# Clinical trial results:
# A Randomized Two-by-Two, Multicenter, Open-Label Phase III Study of BMS-354825 Administered Orally at a Dose of 50 mg or 70 mg Twice Daily or 100 mg or 140 mg Once Daily in Subjects with Chronic Phase Philadelphia Chromosome or BCR-ABL Positive Chronic Myelogenous Leukemia Who are Resistant or Intolerant to Imatinib Mesylate.

## Summary

| | |
|---|---|
| EudraCT number | 2005-001294-99 |
| Trial protocol | AT SE GB HU DK IE CZ FI IT EE ES DE BE |
| Global end of trial date | 14 July 2014 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 22 April 2016 |
| First version publication date | 22 April 2016 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | CA180-034 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00123474 |
| 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 | Bristol-Myers Squibb Study Director, Bristol-Myers Squibb, 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) | 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 | 14 July 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 14 July 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of the study was to compare the efficacy of BMS-354825 as defined by major cytogenetic response when administered once daily relative to BMS-354825 administered twice daily in the treatment of chronic phase chronic myelogenous leukemia imatinib-resistant subjects.

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 July 2005 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 7 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Argentina: 36 |
| Country: Number of subjects enrolled | Australia: 18 |
| Country: Number of subjects enrolled | Brazil: 45 |
| Country: Number of subjects enrolled | Canada: 14 |
| Country: Number of subjects enrolled | Finland: 2 |
| Country: Number of subjects enrolled | Israel: 5 |
| Country: Number of subjects enrolled | Korea, Republic of: 46 |
| Country: Number of subjects enrolled | Mexico: 15 |
| Country: Number of subjects enrolled | Netherlands: 8 |
| Country: Number of subjects enrolled | Peru: 2 |
| Country: Number of subjects enrolled | Philippines: 7 |
| Country: Number of subjects enrolled | Poland: 19 |
| Country: Number of subjects enrolled | Russian Federation: 18 |
| Country: Number of subjects enrolled | South Africa: 9 |
| Country: Number of subjects enrolled | Singapore: 7 |
| Country: Number of subjects enrolled | Switzerland: 11 |
| Country: Number of subjects enrolled | Taiwan: 4 |

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 224 |
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | Spain: 5 |
| Country: Number of subjects enrolled | Sweden: 10 |
| Country: Number of subjects enrolled | United Kingdom: 31 |
| Country: Number of subjects enrolled | Austria: 2 |
| Country: Number of subjects enrolled | Belgium: 19 |
| Country: Number of subjects enrolled | Czech Republic: 8 |
| Country: Number of subjects enrolled | Denmark: 16 |
| Country: Number of subjects enrolled | France: 69 |
| Country: Number of subjects enrolled | Germany: 42 |
| Country: Number of subjects enrolled | Hungary: 1 |
| Country: Number of subjects enrolled | Ireland: 11 |
| Country: Number of subjects enrolled | Italy: 19 |
| Worldwide total number of subjects | 724 |
| EEA total number of subjects | 263 |

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) | 534 |
| From 65 to 84 years | 190 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Study initiated July 2005 and completed July 2014.

### Pre-assignment

Screening details:

724 subjects were enrolled, 670 were randomized, and 662 were treated with study drug. Reasons for non-randomization: 38 no longer met criteria, 8 other reasons, 7 withdrew consent, and 1 death. 1 subject was randomized to 100 mg once daily but received 50 mg twice daily; 1 subject was randomized to 50 mg twice daily but received 100 mg once daily.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Dasatinib 100 mg QD |

Arm description:

Subjects received dasatinib 100 mg once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Dasatinib |
| Investigational medicinal product code | BMS-354825-03 |
| Other name | Sprycel |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

2 Dasatinib 50-mg tablets were administered once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw.

| | |
|---|---|
| **Arm title** | Dasatinib 140 mg QD |

Arm description:

Subjects received dasatinib 140 mg once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Dasatinib |
| Investigational medicinal product code | BMS-354825-03 |
| Other name | Sprycel |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

2 Dasatinib 20-mg and 50-mg tablets were administered once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw.

| | |
|---|---|
| **Arm title** | Dasatinib 50 mg BID |

Arm description:

Subjects received dasatinib 50 mg twice daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. After the 2-year analysis, and with Protocol Amendment 02, subjects on a twice daily dosing schedule were allowed to switch to a once daily dosing schedule.

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Dasatinib |
| Investigational medicinal product code | BMS-354825-03 |
| Other name | Sprycel |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Dasatinib 50-mg tablet was administered twice daily and switching to once daily was allowed after the 2-year analysis, and with protocol amendment 02, until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw.

| | |
|---|---|
| **Arm title** | Dasatinib 70 mg BID |

Arm description:

Subjects received dasatinib 70 mg twice daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. After the 2-year analysis, and with Protocol Amendment 02, subjects on a BID dosing schedule were allowed to switch to a QD dosing schedule.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Dasatinib |
| Investigational medicinal product code | BMS-354825-03 |
| Other name | Sprycel |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Dasatinib 50-mg and 20-mg tablets were administered twice daily and switching to once daily was allowed after the 2-year analysis, and with protocol amendment 02, until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw.

| **Number of subjects in period 1[1]** | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID |
|---|---|---|---|
| Started | 167 | 167 | 168 |
| Randomized | 167 | 167 | 168 |
| Completed | 0 | 0 | 0 |
| Not completed | 167 | 167 | 168 |
| Consent withdrawn by subject | 14 | 19 | 18 |
| Disease progression | 35 | 42 | 29 |
| Adverse event, non-fatal | 10 | 4 | 10 |
| Study drug toxicity | 39 | 45 | 45 |
| Not reported | 1 | - | - |
| Randomized, never treated | 1 | 4 | 2 |
| Treated in 50 mg BID arm | 1 | - | - |
| Other reasons | 54 | 47 | 57 |
| Investigator request | 12 | 6 | 7 |

| **Number of subjects in period 1[1]** | Dasatinib 70 mg BID |
|---|---|
| Started | 168 |
| Randomized | 168 |

| | |
|---|---|
| Completed | 0 |
| Not completed | 168 |
| Consent withdrawn by subject | 16 |
| Disease progression | 27 |
| Adverse event, non-fatal | 8 |
| Study drug toxicity | 51 |
| Not reported | - |
| Randomized, never treated | 1 |
| Treated in 50 mg BID arm | - |
| Other reasons | 60 |
| Investigator request | 5 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 724 subjects were enrolled, 670 were randomized. Reasons for non-randomization: 38 no longer met criteria, 8 other reasons, 7 withdrew consent, and 1 death.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Dasatinib 100 mg QD |
| Reporting group description: | |
| Subjects received dasatinib 100 mg once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Reporting group title | Dasatinib 140 mg QD |
| Reporting group description: | |
| Subjects received dasatinib 140 mg once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Reporting group title | Dasatinib 50 mg BID |
| Reporting group description: | |
| Subjects received dasatinib 50 mg twice daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. After the 2-year analysis, and with Protocol Amendment 02, subjects on a twice daily dosing schedule were allowed to switch to a once daily dosing schedule. | |
| Reporting group title | Dasatinib 70 mg BID |
| Reporting group description: | |
| Subjects received dasatinib 70 mg twice daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. After the 2-year analysis, and with Protocol Amendment 02, subjects on a BID dosing schedule were allowed to switch to a QD dosing schedule. | |

| Reporting group values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID |
|---|---|---|---|
| Number of subjects | 167 | 167 | 168 |
| Age categorical | | | |
| Units: Subjects | | | |
| <=65 years | 121 | 128 | 130 |
| >65 years | 46 | 39 | 38 |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 54.6 | 53.7 | 53.3 |
| standard deviation | ± 13.6 | ± 15 | ± 14.6 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 83 | 97 | 83 |
| Male | 84 | 70 | 85 |
| Imatinib status | | | |
| Primary Resistance: no decrease in white blood cell count after >=4 weeks imatinib/not achieved a complete hematologic response after 3 months, a major cytogenetic response (MCyR) after 6 months, or a complete cytogenetic response (CCyR) after 12 months. Acquired resistance: achieved MCyR and no longer met the criteria for MCyR. Intolerance: Grade >=3 toxicity considered at least possibly related to imatinib at a dose of <=400 mg/day which led to discontinuation of therapy; tolerated the dose of 400 mg but did not achieve a CCyR and subsequently did not tolerate doses >=600 mg. | | | |
| Units: Subjects | | | |
| Primary Resistance to Imatinib | 75 | 78 | 88 |
| Acquired Resistance to Imatinib | 49 | 45 | 36 |
| Intolerant to Imatinib | 43 | 44 | 44 |

| Reporting group values | Dasatinib 70 mg BID | Total | |
|---|---|---|---|
| Number of subjects | 168 | 670 | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| <=65 years | 125 | 504 | |
| >65 years | 43 | 166 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 53.7 | | |
| standard deviation | ± 15 | - | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 91 | 354 | |
| Male | 77 | 316 | |
| Imatinib status | | | |
| Primary Resistance: no decrease in white blood cell count after >=4 weeks imatinib/not achieved a complete hematologic response after 3 months, a major cytogenetic response (MCyR) after 6 months, or a complete cytogenetic response (CCyR) after 12 months. Acquired resistance: achieved MCyR and no longer met the criteria for MCyR. Intolerance: Grade >=3 toxicity considered at least possibly related to imatinib at a dose of <=400 mg/day which led to discontinuation of therapy; tolerated the dose of 400 mg but did not achieve a CCyR and subsequently did not tolerate doses >=600 mg. | | | |
| Units: Subjects | | | |
| Primary Resistance to Imatinib | 81 | 322 | |
| Acquired Resistance to Imatinib | 45 | 175 | |
| Intolerant to Imatinib | 42 | 173 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Dasatinib 100 mg QD |
| Reporting group description: | |
| Subjects received dasatinib 100 mg once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Reporting group title | Dasatinib 140 mg QD |
| Reporting group description: | |
| Subjects received dasatinib 140 mg once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Reporting group title | Dasatinib 50 mg BID |
| Reporting group description: | |
| Subjects received dasatinib 50 mg twice daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. After the 2-year analysis, and with Protocol Amendment 02, subjects on a twice daily dosing schedule were allowed to switch to a once daily dosing schedule. | |
| Reporting group title | Dasatinib 70 mg BID |
| Reporting group description: | |
| Subjects received dasatinib 70 mg twice daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. After the 2-year analysis, and with Protocol Amendment 02, subjects on a BID dosing schedule were allowed to switch to a QD dosing schedule. | |
| Subject analysis set title | QD Dasatinib |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects received dasatinib either 100 mg or 140 mg once daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Subject analysis set title | BID Dasatinib |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects received dasatinib either 50 mg or 70 mg twice daily until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Subject analysis set title | Dasatinib 100 mg Total Daily Dose |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects received dasatinib 100 mg as a total daily dose (either 50 mg twice daily or 100 mg once daily) until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Subject analysis set title | Dasatinib 140 mg Total Daily Dose |
| Subject analysis set type | Intention-to-treat |
| Subject analysis set description: | |
| Subjects received dasatinib 140 mg as a total daily dose (either 70 mg twice daily or 140 mg once daily) until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Subject analysis set title | Other Treatment Groups |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Subjects participated in all other treatment arms until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |
| Subject analysis set title | Total |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Subjects received study drug in any schedule or total daily dose until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. | |

