

**Clinical trial results:****A Phase 2 Multi-Center, Historically-Controlled Study of Dasatinib Added to Standard Chemotherapy in Pediatric Patients with Newly Diagnosed Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia
Summary**

| | |
|--------------------------|----------------------|
| EudraCT number | 2011-001123-20 |
| Trial protocol | IT GB Outside EU/EEA |
| Global end of trial date | 01 June 2021 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v2 (current) |
| This version publication date | 24 November 2021 |
| First version publication date | 10 June 2018 |
| Version creation reason | |

Trial information**Trial identification**

| | |
|-----------------------|-----------|
| Sponsor protocol code | CA180-372 |
|-----------------------|-----------|

Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Bristol-Myers Squibb |
| Sponsor organisation address | Chaussée de la Hulpe 185, Brussels, Belgium, 1170 |
| Public contact | EU Study Start-Up Unit, Bristol-Myers Squibb International Corporation, Clinical.Trials@bms.com |
| Scientific contact | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, Clinical.Trials@bms.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000567-PIP09-05 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Interim |
| Date of interim/final analysis | 28 May 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 28 May 2017 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 June 2021 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To compare the 3-year efficacy based on EFS of dasatinib plus chemotherapy with external historical controls, in hierarchical order, as follows: - Superiority over chemotherapy alone of AIEOP-BFM 2000 - Non-inferiority to continuous imatinib plus chemotherapy of the amended EsPhALL trial - Superiority over continuous imatinib plus chemotherapy of the amended EsPhALL trial

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonization Good Clinical Practice Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 13 April 2012 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Australia: 3 |
| Country: Number of subjects enrolled | Canada: 2 |
| Country: Number of subjects enrolled | United Kingdom: 12 |
| Country: Number of subjects enrolled | Italy: 13 |
| Country: Number of subjects enrolled | United States: 76 |
| Worldwide total number of subjects | 106 |
| EEA total number of subjects | 13 |

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 | 4 |

| | |
|---------------------------|----|
| months) | |
| Children (2-11 years) | 67 |
| Adolescents (12-17 years) | 35 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

106 participants were treated with dasatinib (82 participants received dasatinib in the tablet form exclusively and 24 participants received either tablet and/or PFOS).

Period 1

| | |
|------------------------------|----------------------------------|
| Period 1 title | Treatment Phase (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|------------------|
| Arm title | Dasatinib Cohort |
|-----------|------------------|

Arm description:

Children and adolescents newly diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia (Ph+ ALL) treated with standard multiagent chemotherapy and Dasatinib (either in tablets or Powder For Oral Suspension (PFOS)) at a dose of 60 mg/m² daily.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | Dasatinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

60 mg/m² daily

| | |
|--|--------------------|
| Investigational medicinal product name | Dasatinib |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Film-coated tablet |
| Routes of administration | Oral use |

Dosage and administration details:

60 mg/m² daily

| Number of subjects in period 1 | Dasatinib Cohort |
|--------------------------------|------------------|
| Started | 106 |
| Completed | 78 |
| Not completed | 28 |
| Adverse event, serious fatal | 2 |
| Consent withdrawn by subject | 4 |
| Adverse event, non-fatal | 8 |
| Other reasons | 9 |
| Study Drug Toxicity | 2 |

| | |
|------------------|---|
| Lack of efficacy | 3 |
|------------------|---|

Baseline characteristics

Reporting groups

| | |
|-----------------------|------------------|
| Reporting group title | Dasatinib Cohort |
|-----------------------|------------------|

Reporting group description:

Children and adolescents newly diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia (Ph+ ALL) treated with standard multiagent chemotherapy and Dasatinib (either in tablets or Powder For Oral Suspension (PFOS)) at a dose of 60 mg/m² daily.

| Reporting group values | Dasatinib Cohort | Total | |
|--|------------------|-------|--|
| Number of subjects | 106 | 106 | |
| 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) | 4 | 4 | |
| Children (2-11 years) | 67 | 67 | |
| Adolescents (12-17 years) | 35 | 35 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 9.29 | | |
| standard deviation | ± 4.467 | - | |
| Sex: Female, Male | | | |
| Units: Participants | | | |
| Female | 49 | 49 | |
| Male | 57 | 57 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 1 | 1 | |
| Asian | 5 | 5 | |
| Native Hawaiian or Other Pacific Islander | 1 | 1 | |
| Black or African American | 13 | 13 | |
| White | 85 | 85 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 1 | 1 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 24 | 24 | |
| Not Hispanic or Latino | 55 | 55 | |
| Unknown or Not Reported | 27 | 27 | |

End points

End points reporting groups

| | |
|---|---------------------|
| Reporting group title | Dasatinib Cohort |
| Reporting group description: Children and adolescents newly diagnosed with Philadelphia chromosome positive acute lymphocytic leukemia (Ph+ ALL) treated with standard multiagent chemotherapy and Dasatinib (either in tablets or Powder For Oral Suspension (PFOS)) at a dose of 60 mg/m ² daily. | |
| Subject analysis set title | Historical Controls |
| Subject analysis set type | Per protocol |
| Subject analysis set description: This subset represents the totality of historical controls used for the statistical analyses. The number of subjects are: AIEOP-BFM: N=61 EsPhALL: N=137 COG AALL0031: N=56 | |

Primary: 3-year Event-free Survival (EFS) Rate

| | |
|---|---------------------------------------|
| End point title | 3-year Event-free Survival (EFS) Rate |
| End point description: 3-year EFS rate is defined as the percentage of participants without event after 3 years since the start of study treatment. Events for EFS are defined as ANY first one of the following: · Lack of complete response in bone marrow · Relapse at any site · Development of second malignant neoplasm · Death from any cause | |
| End point type | Primary |
| End point timeframe: From first dose to 3 years following first dose | |

| End point values | Dasatinib Cohort | Historical Controls | | |
|-----------------------------------|---------------------|------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 106 | 1 ^[1] | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 90%) | 66.0 (57.7 to 73.7) | 99999 (99999 to 99999) | | |

