



Clinical trial results:

Randomized study with a run-in feasibility phase to assess the added value of Clofarabine in combination with standard remission-induction chemotherapy in patients aged 18-65 years with previously untreated acute myeloid leukemia (AML) or myelodysplasia (MDS) (RAEB with IPSS 1.5)

Summary

EudraCT number	2009-011613-24
Trial protocol	NL BE SE
Global end of trial date	07 May 2024

Results information

Result version number	v1 (current)
This version publication date	05 April 2025
First version publication date	05 April 2025

Trial information

Trial identification

Sponsor protocol code	HOVON102AML/SAKK30/09
-----------------------	-----------------------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	HOVON
Sponsor organisation address	Dr. Molewaterplein 40, Rotterdam, Netherlands,
Public contact	HOVON , HOVON, +31 107041560, hovan@erasmusmc.nl
Scientific contact	HOVON , HOVON, +31 107041560, hovan@erasmusmc.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 January 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 October 2015
Global end of trial reached?	Yes
Global end of trial date	07 May 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

For part A of the study:

.. To determine the feasibility of Clofarabine when given at three possible dose levels together with standard induction cycles I and II in patients with AML/ RAEB with IPSS \geq 1.5 in a prospective comparison to standard induction cycles I and II without Clofarabine.

For part B of the study:

.. To evaluate the effect of Clofarabine at the selected feasible dose level when combined with remission induction chemotherapy cycles I and II as regards clinical outcome ("event-free survival") in comparison to remission induction cycles I and II with no addition of Clofarabine in a phase III study.

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 February 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Switzerland: 225
Country: Number of subjects enrolled	Netherlands: 483
Country: Number of subjects enrolled	Norway: 14
Country: Number of subjects enrolled	Sweden: 1
Country: Number of subjects enrolled	Belgium: 167
Worldwide total number of subjects	890
EEA total number of subjects	665

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	831
From 65 to 84 years	59
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

All subjects gave written informed consent and were screened according to the inclusion- and exclusion criteria

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Control group

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Idarubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

12 mg/m² 3 hr infusion Days 1, 2, 3

Arm title	Experimental 10 mg
------------------	--------------------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Clofarabine 10mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

10 mg/m², 1 hr infusion Days 1 thru 5

Arm title	Experimental 15 mg
------------------	--------------------

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Clofarabine 15mg
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Infusion

Dosage and administration details:

15 mg/m², 1 hr infusion Days 1 thru 5

Number of subjects in period 1	Control group	Experimental 10 mg	Experimental 15 mg
Started	445	413	32
Completed	313	257	15
Not completed	132	156	17
Adverse events, all combined	5	28	2
Other	35	38	2
Unknown	1	3	-
Lack of efficacy	91	87	13

Baseline characteristics

Reporting groups

Reporting group title	Overall period
-----------------------	----------------

Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	890	890	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	890	890	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	387	387	
Male	503	503	

End points

End points reporting groups

Reporting group title	Control group
Reporting group description: -	
Reporting group title	Experimental 10 mg
Reporting group description: -	
Reporting group title	Experimental 15 mg
Reporting group description: -	

Primary: Primary endpoint

End point title	Primary endpoint ^[1]
End point description:	
End point type	Primary
End point timeframe:	
See publication	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: See HO102 statistical data section from publication 23-03-20217

End point values	Control group	Experimental 10 mg	Experimental 15 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	445	413	32	
Units: Whole	445	413	32	

Attachments (see zip file)	HO102_Statistical data section from publication_23-03-2017 HO102 List of reported non-Sae's (1).pdf HO102 List of reported SAE's (1).pdf
-----------------------------------	--

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs of CTCAE grade 2 or higher, with the exception of alopecia, nausea/vomiting and progression of the disease under study, have to be reported on the Adverse Events CRF.

Assessment type	Systematic
-----------------	------------

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Control group
Reporting group description: -	
Reporting group title	Clofa 10mg
Reporting group description: -	
Reporting group title	Clofa 15mg
Reporting group description: -	

Serious adverse events	Control group	Clofa 10mg	Clofa 15mg
Total subjects affected by serious adverse events			
subjects affected / exposed	161 / 440 (36.59%)	197 / 407 (48.40%)	18 / 32 (56.25%)
number of deaths (all causes)	281	243	18
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma in lung			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large B-cell lymphoma			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteosarcoma			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Solitary fibrous tumour			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Acute vascular leak syndrome			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemorrhage			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemorrhagic shock			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic event			
subjects affected / exposed	2 / 440 (0.45%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Capillary leak			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Shock			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Reversal of colostomy right and jejunostomy left			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Constipation			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	1 / 440 (0.23%)	4 / 407 (0.98%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	4 / 440 (0.91%)	5 / 407 (1.23%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	2 / 4	2 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever (in the absence of neutropenia)			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever eci			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever no focus			

subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gall bladder necrosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucositis			
subjects affected / exposed	1 / 440 (0.23%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi organ failure			
subjects affected / exposed	2 / 440 (0.45%)	1 / 407 (0.25%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	1 / 2	0 / 1	2 / 2
deaths causally related to treatment / all	1 / 2	0 / 1	1 / 1
Malaise			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SIRS			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever (with cough)			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Allergic reaction			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cutaneous GvHD grade 3			

subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GvHD			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ARDS			
subjects affected / exposed	2 / 440 (0.45%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis right lung			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	6 / 440 (1.36%)	1 / 407 (0.25%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	1 / 6	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	1 / 1
Hemoptysis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Interstitial pneumonia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 440 (0.45%)	1 / 407 (0.25%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	7 / 440 (1.59%)	4 / 407 (0.98%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	4 / 7	3 / 4	0 / 0
deaths causally related to treatment / all	1 / 1	2 / 2	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 440 (0.23%)	2 / 407 (0.49%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Respiratory insufficiency			
subjects affected / exposed	6 / 440 (1.36%)	19 / 407 (4.67%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	4 / 5	16 / 19	0 / 0
deaths causally related to treatment / all	2 / 2	3 / 4	0 / 0
Bronchopulmonary hemorrhage			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hypoxia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung embolism			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary infiltrates			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism with ARDS			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute dyspnoe due to pulmonary oedema			
subjects affected / exposed	0 / 440 (0.00%)	0 / 407 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute psychosis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
C-difficile toxin intoxication			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
ECG QT time corrected prolonged			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GGT elevated			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Low potassium				
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Platelet count decreased				
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Prolonged QT time				
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Increased liver values				
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Surgical procedure: biopsy vertebral body				
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Weight loss				
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
AST, ALT increased				
subjects affected / exposed	0 / 440 (0.00%)	0 / 407 (0.00%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
Elevated liverenzymes				
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	1 / 32 (3.13%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0	
GGT increased				

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic rupture			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Neoral toxicity			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic rupture			
subjects affected / exposed	2 / 440 (0.45%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tacrolimus intoxication			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug toxicity			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			

Prolonged aplasia			
subjects affected / exposed	2 / 440 (0.45%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	2 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 440 (0.45%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 440 (0.23%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Heart failure			
subjects affected / exposed	3 / 440 (0.68%)	4 / 407 (0.98%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	3 / 3	4 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
Left ventricular systolic dysfunction			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infection (non SCT elevated)			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pericarditis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Symptomatic bradycardia with possible circulation arrest			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardic atrial fibrillation			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Torsade			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Asystole			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block			
subjects affected / exposed	0 / 440 (0.00%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardial ischemia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathie			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrhythmia grade 4			
subjects affected / exposed	0 / 440 (0.00%)	0 / 407 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CVA			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Carbonarcosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cognitive disturbance			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	1 / 440 (0.23%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy crisis			

subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plexitis right thigh			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stroke			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
CNS hemorrhage			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral bleeding			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cerebral edema			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cerebral hemorrhage			
subjects affected / exposed	0 / 440 (0.00%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
Cerebrovascular accident			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Dysarthria			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epileptic insult			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Intercranial hemorrhage			
subjects affected / exposed	4 / 440 (0.91%)	3 / 407 (0.74%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	3 / 4	3 / 3	0 / 0
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Neurologic toxicity			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral motor neuropathy			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 440 (0.00%)	0 / 407 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Bone marrow hypocellular			

subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 440 (0.23%)	3 / 407 (0.74%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever in aplasia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic fever			
subjects affected / exposed	2 / 440 (0.45%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	3 / 3	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Thrombopenia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Agranulocytosis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	3 / 440 (0.68%)	0 / 407 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	2 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			

subjects affected / exposed	0 / 440 (0.00%)	0 / 407 (0.00%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Monocular diplopia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	3 / 440 (0.68%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Colonic perforation			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhea			
subjects affected / exposed	2 / 440 (0.45%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Digestive hemorrhage			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Gastric hemorrhage			

subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Gastric perforation			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	3 / 440 (0.68%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 3	0 / 0	0 / 0
Ileus grade 4			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic colitis			
subjects affected / exposed	2 / 440 (0.45%)	1 / 407 (0.25%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	2 / 2	1 / 1	1 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Neutropenic enterocolitis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Obstipation			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Esophageal hemorrhage			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastro intestinal disorders			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Jejunal hemorrhage			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mallory Weiss syndrome			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paralytic Ileus			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Typhlitis			
subjects affected / exposed	0 / 440 (0.00%)	4 / 407 (0.98%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	4 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	3 / 440 (0.68%)	2 / 407 (0.49%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	1 / 3	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Toxic hepatic cytolysis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gall bladder inflammation			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepathotoxicity			
subjects affected / exposed	0 / 440 (0.00%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Hepatic toxicity			
subjects affected / exposed	0 / 440 (0.00%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyper bilirubinemia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver dysfunction			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Intestinal obstruction			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bullous dermatitis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythroderma			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leucocytoclastic vasculitis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palmar erythema			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 440 (0.00%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin toxicity			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute renal insufficiency			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Kidney insufficiency			

subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hematuria			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrolithiasis			
subjects affected / exposed	0 / 440 (0.00%)	0 / 407 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
SIADH			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Fasciitis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CPK increased			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Osteonecrosis of jaw			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Infections and infestations			
(Aspergillosis) pulmonary infection			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	1 / 1
Spondylodiscitis			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergilloma			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspergillosis			
subjects affected / exposed	1 / 440 (0.23%)	3 / 407 (0.74%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration pneumonia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bilateral pneumonia			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial infection			
subjects affected / exposed	2 / 440 (0.45%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida sepsis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter related infection			

subjects affected / exposed	3 / 440 (0.68%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
E-coli - sepsis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Gastro -enteritis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection Tyflitt			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection billiary tract			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Infection upper way			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myositis			

subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	10 / 440 (2.27%)	2 / 407 (0.49%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	9 / 10	1 / 2	1 / 1
deaths causally related to treatment / all	2 / 3	0 / 0	0 / 0
Lung infection (abscess)			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinal infection			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Necrotizing fasciitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Neutropenic streptococcus sepsis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumocystis carinii - pneumonia			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	9 / 440 (2.05%)	11 / 407 (2.70%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	9 / 9	11 / 12	1 / 1
deaths causally related to treatment / all	5 / 5	6 / 6	0 / 0
Pneumosepsis (coli +)			

subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pulmonary infection			
subjects affected / exposed	1 / 440 (0.23%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pulmonary invasive aspergillosis			
subjects affected / exposed	1 / 440 (0.23%)	2 / 407 (0.49%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	1 / 1	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Sepsis			
subjects affected / exposed	22 / 440 (5.00%)	30 / 407 (7.37%)	2 / 32 (6.25%)
occurrences causally related to treatment / all	18 / 24	29 / 33	3 / 3
deaths causally related to treatment / all	7 / 10	10 / 12	1 / 1
Sepsis (septic pneumonia)			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis E-coli ESBL			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	4 / 440 (0.91%)	10 / 407 (2.46%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	2 / 4	6 / 10	0 / 0
deaths causally related to treatment / all	1 / 2	4 / 4	0 / 0
Septicemia			
subjects affected / exposed	1 / 440 (0.23%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Sinusitis			

subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis maxillaris both sides			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adeno viremia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Bacteremia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candidemia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral aspergillosis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EBV reactivation			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive infection cerebral			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningo encephalitis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Mucormycosis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Mucosal infection			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CMV reactivation			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Para influenza type 3			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary fungal infection			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection both thighs			

subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subacute cutaneous abcess			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suspicion of pulmonary aspergillosis			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Zona			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Zygomycetes infection			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Iatrogenic pneumothorax			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT interval prolonged			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster			
subjects affected / exposed	0 / 440 (0.00%)	0 / 407 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection other-blood			

subjects affected / exposed	0 / 440 (0.00%)	0 / 407 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Metabolism and nutrition disorders			
Diabetic ketoacidosis			
subjects affected / exposed	1 / 440 (0.23%)	0 / 407 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	1 / 440 (0.23%)	2 / 407 (0.49%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorexia			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumor lysis syndrome			
subjects affected / exposed	0 / 440 (0.00%)	1 / 407 (0.25%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Control group	Clofa 10mg	Clofa 15mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	435 / 440 (98.86%)	403 / 407 (99.02%)	31 / 32 (96.88%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified	Additional description: All combined		
subjects affected / exposed	4 / 440 (0.91%)	6 / 407 (1.47%)	0 / 32 (0.00%)
occurrences (all)	4	7	0
Vascular disorders			
Vascular disorders	Additional description: All combined		
subjects affected / exposed	111 / 440 (25.23%)	111 / 407 (27.27%)	7 / 32 (21.88%)
occurrences (all)	145	170	9

Surgical and medical procedures			
Surgical and medical procedures	Additional description: All combined		
subjects affected / exposed	3 / 440 (0.68%)	4 / 407 (0.98%)	1 / 32 (3.13%)
occurrences (all)	4	4	1
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All combined		
subjects affected / exposed	154 / 440 (35.00%)	156 / 407 (38.33%)	9 / 32 (28.13%)
occurrences (all)	268	296	17
Immune system disorders			
Immune system disorders	Additional description: All combined		
subjects affected / exposed	32 / 440 (7.27%)	42 / 407 (10.32%)	2 / 32 (6.25%)
occurrences (all)	38	58	2
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined		
subjects affected / exposed	20 / 440 (4.55%)	15 / 407 (3.69%)	2 / 32 (6.25%)
occurrences (all)	25	17	2
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined		
subjects affected / exposed	136 / 440 (30.91%)	141 / 407 (34.64%)	8 / 32 (25.00%)
occurrences (all)	203	243	18
Psychiatric disorders			
Psychiatric disorders	Additional description: All combined		
subjects affected / exposed	57 / 440 (12.95%)	80 / 407 (19.66%)	3 / 32 (9.38%)
occurrences (all)	74	111	4
Investigations			
Investigations	Additional description: All combined		
subjects affected / exposed	178 / 440 (40.45%)	203 / 407 (49.88%)	16 / 32 (50.00%)
occurrences (all)	607	786	45
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All combined		
subjects affected / exposed	16 / 440 (3.64%)	11 / 407 (2.70%)	2 / 32 (6.25%)
occurrences (all)	19	12	5
Congenital, familial and genetic disorders			

Congenital, familial and genetic disorders	Additional description: All combined		
subjects affected / exposed	1 / 440 (0.23%)	2 / 407 (0.49%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
Cardiac disorders	Additional description: All combined		
Cardiac disorders	Additional description: All combined		
subjects affected / exposed	60 / 440 (13.64%)	71 / 407 (17.44%)	7 / 32 (21.88%)
occurrences (all)	70	91	10
Nervous system disorders	Additional description: All combined		
Nervous system disorders	Additional description: All combined		
subjects affected / exposed	93 / 440 (21.14%)	98 / 407 (24.08%)	3 / 32 (9.38%)
occurrences (all)	126	150	3
Blood and lymphatic system disorders	Additional description: All combined		
Blood and lymphatic system disorders	Additional description: All combined		
subjects affected / exposed	318 / 440 (72.27%)	276 / 407 (67.81%)	20 / 32 (62.50%)
occurrences (all)	721	704	42
Ear and labyrinth disorders	Additional description: All combined		
Ear and labyrinth disorders	Additional description: All combined		
subjects affected / exposed	8 / 440 (1.82%)	12 / 407 (2.95%)	0 / 32 (0.00%)
occurrences (all)	8	13	0
Eye disorders	Additional description: All combined		
Eye disorders	Additional description: All combined		
subjects affected / exposed	60 / 440 (13.64%)	56 / 407 (13.76%)	3 / 32 (9.38%)
occurrences (all)	62	61	3
Gastrointestinal disorders	Additional description: All combined		
Gastrointestinal disorders	Additional description: All combined		
subjects affected / exposed	357 / 440 (81.14%)	338 / 407 (83.05%)	25 / 32 (78.13%)
occurrences (all)	945	990	55
Hepatobiliary disorders	Additional description: All combined		
Hepatobiliary disorders	Additional description: All combined		
subjects affected / exposed	30 / 440 (6.82%)	28 / 407 (6.88%)	1 / 32 (3.13%)
occurrences (all)	36	31	1
Skin and subcutaneous tissue disorders	Additional description: All combined		
Skin and subcutaneous tissue disorders	Additional description: All combined		
subjects affected / exposed	280 / 440 (63.64%)	268 / 407 (65.85%)	22 / 32 (68.75%)
occurrences (all)	461	521	52
Renal and urinary disorders			

Renal and urinary disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	52 / 440 (11.82%) 60	64 / 407 (15.72%) 78	2 / 32 (6.25%) 2
Endocrine disorders Endocrine disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	4 / 440 (0.91%) 4	4 / 407 (0.98%) 4	1 / 32 (3.13%) 1
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue dis subjects affected / exposed occurrences (all)	Additional description: All combined		
	55 / 440 (12.50%) 67	56 / 407 (13.76%) 78	2 / 32 (6.25%) 2
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	Additional description: All combined		
	326 / 440 (74.09%) 778	303 / 407 (74.45%) 812	22 / 32 (68.75%) 58
Metabolism and nutrition disorders Metabolism and nutrition disorders subjects affected / exposed occurrences (all)	Additional description: All combined		
	187 / 440 (42.50%) 536	210 / 407 (51.60%) 701	11 / 32 (34.38%) 31

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 January 2010	Addition of Maxima MC as participating site
09 March 2010	Addition of Reinier de Graaf Gasthuis as participating site
27 April 2010	Addition of GZA hospitals as participating site
14 September 2010	Changes in protocol (statistician, number of patients part A)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/34953042>