ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Adverse Events Module

Results Database Train-the-Trainer Workshop
October 2012

http://ClinicalTrials.gov

FDAAA - Adverse Events

"A table of anticipated and unanticipated serious adverse events grouped by organ system, with number and frequency of such event in each arm of the clinical trial."

[Sec. 282(j)(3)(I)(iii)(I)]

FDAAA = Food and Drug Administration Amendments Act of 2007

2

FDAAA – Adverse Events (cont.)

"A table of anticipated and unanticipated adverse events **that are not included in the [Serious Adverse Events] table**…that exceed a frequency of 5 percent within any arm of the clinical trial, grouped by organ system, with number and frequency of such event in each arm of the clinical trial."

[Sec. 282(j)(3)(I)(iii)(II)]

FDAAA = Food and Drug Administration Amendments Act of 2007

3

Purpose

The Adverse Events module is designed to summarize data regarding the serious (SAEs) and other (not including serious) adverse events (AEs) that were collected during the study.

- Summary data at the end of the study
- Not "real time" adverse event reporting while the study is ongoing
- SAEs and AEs are presented in separate tables
- Data reported in accordance with procedures for data collection in protocol

4

ClinicalTrials.gov Format

Serious Adverse Events

	AmphoB Standard	AmphoB+Fluc400	AmphoB + Fluc800
Total, serious adverse events			
# participants affected / at risk	22/45 (48.89%)	17/47 (36.17%)	26/49 (53.06%)
Blood and lymphatic system disorders			
Neutropenia [*2]			
# participants affected / at risk	1/45 (2.22%)	0/47 (0.00%)	2/49 (4.08%)
Anaemia [*2]			
# participants affected / at risk	2/45 (4.44%)	0/47 (0.00%)	0/49 (0.00%)
Thrombocytopenia [*2]			
# participants affected / at risk	0/45 (0.00%)	0/47 (0.00%)	1/49 (2.04%)
Cardiac disorders			
Cardiac failure congestive [*2]			
# participants affected / at risk	0/45 (0.00%)	0/47 (0.00%)	1/49 (2.04%)
Cardio-respiratory arrest [*2]			
# participants affected / at risk	0/45 (0.00%)	0/47 (0.00%)	1/49 (2.04%)

NCT00145249

5

ClinicalTrials.gov Format

Frequency Threshold

Threshold above which other adverse events are reported	5%

Other Adverse Events

	AmphoB Standard	AmphoB+Fluc400	AmphoB + Fluc800
Total, other (not including serious) adverse events			
# participants affected / at risk	44/45	47/47	49/49
Blood and lymphatic system disorders			
Anaemia [*1]			
# participants affected / at risk	21/45 (46.67%)	27/47 (57.45%)	24/49 (48.98%)
Thrombocytopenia [*1]			
# participants affected / at risk	2/45 (4.44%)	4/47 (8.51%)	4/49 (8.16%)
Neutropenia [*1]			
# participants affected / at risk	2/45 (4.44%)	1/47 (2.13%)	3/49 (6.12%)

NCT00145249

6

Serious Adverse Event Template

Time Frame for Adverse Event Reporting			
Adverse Event Reporting Additional Description			
Source Vocabulary Name for Table Default ①			
Assessment Type for Table Default ①	(Circle One) Systematic	Non-Systematic	
Arm/Group Title *	*	*	*
Arm/Group Description ②			

Serious Adverse Events *

		Number Participants Affected *	Number Participants at Risk *	Number Events	Number Participants Affected *	Number Participants at Risk *	Number Events	Number Participants Affected *	Number Participants at Risk *	Number Events
Total Number for Serious Adverse Events *		*	*		*	*		*	*	
Adverse Event Term *	Organ System *									
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	

Other Adverse Event Template

Time Frame for Adverse Event Reporting			
Adverse Event Reporting Additional Description			
Source Vocabulary Name for Table Default ①			
Assessment Type for Table Default ①	(Circle One) Systematic	Non-Systematic	
Arm/Group Title *	*	*	*
Arm/Group Description ②			

Other (Not Including Serious) Adverse Events *

		Number Participants Affected *	Number Participants at Risk *	Number Events	Number Participants Affected *	Number Participants at Risk *	Number Events	Number Participants Affected *	Number Participants at Risk *	Number Events
Total Number for Other (Not Including Serious) Adverse Events *		*	*		*	*		*	*	
Adverse Event Term *	Organ System *									
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	
*	③*	*	④[*]		*	④[*]		*	④[*]	

New - Upload Tab Delimited File

- "Beta" version available in PRS on 18 Oct 2012
- Download a tab delimited file (with Arms/Groups)
- Use spreadsheet program to enter adverse event information
- Upload tab delimited file(s) to populate adverse event table(s) in PRS

9

Best Practices

- Specify the Time Frame for adverse event data collection
- Use the Adverse Event Reporting Additional Description to provide information on the methods for adverse event data collection and on the analysis population (number of participants at risk)

10

Adverse Events
Tutorial

11

Overview

Results : Overview

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	Adverse Events

Title: Example Parallel Study Design***** ID: FDXAR -no results

Edit Protocol Delete Results Preview Results

Safety Issue? No

2	Secondary Outcome	Not Posted	Number of Patients With a 50 Percent or Greater Reduction in Pain as Determined by SPS-11 at Week 12 *[Week 12]* *Safety Issue? Unknown*	
3	Secondary Outcome	Not Posted	Number of Patients With a 50 Percent or Greater Reduction in Pain as Determined by SPS-11 at Week 24 *[Week 24]* *Safety Issue? Unknown*	
4	Secondary Outcome	Not Posted	Patient's Overall Pain Relief (POPR) at Week 24 *[Week 24]* *Safety Issue? Unknown*	

WARNING : [3 occurrences] Outcome Safety Issue? has not been entered.

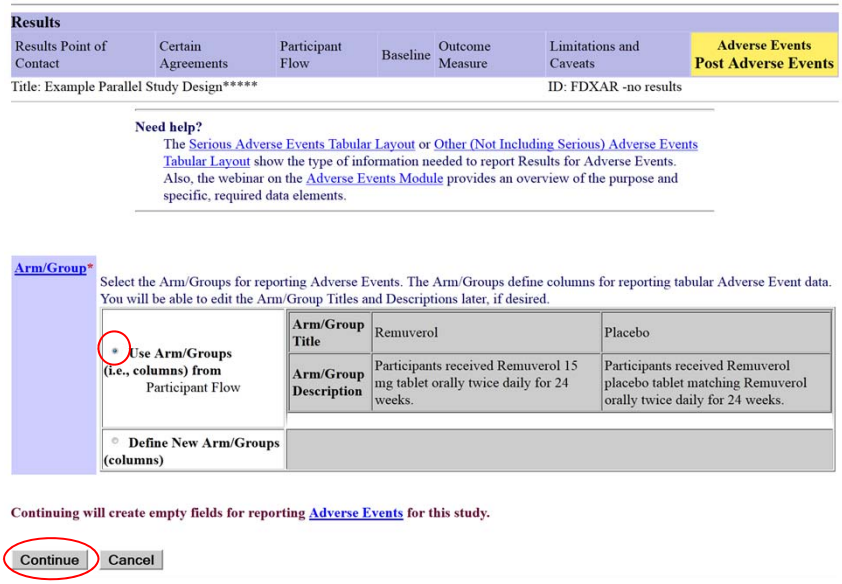
Edit **Limitations and Caveats:**

Adverse Events: Post Adverse Events

ERROR : [1 occurrences] Adverse Events have not been entered.

12

Post Adverse Events



Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events Post Adverse Events**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Need help?
The Serious Adverse Events Tabular Layout or Other (Not Including Serious) Adverse Events Tabular Layout show the type of information needed to report Results for Adverse Events. Also, the webinar on the Adverse Events Module provides an overview of the purpose and specific, required data elements.