Notes:

[1] - Historical controls were used as a comparator for statistical analyses

Statistical analyses

| | |
|---|--|
| Statistical analysis title | EFS rate_1 |
| Statistical analysis description: Difference in 3-year binomial EFS rate in all treated participants (dasatinib plus chemotherapy) vs. chemotherapy alone in AIEOP-BFM 2000 historical control | |
| Comparison groups | Dasatinib Cohort v Historical Controls |

| | |
|---|------------------------|
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.032 ^[2] |
| Method | Chi-squared |
| Parameter estimate | Estimate of Difference |
| Point estimate | 16.86 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | 3.9 |
| upper limit | 29.8 |

Notes:

[2] - Superiority test versus AIEOP-BFM 2000

| | |
|---|--|
| Statistical analysis title | EFS rate_2 |
| Statistical analysis description: | |
| Difference in 3-year binomial EFS rate for all treated participants (dasatinib plus chemotherapy) vs. continuous imatinib plus chemotherapy in the Amended EsPhALL Trial Historical Control | |
| Comparison groups | Dasatinib Cohort v Historical Controls |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.271 ^[3] |
| Method | Chi-squared |
| Parameter estimate | Estimate of difference |
| Point estimate | 6.91 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -3.3 |
| upper limit | 17.2 |

Notes:

[3] - Superiority test versus EsPhALL

| | |
|---|--|
| Statistical analysis title | EFS rate_3 |
| Comparison groups | Dasatinib Cohort v Historical Controls |
| Number of subjects included in analysis | 107 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.157 |
| Method | Chi-squared |
| Parameter estimate | Estimate of difference |
| Point estimate | -10.75 |
| Confidence interval | |
| level | 90 % |
| sides | 2-sided |
| lower limit | -22.7 |
| upper limit | 1.2 |

Secondary: Complete Remission Rate

| | |
|-----------------|-------------------------|
| End point title | Complete Remission Rate |
|-----------------|-------------------------|

End point description:

Complete Remission rate is defined as the percentage of participants achieving a complete remission, i.e. < 5% lymphoblasts in bone marrow and in CSF, with no evidence of other extramedullary disease. Complete remission will be assessed at the end of Induction IA, end of induction IB and end of the consolidation period for all treated participants.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to End of Induction Period Ia (up to 5 weeks) or Ib (up to 9 weeks) or End of Consolidation Period (up to 22 weeks)

| End point values | Dasatinib Cohort | | | |
|-----------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 106 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | | | | |
| End of Induction period Ia | 65.1 | | | |
| End of Induction period Ib | 88.7 | | | |
| End of Consolidation period | 93.4 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Experiencing Adverse Events

| | |
|-----------------|--|
| End point title | Number of Participants Experiencing Adverse Events |
|-----------------|--|

End point description:

Number of participants experiencing different types of all causality all grade adverse events

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 100 days following last dose (up to approximately 23 months)

| End point values | Dasatinib Cohort | | | |
|--------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 106 | | | |
| Units: Participants | | | | |
| Adverse Events (AEs) | 106 | | | |
| Drug-related AEs | 88 | | | |
| AEs leading to discontinuation | 7 | | | |

| | | | | |
|-------------------------------|-----|--|--|--|
| Serious Adverse Events (SAEs) | 101 | | | |
| Deaths | 15 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Event-Free Survival (EFS) Rate (Kaplan-Meier Estimates)

| | |
|-----------------|---|
| End point title | Event-Free Survival (EFS) Rate (Kaplan-Meier Estimates) |
|-----------------|---|

End point description:

Overall estimation of the EFS of dasatinib plus chemotherapy was performed utilizing the Kaplan-Meier (KM) Product Limit method. The 3-year and 5-year EFS rates were computed with the corresponding 95% CI's using Greenwood's formula. Analyses of EFS included KM plots with number of patients at risk. Participants who neither relapse nor die or who are lost to follow-up were censored on the date of their last bone marrow, CSF assessment or physical exam, whichever occurred last.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to 3 years or 5 years following first dose

| | | | | |
|-----------------------------------|---------------------|--|--|--|
| End point values | Dasatinib Cohort | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 106 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| 3-year EFS Estimate | 65.5 (55.5 to 73.7) | | | |
| 5-year EFS Estimate | 53.1 (42.8 to 62.3) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Negative for Minimal Residual Disease (MRD)

| | |
|-----------------|--|
| End point title | Percentage of Participants Negative for Minimal Residual Disease (MRD) |
|-----------------|--|

End point description:

MRD was by real-time qPCR for clone-specific immunoglobulin and T-cell receptor gene rearrangements (IG/TCR). Participants were declared as MRD negative if the MRD level is undetectable providing the assay lower limit of quantification is at least 0.1%

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

From first dose to End of Induction Period Ia (up to 5 weeks) or Ib (up to 9 weeks) or End of Consolidation Period (up to 22 weeks)

| End point values | Dasatinib Cohort | | | |
|-----------------------------------|-----------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 106 | | | |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| End of Induction period Ia | 28.3 (19.98 to 37.88) | | | |
| End of Induction period Ib | 52.8 (42.89 to 62.60) | | | |
| End of Consolidation period | 71.7 (62.12 to 80.02) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with BCR-ABL Mutations at Baseline and at Time of Disease Progression or Relapse

| | |
|-----------------|---|
| End point title | Percentage of Participants with BCR-ABL Mutations at Baseline and at Time of Disease Progression or Relapse |
|-----------------|---|

End point description:

A BCR-ABL mutation is defined as the presence of a detectable amino acid substitution in the ABL kinase domain, assessed by Real-time quantitative PCR.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At baseline (prior to start of study treatment) and at disease progression or relapse (up to approximately 3 years)

| End point values | Dasatinib Cohort | | | |
|-----------------------------------|------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 106 | | | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| At Baseline | 1.3 | | | |
| At Disease Progression or Relapse | 6.5 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All cause mortality was assessed from first dose to study completion.