## Primary: Percentage of Subjects With Major Cytogenetic Response (MCyR) After at Least 6 Months Follow-Up - Imatinib-Resistant Subjects

| End point title | Percentage of Subjects With Major Cytogenetic Response (MCyR) After at Least 6 Months Follow-Up - Imatinib-Resistant Subjects |
|---|---|

End point description:

Cytogenetic response (CyR) was based on the number of Philadelphia chromosome positive (Ph+) metaphases among cells in metaphase on a Bone Marrow (BM) sample. The criteria for CyR were as follows: Complete cytogenetic response (CCyR): 0% Ph+ cells in metaphase in BM; Partial CyR (PCyR): >0 to 35% Ph+ cells in metaphase in BM; Minor cytogenetic response: >35 to 65% Ph+ cells in metaphase in BM; Minimal cytogenetic response: >65 to 95% Ph+ cells in metaphase in BM; No cytogenetic response: >95 to 100% Ph+ cells in metaphase in BM; Best CyR was defined as the best response obtained at any time during the study; MCyR was defined as a best CyR of CCyR or PCyR. Baseline=closest to, but no later than, the first day of study drug for treated subjects and closest to, but no later than, the date of randomization, for those who were randomized but who never received treatment, unless otherwise specified. All randomized imatinib-resistant subjects with available data were summarized

| End point type | Primary |
|---|---|

End point timeframe:

Baseline up to at Least 6 Months follow-up

| **End point values** | QD Dasatinib | BID Dasatinib | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 247 | 251 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 51.8 (45.4 to 58.2) | 49 (42.7 to 55.4) | | |

### Statistical analyses

| **Statistical analysis title** | MCyR: 6 month follow-up analysis |
|---|---|
| Comparison groups | QD Dasatinib v BID Dasatinib |
| Number of subjects included in analysis | 498 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[1] |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 2.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6 |
| upper limit | 11.6 |

Notes:

[1] - Non-inferiority of the QD schedule relative to the BID schedule was deduced if the lower bound of the 95% confidence interval (CI) for the MCyR QD minus MCyR BID difference was greater than or equal to -15%.

## Secondary: Percentage of Subjects With Major Cytogenetic Response (MCyR) at or Prior to 24 Months Follow-Up - Imatinib-Resistant Subjects

| End point title | Percentage of Subjects With Major Cytogenetic Response (MCyR) at or Prior to 24 Months Follow-Up - Imatinib-Resistant |
|---|---|

| | |
|---|---|
| | Subjects |

End point description:

Cytogenetic response (CyR) was based on the number of Philadelphia chromosome positive (Ph+) metaphases among cells in metaphase on a Bone Marrow (BM) sample. The criteria for CyR were as follows: Complete cytogenetic response (CCyR): 0% Ph+ cells in metaphase in BM; Partial CyR (PCyR): >0 to 35% Ph+ cells in metaphase in BM; Minor cytogenetic response: >35 to 65% Ph+ cells in metaphase in BM; Minimal cytogenetic response: >65 to 95% Ph+ cells in metaphase in BM; No cytogenetic response: >95 to 100% Ph+ cells in metaphase in BM; Best CyR was defined as the best response obtained at any time during the study; MCyR was defined as a best CyR of CCyR or PCyR. Baseline=closest to, but no later than, the first day of study drug for treated subjects and closest to, but no later than, the date of randomization, for those who were randomized but who never received treatment, unless otherwise specified. All randomized imatinib-resistant subjects with available data were summarized.

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

End point timeframe:

Baseline up to 24 Months Follow-Up

| **End point values** | QD Dasatinib | BID Dasatinib | Dasatinib 100 mg Total Daily Dose | Dasatinib 140 mg Total Daily Dose |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 247 | 250 | 248 | 249 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | 58.3 (51.9 to 64.5) | 56.4 (50 to 62.6) | 57.3 (50.8 to 63.5) | 57.4 (51 to 63.7) |

**Statistical analyses**

| **Statistical analysis title** | MCyR: At or Prior to 24 Months Follow-Up |
|---|---|
| Comparison groups | QD Dasatinib v BID Dasatinib |
| Number of subjects included in analysis | 497 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[2] |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -6.8 |
| upper limit | 10.6 |

Notes:

[2] - Non-inferiority of the QD schedule relative to the BID schedule was deduced if the lower bound of the 95% CI for the MCyRRQD minus MCyRRBID difference was greater than or equal to -15%.

| **Statistical analysis title** | MCyR: At or Prior to 24 Months Follow-Up |
|---|---|
| Comparison groups | Dasatinib 100 mg Total Daily Dose v Dasatinib 140 mg Total Daily Dose |

| | |
|---|---|
| Number of subjects included in analysis | 497 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[3] |
| Parameter estimate | Risk difference (RD) |
| Point estimate | -0.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -8.9 |
| upper limit | 8.5 |

Notes:

[3] - Non-inferiority of 100 mg total daily dose relative to 140 mg total daily dose was deduced if the lower bound of the 95% CI for the difference was greater than or equal to -15%.

## Secondary: Percentage of Subjects With Complete Hematologic Response (CHR) After at Least 6 and 24 Months Follow-Up - Imatinib-Resistant Subjects

| | |
|---|---|
| End point title | Percentage of Subjects With Complete Hematologic Response (CHR) After at Least 6 and 24 Months Follow-Up - Imatinib-Resistant Subjects |

End point description:

CHR was obtained when all the following criteria were met: White Blood Cells <= institutional upper limit of normal (ULN); Platelets < 450,000/mm³; No blasts or promyelocytes in peripheral blood (PB); < 5% myelocytes plus metamyelocytes in PB; Basophils in PB < 20%; No extramedullary involvement (including no splenomegaly or hepatomegaly). Hematologic responses were counted anytime following 14 days after the dosing start date. All randomized imatinib-resistant subjects with available data were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to at Least 6 and 24 Months Follow-Up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 124 | 123 | 124 | 126 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| 6 Months (n=124, 123, 124, 126) | 86.3 (79 to 91.8) | 85.4 (77.9 to 91.1) | 91.1 (84.7 to 95.5) | 87.4 (80.3 to 92.6) |
| 24 Months (n=124, 123, 124, 126) | 88.7 (81.8 to 93.7) | 86.2 (78.8 to 91.7) | 91.9 (85.7 to 96.1) | 88.9 (82.1 to 93.8) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Time to Major Cytogenetic Response (MCyR) in Subjects With MCyR After At Least 24 Months Follow-Up - Imatinib-Resistant Subjects

| | |
|---|---|
| End point title | Time to Major Cytogenetic Response (MCyR) in Subjects With MCyR After At Least 24 Months Follow-Up - Imatinib-Resistant Subjects |

End point description:

Time to MCyR was defined as the time from the first dosing date until criteria were first met for complete cytogenetic response or partial cytogenetic response, whichever occurred first. Non-responders were censored at the maximum time of all subjects in their respective group (that is, maximum between time to MCyR response for responders and time to last cytogenetic assessment for non-responders). All randomized imatinib-resistant subjects with MCyR and available data were summarized.

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

End point timeframe:

Baseline up to at Least 24 Months Follow-Up

| **End point values** | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 71 | 69 | 72 |
| Units: Months | | | | |
| median (confidence interval 95%) | 2.9 (2.8 to 3.4) | 2.8 (2.8 to 3) | 2.9 (2.8 to 3.3) | 2.9 (2.8 to 3) |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Time to Complete Hematologic Response (CHR) in Subjects With CHR After at Least 24 Months Follow-Up - Imatinib-Resistant Subjects**

| End point title | Time to Complete Hematologic Response (CHR) in Subjects With CHR After at Least 24 Months Follow-Up - Imatinib-Resistant Subjects |
|---|---|

End point description:

Time to CHR was defined as the time from the first dosing date until criteria are first met for the response. Non-responders were censored at the maximum time of all subjects in their respective group (that is, maximum between time to CHR response for responders and time to last hematologic assessment for non-responders). Cytogenetic assessments were not done after the 2 Year Follow-up. All randomized imatinib-resistant subjects with CHR were summarized.

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

End point timeframe:

Baseline up to at Least 24 Months Follow-up

| **End point values** | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 110 | 106 | 114 | 112 |
| Units: Months | | | | |
| median (confidence interval 95%) | 0.5 (0.5 to 0.6) | 0.5 (0.5 to 0.7) | 0.6 (0.5 to 0.9) | 0.7 (0.5 to 0.9) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Major Cytogenetic Response (MCyR) Whose Disease Progressed - Imatinib-Resistant Subjects

| End point title | Number of Subjects With Major Cytogenetic Response (MCyR) Whose Disease Progressed - Imatinib-Resistant Subjects |
|---|---|

End point description:

Progression in a subject=subject achieved a complete hematologic response (CHR) and no longer met the criteria consistently over consecutive 2-weeks after starting their maximum dose; had no CHR after receiving their maximum dose and had a doubling of the white blood cell count from the lowest value to >20,000/mm^3 or an increase by >50,000/mm^3 on two assessments performed at least 2 weeks apart; subject met criteria of accelerated or blast phase chronic myelogenous leukemia at any time; had a MCyR and subsequently no longer met the criteria for MCyR after starting their maximum dose; had a >=30% absolute increase in the number of Philadelphia chromosome positive metaphases. Medium duration of MCyR could not be estimated because the majority of subjects with MCyR continued to respond, or could not be reliably estimated because of the large number of censored subjects. All imatinib-resistant subjects who had achieved MCyR and experienced disease progression were summarized.

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

End point timeframe:

Baseline up to at Least 24 Months Follow-Up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 73 | 71 | 69 | 72 |
| Units: Subjects | 5 | 17 | 6 | 9 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Complete Hematologic Response (CHR) Whose Disease Progressed - Imatinib-Resistant Subjects

| End point title | Number of Subjects With Complete Hematologic Response (CHR) Whose Disease Progressed - Imatinib-Resistant Subjects |
|---|---|

End point description:

Progression in a subject=achieved a CHR and subsequently no longer met the criteria consistently over a consecutive 2-week period after starting their maximum dose; had no CHR after receiving their maximum dose and had a doubling of the white blood cell count from the lowest value to >20,000/mm^3 or an increase by > 50,000/mm^3 on two assessments performed at least 2 weeks apart; met the criteria of accelerated or blast phase chronic myelogenous leukemia at any time; had a major cytogenetic response (MCyR) and subsequently no longer met the criteria for MCyR after starting their maximum dose; had a >= 30% absolute increase in the number of Philadelphia chromosome positive metaphases. Medium duration of CHR could not be estimated because the majority of subjects with CHR continued to respond, or could not be reliably estimated because of the large number of censored subjects. All imatinib-resistant subjects who achieved CHR and then experienced disease progression were summarized.

