# 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 |

**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 |
| **Arm title** | Control group |

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 |

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 |
|---|---|

Reporting group description: -

| Reporting group values | Overall period | Total | |
|---|---|---|---|
| Number of subjects | 376 | 376 | |
| Age categorical<br>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<br>Units: years | | | |
| median | 42 | | |
| full range (min-max) | 18 to 70 | - | |
| Gender categorical<br>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<br>HO100_Statistical data section form publication_220222.pdf<br>saedata100-19Dec2023.pdf |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

1Z97X3840472674552Serious 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 |

### Dictionary used

| | |
|---|---|
| Dictionary name | CTCAE |
| Dictionary version | 3 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Control group |
| Reporting group description: - | |
| Reporting group title | Experimental clofarabine |
| 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 lymfoproliferative 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 | |
| Pneumonthorax | | | |
| 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 hemorrage | | | |

| | | | |
|---|---|---|---|
| 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/billirubin 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 | |
| Consvulsive 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 | | | |

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|---|---|---|---|---|
| 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 | | | | |

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|---|---|---|---|
| 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 punctional 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 | | | |
| Cholecycstitis (acalculeuze) | | | |
| 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 | |
| Hepatoxicity | | | |
| 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 abcess | | | |

| | | | |
|---|---|---|---|
| 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 | | | |

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

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