SAEs and Other AEs were assessed from first dose to 100 days following last dose (up to approximately 23 months).

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 20.0 |

Reporting groups

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|-----------------------|-----------|
| Reporting group title | DASATINIB |
|-----------------------|-----------|

Reporting group description:

Subjects with Philadelphia Chromosome Positive Acute Lymphoblastic Leukemia (Ph+ ALL) were administered Dasatinib tablet (approximately equivalent to 100 mg daily for an adult) or Powder for oral suspension (PFOS) (who are unable to swallow tablets were administered Dasatinib PFOS 10 mg/milliliter) at a dose of 60 milligrams per square meter of body surface area or once daily orally in combination with standard chemotherapy and followed up for 3 years.

| Serious adverse events | DASATINIB | | |
|---|--------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 101 / 106 (95.28%) | | |
| number of deaths (all causes) | 21 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| ACUTE LYMPHOCYTIC LEUKAEMIA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| ASTROCYTOMA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LEUKAEMIA RECURRENT | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| EMBOLISM | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPERTENSION | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPOTENSION | | | |
| subjects affected / exposed | 22 / 106 (20.75%) | | |
| occurrences causally related to treatment / all | 2 / 29 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| CHILLS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DEVICE RELATED THROMBOSIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LOCALISED OEDEMA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 18 / 106 (16.98%) | | |
| occurrences causally related to treatment / all | 2 / 24 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NON-CARDIAC CHEST PAIN | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| OEDEMA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PAIN | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PYREXIA | | | |
| subjects affected / exposed | 52 / 106 (49.06%) | | |
| occurrences causally related to treatment / all | 14 / 132 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| ANAPHYLACTIC REACTION | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences causally related to treatment / all | 0 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| OEDEMA GENITAL | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Respiratory, thoracic and mediastinal disorders | | | |
| CHYLOTHORAX | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COUGH | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DYSPNOEA | | | |
| subjects affected / exposed | 4 / 106 (3.77%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| EPISTAXIS | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMOTHORAX | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPOXIA | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences causally related to treatment / all | 0 / 9 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PLEURAL EFFUSION | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | |
| occurrences causally related to treatment / all | 3 / 11 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PLEURITIC PAIN | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| PNEUMONITIS | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PULMONARY OEDEMA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RESPIRATORY DISTRESS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| STRIDOR | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| ANXIETY | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DELIRIUM | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PERSONALITY CHANGE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 5 / 106 (4.72%) | | |
| occurrences causally related to treatment / all | 2 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|-----------------|--|--|--|
| ASPARTATE AMINOTRANSFERASE INCREASED | | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | | |
| occurrences causally related to treatment / all | 2 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| BLOOD BILIRUBIN INCREASED | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 1 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| BLOOD CREATININE INCREASED | | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | | |
| occurrences causally related to treatment / all | 0 / 7 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| BLOOD CULTURE POSITIVE | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| DRUG CLEARANCE DECREASED | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ENTEROVIRUS TEST POSITIVE | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| NEUTROPHIL COUNT DECREASED | | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | | |
| occurrences causally related to treatment / all | 7 / 12 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PLATELET COUNT DECREASED | | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | | |
| occurrences causally related to treatment / all | 1 / 8 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| TRANSAMINASES INCREASED | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TROPONIN I INCREASED | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| URINE OUTPUT DECREASED | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VIRAL TEST | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| WHITE BLOOD CELL COUNT DECREASED | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences causally related to treatment / all | 1 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| WHITE BLOOD CELL COUNT INCREASED | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Injury, poisoning and procedural complications | | | |
| ALLERGIC TRANSFUSION REACTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| ANAPHYLACTIC TRANSFUSION REACTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| INFUSION RELATED REACTION | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| OVERDOSE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TOXICITY TO VARIOUS AGENTS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TRANSFUSION REACTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TRAUMATIC FRACTURE | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VASCULAR ACCESS COMPLICATION | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| CARDIAC FAILURE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| CARDIAC ARREST | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LEFT VENTRICULAR DYSFUNCTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PERICARDIAL EFFUSION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TACHYCARDIA | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SINUS TACHYCARDIA | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| CEREBRAL ISCHAEMIA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CEREBROVASCULAR ACCIDENT | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DEPRESSED LEVEL OF CONSCIOUSNESS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|-----------------|--|--|--|
| DYSARTHRIA | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ENCEPHALOPATHY | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| FACIAL PARESIS | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HAEMORRHAGE INTRACRANIAL | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HEADACHE | | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | | |
| occurrences causally related to treatment / all | 1 / 8 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HEMIPARESIS | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| LEUKOENCEPHALOPATHY | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PARAESTHESIA | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PERIPHERAL MOTOR NEUROPATHY | | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PERIPHERAL SENSORY NEUROPATHY | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME | | | |
| subjects affected / exposed | 4 / 106 (3.77%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PRESYNCOPE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SEIZURE | | | |
| subjects affected / exposed | 5 / 106 (4.72%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| ANAEMIA | | | |
| subjects affected / exposed | 13 / 106 (12.26%) | | |
| occurrences causally related to treatment / all | 12 / 25 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| FEBRILE NEUTROPENIA | | | |
| subjects affected / exposed | 81 / 106 (76.42%) | | |
| occurrences causally related to treatment / all | 41 / 277 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| FEBRILE BONE MARROW APLASIA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DISSEMINATED INTRAVASCULAR COAGULATION | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMORRHAGIC ANAEMIA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LEUKOPENIA | | | |
| subjects affected / exposed | 4 / 106 (3.77%) | | |
| occurrences causally related to treatment / all | 6 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LYMPHATIC DISORDER | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PANCYTOPENIA | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 1 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NEUTROPENIA | | | |
| subjects affected / exposed | 25 / 106 (23.58%) | | |
| occurrences causally related to treatment / all | 18 / 43 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| THROMBOCYTOPENIA | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences causally related to treatment / all | 11 / 19 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear and labyrinth disorders | | | |
| HYPOACUSIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |

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|---|-------------------|--|--|
| PHOTOPHOBIA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VISION BLURRED | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| ABDOMINAL PAIN LOWER | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ABDOMINAL PAIN | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | | |
| occurrences causally related to treatment / all | 2 / 15 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ASCITES | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ANAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CONSTIPATION | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COLITIS | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences causally related to treatment / all | 5 / 12 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DIARRHOEA | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 21 / 106 (19.81%) | | |
| occurrences causally related to treatment / all | 7 / 33 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DIARRHOEA HAEMORRHAGIC | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ENTERITIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| ENTEROCOLITIS | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTRIC HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTRIC PERFORATION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTRITIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| GASTROINTESTINAL NECROSIS | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMATOECHEZIA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ILEUS | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| INTESTINAL PERFORATION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LARGE INTESTINAL ULCER | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| LOWER GASTROINTESTINAL HAEMORRHAGE | | | |
| subjects affected / exposed | 4 / 106 (3.77%) | | |
| occurrences causally related to treatment / all | 3 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NAUSEA | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences causally related to treatment / all | 2 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NEUTROPENIC COLITIS | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences causally related to treatment / all | 0 / 7 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| OESOPHAGITIS | | | |

| | | | | |
|---|-------------------|--|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PANCREATITIS | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PANCREATITIS ACUTE | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PROCTALGIA | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PROCTITIS | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| RECTAL HAEMORRHAGE | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| STOMATITIS | | | | |
| subjects affected / exposed | 15 / 106 (14.15%) | | | |
| occurrences causally related to treatment / all | 0 / 18 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| UPPER GASTROINTESTINAL HAEMORRHAGE | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| VOMITING | | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 16 / 106 (15.09%) | | |
| occurrences causally related to treatment / all | 3 / 22 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| CHOLECYSTITIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HEPATITIS TOXIC | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VENOOCCLUSIVE LIVER DISEASE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| DERMATITIS ACNEIFORM | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RASH | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RASH GENERALISED | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RASH MACULAR | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RASH MACULO-PAPULAR | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SKIN ULCER | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| ACUTE KIDNEY INJURY | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences causally related to treatment / all | 1 / 11 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BLADDER SPASM | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CYSTITIS NONINFECTIVE | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HAEMATURIA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| NEPHROLITHIASIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| URINARY RETENTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| URINARY TRACT OBSTRUCTION | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Endocrine disorders | | | |
| ADRENAL INSUFFICIENCY | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BONE PAIN | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| MYALGIA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-------------------|--|--|
| OSTEONECROSIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 5 / 106 (4.72%) | | |
| occurrences causally related to treatment / all | 0 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| PAIN IN JAW | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| RHABDOMYOLYSIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| ABDOMINAL INFECTION | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BACTERIAL SEPSIS | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BACTERAEemia | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | | |
| occurrences causally related to treatment / all | 0 / 21 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| BRONCHITIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CANDIDA INFECTION | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 3 / 106 (2.83%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| CANDIDA PNEUMONIA | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| CATHETER SITE INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| CELLULITIS | | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| CELLULITIS OF MALE EXTERNAL GENITAL ORGAN | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| CLOSTRIDIAL INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| CLOSTRIDIUM DIFFICILE COLITIS | | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | | |
| occurrences causally related to treatment / all | 2 / 7 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| CLOSTRIDIUM DIFFICILE INFECTION | | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | | |
| occurrences causally related to treatment / all | 0 / 9 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| COCCIDIOIDOMYCOSIS | | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | | |
| occurrences causally related to treatment / all | 1 / 16 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| CYTOMEGALOVIRUS INFECTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| EMPHYEMA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ENTEROCOLITIS BACTERIAL | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ENTEROCOLITIS INFECTIOUS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ESCHERICHIA BACTERAEMIA | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| ESCHERICHIA SEPSIS | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| ESCHERICHIA URINARY TRACT INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| FUNGAL SEPSIS | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 2 | | | |
| GASTROENTERITIS | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HEPATIC INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HERPES ZOSTER | | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | | |
| occurrences causally related to treatment / all | 2 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| INFECTION | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| INFLUENZA | | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| KIDNEY INFECTION | | | | |

| | | | | |
|---|------------------|--|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| KLEBSIELLA BACTERAEMIA | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| LOCALISED INFECTION | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| LOWER RESPIRATORY TRACT INFECTION | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| LUNG INFECTION | | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | | |
| occurrences causally related to treatment / all | 1 / 13 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| MUCOSAL INFECTION | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| NAIL BED INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| NAIL INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| NEUTROPENIC INFECTION | | | | |

| | | | | |
|---|-----------------|--|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| OSTEOMYELITIS | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| OTITIS MEDIA | | | | |
| subjects affected / exposed | 5 / 106 (4.72%) | | | |
| occurrences causally related to treatment / all | 1 / 5 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PASTEURELLA INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PELVIC INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PERINEAL CELLULITIS | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PERIORBITAL CELLULITIS | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PERITONITIS | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PHARYNGITIS | | | | |