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

End point timeframe:

Baseline up to at Least 24 Months Follow-Up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 110 | 106 | 114 | 112 |
| Units: Subjects | 18 | 28 | 22 | 24 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Subjects With Major Cytogenetic Response (MCyR) and Baseline BCR-ABL Gene Mutation - All Treated Subjects

| End point title | Number of Subjects With Major Cytogenetic Response (MCyR) and Baseline BCR-ABL Gene Mutation - All Treated Subjects |
|---|---|

End point description:

BCR-ABL mutations were assessed in subjects prior to the start of study drug (baseline) and at the time of disease progression or at end of therapy. Quantification of BCR-ABL transcripts in peripheral blood was evaluated using quantitative reverse transcriptase polymerase chain reaction (Q-RT-PCR, RT-PCR). All randomized, treated subjects with available mutation data were summarized.

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

End point timeframe:

Baseline up to 2 Years

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 147 | 139 | 149 | 146 |
| Units: Subjects | | | | |
| Imatinib-resistant mutations | 49 | 49 | 62 | 48 |
| Mutations with unknown Imatinib-resistance status | 0 | 1 | 1 | 2 |
| Imatinib resistant or unknown mutations | 49 | 50 | 63 | 50 |
| Polymorphisms | 0 | 2 | 0 | 0 |
| No mutations | 98 | 87 | 96 | 96 |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Imatinib-Resistant Subjects With Progression Free Survival (PFS) After at Least 24, 36, 48, 60, 72, and 84 Months Follow-Up

| End point title | Percentage of Imatinib-Resistant Subjects With Progression |
|---|---|

| | |
|---|---|
| | Free Survival (PFS) After at Least 24, 36, 48, 60, 72, and 84 Months Follow-Up |

End point description:

PFS=time from randomization until: complete hematologic response (CHR) achieved and subject subsequently no longer met criteria for CHR over 2 weeks; no CHR after receiving maximum dose and had a doubling of the white blood cell count from the lowest value to >20,000/mm^3 or an increase by > 50,000/mm^3 on 2 assessments performed 2 weeks apart); subject met criteria of accelerated phase or blast phase chronic myelogenous leukemia; had MCyR and subsequently no longer met criteria for MCyR after starting maximum dose; >=30% absolute increase in number of Philadelphia chromosome positive metaphases. Deaths without a reported prior progression were considered to have progressed on the date of death; those who neither progressed nor died were censored on the date of their last cytogenetic or hematologic assessment. If the first progression reported during follow-up was death, subject considered to have progressed at date of death. All randomized imatinib-resistant subjects were summarized.

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

End point timeframe:

Baseline up to 84 months follow up

| **End point values** | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 124 | 123 | 124 | 126 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| 24 Months (n=124, 123, 124, 126) | 75.2 (66.3 to 82.1) | 61.3 (52.7 to 69.6) | 70.3 (60.8 to 77.9) | 70.8 (61.6 to 78.2) |
| 36 Months (n=124, 123, 124, 126) | 64.8 (55.2 to 72.9) | 47.4 (37.7 to 56.5) | 67.1 (57.3 to 75.1) | 58.2 (48.4 to 66.8) |
| 48 Months (n=124, 123, 124, 126) | 57.8 (48 to 66.5) | 40 (30.6 to 49.3) | 63.8 (53.7 to 72.2) | 55.1 (45.2 to 64.8) |
| 60 Months (n=124, 123, 124, 126) | 50.2 (40.2 to 59.3) | 36.4 (27.1 to 45.8) | 57.4 (46.9 to 66.5) | 50.2 (40.2 to 59.4) |
| 72 Months (n=124, 123, 124, 126) | 44 (34 to 53.6) | 31.4 (22.4 to 40.8) | 50.7 (40 to 60.4) | 45.3 (35.2 to 54.8) |
| 84 Months (n=124, 123, 124, 126) | 39 (29.2 to 48.7) | 30.2 (21.2 to 39.6) | 42.1 (31.5 to 52.4) | 41.3 (31.3 to 51) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Imatinib-Resistant Subjects With Overall Survival (OS) After at Least 24, 36, 48, 60, 72, and 84 Months Follow-Up

| | |
|---|---|
| End point title | Percentage of Imatinib-Resistant Subjects With Overall Survival (OS) After at Least 24, 36, 48, 60, 72, and 84 Months Follow-Up |

End point description:

OS was defined as the time from randomization until death. Survival data were collected for up to 5 years on subjects who had discontinued dasatinib treatment. Subjects who did not die or who were lost to follow-up were censored on the last date the subject was known to be alive. All randomized imatinib-resistant subjects were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to 84 months follow up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 124 | 123 | 124 | 126 |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| 24 Months (n=124, 123, 124, 126) | 90.1 (83.2 to 94.2) | 93.9 (87.6 to 97) | 88.9 (81.6 to 93.4) | 85.1 (77.3 to 90.3) |
| 36 Months (n=124, 123, 124, 126) | 87.5 (80.2 to 92.3) | 83.8 (75.6 to 89.5) | 83.5 (75.3 to 89.1) | 76.5 (67.7 to 83.1) |
| 48 Months (n=124, 123, 124, 126) | 79.7 (71.3 to 85.9) | 82 (73.4 to 88) | 80.7 (72.1 to 86.9) | 71.1 (61.9 to 78.4) |
| 60 Months (n=124, 123, 124, 126) | 75.1 (66.1 to 82) | 78 (68.9 to 84.7) | 73.6 (64.1 to 80.9) | 69.1 (59.8 to 76.7) |
| 72 Months (n=124, 123, 124, 126) | 67.9 (58.3 to 75.8) | 72.6 (62.9 to 80.1) | 71.4 (61.8 to 79) | 67.1 (57.6 to 74.9) |
| 84 Months (n=124, 123, 124, 126) | 62.6 (52.6 to 71) | 68.1 (58 to 76.2) | 67.9 (57.9 to 76) | 65 (55.3 to 73) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects Intolerant to Imatinib With Major Cytogenetic Response (MCyR) After at Least 6 Months and After at Least 24 Months Follow-Up, by QD and BID Schedules and by Total Daily Dose

| End point title | Percentage of Subjects Intolerant to Imatinib With Major Cytogenetic Response (MCyR) After at Least 6 Months and After at Least 24 Months Follow-Up, by QD and BID Schedules and by Total Daily Dose |
|---|---|

End point description:

Cytogenetic response (CyR) was based on the number of Philadelphia chromosome positive (Ph+) metaphases among cells in metaphase on a Bone Marrow (BM) sample. The criteria for CyR were as follows: complete cytogenetic response (CCyR): 0% Ph+ cells in metaphase in BM; PCyR: >0 to 35% Ph+ cells in metaphase in BM; Minor cytogenetic response: >35 to 65% Ph+ cells in metaphase in BM; Minimal cytogenetic response: >65 to 95% Ph+ cells in metaphase in BM; No CyR: >95 to 100% Ph+ cells in metaphase in BM; Best CyR was defined as the best response obtained at any time during the study; MCyR was defined as a best CyR of CCyR or PCyR. All randomized imatinib-intolerant subjects with available data were summarized.

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

End point timeframe:

Baseline up to at least 6 months and 24 months follow-up

| End point values | QD Dasatinib | BID Dasatinib | Dasatinib 100 mg Total Daily Dose | Dasatinib 140 mg Total Daily Dose |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 87 | 85 | 87 | 86 |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| 6 Month | 72.4 (61.8 to 81.5) | 70.6 (59.7 to 80) | 73.6 (63 to 82.4) | 69.4 (58.5 to 79) |
| 24 Month | 77 (66.8 to 85.4) | 75.6 (65.1 to 84.2) | 77 (66.8 to 85.4) | 75.6 (65.1 to 84.2) |

**Statistical analyses**

| Statistical analysis title | Risk difference: QD Dasatinib and BID Dasatinib |
|---|---|
| Statistical analysis description: 6 month analysis. | |
| Comparison groups | QD Dasatinib v BID Dasatinib |
| Number of subjects included in analysis | 172 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[4] |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1.8 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.7 |
| upper limit | 15.3 |

Notes:

[4] - Non-inferiority of the QD schedule relative to the BID schedule was deduced if the lower bound of the 95% CI for the MCyR QD minus MCyR BID difference was greater than or equal to -15%.

| Statistical analysis title | Risk difference:Total Daily Dose 100 mg and 140 mg |
|---|---|
| Statistical analysis description: 6 month analysis. | |
| Comparison groups | Dasatinib 100 mg Total Daily Dose v Dasatinib 140 mg Total Daily Dose |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[5] |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 4.2 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -9.3 |
| upper limit | 17.6 |

Notes:

[5] - Non-inferiority of 100 mg QD Total Daily Dose relative to 140 mg QD Total Daily Dose was deduced if the lower bound of the 95% CI difference was greater than or equal to -15%.

| Statistical analysis title | Risk difference: QD Dasatinib and BID Dasatinib |
|---|---|

| | |
|---|---|
| Statistical analysis description: | |
| 24 month analysis. | |
| Comparison groups | QD Dasatinib v BID Dasatinib |
| Number of subjects included in analysis | 172 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[6] |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.2 |
| upper limit | 14.1 |

Notes:

[6] - Non-inferiority of the QD schedule relative to the BID schedule was deduced if the lower bound of the 95% CI for the MCyR QD minus MCyR BID difference was greater than or equal to -15%.

| **Statistical analysis title** | Risk difference:Total Daily Dose 100 mg and 140 mg |
|---|---|
| Statistical analysis description: | |
| 24 month analysis. | |
| Comparison groups | Dasatinib 100 mg Total Daily Dose v Dasatinib 140 mg Total Daily Dose |
| Number of subjects included in analysis | 173 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[7] |
| Parameter estimate | Risk difference (RD) |
| Point estimate | 1.4 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -11.2 |
| upper limit | 14.1 |

Notes:

[7] - Non-inferiority of 100 mg QD Total Daily Dose relative to 140 mg QD Total Daily Dose was deduced if the lower bound of the 95% CI difference was greater than or equal to -15%.

