( 2%) | 8 ( 4%) | 10 ( 6%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 5 ( 3%) | 9 ( 5%) | 4 ( 4%) | 2 ( 2%) | 2 ( 1%) | 4 ( 2%) | 3 ( 1%) | 5 ( 3%) |
| CORNEAL EDEMA | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 2 ( 1%) | 2 ( 2%) | 2 ( 2%) | 7 ( 4%) | 1 ( 1%) | 11 ( 5%) | 6 ( 3%) |
| RUBEOSIS IRIDIS | 0 ( 0%) | 1 ( 20%) | 3 ( 2%) | 2 ( 1%) | 4 ( 4%) | 4 ( 4%) | 3 ( 2%) | 3 ( 2%) | 6 ( 3%) | 3 ( 2%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 2 ( 1%) | 4 ( 2%) | 13 ( 6%) | 8 ( 5%) |
| HYPHEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 2 ( 2%) | 1 ( 1%) | 3 ( 2%) | 2 ( 1%) | 3 ( 1%) | 3 ( 2%) |
| MACULAR EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 1 ( 1%) | 2 ( 2%) | 2 ( 1%) | 1 ( 1%) | 4 ( 2%) | 4 ( 2%) |
| UVEITIS NOS | 1 ( 8%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 4 ( 2%) | 0 ( 0%) | 4 ( 2%) |
| VITREOUS DETACHMENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 5 ( 3%) | 1 ( 1%) | 0 ( 0%) | 3 ( 2%) |
| MACULOPATHY | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 3 ( 2%) | 0 ( 0%) | 2 ( 1%) | 2 ( 1%) |
| KERATITIS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 3 ( 3%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 3 ( 2%) |
| CATARACT NEC | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 3 ( 1%) | 1 ( 1%) |
| CATARACT NOS AGGRAVATED | 1 ( 8%) | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 0 ( 0%) | 1 ( 1%) |
| DRY EYE NEC | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 1 ( 0%) | 2 ( 1%) |
| DIPLOPIA | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 3 ( 2%) | 0 ( 0%) | 1 ( 1%) |
| GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 0%) | 1 ( 1%) |
| VISION BLURRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 1 ( 0%) | 1 ( 1%) |
| BLINDNESS NEC | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) |
| HYPOTONY OF EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 3 ( 1%) | 1 ( 1%) |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 18
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| | Control | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| MYDRIASIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 1 ( 1%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 1 ( 1%) |
| CORNEAL EPITHELIUM DEFECT | 1 ( 8%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINOPATHY DIABETIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| VITREOUS DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) |
| CONJUNCTIVITIS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| CORNEAL ABRASION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| CORTICAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIDOCYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| BLEPHARITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL DETACHMENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| MACULAR DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OCULAR HYPERTENSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) |
| PSEUDOPHAKIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| STRABISMUS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| VITREOUS OPACITIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| APHAKIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLINDNESS NIGHT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| BLINDNESS TRANSIENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOODSHOT EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHORIORETINAL ATROPHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COLOUR BLINDNESS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| CORNEAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE ALLERGY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| EYE INFLAMMATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| EYELID DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYELID PTOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOPATHY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| LENTICULAR OPACITIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 18
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| MEIBOMIAN CYST | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OCULAR HYPERAEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC ATROPHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| PAINFUL RED EYES | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PINGUECULA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| RETINAL DEPIGMENTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ISCHEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| RETINAL MICROANEURYSMS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL SCAR | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UVEITIS DIABETIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| INVESTIGATIONS | 0 ( 0%) | 0 ( 0%) | 11 ( 6%) | 13 ( 7%) | 9 ( 9%) | 12 ( 12%) | 17 ( 9%) | 7 ( 4%) | 11 ( 5%) | 9 ( 5%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 0 ( 0%) | 10 ( 5%) | 10 ( 5%) | 8 ( 8%) | 8 ( 8%) | 14 ( 7%) | 4 ( 2%) | 9 ( 4%) | 7 ( 4%) |
| CORNEAL STAINING | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 3 ( 2%) | 1 ( 1%) | 4 ( 4%) | 3 ( 2%) | 3 ( 2%) | 2 ( 1%) | 2 ( 1%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0%) | 0 ( 0%) | 5 ( 3%) | 10 ( 5%) | 5 ( 5%) | 4 ( 4%) | 14 ( 7%) | 15 ( 8%) | 18 ( 8%) | 6 ( 3%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 4 ( 2%) | 4 ( 4%) | 2 ( 2%) | 9 ( 5%) | 13 ( 7%) | 13 ( 6%) | 6 ( 3%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 6 ( 3%) | 2 ( 2%) | 1 ( 1%) | 7 ( 4%) | 7 ( 4%) | 10 ( 5%) | 2 ( 1%) |
| CUTIS LAXA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ECCHYMOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| OCULAR HYPEREMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIORBITAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| SURGICAL AND MEDICAL PROCEDURES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 3 ( 3%) | 1 ( 1%) | 4 ( 2%) | 1 ( 1%) | 1 ( 0%) | 3 ( 2%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 2%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 1 ( 0%) | 1 ( 1%) |
| VITRECTOMY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE IRRITATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCLERAL OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 5 ( 2%) | 1 ( 1%) |
| PUPILLARY DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 3 ( 1%) | 0 ( 0%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| HEADACHE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |



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Integrated Summary of Safety

Table 18
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Sex
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | Male | Female | Male | Female | Male | Female | Male | Female | Male | Female |
| INJURY AND POISONING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEAD INJURY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VASCULAR DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) |

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Integrated Summary of Safety

Table 19
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| NUMBER OF PATIENTS | 3 | 15 | 151 | 224 | 95 | 103 | 164 | 212 | 151 | 240 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | 3 (100%) | 14 ( 93%) | 119 ( 79%) | 177 ( 79%) | 93 ( 98%) | 100 ( 97%) | 141 ( 86%) | 181 ( 85%) | 140 ( 93%) | 209 ( 87%) |
| EYE DISORDERS | 3 (100%) | 14 ( 93%) | 119 ( 79%) | 176 ( 79%) | 93 ( 98%) | 99 ( 96%) | 140 ( 85%) | 181 ( 85%) | 140 ( 93%) | 209 ( 87%) |
| IRITIS | 1 ( 33%) | 3 ( 20%) | 45 ( 30%) | 81 ( 36%) | 56 ( 59%) | 67 ( 65%) | 99 ( 60%) | 123 ( 58%) | 104 ( 69%) | 139 ( 58%) |
| OCULAR HYPEREMIA | 0 ( 0%) | 4 ( 27%) | 58 ( 38%) | 82 ( 37%) | 59 ( 62%) | 54 ( 52%) | 80 ( 49%) | 121 ( 57%) | 92 ( 61%) | 123 ( 51%) |
| EYE IRRITATION | 2 ( 67%) | 8 ( 53%) | 48 ( 32%) | 61 ( 27%) | 47 ( 49%) | 43 ( 42%) | 62 ( 38%) | 69 ( 33%) | 67 ( 44%) | 72 ( 30%) |
| EYE PAIN | 0 ( 0%) | 2 ( 13%) | 33 ( 22%) | 51 ( 23%) | 36 ( 38%) | 36 ( 35%) | 62 ( 38%) | 77 ( 36%) | 66 ( 44%) | 95 ( 40%) |
| LACRIMATION INCREASED | 0 ( 0%) | 4 ( 27%) | 40 ( 26%) | 47 ( 21%) | 35 ( 37%) | 30 ( 29%) | 58 ( 35%) | 66 ( 31%) | 57 ( 38%) | 82 ( 34%) |
| VISUAL ACUITY REDUCED | 0 ( 0%) | 4 ( 27%) | 26 ( 17%) | 48 ( 21%) | 33 ( 35%) | 44 ( 43%) | 44 ( 27%) | 57 ( 27%) | 43 ( 28%) | 55 ( 23%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0%) | 2 ( 13%) | 25 ( 17%) | 43 ( 19%) | 27 ( 28%) | 35 ( 34%) | 43 ( 26%) | 58 ( 27%) | 48 ( 32%) | 66 ( 28%) |
| VITREOUS FLOATERS | 1 ( 33%) | 5 ( 33%) | 24 ( 16%) | 43 ( 19%) | 27 ( 28%) | 36 ( 35%) | 37 ( 23%) | 50 ( 24%) | 44 ( 29%) | 56 ( 23%) |
| VITREOUS HEMORRHAGE | 0 ( 0%) | 2 ( 13%) | 30 ( 20%) | 36 ( 16%) | 32 ( 34%) | 38 ( 37%) | 41 ( 25%) | 50 ( 24%) | 40 ( 26%) | 50 ( 21%) |
| PHOTOPHOBIA | 1 ( 33%) | 5 ( 33%) | 33 ( 22%) | 27 ( 12%) | 31 ( 33%) | 28 ( 27%) | 39 ( 24%) | 47 ( 22%) | 51 ( 34%) | 51 ( 21%) |
| CONJUNCTIVAL EDEMA | 0 ( 0%) | 1 ( 7%) | 32 ( 21%) | 27 ( 12%) | 20 ( 21%) | 28 ( 27%) | 41 ( 25%) | 55 ( 26%) | 41 ( 27%) | 48 ( 20%) |
| CATARACT NUCLEAR | 2 ( 67%) | 3 ( 20%) | 13 ( 9%) | 21 ( 9%) | 14 ( 15%) | 13 ( 13%) | 13 ( 8%) | 24 ( 11%) | 12 ( 8%) | 17 ( 7%) |
| RETINAL DETACHMENT | 1 ( 33%) | 2 ( 13%) | 16 ( 11%) | 10 ( 4%) | 14 ( 15%) | 8 ( 8%) | 22 ( 13%) | 13 ( 6%) | 25 ( 17%) | 20 ( 8%) |
| CATARACT SUBCAPSULAR | 1 ( 33%) | 1 ( 7%) | 15 ( 10%) | 11 ( 5%) | 15 ( 16%) | 18 ( 17%) | 11 ( 7%) | 18 ( 8%) | 16 ( 11%) | 22 ( 9%) |
| PHOTOPSIA | 0 ( 0%) | 0 ( 0%) | 14 ( 9%) | 8 ( 4%) | 14 ( 15%) | 8 ( 8%) | 21 ( 13%) | 24 ( 11%) | 15 ( 10%) | 23 ( 10%) |
| CATARACT CORTICAL | 0 ( 0%) | 5 ( 33%) | 12 ( 8%) | 15 ( 7%) | 4 ( 4%) | 10 ( 10%) | 12 ( 7%) | 18 ( 8%) | 13 ( 9%) | 18 ( 8%) |
| CORNEAL EROSION | 1 ( 33%) | 0 ( 0%) | 10 ( 7%) | 14 ( 6%) | 5 ( 5%) | 5 ( 5%) | 9 ( 5%) | 16 ( 8%) | 8 ( 5%) | 9 ( 4%) |
| CORNEAL EDEMA | 0 ( 0%) | 1 ( 7%) | 1 ( 1%) | 11 ( 5%) | 10 ( 11%) | 7 ( 7%) | 8 ( 5%) | 12 ( 6%) | 7 ( 5%) | 17 ( 7%) |
| RUBEOSIS IRIDIS | 0 ( 0%) | 1 ( 7%) | 10 ( 7%) | 9 ( 4%) | 11 ( 12%) | 5 ( 5%) | 9 ( 5%) | 8 ( 4%) | 12 ( 8%) | 7 ( 3%) |
| EYE DISCHARGE | 0 ( 0%) | 0 ( 0%) | 8 ( 5%) | 10 ( 4%) | 4 ( 4%) | 6 ( 6%) | 8 ( 5%) | 15 ( 7%) | 8 ( 5%) | 12 ( 5%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 8 ( 5%) | 17 ( 8%) | 4 ( 4%) | 7 ( 7%) | 4 ( 2%) | 10 ( 5%) | 12 ( 8%) | 6 ( 3%) |
| IRIS ADHESIONS | 0 ( 0%) | 2 ( 13%) | 7 ( 5%) | 6 ( 3%) | 7 ( 7%) | 2 ( 2%) | 6 ( 4%) | 7 ( 3%) | 15 ( 10%) | 12 ( 5%) |
| MACULAR EDEMA | 0 ( 0%) | 1 ( 7%) | 3 ( 2%) | 8 ( 4%) | 5 ( 5%) | 11 ( 11%) | 6 ( 4%) | 5 ( 2%) | 13 ( 9%) | 6 ( 3%) |
| CORNEAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 8 ( 4%) | 2 ( 2%) | 4 ( 4%) | 6 ( 4%) | 11 ( 5%) | 13 ( 9%) | 12 ( 5%) |
| HYPHEMA | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 3 ( 1%) | 2 ( 2%) | 6 ( 6%) | 4 ( 2%) | 8 ( 4%) | 8 ( 5%) | 7 ( 3%) |
| CATARACT NEC | 0 ( 0%) | 0 ( 0%) | 6 ( 4%) | 4 ( 2%) | 1 ( 1%) | 0 ( 0%) | 3 ( 2%) | 7 ( 3%) | 5 ( 3%) | 4 ( 2%) |
| BLINDNESS NEC | 0 ( 0%) | 1 ( 7%) | 1 ( 1%) | 3 ( 1%) | 7 ( 7%) | 2 ( 2%) | 4 ( 2%) | 2 ( 1%) | 4 ( 3%) | 5 ( 2%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 4 ( 2%) | 2 ( 1%) | 10 ( 7%) | 11 ( 5%) |
| DRY EYE NEC | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 3 ( 1%) | 3 ( 3%) | 4 ( 4%) | 2 ( 1%) | 3 ( 1%) | 3 ( 2%) | 6 ( 3%) |
| GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 2 ( 1%) | 1 ( 1%) | 4 ( 4%) | 2 ( 1%) | 1 ( 0%) | 7 ( 5%) | 5 ( 2%) |
| VISION BLURRED | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 2 ( 1%) | 5 ( 5%) | 5 ( 5%) | 1 ( 1%) | 4 ( 2%) | 0 ( 0%) | 4 ( 2%) |
| CATARACT NOS AGGRAVATED | 0 ( 0%) | 1 ( 7%) | 2 ( 1%) | 6 ( 3%) | 0 ( 0%) | 4 ( 4%) | 1 ( 1%) | 4 ( 2%) | 3 ( 2%) | 0 ( 0%) |
| KERATITIS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 2%) | 2 ( 2%) | 2 ( 2%) | 2 ( 1%) | 2 ( 1%) | 5 ( 3%) | 3 ( 1%) |
| VITREOUS DETACHMENT | 0 ( 0%) | 1 ( 7%) | 1 ( 1%) | 1 ( 0%) | 1 ( 1%) | 2 ( 2%) | 9 ( 5%) | 0 ( 0%) | 2 ( 1%) | 3 ( 1%) |
| MACULOPATHY | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 4 ( 2%) | 3 ( 3%) | 1 ( 1%) | 0 ( 0%) | 5 ( 2%) | 1 ( 1%) | 4 ( 2%) |

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Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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ISTA Pharmaceuticals, Inc.
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Table 19
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 2 ( 2%) | 4 ( 4%) | 1 ( 1%) | 2 ( 1%) | 2 ( 1%) | 4 ( 2%) |
| UVEITIS NOS | 0 ( 0%) | 1 ( 7%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) | 2 ( 2%) | 5 ( 3%) | 2 ( 1%) | 2 ( 1%) | 2 ( 1%) |
| POST-OPERATIVE PAIN | 1 ( 33%) | 0 ( 0%) | 1 ( 1%) | 6 ( 3%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 3 ( 2%) | 2 ( 1%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 1 ( 1%) | 3 ( 2%) | 3 ( 1%) | 3 ( 2%) | 2 ( 1%) |
| RETINOPATHY DIABETIC | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 3 ( 1%) | 1 ( 1%) | 0 ( 0%) | 3 ( 2%) | 0 ( 0%) | 5 ( 3%) | 1 ( 0%) |
| BLEPHARITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 3 ( 3%) | 0 ( 0%) | 3 ( 1%) | 2 ( 1%) | 3 ( 1%) |
| HYPOTONY OF EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 2 ( 1%) | 3 ( 2%) | 3 ( 1%) |
| RETINAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 4 ( 2%) | 2 ( 2%) | 0 ( 0%) | 2 ( 1%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0%) | 1 ( 7%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 2 ( 2%) | 3 ( 2%) | 1 ( 0%) | 1 ( 1%) | 1 ( 0%) |
| DIPLOPIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 3 ( 3%) | 2 ( 1%) | 2 ( 1%) | 2 ( 1%) | 0 ( 0%) |
| RETINAL ISCHEMIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 2 ( 2%) | 1 ( 1%) | 3 ( 2%) | 1 ( 0%) | 1 ( 1%) | 1 ( 0%) |
| CONJUNCTIVITIS NEC | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) | 3 ( 3%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) |
| CORNEAL ABRASION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 2 ( 2%) | 1 ( 1%) | 2 ( 1%) | 1 ( 1%) | 1 ( 0%) |
| MYDRIASIS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 3 ( 1%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 3 ( 1%) | 0 ( 0%) | 2 ( 1%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 3 ( 3%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 3%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| PSEUDOPHAKIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| EYELID PTOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 3 ( 3%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC ATROPHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| VITREOUS DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) |
| APHAKIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| EYE ALLERGY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 1 ( 1%) | 0 ( 0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| OCULAR HYPERTENSION | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| PAINFUL RED EYES | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) |
| CHEMOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CORTICAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| IRIDOCYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LENTICULAR OPACITIES | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| MACULAR DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| RETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| RETINAL MICROANEURYSMS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL SCAR | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 0 ( 0%) |
| BLINDNESS TRANSIENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL DETACHMENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CONJUNCTIVITIS ALLERGIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |

Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 19
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CORNEAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOPATHY BAND | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| KERATOPATHY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MEIBOMIAN CYST | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| PERIORBITAL HEMATOMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ARTERY EMBOLISM | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| RETINAL DEPIGMENTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| STRABISMUS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| VISUAL ACUITY REDUCED TRANSIENTLY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| VITREOUS OPACITIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| ANGLE CLOSURE GLAUCOMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ANISEIKONIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ARCUS SENILIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLEPHAROCONJUNCTIVITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLINDNESS NIGHT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| BLOODSHOT EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| CHALAZION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CHORIORETINAL ATROPHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| COLOUR BLINDNESS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CORNEAL DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL SCAR | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CORNEAL ULCER NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EXOPHTHALMOS ENDOCRINE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE HEMORRHAGE NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION FUNGAL NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION STAPHYLOCOCCAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| EYE INFLAMMATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| EYELID DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HERPES SIMPLEX OPHTHALMIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| IRIS NEVUS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OCULAR HYPERAEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |



Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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Table 19
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| OPTIC DISC HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC NERVE INJURY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PAPILLEDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PINGUECULA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| RETINAL DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL EXUDATES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL VASCULITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| SCLERITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UVEITIS DIABETIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISION ABNORMAL NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| INVESTIGATIONS | 0 ( 0%) | 3 ( 20%) | 17 ( 11%) | 27 ( 12%) | 24 ( 25%) | 24 ( 23%) | 18 ( 11%) | 32 ( 15%) | 24 ( 16%) | 22 ( 9%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 3 ( 20%) | 15 ( 10%) | 24 ( 11%) | 20 ( 21%) | 20 ( 19%) | 15 ( 9%) | 27 ( 13%) | 22 ( 15%) | 18 ( 8%) |
| CORNEAL STAINING | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 4 ( 2%) | 4 ( 4%) | 4 ( 4%) | 3 ( 2%) | 6 ( 3%) | 4 ( 3%) | 4 ( 2%) |
| INTRAOCULAR PRESSURE ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0%) | 0 ( 0%) | 9 ( 6%) | 17 ( 8%) | 13 ( 14%) | 6 ( 6%) | 17 ( 10%) | 22 ( 10%) | 16 ( 11%) | 22 ( 9%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 6 ( 4%) | 9 ( 4%) | 8 ( 8%) | 4 ( 4%) | 14 ( 9%) | 15 ( 7%) | 10 ( 7%) | 15 ( 6%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 3 ( 2%) | 12 ( 5%) | 8 ( 8%) | 0 ( 0%) | 8 ( 5%) | 13 ( 6%) | 9 ( 6%) | 11 ( 5%) |
| OCULAR HYPEREMIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CUTIS LAXA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIORBITAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| DERMATITIS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| ECCHYMOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| PRURITUS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SURGICAL AND MEDICAL PROCEDURES | 1 ( 33%) | 0 ( 0%) | 2 ( 1%) | 12 ( 5%) | 5 ( 5%) | 2 ( 2%) | 7 ( 4%) | 6 ( 3%) | 3 ( 2%) | 5 ( 2%) |
| POST-OPERATIVE COMPLICATIONS NOS | 1 ( 33%) | 0 ( 0%) | 2 ( 1%) | 6 ( 3%) | 2 ( 2%) | 2 ( 2%) | 1 ( 1%) | 4 ( 2%) | 2 ( 1%) | 2 ( 1%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 1 ( 1%) | 3 ( 2%) | 1 ( 0%) | 1 ( 1%) | 1 ( 0%) |
| VITRECTOMY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 2%) | 2 ( 2%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| EYE IRRITATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LENS IMPLANT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCLERAL OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| SUTURE LINE PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |



Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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Table 19
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| NERVOUS SYSTEM DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 4 ( 4%) | 1 ( 1%) | 1 ( 1%) | 3 ( 1%) | 5 ( 3%) | 2 ( 1%) |
| PUPILLARY DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 1 ( 1%) | 1 ( 1%) | 3 ( 1%) | 3 ( 2%) | 0 ( 0%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| FACIAL PALSY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| HEADACHE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| VITH NERVE PARALYSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IMMUNE SYSTEM DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPERSENSITIVITY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MULTIPLE ALLERGIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJURY AND POISONING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHEMICAL BURNS OF EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEAD INJURY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| BENIGN NEOPLASM OF CHOROID | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| RADIOACTIVE IODINE THERAPY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| MECHANICAL COMPLICATION OF IMPLANT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VASCULAR DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |



Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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Table 20
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| NUMBER OF PATIENTS | 3 | 15 | 151 | 224 | 95 | 103 | 164 | 212 | 151 | 240 |
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | 0 ( 0%) | 11 ( 73%) | 107 ( 71%) | 135 ( 60%) | 83 ( 87%) | 85 ( 83%) | 125 ( 76%) | 164 ( 77%) | 132 ( 87%) | 194 ( 81%) |
| EYE DISORDERS | 0 ( 0%) | 11 ( 73%) | 107 ( 71%) | 134 ( 60%) | 83 ( 87%) | 85 ( 83%) | 124 ( 76%) | 163 ( 77%) | 132 ( 87%) | 194 ( 81%) |
| IRITIS | 0 ( 0%) | 1 ( 7%) | 40 ( 26%) | 66 ( 29%) | 43 ( 45%) | 57 ( 55%) | 88 ( 54%) | 114 ( 54%) | 100 ( 66%) | 131 ( 55%) |
| OCULAR HYPEREMIA | 0 ( 0%) | 1 ( 7%) | 49 ( 32%) | 64 ( 29%) | 46 ( 48%) | 39 ( 38%) | 62 ( 38%) | 95 ( 45%) | 76 ( 50%) | 107 ( 45%) |
| EYE PAIN | 0 ( 0%) | 1 ( 7%) | 24 ( 16%) | 33 ( 15%) | 23 ( 24%) | 25 ( 24%) | 47 ( 29%) | 66 ( 31%) | 51 ( 34%) | 77 ( 32%) |
| EYE IRRITATION | 0 ( 0%) | 5 ( 33%) | 38 ( 25%) | 39 ( 17%) | 32 ( 34%) | 29 ( 28%) | 44 ( 27%) | 52 ( 25%) | 48 ( 32%) | 55 ( 23%) |
| LACRIMATION INCREASED | 0 ( 0%) | 1 ( 7%) | 25 ( 17%) | 31 ( 14%) | 22 ( 23%) | 23 ( 22%) | 43 ( 26%) | 51 ( 24%) | 42 ( 28%) | 61 ( 25%) |
| ABNORMAL SENSATION IN EYE | 0 ( 0%) | 1 ( 7%) | 22 ( 15%) | 28 ( 13%) | 17 ( 18%) | 26 ( 25%) | 33 ( 20%) | 45 ( 21%) | 36 ( 24%) | 56 ( 23%) |
| PHOTOPHOBIA | 0 ( 0%) | 3 ( 20%) | 24 ( 16%) | 18 ( 8%) | 19 ( 20%) | 22 ( 21%) | 28 ( 17%) | 35 ( 17%) | 42 ( 28%) | 43 ( 18%) |
| CONJUNCTIVAL EDEMA | 0 ( 0%) | 1 ( 7%) | 30 ( 20%) | 19 ( 8%) | 10 ( 11%) | 20 ( 19%) | 32 ( 20%) | 42 ( 20%) | 36 ( 24%) | 41 ( 17%) |
| VISUAL ACUITY REDUCED | 0 ( 0%) | 2 ( 13%) | 16 ( 11%) | 27 ( 12%) | 19 ( 20%) | 28 ( 27%) | 29 ( 18%) | 37 ( 17%) | 26 ( 17%) | 32 ( 13%) |
| VITREOUS FLOATERS | 0 ( 0%) | 3 ( 20%) | 17 ( 11%) | 25 ( 11%) | 17 ( 18%) | 23 ( 22%) | 23 ( 14%) | 34 ( 16%) | 30 ( 20%) | 44 ( 18%) |
| VITREOUS HEMORRHAGE | 0 ( 0%) | 1 ( 7%) | 15 ( 10%) | 10 ( 4%) | 17 ( 18%) | 15 ( 15%) | 16 ( 10%) | 21 ( 10%) | 11 ( 7%) | 18 ( 8%) |
| PHOTOPSIA | 0 ( 0%) | 0 ( 0%) | 9 ( 6%) | 5 ( 2%) | 11 ( 12%) | 7 ( 7%) | 11 ( 7%) | 14 ( 7%) | 11 ( 7%) | 17 ( 7%) |
| CATARACT SUBCAPSULAR | 0 ( 0%) | 0 ( 0%) | 8 ( 5%) | 3 ( 1%) | 8 ( 8%) | 12 ( 12%) | 7 ( 4%) | 13 ( 6%) | 7 ( 5%) | 10 ( 4%) |
| RETINAL DETACHMENT | 0 ( 0%) | 1 ( 7%) | 6 ( 4%) | 4 ( 2%) | 7 ( 7%) | 5 ( 5%) | 11 ( 7%) | 7 ( 3%) | 12 ( 8%) | 10 ( 4%) |
| CATARACT NUCLEAR | 0 ( 0%) | 1 ( 7%) | 5 ( 3%) | 11 ( 5%) | 6 ( 6%) | 6 ( 6%) | 7 ( 4%) | 15 ( 7%) | 5 ( 3%) | 5 ( 2%) |
| CATARACT CORTICAL | 0 ( 0%) | 1 ( 7%) | 9 ( 6%) | 7 ( 3%) | 1 ( 1%) | 2 ( 2%) | 5 ( 3%) | 14 ( 7%) | 10 ( 7%) | 9 ( 4%) |
| CORNEAL EROSION | 0 ( 0%) | 0 ( 0%) | 8 ( 5%) | 8 ( 4%) | 3 ( 3%) | 3 ( 3%) | 4 ( 2%) | 10 ( 5%) | 4 ( 3%) | 7 ( 3%) |
| CORNEAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 1 ( 1%) | 3 ( 3%) | 4 ( 2%) | 10 ( 5%) | 11 ( 7%) | 10 ( 4%) |
| EYE DISCHARGE | 0 ( 0%) | 0 ( 0%) | 7 ( 5%) | 6 ( 3%) | 1 ( 1%) | 2 ( 2%) | 4 ( 2%) | 8 ( 4%) | 4 ( 3%) | 10 ( 4%) |
| IRIS ADHESIONS | 0 ( 0%) | 2 ( 13%) | 0 ( 0%) | 3 ( 1%) | 3 ( 3%) | 1 ( 1%) | 5 ( 3%) | 5 ( 2%) | 10 ( 7%) | 8 ( 3%) |
| CONJUNCTIVAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 6 ( 4%) | 8 ( 4%) | 3 ( 3%) | 3 ( 3%) | 3 ( 2%) | 3 ( 1%) | 5 ( 3%) | 3 ( 1%) |
| CORNEAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 4 ( 2%) | 1 ( 1%) | 3 ( 3%) | 0 ( 0%) | 8 ( 4%) | 6 ( 4%) | 11 ( 5%) |
| RUBEOSIS IRIDIS | 0 ( 0%) | 1 ( 7%) | 1 ( 1%) | 4 ( 2%) | 6 ( 6%) | 2 ( 2%) | 3 ( 2%) | 3 ( 1%) | 5 ( 3%) | 4 ( 2%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 4 ( 2%) | 2 ( 1%) | 10 ( 7%) | 11 ( 5%) |
| HYPHEMA | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 0%) | 1 ( 1%) | 2 ( 2%) | 0 ( 0%) | 5 ( 2%) | 3 ( 2%) | 3 ( 1%) |
| MACULAR EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 1 ( 1%) | 2 ( 2%) | 1 ( 1%) | 2 ( 1%) | 5 ( 3%) | 3 ( 1%) |
| UVEITIS NOS | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 1%) | 3 ( 2%) | 2 ( 1%) | 2 ( 1%) | 2 ( 1%) |
| VITREOUS DETACHMENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 1%) | 6 ( 4%) | 0 ( 0%) | 2 ( 1%) | 1 ( 0%) |
| MACULOPATHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 1 ( 1%) | 3 ( 1%) |
| KERATITIS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) | 2 ( 2%) | 1 ( 1%) | 1 ( 0%) | 2 ( 1%) | 1 ( 0%) |
| CATARACT NEC | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 3 ( 2%) | 1 ( 0%) |
| CATARACT NOS AGGRAVATED | 0 ( 0%) | 1 ( 7%) | 1 ( 1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 1 ( 1%) | 0 ( 0%) |
| DRY EYE NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 1 ( 1%) | 2 ( 1%) |
| DIPLOPIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 1 ( 1%) | 2 ( 1%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) |

Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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Table 20
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 3 ( 1%) |
| POSTERIOR CAPSULE OPACIFICATION | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 1 ( 1%) | 1 ( 0%) |
| VISION BLURRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 3 ( 1%) | 0 ( 0%) | 2 ( 1%) |
| BLINDNESS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 2 ( 1%) | 0 ( 0%) |
| HYPOTONY OF EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 3 ( 2%) | 1 ( 0%) |
| MYDRIASIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 3 ( 1%) |
| PHOTOPHOBIA AGGRAVATED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| CONJUNCTIVITIS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) |
| CORNEAL EPITHELIUM DEFECT | 0 ( 0%) | 1 ( 7%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| FOREIGN BODY RETAINED IN EYE | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| RETINAL TEAR (EXC DETACHMENT) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| RETINOPATHY DIABETIC | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| VITREOUS DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) |
| CORNEAL ABRASION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CORTICAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| INTRAOCULAR PRESSURE DECREASED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| IRIDOCYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 1 ( 1%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLEPHARITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 0 ( 0%) | 0 ( 0%) |
| CHOROIDAL DETACHMENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| EYE DEGENERATIVE DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| MACULAR DEGENERATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OCULAR HYPERTENSION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| PSEUDOPHAKIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| STRABISMUS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| VITREOUS OPACITIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| APHAKIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLINDNESS NIGHT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| BLINDNESS TRANSIENT | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| BLOODSHOT EYE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CCONJUNCTIVAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| CHORIORETINAL ATROPHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CHORIORETINAL DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| COLOUR BLINDNESS NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CONJUNCTIVITIS VIRAL NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| CORNEAL OPACITY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| CYCLITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |

Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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Table 20
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE ALLERGY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE INFECTION TOXOPLASMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| EYE INFLAMMATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| EYELID DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYELID PTOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOCONJUNCTIVITIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| KERATOPATHY NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| LENTICULAR OPACITIES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| MEIBOMIAN CYST | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OCULAR HYPERAEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| OPEN ANGLE GLAUCOMA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| OPTIC ATROPHY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PAINFUL RED EYES | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PINGUECULA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE PAIN | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| RETINAL DEPIGMENTATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL ISCHEMIA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| RETINAL MICROANEURYSMS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| RETINAL SCAR | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| RETINAL VEIN THROMBOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| UVEITIS DIABETIC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VISUAL DISTURBANCE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| INVESTIGATIONS | 0 ( 0%) | 0 ( 0%) | 8 ( 5%) | 16 ( 7%) | 10 ( 11%) | 11 ( 11%) | 5 ( 3%) | 19 ( 9%) | 11 ( 7%) | 9 ( 4%) |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0%) | 0 ( 0%) | 7 ( 5%) | 13 ( 6%) | 7 ( 7%) | 9 ( 9%) | 3 ( 2%) | 15 ( 7%) | 8 ( 5%) | 8 ( 3%) |
| CORNEAL STAINING | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 3 ( 1%) | 3 ( 3%) | 2 ( 2%) | 2 ( 1%) | 4 ( 2%) | 3 ( 2%) | 1 ( 0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | 0 ( 0%) | 0 ( 0%) | 4 ( 3%) | 11 ( 5%) | 6 ( 6%) | 3 ( 3%) | 13 ( 8%) | 16 ( 8%) | 9 ( 6%) | 15 ( 6%) |
| EYELID EDEMA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 5 ( 2%) | 4 ( 4%) | 2 ( 2%) | 11 ( 7%) | 11 ( 5%) | 6 ( 4%) | 13 ( 5%) |
| ERYTHEMA NEC | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 7 ( 3%) | 3 ( 3%) | 0 ( 0%) | 4 ( 2%) | 10 ( 5%) | 5 ( 3%) | 7 ( 3%) |
| CUTIS LAXA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| ECCHYMOSIS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| OCULAR HYPEREMIA | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| PERIORBITAL EDEMA | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SURGICAL AND MEDICAL PROCEDURES | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 3 ( 3%) | 1 ( 1%) | 5 ( 3%) | 0 ( 0%) | 2 ( 1%) | 2 ( 1%) |



Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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ISTA Pharmaceuticals, Inc.
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Table 20
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Age
Safety Population

| | Control | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | WW | | Saline | | 7.5 IU Vitrase | | 55 IU Vitrase | | 75 IU Vitrase | |
| System Organ Class / Preferred Term | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years | < 60 years | >= 60 years |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) | 1 ( 1%) | 3 ( 2%) | 0 ( 0%) | 1 ( 1%) | 1 ( 0%) |
| VITRECTOMY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| EYE IRRITATION | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| POST-OPERATIVE COMPLICATIONS NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| POST-OPERATIVE HEMORRHAGE | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| SCLERAL OPERATION NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| NERVOUS SYSTEM DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 2 ( 2%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 4 ( 3%) | 2 ( 1%) |
| PUPILLARY DISORDER NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 2 ( 1%) | 3 ( 2%) | 0 ( 0%) |
| VISUAL FIELD DEFECT NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 1 ( 1%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| HEADACHE NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) |
| PUPILLARY REFLEX IMPAIRED | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| INFECTIONS AND INFESTATIONS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HYPOPYON | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| INJURY AND POISONING | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| HEAD INJURY | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) |
| VASCULAR DISORDERS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |
| PERIPHERAL ISCHEMIA NOS | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 0 ( 0%) | 1 ( 1%) | 0 ( 0%) |



Note: One patient in study VIT-02-08961X (Saline) and three patients in study VIT-03-08961X (two Saline and one 55 IU) had calculated ages resolving to zero due to incorrect birth dates recorded. These values are not included in the age calculation. In addition, patients with a missing DOB were not included in the age calculation.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| NUMBER OF PATIENTS | CAUCASIAN | 7 | 255 | 97 | 250 | 265 |
| | HISPANIC | 5 | 65 | 74 | 73 | 70 |
| | OTHER | 6 | 58 | 27 | 54 | 56 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | CAUCASIAN | 6 (85.7%) | 195 (76.5%) | 95 (97.9%) | 201 (80.4%) | 225 (84.9%) |
| | HISPANIC | 5 ( 100%) | 59 (90.8%) | 73 (98.6%) | 72 (98.6%) | 70 ( 100%) |
| | OTHER | 6 ( 100%) | 44 (75.9%) | 25 (92.6%) | 50 (92.6%) | 54 (96.4%) |
| EYE DISORDERS | CAUCASIAN | 6 (85.7%) | 194 (76.1%) | 95 (97.9%) | 201 (80.4%) | 225 (84.9%) |
| | HISPANIC | 5 ( 100%) | 59 (90.8%) | 73 (98.6%) | 72 (98.6%) | 70 ( 100%) |
| | OTHER | 6 ( 100%) | 44 (75.9%) | 24 (88.9%) | 49 (90.7%) | 54 (96.4%) |
| IRITIS | CAUCASIAN | 1 (14.3%) | 68 (26.7%) | 60 (61.9%) | 131 (52.4%) | 145 (54.7%) |
| | HISPANIC | 0 ( 0.0%) | 33 (50.8%) | 48 (64.9%) | 60 (82.2%) | 61 (87.1%) |
| | OTHER | 3 (50.0%) | 25 (43.1%) | 15 (55.6%) | 31 (57.4%) | 37 (66.1%) |
| OCULAR HYPEREMIA | CAUCASIAN | 0 ( 0.0%) | 84 (32.9%) | 62 (63.9%) | 127 (50.8%) | 130 (49.1%) |
| | HISPANIC | 3 (60.0%) | 37 (56.9%) | 38 (51.4%) | 50 (68.5%) | 57 (81.4%) |
| | OTHER | 1 (16.7%) | 19 (32.8%) | 13 (48.1%) | 25 (46.3%) | 28 (50.0%) |
| EYE IRRITATION | CAUCASIAN | 4 (57.1%) | 71 (27.8%) | 46 (47.4%) | 70 (28.0%) | 89 (33.6%) |
| | HISPANIC | 4 (80.0%) | 24 (36.9%) | 32 (43.2%) | 44 (60.3%) | 28 (40.0%) |
| | OTHER | 2 (33.3%) | 16 (27.6%) | 12 (44.4%) | 18 (33.3%) | 22 (39.3%) |
| EYE PAIN | CAUCASIAN | 0 ( 0.0%) | 49 (19.2%) | 34 (35.1%) | 72 (28.8%) | 97 (36.6%) |
| | HISPANIC | 0 ( 0.0%) | 21 (32.3%) | 30 (40.5%) | 45 (61.6%) | 36 (51.4%) |
| | OTHER | 2 (33.3%) | 14 (24.1%) | 8 (29.6%) | 22 (40.7%) | 28 (50.0%) |
| LACRIMATION INCREASED | CAUCASIAN | 0 ( 0.0%) | 48 (18.8%) | 30 (30.9%) | 72 (28.8%) | 82 (30.9%) |
| | HISPANIC | 3 (60.0%) | 26 (40.0%) | 27 (36.5%) | 31 (42.5%) | 32 (45.7%) |
| | OTHER | 1 (16.7%) | 13 (22.4%) | 8 (29.6%) | 21 (38.9%) | 25 (44.6%) |
| VISUAL ACUITY REDUCED | CAUCASIAN | 1 (14.3%) | 50 (19.6%) | 44 (45.4%) | 62 (24.8%) | 63 (23.8%) |
| | HISPANIC | 2 (40.0%) | 11 (16.9%) | 26 (35.1%) | 25 (34.2%) | 20 (28.6%) |
| | OTHER | 1 (16.7%) | 13 (22.4%) | 7 (25.9%) | 14 (25.9%) | 15 (26.8%) |
| ABNORMAL SENSATION IN EYE | CAUCASIAN | 1 (14.3%) | 40 (15.7%) | 31 (32.0%) | 59 (23.6%) | 69 (26.0%) |
| | HISPANIC | 1 (20.0%) | 16 (24.6%) | 23 (31.1%) | 28 (38.4%) | 24 (34.3%) |
| | OTHER | 0 ( 0.0%) | 12 (20.7%) | 8 (29.6%) | 14 (25.9%) | 21 (37.5%) |
| VITREOUS FLOATERS | CAUCASIAN | 3 (42.9%) | 46 (18.0%) | 36 (37.1%) | 54 (21.6%) | 66 (24.9%) |
| | HISPANIC | 1 (20.0%) | 8 (12.3%) | 16 (21.6%) | 24 (32.9%) | 18 (25.7%) |
| | OTHER | 2 (33.3%) | 13 (22.4%) | 11 (40.7%) | 10 (18.5%) | 16 (28.6%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VITREOUS HEMORRHAGE | CAUCASIAN | 1 (14.3%) | 45 (17.6%) | 39 (40.2%) | 64 (25.6%) | 59 (22.3%) |
| | HISPANIC | 0 ( 0.0%) | 11 (16.9%) | 18 (24.3%) | 18 (24.7%) | 14 (20.0%) |
| | OTHER | 1 (16.7%) | 10 (17.2%) | 13 (48.1%) | 9 (16.7%) | 17 (30.4%) |
| PHOTOPHOBIA | CAUCASIAN | 3 (42.9%) | 37 (14.5%) | 31 (32.0%) | 48 (19.2%) | 64 (24.2%) |
| | HISPANIC | 0 ( 0.0%) | 9 (13.8%) | 20 (27.0%) | 23 (31.5%) | 19 (27.1%) |
| | OTHER | 3 (50.0%) | 14 (24.1%) | 8 (29.6%) | 15 (27.8%) | 19 (33.9%) |
| CONJUNCTIVAL EDEMA | CAUCASIAN | 0 ( 0.0%) | 40 (15.7%) | 29 (29.9%) | 56 (22.4%) | 54 (20.4%) |
| | HISPANIC | 1 (20.0%) | 13 (20.0%) | 16 (21.6%) | 29 (39.7%) | 25 (35.7%) |
| | OTHER | 0 ( 0.0%) | 6 (10.3%) | 3 (11.1%) | 11 (20.4%) | 10 (17.9%) |
| CATARACT NUCLEAR | CAUCASIAN | 1 (14.3%) | 21 ( 8.2%) | 13 (13.4%) | 21 ( 8.4%) | 17 ( 6.4%) |
| | HISPANIC | 3 (60.0%) | 7 (10.8%) | 11 (14.9%) | 11 (15.1%) | 5 ( 7.1%) |
| | OTHER | 1 (16.7%) | 6 (10.3%) | 3 (11.1%) | 5 ( 9.3%) | 7 (12.5%) |
| RETINAL DETACHMENT | CAUCASIAN | 0 ( 0.0%) | 16 ( 6.3%) | 16 (16.5%) | 20 ( 8.0%) | 27 (10.2%) |
| | HISPANIC | 1 (20.0%) | 4 ( 6.2%) | 5 ( 6.8%) | 8 (11.0%) | 6 ( 8.6%) |
| | OTHER | 2 (33.3%) | 6 (10.3%) | 1 ( 3.7%) | 7 (13.0%) | 12 (21.4%) |
| CATARACT SUBCAPSULAR | CAUCASIAN | 0 ( 0.0%) | 15 ( 5.9%) | 20 (20.6%) | 19 ( 7.6%) | 23 ( 8.7%) |
| | HISPANIC | 1 (20.0%) | 9 (13.8%) | 11 (14.9%) | 5 ( 6.8%) | 9 (12.9%) |
| | OTHER | 1 (16.7%) | 2 ( 3.4%) | 2 ( 7.4%) | 5 ( 9.3%) | 6 (10.7%) |
| PHOTOPSIA | CAUCASIAN | 0 ( 0.0%) | 12 ( 4.7%) | 10 (10.3%) | 22 ( 8.8%) | 23 ( 8.7%) |
| | HISPANIC | 0 ( 0.0%) | 4 ( 6.2%) | 10 (13.5%) | 16 (21.9%) | 9 (12.9%) |
| | OTHER | 0 ( 0.0%) | 6 (10.3%) | 2 ( 7.4%) | 7 (13.0%) | 6 (10.7%) |
| CATARACT CORTICAL | CAUCASIAN | 1 (14.3%) | 20 ( 7.8%) | 9 ( 9.3%) | 21 ( 8.4%) | 23 ( 8.7%) |
| | HISPANIC | 2 (40.0%) | 3 ( 4.6%) | 3 ( 4.1%) | 8 (11.0%) | 6 ( 8.6%) |
| | OTHER | 2 (33.3%) | 4 ( 6.9%) | 2 ( 7.4%) | 1 ( 1.9%) | 2 ( 3.6%) |
| CORNEAL EROSION | CAUCASIAN | 0 ( 0.0%) | 17 ( 6.7%) | 6 ( 6.2%) | 17 ( 6.8%) | 15 ( 5.7%) |
| | HISPANIC | 0 ( 0.0%) | 5 ( 7.7%) | 3 ( 4.1%) | 6 ( 8.2%) | 2 ( 2.9%) |
| | OTHER | 1 (16.7%) | 2 ( 3.4%) | 1 ( 3.7%) | 2 ( 3.7%) | 0 ( 0.0%) |
| CORNEAL EDEMA | CAUCASIAN | 0 ( 0.0%) | 7 ( 2.7%) | 7 ( 7.2%) | 10 ( 4.0%) | 14 ( 5.3%) |
| | HISPANIC | 0 ( 0.0%) | 4 ( 6.2%) | 9 (12.2%) | 8 (11.0%) | 6 ( 8.6%) |
| | OTHER | 1 (16.7%) | 1 ( 1.7%) | 1 ( 3.7%) | 2 ( 3.7%) | 4 ( 7.1%) |
| RUBEOSIS IRIDIS | CAUCASIAN | 0 ( 0.0%) | 14 ( 5.5%) | 9 ( 9.3%) | 11 ( 4.4%) | 6 ( 2.3%) |
| | HISPANIC | 1 (20.0%) | 3 ( 4.6%) | 6 ( 8.1%) | 6 ( 8.2%) | 6 ( 8.6%) |
| | OTHER | 0 ( 0.0%) | 2 ( 3.4%) | 1 ( 3.7%) | 0 ( 0.0%) | 7 (12.5%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| EYE DISCHARGE | CAUCASIAN | 0 ( 0.0%) | 9 ( 3.5%) | 4 ( 4.1%) | 13 ( 5.2%) | 10 ( 3.8%) |
| | HISPANIC | 0 ( 0.0%) | 8 (12.3%) | 6 ( 8.1%) | 9 (12.3%) | 7 (10.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 1 ( 1.9%) | 3 ( 5.4%) |
| CONJUNCTIVAL HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 16 ( 6.3%) | 4 ( 4.1%) | 6 ( 2.4%) | 9 ( 3.4%) |
| | HISPANIC | 0 ( 0.0%) | 6 ( 9.2%) | 7 ( 9.5%) | 8 (11.0%) | 7 (10.0%) |
| | OTHER | 0 ( 0.0%) | 3 ( 5.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.6%) |
| IRIS ADHESIONS | CAUCASIAN | 0 ( 0.0%) | 7 ( 2.7%) | 4 ( 4.1%) | 9 ( 3.6%) | 14 ( 5.3%) |
| | HISPANIC | 0 ( 0.0%) | 3 ( 4.6%) | 5 ( 6.8%) | 3 ( 4.1%) | 7 (10.0%) |
| | OTHER | 2 (33.3%) | 3 ( 5.2%) | 0 ( 0.0%) | 1 ( 1.9%) | 6 (10.7%) |
| MACULAR EDEMA | CAUCASIAN | 0 ( 0.0%) | 6 ( 2.4%) | 11 (11.3%) | 8 ( 3.2%) | 10 ( 3.8%) |
| | HISPANIC | 1 (20.0%) | 5 ( 7.7%) | 5 ( 6.8%) | 3 ( 4.1%) | 7 (10.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.6%) |
| CORNEAL DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 6 ( 2.4%) | 2 ( 2.1%) | 14 ( 5.6%) | 15 ( 5.7%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 2 ( 2.7%) | 3 ( 4.1%) | 5 ( 7.1%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 2 ( 7.4%) | 0 ( 0.0%) | 5 ( 8.9%) |
| HYPHEMA | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 6 ( 6.2%) | 6 ( 2.4%) | 8 ( 3.0%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 1 ( 1.4%) | 5 ( 6.8%) | 3 ( 4.3%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 1 ( 3.7%) | 1 ( 1.9%) | 4 ( 7.1%) |
| CATARACT NEC | CAUCASIAN | 0 ( 0.0%) | 8 ( 3.1%) | 0 ( 0.0%) | 4 ( 1.6%) | 6 ( 2.3%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 1.4%) | 2 ( 2.7%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 4 ( 7.4%) | 2 ( 3.6%) |
| BLINDNESS NEC | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 3 ( 3.1%) | 3 ( 1.2%) | 5 ( 1.9%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 5 ( 6.8%) | 2 ( 2.7%) | 0 ( 0.0%) |
| | OTHER | 1 (16.7%) | 0 ( 0.0%) | 1 ( 3.7%) | 1 ( 1.9%) | 4 ( 7.1%) |
| HYPOPYON | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.8%) | 10 ( 3.8%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 3 ( 4.1%) | 9 (12.9%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 2 ( 3.6%) |
| DRY EYE NEC | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 2 ( 2.1%) | 4 ( 1.6%) | 6 ( 2.3%) |
| | HISPANIC | 0 ( 0.0%) | 3 ( 4.6%) | 3 ( 4.1%) | 1 ( 1.4%) | 3 ( 4.3%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 7.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLAUCOMA NOS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 4 ( 4.1%) | 0 ( 0.0%) | 9 ( 3.4%) |
| | HISPANIC | 0 ( 0.0%) | 3 ( 4.6%) | 1 ( 1.4%) | 1 ( 1.4%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 2 ( 3.7%) | 2 ( 3.6%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISION BLURRED | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 4 ( 4.1%) | 4 ( 1.6%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 5 ( 6.8%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 1 ( 1.9%) | 0 ( 0.0%) |
| CATARACT NOS AGGRAVATED | CAUCASIAN | 0 ( 0.0%) | 6 ( 2.4%) | 3 ( 3.1%) | 4 ( 1.6%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 1.4%) | 2 ( 2.9%) |
| | OTHER | 1 (16.7%) | 1 ( 1.7%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATITIS NEC | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 1 ( 1.0%) | 2 ( 0.8%) | 8 ( 3.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 4.1%) | 2 ( 2.7%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 2 ( 2.1%) | 4 ( 1.6%) | 2 ( 0.8%) |
| | HISPANIC | 1 (20.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 5 ( 6.8%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 2 ( 3.6%) |
| MACULOPATHY | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 2 ( 2.1%) | 3 ( 1.2%) | 4 ( 1.5%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 2 ( 2.7%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 1 ( 1.9%) | 1 ( 1.8%) |
| INTRAOCULAR PRESSURE INCREASED | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 5 ( 5.2%) | 1 ( 0.4%) | 5 ( 1.9%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 2 ( 2.7%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS NOS | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 2 ( 2.1%) | 5 ( 2.0%) | 4 ( 1.5%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 1 (16.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.7%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | CAUCASIAN | 0 ( 0.0%) | 6 ( 2.4%) | 0 ( 0.0%) | 2 ( 0.8%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.9%) |
| | OTHER | 1 (16.7%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 1 ( 1.0%) | 5 ( 2.0%) | 4 ( 1.5%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| RETINOPATHY DIABETIC | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 1 ( 1.0%) | 2 ( 0.8%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 5.4%) |
| BLEPHARITIS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 2 ( 2.1%) | 2 ( 0.8%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 1 ( 1.8%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| HYPOTONY OF EYE | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 2 ( 2.1%) | 1 ( 0.4%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.9%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 1 ( 1.8%) |
| RETINAL HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 1 ( 1.0%) | 3 ( 1.2%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 1 ( 1.4%) | 2 ( 2.7%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 2 ( 0.8%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 1.4%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 1 (16.7%) | 0 ( 0.0%) | 1 ( 3.7%) | 1 ( 1.9%) | 1 ( 1.8%) |
| DIPLOPIA | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 1 ( 1.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 2 ( 2.7%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 1 ( 1.9%) | 1 ( 1.8%) |
| RETINAL ISCHEMIA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.1%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 1.4%) | 3 ( 4.1%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |
| CONJUNCTIVITIS NEC | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.7%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 3 ( 1.2%) | 2 ( 0.8%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYDRIASIS | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.5%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL TEAR (EXC DETACHMENT) | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.6%) | 2 ( 0.8%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 7.4%) | 1 ( 1.9%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.7%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| PSEUDOPHAKIA | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 0 ( 0.0%) | 2 ( 0.8%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 1 ( 1.8%) |
| INTRAOCULAR PRESSURE DECREASED | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 2 ( 2.1%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 2 ( 2.7%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 2 ( 0.8%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| APHAKIA | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| EYE ALLERGY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.2%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |
| PAINFUL RED EYES | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
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Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CHEMOSIS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.1%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| RETINAL MICROANEURYSMS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 1.4%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL SCAR | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.8%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS TRANSIENT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CONJUNCTIVITIS (INFECTIVE) NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS ALLERGIC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 1 (16.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL OPACITY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |
| KERATOPATHY BAND | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MEIBOMIAN CYST | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL HEMATOMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ARTERY EMBOLISM | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEPIGMENTATION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STRABISMUS NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISUAL ACUITY REDUCED TRANSIENTLY | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS OPACITIES | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANGLE CLOSURE GLAUCOMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANISEIKONIA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ARCUS SENILIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHAROCONJUNCTIVITIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| CHALAZION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL ATROPHY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CHORIORETINAL DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL DEGENERATION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL SCAR | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ULCER NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EXOPHTHALMOS ENDOCRINE | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE HEMORRHAGE NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| EYE INFECTION NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION STAPHYLOCOCCAL | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HERPES SIMPLEX OPHTHALMIC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS NEVUS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC DISC HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| OPTIC NERVE INJURY NOS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAPILLEDEMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEGENERATION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL EXUDATES | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VASCULITIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| SCLERITIS NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISION ABNORMAL NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| INVESTIGATIONS | CAUCASIAN | 1 (14.3%) | 25 ( 9.8%) | 31 (32.0%) | 32 (12.8%) | 29 (10.9%) |
| | HISPANIC | 0 ( 0.0%) | 10 (15.4%) | 13 (17.6%) | 8 (11.0%) | 7 (10.0%) |
| | OTHER | 2 (33.3%) | 9 (15.5%) | 4 (14.8%) | 10 (18.5%) | 10 (17.9%) |
| INTRAOCULAR PRESSURE INCREASED | CAUCASIAN | 1 (14.3%) | 22 ( 8.6%) | 26 (26.8%) | 24 ( 9.6%) | 24 ( 9.1%) |
| | HISPANIC | 0 ( 0.0%) | 8 (12.3%) | 10 (13.5%) | 8 (11.0%) | 6 ( 8.6%) |
| | OTHER | 2 (33.3%) | 9 (15.5%) | 4 (14.8%) | 10 (18.5%) | 10 (17.9%) |
| CORNEAL STAINING | CAUCASIAN | 0 ( 0.0%) | 4 ( 1.6%) | 4 ( 4.1%) | 8 ( 3.2%) | 5 ( 1.9%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 4 ( 5.4%) | 1 ( 1.4%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.6%) |
| INTRAOCULAR PRESSURE ABNORMAL | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | CAUCASIAN | 0 ( 0.0%) | 15 ( 5.9%) | 12 (12.4%) | 20 ( 8.0%) | 20 ( 7.5%) |
| | HISPANIC | 0 ( 0.0%) | 8 (12.3%) | 7 ( 9.5%) | 11 (15.1%) | 13 (18.6%) |
| | OTHER | 0 ( 0.0%) | 3 ( 5.2%) | 0 ( 0.0%) | 8 (14.8%) | 5 ( 8.9%) |
| EYELID EDEMA | CAUCASIAN | 0 ( 0.0%) | 7 ( 2.7%) | 6 ( 6.2%) | 14 ( 5.6%) | 14 ( 5.3%) |
| | HISPANIC | 0 ( 0.0%) | 5 ( 7.7%) | 6 ( 8.1%) | 9 (12.3%) | 9 (12.9%) |
| | OTHER | 0 ( 0.0%) | 3 ( 5.2%) | 0 ( 0.0%) | 6 (11.1%) | 2 ( 3.6%) |
| ERYTHEMA NEC | CAUCASIAN | 0 ( 0.0%) | 11 ( 4.3%) | 4 ( 4.1%) | 13 ( 5.2%) | 13 ( 4.9%) |
| | HISPANIC | 0 ( 0.0%) | 4 ( 6.2%) | 4 ( 5.4%) | 5 ( 6.8%) | 4 ( 5.7%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 5.6%) | 3 ( 5.4%) |
| OCULAR HYPEREMIA | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CUTIS LAXA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.1%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| PERIORBITAL EDEMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |
| DERMATITIS NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| PRURITUS NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | CAUCASIAN | 0 ( 0.0%) | 9 ( 3.5%) | 4 ( 4.1%) | 8 ( 3.2%) | 6 ( 2.3%) |
| | HISPANIC | 0 ( 0.0%) | 5 ( 7.7%) | 2 ( 2.7%) | 2 ( 2.7%) | 1 ( 1.4%) |
| | OTHER | 1 (16.7%) | 0 ( 0.0%) | 1 ( 3.7%) | 3 ( 5.6%) | 1 ( 1.8%) |
| POST-OPERATIVE COMPLICATIONS NOS | CAUCASIAN | 0 ( 0.0%) | 7 ( 2.7%) | 3 ( 3.1%) | 3 ( 1.2%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) |
| | OTHER | 1 (16.7%) | 0 ( 0.0%) | 1 ( 3.7%) | 1 ( 1.9%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 2 ( 2.1%) | 3 ( 1.2%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 1 ( 1.8%) |
| VITRECTOMY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 4 ( 6.2%) | 2 ( 2.7%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENS IMPLANT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| SCLERAL OPERATION NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUTURE LINE PAIN | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.1%) | 2 ( 0.8%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) | 2 ( 2.9%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 2 ( 7.4%) | 1 ( 1.9%) | 2 ( 3.6%) |
| PUPILLARY DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.8%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 7.4%) | 1 ( 1.9%) | 1 ( 1.8%) |
| VISUAL FIELD DEFECT NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FACIAL PALSY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEADACHE NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| PUPILLARY REFLEX IMPAIRED | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITH NERVE PARALYSIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IMMUNE SYSTEM DISORDERS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.1%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERSENSITIVITY NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
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Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| MULTIPLE ALLERGIES | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEMICAL BURNS OF EYE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BENIGN NEOPLASM OF CHOROID | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RADIOACTIVE IODINE THERAPY | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MECHANICAL COMPLICATION OF IMPLANT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 21
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VASCULAR DISORDERS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL ISCHEMIA NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| NUMBER OF PATIENTS | CAUCASIAN | 7 | 255 | 97 | 250 | 265 |
| | HISPANIC | 5 | 65 | 74 | 73 | 70 |
| | OTHER | 6 | 58 | 27 | 54 | 56 |
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | CAUCASIAN | 5 (71.4%) | 156 (61.2%) | 82 (84.5%) | 173 (69.2%) | 205 (77.4%) |
| | HISPANIC | 4 (80.0%) | 51 (78.5%) | 66 (89.2%) | 71 (97.3%) | 70 ( 100%) |
| | OTHER | 2 (33.3%) | 37 (63.8%) | 20 (74.1%) | 46 (85.2%) | 51 (91.1%) |
| EYE DISORDERS | CAUCASIAN | 5 (71.4%) | 155 (60.8%) | 82 (84.5%) | 173 (69.2%) | 205 (77.4%) |
| | HISPANIC | 4 (80.0%) | 51 (78.5%) | 66 (89.2%) | 71 (97.3%) | 70 ( 100%) |
| | OTHER | 2 (33.3%) | 37 (63.8%) | 20 (74.1%) | 44 (81.5%) | 51 (91.1%) |
| IRITIS | CAUCASIAN | 0 ( 0.0%) | 58 (22.7%) | 47 (48.5%) | 116 (46.4%) | 135 (50.9%) |
| | HISPANIC | 0 ( 0.0%) | 27 (41.5%) | 41 (55.4%) | 57 (78.1%) | 61 (87.1%) |
| | OTHER | 1 (16.7%) | 21 (36.2%) | 12 (44.4%) | 29 (53.7%) | 35 (62.5%) |
| OCULAR HYPEREMIA | CAUCASIAN | 0 ( 0.0%) | 68 (26.7%) | 46 (47.4%) | 102 (40.8%) | 113 (42.6%) |
| | HISPANIC | 1 (20.0%) | 29 (44.6%) | 28 (37.8%) | 35 (47.9%) | 47 (67.1%) |
| | OTHER | 0 ( 0.0%) | 16 (27.6%) | 11 (40.7%) | 21 (38.9%) | 23 (41.1%) |
| EYE PAIN | CAUCASIAN | 0 ( 0.0%) | 35 (13.7%) | 21 (21.6%) | 60 (24.0%) | 77 (29.1%) |
| | HISPANIC | 0 ( 0.0%) | 11 (16.9%) | 21 (28.4%) | 35 (47.9%) | 28 (40.0%) |
| | OTHER | 1 (16.7%) | 11 (19.0%) | 6 (22.2%) | 18 (33.3%) | 23 (41.1%) |
| EYE IRRITATION | CAUCASIAN | 4 (57.1%) | 51 (20.0%) | 30 (30.9%) | 56 (22.4%) | 67 (25.3%) |
| | HISPANIC | 1 (20.0%) | 15 (23.1%) | 24 (32.4%) | 29 (39.7%) | 20 (28.6%) |
| | OTHER | 0 ( 0.0%) | 13 (22.4%) | 7 (25.9%) | 11 (20.4%) | 16 (28.6%) |
| LACRIMATION INCREASED | CAUCASIAN | 0 ( 0.0%) | 31 (12.2%) | 23 (23.7%) | 55 (22.0%) | 61 (23.0%) |
| | HISPANIC | 1 (20.0%) | 17 (26.2%) | 15 (20.3%) | 23 (31.5%) | 24 (34.3%) |
| | OTHER | 0 ( 0.0%) | 8 (13.8%) | 7 (25.9%) | 16 (29.6%) | 18 (32.1%) |
| ABNORMAL SENSATION IN EYE | CAUCASIAN | 1 (14.3%) | 28 (11.0%) | 22 (22.7%) | 48 (19.2%) | 57 (21.5%) |
| | HISPANIC | 0 ( 0.0%) | 13 (20.0%) | 13 (17.6%) | 19 (26.0%) | 20 (28.6%) |
| | OTHER | 0 ( 0.0%) | 9 (15.5%) | 8 (29.6%) | 11 (20.4%) | 15 (26.8%) |
| PHOTOPHOBIA | CAUCASIAN | 3 (42.9%) | 26 (10.2%) | 20 (20.6%) | 38 (15.2%) | 53 (20.0%) |
| | HISPANIC | 0 ( 0.0%) | 7 (10.8%) | 14 (18.9%) | 17 (23.3%) | 16 (22.9%) |
| | OTHER | 0 ( 0.0%) | 9 (15.5%) | 7 (25.9%) | 8 (14.8%) | 16 (28.6%) |
| CONJUNCTIVAL EDEMA | CAUCASIAN | 0 ( 0.0%) | 34 (13.3%) | 17 (17.5%) | 44 (17.6%) | 46 (17.4%) |
| | HISPANIC | 1 (20.0%) | 11 (16.9%) | 10 (13.5%) | 21 (28.8%) | 22 (31.4%) |
| | OTHER | 0 ( 0.0%) | 4 ( 6.9%) | 3 (11.1%) | 9 (16.7%) | 9 (16.1%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VITREOUS FLOATERS | CAUCASIAN | 3 (42.9%) | 29 (11.4%) | 21 (21.6%) | 37 (14.8%) | 52 (19.6%) |
| | HISPANIC | 0 ( 0.0%) | 3 ( 4.6%) | 11 (14.9%) | 13 (17.8%) | 12 (17.1%) |
| | OTHER | 0 ( 0.0%) | 10 (17.2%) | 8 (29.6%) | 8 (14.8%) | 10 (17.9%) |
| VISUAL ACUITY REDUCED | CAUCASIAN | 0 ( 0.0%) | 27 (10.6%) | 26 (26.8%) | 40 (16.0%) | 39 (14.7%) |
| | HISPANIC | 1 (20.0%) | 6 ( 9.2%) | 16 (21.6%) | 15 (20.5%) | 11 (15.7%) |
| | OTHER | 1 (16.7%) | 10 (17.2%) | 5 (18.5%) | 11 (20.4%) | 8 (14.3%) |
| VITREOUS HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 18 ( 7.1%) | 19 (19.6%) | 26 (10.4%) | 20 ( 7.5%) |
| | HISPANIC | 0 ( 0.0%) | 3 ( 4.6%) | 9 (12.2%) | 9 (12.3%) | 5 ( 7.1%) |
| | OTHER | 1 (16.7%) | 4 ( 6.9%) | 4 (14.8%) | 2 ( 3.7%) | 4 ( 7.1%) |
| PHOTOPSIA | CAUCASIAN | 0 ( 0.0%) | 8 ( 3.1%) | 8 ( 8.2%) | 13 ( 5.2%) | 18 ( 6.8%) |
| | HISPANIC | 0 ( 0.0%) | 4 ( 6.2%) | 8 (10.8%) | 8 (11.0%) | 6 ( 8.6%) |
| | OTHER | 0 ( 0.0%) | 2 ( 3.4%) | 2 ( 7.4%) | 4 ( 7.4%) | 4 ( 7.1%) |
| CATARACT SUBCAPSULAR | CAUCASIAN | 0 ( 0.0%) | 6 ( 2.4%) | 13 (13.4%) | 14 ( 5.6%) | 11 ( 4.2%) |
| | HISPANIC | 0 ( 0.0%) | 4 ( 6.2%) | 6 ( 8.1%) | 3 ( 4.1%) | 3 ( 4.3%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 1 ( 3.7%) | 3 ( 5.6%) | 3 ( 5.4%) |
| RETINAL DETACHMENT | CAUCASIAN | 0 ( 0.0%) | 4 ( 1.6%) | 9 ( 9.3%) | 12 ( 4.8%) | 12 ( 4.5%) |
| | HISPANIC | 1 (20.0%) | 2 ( 3.1%) | 3 ( 4.1%) | 2 ( 2.7%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 4 ( 6.9%) | 0 ( 0.0%) | 4 ( 7.4%) | 9 (16.1%) |
| CATARACT NUCLEAR | CAUCASIAN | 0 ( 0.0%) | 9 ( 3.5%) | 4 ( 4.1%) | 14 ( 5.6%) | 5 ( 1.9%) |
| | HISPANIC | 1 (20.0%) | 2 ( 3.1%) | 7 ( 9.5%) | 6 ( 8.2%) | 3 ( 4.3%) |
| | OTHER | 0 ( 0.0%) | 5 ( 8.6%) | 1 ( 3.7%) | 2 ( 3.7%) | 2 ( 3.6%) |
| CATARACT CORTICAL | CAUCASIAN | 0 ( 0.0%) | 10 ( 3.9%) | 2 ( 2.1%) | 14 ( 5.6%) | 13 ( 4.9%) |
| | HISPANIC | 1 (20.0%) | 2 ( 3.1%) | 1 ( 1.4%) | 4 ( 5.5%) | 4 ( 5.7%) |
| | OTHER | 0 ( 0.0%) | 4 ( 6.9%) | 0 ( 0.0%) | 1 ( 1.9%) | 2 ( 3.6%) |
| CORNEAL EROSION | CAUCASIAN | 0 ( 0.0%) | 11 ( 4.3%) | 4 ( 4.1%) | 11 ( 4.4%) | 10 ( 3.8%) |
| | HISPANIC | 0 ( 0.0%) | 3 ( 4.6%) | 1 ( 1.4%) | 2 ( 2.7%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 2 ( 3.4%) | 1 ( 3.7%) | 1 ( 1.9%) | 0 ( 0.0%) |
| CORNEAL DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 1 ( 1.0%) | 13 ( 5.2%) | 12 ( 4.5%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) | 5 ( 7.1%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 7.4%) | 0 ( 0.0%) | 4 ( 7.1%) |
| EYE DISCHARGE | CAUCASIAN | 0 ( 0.0%) | 7 ( 2.7%) | 1 ( 1.0%) | 10 ( 4.0%) | 9 ( 3.4%) |
| | HISPANIC | 0 ( 0.0%) | 5 ( 7.7%) | 2 ( 2.7%) | 2 ( 2.7%) | 2 ( 2.9%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 5.4%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| IRIS ADHESIONS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 8 ( 3.2%) | 11 ( 4.2%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 3 ( 4.1%) | 2 ( 2.7%) | 4 ( 5.7%) |
| | OTHER | 2 (33.3%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 5.4%) |
| CONJUNCTIVAL HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 10 ( 3.9%) | 3 ( 3.1%) | 3 ( 1.2%) | 4 ( 1.5%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 3 ( 4.1%) | 3 ( 4.1%) | 2 ( 2.9%) |
| | OTHER | 0 ( 0.0%) | 2 ( 3.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.6%) |
| CORNEAL EDEMA | CAUCASIAN | 0 ( 0.0%) | 4 ( 1.6%) | 2 ( 2.1%) | 8 ( 3.2%) | 10 ( 3.8%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 6 ( 8.6%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 1 ( 1.8%) |
| RUBEOSIS IRIDIS | CAUCASIAN | 0 ( 0.0%) | 4 ( 1.6%) | 4 ( 4.1%) | 4 ( 1.6%) | 4 ( 1.5%) |
| | HISPANIC | 1 (20.0%) | 0 ( 0.0%) | 4 ( 5.4%) | 2 ( 2.7%) | 3 ( 4.3%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.6%) |
| HYPOPYON | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.8%) | 10 ( 3.8%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 3 ( 4.1%) | 9 (12.9%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 2 ( 3.6%) |
| HYPHEMA | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 2 ( 2.1%) | 5 ( 2.0%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 5.4%) |
| MACULAR EDEMA | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 3 ( 3.1%) | 2 ( 0.8%) | 6 ( 2.3%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 0 ( 0.0%) | 1 ( 1.4%) | 2 ( 2.9%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS NOS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 3 ( 1.2%) | 4 ( 1.5%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 1 (16.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.7%) | 0 ( 0.0%) |
| VITREOUS DETACHMENT | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 2 ( 0.8%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 5.5%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.6%) |
| MACULOPATHY | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 2 ( 0.8%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 1 ( 1.8%) |
| KERATITIS NEC | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 1 ( 0.4%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.7%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CATARACT NEC | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 2 ( 0.8%) | 2 ( 0.8%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.6%) |
| CATARACT NOS AGGRAVATED | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 0 ( 0.0%) | 3 ( 1.2%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 1 (16.7%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRY EYE NEC | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 1 ( 0.4%) | 2 ( 0.8%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 1.4%) | 1 ( 1.4%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DIPLOPIA | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 2 ( 2.7%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 1 ( 1.8%) |
| GLAUCOMA NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 5 ( 1.9%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POSTERIOR CAPSULE OPACIFICATION | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 2 ( 0.8%) | 2 ( 0.8%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISION BLURRED | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.2%) | 2 ( 0.8%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NEC | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.6%) |
| HYPOTONY OF EYE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 2 ( 0.8%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| MYDRIASIS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.5%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 2 ( 0.8%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
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Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CONJUNCTIVITIS NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 1 (16.7%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.1%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL TEAR (EXC DETACHMENT) | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.2%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| VITREOUS DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| CORNEAL ABRASION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 2 ( 2.1%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| RETINAL HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 1.4%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHARITIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.8%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PSEUDOPHAKIA | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| STRABISMUS NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS OPACITIES | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| APHAKIA | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS TRANSIENT | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| CHORIORETINAL ATROPHY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL OPACITY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| ERYTHEMA NEC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFLAMMATION NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MEIBOMIAN CYST | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| OCULAR HYPERAEMIA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAINFUL RED EYES | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEPIGMENTATION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL SCAR | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| TOPOGRAPHY CORNEAL ABNORMAL | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| INVESTIGATIONS | CAUCASIAN | 0 ( 0.0%) | 16 ( 6.3%) | 13 (13.4%) | 19 ( 7.6%) | 14 ( 5.3%) |
| | HISPANIC | 0 ( 0.0%) | 3 ( 4.6%) | 6 ( 8.1%) | 3 ( 4.1%) | 3 ( 4.3%) |
| | OTHER | 0 ( 0.0%) | 5 ( 8.6%) | 2 ( 7.4%) | 2 ( 3.7%) | 3 ( 5.4%) |
| INTRAOCULAR PRESSURE INCREASED | CAUCASIAN | 0 ( 0.0%) | 13 ( 5.1%) | 11 (11.3%) | 13 ( 5.2%) | 12 ( 4.5%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 3 ( 4.1%) | 3 ( 4.1%) | 2 ( 2.9%) |
| | OTHER | 0 ( 0.0%) | 5 ( 8.6%) | 2 ( 7.4%) | 2 ( 3.7%) | 2 ( 3.6%) |
| CORNEAL STAINING | CAUCASIAN | 0 ( 0.0%) | 3 ( 1.2%) | 2 ( 2.1%) | 6 ( 2.4%) | 2 ( 0.8%) |
| | HISPANIC | 0 ( 0.0%) | 1 ( 1.5%) | 3 ( 4.1%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | CAUCASIAN | 0 ( 0.0%) | 9 ( 3.5%) | 7 ( 7.2%) | 16 ( 6.4%) | 14 ( 5.3%) |
| | HISPANIC | 0 ( 0.0%) | 5 ( 7.7%) | 2 ( 2.7%) | 7 ( 9.6%) | 6 ( 8.6%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 6 (11.1%) | 4 ( 7.1%) |
| EYELID EDEMA | CAUCASIAN | 0 ( 0.0%) | 2 ( 0.8%) | 4 ( 4.1%) | 12 ( 4.8%) | 13 ( 4.9%) |
| | HISPANIC | 0 ( 0.0%) | 3 ( 4.6%) | 2 ( 2.7%) | 6 ( 8.2%) | 5 ( 7.1%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 4 ( 7.4%) | 1 ( 1.8%) |
| ERYTHEMA NEC | CAUCASIAN | 0 ( 0.0%) | 7 ( 2.7%) | 3 ( 3.1%) | 11 ( 4.4%) | 8 ( 3.0%) |
| | HISPANIC | 0 ( 0.0%) | 2 ( 3.1%) | 0 ( 0.0%) | 1 ( 1.4%) | 2 ( 2.9%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.7%) | 2 ( 3.6%) |
| CUTIS LAXA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |

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Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| OCULAR HYPEREMIA | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 2 ( 2.1%) | 3 ( 1.2%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.7%) | 1 ( 1.8%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 2 ( 2.1%) | 2 ( 0.8%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 1 ( 1.8%) |
| VITRECTOMY | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.7%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.9%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 0.4%) | 3 ( 1.1%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 1 ( 3.7%) | 1 ( 1.9%) | 2 ( 3.6%) |
| PUPILLARY DISORDER NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 3.7%) | 1 ( 1.9%) | 1 ( 1.8%) |

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Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 22
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Race
Safety Population

| System Organ Class / Preferred Term | Race | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISUAL FIELD DEFECT NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 1 ( 1.7%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEADACHE NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.8%) |
| PUPILLARY REFLEX IMPAIRED | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.4%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | CAUCASIAN | 0 ( 0.0%) | 1 ( 0.4%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIPHERAL ISCHEMIA NOS | CAUCASIAN | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | HISPANIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.4%) |
| | OTHER | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given race within each dose group.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| NUMBER OF PATIENTS | NON-DIABETIC | 2 | 86 | 25 | 104 | 80 |
| | DIABETIC: TYPE I | 5 | 169 | 106 | 164 | 187 |
| | DIABETIC: TYPE II | 11 | 123 | 67 | 109 | 124 |
| NUMBER OF PATIENTS WITH AT LEAST ONE ADVERSE EVENT | NON-DIABETIC | 1 (50.0%) | 63 (73.3%) | 25 ( 100%) | 84 (80.8%) | 72 (90.0%) |
| | DIABETIC: TYPE I | 5 ( 100%) | 132 (78.1%) | 101 (95.3%) | 135 (82.3%) | 164 (87.7%) |
| | DIABETIC: TYPE II | 11 ( 100%) | 103 (83.7%) | 67 ( 100%) | 104 (95.4%) | 113 (91.1%) |
| EYE DISORDERS | NON-DIABETIC | 1 (50.0%) | 63 (73.3%) | 25 ( 100%) | 84 (80.8%) | 72 (90.0%) |
| | DIABETIC: TYPE I | 5 ( 100%) | 132 (78.1%) | 100 (94.3%) | 135 (82.3%) | 164 (87.7%) |
| | DIABETIC: TYPE II | 11 ( 100%) | 102 (82.9%) | 67 ( 100%) | 103 (94.5%) | 113 (91.1%) |
| IRITIS | NON-DIABETIC | 1 (50.0%) | 29 (33.7%) | 17 (68.0%) | 54 (51.9%) | 45 (56.3%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 48 (28.4%) | 65 (61.3%) | 90 (54.9%) | 117 (62.6%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 49 (39.8%) | 41 (61.2%) | 78 (71.6%) | 81 (65.3%) |
| OCULAR HYPEREMIA | NON-DIABETIC | 0 ( 0.0%) | 33 (38.4%) | 15 (60.0%) | 50 (48.1%) | 40 (50.0%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 56 (33.1%) | 62 (58.5%) | 88 (53.7%) | 100 (53.5%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 51 (41.5%) | 36 (53.7%) | 64 (58.7%) | 75 (60.5%) |
| EYE IRRITATION | NON-DIABETIC | 1 (50.0%) | 23 (26.7%) | 11 (44.0%) | 25 (24.0%) | 24 (30.0%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 43 (25.4%) | 53 (50.0%) | 54 (32.9%) | 73 (39.0%) |
| | DIABETIC: TYPE II | 7 (63.6%) | 45 (36.6%) | 26 (38.8%) | 53 (48.6%) | 42 (33.9%) |
| EYE PAIN | NON-DIABETIC | 0 ( 0.0%) | 16 (18.6%) | 12 (48.0%) | 34 (32.7%) | 31 (38.8%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 35 (20.7%) | 37 (34.9%) | 50 (30.5%) | 76 (40.6%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 33 (26.8%) | 23 (34.3%) | 55 (50.5%) | 54 (43.5%) |
| LACRIMATION INCREASED | NON-DIABETIC | 0 ( 0.0%) | 13 (15.1%) | 7 (28.0%) | 27 (26.0%) | 25 (31.3%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 40 (23.7%) | 36 (34.0%) | 47 (28.7%) | 62 (33.2%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 34 (27.6%) | 22 (32.8%) | 50 (45.9%) | 52 (41.9%) |
| VISUAL ACUITY REDUCED | NON-DIABETIC | 0 ( 0.0%) | 13 (15.1%) | 6 (24.0%) | 23 (22.1%) | 13 (16.3%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 37 (21.9%) | 49 (46.2%) | 43 (26.2%) | 53 (28.3%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 24 (19.5%) | 22 (32.8%) | 35 (32.1%) | 32 (25.8%) |
| ABNORMAL SENSATION IN EYE | NON-DIABETIC | 0 ( 0.0%) | 12 (14.0%) | 11 (44.0%) | 23 (22.1%) | 30 (37.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 27 (16.0%) | 29 (27.4%) | 44 (26.8%) | 54 (28.9%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 29 (23.6%) | 22 (32.8%) | 34 (31.2%) | 30 (24.2%) |
| VITREOUS FLOATERS | NON-DIABETIC | 0 ( 0.0%) | 13 (15.1%) | 7 (28.0%) | 18 (17.3%) | 18 (22.5%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 33 (19.5%) | 37 (34.9%) | 42 (25.6%) | 58 (31.0%) |
| | DIABETIC: TYPE II | 4 (36.4%) | 21 (17.1%) | 19 (28.4%) | 28 (25.7%) | 24 (19.4%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VITREOUS HEMORRHAGE | NON-DIABETIC | 1 (50.0%) | 9 (10.5%) | 7 (28.0%) | 12 (11.5%) | 9 (11.3%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 36 (21.3%) | 41 (38.7%) | 51 (31.1%) | 57 (30.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 21 (17.1%) | 22 (32.8%) | 28 (25.7%) | 24 (19.4%) |
| PHOTOPHOBIA | NON-DIABETIC | 0 ( 0.0%) | 8 ( 9.3%) | 7 (28.0%) | 14 (13.5%) | 18 (22.5%) |
| | DIABETIC: TYPE I | 3 (60.0%) | 30 (17.8%) | 34 (32.1%) | 40 (24.4%) | 51 (27.3%) |
| | DIABETIC: TYPE II | 3 (27.3%) | 22 (17.9%) | 18 (26.9%) | 32 (29.4%) | 33 (26.6%) |
| CONJUNCTIVAL EDEMA | NON-DIABETIC | 0 ( 0.0%) | 15 (17.4%) | 6 (24.0%) | 23 (22.1%) | 18 (22.5%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 26 (15.4%) | 29 (27.4%) | 44 (26.8%) | 37 (19.8%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 18 (14.6%) | 13 (19.4%) | 29 (26.6%) | 34 (27.4%) |
| CATARACT NUCLEAR | NON-DIABETIC | 0 ( 0.0%) | 7 ( 8.1%) | 6 (24.0%) | 8 ( 7.7%) | 11 (13.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 14 ( 8.3%) | 15 (14.2%) | 13 ( 7.9%) | 11 ( 5.9%) |
| | DIABETIC: TYPE II | 5 (45.5%) | 13 (10.6%) | 6 ( 9.0%) | 16 (14.7%) | 7 ( 5.6%) |
| RETINAL DETACHMENT | NON-DIABETIC | 0 ( 0.0%) | 5 ( 5.8%) | 3 (12.0%) | 11 (10.6%) | 9 (11.3%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 12 ( 7.1%) | 13 (12.3%) | 11 ( 6.7%) | 23 (12.3%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 9 ( 7.3%) | 6 ( 9.0%) | 13 (11.9%) | 13 (10.5%) |
| CATARACT SUBCAPSULAR | NON-DIABETIC | 0 ( 0.0%) | 5 ( 5.8%) | 5 (20.0%) | 9 ( 8.7%) | 12 (15.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 11 ( 6.5%) | 19 (17.9%) | 14 ( 8.5%) | 16 ( 8.6%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 10 ( 8.1%) | 9 (13.4%) | 6 ( 5.5%) | 10 ( 8.1%) |
| PHOTOPSIA | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 1 ( 4.0%) | 5 ( 4.8%) | 4 ( 5.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 12 ( 7.1%) | 14 (13.2%) | 14 ( 8.5%) | 19 (10.2%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 8 ( 6.5%) | 7 (10.4%) | 26 (23.9%) | 15 (12.1%) |
| CATARACT CORTICAL | NON-DIABETIC | 1 (50.0%) | 6 ( 7.0%) | 1 ( 4.0%) | 9 ( 8.7%) | 8 (10.0%) |
| | DIABETIC: TYPE I | 3 (60.0%) | 12 ( 7.1%) | 9 ( 8.5%) | 8 ( 4.9%) | 18 ( 9.6%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 9 ( 7.3%) | 4 ( 6.0%) | 13 (11.9%) | 5 ( 4.0%) |
| CORNEAL EROSION | NON-DIABETIC | 0 ( 0.0%) | 5 ( 5.8%) | 0 ( 0.0%) | 5 ( 4.8%) | 5 ( 6.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 12 ( 7.1%) | 7 ( 6.6%) | 11 ( 6.7%) | 9 ( 4.8%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 7 ( 5.7%) | 3 ( 4.5%) | 9 ( 8.3%) | 3 ( 2.4%) |
| CORNEAL EDEMA | NON-DIABETIC | 0 ( 0.0%) | 6 ( 7.0%) | 1 ( 4.0%) | 5 ( 4.8%) | 7 ( 8.8%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 5 ( 3.0%) | 11 (10.4%) | 9 ( 5.5%) | 6 ( 3.2%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 5 ( 7.5%) | 6 ( 5.5%) | 11 ( 8.9%) |
| RUBEOSIS IRIDIS | NON-DIABETIC | 0 ( 0.0%) | 3 ( 3.5%) | 2 ( 8.0%) | 2 ( 1.9%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 9 ( 5.3%) | 8 ( 7.5%) | 9 ( 5.5%) | 10 ( 5.3%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 7 ( 5.7%) | 6 ( 9.0%) | 6 ( 5.5%) | 6 ( 4.8%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| EYE DISCHARGE | NON-DIABETIC | 0 ( 0.0%) | 7 ( 8.1%) | 2 ( 8.0%) | 4 ( 3.8%) | 6 ( 7.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 8 ( 4.7%) | 3 ( 2.8%) | 12 ( 7.3%) | 7 ( 3.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 3 ( 2.4%) | 5 ( 7.5%) | 7 ( 6.4%) | 7 ( 5.6%) |
| CONJUNCTIVAL HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 5 ( 5.8%) | 1 ( 4.0%) | 2 ( 1.9%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 8 ( 4.7%) | 6 ( 5.7%) | 4 ( 2.4%) | 6 ( 3.2%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 12 ( 9.8%) | 4 ( 6.0%) | 8 ( 7.3%) | 9 ( 7.3%) |
| IRIS ADHESIONS | NON-DIABETIC | 0 ( 0.0%) | 3 ( 3.5%) | 1 ( 4.0%) | 5 ( 4.8%) | 7 ( 8.8%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 8 ( 4.7%) | 5 ( 4.7%) | 6 ( 3.7%) | 12 ( 6.4%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 2 ( 1.6%) | 3 ( 4.5%) | 2 ( 1.8%) | 8 ( 6.5%) |
| MACULAR EDEMA | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 1 ( 4.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 7 ( 4.1%) | 11 (10.4%) | 7 ( 4.3%) | 11 ( 5.9%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 3 ( 2.4%) | 4 ( 6.0%) | 4 ( 3.7%) | 8 ( 6.5%) |
| CORNEAL DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 3 ( 3.5%) | 0 ( 0.0%) | 4 ( 3.8%) | 6 ( 7.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 4 ( 2.4%) | 4 ( 3.8%) | 8 ( 4.9%) | 13 ( 7.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 2 ( 3.0%) | 5 ( 4.6%) | 6 ( 4.8%) |
| HYPHEMA | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 3 (12.0%) | 4 ( 3.8%) | 2 ( 2.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 2 ( 1.9%) | 3 ( 1.8%) | 7 ( 3.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 3 ( 2.4%) | 3 ( 4.5%) | 5 ( 4.6%) | 6 ( 4.8%) |
| CATARACT NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 5.8%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 7 ( 4.1%) | 0 ( 0.0%) | 3 ( 1.8%) | 3 ( 1.6%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 3 ( 2.4%) | 1 ( 1.5%) | 1 ( 0.9%) | 3 ( 2.4%) |
| BLINDNESS NEC | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 1 ( 4.0%) | 1 ( 1.0%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 0 ( 0.0%) | 7 ( 6.6%) | 3 ( 1.8%) | 4 ( 2.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 3 ( 2.4%) | 1 ( 1.5%) | 2 ( 1.8%) | 2 ( 1.6%) |
| HYPOPYON | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 4 ( 5.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 3 ( 1.8%) | 5 ( 2.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.8%) | 12 ( 9.7%) |
| DRY EYE NEC | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 2 ( 1.9%) | 4 ( 2.4%) | 4 ( 2.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 2 ( 1.6%) | 5 ( 7.5%) | 1 ( 0.9%) | 2 ( 1.6%) |
| GLAUCOMA NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 4 ( 3.8%) | 2 ( 1.2%) | 8 ( 4.3%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 4 ( 3.3%) | 1 ( 1.5%) | 1 ( 0.9%) | 3 ( 2.4%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISION BLURRED | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 8.0%) | 2 ( 1.9%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 4 ( 2.4%) | 3 ( 2.8%) | 2 ( 1.2%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 5 ( 7.5%) | 1 ( 0.9%) | 2 ( 1.6%) |
| CATARACT NOS AGGRAVATED | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 1 ( 4.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 3 ( 1.8%) | 3 ( 2.8%) | 3 ( 1.8%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 3 ( 2.4%) | 0 ( 0.0%) | 1 ( 0.9%) | 2 ( 1.6%) |
| KERATITIS NEC | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 4 ( 3.8%) | 1 ( 0.6%) | 6 ( 3.2%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 2 ( 1.8%) | 1 ( 0.8%) |
| VITREOUS DETACHMENT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.5%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 2 ( 1.2%) | 1 ( 0.9%) | 3 ( 1.8%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.0%) | 6 ( 5.5%) | 1 ( 0.8%) |
| MACULOPATHY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 3 ( 1.8%) | 3 ( 2.8%) | 2 ( 1.2%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 2 ( 1.6%) | 1 ( 1.5%) | 2 ( 1.8%) | 2 ( 1.6%) |
| INTRAOCULAR PRESSURE INCREASED | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 3 (12.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 3 ( 1.8%) | 3 ( 2.8%) | 1 ( 0.6%) | 5 ( 2.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| UVEITIS NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 3 ( 1.8%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 2 ( 1.6%) | 0 ( 0.0%) | 4 ( 3.7%) | 1 ( 0.8%) |
| POST-OPERATIVE PAIN | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 1 ( 1.0%) | 2 ( 2.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 4 ( 2.4%) | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.6%) |
| POSTERIOR CAPSULE OPACIFICATION | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.9%) | 3 ( 1.8%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 2.8%) | 3 ( 2.4%) |
| RETINOPATHY DIABETIC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.9%) | 2 ( 1.2%) | 6 ( 3.2%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 2 ( 1.6%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| BLEPHARITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 2 ( 1.9%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.6%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 2 ( 3.0%) | 1 ( 0.9%) | 1 ( 0.8%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| HYPOTONY OF EYE | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.6%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 1 ( 1.5%) | 1 ( 0.9%) | 3 ( 2.4%) |
| RETINAL HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.9%) | 2 ( 1.2%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 2 ( 1.6%) | 1 ( 1.5%) | 2 ( 1.8%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.9%) | 2 ( 1.2%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 0 ( 0.0%) | 2 ( 3.0%) | 2 ( 1.8%) | 0 ( 0.0%) |
| DIPLOPIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 3 ( 2.8%) | 2 ( 1.2%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 3 ( 2.8%) | 2 ( 1.2%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.8%) | 0 ( 0.0%) |
| CONJUNCTIVITIS NEC | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 1 ( 0.6%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ABRASION | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.6%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MYDRIASIS | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.9%) | 0 ( 0.0%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| RETINAL TEAR (EXC DETACHMENT) | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 2 ( 1.9%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.2%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.8%) |
| FOREIGN BODY RETAINED IN EYE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 1 ( 1.5%) | 1 ( 0.9%) | 0 ( 0.0%) |
| EYE DEGENERATIVE DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 0.9%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| PSEUDOPHAKIA | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 2 ( 1.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 0.8%) |
| INTRAOCULAR PRESSURE DECREASED | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 2 ( 1.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 2 ( 1.8%) | 0 ( 0.0%) |
| PHOTOPHOBIA AGGRAVATED | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| APHAKIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.2%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.8%) |
| PAINFUL RED EYES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 1 ( 0.6%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CHEMOSIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIDOCYCLITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| MACULAR DEGENERATION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 0.8%) |
| RETINAL DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 1 ( 1.5%) | 1 ( 0.9%) | 0 ( 0.0%) |
| RETINAL SCAR | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| BLINDNESS TRANSIENT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CONJUNCTIVITIS (INFECTIVE) NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| CONJUNCTIVITIS ALLERGIC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| CORNEAL OPACITY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY BAND | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MEIBOMIAN CYST | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL HEMATOMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| RETINAL ARTERY EMBOLISM | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 0.8%) |
| RETINAL DEPIGMENTATION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STRABISMUS NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISUAL ACUITY REDUCED TRANSIENTLY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS OPACITIES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANGLE CLOSURE GLAUCOMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ANISEIKONIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| ARCUS SENILIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHAROCONJUNCTIVITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| BLOODSHOT EYE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHALAZION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL ATROPHY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CHORIORETINAL DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL DEGENERATION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| CORNEAL SCAR | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL ULCER NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CYCLITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EXOPHTHALMOS ENDOCRINE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE HEMORRHAGE NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION FUNGAL NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Integrated Summary of Safety

Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| EYE INFECTION NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION STAPHYLOCOCCAL | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| EYE INFLAMMATION NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HERPES SIMPLEX OPHTHALMIC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IRIS NEVUS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LACRIMAL DUCT OBSTRUCTION NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC DISC HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| OPTIC NERVE INJURY NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAPILLEDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DEGENERATION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL EXUDATES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VASCULITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL VEIN THROMBOSIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| SCLERITIS NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| TOPOGRAPHY CORNEAL ABNORMAL | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VISION ABNORMAL NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | NON-DIABETIC | 0 ( 0.0%) | 8 ( 9.3%) | 6 (24.0%) | 12 (11.5%) | 6 ( 7.5%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 18 (10.7%) | 24 (22.6%) | 23 (14.0%) | 29 (15.5%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 18 (14.6%) | 18 (26.9%) | 15 (13.8%) | 11 ( 8.9%) |
| INTRAOCULAR PRESSURE INCREASED | NON-DIABETIC | 0 ( 0.0%) | 6 ( 7.0%) | 6 (24.0%) | 9 ( 8.7%) | 4 ( 5.0%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 17 (10.1%) | 20 (18.9%) | 19 (11.6%) | 25 (13.4%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 16 (13.0%) | 14 (20.9%) | 14 (12.8%) | 11 ( 8.9%) |
| CORNEAL STAINING | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 3 ( 2.9%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 5 ( 4.7%) | 4 ( 2.4%) | 5 ( 2.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 3 ( 2.4%) | 3 ( 4.5%) | 2 ( 1.8%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE ABNORMAL | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | NON-DIABETIC | 0 ( 0.0%) | 4 ( 4.7%) | 3 (12.0%) | 8 ( 7.7%) | 6 ( 7.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 14 ( 8.3%) | 11 (10.4%) | 17 (10.4%) | 14 ( 7.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 8 ( 6.5%) | 5 ( 7.5%) | 14 (12.8%) | 18 (14.5%) |
| EYELID EDEMA | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 2 ( 8.0%) | 7 ( 6.7%) | 4 ( 5.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 9 ( 5.3%) | 8 ( 7.5%) | 12 ( 7.3%) | 8 ( 4.3%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 5 ( 4.1%) | 2 ( 3.0%) | 10 ( 9.2%) | 13 (10.5%) |
| ERYTHEMA NEC | NON-DIABETIC | 0 ( 0.0%) | 3 ( 3.5%) | 0 ( 0.0%) | 6 ( 5.8%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 9 ( 5.3%) | 6 ( 5.7%) | 9 ( 5.5%) | 7 ( 3.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 3 ( 2.4%) | 2 ( 3.0%) | 6 ( 5.5%) | 10 ( 8.1%) |
| OCULAR HYPEREMIA | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 1 ( 4.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CUTIS LAXA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| PERIORBITAL EDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.8%) |
| DERMATITIS NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ECCHYMOSIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PRURITUS NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | NON-DIABETIC | 0 ( 0.0%) | 3 ( 3.5%) | 1 ( 4.0%) | 2 ( 1.9%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 8 ( 4.7%) | 4 ( 3.8%) | 4 ( 2.4%) | 7 ( 3.7%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 3 ( 2.4%) | 2 ( 3.0%) | 7 ( 6.4%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 1 ( 4.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 5 ( 3.0%) | 2 ( 1.9%) | 2 ( 1.2%) | 4 ( 2.1%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 1 ( 0.8%) | 1 ( 1.5%) | 2 ( 1.8%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 2 ( 1.9%) | 1 ( 0.6%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 2.8%) | 0 ( 0.0%) |
| VITRECTOMY | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 2 ( 1.6%) | 1 ( 1.5%) | 1 ( 0.9%) | 0 ( 0.0%) |
| EYE IRRITATION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENS IMPLANT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| SCLERAL OPERATION NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| SUTURE LINE PAIN | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 3.8%) | 0 ( 0.0%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 1 ( 1.5%) | 3 ( 2.8%) | 4 ( 3.2%) |
| PUPILLARY DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 3 ( 2.8%) | 1 ( 0.8%) |
| VISUAL FIELD DEFECT NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FACIAL PALSY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| HEADACHE NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| PUPILLARY REFLEX IMPAIRED | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| VITH NERVE PARALYSIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| IMMUNE SYSTEM DISORDERS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPERSENSITIVITY NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
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Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| MULTIPLE ALLERGIES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHEMICAL BURNS OF EYE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NEOPLASMS BENIGN AND MALIGNANT (INCLUDING CYSTS AND POLYPS) | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BENIGN NEOPLASM OF CHOROID | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RADIOACTIVE IODINE THERAPY | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| MECHANICAL COMPLICATION OF IMPLANT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INFECTIONS AND INFESTATIONS | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 23
Incidence of Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| HYPOPYON | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| PERIPHERAL ISCHEMIA NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Integrated Summary of Safety

Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| NUMBER OF PATIENTS | NON-DIABETIC | 2 | 86 | 25 | 104 | 80 |
| | DIABETIC: TYPE I | 5 | 169 | 106 | 164 | 187 |
| | DIABETIC: TYPE II | 11 | 123 | 67 | 109 | 124 |
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED ADVERSE EVENT | NON-DIABETIC | 1 (50.0%) | 45 (52.3%) | 22 (88.0%) | 75 (72.1%) | 66 (82.5%) |
| | DIABETIC: TYPE I | 3 (60.0%) | 110 (65.1%) | 88 (83.0%) | 118 (72.0%) | 153 (81.8%) |
| | DIABETIC: TYPE II | 7 (63.6%) | 89 (72.4%) | 58 (86.6%) | 97 (89.0%) | 107 (86.3%) |
| EYE DISORDERS | NON-DIABETIC | 1 (50.0%) | 45 (52.3%) | 22 (88.0%) | 75 (72.1%) | 66 (82.5%) |
| | DIABETIC: TYPE I | 3 (60.0%) | 110 (65.1%) | 88 (83.0%) | 117 (71.3%) | 153 (81.8%) |
| | DIABETIC: TYPE II | 7 (63.6%) | 88 (71.5%) | 58 (86.6%) | 96 (88.1%) | 107 (86.3%) |
| IRITIS | NON-DIABETIC | 0 ( 0.0%) | 24 (27.9%) | 14 (56.0%) | 51 (49.0%) | 41 (51.3%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 41 (24.3%) | 47 (44.3%) | 81 (49.4%) | 111 (59.4%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 41 (33.3%) | 39 (58.2%) | 70 (64.2%) | 79 (63.7%) |
| OCULAR HYPEREMIA | NON-DIABETIC | 0 ( 0.0%) | 23 (26.7%) | 12 (48.0%) | 41 (39.4%) | 35 (43.8%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 48 (28.4%) | 49 (46.2%) | 70 (42.7%) | 84 (44.9%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 42 (34.1%) | 24 (35.8%) | 47 (43.1%) | 64 (51.6%) |
| EYE PAIN | NON-DIABETIC | 0 ( 0.0%) | 14 (16.3%) | 6 (24.0%) | 29 (27.9%) | 23 (28.8%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 20 (11.8%) | 23 (21.7%) | 41 (25.0%) | 59 (31.6%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 23 (18.7%) | 19 (28.4%) | 43 (39.4%) | 46 (37.1%) |
| EYE IRRITATION | NON-DIABETIC | 1 (50.0%) | 13 (15.1%) | 8 (32.0%) | 18 (17.3%) | 15 (18.8%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 30 (17.8%) | 35 (33.0%) | 40 (24.4%) | 54 (28.9%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 36 (29.3%) | 18 (26.9%) | 38 (34.9%) | 34 (27.4%) |
| LACRIMATION INCREASED | NON-DIABETIC | 0 ( 0.0%) | 8 ( 9.3%) | 6 (24.0%) | 22 (21.2%) | 18 (22.5%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 26 (15.4%) | 25 (23.6%) | 33 (20.1%) | 47 (25.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 22 (17.9%) | 14 (20.9%) | 39 (35.8%) | 38 (30.6%) |
| ABNORMAL SENSATION IN EYE | NON-DIABETIC | 0 ( 0.0%) | 8 ( 9.3%) | 9 (36.0%) | 17 (16.3%) | 23 (28.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 19 (11.2%) | 19 (17.9%) | 37 (22.6%) | 45 (24.1%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 23 (18.7%) | 15 (22.4%) | 24 (22.0%) | 24 (19.4%) |
| PHOTOPHOBIA | NON-DIABETIC | 0 ( 0.0%) | 6 ( 7.0%) | 5 (20.0%) | 12 (11.5%) | 14 (17.5%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 19 (11.2%) | 22 (20.8%) | 28 (17.1%) | 43 (23.0%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 17 (13.8%) | 14 (20.9%) | 23 (21.1%) | 28 (22.6%) |
| CONJUNCTIVAL EDEMA | NON-DIABETIC | 0 ( 0.0%) | 13 (15.1%) | 2 ( 8.0%) | 17 (16.3%) | 13 (16.3%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 21 (12.4%) | 17 (16.0%) | 37 (22.6%) | 32 (17.1%) |

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Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CONJUNCTIVAL EDEMA | DIABETIC: TYPE II | 0 ( 0.0%) | 15 (12.2%) | 11 (16.4%) | 20 (18.3%) | 32 (25.8%) |
| VITREOUS FLOATERS | NON-DIABETIC | 0 ( 0.0%) | 6 ( 7.0%) | 6 (24.0%) | 13 (12.5%) | 14 (17.5%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 22 (13.0%) | 21 (19.8%) | 26 (15.9%) | 45 (24.1%) |
| | DIABETIC: TYPE II | 2 (18.2%) | 14 (11.4%) | 13 (19.4%) | 19 (17.4%) | 15 (12.1%) |
| VISUAL ACUITY REDUCED | NON-DIABETIC | 0 ( 0.0%) | 4 ( 4.7%) | 3 (12.0%) | 17 (16.3%) | 6 ( 7.5%) |
| | DIABETIC: TYPE I | 2 (40.0%) | 23 (13.6%) | 31 (29.2%) | 28 (17.1%) | 34 (18.2%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 16 (13.0%) | 13 (19.4%) | 21 (19.3%) | 18 (14.5%) |
| VITREOUS HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 3 ( 3.5%) | 2 ( 8.0%) | 6 ( 5.8%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 11 ( 6.5%) | 20 (18.9%) | 19 (11.6%) | 17 ( 9.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 11 ( 8.9%) | 10 (14.9%) | 12 (11.0%) | 9 ( 7.3%) |
| PHOTOPSIA | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 1 ( 4.0%) | 3 ( 2.9%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 8 ( 4.7%) | 11 (10.4%) | 7 ( 4.3%) | 16 ( 8.6%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 5 ( 4.1%) | 6 ( 9.0%) | 15 (13.8%) | 9 ( 7.3%) |
| CATARACT SUBCAPSULAR | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 4 (16.0%) | 8 ( 7.7%) | 6 ( 7.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 5 ( 3.0%) | 12 (11.3%) | 10 ( 6.1%) | 7 ( 3.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 6 ( 4.9%) | 4 ( 6.0%) | 2 ( 1.8%) | 4 ( 3.2%) |
| RETINAL DETACHMENT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 9 ( 8.7%) | 6 ( 7.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 4 ( 2.4%) | 7 ( 6.6%) | 5 ( 3.0%) | 10 ( 5.3%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 6 ( 4.9%) | 4 ( 6.0%) | 4 ( 3.7%) | 6 ( 4.8%) |
| CATARACT NUCLEAR | NON-DIABETIC | 0 ( 0.0%) | 3 ( 3.5%) | 2 ( 8.0%) | 6 ( 5.8%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 7 ( 4.1%) | 6 ( 5.7%) | 9 ( 5.5%) | 5 ( 2.7%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 6 ( 4.9%) | 4 ( 6.0%) | 7 ( 6.4%) | 2 ( 1.6%) |
| CATARACT CORTICAL | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 7 ( 6.7%) | 4 ( 5.0%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 6 ( 3.6%) | 3 ( 2.8%) | 7 ( 4.3%) | 12 ( 6.4%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 8 ( 6.5%) | 0 ( 0.0%) | 5 ( 4.6%) | 3 ( 2.4%) |
| CORNEAL EROSION | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 4 ( 3.8%) | 3 ( 3.8%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 8 ( 4.7%) | 4 ( 3.8%) | 6 ( 3.7%) | 5 ( 2.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 6 ( 4.9%) | 2 ( 3.0%) | 4 ( 3.7%) | 3 ( 2.4%) |
| CORNEAL DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 4 ( 3.8%) | 4 ( 5.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 2 ( 1.9%) | 8 ( 4.9%) | 11 ( 5.9%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.0%) | 2 ( 1.8%) | 6 ( 4.8%) |
| I EYE DISCHARGE | NON-DIABETIC | 0 ( 0.0%) | 5 ( 5.8%) | 1 ( 4.0%) | 3 ( 2.9%) | 5 ( 6.3%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| EYE DISCHARGE | DIABETIC: TYPE I | 0 ( 0.0%) | 6 ( 3.6%) | 0 ( 0.0%) | 8 ( 4.9%) | 6 ( 3.2%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 2 ( 1.6%) | 2 ( 3.0%) | 1 ( 0.9%) | 3 ( 2.4%) |
| IRIS ADHESIONS | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 5 ( 4.8%) | 5 ( 6.3%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 1 ( 0.6%) | 2 ( 1.9%) | 4 ( 2.4%) | 7 ( 3.7%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 1 ( 0.8%) | 2 ( 3.0%) | 1 ( 0.9%) | 6 ( 4.8%) |
| CONJUNCTIVAL HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 4 ( 4.7%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 3 ( 1.8%) | 3 ( 2.8%) | 1 ( 0.6%) | 5 ( 2.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 7 ( 5.7%) | 3 ( 4.5%) | 4 ( 3.7%) | 2 ( 1.6%) |
| CORNEAL EDEMA | NON-DIABETIC | 0 ( 0.0%) | 4 ( 4.7%) | 0 ( 0.0%) | 4 ( 3.8%) | 4 ( 5.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 2.8%) | 4 ( 2.4%) | 3 ( 1.6%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 10 ( 8.1%) |
| RUBEOSIS IRIDIS | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 1 ( 4.0%) | 2 ( 1.9%) | 2 ( 2.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 4 ( 3.8%) | 4 ( 2.4%) | 3 ( 1.6%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 3 ( 2.4%) | 3 ( 4.5%) | 0 ( 0.0%) | 4 ( 3.2%) |
| HYPOPYON | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 4 ( 5.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 3 ( 1.8%) | 5 ( 2.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.8%) | 12 ( 9.7%) |
| HYPHEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 4 ( 3.8%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 2 ( 3.0%) | 1 ( 0.9%) | 3 ( 2.4%) |
| MACULAR EDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 3 ( 1.8%) | 1 ( 0.9%) | 3 ( 1.8%) | 5 ( 2.7%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 3 ( 2.4%) |
| UVEITIS NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 3 ( 1.8%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 2 ( 1.8%) | 1 ( 0.8%) |
| VITREOUS DETACHMENT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 2.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 4 ( 3.7%) | 0 ( 0.0%) |
| MACULOPATHY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.9%) | 2 ( 1.2%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.6%) |

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Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| KERATITIS NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 3 ( 2.8%) | 0 ( 0.0%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.8%) | 1 ( 0.8%) |
| CATARACT NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.6%) |
| CATARACT NOS AGGRAVATED | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 1 (20.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| DRY EYE NEC | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 1 ( 1.5%) | 1 ( 0.9%) | 0 ( 0.0%) |
| DIPLOPIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.9%) | 2 ( 1.2%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| GLAUCOMA NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 4 ( 2.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| POSTERIOR CAPSULE OPACIFICATION | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 1 ( 0.8%) |
| VISION BLURRED | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 0.9%) | 1 ( 0.8%) |
| BLINDNESS NEC | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOTONY OF EYE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.6%) |
| MYDRIASIS | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| PHOTOPHOBIA AGGRAVATED | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 2 ( 1.2%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| CONJUNCTIVITIS NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORNEAL EPITHELIUM DEFECT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 1 ( 9.1%) | 0 ( 0.0%) | 2 ( 3.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| FOREIGN BODY RETAINED IN EYE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE INCREASED | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| RETINAL TEAR (EXC DETACHMENT) | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| RETINOPATHY DIABETIC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VITREOUS DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| CORNEAL ABRASION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CORTICAL OPACITY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INTRAOCULAR PRESSURE DECREASED | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| IRIDOCYCLITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 3.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| RETINAL HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLEPHARITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHOROIDAL DETACHMENT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS (INFECTIVE) NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| EYE DEGENERATIVE DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 0.9%) | 0 ( 0.0%) |
| MACULAR DEGENERATION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERTENSION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| PSEUDOPHAKIA | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| STRABISMUS NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| VITREOUS OPACITIES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| APHAKIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLINDNESS NIGHT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| BLINDNESS TRANSIENT | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| BLOODSHOT EYE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CCONJUNCTIVAL EDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL ATROPHY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CHORIORETINAL DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| COLOUR BLINDNESS NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| CONJUNCTIVITIS VIRAL NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| CORNEAL OPACITY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| CYCLITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| ERYTHEMA NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE ALLERGY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE INFECTION TOXOPLASMAL | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| EYE INFLAMMATION NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID EDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYELID PTOSIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOCONJUNCTIVITIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| KERATOPATHY NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| LENTICULAR OPACITIES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| MEIBOMIAN CYST | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPERAEMIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPEN ANGLE GLAUCOMA NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OPTIC ATROPHY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PAINFUL RED EYES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PINGUECULA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE PAIN | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| RETINAL DEPIGMENTATION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL ISCHEMIA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL MICROANEURYSMS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| RETINAL SCAR | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| RETINAL VEIN THROMBOSIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| TOPOGRAPHY CORNEAL ABNORMAL | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| UVEITIS DIABETIC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VISUAL DISTURBANCE NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INVESTIGATIONS | NON-DIABETIC | 0 ( 0.0%) | 6 ( 7.0%) | 2 ( 8.0%) | 7 ( 6.7%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 9 ( 5.3%) | 11 (10.4%) | 12 ( 7.3%) | 12 ( 6.4%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 9 ( 7.3%) | 8 (11.9%) | 5 ( 4.6%) | 8 ( 6.5%) |
| INTRAOCULAR PRESSURE INCREASED | NON-DIABETIC | 0 ( 0.0%) | 4 ( 4.7%) | 2 ( 8.0%) | 5 ( 4.8%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 9 ( 5.3%) | 7 ( 6.6%) | 9 ( 5.5%) | 8 ( 4.3%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 7 ( 5.7%) | 7 (10.4%) | 4 ( 3.7%) | 8 ( 6.5%) |
| CORNEAL STAINING | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 0 ( 0.0%) | 2 ( 1.9%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 3.8%) | 3 ( 1.8%) | 4 ( 2.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 2 ( 1.6%) | 1 ( 1.5%) | 1 ( 0.9%) | 0 ( 0.0%) |
| SKIN & SUBCUTANEOUS TISSUE DISORDERS | NON-DIABETIC | 0 ( 0.0%) | 2 ( 2.3%) | 1 ( 4.0%) | 6 ( 5.8%) | 2 ( 2.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 6 ( 3.6%) | 5 ( 4.7%) | 12 ( 7.3%) | 10 ( 5.3%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 7 ( 5.7%) | 3 ( 4.5%) | 11 (10.1%) | 12 ( 9.7%) |
| EYELID EDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 4.0%) | 5 ( 4.8%) | 2 ( 2.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 2 ( 1.2%) | 4 ( 3.8%) | 10 ( 6.1%) | 6 ( 3.2%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 4 ( 3.3%) | 1 ( 1.5%) | 7 ( 6.4%) | 11 ( 8.9%) |
| ERYTHEMA NEC | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 5 ( 4.8%) | 2 ( 2.5%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 5 ( 3.0%) | 2 ( 1.9%) | 4 ( 2.4%) | 4 ( 2.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 3 ( 2.4%) | 1 ( 1.5%) | 5 ( 4.6%) | 6 ( 4.8%) |
| CUTIS LAXA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| ECCHYMOSIS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| OCULAR HYPEREMIA | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| PERIORBITAL EDEMA | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| SURGICAL AND MEDICAL PROCEDURES | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 3 ( 2.8%) | 1 ( 0.6%) | 4 ( 2.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 4 ( 3.7%) | 0 ( 0.0%) |
| UNSPECIFIED COMPLICATION OF PROCEDURE NEC | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 1 ( 0.6%) | 2 ( 1.9%) | 0 ( 0.0%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 2.8%) | 0 ( 0.0%) |
| VITRECTOMY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| EYE IRRITATION | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.6%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE COMPLICATIONS NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| POST-OPERATIVE HEMORRHAGE | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) |
| SCLERAL OPERATION NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| NERVOUS SYSTEM DISORDERS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 2 ( 1.1%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 1 ( 1.5%) | 1 ( 0.9%) | 3 ( 2.4%) |

Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 24
Incidence of Related Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Diabetic Status
Safety Population

| System Organ Class / Preferred Term | Diabetic Status | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| PUPILLARY DISORDER NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.0%) | 1 ( 1.3%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 1.5%) | 1 ( 0.9%) | 1 ( 0.8%) |
| VISUAL FIELD DEFECT NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.9%) | 0 ( 0.0%) | 1 ( 0.5%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEADACHE NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| PUPILLARY REFLEX IMPAIRED | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| INFECTIONS AND INFESTATIONS | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HYPOPYON | NON-DIABETIC | 0 ( 0.0%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| INJURY AND POISONING | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| HEAD INJURY | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 1 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| VASCULAR DISORDERS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |
| PERIPHERAL ISCHEMIA NOS | NON-DIABETIC | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE I | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | DIABETIC: TYPE II | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.8%) |



Note: Percentages based on the total number of patients of the given diabetic status within each dose group.
Type I Diabetes includes all insulin-dependent diabetics.

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Table 25
Analysis of Selected Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Saline Control | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase | p-Values [1] Overall | 7.5 vs. Saline | 55 vs. Saline | 75 vs. Saline |
|---|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 378 | 180 | 359 | 374 | | | | |
| NUMBER OF PATIENTS WITH AT LEAST ONE SELECTED ADVERSE EVENT | 288 (76.2%) | 174 (96.7%) | 299 (83.3%) | 327 (87.4%) | | | | |
| EYE DISORDERS | 287 (75.9%) | 174 (96.7%) | 298 (83.0%) | 327 (87.4%) | | | | |
| ABNORMAL SENSATION IN EYE | 68 (18.0%) | 54 (30.0%) | 91 (25.3%) | 105 (28.1%) | 0.00203 | 0.00206 | 0.01576 | 0.00131 |
| BLINDNESS NEC | 4 ( 1.1%) | 5 ( 2.8%) | 5 ( 1.4%) | 6 ( 1.6%) | 0.48492 | 0.15614 | 0.74679 | 0.54419 |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0.70720 | N/A | N/A | 0.49734 |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 1 ( 0.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 0.17412 | 0.32258 | 0.48711 | N/A |
| CATARACT CORTICAL | 27 ( 7.1%) | 9 ( 5.0%) | 26 ( 7.2%) | 29 ( 7.8%) | 0.70308 | 0.46093 | 1.00000 | 0.78241 |
| CATARACT NEC | 10 ( 2.6%) | 1 ( 0.6%) | 10 ( 2.8%) | 8 ( 2.1%) | 0.35474 | 0.11482 | 1.00000 | 0.81232 |
| CATARACT NOS AGGRAVATED | 8 ( 2.1%) | 4 ( 2.2%) | 5 ( 1.4%) | 2 ( 0.5%) | 0.19545 | 1.00000 | 0.57931 | 0.10708 |
| CATARACT NUCLEAR | 34 ( 9.0%) | 20 (11.1%) | 29 ( 8.1%) | 27 ( 7.2%) | 0.46070 | 0.44572 | 0.69389 | 0.42353 |
| CATARACT SUBCAPSULAR | 26 ( 6.9%) | 30 (16.7%) | 23 ( 6.4%) | 32 ( 8.6%) | 0.00106 | 0.00076 | 0.88269 | 0.41441 |
| CONJUNCTIVAL EDEMA | 59 (15.6%) | 41 (22.8%) | 86 (24.0%) | 87 (23.3%) | 0.01553 | 0.04476 | 0.00532 | 0.00970 |
| EYE IRRITATION | 111 (29.4%) | 80 (44.4%) | 121 (33.7%) | 128 (34.2%) | 0.00683 | 0.00058 | 0.23398 | 0.15923 |
| EYE PAIN | 84 (22.2%) | 63 (35.0%) | 129 (35.9%) | 149 (39.8%) | <0.00001 | 0.00197 | 0.00005 | <0.00001 |
| HYPOPYON | 0 ( 0.0%) | 1 ( 0.6%) | 6 ( 1.7%) | 20 ( 5.3%) | <0.00001 | 0.32258 | 0.01307 | <0.00001 |
| INTRAOCULAR PRESSURE INCREASED | 3 ( 0.8%) | 6 ( 3.3%) | 3 ( 0.8%) | 4 ( 1.1%) | 0.09359 | 0.03499 | 1.00000 | 0.72402 |
| IRITIS | 126 (33.3%) | 110 (61.1%) | 208 (57.9%) | 230 (61.5%) | <0.00001 | <0.00001 | <0.00001 | <0.00001 |
| LACRIMATION INCREASED | 87 (23.0%) | 56 (31.1%) | 114 (31.8%) | 129 (34.5%) | 0.00394 | 0.04857 | 0.00817 | 0.00053 |
| OCULAR HYPEREMIA | 140 (37.0%) | 101 (56.1%) | 192 (53.5%) | 202 (54.0%) | <0.00001 | 0.00003 | <0.00001 | <0.00001 |
| PHOTOPHOBIA | 60 (15.9%) | 52 (28.9%) | 79 (22.0%) | 94 (25.1%) | 0.00130 | 0.00045 | 0.03814 | 0.00206 |
| PHOTOPSIA | 22 ( 5.8%) | 21 (11.7%) | 44 (12.3%) | 37 ( 9.9%) | 0.01302 | 0.02599 | 0.00279 | 0.04204 |
| RETINAL DETACHMENT | 26 ( 6.9%) | 19 (10.6%) | 31 ( 8.6%) | 41 (11.0%) | 0.21205 | 0.13817 | 0.40925 | 0.05500 |
| VISUAL ACUITY REDUCED | 74 (19.6%) | 70 (38.9%) | 92 (25.6%) | 90 (24.1%) | 0.00003 | <0.00001 | 0.05259 | 0.15757 |
| VITREOUS FLOATERS | 67 (17.7%) | 55 (30.6%) | 79 (22.0%) | 91 (24.3%) | 0.00650 | 0.00095 | 0.16547 | 0.03150 |
| VITREOUS HEMORRHAGE | 66 (17.5%) | 64 (35.6%) | 84 (23.4%) | 82 (21.9%) | 0.00007 | <0.00001 | 0.05440 | 0.14214 |
| INVESTIGATIONS | 39 (10.3%) | 38 (21.1%) | 39 (10.9%) | 37 ( 9.9%) | | | | |
| INTRAOCULAR PRESSURE INCREASED | 39 (10.3%) | 38 (21.1%) | 39 (10.9%) | 37 ( 9.9%) | 0.00163 | 0.00093 | 0.81206 | 0.90390 |
| INFECTIONS AND INFESTATIONS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | | | | |
| HYPOPYON | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1.00000 | 1.00000 | 1.00000 | 1.00000 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract, or events occurring in 10% or more of patients in any one treatment group.
Does NOT include patients in any treatment group in the Watchful Waiting cohort in study VIT-02-08961X
[1] p-Values for comparing across all treatment groups and for pairwise comparisons vs. Saline determined by Fisher's Exact Test.

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Table 26
Analysis of Related Selected Ocular Adverse Events Affecting the Study Eye by System Organ Class
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Saline Control | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase | p-Values [1] Overall | 7.5 vs. Saline | 55 vs. Saline | 75 vs. Saline |
|---|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 378 | 180 | 359 | 374 | | | | |
| NUMBER OF PATIENTS WITH AT LEAST ONE RELATED SELECTED ADVERSE EVENT | 234 (61.9%) | 151 (83.9%) | 265 (73.8%) | 303 (81.0%) | | | | |
| EYE DISORDERS | 233 (61.6%) | 151 (83.9%) | 264 (73.5%) | 303 (81.0%) | | | | |
| ABNORMAL SENSATION IN EYE | 50 (13.2%) | 38 (21.1%) | 73 (20.3%) | 85 (22.7%) | 0.00442 | 0.01865 | 0.01026 | 0.00084 |
| BLINDNESS NEC | 1 ( 0.3%) | 1 ( 0.6%) | 1 ( 0.3%) | 1 ( 0.3%) | 0.83480 | 0.54150 | 1.00000 | 1.00000 |
| BLINDNESS NIGHT | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0.70720 | N/A | N/A | 0.49734 |
| BLINDNESS TRANSIENT | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0.41751 | N/A | 0.48711 | N/A |
| CATARACT CORTICAL | 16 ( 4.2%) | 1 ( 0.6%) | 16 ( 4.5%) | 19 ( 5.1%) | 0.03359 | 0.01657 | 1.00000 | 0.60762 |
| CATARACT NEC | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.6%) | 3 ( 0.8%) | 0.84779 | 1.00000 | 1.00000 | 0.68501 |
| CATARACT NOS AGGRAVATED | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) | 0.55776 | 0.55469 | 1.00000 | 0.62402 |
| CATARACT NUCLEAR | 16 ( 4.2%) | 9 ( 5.0%) | 17 ( 4.7%) | 10 ( 2.7%) | 0.39552 | 0.66687 | 0.85895 | 0.31856 |
| CATARACT SUBCAPSULAR | 11 ( 2.9%) | 17 ( 9.4%) | 15 ( 4.2%) | 17 ( 4.5%) | 0.01336 | 0.00160 | 0.42578 | 0.25374 |
| CONJUNCTIVAL EDEMA | 49 (13.0%) | 26 (14.4%) | 69 (19.2%) | 76 (20.3%) | 0.02374 | 0.69061 | 0.02116 | 0.00803 |
| EYE IRRITATION | 79 (20.9%) | 57 (31.7%) | 90 (25.1%) | 96 (25.7%) | 0.05226 | 0.00818 | 0.18918 | 0.14223 |
| EYE PAIN | 57 (15.1%) | 45 (25.0%) | 105 (29.2%) | 118 (31.6%) | <0.00001 | 0.00680 | <0.00001 | <0.00001 |
| HYPOPYON | 0 ( 0.0%) | 1 ( 0.6%) | 6 ( 1.7%) | 20 ( 5.3%) | <0.00001 | 0.32258 | 0.01307 | <0.00001 |
| INTRAOCULAR PRESSURE INCREASED | 0 ( 0.0%) | 2 ( 1.1%) | 1 ( 0.3%) | 1 ( 0.3%) | 0.11662 | 0.10367 | 0.48711 | 0.49734 |
| IRITIS | 106 (28.0%) | 91 (50.6%) | 188 (52.4%) | 218 (58.3%) | <0.00001 | <0.00001 | <0.00001 | <0.00001 |
| LACRIMATION INCREASED | 56 (14.8%) | 38 (21.1%) | 89 (24.8%) | 95 (25.4%) | 0.00096 | 0.06991 | 0.00081 | 0.00036 |
| OCULAR HYPEREMIA | 113 (29.9%) | 76 (42.2%) | 151 (42.1%) | 171 (45.7%) | 0.00005 | 0.00543 | 0.00071 | <0.00001 |
| PHOTOPHOBIA | 42 (11.1%) | 37 (20.6%) | 58 (16.2%) | 80 (21.4%) | 0.00075 | 0.00405 | 0.05261 | 0.00016 |
| RETINAL DETACHMENT | 10 ( 2.6%) | 11 ( 6.1%) | 16 ( 4.5%) | 21 ( 5.6%) | 0.12926 | 0.05633 | 0.23114 | 0.04452 |
| VISUAL ACUITY REDUCED | 43 (11.4%) | 42 (23.3%) | 60 (16.7%) | 53 (14.2%) | 0.00311 | 0.00038 | 0.04323 | 0.27512 |
| VITREOUS FLOATERS | 42 (11.1%) | 34 (18.9%) | 54 (15.0%) | 68 (18.2%) | 0.02213 | 0.01699 | 0.12564 | 0.00715 |
| VITREOUS HEMORRHAGE | 25 ( 6.6%) | 30 (16.7%) | 33 ( 9.2%) | 27 ( 7.2%) | 0.00162 | 0.00039 | 0.21887 | 0.77520 |
| INVESTIGATIONS | 20 ( 5.3%) | 16 ( 8.9%) | 18 ( 5.0%) | 16 ( 4.3%) | | | | |
| INTRAOCULAR PRESSURE INCREASED | 20 ( 5.3%) | 16 ( 8.9%) | 18 ( 5.0%) | 16 ( 4.3%) | 0.17723 | 0.13890 | 1.00000 | 0.60914 |
| INFECTIONS AND INFESTATIONS | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | | | | |
| HYPOPYON | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1.00000 | 1.00000 | 1.00000 | 1.00000 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract, or events occurring in 10% or more of patients in any one treatment group.
Does NOT include patients in any treatment group in the Watchful Waiting cohort in study VIT-02-08961X
[1] p-Values for comparing across all treatment groups and for pairwise comparisons vs. Saline determined by Fisher's Exact Test.

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Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| EYE DISORDERS | | | | | |
| BLINDNESS NEC | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 1 | 4 | 9 | 6 | 9 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 1 | 4 | 8 | 5 | 10 |
| Mean (SE) | 18.0 ( N/A) | 72.0 (64.9) | 238.3 ( 119) | 82.0 (50.3) | 226.3 (65.8) |
| Min-Max | 18.0 - 18.0 | 0.0 - 266.0 | 0.0 - 815.0 | 0.0 - 220.0 | 0.0 - 570.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 1 | 0 | 1 | 0 | 2 |
| Mean (SE) | 18.0 ( N/A) | N/A | 27.0 ( N/A) | N/A | 171.5 ( 144) |
| Min-Max | 18.0 - 18.0 | N/A | 27.0 - 27.0 | N/A | 28.0 - 315.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 1 | 4 | 8 | 5 | 9 |
| Mean (SE) | 18.0 ( N/A) | 72.0 (64.9) | 238.3 ( 119) | 82.0 (50.3) | 248.3 (69.3) |
| Min-Max | 18.0 - 18.0 | 0.0 - 266.0 | 0.0 - 815.0 | 0.0 - 220.0 | 0.0 - 570.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 1 | 4 | 8 | 5 | 9 |
| Mean (SE) | 18.0 ( N/A) | 72.0 (64.9) | 238.3 ( 119) | 82.0 (50.3) | 248.3 (69.3) |
| Min-Max | 18.0 - 18.0 | 0.0 - 266.0 | 0.0 - 815.0 | 0.0 - 220.0 | 0.0 - 570.0 |
| BLINDNESS NIGHT | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 0 | 0 | 0 | 1 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 0 | 0 | 1 |
| Mean (SE) | N/A | N/A | N/A | N/A | 27.0 ( N/A) |
| Min-Max | N/A | N/A | N/A | N/A | 27.0 - 27.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 0 | 0 | 0 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | N/A | N/A | N/A | N/A |
| Min-Max | N/A | N/A | N/A | N/A | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 0 | 0 | 1 |
| Mean (SE) | N/A | N/A | N/A | N/A | 27.0 ( N/A) |
| Min-Max | N/A | N/A | N/A | N/A | 27.0 - 27.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 0 | 0 | 1 |
| Mean (SE) | N/A | N/A | N/A | N/A | 27.0 ( N/A) |
| Min-Max | N/A | N/A | N/A | N/A | 27.0 - 27.0 |
| BLINDNESS TRANSIENT | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 0 | 1 | 1 | 0 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 1 | 1 | 0 |
| Mean (SE) | N/A | N/A | 1.0 ( N/A) | 49.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | 1.0 - 1.0 | 49.0 - 49.0 | N/A |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 1 | 1 | 0 |
| Mean (SE) | N/A | N/A | 1.0 ( N/A) | 49.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | 1.0 - 1.0 | 49.0 - 49.0 | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 1 | 0 |
| Mean (SE) | N/A | N/A | 1.0 ( N/A) | 49.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | 1.0 - 1.0 | 49.0 - 49.0 | N/A |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 1 | 0 |
| Mean (SE) | N/A | N/A | 1.0 ( N/A) | 49.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | 1.0 - 1.0 | 49.0 - 49.0 | N/A |
| CATARACT CORTICAL | | | | | |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS WITH EVENT | 5 | 27 | 14 | 30 | 31 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 5 | 29 | 16 | 35 | 32 |
| Mean (SE) | 354.2 ( 155) | 186.2 (28.9) | 202.7 (57.9) | 201.0 (41.8) | 228.5 (32.4) |
| Min-Max | 42.0 - 875.0 | 0.0 - 549.0 | 0.0 - 714.0 | 0.0 - 942.0 | 0.0 - 658.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 2 | 9 | 8 | 15 | 14 |
| Mean (SE) | 47.0 ( 5.0) | 161.7 (48.3) | 164.0 (62.5) | 143.9 (63.2) | 169.2 (39.9) |
| Min-Max | 42.0 - 52.0 | 0.0 - 455.0 | 24.0 - 482.0 | 5.0 - 942.0 | 9.0 - 469.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 5 | 27 | 14 | 29 | 30 |
| Mean (SE) | 354.2 ( 155) | 193.0 (30.2) | 205.6 (64.4) | 199.1 (41.7) | 232.9 (34.4) |
| Min-Max | 42.0 - 875.0 | 0.0 - 549.0 | 0.0 - 714.0 | 0.0 - 735.0 | 0.0 - 658.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 5 | 27 | 14 | 29 | 30 |
| Mean (SE) | 354.2 ( 155) | 199.9 (29.3) | 231.1 (62.6) | 240.9 (47.2) | 242.5 (32.9) |
| Min-Max | 42.0 - 875.0 | 0.0 - 549.0 | 0.0 - 714.0 | 0.0 - 942.0 | 0.0 - 658.0 |
| CATARACT NEC | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 10 | 1 | 10 | 9 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 9 | 1 | 8 | 9 |
| Mean (SE) | N/A | 96.4 (48.1) | 0.0 ( N/A) | 59.0 (26.2) | 54.8 (30.6) |
| Min-Max | N/A | 0.0 - 345.0 | 0.0 - 0.0 | 0.0 - 220.0 | 0.0 - 224.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 5 | 1 | 5 | 6 |
| Mean (SE) | N/A | 76.2 (64.1) | 0.0 ( N/A) | 40.6 (18.9) | 11.2 ( 9.7) |
| Min-Max | N/A | 0.0 - 330.0 | 0.0 - 0.0 | 2.0 - 103.0 | 0.0 - 59.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 9 | 1 | 7 | 9 |

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Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | 96.4 (48.1) | 0.0 ( N/A) | 67.1 (28.7) | 54.8 (30.6) |
| Min-Max | N/A | 0.0 - 345.0 | 0.0 - 0.0 | 0.0 - 220.0 | 0.0 - 224.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 9 | 1 | 7 | 9 |
| Mean (SE) | N/A | 96.4 (48.1) | 0.0 ( N/A) | 67.1 (28.7) | 54.8 (30.6) |
| Min-Max | N/A | 0.0 - 345.0 | 0.0 - 0.0 | 0.0 - 220.0 | 0.0 - 224.0 |
| CATARACT NOS AGGRAVATED | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 1 | 8 | 4 | 5 | 3 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 1 | 9 | 4 | 6 | 3 |
| Mean (SE) | 121.0 ( N/A) | 130.2 (48.1) | 107.5 (63.4) | 63.7 (39.8) | 0.0 ( 0.0) |
| Min-Max | 121.0 - 121.0 | 0.0 - 372.0 | 0.0 - 247.0 | 0.0 - 245.0 | 0.0 - 0.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 1 | 3 | 2 | 4 | 0 |
| Mean (SE) | 121.0 ( N/A) | 50.0 (28.0) | 215.0 (32.0) | 95.5 (54.3) | N/A |
| Min-Max | 121.0 - 121.0 | 13.0 - 105.0 | 183.0 - 247.0 | 9.0 - 245.0 | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 1 | 8 | 4 | 5 | 3 |
| Mean (SE) | 121.0 ( N/A) | 133.4 (54.4) | 107.5 (63.4) | 55.2 (47.6) | 0.0 ( 0.0) |
| Min-Max | 121.0 - 121.0 | 0.0 - 372.0 | 0.0 - 247.0 | 0.0 - 245.0 | 0.0 - 0.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 1 | 8 | 4 | 5 | 3 |
| Mean (SE) | 121.0 ( N/A) | 133.4 (54.4) | 107.5 (63.4) | 74.6 (46.9) | 0.0 ( 0.0) |
| Min-Max | 121.0 - 121.0 | 0.0 - 372.0 | 0.0 - 247.0 | 0.0 - 245.0 | 0.0 - 0.0 |
| CATARACT NUCLEAR | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 5 | 34 | 27 | 37 | 29 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 5 | 36 | 33 | 42 | 30 |
| Mean (SE) | 349.0 ( 125) | 210.0 (24.8) | 186.7 (30.7) | 190.6 (31.3) | 161.0 (27.1) |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Min-Max | 0.0 - 674.0 | 0.0 - 518.0 | 0.0 - 698.0 | 0.0 - 888.0 | 0.0 - 535.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 2 | 14 | 15 | 21 | 13 |
| Mean (SE) | 407.0 ( 267) | 237.1 (40.5) | 174.3 (33.1) | 167.2 (33.8) | 110.2 (38.2) |
| Min-Max | 140.0 - 674.0 | 51.0 - 506.0 | 23.0 - 378.0 | 5.0 - 600.0 | 9.0 - 526.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 5 | 34 | 27 | 37 | 29 |
| Mean (SE) | 349.0 ( 125) | 208.1 (24.1) | 164.2 (34.2) | 199.4 (35.0) | 166.0 (27.5) |
| Min-Max | 0.0 - 674.0 | 0.0 - 518.0 | 0.0 - 698.0 | 0.0 - 888.0 | 0.0 - 535.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 5 | 34 | 27 | 37 | 29 |
| Mean (SE) | 349.0 ( 125) | 217.6 (25.4) | 221.9 (33.7) | 200.5 (34.8) | 166.0 (27.5) |
| Min-Max | 0.0 - 674.0 | 0.0 - 518.0 | 0.0 - 698.0 | 0.0 - 888.0 | 0.0 - 535.0 |
| CATARACT SUBCAPSULAR | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 2 | 26 | 33 | 29 | 38 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 2 | 27 | 36 | 34 | 39 |
| Mean (SE) | 117.5 (57.5) | 186.2 (25.4) | 227.9 (31.4) | 187.9 (28.4) | 185.5 (22.7) |
| Min-Max | 60.0 - 175.0 | 0.0 - 456.0 | 0.0 - 821.0 | 0.0 - 656.0 | 0.0 - 518.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 1 | 8 | 18 | 17 | 17 |
| Mean (SE) | 60.0 ( N/A) | 172.4 (38.4) | 206.2 (41.0) | 188.3 (36.3) | 184.2 (31.7) |
| Min-Max | 60.0 - 60.0 | 54.0 - 364.0 | 6.0 - 553.0 | 2.0 - 656.0 | 0.0 - 409.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 2 | 25 | 33 | 29 | 38 |
| Mean (SE) | 117.5 (57.5) | 190.2 (27.3) | 228.0 (33.5) | 199.4 (31.9) | 180.7 (22.8) |
| Min-Max | 60.0 - 175.0 | 0.0 - 456.0 | 0.0 - 821.0 | 0.0 - 656.0 | 0.0 - 518.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 2 | 25 | 33 | 29 | 38 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | 117.5 (57.5) | 190.2 (27.3) | 228.0 (33.5) | 205.2 (31.7) | 185.6 (23.3) |
| Min-Max | 60.0 - 175.0 | 0.0 - 456.0 | 0.0 - 821.0 | 0.0 - 656.0 | 0.0 - 518.0 |
| EYE PAIN | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 2 | 84 | 72 | 139 | 161 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 1 | 119 | 99 | 183 | 203 |
| Mean (SE) | 2.0 ( N/A) | 36.5 ( 6.5) | 50.2 ( 8.8) | 33.6 ( 4.6) | 39.7 ( 6.2) |
| Min-Max | 2.0 - 2.0 | 0.0 - 393.0 | 0.0 - 462.0 | 0.0 - 422.0 | 0.0 - 573.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 1 | 112 | 92 | 174 | 187 |
| Mean (SE) | 2.0 ( N/A) | 30.0 ( 5.7) | 43.1 ( 8.1) | 30.6 ( 4.4) | 32.3 ( 5.4) |
| Min-Max | 2.0 - 2.0 | 0.0 - 372.0 | 0.0 - 462.0 | 0.0 - 422.0 | 0.0 - 573.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3] [5] | | | | | |
| Number of patients | 1 | 84 | 72 | 138 | 159 |
| Mean (SE) | 2.0 ( N/A) | 43.2 ( 8.8) | 61.3 (11.7) | 33.1 ( 5.6) | 47.4 ( 7.7) |
| Min-Max | 2.0 - 2.0 | 0.0 - 393.0 | 0.0 - 462.0 | 0.0 - 422.0 | 0.0 - 573.0 |
| DURATION OF LONGEST EVENT (DAYS) [4] [5] | | | | | |
| Number of patients | 1 | 84 | 72 | 138 | 159 |
| Mean (SE) | 2.0 ( N/A) | 48.1 ( 8.9) | 61.9 (11.7) | 39.5 ( 5.9) | 48.0 ( 7.7) |
| Min-Max | 2.0 - 2.0 | 0.0 - 393.0 | 0.0 - 462.0 | 0.0 - 422.0 | 0.0 - 573.0 |
| HYPOPYON | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 0 | 1 | 6 | 21 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 1 | 6 | 21 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 7.8 ( 2.0) | 10.3 ( 3.9) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 85.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 1 | 6 | 21 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 7.8 ( 2.0) | 10.3 ( 3.9) |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 85.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 6 | 21 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 7.8 ( 2.0) | 10.3 ( 3.9) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 85.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 6 | 21 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 7.8 ( 2.0) | 10.3 ( 3.9) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 85.0 |
| INTRAOCULAR PRESSURE INCREASED | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 3 | 6 | 3 | 6 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 3 | 7 | 4 | 6 |
| Mean (SE) | N/A | 4.3 ( 2.8) | 69.1 (32.1) | 18.8 (11.3) | 19.0 ( 8.9) |
| Min-Max | N/A | 1.0 - 10.0 | 0.0 - 225.0 | 4.0 - 52.0 | 0.0 - 61.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 3 | 6 | 4 | 6 |
| Mean (SE) | N/A | 4.3 ( 2.8) | 56.2 (34.8) | 18.8 (11.3) | 19.0 ( 8.9) |
| Min-Max | N/A | 1.0 - 10.0 | 0.0 - 225.0 | 4.0 - 52.0 | 0.0 - 61.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 3 | 6 | 3 | 6 |
| Mean (SE) | N/A | 4.3 ( 2.8) | 77.3 (36.7) | 23.3 (14.6) | 19.0 ( 8.9) |
| Min-Max | N/A | 1.0 - 10.0 | 0.0 - 225.0 | 4.0 - 52.0 | 0.0 - 61.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 3 | 6 | 3 | 6 |
| Mean (SE) | N/A | 4.3 ( 2.8) | 77.3 (36.7) | 23.7 (14.4) | 19.0 ( 8.9) |
| Min-Max | N/A | 1.0 - 10.0 | 0.0 - 225.0 | 5.0 - 52.0 | 0.0 - 61.0 |
| IRITIS | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 4 | 126 | 123 | 222 | 243 |

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Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Integrated Summary of Safety

Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 4 | 229 | 255 | 454 | 496 |
| Mean (SE) | 106.3 (75.6) | 39.5 ( 4.8) | 52.1 ( 6.2) | 31.0 ( 2.7) | 26.8 ( 2.2) |
| Min-Max | 30.0 - 333.0 | 0.0 - 587.0 | 0.0 - 782.0 | 0.0 - 595.0 | 0.0 - 367.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 3 | 212 | 233 | 438 | 479 |
| Mean (SE) | 30.7 ( 0.3) | 35.8 ( 4.8) | 40.9 ( 4.2) | 27.7 ( 2.3) | 22.1 ( 1.6) |
| Min-Max | 30.0 - 31.0 | 1.0 - 587.0 | 2.0 - 465.0 | 3.0 - 595.0 | 0.0 - 363.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 3 | 126 | 123 | 222 | 243 |
| Mean (SE) | 131.3 ( 101) | 36.8 ( 6.1) | 53.1 ( 8.6) | 27.4 ( 3.8) | 25.1 ( 3.3) |
| Min-Max | 30.0 - 333.0 | 0.0 - 542.0 | 0.0 - 782.0 | 0.0 - 595.0 | 0.0 - 367.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 3 | 126 | 123 | 222 | 243 |
| Mean (SE) | 131.3 ( 101) | 45.4 ( 7.7) | 66.1 (10.1) | 37.9 ( 4.7) | 32.1 ( 3.5) |
| Min-Max | 30.0 - 333.0 | 0.0 - 587.0 | 0.0 - 782.0 | 0.0 - 595.0 | 0.0 - 367.0 |
| RETINAL DETACHMENT | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 3 | 26 | 22 | 35 | 45 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 3 | 29 | 23 | 38 | 53 |
| Mean (SE) | 12.3 (10.4) | 68.0 (19.1) | 122.1 (52.0) | 81.3 (20.8) | 69.8 (15.7) |
| Min-Max | 0.0 - 33.0 | 0.0 - 331.0 | 0.0 - 861.0 | 0.0 - 538.0 | 0.0 - 468.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 3 | 22 | 17 | 27 | 35 |
| Mean (SE) | 12.3 (10.4) | 34.6 (11.0) | 19.7 ( 8.0) | 24.8 ( 9.3) | 27.7 ( 6.0) |
| Min-Max | 0.0 - 33.0 | 0.0 - 189.0 | 0.0 - 120.0 | 0.0 - 248.0 | 0.0 - 126.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 3 | 25 | 21 | 34 | 44 |
| Mean (SE) | 12.3 (10.4) | 78.2 (21.5) | 133.1 (56.5) | 89.1 (22.9) | 73.9 (18.1) |
| Min-Max | 0.0 - 33.0 | 0.0 - 331.0 | 0.0 - 861.0 | 0.0 - 538.0 | 0.0 - 468.0 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Integrated Summary of Safety

Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 3 | 25 | 21 | 34 | 44 |
| Mean (SE) | 12.3 (10.4) | 78.6 (21.5) | 133.1 (56.5) | 89.1 (22.9) | 81.1 (18.4) |
| Min-Max | 0.0 - 33.0 | 0.0 - 331.0 | 0.0 - 861.0 | 0.0 - 538.0 | 0.0 - 468.0 |
| INFECTIONS AND INFESTATIONS | | | | | |
| HYPOPYON | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 1 | 0 | 0 | 0 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 1 | 0 | 0 | 0 |
| Mean (SE) | N/A | 175.0 ( N/A) | N/A | N/A | N/A |
| Min-Max | N/A | 175.0 - 175.0 | N/A | N/A | N/A |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 1 | 0 | 0 | 0 |
| Mean (SE) | N/A | 175.0 ( N/A) | N/A | N/A | N/A |
| Min-Max | N/A | 175.0 - 175.0 | N/A | N/A | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 1 | 0 | 0 | 0 |
| Mean (SE) | N/A | 175.0 ( N/A) | N/A | N/A | N/A |
| Min-Max | N/A | 175.0 - 175.0 | N/A | N/A | N/A |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 1 | 0 | 0 | 0 |
| Mean (SE) | N/A | 175.0 ( N/A) | N/A | N/A | N/A |
| Min-Max | N/A | 175.0 - 175.0 | N/A | N/A | N/A |
| INVESTIGATIONS | | | | | |
| INTRAOCULAR PRESSURE INCREASED | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 3 | 39 | 40 | 42 | 40 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 3 | 44 | 50 | 49 | 56 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Integrated Summary of Safety

Table 27
Duration of Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | 57.7 (31.9) | 55.1 (13.7) | 45.2 (10.9) | 45.7 ( 9.6) | 34.8 ( 8.7) |
| Min-Max | 0.0 - 110.0 | 0.0 - 390.0 | 0.0 - 329.0 | 0.0 - 298.0 | 0.0 - 366.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 2 | 37 | 45 | 43 | 52 |
| Mean (SE) | 86.5 (23.5) | 49.6 (14.3) | 39.6 (10.2) | 36.8 ( 7.4) | 37.5 ( 9.3) |
| Min-Max | 63.0 - 110.0 | 0.0 - 390.0 | 0.0 - 262.0 | 0.0 - 202.0 | 0.0 - 366.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 3 | 39 | 40 | 41 | 39 |
| Mean (SE) | 57.7 (31.9) | 58.9 (15.4) | 54.6 (13.2) | 53.5 (11.0) | 39.9 (11.3) |
| Min-Max | 0.0 - 110.0 | 0.0 - 390.0 | 0.0 - 329.0 | 0.0 - 298.0 | 0.0 - 366.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 3 | 39 | 40 | 41 | 39 |
| Mean (SE) | 57.7 (31.9) | 60.3 (15.3) | 54.8 (13.2) | 53.5 (11.0) | 48.1 (11.9) |
| Min-Max | 0.0 - 110.0 | 0.0 - 390.0 | 0.0 - 329.0 | 0.0 - 298.0 | 0.0 - 366.0 |

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Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| EYE DISORDERS | | | | | |
| BLINDNESS NEC | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 1 | 1 | 1 | 2 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 1 | 1 | 1 | 2 |
| Mean (SE) | N/A | 266.0 ( N/A) | 0.0 ( N/A) | 0.0 ( N/A) | 368.0 (53.0) |
| Min-Max | N/A | 266.0 - 266.0 | 0.0 - 0.0 | 0.0 - 0.0 | 315.0 - 421.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 0 | 0 | 1 |
| Mean (SE) | N/A | N/A | N/A | N/A | 315.0 ( N/A) |
| Min-Max | N/A | N/A | N/A | N/A | 315.0 - 315.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 1 | 1 | 1 | 2 |
| Mean (SE) | N/A | 266.0 ( N/A) | 0.0 ( N/A) | 0.0 ( N/A) | 368.0 (53.0) |
| Min-Max | N/A | 266.0 - 266.0 | 0.0 - 0.0 | 0.0 - 0.0 | 315.0 - 421.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 1 | 1 | 1 | 2 |
| Mean (SE) | N/A | 266.0 ( N/A) | 0.0 ( N/A) | 0.0 ( N/A) | 368.0 (53.0) |
| Min-Max | N/A | 266.0 - 266.0 | 0.0 - 0.0 | 0.0 - 0.0 | 315.0 - 421.0 |
| BLINDNESS NIGHT | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 0 | 0 | 0 | 1 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 0 | 0 | 1 |
| Mean (SE) | N/A | N/A | N/A | N/A | 27.0 ( N/A) |
| Min-Max | N/A | N/A | N/A | N/A | 27.0 - 27.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 0 | 0 | 0 |

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Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | N/A | N/A | N/A | N/A |
| Min-Max | N/A | N/A | N/A | N/A | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 0 | 0 | 1 |
| Mean (SE) | N/A | N/A | N/A | N/A | 27.0 ( N/A) |
| Min-Max | N/A | N/A | N/A | N/A | 27.0 - 27.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 0 | 0 | 1 |
| Mean (SE) | N/A | N/A | N/A | N/A | 27.0 ( N/A) |
| Min-Max | N/A | N/A | N/A | N/A | 27.0 - 27.0 |
| BLINDNESS TRANSIENT | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 0 | 0 | 1 | 0 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 0 | 1 | 0 |
| Mean (SE) | N/A | N/A | N/A | 49.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | N/A | 49.0 - 49.0 | N/A |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 0 | 1 | 0 |
| Mean (SE) | N/A | N/A | N/A | 49.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | N/A | 49.0 - 49.0 | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 0 | 1 | 0 |
| Mean (SE) | N/A | N/A | N/A | 49.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | N/A | 49.0 - 49.0 | N/A |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 0 | 1 | 0 |
| Mean (SE) | N/A | N/A | N/A | 49.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | N/A | 49.0 - 49.0 | N/A |
| CATARACT CORTICAL | | | | | |

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Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Integrated Summary of Safety

Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 1 | 16 | 3 | 19 | 19 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 1 | 17 | 4 | 21 | 21 |
| Mean (SE) | 42.0 ( N/A) | 209.2 (41.3) | 174.0 (90.2) | 172.6 (49.4) | 246.0 (41.1) |
| Min-Max | 42.0 - 42.0 | 0.0 - 549.0 | 8.0 - 336.0 | 0.0 - 942.0 | 0.0 - 658.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 1 | 7 | 2 | 10 | 11 |
| Mean (SE) | 42.0 ( N/A) | 180.6 (57.6) | 182.0 ( 154) | 173.1 (93.7) | 156.0 (43.8) |
| Min-Max | 42.0 - 42.0 | 0.0 - 455.0 | 28.0 - 336.0 | 17.0 - 942.0 | 9.0 - 469.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 1 | 16 | 3 | 18 | 19 |
| Mean (SE) | 42.0 ( N/A) | 222.3 (41.7) | 222.7 ( 107) | 193.8 (56.2) | 254.7 (45.0) |
| Min-Max | 42.0 - 42.0 | 0.0 - 549.0 | 8.0 - 336.0 | 0.0 - 942.0 | 0.0 - 658.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 1 | 16 | 3 | 18 | 19 |
| Mean (SE) | 42.0 ( N/A) | 222.3 (41.7) | 229.3 ( 101) | 199.0 (55.4) | 269.9 (41.7) |
| Min-Max | 42.0 - 42.0 | 0.0 - 549.0 | 28.0 - 336.0 | 0.0 - 942.0 | 9.0 - 658.0 |
| CATARACT NEC | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 2 | 0 | 2 | 4 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 2 | 0 | 1 | 4 |
| Mean (SE) | N/A | 188.5 ( 142) | N/A | 220.0 ( N/A) | 16.8 (14.2) |
| Min-Max | N/A | 47.0 - 330.0 | N/A | 220.0 - 220.0 | 0.0 - 59.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 2 | 0 | 0 | 4 |
| Mean (SE) | N/A | 188.5 ( 142) | N/A | N/A | 16.8 (14.2) |
| Min-Max | N/A | 47.0 - 330.0 | N/A | N/A | 0.0 - 59.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 2 | 0 | 1 | 4 |

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Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Integrated Summary of Safety

Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | 188.5 ( 142) | N/A | 220.0 ( N/A) | 16.8 (14.2) |
| Min-Max | N/A | 47.0 - 330.0 | N/A | 220.0 - 220.0 | 0.0 - 59.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 2 | 0 | 1 | 4 |
| Mean (SE) | N/A | 188.5 ( 142) | N/A | 220.0 ( N/A) | 16.8 (14.2) |
| Min-Max | N/A | 47.0 - 330.0 | N/A | 220.0 - 220.0 | 0.0 - 59.0 |
| CATARACT NOS AGGRAVATED | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 1 | 3 | 0 | 3 | 1 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 1 | 4 | 0 | 3 | 1 |
| Mean (SE) | 121.0 ( N/A) | 213.3 (84.8) | N/A | 10.3 ( 6.4) | 0.0 ( N/A) |
| Min-Max | 121.0 - 121.0 | 33.0 - 372.0 | N/A | 0.0 - 22.0 | 0.0 - 0.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 1 | 1 | 0 | 2 | 0 |
| Mean (SE) | 121.0 ( N/A) | 105.0 ( N/A) | N/A | 15.5 ( 6.5) | N/A |
| Min-Max | 121.0 - 121.0 | 105.0 - 105.0 | N/A | 9.0 - 22.0 | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 1 | 3 | 0 | 3 | 1 |
| Mean (SE) | 121.0 ( N/A) | 249.3 ( 108) | N/A | 10.3 ( 6.4) | 0.0 ( N/A) |
| Min-Max | 121.0 - 121.0 | 33.0 - 372.0 | N/A | 0.0 - 22.0 | 0.0 - 0.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 1 | 3 | 0 | 3 | 1 |
| Mean (SE) | 121.0 ( N/A) | 249.3 ( 108) | N/A | 10.3 ( 6.4) | 0.0 ( N/A) |
| Min-Max | 121.0 - 121.0 | 33.0 - 372.0 | N/A | 0.0 - 22.0 | 0.0 - 0.0 |
| CATARACT NUCLEAR | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 1 | 16 | 12 | 22 | 10 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 1 | 16 | 14 | 23 | 10 |
| Mean (SE) | 546.0 ( N/A) | 271.5 (34.8) | 216.6 (41.5) | 208.0 (50.8) | 271.7 (58.3) |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Min-Max | 546.0 - 546.0 | 9.0 - 518.0 | 0.0 - 475.0 | 0.0 - 888.0 | 21.0 - 535.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 8 | 6 | 9 | 4 |
| Mean (SE) | N/A | 280.0 (45.0) | 239.0 (52.5) | 167.9 (62.9) | 169.3 ( 121) |
| Min-Max | N/A | 112.0 - 506.0 | 37.0 - 378.0 | 5.0 - 600.0 | 21.0 - 526.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 1 | 16 | 12 | 22 | 10 |
| Mean (SE) | 546.0 ( N/A) | 271.5 (34.8) | 187.3 (42.8) | 210.5 (53.1) | 271.7 (58.3) |
| Min-Max | 546.0 - 546.0 | 9.0 - 518.0 | 0.0 - 475.0 | 0.0 - 888.0 | 21.0 - 535.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 1 | 16 | 12 | 22 | 10 |
| Mean (SE) | 546.0 ( N/A) | 271.5 (34.8) | 252.7 (39.4) | 210.5 (53.1) | 271.7 (58.3) |
| Min-Max | 546.0 - 546.0 | 9.0 - 518.0 | 37.0 - 475.0 | 0.0 - 888.0 | 21.0 - 535.0 |
| CATARACT SUBCAPSULAR | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 11 | 20 | 20 | 17 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 11 | 22 | 23 | 17 |
| Mean (SE) | N/A | 243.7 (34.6) | 233.1 (46.3) | 190.3 (38.9) | 176.5 (23.8) |
| Min-Max | N/A | 57.0 - 456.0 | 0.0 - 821.0 | 0.0 - 656.0 | 0.0 - 342.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 2 | 10 | 11 | 8 |
| Mean (SE) | N/A | 210.5 ( 154) | 205.2 (58.6) | 182.6 (54.2) | 206.9 (31.4) |
| Min-Max | N/A | 57.0 - 364.0 | 18.0 - 553.0 | 2.0 - 656.0 | 105.0 - 342.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 11 | 20 | 20 | 17 |
| Mean (SE) | N/A | 243.7 (34.6) | 236.8 (49.6) | 206.1 (42.5) | 176.5 (23.8) |
| Min-Max | N/A | 57.0 - 456.0 | 0.0 - 821.0 | 0.0 - 656.0 | 0.0 - 342.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 11 | 20 | 20 | 17 |

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Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | 243.7 (34.6) | 236.8 (49.6) | 214.4 (42.1) | 176.5 (23.8) |
| Min-Max | N/A | 57.0 - 456.0 | 0.0 - 821.0 | 0.0 - 656.0 | 0.0 - 342.0 |
| EYE PAIN | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 1 | 57 | 48 | 113 | 128 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 61 | 56 | 135 | 144 |
| Mean (SE) | N/A | 30.4 ( 9.5) | 36.3 ( 8.5) | 27.8 ( 5.1) | 33.0 ( 6.2) |
| Min-Max | N/A | 0.0 - 393.0 | 0.0 - 364.0 | 0.0 - 422.0 | 0.0 - 573.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 58 | 53 | 131 | 138 |
| Mean (SE) | N/A | 18.7 ( 6.5) | 28.0 ( 5.6) | 25.6 ( 4.8) | 31.4 ( 6.5) |
| Min-Max | N/A | 0.0 - 372.0 | 0.0 - 214.0 | 0.0 - 422.0 | 0.0 - 573.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 57 | 48 | 113 | 127 |
| Mean (SE) | N/A | 31.9 (10.1) | 37.5 ( 9.8) | 27.4 ( 5.9) | 35.6 ( 7.0) |
| Min-Max | N/A | 1.0 - 393.0 | 0.0 - 364.0 | 0.0 - 422.0 | 0.0 - 573.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 57 | 48 | 113 | 127 |
| Mean (SE) | N/A | 31.9 (10.1) | 37.8 ( 9.8) | 30.7 ( 6.1) | 35.6 ( 7.0) |
| Min-Max | N/A | 1.0 - 393.0 | 0.0 - 364.0 | 0.0 - 422.0 | 0.0 - 573.0 |
| HYPOPYON | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 0 | 1 | 6 | 21 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 1 | 6 | 21 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 7.8 ( 2.0) | 10.3 ( 3.9) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 85.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 1 | 6 | 21 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 7.8 ( 2.0) | 10.3 ( 3.9) |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 85.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 6 | 21 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 7.8 ( 2.0) | 10.3 ( 3.9) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 85.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 6 | 21 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 7.8 ( 2.0) | 10.3 ( 3.9) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 85.0 |
| INTRAOCULAR PRESSURE INCREASED | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 0 | 2 | 1 | 1 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 2 | 2 | 1 |
| Mean (SE) | N/A | N/A | 73.5 (73.5) | 4.5 ( 0.5) | 0.0 ( N/A) |
| Min-Max | N/A | N/A | 0.0 - 147.0 | 4.0 - 5.0 | 0.0 - 0.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 1 | 2 | 1 |
| Mean (SE) | N/A | N/A | 0.0 ( N/A) | 4.5 ( 0.5) | 0.0 ( N/A) |
| Min-Max | N/A | N/A | 0.0 - 0.0 | 4.0 - 5.0 | 0.0 - 0.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 2 | 1 | 1 |
| Mean (SE) | N/A | N/A | 73.5 (73.5) | 4.0 ( N/A) | 0.0 ( N/A) |
| Min-Max | N/A | N/A | 0.0 - 147.0 | 4.0 - 4.0 | 0.0 - 0.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 2 | 1 | 1 |
| Mean (SE) | N/A | N/A | 73.5 (73.5) | 5.0 ( N/A) | 0.0 ( N/A) |
| Min-Max | N/A | N/A | 0.0 - 147.0 | 5.0 - 5.0 | 0.0 - 0.0 |
| IRITIS | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 1 | 106 | 100 | 202 | 231 |

Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 175 | 182 | 381 | 436 |
| Mean (SE) | N/A | 30.1 ( 4.8) | 34.3 ( 4.6) | 25.1 ( 2.6) | 21.5 ( 1.9) |
| Min-Max | N/A | 0.0 - 587.0 | 0.0 - 458.0 | 0.0 - 595.0 | 0.0 - 367.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 169 | 172 | 371 | 431 |
| Mean (SE) | N/A | 29.6 ( 4.8) | 28.0 ( 3.1) | 22.9 ( 2.1) | 19.4 ( 1.5) |
| Min-Max | N/A | 1.0 - 587.0 | 2.0 - 266.0 | 3.0 - 595.0 | 0.0 - 363.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 106 | 100 | 202 | 231 |
| Mean (SE) | N/A | 24.4 ( 4.0) | 36.9 ( 5.8) | 23.3 ( 3.6) | 19.6 ( 2.6) |
| Min-Max | N/A | 0.0 - 324.0 | 2.0 - 365.0 | 0.0 - 595.0 | 1.0 - 367.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 106 | 100 | 202 | 231 |
| Mean (SE) | N/A | 33.2 ( 7.0) | 44.4 ( 7.7) | 31.6 ( 4.6) | 24.8 ( 2.9) |
| Min-Max | N/A | 3.0 - 587.0 | 2.0 - 458.0 | 0.0 - 595.0 | 1.0 - 367.0 |
| RETINAL DETACHMENT | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 1 | 10 | 12 | 18 | 22 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 1 | 12 | 12 | 21 | 25 |
| Mean (SE) | 4.0 ( N/A) | 58.5 (27.2) | 91.3 (70.8) | 57.2 (19.4) | 94.6 (23.6) |
| Min-Max | 4.0 - 4.0 | 0.0 - 301.0 | 0.0 - 861.0 | 0.0 - 301.0 | 0.0 - 445.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 1 | 11 | 10 | 17 | 14 |
| Mean (SE) | 4.0 ( N/A) | 36.5 (17.4) | 23.5 (13.2) | 19.1 ( 5.3) | 40.8 (10.9) |
| Min-Max | 4.0 - 4.0 | 0.0 - 189.0 | 0.0 - 120.0 | 0.0 - 70.0 | 0.0 - 126.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 1 | 10 | 11 | 18 | 22 |
| Mean (SE) | 4.0 ( N/A) | 70.2 (31.5) | 99.5 (77.1) | 64.9 (22.2) | 94.8 (25.3) |
| Min-Max | 4.0 - 4.0 | 0.0 - 301.0 | 0.0 - 861.0 | 0.0 - 301.0 | 0.0 - 445.0 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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ISTA Pharmaceuticals, Inc.
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Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 1 | 10 | 11 | 18 | 22 |
| Mean (SE) | 4.0 ( N/A) | 70.2 (31.5) | 99.5 (77.1) | 64.9 (22.2) | 102.5 (26.3) |
| Min-Max | 4.0 - 4.0 | 0.0 - 301.0 | 0.0 - 861.0 | 0.0 - 301.0 | 0.0 - 445.0 |
| INFECTIONS AND INFESTATIONS | | | | | |
| HYPOPYON | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 1 | 0 | 0 | 0 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 1 | 0 | 0 | 0 |
| Mean (SE) | N/A | 175.0 ( N/A) | N/A | N/A | N/A |
| Min-Max | N/A | 175.0 - 175.0 | N/A | N/A | N/A |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 1 | 0 | 0 | 0 |
| Mean (SE) | N/A | 175.0 ( N/A) | N/A | N/A | N/A |
| Min-Max | N/A | 175.0 - 175.0 | N/A | N/A | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 1 | 0 | 0 | 0 |
| Mean (SE) | N/A | 175.0 ( N/A) | N/A | N/A | N/A |
| Min-Max | N/A | 175.0 - 175.0 | N/A | N/A | N/A |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 1 | 0 | 0 | 0 |
| Mean (SE) | N/A | 175.0 ( N/A) | N/A | N/A | N/A |
| Min-Max | N/A | 175.0 - 175.0 | N/A | N/A | N/A |
| INVESTIGATIONS | | | | | |
| INTRAOCULAR PRESSURE INCREASED | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 20 | 16 | 18 | 16 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 23 | 19 | 20 | 20 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 28
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | 43.0 (15.2) | 45.4 (14.9) | 30.1 ( 8.1) | 36.4 (18.7) |
| Min-Max | N/A | 0.0 - 303.0 | 0.0 - 240.0 | 0.0 - 132.0 | 0.0 - 366.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 20 | 18 | 16 | 19 |
| Mean (SE) | N/A | 32.5 (10.9) | 45.6 (15.7) | 31.4 ( 9.6) | 38.3 (19.6) |
| Min-Max | N/A | 0.0 - 210.0 | 0.0 - 240.0 | 0.0 - 132.0 | 0.0 - 366.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 20 | 16 | 18 | 16 |
| Mean (SE) | N/A | 44.2 (17.4) | 51.5 (17.3) | 33.1 ( 8.8) | 44.8 (23.0) |
| Min-Max | N/A | 0.0 - 303.0 | 0.0 - 240.0 | 0.0 - 132.0 | 0.0 - 366.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 20 | 16 | 18 | 16 |
| Mean (SE) | N/A | 46.9 (17.3) | 51.5 (17.3) | 33.1 ( 8.8) | 44.8 (23.0) |
| Min-Max | N/A | 0.0 - 303.0 | 0.0 - 240.0 | 0.0 - 132.0 | 0.0 - 366.0 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 29
Duration of Selected Ocular Adverse Events Affecting the Study Eye that Required Medication
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| EYE DISORDERS | | | | | |
| BLINDNESS NEC | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 1 | 1 | 0 | 0 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 1 | 1 | 0 | 0 |
| Mean (SE) | N/A | 0.0 ( N/A) | 257.0 ( N/A) | N/A | N/A |
| Min-Max | N/A | 0.0 - 0.0 | 257.0 - 257.0 | N/A | N/A |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 0 | 0 | 0 |
| Mean (SE) | N/A | N/A | N/A | N/A | N/A |
| Min-Max | N/A | N/A | N/A | N/A | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 1 | 1 | 0 | 0 |
| Mean (SE) | N/A | 0.0 ( N/A) | 257.0 ( N/A) | N/A | N/A |
| Min-Max | N/A | 0.0 - 0.0 | 257.0 - 257.0 | N/A | N/A |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 1 | 1 | 0 | 0 |
| Mean (SE) | N/A | 0.0 ( N/A) | 257.0 ( N/A) | N/A | N/A |
| Min-Max | N/A | 0.0 - 0.0 | 257.0 - 257.0 | N/A | N/A |
| EYE PAIN | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 23 | 21 | 44 | 38 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 28 | 24 | 50 | 40 |
| Mean (SE) | N/A | 24.6 ( 7.6) | 44.6 (20.8) | 41.0 (11.5) | 20.2 ( 4.5) |
| Min-Max | N/A | 0.0 - 191.0 | 0.0 - 462.0 | 0.0 - 380.0 | 0.0 - 141.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 27 | 22 | 47 | 38 |

Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 29
Duration of Selected Ocular Adverse Events Affecting the Study Eye that Required Medication
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | 23.9 ( 7.9) | 40.7 (21.9) | 35.3 (10.9) | 18.2 ( 4.4) |
| Min-Max | N/A | 0.0 - 191.0 | 0.0 - 462.0 | 0.0 - 380.0 | 0.0 - 141.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 23 | 21 | 44 | 36 |
| Mean (SE) | N/A | 27.6 ( 9.2) | 47.9 (23.7) | 42.3 (12.6) | 21.2 ( 4.9) |
| Min-Max | N/A | 0.0 - 191.0 | 0.0 - 462.0 | 0.0 - 380.0 | 0.0 - 141.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 23 | 21 | 44 | 36 |
| Mean (SE) | N/A | 29.0 ( 9.1) | 47.9 (23.7) | 42.9 (12.7) | 21.4 ( 4.9) |
| Min-Max | N/A | 0.0 - 191.0 | 0.0 - 462.0 | 0.0 - 380.0 | 0.0 - 141.0 |
| HYPOPYON | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 0 | 1 | 5 | 16 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 1 | 5 | 16 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 6.6 ( 2.0) | 7.2 ( 1.5) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 28.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 1 | 5 | 16 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 6.6 ( 2.0) | 7.2 ( 1.5) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 28.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 5 | 16 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 6.6 ( 2.0) | 7.2 ( 1.5) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 28.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 5 | 16 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 6.6 ( 2.0) | 7.2 ( 1.5) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 28.0 |
| INTRAOCULAR PRESSURE INCREASED | | | | | |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 29
Duration of Selected Ocular Adverse Events Affecting the Study Eye that Required Medication
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS WITH EVENT | 0 | 2 | 3 | 3 | 3 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 2 | 3 | 4 | 3 |
| Mean (SE) | N/A | 5.5 ( 4.5) | 58.0 (44.7) | 18.8 (11.3) | 16.0 ( 1.5) |
| Min-Max | N/A | 1.0 - 10.0 | 7.0 - 147.0 | 4.0 - 52.0 | 13.0 - 18.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 2 | 2 | 4 | 3 |
| Mean (SE) | N/A | 5.5 ( 4.5) | 13.5 ( 6.5) | 18.8 (11.3) | 16.0 ( 1.5) |
| Min-Max | N/A | 1.0 - 10.0 | 7.0 - 20.0 | 4.0 - 52.0 | 13.0 - 18.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 2 | 3 | 3 | 3 |
| Mean (SE) | N/A | 5.5 ( 4.5) | 58.0 (44.7) | 23.3 (14.6) | 16.0 ( 1.5) |
| Min-Max | N/A | 1.0 - 10.0 | 7.0 - 147.0 | 4.0 - 52.0 | 13.0 - 18.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 2 | 3 | 3 | 3 |
| Mean (SE) | N/A | 5.5 ( 4.5) | 58.0 (44.7) | 23.7 (14.4) | 16.0 ( 1.5) |
| Min-Max | N/A | 1.0 - 10.0 | 7.0 - 147.0 | 5.0 - 52.0 | 13.0 - 18.0 |
| IRITIS | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 1 | 53 | 46 | 129 | 124 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 95 | 80 | 225 | 231 |
| Mean (SE) | N/A | 40.2 (10.0) | 50.8 ( 9.1) | 24.1 ( 3.1) | 19.3 ( 1.8) |
| Min-Max | N/A | 0.0 - 587.0 | 4.0 - 465.0 | 3.0 - 595.0 | 2.0 - 187.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 89 | 78 | 223 | 229 |
| Mean (SE) | N/A | 36.4 (10.2) | 49.9 ( 9.2) | 24.0 ( 3.2) | 18.2 ( 1.6) |
| Min-Max | N/A | 1.0 - 587.0 | 4.0 - 465.0 | 3.0 - 595.0 | 2.0 - 187.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 53 | 46 | 129 | 124 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 29
Duration of Selected Ocular Adverse Events Affecting the Study Eye that Required Medication
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | 39.2 (12.4) | 41.4 ( 8.2) | 24.8 ( 5.0) | 17.0 ( 2.1) |
| Min-Max | N/A | 1.0 - 542.0 | 4.0 - 204.0 | 3.0 - 595.0 | 2.0 - 187.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 53 | 46 | 129 | 124 |
| Mean (SE) | N/A | 51.4 (16.3) | 57.2 (13.3) | 28.1 ( 5.1) | 21.9 ( 2.7) |
| Min-Max | N/A | 1.0 - 587.0 | 4.0 - 465.0 | 3.0 - 595.0 | 2.0 - 187.0 |
| INVESTIGATIONS | | | | | |
| INTRAOCULAR PRESSURE INCREASED | | | | | |
| NUMBER OF PATIENTS WITH EVENT | 3 | 31 | 32 | 34 | 35 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 3 | 34 | 37 | 39 | 48 |
| Mean (SE) | 57.7 (31.9) | 67.3 (17.2) | 45.8 (13.2) | 40.4 ( 9.7) | 34.1 ( 9.1) |
| Min-Max | 0.0 - 110.0 | 0.0 - 390.0 | 0.0 - 329.0 | 0.0 - 298.0 | 0.0 - 366.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 2 | 28 | 34 | 35 | 45 |
| Mean (SE) | 86.5 (23.5) | 60.7 (18.3) | 37.0 (11.6) | 34.6 ( 7.5) | 36.4 ( 9.7) |
| Min-Max | 63.0 - 110.0 | 0.0 - 390.0 | 0.0 - 262.0 | 0.0 - 168.0 | 0.0 - 366.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 3 | 31 | 32 | 33 | 34 |
| Mean (SE) | 57.7 (31.9) | 70.8 (18.7) | 51.4 (15.1) | 46.8 (11.1) | 41.8 (12.3) |
| Min-Max | 0.0 - 110.0 | 0.0 - 390.0 | 0.0 - 329.0 | 0.0 - 298.0 | 0.0 - 366.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 3 | 31 | 32 | 33 | 34 |
| Mean (SE) | 57.7 (31.9) | 72.5 (18.6) | 51.7 (15.1) | 46.8 (11.1) | 46.7 (12.3) |
| Min-Max | 0.0 - 110.0 | 0.0 - 390.0 | 0.0 - 329.0 | 0.0 - 298.0 | 0.0 - 366.0 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 30
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye that Required Medication
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| EYE DISORDERS | | | | | |
| EYE PAIN | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 4 | 5 | 33 | 25 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 4 | 5 | 35 | 26 |
| Mean (SE) | N/A | 21.3 ( 8.7) | 13.4 ( 5.8) | 28.8 (13.1) | 19.4 ( 6.4) |
| Min-Max | N/A | 6.0 - 46.0 | 0.0 - 30.0 | 0.0 - 380.0 | 0.0 - 141.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 4 | 5 | 34 | 25 |
| Mean (SE) | N/A | 21.3 ( 8.7) | 13.4 ( 5.8) | 21.4 (11.2) | 17.6 ( 6.4) |
| Min-Max | N/A | 6.0 - 46.0 | 0.0 - 30.0 | 0.0 - 380.0 | 0.0 - 141.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 4 | 5 | 33 | 24 |
| Mean (SE) | N/A | 21.3 ( 8.7) | 13.4 ( 5.8) | 30.3 (13.9) | 19.7 ( 6.9) |
| Min-Max | N/A | 6.0 - 46.0 | 0.0 - 30.0 | 0.0 - 380.0 | 0.0 - 141.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 4 | 5 | 33 | 24 |
| Mean (SE) | N/A | 21.3 ( 8.7) | 13.4 ( 5.8) | 30.3 (13.9) | 19.7 ( 6.9) |
| Min-Max | N/A | 6.0 - 46.0 | 0.0 - 30.0 | 0.0 - 380.0 | 0.0 - 141.0 |
| HYPOPYON | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 0 | 1 | 5 | 16 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 1 | 5 | 16 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 6.6 ( 2.0) | 7.2 ( 1.5) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 28.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 1 | 5 | 16 |

Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 30
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye that Required Medication
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 6.6 ( 2.0) | 7.2 ( 1.5) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 28.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 5 | 16 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 6.6 ( 2.0) | 7.2 ( 1.5) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 28.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 5 | 16 |
| Mean (SE) | N/A | N/A | 19.0 ( N/A) | 6.6 ( 2.0) | 7.2 ( 1.5) |
| Min-Max | N/A | N/A | 19.0 - 19.0 | 2.0 - 14.0 | 2.0 - 28.0 |
| INTRAOCULAR PRESSURE INCREASED | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 0 | 1 | 1 | 0 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 0 | 1 | 2 | 0 |
| Mean (SE) | N/A | N/A | 147.0 ( N/A) | 4.5 ( 0.5) | N/A |
| Min-Max | N/A | N/A | 147.0 - 147.0 | 4.0 - 5.0 | N/A |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 0 | 0 | 2 | 0 |
| Mean (SE) | N/A | N/A | N/A | 4.5 ( 0.5) | N/A |
| Min-Max | N/A | N/A | N/A | 4.0 - 5.0 | N/A |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 1 | 0 |
| Mean (SE) | N/A | N/A | 147.0 ( N/A) | 4.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | 147.0 - 147.0 | 4.0 - 4.0 | N/A |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 0 | 1 | 1 | 0 |
| Mean (SE) | N/A | N/A | 147.0 ( N/A) | 5.0 ( N/A) | N/A |
| Min-Max | N/A | N/A | 147.0 - 147.0 | 5.0 - 5.0 | N/A |
| IRITIS | | | | | |

Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 30
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye that Required Medication
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 1 | 43 | 31 | 116 | 117 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 76 | 50 | 195 | 210 |
| Mean (SE) | N/A | 32.6 ( 9.8) | 25.6 ( 5.7) | 21.7 ( 3.4) | 18.1 ( 1.8) |
| Min-Max | N/A | 0.0 - 587.0 | 4.0 - 204.0 | 3.0 - 595.0 | 2.0 - 187.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 74 | 50 | 194 | 208 |
| Mean (SE) | N/A | 33.5 (10.1) | 25.6 ( 5.7) | 21.6 ( 3.4) | 16.9 ( 1.6) |
| Min-Max | N/A | 1.0 - 587.0 | 4.0 - 204.0 | 3.0 - 595.0 | 2.0 - 187.0 |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 43 | 31 | 116 | 117 |
| Mean (SE) | N/A | 24.0 ( 8.1) | 26.9 ( 8.4) | 22.5 ( 5.3) | 15.8 ( 2.1) |
| Min-Max | N/A | 1.0 - 324.0 | 4.0 - 204.0 | 3.0 - 595.0 | 2.0 - 187.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 43 | 31 | 116 | 117 |
| Mean (SE) | N/A | 39.0 (15.6) | 26.9 ( 8.4) | 25.6 ( 5.4) | 19.6 ( 2.6) |
| Min-Max | N/A | 1.0 - 587.0 | 4.0 - 204.0 | 3.0 - 595.0 | 2.0 - 187.0 |
| INVESTIGATIONS | | | | | |
| INTRAOCULAR PRESSURE INCREASED | | | | | |
| NUMBER OF PATIENTS WITH RELATED EVENT | 0 | 15 | 12 | 12 | 14 |
| DURATION OF EVENTS (DAYS) [1] | | | | | |
| Number of events | 0 | 17 | 13 | 14 | 17 |
| Mean (SE) | N/A | 51.8 (20.0) | 54.4 (21.0) | 33.5 (11.1) | 41.5 (21.9) |
| Min-Max | N/A | 0.0 - 303.0 | 0.0 - 240.0 | 0.0 - 132.0 | 0.0 - 366.0 |
| DURATION OF EVENTS WITH RESOLVED DATES (DAYS) [2] | | | | | |
| Number of events | 0 | 14 | 13 | 11 | 16 |
| Mean (SE) | N/A | 38.6 (14.9) | 54.4 (21.0) | 36.7 (13.1) | 44.1 (23.1) |
| Min-Max | N/A | 0.0 - 210.0 | 0.0 - 240.0 | 2.0 - 132.0 | 0.0 - 366.0 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 30
Duration of Related Selected Ocular Adverse Events Affecting the Study Eye that Required Medication
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| System Organ Class / Preferred Term | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| DURATION OF MOST SEVERE EVENT (DAYS) [3][5] | | | | | |
| Number of patients | 0 | 15 | 12 | 12 | 14 |
| Mean (SE) | N/A | 53.9 (22.5) | 56.8 (22.6) | 38.5 (12.4) | 49.6 (26.2) |
| Min-Max | N/A | 0.0 - 303.0 | 0.0 - 240.0 | 0.0 - 132.0 | 0.0 - 366.0 |
| DURATION OF LONGEST EVENT (DAYS) [4][5] | | | | | |
| Number of patients | 0 | 15 | 12 | 12 | 14 |
| Mean (SE) | N/A | 57.5 (22.3) | 56.8 (22.6) | 38.5 (12.4) | 49.6 (26.2) |
| Min-Max | N/A | 0.0 - 303.0 | 0.0 - 240.0 | 0.0 - 132.0 | 0.0 - 366.0 |



Note: Table only lists events related to Hypopyon, Retinal Detachment, Iritis, Hyperemia, Recurrent Vitreous Hemorrhage, Eye Pain, Intraocular Pressure Increased, No Light Perception, or Cataract.
[1] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. Each event having the selected preferred term is counted.
[2] Each event having the selected preferred term is counted unless the resolved date is missing.
[3] For each patient the most severe event is used.
[4] For each patient the longest event is used.
[5] The date of the patient's last visit is used for the resolved date of the event when the resolved date is missing. The number of patients may not be equal to the number of patients with the event if the start date is missing.
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Table 31
Incidence of Cataract Affecting the Study Eye
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment and Time Period of Onset
Safety Population

| | Control | | | | |
|---|---|---|---|---|---|
| | WW | Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| NUMBER OF PATIENTS WITH CATARACTS | 9 (50.0%) | 99 (26.2%) | 69 (34.8%) | 91 (24.1%) | 95 (24.3%) |
| DAY 0 to DAY 1 | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 4 ( 1.1%) | 6 ( 1.5%) |
| DAY 2 - DAY 7 | 1 ( 5.6%) | 2 ( 0.5%) | 3 ( 1.5%) | 4 ( 1.1%) | 3 ( 0.8%) |
| DAY 8 - DAY 30 | 1 ( 5.6%) | 9 ( 2.4%) | 4 ( 2.0%) | 13 ( 3.4%) | 6 ( 1.5%) |
| DAY 31 - DAY 60 | 1 ( 5.6%) | 7 ( 1.9%) | 11 ( 5.6%) | 6 ( 1.6%) | 10 ( 2.6%) |
| DAY 61 - DAY 90 | 1 ( 5.6%) | 6 ( 1.6%) | 5 ( 2.5%) | 14 ( 3.7%) | 13 ( 3.3%) |
| DAY 91 - DAY 180 | 1 ( 5.6%) | 30 ( 7.9%) | 19 ( 9.6%) | 14 ( 3.7%) | 20 ( 5.1%) |
| > DAY 180 | 4 (22.2%) | 44 (11.6%) | 26 (13.1%) | 36 ( 9.5%) | 37 ( 9.5%) |



Events are included in the period in which they began.
Cataracts are included when recorded as an adverse event, as a change in lens status from phakia to pseudophakia, or as a procedure indication.

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Table 32.1
Summary of Ocular Symptoms Post-Treatment
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| Symptom | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| NUMBER OF PATIENTS | 18 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| PAIN | 3 (16.7%) | 146 (35.0%) | 140 (42.8%) | 100 (76.9%) | 174 (46.2%) | 366 (60.1%) | 780 (54.1%) | 53 (63.1%) | 11 (52.4%) | 44 (62.9%) |
| BURNING / STINGING | 4 (22.2%) | 119 (28.5%) | 101 (30.9%) | 66 (50.8%) | 125 (33.2%) | 240 (39.4%) | 532 (36.9%) | 37 (44.0%) | 11 (52.4%) | 25 (35.7%) |
| TEARING | 8 (44.4%) | 191 (45.8%) | 177 (54.1%) | 79 (60.8%) | 200 (53.1%) | 374 (61.4%) | 830 (57.5%) | 46 (54.8%) | 8 (38.1%) | 51 (72.9%) |
| ITCHING | 12 (66.7%) | 164 (39.3%) | 163 (49.8%) | 54 (41.5%) | 151 (40.1%) | 277 (45.5%) | 645 (44.7%) | 40 (47.6%) | 9 (42.9%) | 39 (55.7%) |
| FOREIGN BODY SENSATION | 6 (33.3%) | 149 (35.7%) | 149 (45.6%) | 78 (60.0%) | 166 (44.0%) | 290 (47.6%) | 683 (47.3%) | 55 (65.5%) | 13 (61.9%) | 44 (62.9%) |
| PHOTOPHOBIA | 12 (66.7%) | 133 (31.9%) | 166 (50.8%) | 79 (60.8%) | 150 (39.8%) | 315 (51.7%) | 710 (49.2%) | 56 (66.7%) | 11 (52.4%) | 53 (75.7%) |
| PHOTOPSIA | 0 ( 0.0%) | 57 (13.7%) | 59 (18.0%) | 23 (17.7%) | 73 (19.4%) | 119 (19.5%) | 274 (19.0%) | 6 ( 7.1%) | 7 (33.3%) | 6 ( 8.6%) |
| OTHER [2] | 16 (88.9%) | 253 (60.7%) | 173 (52.9%) | 25 (19.2%) | 262 (69.5%) | 316 (51.9%) | 776 (53.8%) | 67 (79.8%) | 13 (61.9%) | 59 (84.3%) |

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Note: One patient in study ACS201-HYA-002A received both 75 IU Vitrase and Saline. This patient is included in both groups here. Twelve patients in the "Probe Study" received two injections of 75 IU Vitrase. These patients are only counted once here.
[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups
[2] Other symptoms include any symptoms recorded in the individual studies not listed here, or those recorded as 'Other (specify)'. For studies VIT-02-08961X and VIT-03-08961X, the 'Other' symptom was floaters. See Table 32.3, for incidence of floaters.

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Table 32.2
Summary of Ocular Symptoms Post-Treatment
All Studies by Study for Vitrase Groups Only
Safety Population

| Symptom | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 68 | 31 | 153 | 225 | 602 | 364 | 84 |
| PAIN | 45 (66.2%) | 24 (77.4%) | 98 (64.1%) | 164 (72.9%) | 304 (50.5%) | 145 (39.8%) | 53 (63.1%) |
| BURNING / STINGING | 38 (55.9%) | 15 (48.4%) | 63 (41.2%) | 97 (43.1%) | 218 (36.2%) | 101 (27.7%) | 37 (44.0%) |
| TEARING | 48 (70.6%) | 26 (83.9%) | 108 (70.6%) | 123 (54.7%) | 379 (63.0%) | 146 (40.1%) | 46 (54.8%) |
| ITCHING | 47 (69.1%) | 7 (22.6%) | 79 (51.6%) | 100 (44.4%) | 303 (50.3%) | 109 (29.9%) | 40 (47.6%) |
| FOREIGN BODY SENSATION | 47 (69.1%) | 12 (38.7%) | 89 (58.2%) | 111 (49.3%) | 306 (50.8%) | 118 (32.4%) | 55 (65.5%) |
| PHOTOPHOBIA | 53 (77.9%) | 10 (32.3%) | 110 (71.9%) | 109 (48.4%) | 320 (53.2%) | 108 (29.7%) | 56 (66.7%) |
| PHOTOPSIA | 20 (29.4%) | 8 (25.8%) | 34 (22.2%) | 21 ( 9.3%) | 140 (23.3%) | 51 (14.0%) | 6 ( 7.1%) |
| OTHER [3] | 30 (44.1%) | 3 ( 9.7%) | 53 (34.6%) | 3 ( 1.3%) | 471 (78.2%) | 216 (59.3%) | 67 (79.8%) |



[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X
[3] Other symptoms include any symptoms recorded in the individual studies not listed here, or those recorded as 'Other (specify)'. For studies VIT-02-08961X and VIT-03-08961X, the 'Other' symptom was floaters. See Table 32.3, for incidence of floaters.

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Table 32.3
Summary of Ocular Symptoms Post-Treatment
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| PAIN | 3 (16.7%) | 128 (33.9%) | 77 (38.9%) | 174 (46.2%) | 198 (50.6%) |
| BURNING / STINGING | 4 (22.2%) | 108 (28.6%) | 62 (31.3%) | 125 (33.2%) | 132 (33.8%) |
| TEARING | 8 (44.4%) | 162 (42.9%) | 107 (54.0%) | 200 (53.1%) | 218 (55.8%) |
| ITCHING | 12 (66.7%) | 153 (40.5%) | 102 (51.5%) | 151 (40.1%) | 159 (40.7%) |
| FOREIGN BODY SENSATION | 6 (33.3%) | 133 (35.2%) | 85 (42.9%) | 166 (44.0%) | 173 (44.2%) |
| PHOTOPHOBIA | 12 (66.7%) | 126 (33.3%) | 104 (52.5%) | 150 (39.8%) | 174 (44.5%) |
| PHOTOPSIA | 0 ( 0.0%) | 55 (14.6%) | 47 (23.7%) | 73 (19.4%) | 71 (18.2%) |
| FLOATERS | 13 (72.2%) | 205 (54.2%) | 128 (64.6%) | 211 (56.0%) | 233 (59.6%) |

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Table 32.4
Summary of Ocular Symptoms Post-Treatment
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| Symptom | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| NUMBER OF PATIENTS | 15 | 15 | 14 | 16 |
| PAIN | 7 (46.7%) | 4 (26.7%) | 9 (64.3%) | 8 (50.0%) |
| BURNING / STINGING | 8 (53.3%) | 4 (26.7%) | 6 (42.9%) | 9 (56.3%) |
| TEARING | 9 (60.0%) | 10 (66.7%) | 6 (42.9%) | 8 (50.0%) |
| ITCHING | 6 (40.0%) | 5 (33.3%) | 6 (42.9%) | 7 (43.8%) |
| FOREIGN BODY SENSATION | 12 (80.0%) | 6 (40.0%) | 8 (57.1%) | 10 (62.5%) |
| PHOTOPHOBIA | 9 (60.0%) | 9 (60.0%) | 10 (71.4%) | 8 (50.0%) |
| PHOTOPSIA | 4 (26.7%) | 4 (26.7%) | 2 (14.3%) | 7 (43.8%) |
| FLOATERS | 11 (73.3%) | 14 (93.3%) | 9 (64.3%) | 9 (56.3%) |

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Table 33
Summary of Ocular Symptoms Maximum Severity Post-Treatment
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom | Max. Severity Post Treatment | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | | 18 | 378 | 198 | 377 | 391 |
| PAIN | MILD | 2 (11.1%) | 103 (27.2%) | 65 (32.8%) | 119 (31.6%) | 135 (34.5%) |
| | MODERATE | 1 ( 5.6%) | 22 ( 5.8%) | 9 ( 4.5%) | 38 (10.1%) | 41 (10.5%) |
| | SEVERE | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 1.5%) | 17 ( 4.5%) | 22 ( 5.6%) |
| BURNING / STINGING | MILD | 4 (22.2%) | 98 (25.9%) | 54 (27.3%) | 93 (24.7%) | 99 (25.3%) |
| | MODERATE | 0 ( 0.0%) | 9 ( 2.4%) | 6 ( 3.0%) | 25 ( 6.6%) | 27 ( 6.9%) |
| | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 7 ( 1.9%) | 6 ( 1.5%) |
| TEARING | MILD | 6 (33.3%) | 125 (33.1%) | 77 (38.9%) | 135 (35.8%) | 139 (35.5%) |
| | MODERATE | 2 (11.1%) | 28 ( 7.4%) | 21 (10.6%) | 46 (12.2%) | 53 (13.6%) |
| | SEVERE | 0 ( 0.0%) | 9 ( 2.4%) | 9 ( 4.5%) | 19 ( 5.0%) | 26 ( 6.6%) |
| ITCHING | MILD | 11 (61.1%) | 129 (34.1%) | 88 (44.4%) | 124 (32.9%) | 122 (31.2%) |
| | MODERATE | 0 ( 0.0%) | 21 ( 5.6%) | 13 ( 6.6%) | 21 ( 5.6%) | 29 ( 7.4%) |
| | SEVERE | 1 ( 5.6%) | 3 ( 0.8%) | 1 ( 0.5%) | 6 ( 1.6%) | 8 ( 2.0%) |
| FOREIGN BODY SENSATION | MILD | 5 (27.8%) | 113 (29.9%) | 58 (29.3%) | 125 (33.2%) | 128 (32.7%) |
| | MODERATE | 0 ( 0.0%) | 17 ( 4.5%) | 21 (10.6%) | 35 ( 9.3%) | 33 ( 8.4%) |
| | SEVERE | 1 ( 5.6%) | 3 ( 0.8%) | 6 ( 3.0%) | 6 ( 1.6%) | 12 ( 3.1%) |
| PHOTOPHOBIA | MILD | 7 (38.9%) | 82 (21.7%) | 61 (30.8%) | 73 (19.4%) | 85 (21.7%) |
| | MODERATE | 2 (11.1%) | 27 ( 7.1%) | 20 (10.1%) | 52 (13.8%) | 51 (13.0%) |
| | SEVERE | 3 (16.7%) | 17 ( 4.5%) | 23 (11.6%) | 25 ( 6.6%) | 38 ( 9.7%) |
| PHOTOPSIA | MILD | 0 ( 0.0%) | 43 (11.4%) | 34 (17.2%) | 52 (13.8%) | 45 (11.5%) |
| | MODERATE | 0 ( 0.0%) | 9 ( 2.4%) | 11 ( 5.6%) | 19 ( 5.0%) | 19 ( 4.9%) |
| | SEVERE | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 2 ( 0.5%) | 7 ( 1.8%) |
| FLOATERS | MILD | 3 (16.7%) | 98 (25.9%) | 55 (27.8%) | 108 (28.6%) | 106 (27.1%) |
| | MODERATE | 5 (27.8%) | 56 (14.8%) | 41 (20.7%) | 53 (14.1%) | 67 (17.1%) |
| | SEVERE | 5 (27.8%) | 51 (13.5%) | 32 (16.2%) | 50 (13.3%) | 60 (15.3%) |

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Table 34
Summary of Ocular Symptoms Maximum Severity Post-Treatment, Stratified by Baseline Severity
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom | Baseline Severity | Max. Severity Post Treatment | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| | | | WW | Saline | | | |
| NUMBER OF PATIENTS | | | 18 | 378 | 198 | 377 | 391 |
| PAIN | NONE | NONE | 15 (83.3%) | 245 (64.8%) | 115 (58.1%) | 195 (51.7%) | 190 (48.6%) |
| | | MILD | 1 ( 5.6%) | 86 (22.8%) | 55 (27.8%) | 109 (28.9%) | 120 (30.7%) |
| | | MODERATE | 1 ( 5.6%) | 15 ( 4.0%) | 6 ( 3.0%) | 29 ( 7.7%) | 33 ( 8.4%) |
| | | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 11 ( 2.9%) | 15 ( 3.8%) |
| | MILD | NONE | 0 ( 0.0%) | 5 ( 1.3%) | 5 ( 2.5%) | 7 ( 1.9%) | 2 ( 0.5%) |
| | | MILD | 1 ( 5.6%) | 16 ( 4.2%) | 8 ( 4.0%) | 8 ( 2.1%) | 15 ( 3.8%) |
| | | MODERATE | 0 ( 0.0%) | 5 ( 1.3%) | 2 ( 1.0%) | 7 ( 1.9%) | 8 ( 2.0%) |
| | | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 4 ( 1.1%) | 5 ( 1.3%) |
| | MODERATE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | SEVERE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| BURNING / STINGING | NONE | NONE | 13 (72.2%) | 264 (69.8%) | 129 (65.2%) | 246 (65.3%) | 253 (64.7%) |
| | | MILD | 3 (16.7%) | 77 (20.4%) | 43 (21.7%) | 78 (20.7%) | 77 (19.7%) |
| | | MODERATE | 0 ( 0.0%) | 7 ( 1.9%) | 5 ( 2.5%) | 18 ( 4.8%) | 22 ( 5.6%) |
| | | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 4 ( 1.1%) | 5 ( 1.3%) |
| | MILD | NONE | 1 ( 5.6%) | 5 ( 1.3%) | 6 ( 3.0%) | 6 ( 1.6%) | 4 ( 1.0%) |
| | | MILD | 1 ( 5.6%) | 17 ( 4.5%) | 10 ( 5.1%) | 15 ( 4.0%) | 22 ( 5.6%) |
| | | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | MODERATE | NONE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 0.8%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 34
Summary of Ocular Symptoms Maximum Severity Post-Treatment, Stratified by Baseline Severity
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
*Safety Population*

| Symptom | Baseline Severity | Max. Severity Post Treatment | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| | | | WW | Saline | | | |
| TEARING | NONE | NONE | 10 (55.6%) | 202 (53.4%) | 86 (43.4%) | 163 (43.2%) | 162 (41.4%) |
| | | MILD | 1 ( 5.6%) | 80 (21.2%) | 46 (23.2%) | 90 (23.9%) | 90 (23.0%) |
| | | MODERATE | 1 ( 5.6%) | 14 ( 3.7%) | 6 ( 3.0%) | 29 ( 7.7%) | 30 ( 7.7%) |
| | | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 5 ( 2.5%) | 8 ( 2.1%) | 14 ( 3.6%) |
| | MILD | NONE | 0 ( 0.0%) | 12 ( 3.2%) | 5 ( 2.5%) | 14 ( 3.7%) | 10 ( 2.6%) |
| | | MILD | 5 (27.8%) | 43 (11.4%) | 29 (14.6%) | 44 (11.7%) | 44 (11.3%) |
| | | MODERATE | 1 ( 5.6%) | 8 ( 2.1%) | 10 ( 5.1%) | 13 ( 3.4%) | 17 ( 4.3%) |
| | | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 1.5%) | 5 ( 1.3%) | 6 ( 1.5%) |
| | MODERATE | NONE | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | | MODERATE | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 2.5%) | 4 ( 1.1%) | 6 ( 1.5%) |
| | | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | SEVERE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 1.0%) |
| ITCHING | NONE | NONE | 6 (33.3%) | 218 (57.7%) | 89 (44.9%) | 218 (57.8%) | 215 (55.0%) |
| | | MILD | 9 (50.0%) | 77 (20.4%) | 62 (31.3%) | 75 (19.9%) | 78 (19.9%) |
| | | MODERATE | 0 ( 0.0%) | 9 ( 2.4%) | 9 ( 4.5%) | 11 ( 2.9%) | 12 ( 3.1%) |
| | | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 3 ( 0.8%) | 3 ( 0.8%) |
| | MILD | NONE | 0 ( 0.0%) | 6 ( 1.6%) | 7 ( 3.5%) | 8 ( 2.1%) | 16 ( 4.1%) |
| | | MILD | 2 (11.1%) | 50 (13.2%) | 23 (11.6%) | 48 (12.7%) | 41 (10.5%) |
| | | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 5 ( 1.3%) | 9 ( 2.3%) |
| | | SEVERE | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | MODERATE | NONE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MILD | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | | MODERATE | 0 ( 0.0%) | 9 ( 2.4%) | 1 ( 0.5%) | 5 ( 1.3%) | 8 ( 2.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | SEVERE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

ISTA Pharmaceuticals, Inc.
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Table 34
Summary of Ocular Symptoms Maximum Severity Post-Treatment, Stratified by Baseline Severity
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom | Baseline Severity | Max. Severity Post Treatment | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| | | | WW | Saline | | | |
| FOREIGN BODY SENSATION | NONE | NONE | 11 (61.1%) | 239 (63.2%) | 109 (55.1%) | 202 (53.6%) | 209 (53.5%) |
| | | MILD | 2 (11.1%) | 85 (22.5%) | 38 (19.2%) | 92 (24.4%) | 99 (25.3%) |
| | | MODERATE | 0 ( 0.0%) | 13 ( 3.4%) | 12 ( 6.1%) | 23 ( 6.1%) | 23 ( 5.9%) |
| | | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 2.0%) | 3 ( 0.8%) | 6 ( 1.5%) |
| | MILD | NONE | 1 ( 5.6%) | 5 ( 1.3%) | 3 ( 1.5%) | 9 ( 2.4%) | 7 ( 1.8%) |
| | | MILD | 3 (16.7%) | 27 ( 7.1%) | 17 ( 8.6%) | 33 ( 8.8%) | 29 ( 7.4%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 3.0%) | 9 ( 2.4%) | 7 ( 1.8%) |
| | | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | MODERATE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 1.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | SEVERE | NONE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | SEVERE | 1 ( 5.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| PHOTOPHOBIA | NONE | NONE | 5 (27.8%) | 242 (64.0%) | 88 (44.4%) | 220 (58.4%) | 209 (53.5%) |
| | | MILD | 3 (16.7%) | 48 (12.7%) | 28 (14.1%) | 39 (10.3%) | 50 (12.8%) |
| | | MODERATE | 1 ( 5.6%) | 12 ( 3.2%) | 6 ( 3.0%) | 22 ( 5.8%) | 28 ( 7.2%) |
| | | SEVERE | 1 ( 5.6%) | 3 ( 0.8%) | 9 ( 4.5%) | 6 ( 1.6%) | 13 ( 3.3%) |
| | MILD | NONE | 0 ( 0.0%) | 8 ( 2.1%) | 4 ( 2.0%) | 6 ( 1.6%) | 5 ( 1.3%) |
| | | MILD | 4 (22.2%) | 29 ( 7.7%) | 27 (13.6%) | 30 ( 8.0%) | 28 ( 7.2%) |
| | | MODERATE | 1 ( 5.6%) | 4 ( 1.1%) | 6 ( 3.0%) | 19 ( 5.0%) | 17 ( 4.3%) |
| | | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 2.0%) | 7 ( 1.9%) | 6 ( 1.5%) |
| | MODERATE | NONE | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MILD | 0 ( 0.0%) | 4 ( 1.1%) | 4 ( 2.0%) | 4 ( 1.1%) | 6 ( 1.5%) |
| | | MODERATE | 0 ( 0.0%) | 9 ( 2.4%) | 7 ( 3.5%) | 10 ( 2.7%) | 3 ( 0.8%) |
| | | SEVERE | 1 ( 5.6%) | 3 ( 0.8%) | 0 ( 0.0%) | 5 ( 1.3%) | 5 ( 1.3%) |
| | SEVERE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | | SEVERE | 1 ( 5.6%) | 9 ( 2.4%) | 10 ( 5.1%) | 7 ( 1.9%) | 14 ( 3.6%) |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 34
Summary of Ocular Symptoms Maximum Severity Post-Treatment, Stratified by Baseline Severity
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom | Baseline Severity | Max. Severity Post Treatment | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| | | | WW | Saline | | | |
| PHOTOPSIA | NONE | NONE | 6 (33.3%) | 291 (77.0%) | 115 (58.1%) | 272 (72.1%) | 274 (70.1%) |
| | | MILD | 0 ( 0.0%) | 27 ( 7.1%) | 18 ( 9.1%) | 34 ( 9.0%) | 31 ( 7.9%) |
| | | MODERATE | 0 ( 0.0%) | 4 ( 1.1%) | 8 ( 4.0%) | 11 ( 2.9%) | 13 ( 3.3%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 1 ( 0.3%) | 5 ( 1.3%) |
| | MILD | NONE | 0 ( 0.0%) | 8 ( 2.1%) | 2 ( 1.0%) | 2 ( 0.5%) | 6 ( 1.5%) |
| | | MILD | 0 ( 0.0%) | 13 ( 3.4%) | 9 ( 4.5%) | 7 ( 1.9%) | 10 ( 2.6%) |
| | | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MODERATE | NONE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MODERATE | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| FLOATERS | NONE | NONE | 4 (22.2%) | 162 (42.9%) | 64 (32.3%) | 155 (41.1%) | 148 (37.9%) |
| | | MILD | 3 (16.7%) | 36 ( 9.5%) | 31 (15.7%) | 60 (15.9%) | 55 (14.1%) |
| | | MODERATE | 0 ( 0.0%) | 18 ( 4.8%) | 11 ( 5.6%) | 11 ( 2.9%) | 20 ( 5.1%) |
| | | SEVERE | 2 (11.1%) | 3 ( 0.8%) | 8 ( 4.0%) | 8 ( 2.1%) | 12 ( 3.1%) |
| | MILD | NONE | 1 ( 5.6%) | 7 ( 1.9%) | 2 ( 1.0%) | 6 ( 1.6%) | 8 ( 2.0%) |
| | | MILD | 0 ( 0.0%) | 49 (13.0%) | 20 (10.1%) | 43 (11.4%) | 38 ( 9.7%) |
| | | MODERATE | 0 ( 0.0%) | 4 ( 1.1%) | 7 ( 3.5%) | 7 ( 1.9%) | 8 ( 2.0%) |
| | | SEVERE | 0 ( 0.0%) | 5 ( 1.3%) | 1 ( 0.5%) | 4 ( 1.1%) | 4 ( 1.0%) |
| | MODERATE | NONE | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 2.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | | MILD | 0 ( 0.0%) | 10 ( 2.6%) | 4 ( 2.0%) | 3 ( 0.8%) | 10 ( 2.6%) |
| | | MODERATE | 4 (22.2%) | 28 ( 7.4%) | 16 ( 8.1%) | 27 ( 7.2%) | 36 ( 9.2%) |
| | | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 2.5%) | 7 ( 1.9%) | 4 ( 1.0%) |
| | SEVERE | NONE | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| | | MODERATE | 1 ( 5.6%) | 6 ( 1.6%) | 6 ( 3.0%) | 8 ( 2.1%) | 3 ( 0.8%) |
| | | SEVERE | 3 (16.7%) | 39 (10.3%) | 18 ( 9.1%) | 31 ( 8.2%) | 40 (10.2%) |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 35
Summary of Ocular Symptoms Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom [1] | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| | | NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| PAIN | DAY 1 | DECREASE | 0 ( 0.0%) | 12 ( 3.2%) | 10 ( 5.1%) | 11 ( 2.9%) | 5 ( 1.3%) |
| | | NO CHANGE | 17 (94.4%) | 287 (75.9%) | 147 (74.2%) | 233 (61.8%) | 235 (60.1%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 67 (17.7%) | 35 (17.7%) | 95 (25.2%) | 108 (27.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 7 ( 1.9%) | 1 ( 0.5%) | 24 ( 6.4%) | 27 ( 6.9%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 8 ( 2.1%) | 10 ( 2.6%) |
| | WEEK 1 | DECREASE | 0 ( 0.0%) | 21 ( 5.6%) | 12 ( 6.1%) | 22 ( 5.8%) | 22 ( 5.6%) |
| | | NO CHANGE | 17 (94.4%) | 327 (86.5%) | 162 (81.8%) | 309 (82.0%) | 327 (83.6%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 14 ( 3.7%) | 13 ( 6.6%) | 25 ( 6.6%) | 21 ( 5.4%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 5 ( 1.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MONTH 1 | DECREASE | 0 ( 0.0%) | 21 ( 5.6%) | 13 ( 6.6%) | 23 ( 6.1%) | 19 ( 4.9%) |
| | | NO CHANGE | 14 (77.8%) | 301 (79.6%) | 145 (73.2%) | 286 (75.9%) | 300 (76.7%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 12 ( 3.2%) | 4 ( 2.0%) | 7 ( 1.9%) | 18 ( 4.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 2 | DECREASE | 1 ( 5.6%) | 16 ( 4.2%) | 11 ( 5.6%) | 19 ( 5.0%) | 19 ( 4.9%) |
| | | NO CHANGE | 12 (66.7%) | 256 (67.7%) | 121 (61.1%) | 246 (65.3%) | 239 (61.1%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 8 ( 2.1%) | 9 ( 4.5%) | 6 ( 1.6%) | 13 ( 3.3%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | MONTH 3 | DECREASE | 1 ( 5.6%) | 22 ( 5.8%) | 15 ( 7.6%) | 25 ( 6.6%) | 26 ( 6.6%) |
| | | NO CHANGE | 12 (66.7%) | 314 (83.1%) | 154 (77.8%) | 307 (81.4%) | 317 (81.1%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 15 ( 4.0%) | 7 ( 3.5%) | 9 ( 2.4%) | 15 ( 3.8%) |
| | | INCREASE BY 2 | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.3%) |



[1] Symptoms were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 35
Summary of Ocular Symptoms Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom [1] | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| BURNING / STINGING | DAY 1 | DECREASE | 1 ( 5.6%) | 16 ( 4.2%) | 9 ( 4.5%) | 13 ( 3.4%) | 14 ( 3.6%) |
| | | NO CHANGE | 16 (88.9%) | 305 (80.7%) | 153 (77.3%) | 295 (78.2%) | 303 (77.5%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 46 (12.2%) | 27 (13.6%) | 48 (12.7%) | 53 (13.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 2.0%) | 12 ( 3.2%) | 12 ( 3.1%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 3 ( 0.8%) |
| | WEEK 1 | DECREASE | 1 ( 5.6%) | 22 ( 5.8%) | 14 ( 7.1%) | 22 ( 5.8%) | 20 ( 5.1%) |
| | | NO CHANGE | 15 (83.3%) | 326 (86.2%) | 167 (84.3%) | 319 (84.6%) | 332 (84.9%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 15 ( 4.0%) | 7 ( 3.5%) | 15 ( 4.0%) | 22 ( 5.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 1 | DECREASE | 1 ( 5.6%) | 22 ( 5.8%) | 17 ( 8.6%) | 23 ( 6.1%) | 19 ( 4.9%) |
| | | NO CHANGE | 13 (72.2%) | 298 (78.8%) | 144 (72.7%) | 278 (73.7%) | 302 (77.2%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 13 ( 3.4%) | 2 ( 1.0%) | 14 ( 3.7%) | 17 ( 4.3%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 2 | DECREASE | 2 (11.1%) | 20 ( 5.3%) | 10 ( 5.1%) | 17 ( 4.5%) | 17 ( 4.3%) |
| | | NO CHANGE | 11 (61.1%) | 249 (65.9%) | 129 (65.2%) | 251 (66.6%) | 244 (62.4%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 13 ( 3.4%) | 3 ( 1.5%) | 6 ( 1.6%) | 9 ( 2.3%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 3 | DECREASE | 2 (11.1%) | 22 ( 5.8%) | 14 ( 7.1%) | 22 ( 5.8%) | 20 ( 5.1%) |
| | | NO CHANGE | 11 (61.1%) | 312 (82.5%) | 155 (78.3%) | 310 (82.2%) | 321 (82.1%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 16 ( 4.2%) | 8 ( 4.0%) | 11 ( 2.9%) | 15 ( 3.8%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |



[1] Symptoms were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 35
Summary of Ocular Symptoms Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom [1] | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| TEARING | DAY 1 | DECREASE | 1 ( 5.6%) | 37 ( 9.8%) | 15 ( 7.6%) | 29 ( 7.7%) | 31 ( 7.9%) |
| | | NO CHANGE | 15 (83.3%) | 284 (75.1%) | 149 (75.3%) | 244 (64.7%) | 251 (64.2%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 44 (11.6%) | 27 (13.6%) | 67 (17.8%) | 70 (17.9%) |
| | | INCREASE BY 2 | 1 ( 5.6%) | 8 ( 2.1%) | 2 ( 1.0%) | 24 ( 6.4%) | 24 ( 6.1%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 7 ( 1.9%) | 9 ( 2.3%) |
| | WEEK 1 | DECREASE | 2 (11.1%) | 44 (11.6%) | 33 (16.7%) | 48 (12.7%) | 45 (11.5%) |
| | | NO CHANGE | 14 (77.8%) | 293 (77.5%) | 144 (72.7%) | 283 (75.1%) | 296 (75.7%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 26 ( 6.9%) | 8 ( 4.0%) | 23 ( 6.1%) | 31 ( 7.9%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | MONTH 1 | DECREASE | 1 ( 5.6%) | 42 (11.1%) | 27 (13.6%) | 42 (11.1%) | 45 (11.5%) |
| | | NO CHANGE | 12 (66.7%) | 268 (70.9%) | 124 (62.6%) | 254 (67.4%) | 258 (66.0%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 20 ( 5.3%) | 11 ( 5.6%) | 20 ( 5.3%) | 29 ( 7.4%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 4 ( 1.1%) | 1 ( 0.5%) | 3 ( 0.8%) | 6 ( 1.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MONTH 2 | DECREASE | 2 (11.1%) | 36 ( 9.5%) | 23 (11.6%) | 42 (11.1%) | 41 (10.5%) |
| | | NO CHANGE | 10 (55.6%) | 223 (59.0%) | 112 (56.6%) | 213 (56.5%) | 207 (52.9%) |
| | | INCREASE BY 1 | 2 (11.1%) | 19 ( 5.0%) | 6 ( 3.0%) | 17 ( 4.5%) | 21 ( 5.4%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MONTH 3 | DECREASE | 1 ( 5.6%) | 52 (13.8%) | 24 (12.1%) | 54 (14.3%) | 57 (14.6%) |
| | | NO CHANGE | 11 (61.1%) | 274 (72.5%) | 141 (71.2%) | 270 (71.6%) | 276 (70.6%) |
| | | INCREASE BY 1 | 2 (11.1%) | 23 ( 6.1%) | 9 ( 4.5%) | 17 ( 4.5%) | 24 ( 6.1%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 3 ( 0.8%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |



[1] Symptoms were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 35
Summary of Ocular Symptoms Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom [1] | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| ITCHING | DAY 1 | DECREASE | 1 ( 5.6%) | 30 ( 7.9%) | 21 (10.6%) | 37 ( 9.8%) | 42 (10.7%) |
| | | NO CHANGE | 15 (83.3%) | 304 (80.4%) | 149 (75.3%) | 294 (78.0%) | 308 (78.8%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 38 (10.1%) | 22 (11.1%) | 34 ( 9.0%) | 32 ( 8.2%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.3%) |
| | WEEK 1 | DECREASE | 1 ( 5.6%) | 39 (10.3%) | 20 (10.1%) | 37 ( 9.8%) | 44 (11.3%) |
| | | NO CHANGE | 15 (83.3%) | 297 (78.6%) | 150 (75.8%) | 295 (78.2%) | 297 (76.0%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 22 ( 5.8%) | 17 ( 8.6%) | 24 ( 6.4%) | 34 ( 8.7%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 5 ( 1.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 1 | DECREASE | 1 ( 5.6%) | 36 ( 9.5%) | 20 (10.1%) | 34 ( 9.0%) | 42 (10.7%) |
| | | NO CHANGE | 12 (66.7%) | 273 (72.2%) | 129 (65.2%) | 268 (71.1%) | 275 (70.3%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 24 ( 6.3%) | 12 ( 6.1%) | 17 ( 4.5%) | 20 ( 5.1%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MONTH 2 | DECREASE | 1 ( 5.6%) | 40 (10.6%) | 15 ( 7.6%) | 27 ( 7.2%) | 36 ( 9.2%) |
| | | NO CHANGE | 10 (55.6%) | 216 (57.1%) | 108 (54.5%) | 227 (60.2%) | 218 (55.8%) |
| | | INCREASE BY 1 | 3 (16.7%) | 25 ( 6.6%) | 18 ( 9.1%) | 19 ( 5.0%) | 16 ( 4.1%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 4 ( 1.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 3 | DECREASE | 2 (11.1%) | 47 (12.4%) | 23 (11.6%) | 35 ( 9.3%) | 53 (13.6%) |
| | | NO CHANGE | 6 (33.3%) | 283 (74.9%) | 138 (69.7%) | 290 (76.9%) | 279 (71.4%) |
| | | INCREASE BY 1 | 5 (27.8%) | 18 ( 4.8%) | 14 ( 7.1%) | 18 ( 4.8%) | 27 ( 6.9%) |
| | | INCREASE BY 2 | 1 ( 5.6%) | 3 ( 0.8%) | 2 ( 1.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |



[1] Symptoms were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 35
Summary of Ocular Symptoms Change from Baseline at Specified Visits
*Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X* by Treatment
Safety Population

| Symptom [1] | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| FOREIGN BODY SENSATION | DAY 1 | DECREASE | 2 (11.1%) | 14 ( 3.7%) | 10 ( 5.1%) | 14 ( 3.7%) | 17 ( 4.3%) |
| | | NO CHANGE | 15 (83.3%) | 293 (77.5%) | 148 (74.7%) | 261 (69.2%) | 273 (69.8%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 55 (14.6%) | 27 (13.6%) | 78 (20.7%) | 74 (18.9%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 10 ( 2.6%) | 6 ( 3.0%) | 16 ( 4.2%) | 17 ( 4.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 2 ( 0.5%) | 4 ( 1.0%) |
| | WEEK 1 | DECREASE | 2 (11.1%) | 21 ( 5.6%) | 21 (10.6%) | 33 ( 8.8%) | 24 ( 6.1%) |
| | | NO CHANGE | 15 (83.3%) | 319 (84.4%) | 157 (79.3%) | 293 (77.7%) | 315 (80.6%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 22 ( 5.8%) | 8 ( 4.0%) | 28 ( 7.4%) | 33 ( 8.4%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 4 ( 1.1%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 0.5%) |
| | MONTH 1 | DECREASE | 3 (16.7%) | 19 ( 5.0%) | 21 (10.6%) | 35 ( 9.3%) | 27 ( 6.9%) |
| | | NO CHANGE | 10 (55.6%) | 290 (76.7%) | 132 (66.7%) | 261 (69.2%) | 289 (73.9%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 24 ( 6.3%) | 8 ( 4.0%) | 21 ( 5.6%) | 20 ( 5.1%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 2 ( 0.5%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 2 | DECREASE | 4 (22.2%) | 21 ( 5.6%) | 14 ( 7.1%) | 29 ( 7.7%) | 22 ( 5.6%) |
| | | NO CHANGE | 9 (50.0%) | 244 (64.6%) | 122 (61.6%) | 233 (61.8%) | 235 (60.1%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 14 ( 3.7%) | 6 ( 3.0%) | 13 ( 3.4%) | 14 ( 3.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 3 | DECREASE | 4 (22.2%) | 28 ( 7.4%) | 23 (11.6%) | 37 ( 9.8%) | 37 ( 9.5%) |
| | | NO CHANGE | 10 (55.6%) | 307 (81.2%) | 143 (72.2%) | 292 (77.5%) | 295 (75.4%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 15 ( 4.0%) | 8 ( 4.0%) | 14 ( 3.7%) | 28 ( 7.2%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 2 ( 0.5%) | 1 ( 0.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) |



[1] Symptoms were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 35
Summary of Ocular Symptoms Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom [1] | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| PHOTOPHOBIA | DAY 1 | DECREASE | 2 (11.1%) | 30 ( 7.9%) | 28 (14.1%) | 26 ( 6.9%) | 33 ( 8.4%) |
| | | NO CHANGE | 11 (61.1%) | 321 (84.9%) | 151 (76.3%) | 299 (79.3%) | 286 (73.1%) |
| | | INCREASE BY 1 | 2 (11.1%) | 20 ( 5.3%) | 10 ( 5.1%) | 32 ( 8.5%) | 39 (10.0%) |
| | | INCREASE BY 2 | 1 ( 5.6%) | 2 ( 0.5%) | 1 ( 0.5%) | 11 ( 2.9%) | 17 ( 4.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 3 ( 0.8%) | 7 ( 1.8%) |
| | WEEK 1 | DECREASE | 3 (16.7%) | 29 ( 7.7%) | 28 (14.1%) | 42 (11.1%) | 31 ( 7.9%) |
| | | NO CHANGE | 11 (61.1%) | 310 (82.0%) | 147 (74.2%) | 279 (74.0%) | 304 (77.7%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 24 ( 6.3%) | 9 ( 4.5%) | 35 ( 9.3%) | 31 ( 7.9%) |
| | | INCREASE BY 2 | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 2 ( 0.5%) | 5 ( 1.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MONTH 1 | DECREASE | 3 (16.7%) | 30 ( 7.9%) | 30 (15.2%) | 41 (10.9%) | 35 ( 9.0%) |
| | | NO CHANGE | 10 (55.6%) | 277 (73.3%) | 112 (56.6%) | 253 (67.1%) | 275 (70.3%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 20 ( 5.3%) | 15 ( 7.6%) | 17 ( 4.5%) | 22 ( 5.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 1.5%) | 7 ( 1.9%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 3 ( 0.8%) | 1 ( 0.5%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | MONTH 2 | DECREASE | 3 (16.7%) | 33 ( 8.7%) | 25 (12.6%) | 40 (10.6%) | 30 ( 7.7%) |
| | | NO CHANGE | 8 (44.4%) | 220 (58.2%) | 99 (50.0%) | 217 (57.6%) | 218 (55.8%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 23 ( 6.1%) | 13 ( 6.6%) | 13 ( 3.4%) | 15 ( 3.8%) |
| | | INCREASE BY 2 | 1 ( 5.6%) | 4 ( 1.1%) | 2 ( 1.0%) | 3 ( 0.8%) | 6 ( 1.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| | MONTH 3 | DECREASE | 3 (16.7%) | 44 (11.6%) | 30 (15.2%) | 52 (13.8%) | 53 (13.6%) |
| | | NO CHANGE | 10 (55.6%) | 288 (76.2%) | 121 (61.1%) | 266 (70.6%) | 280 (71.6%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 16 ( 4.2%) | 17 ( 8.6%) | 18 ( 4.8%) | 20 ( 5.1%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 4 ( 1.1%) | 5 ( 2.5%) | 5 ( 1.3%) | 6 ( 1.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 3 ( 0.8%) | 0 ( 0.0%) |



[1] Symptoms were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 35
Summary of Ocular Symptoms Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom [1] | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| PHOTOPSIA | DAY 1 | DECREASE | 0 ( 0.0%) | 15 ( 4.0%) | 5 ( 2.5%) | 7 ( 1.9%) | 12 ( 3.1%) |
| | | NO CHANGE | 5 (27.8%) | 323 (85.4%) | 142 (71.7%) | 313 (83.0%) | 313 (80.1%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 3 ( 0.8%) | 5 ( 2.5%) | 8 ( 2.1%) | 8 ( 2.0%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| | WEEK 1 | DECREASE | 0 ( 0.0%) | 20 ( 5.3%) | 9 ( 4.5%) | 6 ( 1.6%) | 11 ( 2.8%) |
| | | NO CHANGE | 5 (27.8%) | 305 (80.7%) | 134 (67.7%) | 297 (78.8%) | 302 (77.2%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 9 ( 2.4%) | 6 ( 3.0%) | 11 ( 2.9%) | 10 ( 2.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 3 ( 0.8%) | 4 ( 1.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 1 | DECREASE | 0 ( 0.0%) | 15 ( 4.0%) | 8 ( 4.0%) | 8 ( 2.1%) | 11 ( 2.8%) |
| | | NO CHANGE | 3 (16.7%) | 289 (76.5%) | 117 (59.1%) | 264 (70.0%) | 274 (70.1%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 2.0%) | 14 ( 3.7%) | 13 ( 3.3%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 1.3%) | 4 ( 1.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 2 | DECREASE | 0 ( 0.0%) | 11 ( 2.9%) | 5 ( 2.5%) | 8 ( 2.1%) | 12 ( 3.1%) |
| | | NO CHANGE | 4 (22.2%) | 242 (64.0%) | 101 (51.0%) | 226 (59.9%) | 225 (57.5%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 6 ( 1.6%) | 7 ( 3.5%) | 11 ( 2.9%) | 6 ( 1.5%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MONTH 3 | DECREASE | 0 ( 0.0%) | 19 ( 5.0%) | 10 ( 5.1%) | 12 ( 3.2%) | 14 ( 3.6%) |
| | | NO CHANGE | 3 (16.7%) | 296 (78.3%) | 125 (63.1%) | 283 (75.1%) | 290 (74.2%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 8 ( 2.1%) | 8 ( 4.0%) | 10 ( 2.7%) | 10 ( 2.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 0 ( 0.0%) | 4 ( 1.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |



[1] Symptoms were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 35
Summary of Ocular Symptoms Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Symptom [1] | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| FLOATERS | DAY 1 | DECREASE | 5 (27.8%) | 56 (14.8%) | 25 (12.6%) | 40 (10.6%) | 45 (11.5%) |
| | | NO CHANGE | 11 (61.1%) | 306 (81.0%) | 147 (74.2%) | 306 (81.2%) | 301 (77.0%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 9 ( 2.4%) | 14 ( 7.1%) | 21 ( 5.6%) | 28 ( 7.2%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 4 ( 1.1%) | 6 ( 1.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 2.5%) | 0 ( 0.0%) | 5 ( 1.3%) |
| | WEEK 1 | DECREASE | 5 (27.8%) | 60 (15.9%) | 45 (22.7%) | 68 (18.0%) | 67 (17.1%) |
| | | NO CHANGE | 11 (61.1%) | 277 (73.3%) | 120 (60.6%) | 255 (67.6%) | 268 (68.5%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 20 ( 5.3%) | 17 ( 8.6%) | 27 ( 7.2%) | 30 ( 7.7%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 7 ( 1.9%) | 3 ( 1.5%) | 6 ( 1.6%) | 7 ( 1.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| | MONTH 1 | DECREASE | 6 (33.3%) | 76 (20.1%) | 35 (17.7%) | 68 (18.0%) | 72 (18.4%) |
| | | NO CHANGE | 7 (38.9%) | 234 (61.9%) | 95 (48.0%) | 213 (56.5%) | 220 (56.3%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 20 ( 5.3%) | 23 (11.6%) | 29 ( 7.7%) | 34 ( 8.7%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 3 ( 0.8%) | 7 ( 3.5%) | 7 ( 1.9%) | 13 ( 3.3%) |
| | | INCREASE BY 3 | 1 ( 5.6%) | 1 ( 0.3%) | 3 ( 1.5%) | 2 ( 0.5%) | 0 ( 0.0%) |
| | MONTH 2 | DECREASE | 4 (22.2%) | 72 (19.0%) | 37 (18.7%) | 65 (17.2%) | 58 (14.8%) |
| | | NO CHANGE | 8 (44.4%) | 191 (50.5%) | 80 (40.4%) | 172 (45.6%) | 187 (47.8%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 17 ( 4.5%) | 23 (11.6%) | 30 ( 8.0%) | 21 ( 5.4%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 5 ( 1.3%) | 8 ( 2.0%) |
| | | INCREASE BY 3 | 1 ( 5.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) |
| | MONTH 3 | DECREASE | 7 (38.9%) | 95 (25.1%) | 52 (26.3%) | 81 (21.5%) | 91 (23.3%) |
| | | NO CHANGE | 7 (38.9%) | 229 (60.6%) | 104 (52.5%) | 220 (58.4%) | 232 (59.3%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 19 ( 5.0%) | 15 ( 7.6%) | 35 ( 9.3%) | 29 ( 7.4%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 7 ( 1.9%) | 3 ( 1.5%) | 6 ( 1.6%) | 7 ( 1.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 3 ( 0.8%) | 2 ( 0.5%) |



[1] Symptoms were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 36.1
Summary of Anterior Chamber Signs Post-Treatment
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| Sign | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| NUMBER OF PATIENTS | 18 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| CELLS | 4 (22.2%) | 139 (33.3%) | 198 (60.6%) | 118 (90.8%) | 229 (60.7%) | 449 (73.7%) | 994 (68.9%) | 39 (46.4%) | 3 (14.3%) | 29 (41.4%) |
| FLARE | 4 (22.2%) | 119 (28.5%) | 176 (53.8%) | 103 (79.2%) | 184 (48.8%) | 361 (59.3%) | 824 (57.1%) | 30 (35.7%) | 4 (19.0%) | 24 (34.3%) |

337

[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
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Table 36.2
Summary of Anterior Chamber Signs Post-Treatment
All Studies by Study for Vitrase Groups Only
*Safety Population*

| Sign | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 68 | 31 | 153 | 225 | 602 | 364 | 84 |
| CELLS | 45 (66.2%) | 31 ( 100%) | 144 (94.1%) | 186 (82.7%) | 412 (68.4%) | 176 (48.4%) | 39 (46.4%) |
| FLARE | 45 (66.2%) | 28 (90.3%) | 136 (88.9%) | 143 (63.6%) | 352 (58.5%) | 120 (33.0%) | 30 (35.7%) |



[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 36.3
Summary of Anterior Chamber Signs Post-Treatment
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Sign | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| CELLS | 4 (22.2%) | 110 (29.1%) | 101 (51.0%) | 229 (60.7%) | 258 (66.0%) |
| FLARE | 4 (22.2%) | 110 (29.1%) | 93 (47.0%) | 184 (48.8%) | 195 (49.9%) |

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Table 36.4
Summary of Anterior Chamber Signs Post-Treatment
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| Sign | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| NUMBER OF PATIENTS | 15 | 15 | 14 | 16 |
| CELLS | 8 (53.3%) | 3 (20.0%) | 9 (64.3%) | 2 (12.5%) |
| FLARE | 12 (80.0%) | 6 (40.0%) | 11 (78.6%) | 4 (25.0%) |

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Table 37
Summary of Anterior Chamber Signs Maximum Severity Post-Treatment
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Sign | Max. Severity Post Treatment | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| NUMBER OF PATIENTS | | 18 | 378 | 198 | 377 | 391 |
| CELLS | MILD | 4 (22.2%) | 76 (20.1%) | 71 (35.9%) | 104 (27.6%) | 95 (24.3%) |
| | MODERATE | 0 ( 0.0%) | 23 ( 6.1%) | 21 (10.6%) | 78 (20.7%) | 100 (25.6%) |
| | SEVERE | 0 ( 0.0%) | 10 ( 2.6%) | 8 ( 4.0%) | 42 (11.1%) | 41 (10.5%) |
| | HYPOPYON | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 5 ( 1.3%) | 22 ( 5.6%) |
| FLARE | MILD | 3 (16.7%) | 90 (23.8%) | 71 (35.9%) | 121 (32.1%) | 112 (28.6%) |
| | MODERATE | 1 ( 5.6%) | 16 ( 4.2%) | 16 ( 8.1%) | 46 (12.2%) | 53 (13.6%) |
| | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 6 ( 3.0%) | 17 ( 4.5%) | 29 ( 7.4%) |
| | HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |

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Table 38
Summary of Anterior Chamber Signs Maximum Severity Post-Treatment Stratified by Baseline Severity
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Sign | Baseline Severity | Max. Severity Post Treatment | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | | | 18 | 378 | 198 | 377 | 391 |
| CELLS | NONE | NONE | 13 (72.2%) | 267 (70.6%) | 96 (48.5%) | 148 (39.3%) | 132 (33.8%) |
| | | MILD | 4 (22.2%) | 72 (19.0%) | 68 (34.3%) | 97 (25.7%) | 90 (23.0%) |
| | | MODERATE | 0 ( 0.0%) | 18 ( 4.8%) | 20 (10.1%) | 75 (19.9%) | 91 (23.3%) |
| | | SEVERE | 0 ( 0.0%) | 8 ( 2.1%) | 8 ( 4.0%) | 41 (10.9%) | 37 ( 9.5%) |
| | | HYPOPYON | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 5 ( 1.3%) | 21 ( 5.4%) |
| | MILD | NONE | 1 ( 5.6%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | MILD | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 1.5%) | 7 ( 1.9%) | 5 ( 1.3%) |
| | | MODERATE | 0 ( 0.0%) | 5 ( 1.3%) | 1 ( 0.5%) | 3 ( 0.8%) | 9 ( 2.3%) |
| | | SEVERE | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 4 ( 1.0%) |
| | | HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | SEVERE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

ISTA Pharmaceuticals, Inc.
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Table 38
Summary of Anterior Chamber Signs Maximum Severity Post-Treatment Stratified by Baseline Severity
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Sign | Baseline Severity | Max. Severity Post Treatment | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| | | | WW | Saline | | | |
| FLARE | NONE | NONE | 12 (66.7%) | 267 (70.6%) | 104 (52.5%) | 193 (51.2%) | 196 (50.1%) |
| | | MILD | 3 (16.7%) | 84 (22.2%) | 68 (34.3%) | 118 (31.3%) | 103 (26.3%) |
| | | MODERATE | 1 ( 5.6%) | 13 ( 3.4%) | 16 ( 8.1%) | 43 (11.4%) | 48 (12.3%) |
| | | SEVERE | 0 ( 0.0%) | 4 ( 1.1%) | 6 ( 3.0%) | 16 ( 4.2%) | 27 ( 6.9%) |
| | | HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MILD | NONE | 2 (11.1%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 6 ( 1.6%) | 3 ( 1.5%) | 3 ( 0.8%) | 9 ( 2.3%) |
| | | MODERATE | 0 ( 0.0%) | 3 ( 0.8%) | 0 ( 0.0%) | 2 ( 0.5%) | 5 ( 1.3%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | | HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MODERATE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | SEVERE | NONE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MILD | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | MODERATE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | SEVERE | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | HYPOPYON | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |

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Table 39
Summary of Anterior Chamber Signs Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Sign | Visit | | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| | | NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| CELLS | DAY 1 | DECREASE | 1 ( 5.6%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | | NO CHANGE | 16 (88.9%) | 295 (78.0%) | 118 (59.6%) | 171 (45.4%) | 142 (36.3%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 59 (15.6%) | 59 (29.8%) | 88 (23.3%) | 94 (24.0%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 14 ( 3.7%) | 13 ( 6.6%) | 68 (18.0%) | 94 (24.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 1.5%) | 40 (10.6%) | 34 ( 8.7%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.8%) | 20 ( 5.1%) |
| | WEEK 1 | DECREASE | 1 ( 5.6%) | 2 ( 0.5%) | 1 ( 0.5%) | 5 ( 1.3%) | 8 ( 2.0%) |
| | | NO CHANGE | 16 (88.9%) | 325 (86.0%) | 153 (77.3%) | 277 (73.5%) | 279 (71.4%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 27 ( 7.1%) | 24 (12.1%) | 56 (14.9%) | 74 (18.9%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 5 ( 1.3%) | 8 ( 4.0%) | 18 ( 4.8%) | 12 ( 3.1%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 4 ( 1.1%) | 2 ( 1.0%) | 1 ( 0.3%) | 2 ( 0.5%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | MONTH 1 | DECREASE | 0 ( 0.0%) | 6 ( 1.6%) | 2 ( 1.0%) | 4 ( 1.1%) | 17 ( 4.3%) |
| | | NO CHANGE | 12 (66.7%) | 310 (82.0%) | 152 (76.8%) | 291 (77.2%) | 304 (77.7%) |
| | | INCREASE BY 1 | 2 (11.1%) | 13 ( 3.4%) | 7 ( 3.5%) | 17 ( 4.5%) | 16 ( 4.1%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 3 ( 0.8%) | 2 ( 1.0%) | 6 ( 1.6%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MONTH 2 | DECREASE | 1 ( 5.6%) | 8 ( 2.1%) | 1 ( 0.5%) | 1 ( 0.3%) | 11 ( 2.8%) |
| | | NO CHANGE | 10 (55.6%) | 262 (69.3%) | 134 (67.7%) | 266 (70.6%) | 253 (64.7%) |
| | | INCREASE BY 1 | 3 (16.7%) | 9 ( 2.4%) | 4 ( 2.0%) | 5 ( 1.3%) | 8 ( 2.0%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 1 ( 0.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 3 | DECREASE | 1 ( 5.6%) | 6 ( 1.6%) | 2 ( 1.0%) | 7 ( 1.9%) | 14 ( 3.6%) |
| | | NO CHANGE | 11 (61.1%) | 331 (87.6%) | 165 (83.3%) | 328 (87.0%) | 334 (85.4%) |
| | | INCREASE BY 1 | 2 (11.1%) | 9 ( 2.4%) | 7 ( 3.5%) | 6 ( 1.6%) | 8 ( 2.0%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 1.5%) | 4 ( 1.1%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 2 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



[1] Anterior Chamber signs were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe, 4 = Hypopyon

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Table 39
Summary of Anterior Chamber Signs Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Sign | Visit | | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|---|
| | | | WW | Saline | | | |
| FLARE | DAY 1 | DECREASE | 2 (11.1%) | 2 ( 0.5%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | | NO CHANGE | 15 (83.3%) | 298 (78.8%) | 132 (66.7%) | 207 (54.9%) | 210 (53.7%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 64 (16.9%) | 53 (26.8%) | 110 (29.2%) | 104 (26.6%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 7 ( 1.9%) | 8 ( 4.0%) | 37 ( 9.8%) | 44 (11.3%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.5%) | 15 ( 4.0%) | 25 ( 6.4%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | WEEK 1 | DECREASE | 2 (11.1%) | 2 ( 0.5%) | 0 ( 0.0%) | 2 ( 0.5%) | 6 ( 1.5%) |
| | | NO CHANGE | 15 (83.3%) | 329 (87.0%) | 158 (79.8%) | 298 (79.0%) | 308 (78.8%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 29 ( 7.7%) | 24 (12.1%) | 48 (12.7%) | 52 (13.3%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 2 ( 0.5%) | 6 ( 3.0%) | 9 ( 2.4%) | 8 ( 2.0%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.3%) |
| | MONTH 1 | DECREASE | 1 ( 5.6%) | 4 ( 1.1%) | 1 ( 0.5%) | 2 ( 0.5%) | 13 ( 3.3%) |
| | | NO CHANGE | 13 (72.2%) | 317 (83.9%) | 156 (78.8%) | 295 (78.2%) | 316 (80.8%) |
| | | INCREASE BY 1 | 0 ( 0.0%) | 12 ( 3.2%) | 4 ( 2.0%) | 18 ( 4.8%) | 9 ( 2.3%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 1.5%) | 4 ( 1.1%) | 2 ( 0.5%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 2 | DECREASE | 2 (11.1%) | 7 ( 1.9%) | 1 ( 0.5%) | 2 ( 0.5%) | 11 ( 2.8%) |
| | | NO CHANGE | 9 (50.0%) | 269 (71.2%) | 133 (67.2%) | 268 (71.1%) | 255 (65.2%) |
| | | INCREASE BY 1 | 3 (16.7%) | 5 ( 1.3%) | 5 ( 2.5%) | 4 ( 1.1%) | 6 ( 1.5%) |
| | | INCREASE BY 2 | 0 ( 0.0%) | 0 ( 0.0%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | MONTH 3 | DECREASE | 2 (11.1%) | 6 ( 1.6%) | 2 ( 1.0%) | 5 ( 1.3%) | 11 ( 2.8%) |
| | | NO CHANGE | 10 (55.6%) | 338 (89.4%) | 168 (84.8%) | 334 (88.6%) | 342 (87.5%) |
| | | INCREASE BY 1 | 1 ( 5.6%) | 7 ( 1.9%) | 6 ( 3.0%) | 5 ( 1.3%) | 4 ( 1.0%) |
| | | INCREASE BY 2 | 1 ( 5.6%) | 1 ( 0.3%) | 1 ( 0.5%) | 1 ( 0.3%) | 3 ( 0.8%) |
| | | INCREASE BY 3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| | | INCREASE BY 4 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |



[1] Anterior Chamber signs were scored on the following scale: 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe, 4 = Hypopyon

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Table 40.1
Summary of Minimum and Maximum Intraocular Pressure Post-Treatment
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| IOP (mmHg) | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| NUMBER OF PATIENTS | 18 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| MINIMUM IOP | | | | | | | | | | |
| <1 | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.9%) | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 0.5%) | 8 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| 1 - <3 | 0 ( 0.0%) | 1 ( 0.2%) | 2 ( 0.6%) | 0 ( 0.0%) | 2 ( 0.5%) | 4 ( 0.7%) | 8 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| 3 - <6 | 1 ( 5.6%) | 1 ( 0.2%) | 7 ( 2.1%) | 3 ( 2.3%) | 3 ( 0.8%) | 12 ( 2.0%) | 25 ( 1.7%) | 1 ( 1.2%) | 0 ( 0.0%) | 0 ( 0.0%) |
| >=6 | 17 (94.4%) | 413 (99.0%) | 315 (96.3%) | 127 (97.7%) | 370 (98.1%) | 552 (90.6%) | 1364 (94.5%) | 83 (98.8%) | 21 ( 100%) | 69 (98.6%) |
| n | 18 | 417 | 327 | 130 | 377 | 571 | 1405 | 84 | 21 | 69 |
| Mean (SE) | 11.7 ( 0.8) | 12.1 ( 0.1) | 11.3 ( 0.2) | 11.2 ( 0.3) | 11.4 ( 0.1) | 11.1 ( 0.1) | 11.3 ( 0.1) | 9.8 ( 0.3) | 12.5 ( 0.6) | 10.4 ( 0.3) |
| Range | 3.0 - 16.0 | 0.0 - 27.0 | 0.0 - 29.0 | 4.0 - 24.0 | 0.0 - 20.0 | 0.0 - 38.0 | 0.0 - 38.0 | 5.0 - 16.0 | 8.0 - 16.0 | 6.0 - 16.0 |
| MAXIMUM IOP | | | | | | | | | | |
| <=23 | 17 (94.4%) | 380 (91.1%) | 292 (89.3%) | 116 (89.2%) | 349 (92.6%) | 521 (85.6%) | 1278 (88.6%) | 84 ( 100%) | 20 (95.2%) | 69 (98.6%) |
| >23 - 30 | 1 ( 5.6%) | 24 ( 5.8%) | 20 ( 6.1%) | 10 ( 7.7%) | 22 ( 5.8%) | 36 ( 5.9%) | 88 ( 6.1%) | 0 ( 0.0%) | 1 ( 4.8%) | 0 ( 0.0%) |
| >30 - 35 | 0 ( 0.0%) | 5 ( 1.2%) | 3 ( 0.9%) | 1 ( 0.8%) | 3 ( 0.8%) | 4 ( 0.7%) | 11 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| >35 - 40 | 0 ( 0.0%) | 1 ( 0.2%) | 4 ( 1.2%) | 2 ( 1.5%) | 2 ( 0.5%) | 4 ( 0.7%) | 12 ( 0.8%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| >40 - 50 | 0 ( 0.0%) | 3 ( 0.7%) | 4 ( 1.2%) | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 0.3%) | 7 ( 0.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| >50 - 60 | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.6%) | 1 ( 0.8%) | 0 ( 0.0%) | 1 ( 0.2%) | 4 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| >60 | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 0.6%) | 0 ( 0.0%) | 0 ( 0.0%) | 3 ( 0.5%) | 5 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| n | 18 | 417 | 327 | 130 | 377 | 571 | 1405 | 84 | 21 | 69 |
| Mean (SE) | 17.5 ( 0.9) | 18.6 ( 0.3) | 19.0 ( 0.4) | 18.9 ( 0.5) | 17.8 ( 0.2) | 18.3 ( 0.2) | 18.3 ( 0.2) | 17.0 ( 0.2) | 18.3 ( 0.5) | 17.4 ( 0.2) |
| Range | 10.0 - 26.0 | 5.0 - 63.0 | 10.0 - 68.0 | 10.0 - 52.0 | 9.0 - 50.0 | 5.0 - 65.0 | 5.0 - 68.0 | 12.0 - 23.0 | 14.0 - 24.0 | 12.0 - 21.0 |



[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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ISTA Pharmaceuticals, Inc.
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Table 40.2
Summary of Minimum and Maximum Intraocular Pressure Post-Treatment
All Studies by Study for Vitrase Groups Only
Safety Population

| IOP (mmHg) | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 68 | 31 | 153 | 225 | 602 | 364 | 84 |
| MINIMUM IOP | | | | | | | |
| <1 | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 1 ( 0.3%) | 0 ( 0.0%) |
| 1 - <3 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 6 ( 1.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| 3 - <6 | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 2.6%) | 5 ( 2.2%) | 11 ( 1.8%) | 5 ( 1.4%) | 1 ( 1.2%) |
| >=6 | 29 (42.6%) | 31 ( 100%) | 149 (97.4%) | 220 (97.8%) | 579 (96.2%) | 356 (97.8%) | 83 (98.8%) |
| n | 30 | 31 | 153 | 225 | 602 | 364 | 84 |
| Mean (SE) | 12.5 ( 1.2) | 10.6 ( 0.3) | 10.9 ( 0.3) | 11.2 ( 0.2) | 11.1 ( 0.1) | 11.6 ( 0.2) | 9.8 ( 0.3) |
| Range | 0.0 - 38.0 | 7.0 - 14.0 | 4.0 - 18.0 | 4.0 - 18.0 | 0.0 - 29.0 | 0.0 - 20.0 | 5.0 - 16.0 |
| MAXIMUM IOP | | | | | | | |
| <=23 | 21 (30.9%) | 28 (90.3%) | 137 (89.5%) | 211 (93.8%) | 535 (88.9%) | 346 (95.1%) | 84 ( 100%) |
| >23 - 30 | 5 ( 7.4%) | 2 ( 6.5%) | 13 ( 8.5%) | 12 ( 5.3%) | 44 ( 7.3%) | 12 ( 3.3%) | 0 ( 0.0%) |
| >30 - 35 | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 0.7%) | 1 ( 0.4%) | 6 ( 1.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| >35 - 40 | 1 ( 1.5%) | 1 ( 3.2%) | 1 ( 0.7%) | 1 ( 0.4%) | 6 ( 1.0%) | 2 ( 0.5%) | 0 ( 0.0%) |
| >40 - 50 | 1 ( 1.5%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 5 ( 0.8%) | 1 ( 0.3%) | 0 ( 0.0%) |
| >50 - 60 | 1 ( 1.5%) | 0 ( 0.0%) | 1 ( 0.7%) | 0 ( 0.0%) | 2 ( 0.3%) | 0 ( 0.0%) | 0 ( 0.0%) |
| >60 | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 0 ( 0.0%) | 4 ( 0.7%) | 1 ( 0.3%) | 0 ( 0.0%) |
| n | 30 | 31 | 153 | 225 | 602 | 364 | 84 |
| Mean (SE) | 23.3 ( 1.8) | 19.0 ( 0.9) | 18.1 ( 0.4) | 17.7 ( 0.3) | 19.0 ( 0.3) | 17.3 ( 0.2) | 17.0 ( 0.2) |
| Range | 11.0 - 58.0 | 12.0 - 40.0 | 10.0 - 52.0 | 10.0 - 37.0 | 5.0 - 68.0 | 8.0 - 62.0 | 12.0 - 23.0 |



[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

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ISTA Pharmaceuticals, Inc.
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Table 40.3
Summary of Minimum and Maximum Intraocular Pressure Post-Treatment
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| IOP (mmHg) | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| MINIMUM IOP | | | | | |
| <1 | 0 ( 0.0%) | 2 ( 0.5%) | 3 ( 1.5%) | 2 ( 0.5%) | 2 ( 0.5%) |
| 1 - <3 | 0 ( 0.0%) | 0 ( 0.0%) | 2 ( 1.0%) | 2 ( 0.5%) | 4 ( 1.0%) |
| 3 - <6 | 1 ( 5.6%) | 1 ( 0.3%) | 5 ( 2.5%) | 3 ( 0.8%) | 8 ( 2.0%) |
| >=6 | 17 (94.4%) | 375 (99.2%) | 188 (94.9%) | 370 (98.1%) | 377 (96.4%) |
| n | 18 | 378 | 198 | 377 | 391 |
| Mean (SE) | 11.7 ( 0.8) | 12.1 ( 0.1) | 11.3 ( 0.2) | 11.4 ( 0.1) | 11.2 ( 0.2) |
| Range | 3.0 - 16.0 | 0.0 - 27.0 | 0.0 - 29.0 | 0.0 - 20.0 | 0.0 - 23.0 |
| MAXIMUM IOP | | | | | |
| <=23 | 17 (94.4%) | 349 (92.3%) | 169 (85.4%) | 349 (92.6%) | 363 (92.8%) |
| >23 - 30 | 1 ( 5.6%) | 18 ( 4.8%) | 15 ( 7.6%) | 22 ( 5.8%) | 19 ( 4.9%) |
| >30 - 35 | 0 ( 0.0%) | 4 ( 1.1%) | 3 ( 1.5%) | 3 ( 0.8%) | 2 ( 0.5%) |
| >35 - 40 | 0 ( 0.0%) | 1 ( 0.3%) | 3 ( 1.5%) | 2 ( 0.5%) | 3 ( 0.8%) |
| >40 - 50 | 0 ( 0.0%) | 3 ( 0.8%) | 4 ( 2.0%) | 1 ( 0.3%) | 1 ( 0.3%) |
| >50 - 60 | 0 ( 0.0%) | 2 ( 0.5%) | 2 ( 1.0%) | 0 ( 0.0%) | 0 ( 0.0%) |
| >60 | 0 ( 0.0%) | 1 ( 0.3%) | 2 ( 1.0%) | 0 ( 0.0%) | 3 ( 0.8%) |
| n | 18 | 378 | 198 | 377 | 391 |
| Mean (SE) | 17.5 ( 0.9) | 18.4 ( 0.3) | 20.2 ( 0.6) | 17.8 ( 0.2) | 18.0 ( 0.3) |
| Range | 10.0 - 26.0 | 5.0 - 62.0 | 11.0 - 68.0 | 9.0 - 50.0 | 5.0 - 65.0 |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 40.4
Summary of Minimum and Maximum Intraocular Pressure Post-Treatment
PVD Study (PVD-01-08961X) by Treatment
Safety Population

| IOP (mmHg) | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| NUMBER OF PATIENTS | 15 | 15 | 14 | 16 |
| MINIMUM IOP | | | | |
| >=6 | 15 ( 100%) | 15 ( 100%) | 14 ( 100%) | 16 ( 100%) |
| n | 15 | 15 | 14 | 16 |
| Mean (SE) | 12.1 ( 0.4) | 12.7 ( 0.6) | 11.7 ( 0.5) | 13.4 ( 0.5) |
| Range | 8.0 - 14.0 | 9.0 - 16.0 | 8.0 - 16.0 | 10.0 - 16.0 |
| MAXIMUM IOP | | | | |
| <=23 | 15 ( 100%) | 15 ( 100%) | 14 ( 100%) | 16 ( 100%) |
| n | 15 | 15 | 14 | 16 |
| Mean (SE) | 18.1 ( 0.4) | 18.1 ( 0.2) | 18.6 ( 0.4) | 18.5 ( 0.3) |
| Range | 16.0 - 23.0 | 17.0 - 21.0 | 16.0 - 21.0 | 17.0 - 20.0 |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 41.1
Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Change from Baseline
All Studies by Treatment
Safety Population

| | Hemorrhage Clearance Studies | | | | | | | Other Indications | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Control | | Vitrase | | | | | | | |
| IOP (mmHg) | WW | Saline | 7.5 IU | 37.5 IU | 55 IU | 75 IU | Total Vitrase | Vitrase 50-500 IU | Saline Control | Other Active [1] |
| NUMBER OF PATIENTS | 18 | 417 | 327 | 130 | 377 | 609 | 1443 | 84 | 21 | 70 |
| BASELINE IOP | | | | | | | | | | |
| n | 17 | 413 | 326 | 130 | 377 | 562 | 1395 | 84 | 21 | 70 |
| Mean (SE) | 16.2 ( 1.0) | 15.0 ( 0.2) | 15.0 ( 0.2) | 14.8 ( 0.3) | 14.9 ( 0.2) | 14.8 ( 0.2) | 14.9 ( 0.1) | 14.6 ( 0.3) | 15.2 ( 0.7) | 14.5 ( 0.3) |
| Range | 9.0 - 28.0 | 4.0 - 28.0 | 5.0 - 41.0 | 7.0 - 26.0 | 7.0 - 33.0 | 5.0 - 35.0 | 5.0 - 41.0 | 8.0 - 26.0 | 8.0 - 20.0 | 9.0 - 20.0 |
| MINIMUM IOP CHANGE FROM BASELINE | | | | | | | | | | |
| n | 17 | 413 | 326 | 130 | 377 | 562 | 1395 | 84 | 21 | 69 |
| Mean (SE) | -4.8 ( 0.8) | -2.9 ( 0.1) | -3.7 ( 0.2) | -3.6 ( 0.3) | -3.5 ( 0.2) | -3.7 ( 0.1) | -3.7 ( 0.1) | -4.8 ( 0.3) | -2.7 ( 0.9) | -4.1 ( 0.3) |
| Range | -12 - 2.0 | -15 - 5.0 | -22 - 11.0 | -14 - 4.0 | -19 - 9.0 | -19 - 6.0 | -22 - 11.0 | -17 - 2.0 | -9.0 - 4.0 | -10 - 2.0 |
| MAXIMUM IOP CHANGE FROM BASELINE | | | | | | | | | | |
| n | 17 | 413 | 326 | 130 | 377 | 562 | 1395 | 84 | 21 | 69 |
| Mean (SE) | 0.8 ( 1.1) | 3.5 ( 0.3) | 4.0 ( 0.4) | 4.1 ( 0.5) | 2.8 ( 0.2) | 3.3 ( 0.2) | 3.4 ( 0.1) | 2.4 ( 0.4) | 3.1 ( 0.8) | 2.9 ( 0.3) |
| Range | -7.0 - 10.0 | -7.0 - 44.0 | -18 - 48.0 | -5.0 - 36.0 | -13 - 28.0 | -10 - 55.0 | -18 - 55.0 | -11 - 10.9 | -3.0 - 12.0 | -5.0 - 9.0 |



[1] Other Active treatments include SF6 (PVD-01-08961X) and ACS-101C (COR-01-08961X). Patients who received both Vitrase and another active study treatment are included in both groups.

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Table 41.2
Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Change from Baseline
All Studies by Study for Vitrase Groups Only
Safety Population

| IOP (mmHg) | Phase I [1] | V-01-VIT-08961X | ACS202-HYA-001US | ACS203-HYA-001MEX | VIT-02-08961X | VIT-03-08961X | Other Indications [2] |
|---|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | 68 | 31 | 153 | 225 | 602 | 364 | 84 |
| BASELINE IOP | | | | | | | |
| n | 21 | 31 | 153 | 225 | 601 | 364 | 84 |
| Mean (SE) | 18.8 ( 1.4) | 14.4 ( 0.7) | 15.2 ( 0.3) | 14.2 ( 0.2) | 15.0 ( 0.2) | 14.8 ( 0.2) | 14.6 ( 0.3) |
| Range | 11.0 - 35.0 | 10.0 - 30.0 | 7.0 - 26.0 | 8.5 - 20.0 | 5.0 - 41.0 | 6.0 - 32.0 | 8.0 - 26.0 |
| MINIMUM IOP CHANGE FROM BASELINE | | | | | | | |
| n | 21 | 31 | 153 | 225 | 601 | 364 | 84 |
| Mean (SE) | -6.9 ( 1.3) | -3.8 ( 0.6) | -4.3 ( 0.3) | -3.0 ( 0.2) | -3.9 ( 0.2) | -3.2 ( 0.2) | -4.8 ( 0.3) |
| Range | -19 - 4.0 | -16 - 0.0 | -14 - 3.0 | -13 - 6.5 | -22 - 11.0 | -18 - 9.0 | -17 - 2.0 |
| MAXIMUM IOP CHANGE FROM BASELINE | | | | | | | |
| n | 21 | 31 | 153 | 225 | 601 | 364 | 84 |
| Mean (SE) | 3.9 ( 1.5) | 4.6 ( 1.1) | 3.0 ( 0.4) | 3.5 ( 0.3) | 4.0 ( 0.3) | 2.5 ( 0.2) | 2.4 ( 0.4) |
| Range | -10 - 19.0 | -10 - 24.0 | -6.0 - 36.0 | -4.0 - 23.0 | -18 - 55.0 | -6.0 - 45.0 | -11 - 10.9 |



[1] Includes ACS201-HYA-001A, ACS201-HYA-002A, Probe Study
[2] Includes PVD-01-08961X, COR-01-08961X, COP-01-08961X

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Table 41.3
Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Change from Baseline
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| IOP (mmHg) | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|
| | WW | Saline | | | |
| NUMBER OF PATIENTS | 18 | 378 | 198 | 377 | 391 |
| BASELINE IOP | | | | | |
| n | 17 | 378 | 197 | 377 | 391 |
| Mean (SE) | 16.2 ( 1.0) | 15.0 ( 0.2) | 15.4 ( 0.3) | 14.9 ( 0.2) | 14.7 ( 0.2) |
| Range | 9.0 - 28.0 | 4.0 - 28.0 | 5.0 - 41.0 | 7.0 - 33.0 | 5.0 - 32.0 |
| MINIMUM IOP CHANGE FROM BASELINE | | | | | |
| n | 17 | 378 | 197 | 377 | 391 |
| Mean (SE) | -4.8 ( 0.8) | -2.9 ( 0.2) | -4.2 ( 0.3) | -3.5 ( 0.2) | -3.5 ( 0.2) |
| Range | -12 - 2.0 | -15 - 5.0 | -22 - 11.0 | -19 - 9.0 | -17 - 4.0 |
| MAXIMUM IOP CHANGE FROM BASELINE | | | | | |
| n | 17 | 378 | 197 | 377 | 391 |
| Mean (SE) | 0.8 ( 1.1) | 3.4 ( 0.3) | 4.8 ( 0.6) | 2.8 ( 0.2) | 3.3 ( 0.3) |
| Range | -7.0 - 10.0 | -7.0 - 44.0 | -18 - 48.0 | -13 - 28.0 | -6.0 - 55.0 |

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Integrated Summary of Safety

Table 41.4
Summary of Minimum and Maximum Intraocular Pressure Post-Treatment Change from Baseline
All Studies by Treatment
Safety Population

| IOP (mmHg) | Vitrase 75 IU | SF6 | Vitrase 75 IU + SF6 | Saline |
|---|---|---|---|---|
| NUMBER OF PATIENTS | 15 | 15 | 14 | 16 |
| BASELINE IOP | | | | |
| n | 15 | 15 | 14 | 16 |
| Mean (SE) | 16.1 ( 0.5) | 15.5 ( 0.6) | 14.4 ( 0.6) | 16.0 ( 0.6) |
| Range | 12.0 - 19.0 | 10.0 - 18.0 | 11.0 - 18.0 | 11.0 - 20.0 |
| MINIMUM IOP CHANGE FROM BASELINE | | | | |
| n | 15 | 15 | 14 | 16 |
| Mean (SE) | -3.9 ( 0.7) | -2.8 ( 0.7) | -2.7 ( 0.7) | -2.6 ( 1.0) |
| Range | -8.0 - 2.0 | -9.0 - 2.0 | -8.0 - 0.0 | -8.0 - 4.0 |
| MAXIMUM IOP CHANGE FROM BASELINE | | | | |
| n | 15 | 15 | 14 | 16 |
| Mean (SE) | 2.1 ( 0.7) | 2.7 ( 0.6) | 4.2 ( 0.7) | 2.5 ( 0.7) |
| Range | -1.0 - 7.0 | 0.0 - 8.0 | 0.0 - 9.0 | -2.0 - 8.0 |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 42
Summary of Intraocular Pressure at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Visit | IOP (mmHg) | Control | | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| | | WW | Saline | | | |
| NUMBER OF PATIENTS | | 18 | 378 | 198 | 377 | 391 |
| BASELINE | n | 17 | 378 | 197 | 377 | 391 |
| | Mean (SE) | 16.2 ( 1.0) | 15.0 ( 0.2) | 15.4 ( 0.3) | 14.9 ( 0.2) | 14.7 ( 0.2) |
| | Range | 9.0 - 28.0 | 4.0 - 28.0 | 5.0 - 41.0 | 7.0 - 33.0 | 5.0 - 32.0 |
| DAY 1 | n | 17 | 372 | 194 | 371 | 385 |
| | Mean (SE) | 13.4 ( 0.8) | 14.6 ( 0.2) | 14.3 ( 0.3) | 14.0 ( 0.2) | 14.1 ( 0.2) |
| | Range | 8.0 - 19.0 | 5.0 - 35.0 | 5.0 - 29.0 | 3.0 - 30.0 | 2.0 - 38.0 |
| WEEK 1 | n | 17 | 363 | 188 | 357 | 375 |
| | Mean (SE) | 14.8 ( 1.0) | 15.1 ( 0.2) | 15.0 ( 0.4) | 13.8 ( 0.2) | 13.7 ( 0.2) |
| | Range | 6.0 - 21.0 | 5.0 - 62.0 | 8.0 - 61.0 | 6.0 - 29.0 | 4.0 - 37.0 |
| MONTH 1 | n | 14 | 335 | 163 | 318 | 339 |
| | Mean (SE) | 14.6 ( 0.9) | 15.1 ( 0.2) | 15.7 ( 0.5) | 14.6 ( 0.2) | 14.0 ( 0.2) |
| | Range | 9.0 - 19.0 | 1.0 - 53.0 | 6.0 - 60.0 | 6.0 - 50.0 | 3.0 - 38.0 |
| MONTH 2 | n | 14 | 282 | 142 | 274 | 274 |
| | Mean (SE) | 14.3 ( 0.7) | 15.0 ( 0.2) | 15.7 ( 0.5) | 14.6 ( 0.2) | 14.7 ( 0.2) |
| | Range | 10.0 - 18.0 | 1.0 - 35.0 | 2.0 - 56.0 | 4.0 - 36.0 | 4.0 - 33.0 |
| MONTH 3 | n | 14 | 353 | 178 | 344 | 361 |
| | Mean (SE) | 13.6 ( 1.1) | 14.9 ( 0.2) | 15.6 ( 0.5) | 14.9 ( 0.2) | 14.6 ( 0.2) |
| | Range | 3.0 - 18.0 | 4.0 - 38.0 | 3.0 - 68.0 | 6.0 - 40.0 | 4.0 - 40.0 |

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Table 43
Summary of Intraocular Pressure Change from Baseline at Specified Visits
Primary Phase III Studies: VIT-02-08961X, VIT-03-08961X by Treatment
Safety Population

| Visit | IOP (mmHg) | Control: WW | Control: Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
|---|---|---|---|---|---|---|
| NUMBER OF PATIENTS | | 18 | 378 | 198 | 377 | 391 |
| BASELINE | n | 17 | 378 | 197 | 377 | 391 |
| | Mean (SE) | 16.2 ( 1.0) | 15.0 ( 0.2) | 15.4 ( 0.3) | 14.9 ( 0.2) | 14.7 ( 0.2) |
| | Range | 9.0 - 28.0 | 4.0 - 28.0 | 5.0 - 41.0 | 7.0 - 33.0 | 5.0 - 32.0 |
| CHANGE FROM BASELINE | | | | | | |
| DAY 1 | n | 16 | 372 | 194 | 371 | 385 |
| | Mean (SE) | -3.2 ( 0.9) | -0.4 ( 0.2) | -1.2 ( 0.3) | -1.0 ( 0.2) | -0.6 ( 0.2) |
| | Range | -9.0 - 2.0 | -14 - 25.0 | -21 - 15.0 | -18 - 15.0 | -12 - 21.0 |
| WEEK 1 | n | 16 | 363 | 188 | 357 | 375 |
| | Mean (SE) | -1.6 ( 1.0) | 0.1 ( 0.2) | -0.3 ( 0.4) | -1.1 ( 0.2) | -0.9 ( 0.2) |
| | Range | -9.0 - 5.0 | -12 - 44.0 | -10 - 43.0 | -17 - 9.0 | -15 - 12.0 |
| MONTH 1 | n | 14 | 335 | 163 | 318 | 339 |
| | Mean (SE) | -1.6 ( 1.4) | 0.1 ( 0.2) | 0.0 ( 0.5) | -0.4 ( 0.2) | -0.7 ( 0.2) |
| | Range | -12 - 6.0 | -10 - 41.0 | -18 - 45.0 | -18 - 20.0 | -16 - 14.0 |
| MONTH 2 | n | 13 | 282 | 142 | 274 | 274 |
| | Mean (SE) | -1.8 ( 1.1) | -0.0 ( 0.2) | 0.0 ( 0.5) | -0.3 ( 0.2) | -0.1 ( 0.2) |
| | Range | -10 - 4.0 | -12 - 13.0 | -21 - 34.0 | -16 - 16.0 | -11 - 21.0 |
| MONTH 3 | n | 13 | 353 | 177 | 344 | 361 |
| | Mean (SE) | -1.7 ( 1.0) | -0.2 ( 0.2) | 0.1 ( 0.5) | -0.2 ( 0.2) | -0.1 ( 0.2) |
| | Range | -6.0 - 5.0 | -12 - 24.0 | -19 - 48.0 | -17 - 28.0 | -12 - 24.0 |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 44
Summary of Intraocular Pressure at Specified Visits
Study V-01-VIT-08961X by Treatment
Safety Population

| Visit | IOP (mmHg) | Saline | 75 IU Vitrase |
|---|---|---|---|
| NUMBER OF PATIENTS | | 30 | 31 |
| BASELINE | n | 30 | 31 |
| | Mean (SE) | 14.9 ( 0.6) | 14.4 ( 0.7) |
| | Range | 10.0 - 20.0 | 10.0 - 30.0 |
| DAY 1 | n | 30 | 30 |
| | Mean (SE) | 14.1 ( 0.6) | 14.7 ( 0.7) |
| | Range | 10.0 - 22.0 | 10.0 - 27.0 |
| WEEK 1 | n | 30 | 31 |
| | Mean (SE) | 13.6 ( 0.6) | 12.6 ( 0.4) |
| | Range | 10.0 - 24.0 | 10.0 - 18.0 |
| MONTH 1 | n | 30 | 31 |
| | Mean (SE) | 14.4 ( 0.6) | 13.5 ( 0.5) |
| | Range | 10.0 - 20.0 | 7.0 - 20.0 |
| MONTH 2 | n | 29 | 31 |
| | Mean (SE) | 14.0 ( 0.7) | 13.4 ( 0.5) |
| | Range | 8.0 - 28.0 | 9.0 - 18.0 |
| MONTH 3 | n | 30 | 31 |
| | Mean (SE) | 14.3 ( 0.6) | 13.6 ( 0.5) |
| | Range | 10.0 - 20.0 | 9.0 - 20.0 |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 45
Summary of Intraocular Pressure Change from Baseline at Specified Visits
Study V-01-VIT-08961X by Treatment
Safety Population

| Visit | IOP (mmHg) | Saline | 75 IU Vitrase |
|---|---|---|---|
| NUMBER OF PATIENTS | | 30 | 31 |
| BASELINE | n | 30 | 31 |
| | Mean (SE) | 14.9 ( 0.6) | 14.4 ( 0.7) |
| | Range | 10.0 - 20.0 | 10.0 - 30.0 |
| CHANGE FROM BASELINE | | | |
| DAY 1 | n | 30 | 30 |
| | Mean (SE) | -0.8 ( 0.4) | 0.8 ( 0.8) |
| | Range | -8.0 - 2.0 | -8.0 - 15.0 |
| WEEK 1 | n | 30 | 31 |
| | Mean (SE) | -1.2 ( 0.6) | -1.8 ( 0.7) |
| | Range | -8.0 - 4.0 | -16 - 4.0 |
| MONTH 1 | n | 30 | 31 |
| | Mean (SE) | -0.5 ( 0.6) | -0.9 ( 0.6) |
| | Range | -8.0 - 4.0 | -12 - 4.0 |
| MONTH 2 | n | 29 | 31 |
| | Mean (SE) | -0.7 ( 0.7) | -1.1 ( 0.7) |
| | Range | -8.0 - 8.0 | -12 - 6.0 |
| MONTH 3 | n | 30 | 31 |
| | Mean (SE) | -0.5 ( 0.5) | -0.8 ( 0.6) |
| | Range | -8.0 - 4.0 | -10 - 4.0 |

ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 46
Incidence of Deaths
All Studies
Safety Population

| Study | Number of Deaths | Safety Population | Incidence of Deaths |
|---|---|---|---|
| ACS201-HYA-001A | 0 | 14 | 0.0% |
| ACS201-HYA-002A | 0 | 28 | 0.0% |
| PROBE STUDY | 0 | 34 | 0.0% |
| V-01-VIT-08961X | 3 | 61 | 4.9% |
| ACS202-HYA-001US | 0 | 153 | 0.0% |
| ACS203-HYA-001MEX | 0 | 225 | 0.0% |
| VIT-02-08961X (WW) | 7 | 71 | 9.9% |
| VIT-02-08961X | 33 | 740 | 4.5% |
| VIT-03-08961X | 28 | 551 | 5.1% |
| PVD-01-08961X | 1 | 60 | 1.7% |
| COR-01-08961X | 0 | 41 | 0.0% |
| COP-01-08961X | 0 | 30 | 0.0% |



Patient 149-3702 in study VIT-02-08961X died 450 days after discontinuing due to Lost to Follow-up. This patient's death is not included here.

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ISTA Pharmaceuticals, Inc.
Integrated Summary of Safety

Table 47
Incidence of Deaths by Treatment
Primary Phase III Studies: VIT-02-08961X and VIT-03-08961X
Safety Population

| | Control | | | | |
|---|---|---|---|---|---|
| | WW | Saline | 7.5 IU Vitrase | 55 IU Vitrase | 75 IU Vitrase |
| *NUMBER OF PATIENTS* | 18 | 378 | 198 | 377 | 391 |
| INCIDENCE OF DEATHS | 6 (33.3%) | 16 ( 4.2%) | 8 ( 4.0%) | 17 ( 4.5%) | 21 ( 5.4%) |



Patient 149-3702 in study VIT-02-08961X died 450 days after discontinuing due to Lost to Follow-up. This patient's death is not included here.

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