| | | | | |
|---|------------------|--|--|--|
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PNEUMONIA | | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | | |
| occurrences causally related to treatment / all | 1 / 11 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PNEUMONIA BACTERIAL | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PNEUMONIA VIRAL | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| POSTOPERATIVE WOUND INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| PSEUDOMONAL BACTERAEMIA | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| RASH PUSTULAR | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| RESPIRATORY SYNCYTIAL VIRUS INFECTION | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| SEPSIS | | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 20 / 106 (18.87%) | | |
| occurrences causally related to treatment / all | 7 / 31 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| SEPTIC EMBOLUS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SEPTIC SHOCK | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SINUSITIS | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SKIN INFECTION | | | |
| subjects affected / exposed | 4 / 106 (3.77%) | | |
| occurrences causally related to treatment / all | 2 / 9 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SPLENIC INFECTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| STREPTOCOCCAL SEPSIS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SYSTEMIC CANDIDA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| SYSTEMIC MYCOSIS | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TOOTH ABSCESS | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| TOOTH INFECTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| URINARY TRACT INFECTION | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | |
| occurrences causally related to treatment / all | 1 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| URINARY TRACT INFECTION ENTEROCOCCAL | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VIRAL DIARRHOEA | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| VIRAL UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |

| | | | | |
|---|-------------------|--|--|--|
| DECREASED APPETITE | | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | | |
| occurrences causally related to treatment / all | 1 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| DEHYDRATION | | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | | | |
| occurrences causally related to treatment / all | 3 / 17 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HYPERGLYCAEMIA | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HYPERKALAEMIA | | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HYPERNATRAEMIA | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HYPERTRIGLYCERIDAEMIA | | | | |
| subjects affected / exposed | 1 / 106 (0.94%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HYPOALBUMINAEMIA | | | | |
| subjects affected / exposed | 3 / 106 (2.83%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HYPOKALAEMIA | | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | | |
| occurrences causally related to treatment / all | 2 / 10 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| HYPONATRAEMIA | | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences causally related to treatment / all | 2 / 10 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 2 / 106 (1.89%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | DASATINIB | | |
|---|---------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 106 / 106 (100.00%) | | |
| Vascular disorders | | | |
| FLUSHING | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 13 | | |
| HAEMATOMA | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences (all) | 8 | | |
| HYPERTENSION | | | |
| subjects affected / exposed | 41 / 106 (38.68%) | | |
| occurrences (all) | 93 | | |
| HYPOTENSION | | | |
| subjects affected / exposed | 28 / 106 (26.42%) | | |
| occurrences (all) | 55 | | |
| PALLOR | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | | |
| occurrences (all) | 19 | | |
| General disorders and administration site conditions | | | |
| CATHETER SITE ERYTHEMA | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences (all) | 7 | | |
| ASTHENIA | | | |

| | | | |
|-----------------------------|-------------------|--|--|
| subjects affected / exposed | 11 / 106 (10.38%) | | |
| occurrences (all) | 19 | | |
| CATHETER SITE PAIN | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | | |
| occurrences (all) | 18 | | |
| CHILLS | | | |
| subjects affected / exposed | 20 / 106 (18.87%) | | |
| occurrences (all) | 37 | | |
| FACE OEDEMA | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 11 | | |
| FATIGUE | | | |
| subjects affected / exposed | 58 / 106 (54.72%) | | |
| occurrences (all) | 151 | | |
| INFLUENZA LIKE ILLNESS | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences (all) | 7 | | |
| GAIT DISTURBANCE | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 16 | | |
| MALAISE | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 8 | | |
| NON-CARDIAC CHEST PAIN | | | |
| subjects affected / exposed | 18 / 106 (16.98%) | | |
| occurrences (all) | 30 | | |
| MUCOSAL INFLAMMATION | | | |
| subjects affected / exposed | 51 / 106 (48.11%) | | |
| occurrences (all) | 88 | | |
| OEDEMA PERIPHERAL | | | |
| subjects affected / exposed | 17 / 106 (16.04%) | | |
| occurrences (all) | 32 | | |
| OEDEMA | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 11 | | |
| PAIN | | | |

| | | | |
|---|-------------------|--|--|
| subjects affected / exposed | 28 / 106 (26.42%) | | |
| occurrences (all) | 46 | | |
| PYREXIA | | | |
| subjects affected / exposed | 79 / 106 (74.53%) | | |
| occurrences (all) | 356 | | |
| Immune system disorders | | | |
| DRUG HYPERSENSITIVITY | | | |
| subjects affected / exposed | 17 / 106 (16.04%) | | |
| occurrences (all) | 21 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| COUGH | | | |
| subjects affected / exposed | 78 / 106 (73.58%) | | |
| occurrences (all) | 249 | | |
| ATELECTASIS | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 9 | | |
| DYSPNOEA | | | |
| subjects affected / exposed | 18 / 106 (16.98%) | | |
| occurrences (all) | 26 | | |
| EPISTAXIS | | | |
| subjects affected / exposed | 27 / 106 (25.47%) | | |
| occurrences (all) | 48 | | |
| HYPOXIA | | | |
| subjects affected / exposed | 15 / 106 (14.15%) | | |
| occurrences (all) | 22 | | |
| NASAL CONGESTION | | | |
| subjects affected / exposed | 28 / 106 (26.42%) | | |
| occurrences (all) | 52 | | |
| OROPHARYNGEAL PAIN | | | |
| subjects affected / exposed | 35 / 106 (33.02%) | | |
| occurrences (all) | 67 | | |
| PRODUCTIVE COUGH | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 13 | | |
| PLEURAL EFFUSION | | | |