Arm/Group*

Select the Arm/Groups for reporting Adverse Events. The Arm/Groups define columns for reporting tabular Adverse Event data. You will be able to edit the Arm/Group Titles and Descriptions later, if desired.

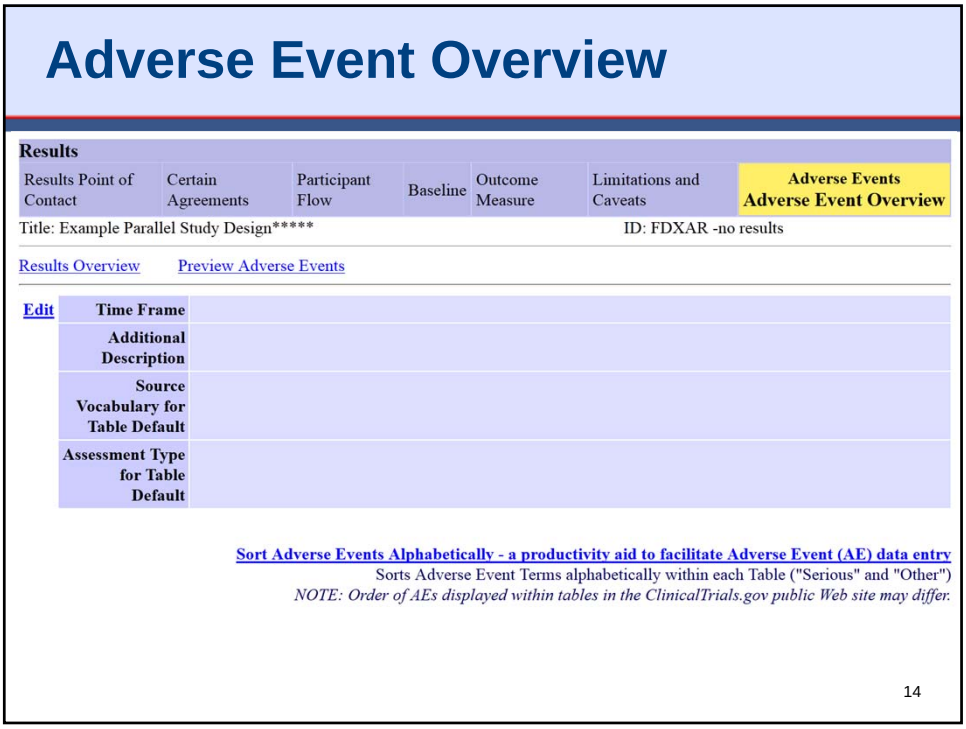
	Arm/Group Title	Remuverol	Placebo
(•) Use Arm/Groups (i.e., columns) from Participant Flow	Arm/Group Description	Participants received Remuverol 15 mg tablet orally twice daily for 24 weeks.	Participants received Remuverol placebo tablet matching Remuverol orally twice daily for 24 weeks.
( ) Define New Arm/Groups (columns)			

Continuing will create empty fields for reporting Adverse Events for this study.

Continue Cancel

13

Adverse Event Overview



Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events Adverse Event Overview**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Results Overview Preview Adverse Events

Edit		
	Time Frame	
	Additional Description	
	Source Vocabulary for Table Default	
	Assessment Type for Table Default	

Sort Adverse Events Alphabetically - a productivity aid to facilitate Adverse Event (AE) data entry
Sorts Adverse Event Terms alphabetically within each Table ("Serious" and "Other")
NOTE: Order of AEs displayed within tables in the ClinicalTrials.gov public Web site may differ.

14

Adverse Event Overview (cont.)

Add Arm/Group

Add Serious Adverse Event List all Serious Adverse Events.

		Remuverol *Participants received Remuvero...* Modify/Delete	Placebo *Participants received Remuvero...* Modify/Delete
Edit	**Total for Serious Adverse Events**	<> *Affected out of* <> *At Risk* ( ) **ERROR : The Total Number Affected has not been entered.** **ERROR : The Total Number of Participants at Risk for Serious Adverse Event has not been entered.**	<> *Affected out of* <> *At Risk* ( ) **ERROR : The Total Number Affected has not been entered.** **ERROR : The Total Number of Participants at Risk for Serious Adverse Event has not been entered.**
	Maximum for a single	*participants Affected by a Serious Adverse Event*	*participants Affected by a Serious Adverse Event*
	Sum for all	*0 participants Affected by all Serious Adverse Events*	*0 participants Affected by all Serious Adverse Events*

15

Edit Serious Adverse Event Total

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events** **Edit Serious Adverse Event Total**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Please enter the Total Number of Participants Affected and at Risk as integers.

- The Total Number of Participants at Risk is typically equal to the Number of Participants who Started the first Period in the Participant Flow.
- The Total Number of Participants Affected in an Arm/Group must be less than or equal to the sum of Participants Affected for All Adverse Events in the Arm/Group.
- The Total Number of Participants Affected in an Arm/Group must be greater than or equal to the Maximum Number of Participants Affected for any Adverse Event in the Arm/Group.

Serious Adverse Event(s)	Remuverol *Participants received Remuvero...*		Placebo *Participants received Remuvero...*	
Maximum for a single Serious Adverse Event	<> *(Calculated)*		<> *(Calculated)*	
Sum for all Serious Adverse Events	0 *(Calculated)*		0 *(Calculated)*	
	# Affected *	**# at Risk** *	**# Affected** *	**# at Risk** *
Total	4 **ERROR : The Total Number Affected has not been entered.**	101 **ERROR : The Total Number of Participants at Risk for Serious Adverse Event has not been entered.**	0 **ERROR : The Total Number Affected has not been entered.**	99 **ERROR : The Total Number of Participants at Risk for Serious Adverse Event has not been entered.**

OK Cancel

16

Adverse Event Overview

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events** **Adverse Event Overview**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Add Arm/Group

Add Serious Adverse Event List all Serious Adverse Events.

		Remuverol *Participants received Remuvero...* Modify/Delete	**Placebo** *Participants received Remuvero...* Modify/Delete
Edit	**Total for Serious Adverse Events**	4 *Affected out of* 101 *At Risk* (3.96%) **ERROR : The Total Number of participants Affected in an Arm/Group must be less than or equal to the sum of participants Affected for all Serious Adverse Events listed in the table for that Arm/Group.**	0 *Affected out of* 99 *At Risk* (0%)
	Maximum for a single	*participants Affected by a Serious Adverse Event*	*participants Affected by a Serious Adverse Event*
	Sum for all	*0 participants Affected by all Serious Adverse Events*	*0 participants Affected by all Serious Adverse Events*

17

Add Serious Adverse Event

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events** **Add Serious Adverse Event**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Adverse Event Term:* Idiopathic Thrombocytopenic Purpura

Source Vocabulary Name: Please enter the name and version for the term's source vocabulary, if any, (e.g., SNOMED CT, MedDRA 10.0).

Blank means use table default.
No current default source vocabulary
MedDRA (12.0)

Organ System:* Blood and lymphatic system disorders

Assessment Type: Blank means use table default.
No current default assessment type
Systematic Assessment

Additional Description: Maximum allowed content length (250)

OK Cancel

18

Adverse Event Overview

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events** **Adverse Event Overview**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Add Arm/Group

Add Serious Adverse Event List all Serious Adverse Events.

		Remuverol *Participants received Remuvero...* Modify/Delete	**Placebo** *Participants received Remuvero...* Modify/Delete
Edit	**Total for Serious Adverse Events**	4 *Affected out of* 101 *At Risk* (3.96%) **ERROR : The Total Number of participants Affected in an Arm/Group must be less than or equal to the sum of participants Affected for all Serious Adverse Events listed in the table for that Arm/Group.**	0 *Affected out of* 99 *At Risk* (0%)
	Maximum for a single	*participants Affected by a Serious Adverse Event*	*participants Affected by a Serious Adverse Event*
	Sum for all	*unknown participants Affected by all Serious Adverse Events*	*unknown participants Affected by all Serious Adverse Events*
Edit	Idiopathic Thrombocytopenic Purpura		

ERROR : [2 occurrences] The Number of Affected Participants has not been entered for an Adverse Event.
NOTE : [2 occurrences] Missing Number of Events for an Adverse Event Arm/Group.

19

Adverse Event Subset

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events** **Adverse Event Subset**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Adverse Event Overview

		Remuverol	**Placebo**
Edit	**Total for Serious Adverse Events**	4 *Affected out of* 101 *At Risk* (3.96%) **ERROR : The Total Number of participants Affected in an Arm/Group must be less than or equal to the sum of participants Affected for all Serious Adverse Events listed in the table for that Arm/Group.**	0 *Affected out of* 99 *At Risk* (0%)
	Idiopathic Thrombocytopenic Purpura *MedDRA (12.0)* *Blood and lymphatic system disorders* *Systematic Assessment* Modify/Delete	<> *Affected out of* 101 *At Risk* ( ) <> *Events* NOTE : Missing Number of Events for an Adverse Event Arm/Group. **ERROR : The Number of Affected Participants has not been entered for an Adverse Event.**	<> *Affected out of* 99 *At Risk* ( ) <> *Events* NOTE : Missing Number of Events for an Adverse Event Arm/Group. **ERROR : The Number of Affected Participants has not been entered for an Adverse Event.**

20

Edit Serious Adverse Event Subset

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events** **Edit Serious Adverse Event Subset Data**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Please enter the number of participants affected and at risk as integers. Also, if available, enter the number of events as integers.

Serious Adverse Event(s)	Remuverol *Participants received Remuvero...*			Placebo *Participants received Remuvero...*		
	# Affected *		**# at Risk ***	**# Affected ***		**# at Risk ***
Total	4 ERROR : The Total Number of participants Affected in an Arm/Group must be less than or equal to the sum of participants Affected for all Serious Adverse Events listed in the table for that Arm/Group.		101	0		99
	# Affected *	**# Events**	**# at Risk [blank =Total]**	**# Affected ***	**# Events**	**# at Risk [blank =Total]**
Idiopathic Thrombocytopenic Purpura *Systematic Assessment*	1 ERROR : The Number of Affected Participants has not been entered for an Adverse Event.	NOTE : Missing Number of Events for an Adverse Event Arm/Group.	[101]	0 ERROR : The Number of Affected Participants has not been entered for an Adverse Event.	NOTE : Missing Number of Events for an Adverse Event Arm/Group.	[99]

OK Cancel

Adverse Event Subset

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events** **Adverse Event Subset**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Adverse Event Overview

		Remuverol	Placebo
Edit	**Total for Serious Adverse Events**	4 *Affected out of* 101 *At Risk* (3.96%) ERROR : The Total Number of participants Affected in an Arm/Group must be less than or equal to the sum of participants Affected for all Serious Adverse Events listed in the table for that Arm/Group.	0 *Affected out of* 99 *At Risk* (0%)
	Idiopathic Thrombocytopenic Purpura *MedDRA (12.0)* *Blood and lymphatic system disorders* *Systematic Assessment* Modify/Delete	1 *Affected out of* 101 *At Risk* (0.99%) <> *Events* NOTE : Missing Number of Events for an Adverse Event Arm/Group.	0 *Affected out of* 99 *At Risk* (0%) <> *Events* NOTE : Missing Number of Events for an Adverse Event Arm/Group.

22

Adverse Event Overview

Results

Results Point of Contact	Certain Agreements	Participant Flow	Baseline	Outcome Measure	Limitations and Caveats	**Adverse Events** **Adverse Event Overview**

Title: Example Parallel Study Design***** ID: FDXAR -no results

Add Arm/Group

Add Serious Adverse Event List all Serious Adverse Events.

		Remuverol *Participants received Remuvero...* Modify/Delete	**Placebo** *Participants received Remuvero...* Modify/Delete
Edit	**Total for Serious Adverse Events**	4 *Affected out of* 101 *At Risk* (3.96%) **ERROR : The Total Number of participants Affected in an Arm/Group must be less than or equal to the sum of participants Affected for all Serious Adverse Events listed in the table for that Arm/Group.**	0 *Affected out of* 99 *At Risk* (0%)
	Maximum for a single	*1 participants Affected by a Serious Adverse Event*	*0 participants Affected by a Serious Adverse Event*
	Sum for all	*1 participants Affected by all Serious Adverse Events*	*0 participants Affected by all Serious Adverse Events*
Edit	Idiopathic Thrombocytopenic Purpura		

NOTE : [2 occurrences] Missing Number of Events for an Adverse Event Arm/Group.

23

Enter Adverse Events

- Example Study Designs
  - Crossover
  - Dose Escalation
  - Factorial
  - Multiple Period

24

Additional Issues

- More than one time period of assessment for each Arm/Group
- Participants were not evaluated for adverse events during the study

25

Additional Slides

26

Adverse Events – Example

Time Frame	No text entered.
Additional Description	This is a retrospective study of pre-existing data; thus, no assessments for Serious or Non-serious Adverse Events were performed.

Reporting Groups

	Description
Fondaparinux	All dosages of fondaparinux
Low Molecular Weight Heparins (LMWHs)	All dosages of LMWH, including Enoxaparin, Dalteparin, Nadroparin, and Tinzaparin

Serious Adverse Events

	Fondaparinux	Low Molecular Weight Heparins (LMWHs)
Total, serious adverse events		
# participants affected / at risk	**0/0 (0.00%)**	**0/0 (0.00%)**

NCT01064362

27

Adverse Events - Example

Participant Flow: Overall Study

	Gemcitabine/Carboplatin	Paclitaxel/Carboplatin
STARTED	417	414
Received Induction Therapy	411	409
Received Consolidation Therapy	169	183
Received Crossover Therapy	77	78
COMPLETED	246 [1]	261 [1]
NOT COMPLETED	171	153
Toxicity	26	37
Disease Progression	5	6
Physician Decision	20	11
Withdrawal by Subject	58	39
Protocol Violation	5	7
Death	6	8
Other	33	34
Missing Data	18	11

[1] Completed was defined as the patients treated in either consolidation therapy or crossover therapy.

NCT00191646

28

Adverse Events - Example

	Gemcitabine/Carboplatin Induction	Paclitaxel/Carboplatin Induction	Consolidation (Gemcitabine to Paclitaxel)	Consolidation (Paclitaxel to Paclitaxel)	Crossover (Paclitaxel to Gemcitabine)	Crossover (Gemcitabine to Paclitaxel)
Total, serious adverse events						
# participants affected / at risk	96/412 (23.30%)	72/408 (17.65%)	14/169 (8.28%)	12/183 (6.56%)	8/78 (10.26%)	8/77 (10.39%)
Blood and lymphatic system disorders						
Anaemia † [1]						
# participants affected / at risk	2/412 (0.49%)	0/408 (0.00%)	0/169 (0.00%)	0/183 (0.00%)	0/78 (0.00%)	0/77 (0.00%)
# events	3	0	0	0	0	0
Febrile neutropenia † [1]						
# participants affected / at risk	5/412 (1.21%)	9/408 (2.21%)	0/169 (0.00%)	0/183 (0.00%)	1/78 (1.28%)	1/77 (1.30%)
# events	5	11	0	0	1	2

29

NCT00191646