## Secondary: Percentage of Subjects Intolerant to Imatinib With Complete Hematologic Response (CHR) After at Least 6 Months and After at Least 24 Months Follow-Up

| End point title | Percentage of Subjects Intolerant to Imatinib With Complete Hematologic Response (CHR) After at Least 6 Months and After at Least 24 Months Follow-Up |
|---|---|

End point description:

A CHR was obtained when all the following criteria were met: white blood cells <= institutional upper limit of normal (ULN); Platelets < 450,000/mm$^3$; No blasts or promyelocytes in peripheral blood (PB); < 5% myelocytes plus metamyelocytes in PB; Basophils in PB <20%; No extramedullary involvement (including no splenomegaly or hepatomegaly). Hematologic responses were counted anytime following 14 days after the dosing start date. All randomized imatinib-intolerant subjects were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to at Least 6 months and 24 months follow up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43 | 44 | 44 | 42 |
| Units: Percentage of Subjects | | | | |
| number (not applicable) | | | | |
| 6 Months (n=43, 44, 44, 41) | 100 | 86 | 93 | 85 |
| 24 Months (n=43, 44, 44, 42) | 100 | 89 | 93 | 86 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Imatinib Intolerant Subjects With Progression Free Survival (PFS) After 24, 36, 48, 60, 72, and 84 Months of Follow-Up

| End point title | Percentage of Imatinib Intolerant Subjects With Progression Free Survival (PFS) After 24, 36, 48, 60, 72, and 84 Months of Follow-Up |
|---|---|

End point description:

PFS= From randomization until: complete hematologic response (CHR) achieved and subject subsequently no longer met criteria for CHR over 2 weeks; no CHR after receiving maximum dose and doubling of the white blood cells count from the lowest value to > 20,000/mm^3 or an increase by > 50,000/mm^3 on 2 assessments performed 2 weeks apart; subject met criteria of accelerated phase or blast phase chronic myelogenous leukemia; subject had Major Cytogenetic Response (MCyR) and subsequently no longer met criteria for MCyR after starting maximum dose; >=30% absolute increase in number of Ph+ metaphases. Deaths without a reported prior progression were considered to have progressed on the date of death; those who neither progressed nor died were censored on the date of their last cytogenetic or hematologic assessment. All randomized imatinib-intolerant subjects with available data were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to 84 months follow-up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43 | 44 | 44 | 42 |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| 24 Months (n=43, 44, 44, 42) | 83.6 (67 to 92.3) | 87.7 (72.8 to 94.7) | 77.4 (61 to 87.6) | 83.7 (67.1 to 92.4) |
| 36 Months (n=43, 44, 44, 42) | 71.7 (53.6 to 83.7) | 76 (58.7 to 86.8) | 68.6 (51.1 to 80.9) | 77.4 (59.6 to 88.1) |
| 48 Months (n=43, 44, 44, 42) | 62.7 (44.5 to 76.5) | 76 (58.7 to 86.8) | 62 (44.1 to 75.7) | 66.9 (47.8 to 80.4) |
| 60 Months (n=43, 44, 44, 42) | 59.2 (40.8 to 73.6) | 71.2 (52.1 to 83.8) | 62 (44.1 to 75.7) | 59.5 (40.1 to 74.4) |

| | | | | |
|---|---|---|---|---|
| 72 Months (n=43, 44, 44, 42) | 59.2 (40.8 to 73.6) | 66.5 (46.3 to 80.6) | 58.2 (39.8 to 72.7) | 55.2 (35.7 to 71.1) |
| 84 Months (n=43, 44, 44, 42) | 50.9 (32.1 to 67) | 66.5 (46.3 to 80.6) | 47.5 (27.4 to 65.2) | 50.2 (30.4 to 67.1) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Imatinib Intolerant Subjects With Overall Survival (OS) After 24, 36, 48, 60, 72, and 84 Months of Follow-up

| | |
|---|---|
| End point title | Percentage of Imatinib Intolerant Subjects With Overall Survival (OS) After 24, 36, 48, 60, 72, and 84 Months of Follow-up |

End point description:

OS was defined as the time from randomization until death. Survival data were collected for up to 5 years on subjects who had discontinued dasatinib treatment. Subjects who did not die or who were lost to follow-up were censored on the last date the subject was known to be alive. All randomized imatinib-intolerant subjects were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to 84 months follow-up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 43 | 44 | 44 | 42 |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| 24 Months (n=43, 44, 44, 42) | 94.9 (81.2 to 98.7) | 92.8 (79.2 to 97.6) | 95.3 (82.5 to 98.8) | 97.4 (82.8 to 99.6) |
| 36 Months (n=43, 44, 44, 42) | 89.7 (74.9 to 96) | 92.8 (79.2 to 97.6) | 90.4 (76.4 to 96.3) | 94.7 (80.6 to 98.7) |
| 48 Months (n=43, 44, 44, 42) | 84.5 (68.6 to 92.7) | 87.5 (72.4 to 94.6) | 85.1 (69.7 to 93) | 86.8 (71.2 to 94.3) |
| 60 Months (n=43, 44, 44, 42) | 81.8 (65.6 to 90.9) | 87.5 (72.4 to 94.6) | 82.4 (66.6 to 91.2) | 81.1 (64.3 to 90.5) |
| 72 Months (n=43, 44, 44, 42) | 79 (62.3 to 88.9) | 87.5 (72.4 to 94.6) | 79.6 (63.2 to 89.3) | 81.1 (64.3 to 90.5) |
| 84 Months (n=43, 44, 44, 42) | 70 (52.2 to 82.2) | 87.5 (72.4 to 94.6) | 76.9 (59.7 to 87.2) | 77.7 (60.1 to 88.2) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of All Randomized Subjects With Cytogenic and Hematologic Response by Dosing Schedule (QD or BID) and by Total Daily Dose (100 mg or 140

## mg) After at Least 6 Months Follow-Up

| | |
|---|---|
| End point title | Percentage of All Randomized Subjects With Cytogenic and Hematologic Response by Dosing Schedule (QD or BID) and by Total Daily Dose (100 mg or 140 mg) After at Least 6 Months Follow-Up |

End point description:

Complete cytogenetic response (CCyR): 0% Philadelphia chromosome positive cells in metaphase in Bone Marrow (BM). Partial cytogenetic response (PCyR) >0 to 35% Ph+ cells in metaphase in BM. MCyR: best cytogenetic response of CCyR or PCyR. A complete hematologic response (CHR) was obtained when all the following criteria were met: White Blood Cells <=institutional upper limit of normal (ULN); Platelets <450,000/mm³; No blasts or promyelocytes in peripheral blood (PB); <5% myelocytes plus metamyelocytes in PB; Basophils in PB <20%; No extramedullary involvement (including no splenomegaly or hepatomegaly). Hematologic responses were counted anytime following 14 days after the dosing start date. All randomized subjects were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to at least 6 months follow-up

| **End point values** | QD Dasatinib | BID Dasatinib | Dasatinib 100 mg Total Daily Dose | Dasatinib 140 mg Total Daily Dose |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 334 | 336 | 335 | 335 |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| MCyR (n=334, 336, 335, 335) | 57.2 (51.7 to 62.6) | 54.5 (49 to 59.9) | 56.1 (50.6 to 61.5) | 55.5 (50 to 60.9) |
| CHR (n=334, 336, 335, 335) | 87.7 (83.7 to 91) | 89.3 (85.5 to 92.4) | 90.7 (87.1 to 93.6) | 86.3 (82.1 to 89.8) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of All Randomized Subjects With Cytogenic and Hematologic Response by Dosing Schedule (QD or BID) and by Total Daily Dose (100 mg or 140 mg) After at Least 24 Months Follow-Up

| | |
|---|---|
| End point title | Percentage of All Randomized Subjects With Cytogenic and Hematologic Response by Dosing Schedule (QD or BID) and by Total Daily Dose (100 mg or 140 mg) After at Least 24 Months Follow-Up |

End point description:

Complete cytogenetic response (CCyR): 0% Philadelphia chromosome positive cells in metaphase in Bone Marrow (BM). Partial cytogenetic response (PCyR) : >0 to 35% Ph+ cells in metaphase in BM. Major cytogenetic response: best cytogenetic response of CCyR or PCyR. A complete hematologic response was obtained when all the following criteria were met: White Blood Cells <=institutional upper limit of normal (ULN); Platelets <450,000/mm³; No blasts or promyelocytes in peripheral blood (PB); <5% myelocytes plus metamyelocytes in PB; Basophils in PB <20%; No extramedullary involvement (including no splenomegaly or hepatomegaly). Hematologic responses were counted anytime following 14 days after the dosing start date. No cytogenic assessments were made after 2 years of follow-up. All randomized subjects were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to at least 24 months follow-up

| End point values | QD Dasatinib | BID Dasatinib | Dasatinib 100 mg Total Daily Dose | Dasatinib 140 mg Total Daily Dose |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 334 | 336 | 335 | 335 |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| MCyR (n=334, 336, 335, 335) | 63.2 (57.8 to 68.4) | 61.3 (55.9 to 66.5) | 62.4 (57 to 67.6) | 62.1 (56.7 to 67.3) |
| CHR (n=334, 336, 335, 335) | 89.2 (85.4 to 92.3) | 90.2 (86.5 to 93.1) | 91.9 (88.5 to 94.6) | 87.5 (83.4 to 90.8) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Progression Free Survival (PFS) at 24, 36, 48, 60, 72, and 84 Months Follow-Up by Dose Schedule and Total Daily Dose - All Randomized Subjects

| End point title | Percentage of Subjects With Progression Free Survival (PFS) at 24, 36, 48, 60, 72, and 84 Months Follow-Up by Dose Schedule and Total Daily Dose - All Randomized Subjects |
|---|---|

End point description:

PFS= time from randomization until: complete hematologic response (CHR) achieved and subject subsequently no longer met criteria for CHR over 2 weeks; no CHR after receiving maximum dose and doubling of the white blood cells count from the lowest value to > 20,000/mm^3 or an increase by > 50,000/mm^3 on 2 assessments performed 2 weeks apart); subject met criteria of accelerated phase or blast phase chronic myelogenous leukemia; subject had major cytogenetic response (MCyR) and subsequently no longer met criteria for MCyR after starting maximum dose; >=30% absolute increase in number of Ph+ metaphases. Deaths without a reported prior progression were considered to have progressed on the date of death; those who neither progressed nor died were censored on the date of their last cytogenetic or hematologic assessment. All subjects who were randomized to a treatment arm were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to 84 months follow-up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 167 | 167 | 168 | 168 |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| 24 Months (n=167, 167, 168, 168) | 77.4 (69.9 to 83.2) | 67.7 (59.6 to 74.5) | 72.2 (64.3 to 78.7) | 73.9 (66.1 to 80.1) |

| | | | | |
|---|---|---|---|---|
| 36 Months (n=167, 167, 168, 168) | 66.6 (58.3 to 73.6) | 54 (45.4 to 61.8) | 67.5 (59.2 to 74.5) | 62.8 (54.3 to 70.1) |
| 48 Months (n=167, 167, 168, 168) | 59.1 (50.6 to 66.6) | 48 (39.4 to 56.2) | 63.3 (54.8 to 70.7) | 58.7 (50.1 to 66.3) |
| 60 Months (n=167, 167, 168, 168) | 52.5 (43.8 to 60.5) | 44.2 (35.5 to 52.5) | 58.7 (49.8 to 66.5) | 52.5 (43.7 to 60.5) |
| 72 Months (n=167, 167, 168, 168) | 48 (39.2 to 56.2) | 39.2 (30.6 to 47.7) | 52.8 (43.7 to 61.1) | 47.7 (38.7 to 56) |
| 84 Months (n=167, 167, 168, 168) | 42.1 (33.4 to 50.6) | 38.2 (29.6 to 46.7) | 43.9 (34.5 to 52.9) | 43.5 (34.5 to 52.1) |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of Subjects With Overall Survival (OS) at 24, 36, 48, 60, 72, and 84 Months Follow-Up - All Randomized Subjects

| | |
|---|---|
| End point title | Percentage of Subjects With Overall Survival (OS) at 24, 36, 48, 60, 72, and 84 Months Follow-Up - All Randomized Subjects |

End point description:

OS was defined as the time from randomization until death. Survival data were collected for up to 5 years on subjects who had discontinued dasatinib treatment. Subjects who did not die or who were lost to follow-up were censored on the last date the subject was known to be alive. All subjects who were randomized to a treatment arm were summarized. Here, 'n' signifies evaluable subjects for specified categories in respective treatment arms.

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

End point timeframe:

Baseline up to 84 months follow-up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 167 | 167 | 168 | 168 |
| Units: Percentage of Subjects | | | | |
| number (confidence interval 95%) | | | | |
| 24 Months (n=167, 167, 168, 168) | 91.3 (85.8 to 94.8) | 93.6 (88.4 to 96.5) | 90.6 (84.9 to 94.2) | 88.1 (81.9 to 92.2) |
| 36 Months (n=167, 167, 168, 168) | 88.1 (82 to 92.3) | 86.2 (79.6 to 90.8) | 85.3 (78.7 to 90) | 80.9 (73.9 to 86.3) |
| 48 Months (n=167, 167, 168, 168) | 81 (73.9 to 86.3) | 83.4 (76.4 to 88.5) | 81.8 (74.7 to 87.1) | 74.9 (67.3 to 81) |
| 60 Months (n=167, 167, 168, 168) | 76.8 (69.4 to 82.7) | 80.5 (73.1 to 86) | 75.9 (68.2 to 82) | 72 (64.1 to 78.4) |
| 72 Months (n=167, 167, 168, 168) | 70.9 (62.9 to 77.5) | 76.6 (68.7 to 82.7) | 73.6 (65.6 to 80) | 70.5 (62.5 to 77.1) |
| 84 Months (n=167, 167, 168, 168) | 64.6 (56.1 to 71.8) | 73.4 (65.2 to 79.9) | 70.3 (62 to 77.1) | 68.1 (59.8 to 74.9) |

## Statistical analyses

No statistical analyses for this end point

## Secondary: After 2 Years Follow-Up: Number of Subjects With Death, Serious Adverse Events (SAEs), Adverse Events (AEs) That Led to Treatment Discontinuation

| End point title | After 2 Years Follow-Up: Number of Subjects With Death, Serious Adverse Events (SAEs), Adverse Events (AEs) That Led to Treatment Discontinuation |
|---|---|

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Treatment-related=having certain, probable, possible, or missing relationship to study drug. Baseline=closest to, but no later than, the first day of study drug for treated subjects. All randomized subjects who received at least 1 dose of study drug were summarized.

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

End point timeframe:

Baseline up to 2 years follow-up

| End point values | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID | Dasatinib 70 mg BID |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 165 | 163 | 167 | 167 |
| Units: Subjects | | | | |
| Any SAEs | 58 | 67 | 73 | 78 |
| Drug-Related SAEs | 32 | 40 | 47 | 55 |
| Drug-Related AEs that led to discontinuation | 14 | 24 | 20 | 25 |
| Death within 30 days of last dose of study drug | 3 | 2 | 6 | 5 |

## Statistical analyses

No statistical analyses for this end point

## Secondary: After 7 Years Follow-Up and Study Closure: Number of Subjects With Death, Serious Adverse Events (SAEs), Adverse Events (AEs) That Led to Treatment Discontinuation

| End point title | After 7 Years Follow-Up and Study Closure: Number of Subjects With Death, Serious Adverse Events (SAEs), Adverse Events (AEs) That Led to Treatment Discontinuation[8] |
|---|---|

End point description:

AE=any new unfavorable symptom, sign, or disease or worsening of a preexisting condition that may not have a causal relationship with treatment. SAE=a medical event that at any dose results in death, persistent or significant disability/incapacity, or drug dependency/abuse; is life-threatening, an important medical event, or a congenital anomaly/birth defect; or requires or prolongs hospitalization. Treatment-related=having certain, probable, possible, or missing relationship to study drug. After the 2-year analysis those on a twice daily dosing schedule were allowed to switch to a once daily dosing schedule. Due to the large number of subjects switching from twice daily dosing to once daily dosing, the overall safety data are presented for the 100 mg once daily group and combined for the other

treatment groups. All randomized subjects who received at least 1 dose of study drug were summarized.

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

End point timeframe:

Baseline to 30 days post last dose; 7 years follow up; study closure July 2014

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint was to be evaluated for the specified arms only.

| **End point values** | Dasatinib 100 mg QD | Other Treatment Groups | Total | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 165 | 497 | 662 | |
| Units: Subjects | | | | |
| All Deaths | 51 | 133 | 184 | |
| Deaths on-study or within 30 days post dose | 11 | 15 | 26 | |
| SAEs | 75 | 259 | 334 | |
| AEs Leading to Discontinuation of Treatment | 43 | 153 | 196 | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Baseline to 30 days post last dose; 7 years follow up

Adverse event reporting additional description:

Study closure July 2014.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 17.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Dasatinib 100 mg QD |

Reporting group description:

Subjects received dasatinib 100 mg once a day (QD) until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw.

| | |
|---|---|
| Reporting group title | Dasatinib 140 mg QD |

Reporting group description:

Subjects received dasatinib 140 mg QD until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw.

| | |
|---|---|
| Reporting group title | Dasatinib 50 mg BID |

Reporting group description:

Subjects received 50 mg twice a day (BID) until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. After the 2-year analysis, and with Protocol Amendment 02, subjects on a BID dosing schedule were allowed to switch to a QD dosing schedule.

| | |
|---|---|
| Reporting group title | Dasatinib 70 mg BID |

Reporting group description:

Subjects received 70 mg BID until progression of disease, development of intolerable toxicity, or the subject's decision to withdraw. After the 2-year analysis, and with Protocol Amendment 02, subjects on a BID dosing schedule were allowed to switch to a QD dosing schedule.

| Serious adverse events | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 75 / 165 (45.45%) | 78 / 163 (47.85%) | 89 / 167 (53.29%) |
| number of deaths (all causes) | 15 | 11 | 17 |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenoma benign | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Basal cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blast cell crisis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 3 / 167 (1.80%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Blast cell proliferation | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blast crisis in myelogenous leukaemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Breast cancer | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic lymphocytic leukaemia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic myeloid leukaemia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic myeloid leukaemia transformation | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| Intraductal proliferative breast lesion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukaemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lip neoplasm malignant stage unspecified | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pituitary tumour | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Prostate cancer | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Renal cell carcinoma | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin cancer | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin cancer metastatic | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 165 (1.82%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 1 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thyroid adenoma | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tongue neoplasm malignant stage unspecified | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vulval cancer | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vascular disorders | | | |
| Deep vein thrombosis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Extremity necrosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral artery thrombosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral ischaemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Poor peripheral circulation | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chest pain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 165 (2.42%) | 2 / 163 (1.23%) | 3 / 167 (1.80%) |
| occurrences causally related to treatment / all | 2 / 4 | 3 / 3 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chills | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| Device failure | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device malfunction | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Malaise | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Medical device pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multi-organ failure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 11 / 163 (6.75%) | 6 / 167 (3.59%) |
| occurrences causally related to treatment / all | 2 / 3 | 6 / 13 | 4 / 10 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Serositis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| Thrombosis in device | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholangitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 165 (0.61%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Allergy to arthropod sting | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaphylactoid reaction | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Reproductive system and breast disorders | | | |
| Endometriosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Menorrhagia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 7 / 165 (4.24%) | 15 / 163 (9.20%) | 14 / 167 (8.38%) |
| occurrences causally related to treatment / all | 16 / 16 | 30 / 30 | 23 / 23 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 4 / 165 (2.42%) | 6 / 163 (3.68%) | 7 / 167 (4.19%) |
| occurrences causally related to treatment / all | 8 / 8 | 4 / 7 | 11 / 12 |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| Pneumonitis | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 1 / 1 | 3 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alveolar proteinosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 5 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Interstitial lung disease | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laryngeal oedema | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleurisy | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumothorax | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary arterial hypertension | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary hypertension | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Completed suicide | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Confusional state | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depressed mood | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychotic disorder | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blast cell count increased | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium test positive | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoglobin | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 3 / 4 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemoglobin decreased | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 3 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count decreased | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Platelet count increased | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental overdose | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Brain contusion | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fracture | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Incisional hernia, obstructive | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Jaw fracture | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Joint injury | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Laceration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative thoracic procedure complication | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Procedural intestinal perforation | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rib fracture | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Road traffic accident | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Spinal compression fracture | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Atrial septal defect | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arrhythmia supraventricular | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 4 / 167 (2.40%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Bradycardia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 3 / 163 (1.84%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 3 / 3 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac valve disease | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardio-respiratory arrest | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Cor pulmonale | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Left ventricular dysfunction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 1 / 163 (0.61%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Myocardial ischaemia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 2 / 163 (1.23%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Palpitations | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 3 / 163 (1.84%) | 3 / 167 (1.80%) |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 3 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pericarditis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 2 / 163 (1.23%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 1 / 1 | 2 / 2 | 4 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Restrictive cardiomyopathy | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stress cardiomyopathy | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tachycardia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular arrhythmia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| **Nervous system disorders** | | | |
| Central nervous system haemorrhage | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Cerebellar infarction | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 165 (1.21%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 2 / 3 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Headache | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Migraine | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myasthenia gravis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 165 (0.61%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| VIIth nerve paralysis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| **Blood and lymphatic system disorders** | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 3 / 163 (1.84%) | 3 / 167 (1.80%) |
| occurrences causally related to treatment / all | 1 / 1 | 4 / 4 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 2 / 163 (1.23%) | 3 / 167 (1.80%) |
| occurrences causally related to treatment / all | 4 / 4 | 3 / 3 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 2 / 163 (1.23%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 2 / 2 | 1 / 2 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytopenia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 165 (1.21%) | 4 / 163 (2.45%) | 6 / 167 (3.59%) |
| occurrences causally related to treatment / all | 1 / 2 | 4 / 5 | 8 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Amaurosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cataract | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diplopia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retinal haemorrhage | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vitreous haemorrhage | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 2 / 163 (1.23%) | 4 / 167 (2.40%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 2 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal fistula | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 1 / 2 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 165 (3.03%) | 12 / 163 (7.36%) | 5 / 167 (2.99%) |
| occurrences causally related to treatment / all | 3 / 5 | 10 / 15 | 6 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 2 / 163 (1.23%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 2 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis erosive | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 4 / 167 (2.40%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 3 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal necrosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Irritable bowel syndrome | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Large intestine polyp | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Loose tooth | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nausea | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 3 / 163 (1.84%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 2 / 2 | 2 / 3 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophageal pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rectal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Small intestinal obstruction | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 5 / 163 (3.07%) | 6 / 167 (3.59%) |
| occurrences causally related to treatment / all | 2 / 2 | 3 / 6 | 5 / 6 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Bile duct stone | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cholecystitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 3 / 163 (1.84%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acute febrile neutrophilic dermatosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Angioedema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dermatosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erythema nodosum | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Exfoliative rash | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pruritus | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyoderma gangrenosum | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 3 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rash generalised | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin lesion | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal failure acute | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocrine disorders | | | |
| Goitre | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue | | | |

| | | | |
|---|---|---|---|
| disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Arthritis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myositis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Osteonecrosis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abdominal infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anal abscess | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bacteraemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter gastroenteritis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Campylobacter infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 5 / 165 (3.03%) | 2 / 163 (1.23%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis bacterial | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Endocarditis enterococcal | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enteritis infectious | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Erysipelas | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 2 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis clostridial | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal viral infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematoma infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infection | | | |
| subjects affected / exposed | 5 / 165 (3.03%) | 0 / 163 (0.00%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 3 / 9 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infectious colitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lobar pneumonia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower respiratory tract infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Periodontitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 165 (2.42%) | 15 / 163 (9.20%) | 10 / 167 (5.99%) |
| occurrences causally related to treatment / all | 2 / 5 | 6 / 21 | 9 / 15 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Postoperative wound infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomembranous colitis | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 1 / 163 (0.61%) | 3 / 167 (1.80%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 1 / 3 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin bacterial infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Soft tissue infection | | | |
| subjects affected / exposed | 2 / 165 (1.21%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tuberculosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 2 / 163 (1.23%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 3 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 2 / 167 (1.20%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diabetes mellitus | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid overload | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Fluid retention | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 1 / 163 (0.61%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 0 / 165 (0.00%) | 0 / 163 (0.00%) | 0 / 167 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 0 / 163 (0.00%) | 1 / 167 (0.60%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | Dasatinib 70 mg BID | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 92 / 167 (55.09%) | | |
| number of deaths (all causes) | 22 | | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adenoma benign | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Basal cell carcinoma | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blast cell crisis | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Blast cell proliferation | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Blast crisis in myelogenous leukaemia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Breast cancer | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic lymphocytic leukaemia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic myeloid leukaemia | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chronic myeloid leukaemia transformation | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intraductal proliferative breast lesion | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Leukaemia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lip neoplasm malignant stage | | | | |

| | | | | |
|---|---|---|---|---|
| unspecified | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pituitary tumour | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Prostate cancer | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal cell carcinoma | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin cancer | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin cancer metastatic | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Squamous cell carcinoma of skin | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thyroid adenoma | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tongue neoplasm malignant stage unspecified | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vulval cancer | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vascular disorders | | | | |
| Deep vein thrombosis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Extremity necrosis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematoma | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhage | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypertension | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypotension | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral artery thrombosis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral ischaemia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Poor peripheral circulation | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thrombosis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| Chest discomfort | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chest pain | | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | | |
| occurrences causally related to treatment / all | 2 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Chills | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Death | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device failure | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Device malfunction | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Malaise | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Medical device pain | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multi-organ failure | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedema peripheral | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyrexia | | | | |
| subjects affected / exposed | 9 / 167 (5.39%) | | | |
| occurrences causally related to treatment / all | 4 / 13 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Serositis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sudden death | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Thrombosis in device | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cholangitis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cholecystitis acute | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Immune system disorders | | | | |
| Allergy to arthropod sting | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Anaphylactoid reaction | | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Reproductive system and breast disorders | | | |
| Endometriosis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Menorrhagia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Menstrual disorder | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Uterine haemorrhage | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pleural effusion | | | |
| subjects affected / exposed | 20 / 167 (11.98%) | | |
| occurrences causally related to treatment / all | 32 / 35 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 9 / 167 (5.39%) | | |
| occurrences causally related to treatment / all | 10 / 14 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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|---|---|---|---|
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Asthma | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pulmonary oedema | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | |
| occurrences causally related to treatment / all | 2 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Alveolar proteinosis | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Chronic obstructive pulmonary disease | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cough | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dyspnoea exertional | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Interstitial lung disease | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laryngeal oedema | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Obstructive airways disorder | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oropharyngeal pain | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pleurisy | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumothorax | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary arterial hypertension | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary congestion | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pulmonary hypertension | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory failure | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psychiatric disorders | | | | |
| Completed suicide | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Confusional state | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Depressed mood | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Depression | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Mental status changes | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Psychotic disorder | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Investigations | | | | |
| Alanine aminotransferase increased | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Aspartate aminotransferase increased | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blast cell count increased | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Blood creatinine increased | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium test positive | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Electrocardiogram QT prolonged | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemoglobin | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemoglobin decreased | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neutrophil count decreased | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Platelet count decreased | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Platelet count increased | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| White blood cell count decreased | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Injury, poisoning and procedural complications | | | | |
| Accidental overdose | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Brain contusion | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fibula fracture | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fracture | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Incisional hernia, obstructive | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Injury | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Jaw fracture | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Joint injury | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Laceration | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ligament sprain | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lumbar vertebral fracture | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Muscle strain | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Overdose | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postoperative thoracic procedure complication | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Procedural intestinal perforation | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rib fracture | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Road traffic accident | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Spinal compression fracture | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Congenital, familial and genetic disorders | | | | |

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|---|---|---|---|
| Atrial septal defect | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Acute coronary syndrome | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Angina pectoris | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Arrhythmia supraventricular | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac failure | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure acute | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac failure congestive | | | | |
| subjects affected / exposed | 5 / 167 (2.99%) | | | |
| occurrences causally related to treatment / all | 4 / 7 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardiac valve disease | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cardio-respiratory arrest | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cor pulmonale | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Left ventricular dysfunction | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 3 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myocardial infarction | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myocardial ischaemia | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 0 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Palpitations | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pericardial effusion | | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | | |
| occurrences causally related to treatment / all | 3 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pericarditis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Restrictive cardiomyopathy | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Stress cardiomyopathy | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tachycardia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ventricular arrhythmia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorders | | | | |
| Central nervous system haemorrhage | | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebellar infarction | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral haematoma | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebral ischaemia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dizziness | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Headache | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoaesthesia | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Migraine | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Myasthenia gravis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neuropathy peripheral | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Paraesthesia | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Peripheral sensory neuropathy | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Syncope | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Transient ischaemic attack | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| VIIth nerve paralysis | | | | |

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|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 5 / 167 (2.99%) | | |
| occurrences causally related to treatment / all | 3 / 5 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 1 / 1 | | |
| Lymphadenopathy | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neutropenia | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | |
| occurrences causally related to treatment / all | 4 / 4 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 9 / 167 (5.39%) | | |
| occurrences causally related to treatment / all | 9 / 10 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Amaurosis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cataract | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diplopia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Retinal haemorrhage | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vitreous haemorrhage | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Abdominal pain | | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | | |
| occurrences causally related to treatment / all | 1 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Abdominal pain upper | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Anal fistula | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Colitis | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Constipation | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dental caries | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diarrhoea | | | | |
| subjects affected / exposed | 4 / 167 (2.40%) | | | |
| occurrences causally related to treatment / all | 3 / 5 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enteritis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastritis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastritis erosive | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal necrosis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 1 | | | |
| Gingival bleeding | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haemorrhoids | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileus | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Inguinal hernia | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Intestinal obstruction | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Irritable bowel syndrome | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Large intestine polyp | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Loose tooth | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nausea | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophageal pain | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Oesophagitis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pancreatitis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rectal haemorrhage | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Small intestinal obstruction | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Toothache | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper gastrointestinal haemorrhage | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Vomiting | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hepatobiliary disorders | | | | |
| Bile duct stone | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cholecystitis | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin and subcutaneous tissue disorders | | | | |
| Acute febrile neutrophilic dermatosis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Angioedema | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Decubitus ulcer | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Dermatosis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erythema nodosum | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Exfoliative rash | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pruritus | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyoderma gangrenosum | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 2 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash | | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | | |
| occurrences causally related to treatment / all | 3 / 3 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Rash generalised | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin lesion | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal and urinary disorders | | | | |
| Nephrolithiasis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pollakiuria | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal failure | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Renal failure acute | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endocrine disorders | | | | |
| Goitre | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypothyroidism | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Musculoskeletal and connective tissue disorders | | | | |
| Arthralgia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Arthritis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

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|---|---|---|---|
| Back pain | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Flank pain | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lumbar spinal stenosis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Myositis | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Neck pain | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Osteoarthritis | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Osteonecrosis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pain in extremity | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infections and infestations | | | | |
| Abdominal infection | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Anal abscess | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Appendicitis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bacteraemia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchitis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Bronchopneumonia | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Campylobacter gastroenteritis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Campylobacter infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cellulitis | | | | |
| subjects affected / exposed | 4 / 167 (2.40%) | | | |
| occurrences causally related to treatment / all | 0 / 6 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile colitis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Clostridium difficile infection | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endocarditis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endocarditis bacterial | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Endocarditis enterococcal | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enteritis infectious | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Erysipelas | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis clostridial | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis viral | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal viral infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Haematoma infection | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Herpes zoster | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infection | | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 0 / 2 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Infectious colitis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Influenza | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lobar pneumonia | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lower respiratory tract infection | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Lung infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nasopharyngitis | | | | |

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|---|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Neutropenic sepsis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Periodontitis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pharyngitis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pharyngotonsillitis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 8 / 167 (4.79%) | | | |
| occurrences causally related to treatment / all | 3 / 8 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Postoperative wound infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pseudomembranous colitis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sepsis | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 4 / 167 (2.40%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 1 / 1 | | | |
| Septic shock | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Sinusitis | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin bacterial infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Skin infection | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 1 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Soft tissue infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tuberculosis | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Upper respiratory tract infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Urinary tract infection | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 2 / 167 (1.20%) | | | |
| occurrences causally related to treatment / all | 1 / 5 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Viral infection | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Wound infection | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Metabolism and nutrition disorders | | | | |
| Dehydration | | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | | |
| occurrences causally related to treatment / all | 2 / 4 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Diabetes mellitus | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fluid overload | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Fluid retention | | | | |
| subjects affected / exposed | 0 / 167 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hyperkalaemia | | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hypokalaemia | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hyponatraemia | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Dasatinib 100 mg QD | Dasatinib 140 mg QD | Dasatinib 50 mg BID |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 160 / 165 (96.97%) | 155 / 163 (95.09%) | 160 / 167 (95.81%) |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 9 / 165 (5.45%) | 5 / 163 (3.07%) | 5 / 167 (2.99%) |
| occurrences (all) | 11 | 11 | 6 |
| Hypertension | | | |
| subjects affected / exposed | 15 / 165 (9.09%) | 12 / 163 (7.36%) | 13 / 167 (7.78%) |
| occurrences (all) | 17 | 14 | 15 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 15 / 165 (9.09%) | 16 / 163 (9.82%) | 23 / 167 (13.77%) |
| occurrences (all) | 20 | 18 | 32 |
| Chest pain | | | |
| subjects affected / exposed | 21 / 165 (12.73%) | 16 / 163 (9.82%) | 19 / 167 (11.38%) |
| occurrences (all) | 27 | 19 | 21 |
| Chills | | | |
| subjects affected / exposed | 11 / 165 (6.67%) | 11 / 163 (6.75%) | 16 / 167 (9.58%) |
| occurrences (all) | 15 | 15 | 21 |
| Fatigue | | | |
| subjects affected / exposed | 62 / 165 (37.58%) | 62 / 163 (38.04%) | 56 / 167 (33.53%) |
| occurrences (all) | 80 | 77 | 71 |
| Influenza like illness | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 14 / 165 (8.48%) | 17 / 163 (10.43%) | 9 / 167 (5.39%) |
| occurrences (all) | 21 | 29 | 14 |
| Oedema peripheral | | | |
| subjects affected / exposed | 30 / 165 (18.18%) | 29 / 163 (17.79%) | 30 / 167 (17.96%) |
| occurrences (all) | 41 | 39 | 39 |
| Pain | | | |
| subjects affected / exposed | 19 / 165 (11.52%) | 10 / 163 (6.13%) | 12 / 167 (7.19%) |
| occurrences (all) | 28 | 11 | 14 |
| Pyrexia | | | |
| subjects affected / exposed | 32 / 165 (19.39%) | 40 / 163 (24.54%) | 43 / 167 (25.75%) |
| occurrences (all) | 52 | 88 | 68 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 53 / 165 (32.12%) | 42 / 163 (25.77%) | 57 / 167 (34.13%) |
| occurrences (all) | 68 | 64 | 84 |
| Dyspnoea | | | |
| subjects affected / exposed | 49 / 165 (29.70%) | 51 / 163 (31.29%) | 53 / 167 (31.74%) |
| occurrences (all) | 63 | 71 | 76 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 11 / 165 (6.67%) | 8 / 163 (4.91%) | 9 / 167 (5.39%) |
| occurrences (all) | 11 | 9 | 9 |
| Epistaxis | | | |
| subjects affected / exposed | 15 / 165 (9.09%) | 15 / 163 (9.20%) | 7 / 167 (4.19%) |
| occurrences (all) | 17 | 28 | 9 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 20 / 165 (12.12%) | 16 / 163 (9.82%) | 19 / 167 (11.38%) |
| occurrences (all) | 24 | 20 | 27 |
| Pleural effusion | | | |
| subjects affected / exposed | 41 / 165 (24.85%) | 51 / 163 (31.29%) | 54 / 167 (32.34%) |
| occurrences (all) | 56 | 68 | 71 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 6 / 165 (3.64%) | 9 / 163 (5.52%) | 15 / 167 (8.98%) |
| occurrences (all) | 6 | 11 | 19 |
| Depression | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 16 / 165 (9.70%) | 12 / 163 (7.36%) | 14 / 167 (8.38%) |
| occurrences (all) | 17 | 12 | 17 |
| Insomnia | | | |
| subjects affected / exposed | 19 / 165 (11.52%) | 20 / 163 (12.27%) | 14 / 167 (8.38%) |
| occurrences (all) | 19 | 21 | 16 |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 14 / 165 (8.48%) | 19 / 163 (11.66%) | 18 / 167 (10.78%) |
| occurrences (all) | 14 | 22 | 18 |
| Weight increased | | | |
| subjects affected / exposed | 18 / 165 (10.91%) | 8 / 163 (4.91%) | 13 / 167 (7.78%) |
| occurrences (all) | 20 | 10 | 14 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 4 / 165 (2.42%) | 10 / 163 (6.13%) | 12 / 167 (7.19%) |
| occurrences (all) | 4 | 11 | 12 |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 13 / 165 (7.88%) | 7 / 163 (4.29%) | 8 / 167 (4.79%) |
| occurrences (all) | 16 | 8 | 9 |
| Pericardial effusion | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 9 / 163 (5.52%) | 10 / 167 (5.99%) |
| occurrences (all) | 3 | 9 | 11 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 24 / 165 (14.55%) | 26 / 163 (15.95%) | 25 / 167 (14.97%) |
| occurrences (all) | 30 | 35 | 33 |
| Headache | | | |
| subjects affected / exposed | 75 / 165 (45.45%) | 73 / 163 (44.79%) | 60 / 167 (35.93%) |
| occurrences (all) | 142 | 146 | 95 |
| Paraesthesia | | | |
| subjects affected / exposed | 12 / 165 (7.27%) | 11 / 163 (6.75%) | 10 / 167 (5.99%) |
| occurrences (all) | 12 | 14 | 13 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 23 / 165 (13.94%) | 14 / 163 (8.59%) | 26 / 167 (15.57%) |
| occurrences (all) | 28 | 13 | 38 |
| Neutropenia | | | |
| subjects affected / exposed | 23 / 165 (13.94%) | 28 / 163 (17.18%) | 29 / 167 (17.37%) |
| occurrences (all) | 71 | 70 | 68 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 22 / 165 (13.33%) | 38 / 163 (23.31%) | 29 / 167 (17.37%) |
| occurrences (all) | 43 | 80 | 85 |
| Eye disorders | | | |
| Periorbital oedema | | | |
| subjects affected / exposed | 8 / 165 (4.85%) | 4 / 163 (2.45%) | 17 / 167 (10.18%) |
| occurrences (all) | 9 | 4 | 21 |
| Vision blurred | | | |
| subjects affected / exposed | 11 / 165 (6.67%) | 8 / 163 (4.91%) | 5 / 167 (2.99%) |
| occurrences (all) | 12 | 9 | 6 |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 13 / 165 (7.88%) | 8 / 163 (4.91%) | 9 / 167 (5.39%) |
| occurrences (all) | 16 | 9 | 11 |
| Abdominal pain | | | |
| subjects affected / exposed | 25 / 165 (15.15%) | 26 / 163 (15.95%) | 24 / 167 (14.37%) |
| occurrences (all) | 31 | 39 | 36 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 13 / 165 (7.88%) | 24 / 163 (14.72%) | 17 / 167 (10.18%) |
| occurrences (all) | 15 | 30 | 18 |
| Constipation | | | |
| subjects affected / exposed | 31 / 165 (18.79%) | 20 / 163 (12.27%) | 25 / 167 (14.97%) |
| occurrences (all) | 33 | 29 | 31 |
| Diarrhoea | | | |
| subjects affected / exposed | 67 / 165 (40.61%) | 70 / 163 (42.94%) | 73 / 167 (43.71%) |
| occurrences (all) | 114 | 139 | 152 |
| Dyspepsia | | | |
| subjects affected / exposed | 13 / 165 (7.88%) | 25 / 163 (15.34%) | 13 / 167 (7.78%) |
| occurrences (all) | 14 | 33 | 15 |
| Flatulence | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 9 / 165 (5.45%) | 5 / 163 (3.07%) | 6 / 167 (3.59%) |
| occurrences (all) | 10 | 5 | 6 |
| Gastritis | | | |
| subjects affected / exposed | 4 / 165 (2.42%) | 11 / 163 (6.75%) | 7 / 167 (4.19%) |
| occurrences (all) | 4 | 13 | 7 |
| Nausea | | | |
| subjects affected / exposed | 37 / 165 (22.42%) | 54 / 163 (33.13%) | 52 / 167 (31.14%) |
| occurrences (all) | 63 | 74 | 83 |
| Stomatitis | | | |
| subjects affected / exposed | 5 / 165 (3.03%) | 7 / 163 (4.29%) | 12 / 167 (7.19%) |
| occurrences (all) | 6 | 9 | 16 |
| Toothache | | | |
| subjects affected / exposed | 10 / 165 (6.06%) | 15 / 163 (9.20%) | 8 / 167 (4.79%) |
| occurrences (all) | 15 | 17 | 13 |
| Vomiting | | | |
| subjects affected / exposed | 23 / 165 (13.94%) | 29 / 163 (17.79%) | 32 / 167 (19.16%) |
| occurrences (all) | 33 | 37 | 54 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 5 / 165 (3.03%) | 7 / 163 (4.29%) | 7 / 167 (4.19%) |
| occurrences (all) | 5 | 9 | 9 |
| Alopecia | | | |
| subjects affected / exposed | 13 / 165 (7.88%) | 8 / 163 (4.91%) | 7 / 167 (4.19%) |
| occurrences (all) | 14 | 9 | 7 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 4 / 165 (2.42%) | 8 / 163 (4.91%) | 8 / 167 (4.79%) |
| occurrences (all) | 4 | 10 | 9 |
| Dry skin | | | |
| subjects affected / exposed | 10 / 165 (6.06%) | 8 / 163 (4.91%) | 8 / 167 (4.79%) |
| occurrences (all) | 11 | 9 | 8 |
| Erythema | | | |
| subjects affected / exposed | 5 / 165 (3.03%) | 7 / 163 (4.29%) | 9 / 167 (5.39%) |
| occurrences (all) | 5 | 9 | 13 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 11 / 165 (6.67%) | 4 / 163 (2.45%) | 9 / 167 (5.39%) |
| occurrences (all) | 12 | 4 | 10 |