| | | | |
|------------------------------|-------------------|--|--|
| subjects affected / exposed | 16 / 106 (15.09%) | | |
| occurrences (all) | 18 | | |
| RESPIRATORY TRACT CONGESTION | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 16 | | |
| RHINITIS ALLERGIC | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 9 | | |
| RHINORRHOEA | | | |
| subjects affected / exposed | 37 / 106 (34.91%) | | |
| occurrences (all) | 76 | | |
| TACHYPNOEA | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | | |
| occurrences (all) | 14 | | |
| SNEEZING | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 7 | | |
| WHEEZING | | | |
| subjects affected / exposed | 13 / 106 (12.26%) | | |
| occurrences (all) | 16 | | |
| Psychiatric disorders | | | |
| AGITATION | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 20 | | |
| ANXIETY | | | |
| subjects affected / exposed | 15 / 106 (14.15%) | | |
| occurrences (all) | 29 | | |
| DEPRESSION | | | |
| subjects affected / exposed | 16 / 106 (15.09%) | | |
| occurrences (all) | 20 | | |
| INSOMNIA | | | |
| subjects affected / exposed | 16 / 106 (15.09%) | | |
| occurrences (all) | 21 | | |
| IRRITABILITY | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | | |
| occurrences (all) | 16 | | |

| | | | |
|--------------------------------------|-------------------|--|--|
| Investigations | | | |
| ALANINE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 42 / 106 (39.62%) | | |
| occurrences (all) | 186 | | |
| ASPARTATE AMINOTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 35 / 106 (33.02%) | | |
| occurrences (all) | 102 | | |
| BLOOD BILIRUBIN INCREASED | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | | |
| occurrences (all) | 23 | | |
| BLOOD CREATININE INCREASED | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | |
| occurrences (all) | 16 | | |
| CARDIAC MURMUR | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | | |
| occurrences (all) | 27 | | |
| ELECTROCARDIOGRAM QT PROLONGED | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences (all) | 18 | | |
| GAMMA-GLUTAMYLTRANSFERASE INCREASED | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 15 | | |
| LYMPHOCYTE COUNT DECREASED | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 126 | | |
| NEUTROPHIL COUNT DECREASED | | | |
| subjects affected / exposed | 41 / 106 (38.68%) | | |
| occurrences (all) | 316 | | |
| PLATELET COUNT DECREASED | | | |
| subjects affected / exposed | 39 / 106 (36.79%) | | |
| occurrences (all) | 368 | | |
| WEIGHT DECREASED | | | |
| subjects affected / exposed | 26 / 106 (24.53%) | | |
| occurrences (all) | 38 | | |

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|---|--------------------------|--|--|
| WEIGHT INCREASED subjects affected / exposed occurrences (all) | 11 / 106 (10.38%) 36 | | |
| WHITE BLOOD CELL COUNT DECREASED subjects affected / exposed occurrences (all) | 21 / 106 (19.81%) 192 | | |
| Injury, poisoning and procedural complications | | | |
| ALLERGIC TRANSFUSION REACTION subjects affected / exposed occurrences (all) | 13 / 106 (12.26%) 18 | | |
| ARTHROPOD BITE subjects affected / exposed occurrences (all) | 6 / 106 (5.66%) 8 | | |
| CONTUSION subjects affected / exposed occurrences (all) | 32 / 106 (30.19%) 59 | | |
| SKIN ABRASION subjects affected / exposed occurrences (all) | 8 / 106 (7.55%) 16 | | |
| SUNBURN subjects affected / exposed occurrences (all) | 7 / 106 (6.60%) 7 | | |
| TRANSFUSION REACTION subjects affected / exposed occurrences (all) | 6 / 106 (5.66%) 10 | | |
| Cardiac disorders | | | |
| PERICARDIAL EFFUSION subjects affected / exposed occurrences (all) | 6 / 106 (5.66%) 6 | | |
| SINUS TACHYCARDIA subjects affected / exposed occurrences (all) | 19 / 106 (17.92%) 31 | | |
| TACHYCARDIA subjects affected / exposed occurrences (all) | 35 / 106 (33.02%) 82 | | |
| Nervous system disorders | | | |

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|--|---|--|--|
| <p> DIZZINESS subjects affected / exposed occurrences (all) </p> <p> HEADACHE subjects affected / exposed occurrences (all) </p> <p> LETHARGY subjects affected / exposed occurrences (all) </p> <p> NEUROPATHY PERIPHERAL subjects affected / exposed occurrences (all) </p> <p> PERIPHERAL MOTOR NEUROPATHY subjects affected / exposed occurrences (all) </p> <p> PERIPHERAL SENSORY NEUROPATHY subjects affected / exposed occurrences (all) </p> <p> TREMOR subjects affected / exposed occurrences (all) </p> | <p>14 / 106 (13.21%)</p> <p>30</p> | | |
| | <p>70 / 106 (66.04%)</p> <p>246</p> | | |
| | <p>7 / 106 (6.60%)</p> <p>13</p> | | |
| | <p>6 / 106 (5.66%)</p> <p>12</p> | | |
| | <p>12 / 106 (11.32%)</p> <p>17</p> | | |
| | <p>13 / 106 (12.26%)</p> <p>15</p> | | |
| | <p>8 / 106 (7.55%)</p> <p>8</p> | | |
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| <p>Blood and lymphatic system disorders</p> <p>ANAEMIA subjects affected / exposed occurrences (all)</p> <p>FEBRILE NEUTROPENIA subjects affected / exposed occurrences (all)</p> <p>LEUKOPENIA subjects affected / exposed occurrences (all)</p> <p>NEUTROPENIA subjects affected / exposed occurrences (all)</p> <p>THROMBOCYTOPENIA</p> | <p>83 / 106 (78.30%)</p> <p>773</p> <p>37 / 106 (34.91%)</p> <p>62</p> <p>12 / 106 (11.32%)</p> <p>46</p> <p>43 / 106 (40.57%)</p> <p>181</p> | | |

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|--|---|--|--|
| subjects affected / exposed occurrences (all) | 50 / 106 (47.17%) 385 | | |
| Ear and labyrinth disorders EAR PAIN subjects affected / exposed occurrences (all) | 25 / 106 (23.58%) 44 | | |
| Eye disorders EYE PAIN subjects affected / exposed occurrences (all) OCULAR HYPERAEMIA subjects affected / exposed occurrences (all) PERIORBITAL OEDEMA subjects affected / exposed occurrences (all) VISION BLURRED subjects affected / exposed occurrences (all) | 8 / 106 (7.55%) 10 7 / 106 (6.60%) 8 9 / 106 (8.49%) 12 15 / 106 (14.15%) 18 | | |
| Gastrointestinal disorders ABDOMINAL DISTENSION subjects affected / exposed occurrences (all) ABDOMINAL PAIN subjects affected / exposed occurrences (all) ABDOMINAL PAIN UPPER subjects affected / exposed occurrences (all) ANAL INFLAMMATION subjects affected / exposed occurrences (all) COLITIS subjects affected / exposed occurrences (all) CONSTIPATION | 11 / 106 (10.38%) 17 73 / 106 (68.87%) 238 19 / 106 (17.92%) 35 7 / 106 (6.60%) 9 13 / 106 (12.26%) 19 | | |

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|--|-------------------|--|--|
| subjects affected / exposed | 58 / 106 (54.72%) | | |
| occurrences (all) | 131 | | |
| DIARRHOEA | | | |
| subjects affected / exposed | 75 / 106 (70.75%) | | |
| occurrences (all) | 247 | | |
| DYSPEPSIA | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 11 | | |
| HAEMATOCHESIA | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | | |
| occurrences (all) | 28 | | |
| MOUTH ULCERATION | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 10 | | |
| NAUSEA | | | |
| subjects affected / exposed | 81 / 106 (76.42%) | | |
| occurrences (all) | 325 | | |
| ORAL PAIN | | | |
| subjects affected / exposed | 27 / 106 (25.47%) | | |
| occurrences (all) | 44 | | |
| PROCTALGIA | | | |
| subjects affected / exposed | 15 / 106 (14.15%) | | |
| occurrences (all) | 21 | | |
| STOMATITIS | | | |
| subjects affected / exposed | 49 / 106 (46.23%) | | |
| occurrences (all) | 121 | | |
| TOOTHACHE | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | |
| occurrences (all) | 13 | | |
| VOMITING | | | |
| subjects affected / exposed | 83 / 106 (78.30%) | | |
| occurrences (all) | 436 | | |
| Skin and subcutaneous tissue disorders | | | |
| ALOPECIA | | | |
| subjects affected / exposed | 21 / 106 (19.81%) | | |
| occurrences (all) | 25 | | |

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|-----------------------------|-------------------|--|--|
| DERMATITIS ACNEIFORM | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | |
| occurrences (all) | 14 | | |
| DRY SKIN | | | |
| subjects affected / exposed | 19 / 106 (17.92%) | | |
| occurrences (all) | 26 | | |
| ECCHYMOSIS | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 15 | | |
| ERYTHEMA | | | |
| subjects affected / exposed | 22 / 106 (20.75%) | | |
| occurrences (all) | 36 | | |
| PETECHIAE | | | |
| subjects affected / exposed | 17 / 106 (16.04%) | | |
| occurrences (all) | 28 | | |
| PAIN OF SKIN | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences (all) | 6 | | |
| PRURITUS | | | |
| subjects affected / exposed | 27 / 106 (25.47%) | | |
| occurrences (all) | 39 | | |
| RASH MACULO-PAPULAR | | | |
| subjects affected / exposed | 21 / 106 (19.81%) | | |
| occurrences (all) | 41 | | |
| RASH | | | |
| subjects affected / exposed | 48 / 106 (45.28%) | | |
| occurrences (all) | 120 | | |
| SWELLING FACE | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | |
| occurrences (all) | 9 | | |
| RASH PAPULAR | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 8 | | |
| URTICARIA | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | |
| occurrences (all) | 11 | | |

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|---|-------------------|--|--|
| Renal and urinary disorders | | | |
| DYSURIA | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | | |
| occurrences (all) | 16 | | |
| HAEMATURIA | | | |
| subjects affected / exposed | 13 / 106 (12.26%) | | |
| occurrences (all) | 17 | | |
| URINARY RETENTION | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences (all) | 9 | | |
| Musculoskeletal and connective tissue disorders | | | |
| BACK PAIN | | | |
| subjects affected / exposed | 48 / 106 (45.28%) | | |
| occurrences (all) | 122 | | |
| ARTHRALGIA | | | |
| subjects affected / exposed | 38 / 106 (35.85%) | | |
| occurrences (all) | 103 | | |
| BONE PAIN | | | |
| subjects affected / exposed | 22 / 106 (20.75%) | | |
| occurrences (all) | 40 | | |
| MUSCULAR WEAKNESS | | | |
| subjects affected / exposed | 21 / 106 (19.81%) | | |
| occurrences (all) | 30 | | |
| MUSCULOSKELETAL CHEST PAIN | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 15 | | |
| MYALGIA | | | |
| subjects affected / exposed | 15 / 106 (14.15%) | | |
| occurrences (all) | 30 | | |
| MUSCULOSKELETAL PAIN | | | |
| subjects affected / exposed | 15 / 106 (14.15%) | | |
| occurrences (all) | 20 | | |
| NECK PAIN | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | |
| occurrences (all) | 15 | | |
| OSTEONECROSIS | | | |

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|---------------------------------|-------------------|--|--|
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 8 | | |
| PAIN IN EXTREMITY | | | |
| subjects affected / exposed | 62 / 106 (58.49%) | | |
| occurrences (all) | 191 | | |
| PAIN IN JAW | | | |
| subjects affected / exposed | 18 / 106 (16.98%) | | |
| occurrences (all) | 30 | | |
| Infections and infestations | | | |
| CANDIDA INFECTION | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | | |
| occurrences (all) | 19 | | |
| CELLULITIS | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 10 | | |
| CLOSTRIDIUM DIFFICILE COLITIS | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | | |
| occurrences (all) | 13 | | |
| CONJUNCTIVITIS | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | | |
| occurrences (all) | 15 | | |
| CLOSTRIDIUM DIFFICILE INFECTION | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 9 | | |
| EAR INFECTION | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 7 | | |
| DEVICE RELATED INFECTION | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 9 | | |
| ENTEROCOLITIS INFECTIOUS | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 12 | | |
| INFLUENZA | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 7 | | |

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|-----------------------------------|-------------------|--|--|
| LUNG INFECTION | | | |
| subjects affected / exposed | 8 / 106 (7.55%) | | |
| occurrences (all) | 8 | | |
| ORAL CANDIDIASIS | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | | |
| occurrences (all) | 23 | | |
| PHARYNGITIS | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 11 | | |
| OTITIS MEDIA | | | |
| subjects affected / exposed | 11 / 106 (10.38%) | | |
| occurrences (all) | 15 | | |
| PNEUMONIA | | | |
| subjects affected / exposed | 6 / 106 (5.66%) | | |
| occurrences (all) | 6 | | |
| RHINITIS | | | |
| subjects affected / exposed | 10 / 106 (9.43%) | | |
| occurrences (all) | 17 | | |
| RHINOVIRUS INFECTION | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 7 | | |
| SEPSIS | | | |
| subjects affected / exposed | 7 / 106 (6.60%) | | |
| occurrences (all) | 8 | | |
| SINUSITIS | | | |
| subjects affected / exposed | 18 / 106 (16.98%) | | |
| occurrences (all) | 26 | | |
| SKIN INFECTION | | | |
| subjects affected / exposed | 12 / 106 (11.32%) | | |
| occurrences (all) | 15 | | |
| UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 39 / 106 (36.79%) | | |
| occurrences (all) | 60 | | |
| URINARY TRACT INFECTION | | | |

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|---|-------------------|--|--|
| subjects affected / exposed | 14 / 106 (13.21%) | | |
| occurrences (all) | 17 | | |
| VIRAL UPPER RESPIRATORY TRACT INFECTION | | | |
| subjects affected / exposed | 9 / 106 (8.49%) | | |
| occurrences (all) | 11 | | |
| Metabolism and nutrition disorders | | | |
| DECREASED APPETITE | | | |
| subjects affected / exposed | 40 / 106 (37.74%) | | |
| occurrences (all) | 100 | | |
| DEHYDRATION | | | |
| subjects affected / exposed | 14 / 106 (13.21%) | | |
| occurrences (all) | 18 | | |
| HYPERGLYCAEMIA | | | |
| subjects affected / exposed | 23 / 106 (21.70%) | | |
| occurrences (all) | 34 | | |
| HYPOCALCAEMIA | | | |
| subjects affected / exposed | 30 / 106 (28.30%) | | |
| occurrences (all) | 66 | | |
| HYPOALBUMINAEMIA | | | |
| subjects affected / exposed | 34 / 106 (32.08%) | | |
| occurrences (all) | 54 | | |
| HYPOKALAEMIA | | | |
| subjects affected / exposed | 50 / 106 (47.17%) | | |
| occurrences (all) | 175 | | |
| HYPOMAGNESAEMIA | | | |
| subjects affected / exposed | 19 / 106 (17.92%) | | |
| occurrences (all) | 36 | | |
| HYPONATRAEMIA | | | |
| subjects affected / exposed | 23 / 106 (21.70%) | | |
| occurrences (all) | 41 | | |
| HYPOPHOSPHATAEMIA | | | |
| subjects affected / exposed | 23 / 106 (21.70%) | | |
| occurrences (all) | 43 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-------------------|--|
| 20 September 2011 | The following amendment was developed to incorporate two key changes including: 1) Changing the statistical design of the trial to allow comparison to historical external controls. Specifically, the 3-year event free survival (EFS) of dasatinib plus chemotherapy will be compared to the 3-year EFS of chemotherapy alone from the Associazione Italiana di Ematologia Pediatrica - Berlin-Frankfurt-Muenster ALL 2000 (AIEOP BFM 2000) trial and the 3-year EFS of imatinib plus chemotherapy from the European intergroup Study on post induction treatment of Philadelphia positive Acute Lymphoblastic Leukemia (EsPhALL). This analysis will improve the ability to interpret the safety and efficacy of dasatinib added to chemotherapy among other treatment options for this pediatric leukemia. 2) Incorporating additional supportive care options for chemotherapy to accommodate the standard of care at sites in the United Kingdom (UK). Additionally, typographical errors were also corrected. |
| 07 December 2012 | The key purposes of this amendment are to incorporate the following key changes: 1) Introduce a new pediatric formulation of dasatinib. 2) Address lack of availability of native-asparaginase in the United States and allow use of Peg-Asparaginase upfront in such instances as well as provide more detailed instruction for dose modifications of the various asparaginase formulations. 3) Indicate that the BCR-ABL mutation status will be reported for baseline and at time of progression as a secondary objective instead of as an exploratory objective. 4) Allow Philadelphia chromosome positivity from peripheral blood to be acceptable for study entry. 5) Expand the window for screening activities to 21 days. 6) Modify the definition of high risk group and low/standard risk group in response to Induction 1A treatment. 7) Provides for clarifications, fixes inconsistencies across sections of the protocol and corrects various typographical errors. |
| 31 July 2013 | The key purposes of this amendment are to incorporate the following key changes: 1) Increase the number of treated subjects from 75 to at least 75 and up to 90. 2) Modify language regarding pregnancy prevention. 3) Incorporate recommendations for subject management and supportive care during High Risk (HR) Blocks 1-3. 4) Provides for clarifications, fixes inconsistencies across sections of the protocol and corrects various typographical errors. |
| 28 October 2013 | The key purposes of this amendment are to incorporate the following changes: 1) Add mandatory supportive care measures during the 3 High Risk Blocks 2) Provide updates to the WOCBP language to harmonize this language with the current BMS directives for WOCBP. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported