



Clinical trial results: Clofarabine added to prephase and consolidation therapy in acute lymphoblastic leukemia in adults.

Summary

EudraCT number	2008-005798-36
Trial protocol	NL BE
Global end of trial date	04 September 2023

Results information

Result version number	v1 (current)
This version publication date	12 June 2024
First version publication date	12 June 2024

Trial information

Trial identification

Sponsor protocol code	HOVON100ALL/EORTC06083
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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. Molenwaterplein 40, Rotterdam, Netherlands,
Public contact	Clinical Trial Center, HDC, HOVON, +31 (0)107041560, hdc@erasmusmc.nl
Scientific contact	Clinical Trial Center, HDC, HOVON, +31 (0)107041560, hdc@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	23 April 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 January 2021
Global end of trial reached?	Yes
Global end of trial date	04 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase II part

- To determine the feasibility of adding i.v. clofarabine to standard prephase therapy (followed by induction chemotherapy)

Phase III part

- To improve EFS in adult ALL patients by the addition of i.v. clofarabine to the standard prephase and consolidation therapy

Protection of trial subjects:

Monitoring and Insurance

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 October 2009
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	Netherlands: 308
Country: Number of subjects enrolled	Belgium: 64
Country: Number of subjects enrolled	France: 4
Worldwide total number of subjects	376
EEA total number of subjects	376

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 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	350
From 65 to 84 years	26
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

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
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Arm title	Control group
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Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Prednisolone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Predniso(lo)ne 60 mg/m², divided in 2 daily doses p.o. 1-7

Arm title	Clofarabine
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Arm description: -

Arm type	Experimental
Investigational medicinal product name	Clofarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

At study start, patients are assigned to a dose level Clofarabine of 20 mg/m² /day (x5), if randomized for arm B. If this dose is not feasible according to the decision rules as described in section 17, the dose of clofarabine to be randomized for will be reduced to 15 mg/m² /day (x5). If the dose of 20 mg/m² /day (x5) is feasible, the dose is increased to 30 mg/m² /day (x5). Depending on the advice of the DSMB, the dose of clofarabine will be decreased or increased.

Number of subjects in period 1	Control group	Clofarabine
Started	187	189
Completed	111	101
Not completed	76	88
Adverse events, all combined	13	25
Other	12	19
At patients request	1	1
Lack of efficacy	50	43

Baseline characteristics

Reporting groups

Reporting group title	Overall period
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Reporting group description: -

Reporting group values	Overall period	Total	
Number of subjects	376	376	
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)	376	376	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous			
Units: years			
median	42		
full range (min-max)	18 to 70	-	
Gender categorical			
Units: Subjects			
Female	151	151	
Male	225	225	

End points

End points reporting groups

Reporting group title	Control group
Reporting group description: -	
Reporting group title	Clofarabine
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 attached chart/documents for results

End point values	Control group	Clofarabine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	187	189		
Units: Whole	187	189		

Attachments (see zip file)	nonsaedata100-19Dec2023.pdf HO100_Statistical data section form publication_220222.pdf saedata100-19Dec2023.pdf
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

1Z97X3840472674552 Serious Adverse Events (SAEs) will be reported from the first study-related procedure until 30 days following the last protocol treatment or until the start of subsequent systemic therapy for the disease under study, if earlier.

Assessment type	Systematic
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Dictionary used

Dictionary name	CTCAE
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Dictionary version	3
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Reporting groups

Reporting group title	Control group
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Reporting group description: -

Reporting group title	Experimental clofarabine
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Reporting group description: -

Serious adverse events	Control group	Experimental clofarabine	
Total subjects affected by serious adverse events			
subjects affected / exposed	112 / 186 (60.22%)	142 / 188 (75.53%)	
number of deaths (all causes)	78	72	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Admission based on ebv lymphoproliferative disorder			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Neoplasm malignant			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
EBV + lymphomatoid granulomatosis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Thromboembolic event, pulmonary embolism			

subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bleeding			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Collaps			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 186 (1.08%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	2 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prolonged clotting times (PT/aPTT)			
alternative dictionary used: MedDRA 3			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thromboembolic event			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	2 / 186 (1.08%)	4 / 188 (2.13%)	
occurrences causally related to treatment / all	2 / 2	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombus mass in the right jugular vein & inf vena subclavion			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			

Cholecystectomy			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nefrectomy left			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Death nos			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Extravasation			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever			
subjects affected / exposed	9 / 186 (4.84%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	3 / 10	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever (not neutropenic)			
subjects affected / exposed	2 / 186 (1.08%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fever e.c.i			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Loss of strength in both legs subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection subjects affected / exposed	1 / 186 (0.54%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise subjects affected / exposed	3 / 186 (1.61%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucositis subjects affected / exposed	5 / 186 (2.69%)	5 / 188 (2.66%)	
occurrences causally related to treatment / all	5 / 6	7 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pain thorax subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Edema subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
AGvHD subjects affected / exposed	2 / 186 (1.08%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
GHVD subjects affected / exposed	5 / 186 (2.69%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	3 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Allergic reaction			

subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
GvHD skin			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Peri-engraftment respiratory distress syndrome			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	3 / 186 (1.61%)	3 / 188 (1.60%)	
occurrences causally related to treatment / all	1 / 3	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory insufficiency			
subjects affected / exposed	3 / 186 (1.61%)	5 / 188 (2.66%)	
occurrences causally related to treatment / all	2 / 3	3 / 5	
deaths causally related to treatment / all	1 / 1	0 / 0	
Lung embolism			
subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary hemorrhage			

subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnea			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxemia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusion			
subjects affected / exposed	2 / 186 (1.08%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mood alteration: depression			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychosis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
ASAT/ALAT elevation			
subjects affected / exposed	1 / 186 (0.54%)	3 / 188 (1.60%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood/bilirubin increased			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
GGT increased			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Increased liver enzymes			
subjects affected / exposed	1 / 186 (0.54%)	3 / 188 (1.60%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme disorder			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases elevated			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Allergic reaction on trombocyte transfusion			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Morfine-intoxication			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic vertebral collapse			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Second osteoporotic fracture			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural hematoma bilateral			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
CNS hemorrhage			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radiation pneumonitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spontaneous rupture of the spleen			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcapital fracture left hip			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access complication			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocard infarction			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute coronary syndrome			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest seizure			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
CVA			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral thrombosis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsive syncope			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Critical illness neuropathy (motor-neuropathy)			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug toxicity			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 186 (0.54%)	7 / 188 (3.72%)	
occurrences causally related to treatment / all	0 / 1	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischemia cerebrovascular			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder transient cerebral dysfunction			

subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Neurological symptoms		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Neuropathy		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Seizure		
subjects affected / exposed	2 / 186 (1.08%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sinus thrombosis		
subjects affected / exposed	2 / 186 (1.08%)	2 / 188 (1.06%)
occurrences causally related to treatment / all	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Vasovagal episode		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Acute serotenergic syndrome		
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Insult		
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Admission for dizziness		

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CSF leak			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral encephalopathy			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cortical vein thrombosis (left)			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic cranial hypertension			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periferal motor tremor neuropathy (PNP)			
subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radicular syndrome			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke (heamorrhagic)			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	11 / 186 (5.91%)	14 / 188 (7.45%)	
occurrences causally related to treatment / all	11 / 11	14 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemolytic anemia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic fever			
subjects affected / exposed	7 / 186 (3.76%)	10 / 188 (5.32%)	
occurrences causally related to treatment / all	6 / 7	10 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subfebrile neutropenia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anemia			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile non-neutropenia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal perforation			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute pancreatitis			
subjects affected / exposed	2 / 186 (1.08%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	2 / 186 (1.08%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis, infectious			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	3 / 186 (1.61%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	1 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhea			

subjects affected / exposed	4 / 186 (2.15%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Distal ileitis		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Enterocolitis		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hematemesis		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hemorrhagic gastritis		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nausea vomiting		
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Nausea, throw up		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Obstruction colon		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Oral mucositis		

subjects affected / exposed	2 / 186 (1.08%)	2 / 188 (1.06%)
occurrences causally related to treatment / all	1 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Oral mucositis grade 3		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatitis		
subjects affected / exposed	1 / 186 (0.54%)	3 / 188 (1.60%)
occurrences causally related to treatment / all	1 / 1	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Vomiting		
subjects affected / exposed	3 / 186 (1.61%)	4 / 188 (2.13%)
occurrences causally related to treatment / all	3 / 3	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Gingivostomatitis		
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ileus/ileum		
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	1 / 11
deaths causally related to treatment / all	0 / 0	0 / 0
Stomach antral vascular ectasia		
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Drug induced stomatitis		
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastro intestinal bleeding		

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
High esophageal ulceration			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal mucositis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischemic colitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left sacro ileitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucocutaneous ulcer small intestine			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal reflux			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paralytic ileus			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post functional pain			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis and ulcerative oesophagitis with herpes infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis (acalculouse)			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	2 / 186 (1.08%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hepatic impairment			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic veno-occlusive disease			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function disorder			

subjects affected / exposed	1 / 186 (0.54%)	7 / 188 (3.72%)	
occurrences causally related to treatment / all	1 / 1	6 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug induced hepatitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver failure			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash/desquamation			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute renal insufficiency			
subjects affected / exposed	3 / 186 (1.61%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			

subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute renal toxicity			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney failure			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney stone			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstruction ureter urolithiase			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Muscle pain			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Backpain			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bone pain			
subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain hip			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain right flank			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal infection			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Airway infection			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteremia (Enterobacter cloacae)			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CVL infection (Hickman)			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter related infection			
subjects affected / exposed	2 / 186 (1.08%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catheter sepsis			

subjects affected / exposed	2 / 186 (1.08%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cellulitis orbita sinistra		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dental infection		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Device related infection		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
E. Coli sepsis		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Fungal infection		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastro enteritis		
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
HHV6 pneumonia		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0
Infection		

subjects affected / exposed	2 / 186 (1.08%)	2 / 188 (1.06%)
occurrences causally related to treatment / all	2 / 2	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Infection (CVC with normal ANC)		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infection candida		
subjects affected / exposed	1 / 186 (0.54%)	2 / 188 (1.06%)
occurrences causally related to treatment / all	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Infection catheter related		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infection - wound (retrosternal)		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infection wound (retrosternal)		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infection catheter related (CVC)		
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infection e.c.i.		
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Infection gastrointestinal (norovirus)		

subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection grade 4 ANC			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection normal ANC			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection skin: erysipelas			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection with normal ANC general: blood and pleural			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection urinary tract			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Opportunistic infection (oesophagus)			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PJP infection			

subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	4 / 186 (2.15%)	11 / 188 (5.85%)	
occurrences causally related to treatment / all	4 / 5	11 / 13	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonal aspergillus infection			
subjects affected / exposed	1 / 186 (0.54%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory infection			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rota virus infection			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis with pseudomonas aeruginosa			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	3 / 186 (1.61%)	5 / 188 (2.66%)	
occurrences causally related to treatment / all	2 / 3	3 / 6	
deaths causally related to treatment / all	1 / 2	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylodiscitis			

subjects affected / exposed	2 / 186 (1.08%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory infection			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 186 (1.08%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection with grade 4 neutrophils			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perianal abscess			
subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicular abscess			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
CMV reactivation			
subjects affected / exposed	0 / 186 (0.00%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
CNS bacteriamia			
subjects affected / exposed	0 / 186 (0.00%)	3 / 188 (1.60%)	
occurrences causally related to treatment / all	0 / 0	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
E coli urinary tract infection and e faecalis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
E.coli bacterimia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia coli sepsis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 186 (0.00%)	4 / 188 (2.13%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	1 / 1	
Herpes simplex infection			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection candidaemia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection central venous catheter			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection lung pneumocystis jirovecii			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucormycosis (zymycosis) of sinus			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pansinusitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumococcus pneumonia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytical virus infection			

subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
S.aureus bacteremia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic arthritis at right sacroiliac joint			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcus epidermidis septicemia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella zoster virus infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral pulmonary infection			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glucose intolerance			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertriglyceridaemia			

subjects affected / exposed	1 / 186 (0.54%)	2 / 188 (1.06%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 186 (0.54%)	0 / 188 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatremia			
subjects affected / exposed	1 / 186 (0.54%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorexia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypesthesia lower body			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalemia			
subjects affected / exposed	0 / 186 (0.00%)	1 / 188 (0.53%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Control group	Experimental clofarabine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	177 / 186 (95.16%)	182 / 188 (96.81%)	
Vascular disorders			
Vascular disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	55 / 186 (29.57%)	50 / 188 (26.60%)	
occurrences (all)	68	55	
Surgical and medical procedures			
Surgical and medical procedures	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	3 / 186 (1.61%)	0 / 188 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
General disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	154 / 186 (82.80%)	171 / 188 (90.96%)	
occurrences (all)	178	187	
General disorders and administration site conditions	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	175 / 186 (94.09%)	100 / 188 (53.19%)	
occurrences (all)	185	202	
Immune system disorders			
Immune system disorders	Additional description: All combined, see non-SAE chart for details		
subjects affected / exposed	30 / 186 (16.13%)	12 / 188 (6.38%)	
occurrences (all)	35	15	
Reproductive system and breast disorders			
Reproductive system and breast disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	9 / 186 (4.84%)	3 / 188 (1.60%)	
occurrences (all)	9	5	
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All combined, see non-SAE chart for details.		
subjects affected / exposed	41 / 186 (22.04%)	36 / 188 (19.15%)	
occurrences (all)	56	63	
Investigations			
Investigations	Additional description: All combined, see non SAE chart for details		
subjects affected / exposed	123 / 186 (66.13%)	24 / 188 (12.77%)	
occurrences (all)	291	28	
Cardiac disorders			

Cardiac disorders subjects affected / exposed occurrences (all)	68 / 186 (36.56%) 69	41 / 188 (21.81%) 49	
Nervous system disorders Nervous system disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	90 / 186 (48.39%) 167	99 / 188 (52.66%) 192	
Blood and lymphatic system disorders Blood and lymphatic system disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	72 / 186 (38.71%) 90	58 / 188 (30.85%) 81	
Ear and labyrinth disorders Ear and labyrinth disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	9 / 186 (4.84%) 9	10 / 188 (5.32%) 10	
Eye disorders Eye disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	21 / 186 (11.29%) 26	17 / 188 (9.04%) 17	
Gastrointestinal disorders Gastrointestinal disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.		
	126 / 186 (67.74%) 323	133 / 188 (70.74%) 398	
Hepatobiliary disorders Hepatobiliary disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	130 / 186 (69.89%) 584	122 / 188 (64.89%) 658	
Skin and subcutaneous tissue disorders Skin and subcutaneous tissue disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.		
	77 / 186 (41.40%) 101	96 / 188 (51.06%) 111	
Renal and urinary disorders Renal and urinary disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.		
	18 / 186 (9.68%) 22	28 / 188 (14.89%) 32	
Endocrine disorders			

Endocrine disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details.		
	19 / 186 (10.22%) 19	40 / 188 (21.28%) 40	
Musculoskeletal and connective tissue disorders Musculoskeletal and connective tissue disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	25 / 186 (13.44%) 35	31 / 188 (16.49%) 41	
Infections and infestations Infections and infestations subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	123 / 186 (66.13%) 291	143 / 188 (76.06%) 419	
Metabolism and nutrition disorders Metabolims and nutrition disorders subjects affected / exposed occurrences (all)	Additional description: All combined, see non-SAE chart for details		
	128 / 186 (68.82%) 865	137 / 188 (72.87%) 1003	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 February 2011	Amendment nr. 4 was a substantial protocol amendment concerning: - small adjustments to the treatment - update of SAE chapter - addition of MRD time point
30 November 2011	Amendment nr. 6 was a substantial protocol amendment concerning: -addition of nadroparine prophylaxis to protocol treatment -- addition side study coagulation NL
20 May 2014	Amendment nr. 13 was a substantial protocol amendment concerning: - Change of PI prof. dr. J. Cornelissen to dr. A.W. Rijneveld - The designation of pharmaceuticals companies is adjusted - General clarifications of text throughout the protocol

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/34883506>