| | | | |
|---|---|---|---|
| Night sweats | | | |
| subjects affected / exposed | 7 / 165 (4.24%) | 10 / 163 (6.13%) | 12 / 167 (7.19%) |
| occurrences (all) | 10 | 12 | 14 |
| Petechiae | | | |
| subjects affected / exposed | 1 / 165 (0.61%) | 11 / 163 (6.75%) | 4 / 167 (2.40%) |
| occurrences (all) | 1 | 11 | 4 |
| Pruritus | | | |
| subjects affected / exposed | 24 / 165 (14.55%) | 22 / 163 (13.50%) | 17 / 167 (10.18%) |
| occurrences (all) | 27 | 27 | 29 |
| Rash | | | |
| subjects affected / exposed | 37 / 165 (22.42%) | 52 / 163 (31.90%) | 43 / 167 (25.75%) |
| occurrences (all) | 50 | 83 | 59 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 47 / 165 (28.48%) | 39 / 163 (23.93%) | 36 / 167 (21.56%) |
| occurrences (all) | 59 | 51 | 47 |
| Back pain | | | |
| subjects affected / exposed | 26 / 165 (15.76%) | 29 / 163 (17.79%) | 28 / 167 (16.77%) |
| occurrences (all) | 30 | 36 | 34 |
| Bone pain | | | |
| subjects affected / exposed | 20 / 165 (12.12%) | 25 / 163 (15.34%) | 15 / 167 (8.98%) |
| occurrences (all) | 26 | 31 | 18 |
| Muscle spasms | | | |
| subjects affected / exposed | 10 / 165 (6.06%) | 4 / 163 (2.45%) | 14 / 167 (8.38%) |
| occurrences (all) | 14 | 4 | 20 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 24 / 165 (14.55%) | 13 / 163 (7.98%) | 15 / 167 (8.98%) |
| occurrences (all) | 31 | 14 | 16 |
| Myalgia | | | |
| subjects affected / exposed | 27 / 165 (16.36%) | 26 / 163 (15.95%) | 24 / 167 (14.37%) |
| occurrences (all) | 40 | 36 | 27 |
| Neck pain | | | |
| subjects affected / exposed | 10 / 165 (6.06%) | 6 / 163 (3.68%) | 5 / 167 (2.99%) |
| occurrences (all) | 9 | 9 | 5 |
| Pain in extremity | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 33 / 165 (20.00%) | 29 / 163 (17.79%) | 24 / 167 (14.37%) |
| occurrences (all) | 37 | 35 | 30 |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 14 / 165 (8.48%) | 5 / 163 (3.07%) | 16 / 167 (9.58%) |
| occurrences (all) | 16 | 9 | 21 |
| Conjunctivitis | | | |
| subjects affected / exposed | 3 / 165 (1.82%) | 11 / 163 (6.75%) | 7 / 167 (4.19%) |
| occurrences (all) | 3 | 12 | 8 |
| Infection | | | |
| subjects affected / exposed | 9 / 165 (5.45%) | 4 / 163 (2.45%) | 8 / 167 (4.79%) |
| occurrences (all) | 11 | 6 | 6 |
| Influenza | | | |
| subjects affected / exposed | 13 / 165 (7.88%) | 4 / 163 (2.45%) | 17 / 167 (10.18%) |
| occurrences (all) | 20 | 4 | 20 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 23 / 165 (13.94%) | 13 / 163 (7.98%) | 22 / 167 (13.17%) |
| occurrences (all) | 26 | 21 | 37 |
| Oral herpes | | | |
| subjects affected / exposed | 13 / 165 (7.88%) | 5 / 163 (3.07%) | 9 / 167 (5.39%) |
| occurrences (all) | 16 | 5 | 14 |
| Pneumonia | | | |
| subjects affected / exposed | 5 / 165 (3.03%) | 5 / 163 (3.07%) | 10 / 167 (5.99%) |
| occurrences (all) | 7 | 5 | 7 |
| Sinusitis | | | |
| subjects affected / exposed | 19 / 165 (11.52%) | 8 / 163 (4.91%) | 17 / 167 (10.18%) |
| occurrences (all) | 29 | 11 | 22 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 28 / 165 (16.97%) | 26 / 163 (15.95%) | 35 / 167 (20.96%) |
| occurrences (all) | 46 | 43 | 52 |
| Urinary tract infection | | | |
| subjects affected / exposed | 15 / 165 (9.09%) | 13 / 163 (7.98%) | 12 / 167 (7.19%) |
| occurrences (all) | 23 | 17 | 25 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 16 / 165 (9.70%) | 21 / 163 (12.88%) | 21 / 167 (12.57%) |
| occurrences (all) | 20 | 24 | 28 |

| **Non-serious adverse events** | Dasatinib 70 mg BID | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 165 / 167 (98.80%) | | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | | |
| occurrences (all) | 10 | | |
| Hypertension | | | |
| subjects affected / exposed | 20 / 167 (11.98%) | | |
| occurrences (all) | 20 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 27 / 167 (16.17%) | | |
| occurrences (all) | 34 | | |
| Chest pain | | | |
| subjects affected / exposed | 17 / 167 (10.18%) | | |
| occurrences (all) | 31 | | |
| Chills | | | |
| subjects affected / exposed | 14 / 167 (8.38%) | | |
| occurrences (all) | 14 | | |
| Fatigue | | | |
| subjects affected / exposed | 49 / 167 (29.34%) | | |
| occurrences (all) | 74 | | |
| Influenza like illness | | | |
| subjects affected / exposed | 13 / 167 (7.78%) | | |
| occurrences (all) | 16 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 36 / 167 (21.56%) | | |
| occurrences (all) | 43 | | |
| Pain | | | |
| subjects affected / exposed | 10 / 167 (5.99%) | | |
| occurrences (all) | 12 | | |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 44 / 167 (26.35%) | | |
| occurrences (all) | 69 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 54 / 167 (32.34%) | | |
| occurrences (all) | 81 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 43 / 167 (25.75%) | | |
| occurrences (all) | 58 | | |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 2 / 167 (1.20%) | | |
| occurrences (all) | 2 | | |
| Epistaxis | | | |
| subjects affected / exposed | 12 / 167 (7.19%) | | |
| occurrences (all) | 13 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 17 / 167 (10.18%) | | |
| occurrences (all) | 16 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 51 / 167 (30.54%) | | |
| occurrences (all) | 73 | | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 12 / 167 (7.19%) | | |
| occurrences (all) | 16 | | |
| Depression | | | |
| subjects affected / exposed | 11 / 167 (6.59%) | | |
| occurrences (all) | 13 | | |
| Insomnia | | | |
| subjects affected / exposed | 12 / 167 (7.19%) | | |
| occurrences (all) | 14 | | |
| Investigations | | | |
| Weight decreased | | | |
| subjects affected / exposed | 27 / 167 (16.17%) | | |
| occurrences (all) | 32 | | |
| Weight increased | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 11 / 167 (6.59%) | | |
| occurrences (all) | 12 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | |
| occurrences (all) | 13 | | |
| Cardiac disorders | | | |
| Palpitations | | | |
| subjects affected / exposed | 11 / 167 (6.59%) | | |
| occurrences (all) | 12 | | |
| Pericardial effusion | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | | |
| occurrences (all) | 7 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 25 / 167 (14.97%) | | |
| occurrences (all) | 28 | | |
| Headache | | | |
| subjects affected / exposed | 76 / 167 (45.51%) | | |
| occurrences (all) | 131 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | | |
| occurrences (all) | 8 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 23 / 167 (13.77%) | | |
| occurrences (all) | 35 | | |
| Neutropenia | | | |
| subjects affected / exposed | 28 / 167 (16.77%) | | |
| occurrences (all) | 61 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 27 / 167 (16.17%) | | |
| occurrences (all) | 83 | | |
| Eye disorders | | | |
| Periorbital oedema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 167 (2.99%) | | |
| occurrences (all) | 6 | | |
| Vision blurred | | | |
| subjects affected / exposed | 5 / 167 (2.99%) | | |
| occurrences (all) | 5 | | |
| Gastrointestinal disorders | | | |
| Abdominal distension | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | | |
| occurrences (all) | 10 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 20 / 167 (11.98%) | | |
| occurrences (all) | 24 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 18 / 167 (10.78%) | | |
| occurrences (all) | 21 | | |
| Constipation | | | |
| subjects affected / exposed | 20 / 167 (11.98%) | | |
| occurrences (all) | 22 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 82 / 167 (49.10%) | | |
| occurrences (all) | 151 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 16 / 167 (9.58%) | | |
| occurrences (all) | 17 | | |
| Flatulence | | | |
| subjects affected / exposed | 3 / 167 (1.80%) | | |
| occurrences (all) | 3 | | |
| Gastritis | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | | |
| occurrences (all) | 8 | | |
| Nausea | | | |
| subjects affected / exposed | 69 / 167 (41.32%) | | |
| occurrences (all) | 109 | | |
| Stomatitis | | | |
| subjects affected / exposed | 7 / 167 (4.19%) | | |
| occurrences (all) | 10 | | |

| | | | |
|---|---|---|---|
| Toothache | | | |
| subjects affected / exposed | 8 / 167 (4.79%) | | |
| occurrences (all) | 10 | | |
| Vomiting | | | |
| subjects affected / exposed | 52 / 167 (31.14%) | | |
| occurrences (all) | 89 | | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 9 / 167 (5.39%) | | |
| occurrences (all) | 12 | | |
| Alopecia | | | |
| subjects affected / exposed | 13 / 167 (7.78%) | | |
| occurrences (all) | 13 | | |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 11 / 167 (6.59%) | | |
| occurrences (all) | 12 | | |
| Dry skin | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | | |
| occurrences (all) | 6 | | |
| Erythema | | | |
| subjects affected / exposed | 5 / 167 (2.99%) | | |
| occurrences (all) | 7 | | |
| Hyperhidrosis | | | |
| subjects affected / exposed | 1 / 167 (0.60%) | | |
| occurrences (all) | 1 | | |
| Night sweats | | | |
| subjects affected / exposed | 10 / 167 (5.99%) | | |
| occurrences (all) | 10 | | |
| Petechiae | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | | |
| occurrences (all) | 6 | | |
| Pruritus | | | |
| subjects affected / exposed | 23 / 167 (13.77%) | | |
| occurrences (all) | 31 | | |
| Rash | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 43 / 167 (25.75%) | | |
| occurrences (all) | 63 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 30 / 167 (17.96%) | | |
| occurrences (all) | 39 | | |
| Back pain | | | |
| subjects affected / exposed | 24 / 167 (14.37%) | | |
| occurrences (all) | 37 | | |
| Bone pain | | | |
| subjects affected / exposed | 15 / 167 (8.98%) | | |
| occurrences (all) | 19 | | |
| Muscle spasms | | | |
| subjects affected / exposed | 8 / 167 (4.79%) | | |
| occurrences (all) | 8 | | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 18 / 167 (10.78%) | | |
| occurrences (all) | 20 | | |
| Myalgia | | | |
| subjects affected / exposed | 22 / 167 (13.17%) | | |
| occurrences (all) | 26 | | |
| Neck pain | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | | |
| occurrences (all) | 6 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 22 / 167 (13.17%) | | |
| occurrences (all) | 27 | | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 11 / 167 (6.59%) | | |
| occurrences (all) | 12 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 6 / 167 (3.59%) | | |
| occurrences (all) | 6 | | |
| Infection | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 167 (1.20%) | | |
| occurrences (all) | 2 | | |
| Influenza | | | |
| subjects affected / exposed | 11 / 167 (6.59%) | | |
| occurrences (all) | 13 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 13 / 167 (7.78%) | | |
| occurrences (all) | 16 | | |
| Oral herpes | | | |
| subjects affected / exposed | 8 / 167 (4.79%) | | |
| occurrences (all) | 10 | | |
| Pneumonia | | | |
| subjects affected / exposed | 13 / 167 (7.78%) | | |
| occurrences (all) | 12 | | |
| Sinusitis | | | |
| subjects affected / exposed | 12 / 167 (7.19%) | | |
| occurrences (all) | 15 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 23 / 167 (13.77%) | | |
| occurrences (all) | 43 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 9 / 167 (5.39%) | | |
| occurrences (all) | 9 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 24 / 167 (14.37%) | | |
| occurrences (all) | 39 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 17 April 2006 | The purpose of this amendment was to make minor modifications to the hematologic response criteria and to remove the restriction of concurrent medications that inhibit platelet function. |
| 08 March 2007 | The purpose of this amendment was to allow subjects on the twice daily dosing schedule to switch to once daily dosing, in specific circumstances, to optimize the safety of dasatinib. |
| 28 February 2008 | The purpose of this amendment was to describe the participation requirements and study conduct for subjects who completed 2 years on study: The study will continue until all subjects have discontinued due to death, withdrawn consent or lost to follow up or until all subjects are followed for at least 5 years after study start, whichever occurs first. |
| 19 December 2008 | The purpose of this amendment was to clarify language surrounding study conduct for all enrolled subjects after two years on study in terms of data collection and submission of adverse events. |
| 14 September 2010 | The purpose of this amendment was to extend the duration of the study to subjects who continued to have clinical benefit. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported