ERRATA FDA ODAC BRIEFING DOCUMENT
SEPTEMBER 13, 2005 MEETING
NDA 21473/S-003 TARCEVA
PANCREATIC ADENOCARCINOMA

General: There may be some confusion in the document regarding which analysis is the primary analysis with regard to the timing (number of deaths). It is clear the primary analysis is overall survival and the protocol specified statistical test is the stratified Log Rank. The question is when the primary analysis was supposed to be done. The protocol specified the final analysis would be done when there were 381 deaths. But before the investigators realized it, there were 484 deaths. The question arises whether 381 deaths or 484 deaths should be considered the primary analysis. The Applicant believes it should be 484 deaths. The FDA will look at analyses at several time points. These time are the protocol specified (381 deaths), the data cut-off (484 deaths, 443 deaths in the 100 mg cohort) and the updated data to June 2005 (551 deaths, 504 deaths in the 100 mg cohort).

Page 2, second paragraph: Change "22 PR" in the 100 mg EG group to "20 PR". Change the response rate in the PG group from "8.0%" to "7.9%".

Page 2, second paragraph: Delete "social functioning" from the QOL components that approached statistically significant worsening.

Page 33, fourth paragraph: Change the first 2 sentences to
“In addition, a multivariate Cox model was constructed that included treatment and both of the specified covariates, namely ECOG PS and extent of disease. The adjusted HR for overall survival in the EG arm relative to the PG arm was 0.79 (95% CI: 0.65 to 0.95, p=0.014).

Page 35, Reviewer's note: Change third line to indicate "(Log -rank test, unadjusted)".

Page 35, Reviewer’s note, second paragraph: Change to “When survival data are analyzed using the Cox proportional hazard ratio, again, the unadjusted overall survival was not statistically significantly different for the 381 death group. However, the unadjusted Cox analysis in the 443 death group was statistically significant (p=0.0463)."

Page 55, Table 26: Change Patients who died on treatment or within 30 days from "86 (33) and 72 (27)" to "81 (31) and 68 (27)". Change the last line of the Reviewer's note to "EG group (31%) as compared to PG (27%)."

Page 56, first paragraph line 4: Change to "Moreover, 3 additional patients experienced serious drug-related events with a fatal outcome. However, the Investigators attributed their death to other conditions or circumstances on the CFR. This included 1 patient in the erlotinib arm who was noted to have severe pneumonia and 2 patients in the placebo arm, 1 who had pneumonia, and 1 who had a combination of cancer progression and drug toxicity."

Page 57, Table 27: Replace Table 27 with the following Table.

Table 27 Causes of death in patients that died within 30 days of last dose of treatment

	Erlotinib/Gem (N=81) %*	Placebo/Gem (N =68) %*
Toxicity due to protocol	2 (2.5)	0(0)
Combination Pancreatic cancer and protocol treatment	3 (3.7)	0(0)
Other primary malignancy	1(1.2)	0(0)
Pancreatic cancer progression	65 (80.2)	59(86.8)
Other reasons	10 (12.3)	9 (13.2)

*****% of patients that died within 30 days of last dose

Page 57, Reviewer's comment, line 3: Change to "pancreatic cancer and protocol treatment (6.2%) versus (0%) in all patients who died ≤ 30 days of drug administration".

Page 57, Table 28: Change Deep Venous Thromboses from "6 (2.3) and 5 (2)" to "9 (3.5) and 3 (1.2)". Change Pulmonary embolism from "9 (3.5) and 3 (1.2)" to "6 (2.3) and 5 (2)". Delete "Stent occlusion". This refers to biliary stents, not cardiac.

Page 66, Table 32: Change adverse events to " 37 (14) and 13 (5)".

Page 66, paragraph following Table 32 line 3: Change to "14% versus 5 %, respectively"

Page 67, first paragraph line 2: Change to "A total of 37 (14%) patients discontinued therapy due AE events in the EG group. In contrast, only 13 (5%) patients discontinued therapy due to AE in the PG group."

Page 67, Reviewer's comment: Change line 2 to "erlotinib group 37 versus 13, respectively (14% versus 5%, respectively)"

Page 69, Table 36: Change Erlotinib + gemcitabine "N=261" to "N=259". Change Placebo + gemcitabine "N=260" to "N=256"

Page 73, second paragraph ninth line: delete "social functioning".

Page 73, third paragraph second line: delete "serious".