



Clinical trial results:

A Phase 1b/2 Study to Evaluate the Safety and Efficacy Of PF-04449913, An Oral Hedgehog Inhibitor, in Combination With Intensive Chemotherapy, Low Dose Ara-C or Decitabine In Patients With Acute Myeloid Leukemia or High-risk Myelodysplastic Syndrome

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2012-000684-24 |
| Trial protocol | PL ES IT |
| Global end of trial date | |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 |
| This version publication date | 29 December 2017 |
| First version publication date | 29 December 2017 |

Trial information

Trial identification

| | |
|-----------------------|----------|
| Sponsor protocol code | B1371003 |
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Additional study identifiers

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

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Pfizer, Inc. |
| Sponsor organisation address | 235 E 42nd Street, New York, United States, NY 10017 |
| Public contact | Pfizer Clinical Trials.gov Call Center, Pfizer, Inc., +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc., +1 18007181021, ClinicalTrials.gov_Inquiries@pfizer.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 | Interim |
| Date of interim/final analysis | 03 January 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 03 January 2017 |
| Global end of trial reached? | No |

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the safety and efficacy of glasdegib (PF-04449913) when administered in combination with first line treatment regimens for Acute Myeloid Leukemia (AML) and High Risk Myelodysplastic Syndrome (MDS).

Protection of trial subjects:

This study was conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. In addition, all local regulatory requirements were followed, in particular, those affording greater protection to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

| | |
|---|--------------|
| Actual start date of recruitment | 27 June 2012 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 4 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United States: 147 |
| Country: Number of subjects enrolled | Italy: 14 |
| Country: Number of subjects enrolled | Germany: 43 |
| Country: Number of subjects enrolled | Poland: 20 |
| Country: Number of subjects enrolled | Spain: 22 |
| Country: Number of subjects enrolled | Canada: 9 |
| Worldwide total number of subjects | 255 |
| EEA total number of subjects | 99 |

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) | 57 |
| From 65 to 84 years | 190 |
| 85 years and over | 8 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Phase 1B: Unfit (unfit for intensive chemotherapy) subjects with prior decitabine or azacitidine for high risk MDS or AHD (antecedent hematologic disease) were eligible for the LDAC arm only; with prior cytarabine were eligible for decitabine arm only. Phase 2: Subject's treatment arm assignment was based on the fit or unfit status at screening.

Period 1

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|-----------------------------------|
| Arm title | Phase 1B: Glasdegib 100 mg + LDAC |
|------------------|-----------------------------------|

Arm description:

Subjects received oral doses of glasdegib (PF-04449913) tablets 100 milligram (mg) starting on Day 3 of Cycle 1 for pharmacokinetic (PK) assessment purposes and thereafter once daily (QD) and continuously for 28-day cycles (starting on Day 1 for all other cycles). Low dose Ara-C (LDAC) was given at a dose of 20 mg subcutaneously twice daily (BID) on Days 1-10 of the 28-day cycles.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Glasdegib (PF-04449913) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Glasdegib (PF-04449913) tablets 100 mg were taken orally QD starting on Day 3 of Cycle 1 and continuously for 28-day cycles (starting on Day 1 for all other cycles). Tablets were taken in the morning at approximately the same time each day. Dosing occurred with plenty of water (without adjustment for body size). Study medication were swallowed whole and not chewed, with or without food.

| | |
|--|--|
| Investigational medicinal product name | LDAC (low dose Ara-C) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

LDAC was given at a dose of 20 mg (not adjusted for the subjects weight) subcutaneously (SC) twice daily (morning and evening; approximately 12 hrs apart) on Days 1-10 days of the 28 day cycles.

| | |
|------------------|-----------------------------------|
| Arm title | Phase 1B: Glasdegib 200 mg + LDAC |
|------------------|-----------------------------------|

Arm description:

Subjects received oral doses of glasdegib tablets 200 mg starting on Day 3 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). LDAC was given at a dose of 20 mg subcutaneously BID on Days 1-10 of the 28-day cycles. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 2/Day 1 and Cycle 2/Day 16, respectively.

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

| | |
|--|-------------------------|
| Investigational medicinal product name | Glasdegib (PF-04449913) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Glasdegib (PF-04449913) tablets 200 mg were taken orally QD starting on Day 3 of Cycle 1 and continuously for 28-day cycles (starting on Day 1 for all other cycles). Tablets were taken in the morning at approximately the same time each day. Dosing occurred with plenty of water (without adjustment for body size). Study medication were swallowed whole and not chewed, with or without food. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 2/Day 1 and Cycle 2/Day 16, respectively.

| | |
|--|--|
| Investigational medicinal product name | LDAC (low dose Ara-C) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

LDAC was given at a dose of 20 mg (not adjusted for the subjects weight) subcutaneously (SC) twice daily (morning and evening; approximately 12 hrs apart) on Days 1-10 days of the 28 day cycles.

| | |
|------------------|---|
| Arm title | Phase 1B: Glasdegib 100 mg + Decitabine |
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Arm description:

Subjects received oral doses of glasdegib tablets 100 mg starting on Day 2 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). Decitabine was given at a dose of 20 mg/m² as an intravenous (IV) infusion over 1 hour on Days 1-5 of the 28-day cycles.

| | |
|--|----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Decitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Decitabine was given at a dose of 20 mg/m² over a 1 hour IV infusion on Days 1-5 of a 28 day cycle. Dose was recalculated when the weight changes >10%.

| | |
|--|-------------------------|
| Investigational medicinal product name | Glasdegib (PF-04449913) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Glasdegib (PF-04449913) tablets 100 mg were taken orally QD starting on Day 2 of Cycle 1 and continuously for 28-day cycles (starting on Day 1 for all other cycles). Tablets were taken in the morning at approximately the same time each day. Dosing occurred with plenty of water (without adjustment for body size). Study medication were swallowed whole and not chewed, with or without food.

| | |
|------------------|---|
| Arm title | Phase 1B: Glasdegib 200 mg + Decitabine |
|------------------|---|

Arm description:

Subjects received oral doses of glasdegib tablets 200 mg starting on Day 2 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). Decitabine was given at a dose of 20 mg/m² as an IV infusion over 1 hour on Days 1-5 of the 28-day cycles. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 1/Day 24 and Cycle 5/Day 1, respectively.

| | |
|--|----------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Decitabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Decitabine was given at a dose of 20 mg/m² over a 1 hour IV infusion on Days 1-5 of a 28 day cycle. Dose was recalculated when the weight changes >10%.

| | |
|--|-------------------------|
| Investigational medicinal product name | Glasdegib (PF-04449913) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Glasdegib (PF-04449913) tablets 200 mg were taken orally QD starting on Day 2 of Cycle 1 and continuously for 28-day cycles (starting on Day 1 for all other cycles). Tablets were taken in the morning at approximately the same time each day. Dosing occurred with plenty of water (without adjustment for body size). Study medication were swallowed whole and not chewed, with or without food. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 1/Day 24 and Cycle 5/Day 1, respectively.

| | |
|------------------|--|
| Arm title | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunorubicin |
|------------------|--|

Arm description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 100 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Glasdegib (PF-04449913) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Glasdegib (PF-04449913) tablets 100 mg were taken orally QD on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days. Tablets were taken in the morning at approximately the same time each day. Dosing occurred with plenty of water (without adjustment for body size). Study medication were swallowed whole and not chewed, with or without food.

| | |
|--|----------------------|
| Investigational medicinal product name | Daunorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV for each cycle. Daunorubicin was given as close as possible to the administration of glasdegib.

| | |
|--|--|
| Investigational medicinal product name | Cytarabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |

| | |
|--------------------------|-----------------|
| Routes of administration | Intravenous use |
|--------------------------|-----------------|

Dosage and administration details:

Cytarabine was given on Days 1 through 7 at a dose of 100 mg/m²/day by continuous intravenous infusion (CIV) for each cycle of induction, and given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation.

| | |
|------------------|--|
| Arm title | Phase 1B: Glasdegib 200 mg + Cytarabine/Daunorubicin |
|------------------|--|

Arm description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 200 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. One (1) subject in this cohort had dose reduction to 100 mg starting from Consolidation Cycle 1/Day 21.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Glasdegib (PF-04449913) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Glasdegib (PF-04449913) tablets 200 mg were taken orally QD on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days. Tablets were taken in the morning at approximately the same time each day. Dosing occurred with plenty of water (without adjustment for body size). Study medication were swallowed whole and not chewed, with or without food. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. One (1) subject in this cohort had dose reduction to 100 mg starting from Consolidation Cycle 1/Day 21.

| | |
|--|----------------------|
| Investigational medicinal product name | Daunorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV for each cycle. Daunorubicin was given as close as possible to the administration of glasdegib.

| | |
|--|--|
| Investigational medicinal product name | Cytarabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cytarabine was given on Days 1 through 7 at a dose of 100 mg/m²/day by continuous intravenous infusion (CIV) for each cycle of induction, and given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation.

| | |
|------------------|---|
| Arm title | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunorubicin |
|------------------|---|

Arm description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 100 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of

the study. A cycle was defined as 28 days.

| | |
|--|-------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Glasdegib (PF-04449913) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Glasdegib (PF-04449913) tablets 100 mg were taken orally QD on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days. Tablets were taken in the morning at approximately the same time each day. Dosing occurred with plenty of water (without adjustment for body size). Study medication were swallowed whole and not chewed, with or without food.

| | |
|--|----------------------|
| Investigational medicinal product name | Daunorubicin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder for injection |
| Routes of administration | Intravenous use |

Dosage and administration details:

Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV for each cycle. Daunorubicin was given as close as possible to the administration of glasdegib.

| | |
|--|--|
| Investigational medicinal product name | Cytarabine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Cytarabine was given on Days 1 through 7 at a dose of 100 mg/m²/day by continuous intravenous infusion (CIV) for each cycle of induction, and given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation.

| | |
|------------------|--|
| Arm title | Phase 2 Unfit: Glasdegib 100 mg + LDAC |
|------------------|--|

Arm description:

Subjects received oral doses of glasdegib tablets 100 mg QD in 28-day cycles on a continuous basis, starting on Day 1 of Cycle 1. LDAC was given at a dose of 20 mg subcutaneously BID on Days 1-10 of the 28 day cycles.

| | |
|--|--|
| Arm type | Experimental |
| Investigational medicinal product name | LDAC (low dose Ara-C) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

LDAC was given at a dose of 20 mg (not adjusted for the subjects weight) subcutaneously (SC) twice daily (morning and evening; approximately 12 hrs apart) on Days 1-10 days of the 28 day cycles.

| | |
|--|-------------------------|
| Investigational medicinal product name | Glasdegib (PF-04449913) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Glasdegib (PF-04449913) tablets 100 mg were taken orally QD starting on Day 1 of Cycle 1 and continuously for 28-day cycles. Tablets were taken in the morning at approximately the same time each day. Dosing occurred with plenty of water (without adjustment for body size). Study medication were swallowed whole and not chewed, with or without food.

| | |
|------------------|---------------------------|
| Arm title | Phase 2 Unfit: LDAC alone |
|------------------|---------------------------|

Arm description:

Subjects received LDAC subcutaneously at a dose of 20 mg BID on Days 1-10 of the 28 day cycles.

| | |
|--|--|
| Arm type | Active comparator |
| Investigational medicinal product name | LDAC (low dose Ara-C) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solution for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

LDAC was given at a dose of 20 mg (not adjusted for the subjects weight) subcutaneously (SC) twice daily (morning and evening; approximately 12 hrs apart) on Days 1-10 days of the 28 day cycles.

| Number of subjects in period 1 | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | Phase 1B: Glasdegib 100 mg + Decitabine |
|--------------------------------|--------------------------------------|--------------------------------------|---|
| | | | |
| Started | 17 | 6 | 4 |
| Received treatment | 17 | 6 | 4 |
| Completed | 0 | 0 | 0 |
| Not completed | 17 | 6 | 4 |
| Adverse event, serious fatal | 15 | 6 | 4 |
| Consent withdrawn by subject | 1 | - | - |
| : Study ongoing at cutoff date | 1 | - | - |
| : Randomized, not treated | - | - | - |
| Lost to follow-up | - | - | - |

| Number of subjects in period 1 | Phase 1B: Glasdegib 200 mg + Decitabine | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunoru bicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Daunoru bicin |
|--------------------------------|---|--|--|
| | | | |
| Started | 3 | 16 | 6 |
| Received treatment | 3 | 16 | 6 |
| Completed | 0 | 0 | 0 |
| Not completed | 3 | 16 | 6 |
| Adverse event, serious fatal | 2 | 7 | 3 |
| Consent withdrawn by subject | 1 | - | 1 |
| : Study ongoing at cutoff date | - | 8 | 2 |
| : Randomized, not treated | - | - | - |
| Lost to follow-up | - | 1 | - |

| Number of subjects in period 1 | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunoru bicin | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone |
|--------------------------------|---|--|------------------------------|
| | | | |
| Started | 71 | 88 | 44 |
| Received treatment | 69 | 84 | 41 |
| Completed | 0 | 0 | 0 |
| Not completed | 71 | 88 | 44 |

| | | | |
|--------------------------------|----|----|----|
| Adverse event, serious fatal | 41 | 64 | 40 |
| Consent withdrawn by subject | 3 | 3 | - |
| : Study ongoing at cutoff date | 24 | 16 | 1 |
| : Randomized, not treated | 2 | 4 | 3 |
| Lost to follow-up | 1 | 1 | - |

Baseline characteristics

Reporting groups

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 1B: Glasdegib 100 mg + LDAC |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects received oral doses of glasdegib (PF-04449913) tablets 100 milligram (mg) starting on Day 3 of Cycle 1 for pharmacokinetic (PK) assessment purposes and thereafter once daily (QD) and continuously for 28-day cycles (starting on Day 1 for all other cycles). Low dose Ara-C (LDAC) was given at a dose of 20 mg subcutaneously twice daily (BID) on Days 1-10 of the 28-day cycles.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 1B: Glasdegib 200 mg + LDAC |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects received oral doses of glasdegib tablets 200 mg starting on Day 3 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). LDAC was given at a dose of 20 mg subcutaneously BID on Days 1-10 of the 28-day cycles. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 2/Day 1 and Cycle 2/Day 16, respectively.

| | |
|-----------------------|---|
| Reporting group title | Phase 1B: Glasdegib 100 mg + Decitabine |
|-----------------------|---|

Reporting group description:

Subjects received oral doses of glasdegib tablets 100 mg starting on Day 2 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). Decitabine was given at a dose of 20 mg/m² as an intravenous (IV) infusion over 1 hour on Days 1-5 of the 28-day cycles.

| | |
|-----------------------|---|
| Reporting group title | Phase 1B: Glasdegib 200 mg + Decitabine |
|-----------------------|---|

Reporting group description:

Subjects received oral doses of glasdegib tablets 200 mg starting on Day 2 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). Decitabine was given at a dose of 20 mg/m² as an IV infusion over 1 hour on Days 1-5 of the 28-day cycles. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 1/Day 24 and Cycle 5/Day 1, respectively.

| | |
|-----------------------|--|
| Reporting group title | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunorubicin |
|-----------------------|--|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 100 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days.

| | |
|-----------------------|--|
| Reporting group title | Phase 1B: Glasdegib 200 mg + Cytarabine/Daunorubicin |
|-----------------------|--|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 200 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. One (1) subject in this cohort had dose reduction to 100 mg starting from Consolidation Cycle 1/Day 21.

| | |
|-----------------------|---|
| Reporting group title | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunorubicin |
|-----------------------|---|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of

induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 100 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days.

| | |
|---|--|
| Reporting group title | Phase 2 Unfit: Glasdegib 100 mg + LDAC |
| Reporting group description: | |
| Subjects received oral doses of glasdegib tablets 100 mg QD in 28-day cycles on a continuous basis, starting on Day 1 of Cycle 1. LDAC was given at a dose of 20 mg subcutaneously BID on Days 1-10 of the 28 day cycles. | |
| Reporting group title | Phase 2 Unfit: LDAC alone |
| Reporting group description: | |
| Subjects received LDAC subcutaneously at a dose of 20 mg BID on Days 1-10 of the 28 day cycles. | |

| Reporting group values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | Phase 1B: Glasdegib 100 mg + Decitabine |
|------------------------|-----------------------------------|-----------------------------------|---|
| Number of subjects | 17 | 6 | 4 |
| Age categorical | | | |
| Units: Subjects | | | |
| < 18 years | 0 | 0 | 0 |
| 18 to 44 years | 0 | 0 | 0 |
| 45 to 64 years | 0 | 1 | 0 |
| >=65 years | 17 | 5 | 4 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 76.2 | 74.5 | 75.3 |
| standard deviation | ± 5.7 | ± 8.8 | ± 5.7 |
| Gender, Male/Female | | | |
| Units: Subjects | | | |
| Female | 5 | 3 | 1 |
| Male | 12 | 3 | 3 |

| Reporting group values | Phase 1B: Glasdegib 200 mg + Decitabine | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Daunorubicin |
|------------------------|---|--|--|
| Number of subjects | 3 | 16 | 6 |
| Age categorical | | | |
| Units: Subjects | | | |
| < 18 years | 0 | 0 | 0 |
| 18 to 44 years | 0 | 3 | 1 |
| 45 to 64 years | 0 | 9 | 2 |
| >=65 years | 3 | 4 | 3 |
| Age Continuous | | | |
| Units: Years | | | |
| arithmetic mean | 74.7 | 54.2 | 56.7 |
| standard deviation | ± 2.9 | ± 12.6 | ± 13.9 |
| Gender, Male/Female | | | |
| Units: Subjects | | | |
| Female | 1 | 8 | 2 |
| Male | 2 | 8 | 4 |

| Reporting group values | Phase 2 Fit: Glasdegib 100 mg + | Phase 2 Unfit: Glasdegib 100 mg + | Phase 2 Unfit: LDAC alone |
|------------------------|---------------------------------|-----------------------------------|---------------------------|
|------------------------|---------------------------------|-----------------------------------|---------------------------|

| | Cytarabine/Daunorubicin | LDAC | |
|--|-------------------------|-------|-------|
| Number of subjects | 71 | 88 | 44 |
| Age categorical Units: Subjects | | | |
| < 18 years | 0 | 0 | 0 |
| 18 to 44 years | 5 | 0 | 0 |
| 45 to 64 years | 33 | 2 | 1 |
| >=65 years | 33 | 86 | 43 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 61.9 | 76.2 | 74.5 |
| standard deviation | ± 9.6 | ± 6.2 | ± 4.9 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 28 | 19 | 18 |
| Male | 43 | 69 | 26 |

| | | | |
|--|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 255 | | |
| Age categorical Units: Subjects | | | |
| < 18 years | 0 | | |
| 18 to 44 years | 9 | | |
| 45 to 64 years | 48 | | |
| >=65 years | 198 | | |
| Age Continuous Units: Years | | | |
| arithmetic mean | - | | |
| standard deviation | - | | |
| Gender, Male/Female Units: Subjects | | | |
| Female | 85 | | |
| Male | 170 | | |

Subject analysis sets

| | |
|---|---|
| Subject analysis set title | Phase 1B: Glasdegib + LDAC |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Included all subjects who received oral glasdegib in combination with LDAC in phase 1B portion. | |
| Subject analysis set title | Phase 1B: Glasdegib + Decitabine |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Included all subjects who received oral glasdegib in combination with decitabine in phase 1B portion. | |
| Subject analysis set title | Phase 1B: Glasdegib + Cytarabine/Daunorubicin |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Included all subjects who received oral glasdegib in combination with cytarabine/daunorubicin in phase 1B portion. | |
| Subject analysis set title | Phase 1B: Glasdegib + LDAC (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response).

| | |
|----------------------------|---|
| Subject analysis set title | Phase 1B: Glasdegib + LDAC (Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response.

| | |
|----------------------------|---|
| Subject analysis set title | Phase 1B: Glasdegib + Decitabine (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response).

| | |
|----------------------------|---|
| Subject analysis set title | Phase 1B: Glasdegib + Decitabine (Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response.

| | |
|----------------------------|---|
| Subject analysis set title | Phase 1B: Glasdegib + Cytarabine/Dauno (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response). Dauno is short for daunorubicin.

| | |
|----------------------------|---|
| Subject analysis set title | Phase 1B: Glasdegib+Cytarabine/Dauno(Biomarker,non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response. Dauno is short for daunorubicin.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Phase 2 Fit (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response).

| | |
|----------------------------|--|
| Subject analysis set title | Phase 2 Fit (Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response.

| | |
|----------------------------|---|
| Subject analysis set title | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response).

| | |
|----------------------------|--|
| Subject analysis set title | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response.

| | |
|----------------------------|--|
| Subject analysis set title | Phase 2 Unfit: LDAC alone (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response).

| | |
|----------------------------|--|
| Subject analysis set title | Phase 2 Unfit: LDAC alone (Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response.

| Reporting group values | Phase 1B: Glasdegib + LDAC | Phase 1B: Glasdegib + Decitabine | Phase 1B: Glasdegib + Cytarabine/Daunorubicin |
|--|----------------------------|----------------------------------|---|
| Number of subjects | 23 | 7 | 22 |
| Age categorical Units: Subjects | | | |
| < 18 years | 0 | 0 | 0 |
| 18 to 44 years | 0 | 0 | 4 |
| 45 to 64 years | 1 | 0 | 11 |
| >=65 years | 22 | 7 | 7 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 75.8 | 75.0 | 54.9 |
| standard deviation | ± 6.5 | ± 4.4 | ± 12.7 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 8 | 2 | 10 |
| Male | 15 | 5 | 12 |

| Reporting group values | Phase 1B: Glasdegib + LDAC (Biomarker, Responder) | Phase 1B: Glasdegib + LDAC (Biomarker, non-Responder) | Phase 1B: Glasdegib + Decitabine (Biomarker, Responder) |
|--|---|---|---|
| Number of subjects | 4 | 19 | 5 |
| Age categorical Units: Subjects | | | |
| < 18 years | 0 | 0 | 0 |
| 18 to 44 years | 0 | 0 | 0 |
| 45 to 64 years | 0 | 1 | 0 |
| >=65 years | 4 | 18 | 5 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 75.8 | 75.8 | 74.4 |
| standard deviation | ± 6.1 | ± 6.7 | ± 5.1 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 1 | 7 | 2 |
| Male | 3 | 12 | 3 |

| Reporting group values | Phase 1B: Glasdegib + Decitabine (Biomarker, non-Responder) | Phase 1B: Glasdegib + Cytarabine/Daunorubicin (Biomarker, Responder) | Phase 1B: Glasdegib+Cytarabine/Daunorubicin (Biomarker, non-Responder) |
|------------------------|---|--|--|
| Number of subjects | 2 | 14 | 8 |

| | | | |
|--|-------|--------|--------|
| Age categorical Units: Subjects | | | |
| < 18 years | 0 | 0 | 0 |
| 18 to 44 years | 0 | 3 | 1 |
| 45 to 64 years | 0 | 7 | 4 |
| >=65 years | 2 | 4 | 3 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 76.5 | 53.0 | 58.1 |
| standard deviation | ± 2.1 | ± 13.8 | ± 10.7 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 0 | 8 | 2 |
| Male | 2 | 6 | 6 |

| Reporting group values | Phase 2 Fit (Biomarker, Responder) | Phase 2 Fit (Biomarker, non- Responder) | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) |
|--|--|---|--|
| Number of subjects | 45 | 26 | 33 |
| Age categorical Units: Subjects | | | |
| < 18 years | 0 | 0 | 0 |
| 18 to 44 years | 4 | 1 | 0 |
| 45 to 64 years | 21 | 12 | 1 |
| >=65 years | 20 | 13 | 32 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 61.2 | 62.9 | 75.2 |
| standard deviation | ± 10.7 | ± 7.5 | ± 6.0 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 17 | 11 | 8 |
| Male | 28 | 15 | 25 |

| Reporting group values | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Biomarker, non-Responder) | Phase 2 Unfit: LDAC alone (Biomarker, Responder) | Phase 2 Unfit: LDAC alone (Biomarker, non-Responder) |
|--|---|--|--|
| Number of subjects | 55 | 4 | 40 |
| Age categorical Units: Subjects | | | |
| < 18 years | 0 | 0 | 0 |
| 18 to 44 years | 0 | 0 | 0 |
| 45 to 64 years | 1 | 0 | 1 |
| >=65 years | 54 | 4 | 39 |
| Age Continuous Units: Years | | | |
| arithmetic mean | 76.7 | 77.8 | 74.2 |
| standard deviation | ± 6.3 | ± 4.2 | ± 4.9 |
| Gender, Male/Female Units: Subjects | | | |
| Female | 11 | 2 | 16 |

| | | | |
|------|----|---|----|
| Male | 44 | 2 | 24 |
|------|----|---|----|

| |
|--|
| |
| |

End points

End points reporting groups

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 1B: Glasdegib 100 mg + LDAC |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects received oral doses of glasdegib (PF-04449913) tablets 100 milligram (mg) starting on Day 3 of Cycle 1 for pharmacokinetic (PK) assessment purposes and thereafter once daily (QD) and continuously for 28-day cycles (starting on Day 1 for all other cycles). Low dose Ara-C (LDAC) was given at a dose of 20 mg subcutaneously twice daily (BID) on Days 1-10 of the 28-day cycles.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 1B: Glasdegib 200 mg + LDAC |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects received oral doses of glasdegib tablets 200 mg starting on Day 3 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). LDAC was given at a dose of 20 mg subcutaneously BID on Days 1-10 of the 28-day cycles. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 2/Day 1 and Cycle 2/Day 16, respectively.

| | |
|-----------------------|---|
| Reporting group title | Phase 1B: Glasdegib 100 mg + Decitabine |
|-----------------------|---|

Reporting group description:

Subjects received oral doses of glasdegib tablets 100 mg starting on Day 2 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). Decitabine was given at a dose of 20 mg/m² as an intravenous (IV) infusion over 1 hour on Days 1-5 of the 28-day cycles.

| | |
|-----------------------|---|
| Reporting group title | Phase 1B: Glasdegib 200 mg + Decitabine |
|-----------------------|---|

Reporting group description:

Subjects received oral doses of glasdegib tablets 200 mg starting on Day 2 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). Decitabine was given at a dose of 20 mg/m² as an IV infusion over 1 hour on Days 1-5 of the 28-day cycles. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 1/Day 24 and Cycle 5/Day 1, respectively.

| | |
|-----------------------|--|
| Reporting group title | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunorubicin |
|-----------------------|--|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 100 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days.

| | |
|-----------------------|--|
| Reporting group title | Phase 1B: Glasdegib 200 mg + Cytarabine/Daunorubicin |
|-----------------------|--|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 200 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. One (1) subject in this cohort had dose reduction to 100 mg starting from Consolidation Cycle 1/Day 21.

| | |
|-----------------------|---|
| Reporting group title | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunorubicin |
|-----------------------|---|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of

induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 100 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days.

| | |
|---|---|
| Reporting group title | Phase 2 Unfit: Glasdegib 100 mg + LDAC |
| Reporting group description: | |
| Subjects received oral doses of glasdegib tablets 100 mg QD in 28-day cycles on a continuous basis, starting on Day 1 of Cycle 1. LDAC was given at a dose of 20 mg subcutaneously BID on Days 1-10 of the 28 day cycles. | |
| Reporting group title | Phase 2 Unfit: LDAC alone |
| Reporting group description: | |
| Subjects received LDAC subcutaneously at a dose of 20 mg BID on Days 1-10 of the 28 day cycles. | |
| Subject analysis set title | Phase 1B: Glasdegib + LDAC |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Included all subjects who received oral glasdegib in combination with LDAC in phase 1B portion. | |
| Subject analysis set title | Phase 1B: Glasdegib + Decitabine |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Included all subjects who received oral glasdegib in combination with decitabine in phase 1B portion. | |
| Subject analysis set title | Phase 1B: Glasdegib + Cytarabine/Daunorubicin |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| Included all subjects who received oral glasdegib in combination with cytarabine/daunorubicin in phase 1B portion. | |
| Subject analysis set title | Phase 1B: Glasdegib + LDAC (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response). | |
| Subject analysis set title | Phase 1B: Glasdegib + LDAC (Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response. | |
| Subject analysis set title | Phase 1B: Glasdegib + Decitabine (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response). | |
| Subject analysis set title | Phase 1B: Glasdegib + Decitabine (Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response. | |
| Subject analysis set title | Phase 1B: Glasdegib + Cytarabine/Dauno (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response). Dauno is short for daunorubicin. | |
| Subject analysis set title | Phase 1B: Glasdegib+Cytarabine/Dauno(Biomarker,non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response. Dauno is short for daunorubicin.

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | Phase 2 Fit (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response).

| | |
|----------------------------|--|
| Subject analysis set title | Phase 2 Fit (Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response.

| | |
|----------------------------|---|
| Subject analysis set title | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response).

| | |
|----------------------------|--|
| Subject analysis set title | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response.

| | |
|----------------------------|--|
| Subject analysis set title | Phase 2 Unfit: LDAC alone (Biomarker, Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who achieved CR, CRi, MLFS, PR, or PRi (AML investigator reported best overall response), and MDS subjects who achieved CR, mCR, PR, or SD (MDS investigator reported best overall response).

| | |
|----------------------------|--|
| Subject analysis set title | Phase 2 Unfit: LDAC alone (Biomarker, non-Responder) |
| Subject analysis set type | Sub-group analysis |

Subject analysis set description:

AML subjects who did not achieve CR, CRi, MLFS, PR, or PRi; and MDS subjects who did not achieve CR, mCR, PR or SD were defined as non-responders for best overall response.

Primary: Number of subjects with dose-limiting toxicities (DLTs) at Phase 1B

| | |
|-----------------|---|
| End point title | Number of subjects with dose-limiting toxicities (DLTs) at Phase 1B ^{[1][2]} |
|-----------------|---|

End point description:

A DLT was any of the following adverse events(AEs) in Cycle 1, considered by investigator possibly related to glasdegib in combination with chemotherapy: (1) Grade \geq 3 non-hematologic toxicity, excluding Grade \geq 3 infection, fever, infusion related AEs, electrolyte abnormalities and ALT/AST elevation that returned to Grade \leq 1 or baseline within 7 days; (2) prolonged myelosuppression lasted longer than 42 days from the point of detection, defined as absolute neutrophil count $<$ 500/mL or platelet count $<$ 10×10^9 /L with a normal bone marrow; (3) inability to deliver at least 80% planned study doses for all agents in a combination due to non-hematologic toxicities; (4) Delay of $>$ 28 days in receiving next scheduled cycle due to persisting non-hematologic toxicities. Per protocol analysis set was used, including all enrolled subjects in the dose escalation component who received at least 1 dose of glasdegib, co-administered chemotherapeutics, did not have major treatment deviations during DLT monitoring period.

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

End point timeframe:

Glasdegib+LDAC, Glasdegib+Decitabine: Cycle 1, Day 1 to Day 28;
Glasdegib+Cytarabine/Daunorubicin: Cycle 1, Day -3 to Day 21 or to Day 28 depending on when the next chemotherapy cycle was started

Notes:

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

Justification: Not every reporting arm is required for reporting this endpoint of the study.

[2] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + Decitabine |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 ^[3] | 5 ^[4] | 4 ^[5] | 2 ^[6] |
| Units: Subjects | 0 | 0 | 0 | 0 |

Notes:

[3] - Actual number of subjects that started the Arm: 3

[4] - Actual number of subjects that started the Arm: 6

[5] - Actual number of subjects that started the Arm: 4

[6] - Actual number of subjects that started the Arm: 3

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6 ^[7] | 6 ^[8] | | |
| Units: Subjects | 1 | 0 | | |

Notes:

[7] - Actual number of subjects that started the Arm: 6

[8] - Actual number of subjects that started the Arm: 6

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of subjects with complete response (CR) at Phase 2 Fit

| | |
|-----------------|--|
| End point title | Percentage of subjects with complete response (CR) at Phase 2 Fit ^[9] ^[10] |
|-----------------|--|

End point description:

For AML subjects: CR were those with repeat bone marrow showing <5% myeloblasts, spicules present and no Auer rods, peripheral blood showing neutrophils $\geq 1000/\text{mCL}$ and platelets $\geq 100,000/\text{mCL}$, transfusion independent and no extramedullary disease. For MDS subjects: CR were those with repeat bone marrow showing $\leq 5\%$ myeloblasts, peripheral blood showing neutrophils $\geq 1000/\text{mCL}$, platelets $\geq 100,000/\text{mCL}$, 0% blast and hemoglobin (Hgb) $\geq 11 \text{ g/dL}$, normal maturation of all cell lines. End of treatment: maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first. Full analysis set was used to analyze this end point, including all enrolled subjects of Phase 2 Fit arm who received at least 1 dose of study medication. Number of subjects analyzed is number of subjects in the treatment group. 'n' in the categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Screening (within 28 days Prior to Dosing), Day 21 of each Induction Cycles and final Consolidation Cycle, Day 1 of every third Maintenance Cycles, End of Treatment

Notes:

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

Justification: Not every reporting arm is required for reporting this endpoint of the study.

[10] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|----------------------------------|---|--|--|--|
| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunorubicin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 69 | | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 80%) | | | | |
| Total subjects | 42.0 (34.4 to 49.6) | | | |
| Subject ≥ 55 years old (n = 60) | 36.7 (28.7 to 44.6) | | | |
| Subjects < 55 years old (n = 9) | 77.8 (60.0 to 95.5) | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Overall survival (OS) at Phase 2 Unfit

| | |
|--|--|
| End point title | Overall survival (OS) at Phase 2 Unfit ^[11] |
| End point description: | |
| OS was defined as duration from the date of randomization to the date of death from any cause. Subjects not known to have died at the last follow-up were censored on the date they were last known to be alive. Survival status were collected every month for the first two months after discontinuation of study treatment and thereafter every 2 months until death or 4 years from time of randomization. Full analysis set was used to analyze this end point, including all randomized subjects of Phase 2 Unfit arm. | |
| End point type | Primary |
| End point timeframe: | |
| Randomization to Follow-up (4 years) | |

Notes:

[11] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|----------------------------------|---|------------------------------|--|--|
| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 88 | 44 | | |
| Units: Months | | | | |
| median (confidence interval 80%) | 8.8 (6.9 to 9.9) | 4.9 (3.5 to 6.0) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | Difference between groups in overall survival |
| Comparison groups | Phase 2 Unfit: Glasdegib 100 mg + LDAC v Phase 2 Unfit: LDAC alone |
| Number of subjects included in analysis | 132 |
| Analysis specification | Pre-specified |
| Analysis type | |
| P-value | = 0.0004 ^[12] |
| Method | Logrank |
| Parameter estimate | Hazard ratio (HR) |
| Point estimate | 0.513 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 0.394 |
| upper limit | 0.666 |

Notes:

[12] - 1-sided p-value from the log-rank test stratified by prognosis stratum according to Interactive Voice Response System (IVRS).

Secondary: Overall survival (OS) at Phase 1B

| | |
|---|-----------------------------------|
| End point title | Overall survival (OS) at Phase 1B |
| End point description: | |
| OS was defined as duration from the date of the first dose of any of the study medications to the date of death from any cause. Subjects not known to have died at the last follow up were censored on the date they were last known to be alive. Survival status were collected every month for the first two months after discontinuation of study treatment and thereafter every 2 months until death or 4 years from each subject's first dose. Full analysis set was used to analyze this end point, including all enrolled subjects of Phase 1B portion who received at least 1 dose of study medication. 99999 represents data not estimable (NE) when the number of subjects analyzed is less than or equal to 3. | |
| End point type | Secondary |
| End point timeframe: | |
| First dose to Follow-up (4 years) | |

| End point values | Phase 1B: Glasdegib + LDAC | Phase 1B: Glasdegib + Decitabine | Phase 1B: Glasdegib + Cytarabine/Da unorubicin | |
|----------------------------------|----------------------------------|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 23 | 7 | 22 | |
| Units: Months | | | | |
| median (confidence interval 80%) | 4.4 (2.5 to 6.6) | 11.5 (4.5 to 17.4) | 34.7 (14.5 to 99999) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS) at Phase 2 Fit

| | |
|-----------------|--|
| End point title | Overall survival (OS) at Phase 2 Fit ^[13] |
|-----------------|--|

End point description:

OS was defined as duration from the date of the first dose of any of the study medications to the date of death from any cause. Subjects not known to have died at the last follow up were censored on the date they were last known to be alive. Survival status were collected every month for the first two months after discontinuation of study treatment and thereafter every 2 months until death or 4 years from each subject's first dose. Full analysis set was used to analyze this endpoint, including all enrolled subjects of Phase 2 Fit arm who received at least 1 dose of study medication. Number of subjects analyzed is number of subjects in the treatment group. 'n' in the categories is number of subjects contributing to the summary statistics. 99999 represents data not estimable (NE) when the number of subjects analyzed is less than 3.

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

End point timeframe:

First dose to Follow-up (4 years)

Notes:

[13] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | | | |
|-----------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 69 | | | |
| Units: Months | | | | |
| median (confidence interval 80%) | | | | |
| Total subjects | 14.9 (13.4 to 19.3) | | | |
| Subjects >= 55 years old (n = 60) | 14.7 (13.1 to 17.7) | | | |
| Subjects < 55 years old (n = 9) | 99999 (11.0 to 99999) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with CR / complete response with incomplete blood count recovery (CRi) at Phase 1B

| | |
|-----------------|---|
| End point title | Percentage of subjects with CR / complete response with |
|-----------------|---|

End point description:

For AML subjects:CR were those with repeat bone marrow showing <5% myeloblasts,spicules present and no Auer rods, peripheral blood showing neutrophils \geq 1000/mcL and platelets \geq 100,000/mcL, transfusion independent and no extramedullary disease. For MDS subjects:CR were those with repeat bone marrow showing \leq 5% myeloblasts, peripheral blood showing neutrophils \geq 1000/mcL, platelets \geq 100,000/mcL, 0% blast and hemoglobin (Hgb) \geq 11 g/dL, normal maturation of all cell lines.For AML and MDS subjects,complete response with incomplete blood count recovery(CRi)were those with repeat bone marrow showing <5% myeloblasts with platelets <100,000/mcL or neutrophils <1000/mcL.End of treatment:maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first.Full analysis set was used to analyze this endpoint, defined as all enrolled subjects of Phase 1B portion who received at least 1 dose of study medication.

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

End point timeframe:

Arm A and Arm B: Screening (within 28 days prior to Dosing), Day 1 of every third cycles, End of Treatment; Arm C: Screening, Day 21 of each Induction cycles and final Consolidation Cycle, Day 1 of every third Maintenance Cycles, End of Treatment

| End point values | Phase 1B: Glasdegib + LDAC | Phase 1B: Glasdegib + Decitabine | Phase 1B: Glasdegib + Cytarabine/Da unorubicin | |
|------------------------------------|----------------------------------|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 23 | 7 | 22 | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 80%) | | | | |
| Percentage of subjects with CR/CRi | 8.7 (2.3 to 21.5) | 28.6 (7.9 to 59.6) | 54.5 (38.9 to 69.5) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with complete response (CR) at Phase 2 Unfit

| | |
|-----------------|---|
| End point title | Percentage of subjects with complete response (CR) at Phase 2 Unfit ^[14] |
|-----------------|---|

End point description:

For AML subjects:CR were those with repeat bone marrow showing <5% myeloblasts,spicules present and no Auer rods, peripheral blood showing neutrophils \geq 1000/mcL and platelets \geq 100,000/mcL, transfusion independent and no extramedullary disease. For MDS subjects:CR were those with repeat bone marrow showing \leq 5% myeloblasts, peripheral blood showing neutrophils \geq 1000/mcL, platelets \geq 100,000/mcL, 0% blast and hemoglobin (Hgb) \geq 11 g/dL, normal maturation of all cell lines. End of treatment: maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first. Full analysis set was used to analyze this end point, including all enrolled subjects of Phase 2 Fit arm who received at least 1 dose of study medication.

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

End point timeframe:

Screening (within 28 days prior to Dosing), Day 1 of every third cycles, End of Treatment.

Notes:

[14] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | | |
|----------------------------------|--|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 88 | 44 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 80%) | | | | |
| Percentage of subjects with CR | 17.0 (11.9 to 22.2) | 2.3 (0.0 to 5.2) | | |

Statistical analyses

| Statistical analysis title | Difference between groups in CR rate |
|---|--|
| Comparison groups | Phase 2 Unfit: Glasdegib 100 mg + LDAC v Phase 2 Unfit: LDAC alone |
| Number of subjects included in analysis | 132 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority |
| P-value | = 0.0152 |
| Method | Cochran-Mantel-Haenszel |
| Parameter estimate | Odds ratio (OR) |
| Point estimate | 5.025 |
| Confidence interval | |
| level | Other: 80 % |
| sides | 2-sided |
| lower limit | 1.5896 |
| upper limit | 15.8843 |

Secondary: Percentage of subjects with disease-specific efficacy for Acute Myeloid Leukemia (AML) at Phase 2 Fit and Unfit

| | |
|------------------------|--|
| End point title | Percentage of subjects with disease-specific efficacy for Acute Myeloid Leukemia (AML) at Phase 2 Fit and Unfit ^[15] |
| End point description: | AML subjects,disease specific efficacy measures included:CRi;Morphologic Leukemia Free State(MLFS)(bone marrow<5%myeloblasts with spicules and no auer rods,neutrophils<1000/mcL and platelets<100,000/mcL);partial remission(PR)(bone marrow myeloblasts decrease to 5-25&>=50%decrease from start, neutrophils>=1000/mcL, platelets>=100,000/mcL);PR with incomplete blood count recovery(PRI)(bone marrow myeloblasts decrease to 5-25&>=50%decrease from start,neutrophils<1000/mcL or platelets<100,000/mcL);minor response(MR)(bone marrow myeloblasts decrease to>=25% from start);stable disease(SD)(bone marrow myeloblasts stable+/-25% from screening value);cytogenetic complete response(CRc)(bone marrow<5%myeloblasts, neutrophils>1000/mcL,platelets>100,000/mcL,normal cytogenetics),molecular complete response(CRm)(bone marrow<5%myeloblasts, neutrophils>1000/mcL, platelets>100,000/mcL and molecular-negative).AML subjects in Full analysis set were analyzed. |
| End point type | Secondary |

End point timeframe:

Phase 2 Fit: Screening (within 28 days prior to Dosing), Day 21 of each Induction cycles and final Consolidation Cycle, Day 1 of every third Maintenance Cycles, End of Treatment. Phase 2 Unfit: Screening, Day 1 of every third cycles, End of Treatment.

Notes:

[15] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | |
|----------------------------------|--|--|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 64 | 78 | 38 | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 80%) | | | | |
| CRi | 10.9 (6.2 to 17.7) | 6.4 (3.2 to 11.6) | 2.6 (0.3 to 9.9) | |
| MLFS | 7.8 (3.8 to 14.0) | 2.6 (0.7 to 6.7) | 0.0 (0.0 to 5.9) | |
| PR | 1.6 (0.2 to 5.9) | 6.4 (3.2 to 11.6) | 2.6 (0.3 to 9.9) | |
| PRi | 1.6 (0.2 to 5.9) | 1.3 (0.1 to 4.9) | 0.0 (0.0 to 5.9) | |
| MR | 10.9 (6.2 to 17.7) | 6.4 (3.2 to 11.6) | 10.5 (4.7 to 19.9) | |
| SD | 6.3 (2.8 to 12.1) | 15.4 (10.3 to 21.9) | 21.1 (12.7 to 31.9) | |
| CRc | 35.9 (27.9 to 44.7) | 10.3 (6.1 to 16.1) | 0.0 (0.0 to 5.9) | |
| CRm | 37.5 (29.4 to 46.2) | 15.4 (10.3 to 21.9) | 2.6 (0.3 to 9.9) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of subjects with disease-specific efficacy for Myelodysplastic Syndrome (MDS) at Phase 2 Fit and Unfit

| | |
|-----------------|---|
| End point title | Percentage of subjects with disease-specific efficacy for Myelodysplastic Syndrome (MDS) at Phase 2 Fit and Unfit ^[16] |
|-----------------|---|

End point description:

MDS subjects,disease specific efficacy measures included:CRi(bone marrow showing <5% myeloblasts with platelets <100,000/mcL or neutrophils <1000/mcL, include confirmed and unconfirmed responses);PR(repeat bone marrow myeloblasts showing decreased by >= 50% decrease but still >5%, peripheral blood showing neutrophils >= 1,000/mcL, platelets >= 100,000/mcL and Hgb>=11g/dL; include confirmed and unconfirmed responses); SD(include confirmed and unconfirmed responses, failure to achieve PR and no evidence of progression for >8 weeks); marrow complete response(mCR)(bone marrow showing <=5% myeloblasts and decreased by >= 50%),partial cytogenetic response(>=50% reduction of chromosomal abnormality) and complete cytogenetic response(CRc)(disappearance of chromosomal abnormality with no appearance of new ones).MDS subjects in Full analysis set were analyzed: all enrolled subjects of Phase 2 Fit arm who received at least 1 dose of study medication,all randomized subjects of Phase 2 Unfit arm.

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

End point timeframe:

Phase 2 Fit: Screening (within 28 days Prior to Dosing), Day 21 of each Induction cycles and final Consolidation Cycle, Day 1 of every third Maintenance Cycles, End of Treatment. Phase 2 Unfit: Screening, Day 1 of every third cycles, End of Treatment.

Notes:

[16] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | |
|----------------------------------|--|--|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 5 | 10 | 6 | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 80%) | | | | |
| mCR | 0.0 (0.0 to 36.9) | 10.0 (1.0 to 33.7) | 0.0 (0.0 to 31.9) | |
| PR | 0.0 (0.0 to 36.9) | 0.0 (0.0 to 20.6) | 0.0 (0.0 to 31.9) | |
| SD | 0.0 (0.0 to 36.9) | 0.0 (0.0 to 20.6) | 33.3 (9.3 to 66.7) | |
| CRi | 20.0 (2.1 to 58.4) | 10.0 (1.0 to 33.7) | 0.0 (0.0 to 31.9) | |
| Unconfirmed SD | 0.0 (0.0 to 36.9) | 10.0 (1.0 to 33.7) | 0.0 (0.0 to 31.9) | |
| Unconfirmed CRi | 0.0 (0.0 to 36.9) | 10.0 (1.0 to 33.7) | 0.0 (0.0 to 31.9) | |
| mCR (CRi not included) | 0.0 (0.0 to 36.9) | 10.0 (1.0 to 33.7) | 0.0 (0.0 to 31.9) | |
| CRc | 60.0 (24.7 to 88.8) | 10.0 (1.0 to 33.7) | 0.0 (0.0 to 31.9) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to maximum observed plasma concentration (Tmax) of glasdegib in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 10 and Cycle 2/Day 1

| | |
|-----------------|--|
| End point title | Time to maximum observed plasma concentration (Tmax) of glasdegib in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 10 and Cycle 2/Day 1 ^[17] |
|-----------------|--|

End point description:

Dose compliant group were used to analyze this end point: subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state, part of the "dose compliant" group. Number of subjects analyzed: numbers of subjects in the treatment group. 'n' in categories: number of subjects contributing to the summary statistics. 99999 represents data not estimable (NE) as fewer than 3 subjects had reportable parameter values.

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

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6 and 24 hours post-dose on Cycle 1/Day 10; pre-dose, 0.5, 1, 2, 6 and 24 hours post-dose on Cycle 2/Day 1

Notes:

[17] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + Decitabine | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1/Day 10 (n = 3, 3) | 2.00 (0.500 to 24.0) | 2.05 (1.00 to 5.97) | | |
| Cycle 2/Day 1 (n = 3) | 1.03 (0.567 to 2.00) | 99999 (99999 to 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time profile from time 0 to dosing interval (AUC_{tau}) of glasdegib in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 10 and Cycle 2/Day 1

| | |
|-----------------|---|
| End point title | Area under the plasma concentration-time profile from time 0 to dosing interval (AUC _{tau}) of glasdegib in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 10 and Cycle 2/Day 1 ^[18] |
|-----------------|---|

End point description:

Dose compliant group were used to analyze this end point: subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state, part of the "dose compliant" group. Number of subjects analyzed: numbers of subjects in the treatment group. 'n' in categories: number of subjects contributing to the summary statistics. 99999 represents data not estimable (NE) as fewer than 3 subjects had reportable parameter values.

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

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6 and 24 hours post-dose on Cycle 1/Day 10; pre-dose, 0.5, 1, 2, 6 and 24 hours post-dose on Cycle 2/Day 1

Notes:

[18] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + Decitabine | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |

| | | | | |
|---------------------------|-----------------|-----------------|--|--|
| Cycle 1/Day 10 (n = 2, 3) | 99999 (± 99999) | 28380 (± 11) | | |
| Cycle 2/Day 1 (n = 3) | 17060 (± 29) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum observed plasma concentration (C_{max}) of glasdegib in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 and Day 10

| | |
|-----------------|--|
| End point title | Maximum observed plasma concentration (C _{max}) of glasdegib in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 and Day 10 ^[19] |
|-----------------|--|

End point description:

Dose compliant group was used to analyze this end point. Subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state and part of the "dose compliant" group. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.5, 1, 6 and 24 hours post-dose on Induction Cycle 1/Day 3; pre-dose, 0.5, 1, 4, 6 and 24 hours post-dose on Induction Cycle 1/Day 10

Notes:

[19] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Daunorubicin | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 14 | 6 | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Induction Cycle 1/Day 3 (n = 14, 6) | 674.2 (± 45) | 1622 (± 25) | | |
| Induction Cycle 1/Day 10 (n = 15, 6) | 1135 (± 43) | 2371 (± 43) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: T_{max} of glasdegib in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 and Day 10

| | |
|-----------------|---|
| End point title | T _{max} of glasdegib in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 and Day 10 ^[20] |
|-----------------|---|

End point description:

Dose compliant group was used to analyze this end point. Subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state and part of the "dose compliant" group. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.5, 1, 6 and 24 hours post-dose on Induction Cycle 1/Day 3; pre-dose, 0.5, 1, 4, 6 and 24 hours post-dose on Induction Cycle 1/Day 10

Notes:

[20] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin | | |
|--------------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 6 | | |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| Induction Cycle 1/Day 3 (n = 14, 6) | 5.99 (0.467 to 25.2) | 6.00 (1.00 to 6.07) | | |
| Induction Cycle 1/Day 10 (n = 15, 6) | 4.08 (0.500 to 24.7) | 1.04 (0.583 to 4.12) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AUCtau of glasdegib in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 and Day 10

| | |
|-----------------|---|
| End point title | AUCtau of glasdegib in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 and Day 10 ^[21] |
|-----------------|---|

End point description:

Dose compliant group was used to analyze this end point. Subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state and part of the "dose compliant" group. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.5, 1, 6 and 24 hours post-dose on Induction Cycle 1/Day 3; pre-dose, 0.5, 1, 4, 6 and 24 hours post-dose on Induction Cycle 1/Day 10

Notes:

[21] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 6 | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Induction Cycle 1/Day 3 (n = 12, 5) | 9332 (± 56) | 22840 (± 43) | | |
| Induction Cycle 1/Day 10 (n = 13, 5) | 16300 (± 46) | 26370 (± 39) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of LDAC and Ara-U in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 2 and Cycle 1/Day 10

| | |
|-----------------|---|
| End point title | Cmax of LDAC and Ara-U in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 2 and Cycle 1/Day 10 ^[22] |
|-----------------|---|

End point description:

Ara-U is the major metabolite of cytarabine. LDAC (low dose cytarabine) is rapidly degraded to the stable metabolite Ara-U. PK concentration population were analyzed: all treated participants who had at least 1 concentration of any of the study drugs. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4 and 6 hours post-dose on Cycle 1/Day 2 and Cycle 1/Day 10

Notes:

[22] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| LDAC Cycle 1/Day 2 (n = 16, 6) | 58.50 (± 58) | 100.1 (± 29) | | |
| LDAC Cycle 1/Day 10 (n = 12, 6) | 63.01 (± 88) | 132.5 (± 39) | | |
| Ara-U Cycle 1/Day 2 (n = 17, 6) | 379.5 (± 34) | 569.7 (± 29) | | |
| Ara-U Cycle 1/Day 10 (n = 12, 6) | 452.2 (± 36) | 652.0 (± 27) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of LDAC and Ara-U in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 2 and Cycle 1/Day 10

| | |
|-----------------|---|
| End point title | Tmax of LDAC and Ara-U in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 2 and Cycle 1/Day 10 ^[23] |
|-----------------|---|

End point description:

Ara-U is the major metabolite of cytarabine. LDAC (low dose cytarabine) is rapidly degraded to the stable metabolite Ara-U. PK parameter analysis set was used to analyze this end point, including all treated subjects who had at least 1 of the PK parameters of interest for any of the study drugs. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4 and 6 hours post-dose on Cycle 1/Day 2 and Cycle 1/Day 10

Notes:

[23] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | | |
|----------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| LDAC Cycle 1/Day 2 (n = 16, 6) | 0.250 (0.233 to 1.00) | 0.250 (0.250 to 0.500) | | |
| LDAC Cycle 1/Day 10 (n = 12, 6) | 0.325 (0.233 to 1.00) | 0.250 (0.233 to 0.500) | | |
| Ara-U Cycle 1/Day 2 (n = 17, 6) | 3.97 (1.00 to 6.05) | 4.00 (1.00 to 6.00) | | |
| Ara-U Cycle 1/Day 10 (n = 12, 6) | 2.00 (0.000 to 6.00) | 1.99 (1.02 to 4.08) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time profile from time 0 to infinity (AUCinf) of LDAC in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 2 and Cycle 1/Day 10

| | |
|-----------------|--|
| End point title | Area under the plasma concentration-time profile from time 0 to infinity (AUCinf) of LDAC in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 2 and Cycle 1/Day 10 ^[24] |
|-----------------|--|

End point description:

PK parameter analysis set was used to analyze this end point, including all treated subjects who had at least 1 of the PK parameters of interest for any of the study drugs. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4 and 6 hours post-dose on Cycle 1/Day 2 and Cycle 1/Day 10

Notes:

[24] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| LDAC Cycle 1/Day 2 (n = 14, 6) | 71.10 (± 28) | 89.35 (± 28) | | |
| LDAC Cycle 1/Day 10 (n = 9, 5) | 92.28 (± 25) | 143.9 (± 24) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration (AUClast) of LDAC and Ara-U in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 2 and Cycle 1/Day 10

| | |
|-----------------|--|
| End point title | Area under the plasma concentration-time profile from time 0 to the time of the last quantifiable concentration (AUClast) of LDAC and Ara-U in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 2 and Cycle 1/Day 10 ^[25] |
|-----------------|--|

End point description:

Ara-U is the major metabolite of cytarabine. LDAC (low dose cytarabine) is rapidly degraded to the stable metabolite Ara-U. PK parameter analysis set was used to analyze this end point, including all treated subjects who had at least 1 of the PK parameters of interest for any of the study drugs. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 2, 4 and 6 hours post-dose on Cycle 1/Day 2 and Cycle 1/Day 10

Notes:

[25] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| LDAC Cycle 1/Day 2 (n = 16, 6) | 62.55 (± 41) | 87.49 (± 29) | | |
| LDAC Cycle 1/Day 10 (n = 12, 6) | 65.56 (± 76) | 134.8 (± 26) | | |
| Ara-U Cycle 1/Day 2 (n = 17, 6) | 2036 (± 36) | 3050 (± 29) | | |
| Ara-U Cycle 1/Day 10 (n = 12, 6) | 2283 (± 43) | 3528 (± 29) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of decitabine in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 1 and Cycle 1/Day 2

| | |
|-----------------|--|
| End point title | Cmax of decitabine in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 1 and Cycle 1/Day 2 ^[26] |
|-----------------|--|

End point description:

PK concentration population: all treated subjects who had at least 1 concentration of any of the study drugs.

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

End point timeframe:

Pre-dose, 0.5 hour from start of infusion, 1 hour (at end of infusion) and 2, 3 and 4 hours from start of infusion on Cycle 1/Day 1 and Cycle 1/Day 2

Notes:

[26] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + Decitabine | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 3 | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1/Day 1 | 113.4 (± 59) | 174.2 (± 113) | | |
| Cycle 1/Day 2 | 127.9 (± 43) | 121.7 (± 37) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of decitabine in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 1 and Cycle 1/Day 2

| | |
|-----------------|--|
| End point title | Tmax of decitabine in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 1 and Cycle 1/Day 2 ^[27] |
|-----------------|--|

End point description:

PK parameter analysis set was used to analyze this end point, including all treated subjects who had at least 1 of the PK parameters of interest for any of the study drugs.

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

End point timeframe:

Pre-dose, 0.5 hour from start of infusion, 1 hour (at end of infusion) and 2, 3 and 4 hours from start of infusion on Cycle 1/Day 1 and Cycle 1/Day 2

Notes:

[27] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + Decitabine | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 3 | 3 | | |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1/Day 1 | 0.75 (0.50 to 1.0) | 0.53 (0.52 to 0.75) | | |
| Cycle 1/Day 2 | 0.58 (0.53 to 0.95) | 0.53 (0.52 to 1.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AUCinf of decitabine in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 1 and Cycle 1/Day 2

| | |
|-----------------|--|
| End point title | AUCinf of decitabine in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 1 and Cycle 1/Day 2 ^[28] |
|-----------------|--|

End point description:

PK parameter analysis set was used to analyze this end point, including all treated subjects who had at least 1 of the PK parameters of interest for any of the study drugs. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics. 99999 represents data not estimable (NE) as fewer than 3 subjects had reportable parameter values.

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

End point timeframe:

Pre-dose, 0.5 hour from start of infusion, 1 hour (at end of infusion) and 2, 3 and 4 hours from start of infusion on Cycle 1/Day 1 and Cycle 1/Day 2

Notes:

[28] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + Decitabine | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |

| | | | | |
|--------------------------|-----------------|-----------------|--|--|
| Cycle 1/Day 1 (n = 3, 3) | 133.4 (± 71) | 251.5 (± 140) | | |
| Cycle 1/Day 2 (n = 2, 2) | 99999 (± 99999) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AUCtau of cytarabine and Ara-U in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3

| | |
|-----------------|---|
| End point title | AUCtau of cytarabine and Ara-U in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 ^[29] |
|-----------------|---|

End point description:

Ara-U is the major metabolite of cytarabine. PK parameter analysis set was used to analyze this end point, including all treated subjects who had at least 1 of the PK parameters of interest for any of the study drugs. 99999 represents data not estimable (NE) as fewer than 3 subjects had reportable parameter values.

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

End point timeframe:

Pre-dose, 6 and 24 hours post start of cytarabine infusion on Induction Cycle 1/Day 3

Notes:

[29] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 9 | 2 | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cytarabine | 1070 (± 211) | 99999 (± 99999) | | |
| Ara-U | 28420 (± 32) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of daunorubicin and daunorubicinol in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3

| | |
|-----------------|--|
| End point title | Cmax of daunorubicin and daunorubicinol in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 ^[30] |
|-----------------|--|

End point description:

Daunorubicinol is the major metabolite of daunorubicin, which has anti-neoplastic activity. PK concentration population were analyzed: all treated participants who had at least 1 concentration of any of the study drugs.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 4, 6, 24 hours post administration of daunorubicin on Induction Cycle 1/Day 3

Notes:

[30] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin | | |
|--|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 6 | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Daunorubicin | 275.3 (± 153) | 341.0 (± 82) | | |
| Daunorubicinol | 195.4 (± 139) | 233.4 (± 46) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of daunorubicin and daunorubicinol in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3

| | |
|-----------------|--|
| End point title | Tmax of daunorubicin and daunorubicinol in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 ^[31] |
|-----------------|--|

End point description:

Daunorubicinol is the major metabolite of daunorubicin, which has anti-neoplastic activity. PK parameter analysis set was used to analyze this end point, including all treated subjects who had at least 1 of the PK parameters of interest for any of the study drugs.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 4, 6, 24 hours post administration of daunorubicin on Induction Cycle 1/Day 3

Notes:

[31] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 15 | 6 | | |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| Daunorubicin | 0.500 (0.217 to 1.72) | 0.492 (0.250 to 0.600) | | |
| Daunorubicinol | 1.00 (0.217 to 5.90) | 0.642 (0.283 to 4.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AUCtau of daunorubicin and daunorubicinol in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3

| | |
|-----------------|--|
| End point title | AUCtau of daunorubicin and daunorubicinol in subjects receiving glasdegib and cytarabine/daunorubicin at Phase 1B on Induction Cycle 1/Day 3 ^[32] |
|-----------------|--|

End point description:

Daunorubicinol is the major metabolite of daunorubicin, which has anti-neoplastic activity. PK parameter analysis set was used to analyze this end point, including all treated subjects who had at least 1 of the PK parameters of interest for any of the study drugs. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.25, 0.5, 1, 4, 6, 24 hours post administration of daunorubicin on Induction Cycle 1/Day 3

Notes:

[32] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 6 | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Daunorubicin (n = 14, 4) | 499.3 (± 61) | 424.9 (± 38) | | |
| Daunorubicinol (n = 15, 5) | 2152 (± 24) | 2712 (± 33) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of glasdegib in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 10 and Cycle 1/Day 21

| | |
|-----------------|---|
| End point title | Cmax of glasdegib in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 10 and Cycle 1/Day 21 ^[33] |
|-----------------|---|

End point description:

Dose compliant group were used to analyze this end point: subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state, part of the "dose compliant" group. Number of subjects analyzed: numbers of subjects in the treatment group. 'n' in categories: number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6 and 24 hours post-dose on Cycle 1/Day 10 and Cycle 1/Day 21

Notes:

[33] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1/Day 10 (n = 13, 6) | 1074 (± 63) | 1942 (± 75) | | |
| Cycle 1/Day 21 (n = 8, 5) | 1242 (± 56) | 2577 (± 104) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of glasdegib in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 10 and Cycle 1/Day 21

| | |
|-----------------|---|
| End point title | Tmax of glasdegib in subjects receiving glasdegib and LDAC at Phase 1B on Cycle 1/Day 10 and Cycle 1/Day 21 ^[34] |
|-----------------|---|

End point description:

Dose compliant group were used to analyze this end point: subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state, part of the "dose compliant" group. Number of subjects analyzed: numbers of subjects in the treatment group. 'n' in categories: number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6 and 24 hours post-dose on Cycle 1/Day 10 and Cycle 1/Day 21

Notes:

[34] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | | |
|-------------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| Cycle 1/Day 10 (n = 13, 6) | 1.75 (0.750 to 24.0) | 4.00 (1.02 to 24.0) | | |
| Cycle 1/Day 21 (n = 8, 5) | 1.34 (0.533 to 2.00) | 4.00 (1.00 to 6.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AUCtau of glasdegib in subjects receiving glasdegib and LDAC at phase 1B on Cycle 1/Day 10 and Cycle 1/Day 21

| | |
|-----------------|---|
| End point title | AUCtau of glasdegib in subjects receiving glasdegib and LDAC at phase 1B on Cycle 1/Day 10 and Cycle 1/Day 21 ^[35] |
|-----------------|---|

End point description:

Dose compliant group were used to analyze this end point: subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state, part of the "dose compliant" group. Number of subjects analyzed: numbers of subjects in the treatment group. 'n' in categories: number of subjects contributing to the summary statistics.

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

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6 and 24 hours post-dose on Cycle 1/Day 10 and Cycle 1/Day 21

Notes:

[35] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | | |
|---|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 17 | 6 | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1/Day 10 (n = 10, 4) | 15020 (± 49) | 28600 (± 17) | | |
| Cycle 1/Day 21 (n = 8, 4) | 16660 (± 43) | 31400 (± 119) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of glasdegib in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 10 and Cycle 2/Day 1

| | |
|-----------------|--|
| End point title | Cmax of glasdegib in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 10 and Cycle 2/Day 1 ^[36] |
|-----------------|--|

End point description:

Dose compliant group were used to analyze this end point: subjects who had at least 4 days of uninterrupted dosing for a multiple dose PK assessment were considered to be at steady state, part of the "dose compliant" group. Number of subjects analyzed: numbers of subjects in the treatment group. 'n' in categories: number of subjects contributing to the summary statistics. 99999 represents data not estimable (NE) as fewer than 3 subjects had reportable parameter values.

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

End point timeframe:

Pre-dose, 0.5, 1, 2, 4, 6 and 24 hours post-dose on Cycle 1/Day 10; pre-dose, 0.5, 1, 2, 6 and 24 hours post-dose on Cycle 2/Day 1

Notes:

[36] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + Decitabine | | |
|---|--|--|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 4 | 3 | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cycle 1/Day 10 (n = 3, 3) | 1718 (± 28) | 2381 (± 28) | | |
| Cycle 2/Day 1 (n = 3) | 1826 (± 44) | 99999 (± 99999) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose plasma concentration (Ctough) of glasdegib in Phase 2 Fit on Induction Cycle 1/Day 10

| | |
|-----------------|--|
| End point title | Pre-dose plasma concentration (Ctough) of glasdegib in Phase 2 Fit on Induction Cycle 1/Day 10 ^[37] |
|-----------------|--|

End point description:

Dose compliant, non CYP3A4 group was used to analyze this end point, defined as dose compliant group subjects who did not have administration of any strong or moderate CYP3A4 inhibitors.

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

End point timeframe:

Pre-dose, 1 and 4 hours post-dose on Induction Cycle 1/Day 10

Notes:

[37] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|---|---|--|--|--|
| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 42 | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 308.7 (\pm 74) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Cmax of glasdegib in subjects receiving glasdegib and LDAC at Phase 2 Unfit on Cycle 1/Day 10

| | |
|-----------------|---|
| End point title | Cmax of glasdegib in subjects receiving glasdegib and LDAC at Phase 2 Unfit on Cycle 1/Day 10 ^[38] |
|-----------------|---|

End point description:

Dose compliant, non CYP3A4 group was used to analyze this end point, defined as dose compliant group subjects who did not have administration of any strong or moderate CYP3A4 inhibitors.

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

End point timeframe:

Pre-dose, 1, 2, 4, and 6 hour post-dose on Cycle 1/Day 10

Notes:

[38] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|---|---|--|--|--|
| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | 1525 (\pm 44) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Tmax of glasdegib in subjects receiving glasdegib and LDAC at Phase 2 Unfit on Cycle 1/Day 10

| | |
|-----------------|---|
| End point title | Tmax of glasdegib in subjects receiving glasdegib and LDAC at Phase 2 Unfit on Cycle 1/Day 10 ^[39] |
|-----------------|---|

End point description:

Dose compliant, non CYP3A4 group was used to analyze this end point, defined as dose compliant group subjects who did not have administration of any strong or moderate CYP3A4 inhibitors.

| | | | | |
|--|--|--|--|--|
| End point type | Secondary | | | |
| End point timeframe: | | | | |
| Pre-dose, 1, 2, 4, and 6 hour post-dose on Cycle 1/Day 10 | | | | |
| Notes: | | | | |
| [39] - 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: Not every reporting arm is required for reporting this endpoint of the study. | | | | |
| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 41 | | | |
| Units: Hours | | | | |
| median (full range (min-max)) | | | | |
| Tmax | 1.67 (0.667 to 5.83) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: AUCtau of glasdegib in subjects receiving glasdegib and LDAC at Phase 2 Unfit on Cycle 1/Day 10

| | | | | |
|--|---|--|--|--|
| End point title | AUCtau of glasdegib in subjects receiving glasdegib and LDAC at Phase 2 Unfit on Cycle 1/Day 10 ^[40] | | | |
| End point description: | | | | |
| Dose compliant, non CYP3A4 group was used to analyze this end point, defined as dose compliant group subjects who did not have administration of any strong or moderate CYP3A4 inhibitors. | | | | |
| End point type | Secondary | | | |
| End point timeframe: | | | | |
| Pre-dose, 1, 2, 4, and 6 hour post-dose on Cycle 1/Day 10 | | | | |
| Notes: | | | | |
| [40] - 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: Not every reporting arm is required for reporting this endpoint of the study. | | | | |
| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 37 | | | |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| AUCtau | 17210 (± 54) | | | |

Statistical analyses

Secondary: Number of subjects with disease-related gene mutations at Phase 1B

| | |
|-----------------|--|
| End point title | Number of subjects with disease-related gene mutations at Phase 1B |
|-----------------|--|

End point description:

Peripheral blood and bone marrow aspirate were collected for baseline mutational analyses. Genetic abnormalities frequently associated with AML were analyzed. These genetic abnormalities included known mutations in the genes NPM1, CEBPA, FLT3, RUNX1, IDH1, IDH2, KIT, K Ras, N Ras and WT1. Additional genes with mutations known to be associated with AML and MDS such as TET2 and DNMT3A were also evaluated. Pharmacodynamic (PD) analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 1B portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Baseline (Cycle 1/Day 1 pre-dose for Glasdegib + LDAC and Glasdegib + Decitabine Arms; Induction Cycle 1/Day -3 pre-dose for Glasdegib +Cytarabine/Daunorubicin Arm)

| End point values | Phase 1B: Glasdegib + LDAC (Biomarker, Responder) | Phase 1B: Glasdegib + LDAC (Biomarker, non- Responder) | Phase 1B: Glasdegib + Decitabine (Biomarker, Responder) | Phase 1B: Glasdegib + Decitabine (Biomarker, non- Responder) |
|--|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 0 ^[41] | 9 | 0 ^[42] | 1 |
| Units: Subjects | | | | |
| CEBPA (CCAAT/enhancer-binding protein alpha) | | 3 | | 0 |
| DNMT3A (DNA [cytosine-5]-methyltransferase 3A) | | 2 | | 0 |
| FLT3 (Fms-like tyrosine kinase 3) | | 1 | | 0 |
| FLT3-ITD (FLT3 internal tandem duplications) | | 0 | | 0 |
| IDH1 (Isocitrate dehydrogenase 1) | | 1 | | 0 |
| IDH2 (Isocitrate dehydrogenase 2) | | 0 | | 0 |
| KIT(Tyrosine-protein kinase Kit) | | 0 | | 1 |
| KRAS(Kirsten rat sarcoma 2 viral oncogene homolog) | | 1 | | 0 |
| NPM1 (Nucleophosmin) | | 0 | | 0 |
| NRAS(Neuroblastoma RAS viral oncogene homolog) | | 5 | | 0 |
| RUNX1 (Runt related transcription factor 1) | | 1 | | 0 |
| TET2 (Tet methylcytosine dioxygenase 2) | | 3 | | 0 |
| WT1 (Wilm's tumour tumor suppressor gene1) | | 0 | | 0 |

Notes:

[41] - Sample non-collection/availability, blast count being too low for reliable mutation detection.

[42] - Sample non-collection/availability, blast count being too low for reliable mutation detection.

| End point values | Phase 1B: Glasdegib + Cytarabine/Da | Phase 1B: Glasdegib+Cyt arabine/Dauno | | |
|------------------|---|---|--|--|
|------------------|---|---|--|--|

| | uno (Biomarker, Responder) | (Biomarker,non -Responder) | | |
|--|----------------------------------|-------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 11 | 1 | | |
| Units: Subjects | | | | |
| CEBPA (CCAAT/enhancer-binding protein alpha) | 2 | 0 | | |
| DNMT3A (DNA [cytosine-5]-methyltransferase 3A) | 0 | 0 | | |
| FLT3 (Fms-like tyrosine kinase 3) | 2 | 0 | | |
| FLT3-ITD (FLT3 internal tandem duplications) | 1 | 0 | | |
| IDH1 (Isocitrate dehydrogenase 1) | 0 | 0 | | |
| IDH2 (Isocitrate dehydrogenase 2) | 2 | 0 | | |
| KIT(Tyrosine-protein kinase Kit) | 0 | 0 | | |
| KRAS(Kirsten rat sarcoma 2 viral oncogene homolog) | 0 | 0 | | |
| NPM1 (Nucleophosmin) | 4 | 0 | | |
| NRAS(Neuroblastoma RAS viral oncogene homolog) | 1 | 0 | | |
| RUNX1 (Runt related transcription factor 1) | 1 | 0 | | |
| TET2 (Tet methylcytosine dioxygenase 2) | 1 | 0 | | |
| WT1 (Wilm's tumour tumor suppressor gene1) | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 1B - Baseline

| | |
|-----------------|---|
| End point title | Serum levels of circulating protein analytes at Phase 1B - Baseline |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1(baseline), 1 hour post-dose on Cycle 1/Day 2 and Day 10, pre-dose on Cycle 1/Day 21 and end of treatment for Glasdegib+LADC arm; Cycle 1/Day 1(baseline), 1 hour post-dose on Cycle 1/Day 1 and Day 2 and pre-dose on Cycle 1/Day 10 for Glasdegib+Decitabine arm; pre-dose on Induction Cycle 1/Day -3(baseline), 1 hour post-dose on Induction Cycle 1/Lead-in,Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment for Glasdegib+Cytarabine/Daunorubicin arm. Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. Pharmacodynamic(PD) analysis set was analyzed: all enrolled subjects in the Phase 1B portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Baseline (Induction Cycle 1/Day -3 pre-dose)

| | | | | |
|---|---|--|--|--|
| End point values | Phase 1B: Glasdegib + Cytarabine/Da unorubicin | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 22 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| MMP-3 (Matrix metalloproteinase-3) | 10200 (1700 to 44000) | | | |
| IL-8 (Interleukin-8) | 10.7 (0.00 to 71.00) | | | |
| BDNF (Brain-derived neurotrophic factor) | 1200 (0.00 to 22000) | | | |
| IL-5 (Interleukin-5) | 0.00 (0.00 to 0.00) | | | |
| VEGF (Vascular endothelial growth factor) | 88.00 (32.00 to 2000.00) | | | |
| MCP-1 (Monocyte chemotactic protein-1) | 180.5 (0.00 to 1850.00) | | | |
| ITAC:Interferon-inducible T-cell α chemoattractant | 0.00 (0.00 to 1900.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 1B - Induction Cycle 1/Day 3: MMP-3 (Matrix metalloproteinase-3)

| | |
|-----------------|--|
| End point title | Serum levels of circulating protein analytes at Phase 1B - Induction Cycle 1/Day 3: MMP-3 (Matrix metalloproteinase-3) |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1(baseline), 1 hour post-dose on Cycle 1/Day 2 and Day 10, pre-dose on Cycle 1/Day 21 and end of treatment for Glasdegib+LADC arm; Cycle 1/Day 1(baseline), 1 hour post-dose on Cycle 1/Day 1 and Day 2 and pre-dose on Cycle 1/Day 10 for Glasdegib+Decitabine arm; pre-dose on Induction Cycle 1/Day -3(baseline), 1 hour post-dose on Induction Cycle 1/Lead-in,Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment for Glasdegib+Cytarabine/Daunorubicin arm. Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. Pharmacodynamic(PD) analysis set was analyzed: all enrolled subjects in the Phase 1B portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Induction Cycle 1/Day 3, 1 Hour Post dose

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Phase 1B: Glasdegib + Cytarabine/Da unorubicin | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 21 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | 20000 (1600 to 111000) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 1B - Induction Cycle 1/Day 10

| | |
|---|---|
| End point title | Serum levels of circulating protein analytes at Phase 1B - Induction Cycle 1/Day 10 |
| End point description: Blood samples were collected at pre-dose on Cycle 1/Day 1(baseline), 1 hour post-dose on Cycle 1/Day 2 and Day 10, pre-dose on Cycle 1/Day 21 and end of treatment for Glasdegib+LADC arm; Cycle 1/Day 1(baseline), 1 hour post-dose on Cycle 1/Day 1 and Day 2 and pre-dose on Cycle 1/Day 10 for Glasdegib+Decitabine arm; pre-dose on Induction Cycle 1/Day -3(baseline), 1 hour post-dose on Induction Cycle 1/Lead-in,Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment for Glasdegib+Cytarabine/Daunorubicin arm. Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. Pharmacodynamic(PD) analysis set was analyzed: all enrolled subjects in the Phase 1B portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment. | |
| End point type | Secondary |
| End point timeframe: Induction Cycle 1/Day 10, 1 Hour Post dose | |

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Phase 1B: Glasdegib + Cytarabine/Da unorubicin | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 21 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| IL-8 | 37.00 (7.90 to 128.00) | | | |
| BDNF | 200 (0.00 to 2800) | | | |
| IL-5 | 99.00 (0.00 to 2440.00) | | | |
| VEGF | 51.00 (0.00 to 149.00) | | | |
| MCP-1 | 684.00 (368.00 to 9780.00) | | | |

| | | | | |
|------|-----------------------|--|--|--|
| ITAC | 0.00 (0.00 to 218.00) | | | |
|------|-----------------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline levels of serum circulating protein analytes associated with best overall response at Phase 1B

| | |
|---|---|
| End point title | Baseline levels of serum circulating protein analytes associated with best overall response at Phase 1B |
| End point description: | |
| Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 2 and Day 10, pre-dose on Cycle 1/Day 21 and end of treatment for Glasdegib+LADC arm; Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and Day 2 and pre-dose on Cycle 1/Day 10 for Glasdegib+Decitabine arm; pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Lead-in, Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment for Glasdegib+Cytarabine/Daunorubicin arm. Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. Serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Cycle 1/Day 1 pre-dose for Glasdegib + LDAC and Glasdegib + Decitabine Arms; Induction Cycle 1/Day -3 pre-dose for Glasdegib +Cytarabine/Daunorubicin Arm) | |

| End point values | Phase 1B: Glasdegib + LDAC (Biomarker, Responder) | Phase 1B: Glasdegib + LDAC (Biomarker, non-Responder) | Phase 1B: Glasdegib + Decitabine (Biomarker, Responder) | Phase 1B: Glasdegib + Decitabine (Biomarker, non-Responder) |
|---------------------------------------|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 4 | 19 | 5 | 2 |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| IL-6 (Interleukin-6) | 3.2 (0.00 to 11.00) | 0.00 (0.00 to 232.00) | 0.00 (0.00 to 7.00) | 8.50 (0.00 to 17.00) |
| SDF-1 (Stromal cell-derived factor 1) | 2895.00 (2370.00 to 3330.00) | 2480.00 (1170.00 to 4280.00) | 1720.00 (1440.00 to 3190.00) | 4045.00 (2860.00 to 5230.00) |

| End point values | Phase 1B: Glasdegib + Cytarabine/Daunorubicin (Biomarker, Responder) | Phase 1B: Glasdegib+Cytarabine/Daunorubicin (Biomarker, non-Responder) | | |
|------------------|--|--|--|--|
|------------------|--|--|--|--|

| | | | | |
|---------------------------------------|------------------------------|------------------------------|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 8 | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| IL-6 (Interleukin-6) | 6.90 (0.00 to 25.00) | 0.00 (0.00 to 14.00) | | |
| SDF-1 (Stromal cell-derived factor 1) | 2275.00 (1600.00 to 3700.00) | 3275.00 (1950.00 to 4730.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 1B - Induction Cycle 1/Lead-In: MMP-3 (Matrix metalloproteinase-3)

| | |
|-----------------|--|
| End point title | Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 1B - Induction Cycle 1/Lead-In: MMP-3 (Matrix metalloproteinase-3) |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 2 and Day 10, pre-dose on Cycle 1/Day 21 and end of treatment for Glasdegib+LADC arm; Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and Day 2 and pre-dose on Cycle 1/Day 10 for Glasdegib+Decitabine arm; pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Lead-in, Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment for Glasdegib+Cytarabine/Daunorubicin arm. Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. Serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point.

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

End point timeframe:

Induction Cycle 1/Lead-in, 1 Hour Post dose

| | | | | |
|-------------------------------|---|---|--|--|
| End point values | Phase 1B: Glasdegib + Cytarabine/Dauno (Biomarker, Responder) | Phase 1B: Glasdegib+Cytarabine/Dauno (Biomarker, non-Responder) | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 14 | 8 | | |
| Units: ng/mL | | | | |
| median (full range (min-max)) | 8.90 (2.20 to 51.00) | 10.50 (6.50 to 19.00) | | |

Statistical analyses

Secondary: Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 1B - Induction Cycle 1/Day 3: SDF-1 (Stromal cell-derived factor 1)

| | |
|-----------------|---|
| End point title | Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 1B - Induction Cycle 1/Day 3: SDF-1 (Stromal cell-derived factor 1) |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 2 and Day 10, pre-dose on Cycle 1/Day 21 and end of treatment for Glasdegib+LADC arm; Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and Day 2 and pre-dose on Cycle 1/Day 10 for Glasdegib+Decitabine arm; pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Lead-in, Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment for Glasdegib+Cytarabine/Daunorubicin arm. Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. Serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point.

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

End point timeframe:

Induction Cycle 1/Day 3, 1 Hour Post dose

| End point values | Phase 1B: Glasdegib + Cytarabine/Da uno (Biomarker, Responder) | Phase 1B: Glasdegib+Cyt arabine/Dauno (Biomarker,non -Responder) | | |
|-------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 13 | 8 | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | 2510.00 (1530.00 to 3520.00) | 3260.00 (1350.00 to 4430.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with disease-related gene mutations at Phase 2 Fit and Unfit

| | |
|-----------------|---|
| End point title | Number of subjects with disease-related gene mutations at Phase 2 Fit and Unfit |
|-----------------|---|

End point description:

Peripheral blood and bone marrow aspirate were collected for baseline mutational analyses. Genetic abnormalities frequently associated with AML were analyzed. These genetic abnormalities included known mutations in the genes NPM1, CEBPA, FLT3, RUNX1, IDH1, IDH2, KIT, K Ras, N Ras and WT1. Additional genes with mutations known to be associated with AML and MDS such as TET2 and DNMT3A were also evaluated. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 1B portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Baseline (Induction Cycle 1/Day -3 pre-dose for Phase 2 Fit; Cycle 1/Day 1 pre-dose for Phase 2 Unfit)

| End point values | Phase 2 Fit (Biomarker, Responder) | Phase 2 Fit (Biomarker, non- Responder) | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Bio marker, non- Responder) |
|-----------------------------|--|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 32 | 18 | 21 | 40 |
| Units: Subjects | | | | |
| CEBPA | 6 | 3 | 3 | 5 |
| DNMT3A | 12 | 6 | 2 | 13 |
| FLT3 | 3 | 2 | 1 | 4 |
| FLT3-ITD | 2 | 1 | 1 | 2 |
| IDH1 | 2 | 1 | 5 | 5 |
| IDH2 | 5 | 4 | 2 | 10 |
| KIT | 2 | 1 | 1 | 2 |
| KRAS | 0 | 1 | 0 | 2 |
| NPM1 | 12 | 3 | 2 | 3 |
| NRAS | 5 | 1 | 1 | 4 |
| RUNX1 | 7 | 7 | 10 | 18 |
| TET2 | 7 | 5 | 7 | 8 |
| WT1 | 0 | 1 | 1 | 2 |

| End point values | Phase 2 Unfit: LDAC alone (Biomarker, Responder) | Phase 2 Unfit: LDAC alone (Biomarker, non- Responder) | | |
|-----------------------------|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 1 | 26 | | |
| Units: Subjects | | | | |
| CEBPA | 0 | 3 | | |
| DNMT3A | 0 | 6 | | |
| FLT3 | 0 | 0 | | |
| FLT3-ITD | 0 | 2 | | |
| IDH1 | 0 | 2 | | |
| IDH2 | 0 | 5 | | |
| KIT | 0 | 1 | | |
| KRAS | 0 | 2 | | |
| NPM1 | 0 | 1 | | |
| NRAS | 0 | 3 | | |
| RUNX1 | 0 | 7 | | |
| TET2 | 1 | 8 | | |
| WT1 | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 2 Fit - Induction Cycle 1/Day 3

| | |
|-----------------|---|
| End point title | Serum levels of circulating protein analytes at Phase 2 Fit - Induction Cycle 1/Day 3 ^[43] |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Induction Cycle 1/Day 3, 1 Hour Post dose

Notes:

[43] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|--|---|--|--|--|
| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 57 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| Factor VII(activated blood coagulation factor VII) | 318000 (56000 to 620000) | | | |
| BDNF | 700 (0 to 6200) | | | |
| MMP-3 | 21000 (1700 to 107000) | | | |
| IL-8 | 28.00 (0.00 to 139.00) | | | |
| ITAC | 14.00 (0.00 to 535.00) | | | |

Statistical analyses

Secondary: Serum levels of circulating protein analytes at Phase 2 Fit - Induction Cycle 1/Day 10

| | |
|-----------------|--|
| End point title | Serum levels of circulating protein analytes at Phase 2 Fit - Induction Cycle 1/Day 10 ^[44] |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Induction Cycle 1/Day 10, 1 Hour Post dose

Notes:

[44] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | | | |
|---------------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 62 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| IL-1 β (Interleukin-1 β) | 8.50 (0.00 to 15.00) | | | |
| IL-6 | 17.00 (0.00 to 7320.00) | | | |
| Factor VII | 292500 (45000 to 641000) | | | |
| BDNF | 300 (0 to 15000) | | | |
| VEGF | 69.00 (0.00 to 140.00) | | | |
| MCP-1 | 594.00 (126.00 to 21200.00) | | | |
| MMP-3 | 12000 (3000 to 93000) | | | |
| IL-8 | 55.00 (0.00 to 8930.00) | | | |
| IL-5 | 85.00 (0.00 to 2240.00) | | | |
| ITAC | 0.00 (0.00 to 46.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 2 Fit - Consolidation Cycle 1/Day 1

| | |
|-----------------|---|
| End point title | Serum levels of circulating protein analytes at Phase 2 Fit - Consolidation Cycle 1/Day 1 ^[45] |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Consolidation Cycle 1/Day 1, 1 Hour Post dose

Notes:

[45] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|--|---|--|--|--|
| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 24 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| MIP-1 β (Macrophage Inflammatory Protein-1 β) | 226.00 (0.00 to 6160.00) | | | |
| BDNF | 7000 (370 to 38000) | | | |
| VEGF | 232.50 (41.00 to 834.00) | | | |
| IL-8 | 9.90 (0.00 to 514.00) | | | |
| ITAC | 41.50 (10.00 to 117.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 2 Fit - Consolidation Cycle 1/Day 10

| | |
|-----------------|--|
| End point title | Serum levels of circulating protein analytes at Phase 2 Fit - Consolidation Cycle 1/Day 10 ^[46] |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Consolidation Cycle 1/Day 10, Pre-dose

Notes:

[46] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| MIP-1 β | 239.50 (0.00 to 6560.00) | | | |
| MCP-1 | 581.00 (192.00 to 3880.00) | | | |
| MMP-3 | 12000 (2700 to 48000) | | | |
| IL-8 | 11.00 (0.00 to 74.00) | | | |
| ITAC | 4.10 (0.00 to 27.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 2 Fit - End of Treatment

| | |
|-----------------|--|
| End point title | Serum levels of circulating protein analytes at Phase 2 Fit - End of Treatment ^[47] |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

End of Treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first), Hours not specified

Notes:

[47] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunorubicin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 42 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| MIP-1 β | 338.00 (0.00 to 4480.00) | | | |
| VEGF | 133.00 (0.00 to 2880.00) | | | |
| MCP-1 | 277.00 (0.00 to 7450.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Fit: 6CKINE (C-C motif chemokine 21)

| | |
|-----------------|---|
| End point title | Baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Fit: 6CKINE (C-C motif chemokine 21) |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment. Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. The data of analytes for which the serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Baseline (Induction Cycle 1/Day -3 pre-dose)

| End point values | Phase 2 Fit (Biomarker, Responder) | Phase 2 Fit (Biomarker, non- Responder) | | |
|---------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 43 | 22 | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| 6CKINE (C-C motif chemokine 21) | 323.00 (158.00 to 419.00) | 362.00 (225.00 to 758.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Fit - Induction Cycle 1/Day 3: TNFα (Tumor necrosis factor α)

| | |
|---|---|
| End point title | Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Fit - Induction Cycle 1/Day 3: TNFα (Tumor necrosis factor α) |
| End point description: | |
| Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment treatment. Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. The data of analytes for which the serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment. | |
| End point type | Secondary |
| End point timeframe: | |
| Induction Cycle 1/Day 3, 1 Hour Post dose | |

| End point values | Phase 2 Fit (Biomarker, Responder) | Phase 2 Fit (Biomarker, non- Responder) | | |
|--|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 37 | 20 | | |
| Units: pg/mL | | | | |
| arithmetic mean (full range (min-max)) | 3.20 (0.00 to 26.00) | 10.90 (0.00 to 63.00) | | |

Statistical analyses

Secondary: Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Fit - Induction Cycle 1/Day 10: TNF α (Tumor necrosis factor α)

| | |
|-----------------|--|
| End point title | Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Fit - Induction Cycle 1/Day 10: TNF α (Tumor necrosis factor α) |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment treatment. Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. The data of analytes for which the serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Induction Cycle 1/Day 10, 1 Hour Post dose

| End point values | Phase 2 Fit (Biomarker, Responder) | Phase 2 Fit (Biomarker, non-Responder) | | |
|--|------------------------------------|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 42 | 20 | | |
| Units: pg/mL | | | | |
| arithmetic mean (full range (min-max)) | 1.20 (0.00 to 18.00) | 6.60 (0.00 to 88.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Fit - End of Treatment

| | |
|-----------------|--|
| End point title | Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Fit - End of Treatment |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and Day 10, 1 hour post-dose on Consolidation Cycle 1/Day 1, pre-dose on Consolidation Cycle 1/Day 10, and at end of treatment treatment. Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. The data of analytes for which the serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

End of Treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first), Hours not specified

| End point values | Phase 2 Fit (Biomarker, Responder) | Phase 2 Fit (Biomarker, non- Responder) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 27 | 15 | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| IL-1 β | 9.70 (0.00 to 20.00) | 6.70 (0.00 to 20.00) | | |
| IL-15 (Interleukin-15) | 700 (0 to 1300) | 600 (0 to 850) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 2 Unfit - Cycle 1/Day 1: IL-18 (Interleukin-18)

| | |
|-----------------|---|
| End point title | Serum levels of circulating protein analytes at Phase 2 Unfit - Cycle 1/Day 1: IL-18 (Interleukin-18) ^[48] |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and pre-dose on Cycle 1/Day 10 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Unfit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Cycle 1/Day 1, 1 Hour Post dose

Notes:

[48] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC | | | |
|-------------------------------|--|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 18 | | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | 483.00 (40.00 to 1230.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Serum levels of circulating protein analytes at Phase 2 Unfit - Cycle 1/Day 10

| | |
|-----------------|--|
| End point title | Serum levels of circulating protein analytes at Phase 2 Unfit - Cycle 1/Day 10 ^[49] |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and pre-dose on Cycle 1/Day 10 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Serum levels were determined for 38 circulating proteins. Only the values showing statistically significant change from baseline are reported here. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Unfit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Cycle 1/Day 10, Pre-dose

Notes:

[49] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | | |
|-------------------------------|--|------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 66 | 24 | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| BDNF | 500 (0 to 7200) | 200 (0 to 5100) | | |
| ITAC | 7.5 (0.00 to 226.00) | 0.00 (0.00 to 71.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Unfit

| | |
|-----------------|--|
| End point title | Baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Unfit |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and pre-dose on Cycle 1/Day 10 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. The data of analytes for which the serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Unfit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

| | |
|-----------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Cycle 1/Day 1 pre-dose) | |

| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Bio marker, non- Responder) | | |
|--|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 28 | 44 | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| BDNF | 2000 (170 to 22000) | 900 (0 to 12000) | | |
| ICAM-1 (Intercellular cell adhesion molecule-1) | 128000 (37000 to 287000) | 161000 (82000 to 580000) | | |
| 6CKINE | 223.50 (53.00 to 679.00) | 318.00 (128.00 to 911.00) | | |
| BAFF (B-cell activating factor) | 704.50 (116.00 to 3000.00) | 1295.00 (199.00 to 6190.00) | | |
| MIP-3β | 275.00 (86.00 to 2060.00) | 414.50 (109.00 to 2130.00) | | |
| Eotaxin-1 (C-C motif chemokine 11) | 169.00 (0.00 to 333.00) | 0.00 (0.00 to 260.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Unfit - Cycle 1/Day 1

| | |
|-----------------|---|
| End point title | Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Unfit - Cycle 1/Day 1 |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and pre-dose on Cycle 1/Day 10 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-

reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. The data of analytes for which the serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Unfit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

| | |
|---------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 1/Day 1, 1 Hour Post dose | |

| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Bio marker, non-Responder) | | |
|---|---|---|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 6 | 12 | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | | | | |
| Factor VII:activated blood coagulation factor VII | 311500 (48000 to 661000) | 234500 (147000 to 676000) | | |
| IL-6 (Interleukin-6) | 0.00 (0.00 to 3.50) | 6.80 (0.00 to 62.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Unfit - End of Treatment: IL-6 (Interleukin-6)

| | |
|-----------------|--|
| End point title | Post-baseline levels of serum circulating protein analytes associated with best overall response at Phase 2 Unfit - End of Treatment: IL-6 (Interleukin-6) |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and pre-dose on Cycle 1/Day 10 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. A total of 38 proteins were analyzed. The data of analytes for which the serum level showed statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Unfit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

| | |
|---|-----------|
| End point type | Secondary |
| End point timeframe: | |
| End of Treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first), Hours not specified | |

| | | | | |
|-------------------------------|--|--|--|--|
| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Bio marker, non-Responder) | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 17 | 18 | | |
| Units: pg/mL | | | | |
| median (full range (min-max)) | 0.00 (0.00 to 45.00) | 9.40 (0.00 to 52.00) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Ratios of mRNA levels to baseline at Phase 2 Fit - Induction Cycle 1/Day 3

| | |
|-----------------|--|
| End point title | Ratios of mRNA levels to baseline at Phase 2 Fit - Induction Cycle 1/Day 3 ^[50] |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3(baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Whole blood mRNA analyses were performed on 21 mRNA candidates. Only the values showing statistically significant change from baseline are reported here. CDKN1A: cyclin-dependent kinase inhibitor 1A; SMO: mRNA encoding the glasdegib target Smoothened. PD analysis set was used to analyze this end point: all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

Induction Cycle 1/Day 3, 1 Hour Post dose

Notes:

[50] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 62 | | | |
| Units: Not Applicable | | | | |
| median (full range (min-max)) | | | | |
| CDKN1A (n = 54) | 2.40 (0.08 to 53.17) | | | |
| SMO (n = 18) | 4.80 (0.06 to 51.22) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Ratios of mRNA levels to baseline at Phase 2 Fit - End of Treatment

| | |
|-----------------|---|
| End point title | Ratios of mRNA levels to baseline at Phase 2 Fit - End of Treatment ^[51] |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and end of treatment. Whole blood mRNA analyses were performed on 21 mRNA candidates. Only the values showing statistically significant change from baseline are reported here. CCND2:G1/S-Specific Cyclin D2; MSI2: Musashi RNA Binding Protein 2; PTCH2: Patched 2. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

End of Treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first), Hours not specified

Notes:

[51] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 62 | | | |
| Units: Not Applicable | | | | |
| median (full range (min-max)) | | | | |
| CCND2 (n = 42) | 0.80 (0.23 to 3.23) | | | |
| MSI2 (n = 42) | 0.80 (0.31 to 4.58) | | | |
| PTCH2 (n = 12) | 0.70 (0.29 to 1.90) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Ratios of mRNA levels to baseline at Phase 2 Unfit - End of Treatment

| | |
|-----------------|---|
| End point title | Ratios of mRNA levels to baseline at Phase 2 Unfit - End of Treatment ^[52] |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Whole blood mRNA analyses were performed on 21 mRNA candidates. Only the values showing statistically significant change from baseline are reported here. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Unfit portion who received at least 1 dose of glasdegib, and had at

least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics.

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

End point timeframe:

End of Treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first), Hours not specified

Notes:

[52] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| | | | | |
|-------------------------------|--|--|--|--|
| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 47 | | | |
| Units: Not Applicable | | | | |
| median (full range (min-max)) | | | | |
| CCND2 (n = 30) | 0.70 (0.06 to 2.35) | | | |
| SMO (n = 20) | 0.40 (0.09 to 8.09) | | | |
| CCND1 (n = 17) | 0.40 (0.10 to 13.33) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline mRNA levels associated with best overall response at Phase 2 Fit: CCND2 (G1/S-Specific Cyclin D2)

| | |
|-----------------|--|
| End point title | Baseline mRNA levels associated with best overall response at Phase 2 Fit: CCND2 (G1/S-Specific Cyclin D2) |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. Whole blood mRNA analyses were performed on 21 mRNA candidates. Baseline mRNA level showing statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

Baseline (Induction Cycle 1/Day -3 pre-dose)

| End point values | Phase 2 Fit (Biomarker, Responder) | Phase 2 Fit (Biomarker, non- Responder) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 39 | 22 | | |
| Units: Not Applicable | | | | |
| median (full range (min-max)) | 10.9 (1.61 to 25.26) | 14.80 (5.03 to 23.74) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline mRNA levels associated with best overall response at Phase 2 Unfit

| | |
|--|---|
| End point title | Baseline mRNA levels associated with best overall response at Phase 2 Unfit |
| End point description: | |
| Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and end of treatment. Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. Whole blood mRNA analyses were performed on 21 mRNA candidates. Baseline mRNA level showing statistically significant correlation with clinical response are reported. FOXM1: Forkhead box M1; PTCH1: Patched 1. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Unfit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment. Number of subjects analyzed is number of subjects in the treatment group. 'n' in categories is number of subjects contributing to the summary statistics. | |
| End point type | Secondary |
| End point timeframe: | |
| Baseline (Cycle 1/Day 1 pre-dose) | |

| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Bio marker, non- Responder) | | |
|-------------------------------|---|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 33 | 55 | | |
| Units: Not Applicable | | | | |
| median (full range (min-max)) | | | | |
| FOXM1 (n = 15, 28) | 0.20 (0.05 to 0.77) | 0.40 (0.09 to 1.86) | | |
| PTCH1 (n = 14, 27) | 0.20 (0.07 to 0.58) | 0.10 (0.01 to 0.42) | | |

Statistical analyses

Secondary: Ratios of mRNA levels to baseline associated with best overall response at Phase 2 Fit

| | |
|-----------------|--|
| End point title | Ratios of mRNA levels to baseline associated with best overall response at Phase 2 Fit |
|-----------------|--|

End point description:

Blood samples were collected at pre-dose on Induction Cycle 1/Day -3 (baseline), 1 hour post-dose on Induction Cycle 1/Day 3 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. Whole blood mRNA analyses were performed on 21 mRNA candidates. Ratios of mRNA level to baseline showing statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Fit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a baseline and an adequate post treatment assessment.

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

End point timeframe:

End of Treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first), Hours not specified

| End point values | Phase 2 Fit (Biomarker, Responder) | Phase 2 Fit (Biomarker, non- Responder) | | |
|-------------------------------|--|--|--|--|
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 45 | 26 | | |
| Units: Not Applicable | | | | |
| median (full range (min-max)) | | | | |
| CCNE1 (n = 26, 13) | 0.60 (0.21 to 1.65) | 1.10 (0.28 to 3.82) | | |
| MSI2 (n = 28, 14) | 0.90 (0.31 to 4.58) | 0.50 (0.33 to 1.86) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Ratios of mRNA levels to baseline associated with best overall response at Phase 2 Unfit: MYCN (Neuroblastoma Myc oncogene)

| | |
|-----------------|---|
| End point title | Ratios of mRNA levels to baseline associated with best overall response at Phase 2 Unfit: MYCN (Neuroblastoma Myc oncogene) |
|-----------------|---|

End point description:

Blood samples were collected at pre-dose on Cycle 1/Day 1 (baseline), 1 hour post-dose on Cycle 1/Day 1 and end of treatment (maximum of 12 cycles from start of therapy or until disease progression or relapse, subjects refusal or unacceptable toxicity occurred, whichever came first). Responders were AML subjects who achieved CR, CRi, MLFS, PR or PRi based on investigator-reported best overall response and MDS subjects who achieved CR, mCR, PR or SD based on investigator-reported best overall response. Whole blood mRNA analyses were performed on 21 mRNA candidates. Ratios of mRNA level to baseline showing statistically significant correlation with clinical response are reported. PD analysis set was used to analyze this end point, defined as all enrolled subjects in the Phase 2 Unfit portion who received at least 1 dose of glasdegib, and had at least 1 PD parameter from the corresponding assay sample with a

baseline and an adequate post treatment assessment.

| | |
|---------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Cycle 1/Day 1, 1 Hour Post dose | |

| | | | | |
|-------------------------------|---|--|--|--|
| End point values | Phase 2 Unfit: Glasdegib 100 mg + LDAC (Biomarker, Responder) | Phase 2 Unfit: Glasdegib 100 mg+LDAC(Bio marker, non-Responder) | | |
| Subject group type | Subject analysis set | Subject analysis set | | |
| Number of subjects analysed | 7 | 12 | | |
| Units: Not Applicable | | | | |
| median (full range (min-max)) | 1.60 (0.50 to 40.25) | 0.50 (0.03 to 20.60) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with corrected QT interval using Fridericia's formula (QTcF) values meeting predefined criteria at Phase 1B

| | |
|-----------------|--|
| End point title | Number of subjects with corrected QT interval using Fridericia's formula (QTcF) values meeting predefined criteria at Phase 1B |
|-----------------|--|

End point description:

Maximum absolute values and increases from baseline were summarized for QTcF interval (time from the beginning of Q wave to the end of T wave corresponding to electrical systole corrected for heart rate using Fridericia's formula). Number of subjects with QTcF meeting the following criteria is presented: QTcF interval: <450 msec; QTcF interval: 450 to <480 msec; QTcF interval: 480 to <500 msec; QTcF interval ≥500 msec; QTcF interval increase from baseline: <30 msec; QTcF interval increase from baseline: 30 to <60 msec; QTcF interval increase from baseline ≥60 msec. End of treatment in the time frame were defined as: maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first. QTc analysis set was analyzed: all subjects enrolled in study having at least 1 ECG assessment after receiving at least 1 dose of glasdegib.

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

End point timeframe:

All Arms: Screening (within 28 days prior to Dosing), Day 1 of each cycle, Cycle 1/Day 10, End of Treatment. Additions: Cycle 1/Day 3, Day 21 in Arm A; Cycle 1/Day 2 in Arm B; Lead-in Day -3, Day 10 of Induction and Consolidation Cycles in Arm C.

| | | | | |
|----------------------------------|-------------------------------|-------------------------------------|--|--|
| End point values | Phase 1B: Glasdegib + LDAC | Phase 1B: Glasdegib + Decitabine | Phase 1B: Glasdegib + Cytarabine/Daunorubicin | |
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 21 | 7 | 22 | |
| Units: Subjects | | | | |
| QTcF interval increase < 30 msec | 16 | 2 | 14 | |

| | | | | |
|--|----|---|----|--|
| QTcF interval increase: 30 to < 60 msec | 5 | 3 | 6 | |
| QTcF interval increase ≥ 60 msec | 0 | 2 | 2 | |
| Maximum QTcF interval < 450 msec | 10 | 4 | 10 | |
| Maximum QTcF interval: 450 to < 480 msec | 11 | 2 | 10 | |
| Maximum QTcF interval: 480 to < 500 msec | 0 | 0 | 1 | |
| Maximum QTcF interval ≥ 500 msec | 0 | 1 | 1 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with corrected QT interval using Fridericia's formula (QTcF) values meeting predefined criteria at Phase 2 Fit and Unfit

| | |
|-----------------|---|
| End point title | Number of subjects with corrected QT interval using Fridericia's formula (QTcF) values meeting predefined criteria at Phase 2 Fit and Unfit ^[53] |
|-----------------|---|

End point description:

Maximum absolute values and increases from baseline were summarized for QTcF interval (time from the beginning of Q wave to the end of T wave corresponding to electrical systole corrected for heart rate using Fridericia's formula). Number of subjects with QTcF meeting the following criteria is presented: QTcF interval: <450 msec; QTcF interval: 450 to <480 msec; QTcF interval: 480 to <500 msec; QTcF interval ≥500 msec; QTcF interval increase from baseline: <30 msec; QTcF interval increase from baseline: 30 to <60 msec; QTcF interval increase from baseline ≥60 msec. End of treatment in the time frame were defined as: maximum of 12 cycles from start of therapy or until disease progression or relapse, subject refusal or unacceptable toxicity occurred, whichever came first. QTc analysis set was used to analyze this end point, defined as all subjects enrolled in the study having at least 1 ECG assessment after receiving at least 1 dose of glasdegib.

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

End point timeframe:

All Arms: Screening, Day 1 of each cycle, Cycle 1/Day 10, End of Treatment. Additions: Lead-in Day -3, Day 10 of Induction and Consolidation Cycles in Phase 2 Fit Arm.

Notes:

[53] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | |
|--|---|---|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 68 | 83 | 17 | |
| Units: Subjects | | | | |
| QTcF interval increase < 30 msec | 41 | 60 | 12 | |
| QTcF interval increase: 30 to < 60 msec | 21 | 19 | 4 | |
| QTcF interval increase ≥ 60 msec | 6 | 4 | 1 | |
| Maximum QTcF interval < 450 msec | 46 | 46 | 8 | |
| Maximum QTcF interval: 450 to < 480 msec | 18 | 29 | 4 | |
| Maximum QTcF interval: 480 to < 500 msec | 3 | 3 | 3 | |
| Maximum QTcF interval ≥ 500 msec | 1 | 5 | 2 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent adverse events (AEs) at Phase 1B (All Causality)

| | |
|-----------------|---|
| End point title | Number of subjects with treatment-emergent adverse events (AEs) at Phase 1B (All Causality) |
|-----------------|---|

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event did not necessarily have a causal relationship with the treatment or usage. Treatment Emergent AEs were those with initial onset or increasing in severity after the first dose of study medication. AEs were graded by the investigator according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 : Grade 1: mild AE; Grade 2: moderate AE; Grade 3: severe AE; Grade 4: life-threatening consequences, urgent intervention indicated; Grade 5: death related to AE. Safety analysis set was used to analyze this end point, defined as all enrolled subjects who received at least 1 dose of any of the study medications for each drug combination.

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

End point timeframe:

From the time subjects took at least 1 dose of investigational product to Follow-up (at least 28 days and no more than 35 days after discontinuation of treatment)

| End point values | Phase 1B: Glasdegib + LDAC | Phase 1B: Glasdegib + Decitabine | Phase 1B: Glasdegib + Cytarabine/Da unorubicin | |
|-----------------------------|----------------------------------|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 23 | 7 | 22 | |
| Units: Subjects | | | | |
| Grade 1 AEs | 1 | 1 | 0 | |
| Grade 2 AEs | 2 | 0 | 3 | |
| Grade 3 AEs | 3 | 1 | 8 | |
| Grade 4 AEs | 10 | 4 | 10 | |
| Grade 5 AEs | 7 | 1 | 1 | |
| Missing or unknown AEs | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent adverse events (AEs) at Phase 1B (Treatment-related)

| | |
|-----------------|---|
| End point title | Number of subjects with treatment-emergent adverse events (AEs) at Phase 1B (Treatment-related) |
|-----------------|---|

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event did not necessarily had a causal relationship with the treatment or usage. Treatment Emergent AEs were those with initial onset or increasing in severity after the first dose of study medication. Treatment-related AEs were AEs related to glasdegib and/or backbone chemotherapy. AEs were graded by the investigator according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 : Grade 1: mild AE; Grade 2: moderate AE; Grade 3: severe AE; Grade 4: life-threatening consequences, urgent intervention indicated; Grade 5: death related to AE. Safety analysis set was used to analyze this end point, defined as all enrolled subjects who received at least 1 dose of any of the study medications for each drug combination.

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

End point timeframe:

From the time subjects took at least 1 dose of investigational product to Follow-up (at least 28 days and no more than 35 days after discontinuation of treatment)

| End point values | Phase 1B: Glasdegib + LDAC | Phase 1B: Glasdegib + Decitabine | Phase 1B: Glasdegib + Cytarabine/Da unorubicin | |
|-----------------------------|----------------------------------|--|---|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 23 | 7 | 22 | |
| Units: Subjects | | | | |
| Grade 1 AEs | 3 | 2 | 2 | |
| Grade 2 AEs | 2 | 0 | 7 | |
| Grade 3 AEs | 7 | 0 | 3 | |
| Grade 4 AEs | 6 | 4 | 10 | |
| Grade 5 AEs | 3 | 0 | 0 | |
| Missing or unknown AEs | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent AEs categorized by seriousness at Phase 1B

| | |
|-----------------|---|
| End point title | Number of subjects with treatment-emergent AEs categorized by seriousness at Phase 1B ^[54] |
|-----------------|---|

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event did not necessarily had a causal relationship with the treatment or usage. Treatment Emergent AEs were those with initial onset or increasing in severity after the first dose of study medication. An serious adverse event (SAE) was any untoward medical occurrence at any dose that: resulted in death; was life threatening (immediate risk of death); required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions); resulted in congenital anomaly/birth defect. Safety analysis set was used to analyze this end point, defined as all enrolled subjects who received at least 1 dose of any of the study medications for each drug combination.

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

End point timeframe:

From the time subjects took at least 1 dose of investigational product to Follow-up (at least 28 days and no more than 35 days after discontinuation of treatment)

Notes:

[54] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 200 mg + LDAC | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + Decitabine |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 17 | 6 | 4 | 3 |
| Units: Subjects | | | | |
| AEs | 17 | 6 | 4 | 3 |
| SAEs | 13 | 5 | 4 | 2 |

| End point values | Phase 1B: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin | | |
|-----------------------------|---|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 16 | 6 | | |
| Units: Subjects | | | | |
| AEs | 16 | 6 | | |
| SAEs | 10 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent AEs at Phase 2 Fit and Unfit (All Causality)

| | |
|-----------------|---|
| End point title | Number of subjects with treatment-emergent AEs at Phase 2 Fit and Unfit (All Causality) ^[55] |
|-----------------|---|

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event did not necessarily had a causal relationship with the treatment or usage. Treatment Emergent AEs were those with initial onset or increasing in severity after the first dose of study medication. AEs were graded by the investigator according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 : Grade 1: mild AE; Grade 2: moderate AE; Grade 3: severe AE; Grade 4: life-threatening consequences, urgent intervention indicated; Grade 5: death related to AE. Safety analysis set was used to analyze this end point, defined as all enrolled subjects who received at least 1 dose of any of the study medications for each drug combination.

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

End point timeframe:

From the time subjects took at least 1 dose of investigational product to Follow-up (at least 28 days and no more than 35 days after discontinuation of treatment)

Notes:

[55] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | |
|-----------------------------|---|---|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 69 | 84 | 41 | |
| Units: Subjects | | | | |
| Grade 1 AEs | 0 | 2 | 0 | |
| Grade 2 AEs | 1 | 4 | 1 | |
| Grade 3 AEs | 11 | 15 | 8 | |
| Grade 4 AEs | 52 | 39 | 15 | |
| Grade 5 AEs | 5 | 24 | 17 | |
| Missing or unknown AEs | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent AEs at Phase 2 Fit and Unfit (Treatment-related)

| | |
|-----------------|---|
| End point title | Number of subjects with treatment-emergent AEs at Phase 2 Fit and Unfit (Treatment-related) ^[56] |
|-----------------|---|

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event did not necessarily had a causal relationship with the treatment or usage. Treatment Emergent AEs were those with initial onset or increasing in severity after the first dose of study medication. Treatment-related AEs were AEs related to glasdegib and/or backbone chemotherapy. AEs were graded by the investigator according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 : Grade 1: mild AE; Grade 2: moderate AE; Grade 3: severe AE; Grade 4: life-threatening consequences, urgent intervention indicated; Grade 5: death related to AE. Safety analysis set was used to analyze this end point, defined as all enrolled subjects who received at least 1 dose of any of the study medications for each drug combination.

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

End point timeframe:

From the time subjects took at least 1 dose of investigational product to Follow-up (at least 28 days and no more than 35 days after discontinuation of treatment)

Notes:

[56] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | |
|-----------------------------|---|---|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 69 | 84 | 41 | |
| Units: Subjects | | | | |
| Grade 1 AEs | 0 | 4 | 4 | |
| Grade 2 AEs | 4 | 9 | 6 | |
| Grade 3 AEs | 15 | 20 | 3 | |
| Grade 4 AEs | 46 | 34 | 10 | |

| | | | | |
|------------------------|---|---|---|--|
| Grade 5 AEs | 1 | 1 | 1 | |
| Missing or unknown AEs | 0 | 0 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with treatment-emergent AEs categorized by seriousness at Phase 2 Fit and Unfit

| | |
|-----------------|--|
| End point title | Number of subjects with treatment-emergent AEs categorized by seriousness at Phase 2 Fit and Unfit ^[57] |
|-----------------|--|

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation subject administered a product or medical device; the event did not necessarily had a causal relationship with the treatment or usage. Treatment Emergent AEs were those with initial onset or increasing in severity after the first dose of study medication. AEs were graded by the investigator according to the Common Terminology Criteria for Adverse Events (CTCAE) version 4.0 : Grade 1: mild AE; Grade 2: moderate AE; Grade 3: severe AE; Grade 4: life-threatening consequences, urgent intervention indicated; Grade 5: death related to AE. Safety analysis set was used to analyze this end point, defined as all enrolled subjects who received at least 1 dose of any of the study medications for each drug combination.

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

End point timeframe:

From the time subjects took at least 1 dose of investigational product to Follow-up (at least 28 days and no more than 35 days after discontinuation of treatment)

Notes:

[57] - 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: Not every reporting arm is required for reporting this endpoint of the study.

| End point values | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Da unorubicin | Phase 2 Unfit: Glasdegib 100 mg + LDAC | Phase 2 Unfit: LDAC alone | |
|-----------------------------|---|---|------------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 69 | 84 | 41 | |
| Units: Subjects | | | | |
| AEs | 69 | 84 | 41 | |
| SAEs | 35 | 66 | 32 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the time subjects took at least 1 dose of investigational product to Follow-up (at least 28 days and no more than 35 days after discontinuation of treatment)

Adverse event reporting additional description:

MedDRA 19.0 coding dictionary was applied for phase 1b adverse events (AEs) tables. MedDRA 19.1 coding dictionary was applied for phase 2 Fit and phase 2 Unfit AEs tables.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 1B: Glasdegib 100 mg + LDAC |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects received oral doses of glasdegib (PF-04449913) tablets 100 milligram (mg) starting on Day 3 of Cycle 1 for pharmacokinetic (PK) assessment purposes and thereafter once daily (QD) and continuously for 28-day cycles (starting on Day 1 for all other cycles). Low dose Ara-C (LDAC) was given at a dose of 20 mg subcutaneously twice daily (BID) on Days 1-10 of the 28-day cycles.

| | |
|-----------------------|---|
| Reporting group title | Phase 1B: Glasdegib 100 mg + Decitabine |
|-----------------------|---|

Reporting group description:

Subjects received oral doses of glasdegib tablets 100 mg starting on Day 2 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). Decitabine was given at a dose of 20 mg/m² as an intravenous (IV) infusion over 1 hour on Days 1-5 of the 28-day cycles.

| | |
|-----------------------|-----------------------------------|
| Reporting group title | Phase 1B: Glasdegib 200 mg + LDAC |
|-----------------------|-----------------------------------|

Reporting group description:

Subjects received oral doses of glasdegib tablets 200 mg starting on Day 3 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). LDAC was given at a dose of 20 mg subcutaneously BID on Days 1-10 of the 28-day cycles. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 2/Day 1 and Cycle 2/Day 16, respectively.

| | |
|-----------------------|--|
| Reporting group title | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunorubicin |
|-----------------------|--|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 100 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days.

| | |
|-----------------------|---|
| Reporting group title | Phase 1B: Glasdegib 200 mg + Decitabine |
|-----------------------|---|

Reporting group description:

Subjects received oral doses of glasdegib tablets 200 mg starting on Day 2 of Cycle 1 for PK assessment purposes and thereafter QD and continuously for 28-day cycles (starting on Day 1 for all other cycles). Decitabine was given at a dose of 20 mg/m² as an IV infusion over 1 hour on Days 1-5 of the 28-day cycles. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. Subjects who had glasdegib dose reduction were reported as the starting glasdegib dose level received. Two (2) subjects in this cohort had dose reduction to 100 mg starting from Cycle 1/Day 24 and Cycle 5/Day 1, respectively.

| | |
|-----------------------|--|
| Reporting group title | Phase 2 Unfit: Glasdegib 100 mg + LDAC |
|-----------------------|--|

Reporting group description:

Subjects received oral doses of glasdegib tablets 100 mg QD in 28-day cycles on a continuous basis, starting on Day 1 of Cycle 1. LDAC was given at a dose of 20 mg subcutaneously BID on Days 1-10 of

the 28 day cycles.

| | |
|-----------------------|---|
| Reporting group title | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunorubicin |
|-----------------------|---|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 100 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days.

| | |
|-----------------------|--|
| Reporting group title | Phase 1B: Glasdegib 200 mg + Cytarabine/Daunorubicin |
|-----------------------|--|

Reporting group description:

Subjects received 1-2 cycles of induction (glasdegib and daunorubicin/cytarabine), followed by 2-4 cycles of consolidation (glasdegib and high dose cytarabine) and a maximum of 6 cycles of maintenance (glasdegib alone). Daunorubicin was given on Days 1-3 QD at a dose of 60 mg/m²/day by IV together with cytarabine on Days 1-7 at a dose of 100 mg/m²/day by continuous IV infusion for each cycle of induction. Cytarabine was given on Days 1, 3, and 5 at a dose of 1 g/m² administered as a 3-hour IV infusion every 12 hours (2 g/m²/day) for each cycle of consolidation. Glasdegib tablets 200 mg QD was started on induction Cycle 1/Day -3 and administered continuously QD thereafter for the duration of the study. A cycle was defined as 28 days. In March 2013, all active subjects receiving glasdegib 200 mg were required to reduce dose to 100 mg. One (1) subject in this cohort had dose reduction to 100 mg starting from Consolidation Cycle 1/Day 21.

| | |
|-----------------------|---------------------------|
| Reporting group title | Phase 2 Unfit: LDAC alone |
|-----------------------|---------------------------|

Reporting group description:

Subjects received LDAC subcutaneously at a dose of 20 mg BID on Days 1-10 of the 28 day cycles.

| Serious adverse events | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + LDAC |
|---|-----------------------------------|---|-----------------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 17 (76.47%) | 4 / 4 (100.00%) | 5 / 6 (83.33%) |
| number of deaths (all causes) | 9 | 1 | 2 |
| number of deaths resulting from adverse events | 7 | 1 | 1 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haemorrhage | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 3 / 3 | 1 / 1 | 1 / 1 |
| Fatigue | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 1 / 1 | 0 / 0 |
| Nodule | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Death | | | |

| | | | |
|---|----------------|----------------|---------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (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 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pneumonitis | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Cough | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 embolism | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Respiratory arrest | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Psychiatric disorders | | | |
| Bipolar II disorder | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Mental status changes | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Investigations | | | |
| Lumbar puncture abnormal | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Laboratory test abnormal | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |

| | | | |
|---|----------------|---------------|---------------|
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Splenic rupture | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Angina pectoris | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 failure | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Tachyarrhythmia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Myocarditis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Nervous system disorders | | | |
| Autonomic nervous system imbalance | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (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 |
| Neurotoxicity | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Dyskinesia | | | |

| | | | |
|---|-----------------|---------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Syncope | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 sensorimotor neuropathy | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 0 / 4 (0.00%) | 3 / 6 (50.00%) |
| occurrences causally related to treatment / all | 2 / 3 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Granulocytopenia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Lymphadenitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Eye disorders | | | |
| Mydriasis | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Gastrointestinal disorders | | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (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 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Nausea | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic colitis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Constipation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Retroperitoneal haematoma | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 maculo-papular | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Skin toxicity | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |

| | | | |
|---|----------------|----------------|---------------|
| Back pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (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 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 difficile sepsis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Enterobacter sepsis | | | |

| | | | |
|---|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Neutropenic sepsis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 2 / 4 (50.00%) | 0 / 6 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 1 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Septic shock | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Abscess | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Aspergillus infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 difficile colitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Device related infections | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Infected dermal cyst | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pseudomembranous colitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Septic encephalopathy | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Urogenital infection bacterial | | | |

| | | | |
|---|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Mycobacterium avium complex infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gout | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Hyponatraemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (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 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (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 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (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 |

| Serious adverse events | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunorubicin | Phase 1B: Glasdegib 200 mg + Decitabine | Phase 2 Unfit: Glasdegib 100 mg + LDAC |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 16 (62.50%) | 2 / 3 (66.67%) | 66 / 84 (78.57%) |
| number of deaths (all causes) | 2 | 0 | 31 |
| number of deaths resulting from adverse events | 0 | 0 | 24 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of skin | | | |

| | | | |
|--|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Vascular disorders | | | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 8 / 84 (9.52%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 7 / 7 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 3 / 84 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Multiple organ dysfunction syndrome | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Nodule | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |

| | | | |
|---|----------------|---------------|----------------|
| Pyrexia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 3 / 84 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Death | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Sudden death | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |

| | | | |
|---|----------------|---------------|----------------|
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Pneumonitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Cough | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| 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 embolism | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Respiratory arrest | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Respiratory distress | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Bipolar II disorder | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Investigations | | | |
| Lumbar puncture abnormal | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Laboratory test abnormal | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Splenic rupture | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|---------------|----------------|
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 failure congestive | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| 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 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiogenic shock | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Tachyarrhythmia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocarditis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Nervous system disorders | | | |
| Autonomic nervous system imbalance | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 3 (33.33%) | 0 / 84 (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 |
| Ischaemic stroke | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Neurotoxicity | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Polyneuropathy | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Dyskinesia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 4 / 84 (4.76%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Haemorrhage intracranial | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 3 / 84 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| Peripheral sensorimotor neuropathy | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Transient ischaemic attack | | | |

| | | | |
|---|----------------|----------------|------------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 3 (33.33%) | 24 / 84 (28.57%) |
| occurrences causally related to treatment / all | 1 / 1 | 1 / 1 | 10 / 27 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Pancytopenia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 6 / 84 (7.14%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 6 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Granulocytopenia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphadenitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Eye disorders | | | |
| Mydriasis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Nausea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic colitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Constipation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Pancreatitis acute | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Retroperitoneal haematoma | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Rash generalised | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Rash | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin toxicity | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 3 / 84 (3.57%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 4 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|---------------|----------------|
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| 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 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | | |
|---|-----------------|---------------|------------------|--|
| Clostridium difficile infection | | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (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 | |
| Clostridium difficile sepsis | | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 | |
| Enterobacter sepsis | | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 | |
| Enterocolitis infectious | | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (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 | |
| Lower respiratory tract infection bacterial | | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 | |
| Pneumonia | | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 19 / 84 (22.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 6 / 26 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 9 / 9 | |
| Sepsis | | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 3 / 84 (3.57%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 2 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 | |
| Skin infection | | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Septic shock | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Abscess | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Aspergillus infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Device related infections | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 3 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Herpes zoster | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infected dermal cyst | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Influenza | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| 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 | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pseudomembranous colitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Respiratory tract infection | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic encephalopathy | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Urogenital infection bacterial | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Adenovirus infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Mycobacterium avium complex infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Pseudomonal sepsis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Gout | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (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 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|-------------------------------|--------------|---------------------|---------------------|
| Serious adverse events | Phase 2 Fit: | Phase 1B: Glasdegib | Phase 2 Unfit: LDAC |
|-------------------------------|--------------|---------------------|---------------------|

| | Glasdegib 100 mg + Cytarabine/Daunoru bicin | 200 mg + Cytarabine/Daunoru bicin | alone |
|--|---|---|------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 35 / 69 (50.72%) | 3 / 6 (50.00%) | 32 / 41 (78.05%) |
| number of deaths (all causes) | 8 | 1 | 23 |
| number of deaths resulting from adverse events | 5 | 1 | 19 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma of skin | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| 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 | | | |
| Hypotension | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| General disorders and administration site conditions | | | |
| Disease progression | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 1 / 6 (16.67%) | 5 / 41 (12.20%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 0 / 5 |
| deaths causally related to treatment / all | 2 / 2 | 1 / 1 | 5 / 5 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Multiple organ dysfunction syndrome | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Nodule | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Death | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| General physical health deterioration | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Acute respiratory distress syndrome | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pleuritic pain | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Cough | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| 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 embolism | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Respiratory arrest | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Psychiatric disorders | | | |
| Bipolar II disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Mental status changes | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Confusional state | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Investigations | | | |
| Lumbar puncture abnormal | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Aspartate aminotransferase | | | |

| | | | |
|---|----------------|---------------|----------------|
| increased | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Laboratory test abnormal | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Femur fracture | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |

| | | | |
|---|----------------|---------------|----------------|
| Splenic rupture | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Thoracic vertebral fracture | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac failure congestive | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Angina pectoris | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac arrest | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 failure | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Cardiogenic shock | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Myocardial infarction | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Tachyarrhythmia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Ventricular fibrillation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Myocarditis | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Nervous system disorders | | | |
| Autonomic nervous system imbalance | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Dizziness | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Ischaemic stroke | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Neurotoxicity | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Polyneuropathy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Subarachnoid haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Dyskinesia | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Presyncope | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Syncope | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Cerebral haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Haemorrhage intracranial | | | |

| | | | |
|---|------------------|----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Peripheral sensorimotor neuropathy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Transient ischaemic attack | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Blood and lymphatic system disorders | | | |
| Febrile neutropenia | | | |
| subjects affected / exposed | 14 / 69 (20.29%) | 1 / 6 (16.67%) | 7 / 41 (17.07%) |
| occurrences causally related to treatment / all | 10 / 16 | 0 / 1 | 3 / 8 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Neutropenia | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pancytopenia | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 2 / 41 (4.88%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Anaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Disseminated intravascular coagulation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| Granulocytopenia | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lymphadenitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Thrombocytosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Eye disorders | | | |
| Mydriasis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Gastrointestinal disorders | | | |
| Gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Impaired gastric emptying | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Nausea | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neutropenic colitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Upper gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Constipation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Haematemesis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Lower gastrointestinal haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pancreatitis acute | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Retroperitoneal haematoma | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Skin and subcutaneous tissue disorders | | | |
| Rash generalised | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 maculo-papular | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Skin toxicity | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Myalgia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Back pain | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |

| | | | |
|---|----------------|----------------|----------------|
| Bacteraemia | | | |
| subjects affected / exposed | 2 / 69 (2.90%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (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 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 difficile sepsis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Enterobacter sepsis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Lower respiratory tract infection bacterial | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pneumonia | | | |

| | | | |
|---|----------------|----------------|-----------------|
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 7 / 41 (17.07%) |
| occurrences causally related to treatment / all | 2 / 5 | 0 / 0 | 1 / 12 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 3 / 3 |
| Sepsis | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 0 / 6 (0.00%) | 5 / 41 (12.20%) |
| occurrences causally related to treatment / all | 5 / 7 | 0 / 0 | 1 / 8 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 5 / 5 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Septic shock | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 1 / 1 | 0 / 0 | 1 / 1 |
| Abscess | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Aspergillus infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 difficile colitis | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Cystitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Device related infections | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Infected dermal cyst | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Influenza | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lung infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pneumonia fungal | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pseudomembranous colitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Septic encephalopathy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Urogenital infection bacterial | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Adenovirus infection | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 bacterial | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Mycobacterium avium complex infection | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pharyngitis | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pneumocystis jirovecii pneumonia | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Pseudomonal sepsis | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Gout | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 / 69 (1.45%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Tumour lysis syndrome | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (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 |

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

| Non-serious adverse events | Phase 1B: Glasdegib 100 mg + LDAC | Phase 1B: Glasdegib 100 mg + Decitabine | Phase 1B: Glasdegib 200 mg + LDAC |
|---|--------------------------------------|--|--------------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 16 / 17 (94.12%) | 4 / 4 (100.00%) | 6 / 6 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypotension | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 0 | 3 |
| Ischaemia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Phlebitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombophlebitis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Venous thrombosis | | | |

| | | | |
|--|-----------------|----------------|----------------|
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pallor | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 1 | 2 |
| Catheter site pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site swelling | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chills | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 6 / 17 (35.29%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 8 | 1 | 1 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Generalised oedema | | | |

| | | | |
|------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hernia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nodule | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oedema | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Oedema peripheral | | | |
| subjects affected / exposed | 5 / 17 (29.41%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 6 | 0 | 1 |
| Pain | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Performance status decreased | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pyrexia | | | |

| | | | |
|--|----------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 5 / 17 (29.41%) 5 | 1 / 4 (25.00%) 2 | 0 / 6 (0.00%) 0 |
| Thirst subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| Catheter site erythema subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Catheter site haemorrhage subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 3 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 4 (25.00%) 1 | 0 / 6 (0.00%) 0 |
| Vaginal haemorrhage subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Vulvovaginal pruritus subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Atelectasis subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 4 / 17 (23.53%) 4 | 1 / 4 (25.00%) 1 | 1 / 6 (16.67%) 1 |
| Dysphonia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Dyspnoea | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 2 | 1 |
| Hypoxia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis allergic | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| hiccups | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Anxiety | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Apathy | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Confusional state | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 1 | 1 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Disorientation | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--------------------------------------|-----------------|----------------|----------------|
| Insomnia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 2 / 4 (50.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Panic attack | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Delirium | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 1 | 2 |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood magnesium decreased | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest X-ray abnormal | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eastern Cooperative Oncology Group performance status worsened | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Karnofsky scale worsened | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Platelet count decreased | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 1 | 2 |
| Fall | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Infusion related reaction | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Procedural headache | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin abrasion | | | |

| | | | |
|------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vascular access complication | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Diastolic dysfunction | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |

| | | | |
|-------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Amnesia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 1 | 2 |
| Dysgeusia | | | |
| subjects affected / exposed | 4 / 17 (23.53%) | 1 / 4 (25.00%) | 4 / 6 (66.67%) |
| occurrences (all) | 4 | 2 | 4 |
| Headache | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 3 | 1 | 1 |
| Lethargy | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Mental impairment | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peroneal nerve palsy | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |

| | | | |
|--------------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sedation | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 2 / 4 (50.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 9 | 3 | 2 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 3 / 17 (17.65%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Leukocytosis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Leukopenia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lymphadenitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 7 / 17 (41.18%) | 2 / 4 (50.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 11 | 3 | 0 |
| Spleen disorder | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|--|----------------------|---------------------|---------------------|
| Splenomegaly subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 6 / 17 (35.29%) 9 | 2 / 4 (50.00%) 2 | 1 / 6 (16.67%) 1 |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Eye disorders | | | |
| Diplopia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Eye haemorrhage subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Ocular hyperaemia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Photophobia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Scleral pigmentation subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Vision blurred subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Abdominal distension subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Abdominal pain | | | |

| | | | |
|------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 4 / 17 (23.53%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Anal fissure | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Anal haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Angina bullosa haemorrhagica | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Ascites | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 7 / 17 (41.18%) | 2 / 4 (50.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 7 | 2 | 3 |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 17 (47.06%) | 2 / 4 (50.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 10 | 4 | 2 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 2 / 4 (50.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Faeces discoloured | | | |

| | | | |
|----------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Megacolon | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mouth haemorrhage | | | |

| | | | |
|-----------------------------|-----------------|-----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nausea | | | |
| subjects affected / exposed | 6 / 17 (35.29%) | 4 / 4 (100.00%) | 4 / 6 (66.67%) |
| occurrences (all) | 10 | 6 | 5 |
| Oral disorder | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oral mucosal blistering | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Oral pain | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth loss | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vomiting | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 4 | 2 | 3 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 1 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Erythema | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Macule | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Night sweats | | | |

| | | | |
|-----------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palmar erythema | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Panniculitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 2 / 6 (33.33%) |
| occurrences (all) | 2 | 0 | 4 |
| Plantar erythema | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus allergic | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Purpura | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash papular | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin disorder | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Dysuria | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal cyst | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|----------------------|---------------------|---------------------|
| Renal failure subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Urinary retention subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Endocrine disorders Adrenal insufficiency subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Hypothyroidism subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 4 (0.00%) 0 | 2 / 6 (33.33%) 3 |
| Back pain subjects affected / exposed occurrences (all) | 2 / 17 (11.76%) 2 | 2 / 4 (50.00%) 3 | 1 / 6 (16.67%) 1 |
| Bone pain subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Joint effusion subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Muscle spasms subjects affected / exposed occurrences (all) | 5 / 17 (29.41%) 6 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 3 |
| Muscular weakness subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Musculoskeletal pain | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Pain in jaw | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Plantar fasciitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---------------------------------|----------------|----------------|----------------|
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Candida infection | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 2 | 2 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Clostridium difficile infection | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Device related infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Enterobacter bacteraemia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Enterocolitis bacterial | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Enterocolitis infectious | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Folliculitis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Fungal infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Genital infection viral | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|-----------------------------------|-----------------|----------------|----------------|
| Nasopharyngitis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Onychomycosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 1 | 1 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary mycosis | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 2 | 0 | 1 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Urinary tract infection subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 1 / 4 (25.00%) 2 | 0 / 6 (0.00%) 0 |
| Viral infection subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Oral herpes subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 1 / 4 (25.00%) 1 | 2 / 6 (33.33%) 2 |
| Dehydration subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 1 / 4 (25.00%) 1 | 1 / 6 (16.67%) 1 |
| Gout subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hyperkalaemia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 2 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Hypermagnesaemia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 1 / 6 (16.67%) 1 |
| Hypernatraemia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hyperphosphataemia subjects affected / exposed occurrences (all) | 1 / 17 (5.88%) 1 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hyperuricaemia subjects affected / exposed occurrences (all) | 0 / 17 (0.00%) 0 | 0 / 4 (0.00%) 0 | 0 / 6 (0.00%) 0 |
| Hypoalbuminaemia | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 2 / 17 (11.76%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 4 (25.00%) | 3 / 6 (50.00%) |
| occurrences (all) | 2 | 1 | 5 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 0 | 1 | 2 |
| Hyponatraemia | | | |
| subjects affected / exposed | 2 / 17 (11.76%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 2 | 4 | 0 |
| Hypophagia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 1 / 4 (25.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 3 | 1 |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 1 / 17 (5.88%) | 0 / 4 (0.00%) | 1 / 6 (16.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |

| | | | |
|-----------------------------|----------------|---------------|---------------|
| subjects affected / exposed | 0 / 17 (0.00%) | 0 / 4 (0.00%) | 0 / 6 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Phase 1B: Glasdegib 100 mg + Cytarabine/Daunoru bicin | Phase 1B: Glasdegib 200 mg + Decitabine | Phase 2 Unfit: Glasdegib 100 mg + LDAC |
|--|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 16 / 16 (100.00%) | 3 / 3 (100.00%) | 81 / 84 (96.43%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Squamous cell carcinoma | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 1 / 3 (33.33%) | 6 / 84 (7.14%) |
| occurrences (all) | 3 | 1 | 7 |
| Hypotension | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 0 / 3 (0.00%) | 12 / 84 (14.29%) |
| occurrences (all) | 5 | 0 | 13 |
| Ischaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Phlebitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Venous thrombosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pallor | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 1 / 84 (1.19%) |
| occurrences (all) | 0 | 0 | 1 |
| Haematoma | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 5 / 84 (5.95%) |
| occurrences (all) | 0 | 0 | 7 |

| | | | |
|--|-----------------|----------------|------------------|
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 2 / 3 (66.67%) | 11 / 84 (13.10%) |
| occurrences (all) | 1 | 2 | 17 |
| Catheter site pain | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Catheter site swelling | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 9 / 84 (10.71%) |
| occurrences (all) | 1 | 0 | 9 |
| Chills | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 1 / 3 (33.33%) | 5 / 84 (5.95%) |
| occurrences (all) | 7 | 1 | 5 |
| Fatigue | | | |
| subjects affected / exposed | 6 / 16 (37.50%) | 2 / 3 (66.67%) | 25 / 84 (29.76%) |
| occurrences (all) | 10 | 5 | 65 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hernia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Injection site pain | | | |

| | | | |
|------------------------------|------------------|----------------|------------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 6 / 84 (7.14%) |
| occurrences (all) | 1 | 0 | 10 |
| Nodule | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Oedema | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 6 / 16 (37.50%) | 1 / 3 (33.33%) | 22 / 84 (26.19%) |
| occurrences (all) | 7 | 1 | 34 |
| Pain | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 4 / 84 (4.76%) |
| occurrences (all) | 4 | 0 | 4 |
| Performance status decreased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 10 / 16 (62.50%) | 0 / 3 (0.00%) | 21 / 84 (25.00%) |
| occurrences (all) | 15 | 0 | 38 |
| Thirst | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site erythema | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site haemorrhage | | | |

| | | | |
|--|----------------------|---------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Vaginal haemorrhage subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Vulvovaginal pruritus subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 2 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Atelectasis subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 1 / 3 (33.33%) 1 | 18 / 84 (21.43%) 20 |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Dyspnoea subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 5 | 1 / 3 (33.33%) 3 | 21 / 84 (25.00%) 36 |
| Dyspnoea exertional subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Epistaxis subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 3 | 1 / 3 (33.33%) 1 | 6 / 84 (7.14%) 10 |
| Hypoxia | | | |

| | | | |
|-----------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lung infiltration | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 8 / 84 (9.52%) |
| occurrences (all) | 2 | 0 | 8 |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |

| | | | |
|-----------------------------|-----------------|---------------|------------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| hiccups | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Psychiatric disorders | | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 3 / 84 (3.57%) |
| occurrences (all) | 0 | 0 | 5 |
| Anxiety | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences (all) | 3 | 0 | 2 |
| Apathy | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 7 / 84 (8.33%) |
| occurrences (all) | 0 | 0 | 7 |
| Depressed mood | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Disorientation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 0 / 3 (0.00%) | 10 / 84 (11.90%) |
| occurrences (all) | 5 | 0 | 11 |
| Panic attack | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Delirium | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------------|---------------------|-----------------------|
| Hallucination subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Investigations | | | |
| Alanine aminotransferase increased subjects affected / exposed occurrences (all) | 4 / 16 (25.00%) 5 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Amylase increased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Aspartate aminotransferase increased subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 3 | 0 / 3 (0.00%) 0 | 6 / 84 (7.14%) 9 |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Blood bilirubin increased subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Blood creatinine increased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 3 (33.33%) 1 | 9 / 84 (10.71%) 13 |
| Blood fibrinogen decreased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Blood magnesium decreased subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Blood uric acid increased subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Chest X-ray abnormal subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Eastern Cooperative Oncology Group performance status worsened | | | |

| | | | |
|---|-----------------|---------------|------------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 7 / 84 (8.33%) |
| occurrences (all) | 0 | 0 | 11 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 3 / 84 (3.57%) |
| occurrences (all) | 2 | 0 | 3 |
| Karnofsky scale worsened | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 11 / 84 (13.10%) |
| occurrences (all) | 1 | 0 | 43 |
| Platelet count decreased | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 14 / 84 (16.67%) |
| occurrences (all) | 6 | 0 | 119 |
| Weight decreased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 16 / 84 (19.05%) |
| occurrences (all) | 1 | 0 | 23 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 0 / 3 (0.00%) | 13 / 84 (15.48%) |
| occurrences (all) | 7 | 0 | 46 |
| Activated partial thromboplastin time prolonged | | | |

| | | | |
|--|----------------|---------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| C-reactive protein increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 6 / 84 (7.14%) |
| occurrences (all) | 0 | 0 | 10 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 5 / 84 (5.95%) |
| occurrences (all) | 0 | 0 | 8 |
| Fall | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 9 / 84 (10.71%) |
| occurrences (all) | 1 | 0 | 11 |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Procedural headache | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vascular access complication | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Atrial fibrillation | | | |

| | | | |
|-------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 6 / 84 (7.14%) |
| occurrences (all) | 0 | 0 | 9 |
| Diastolic dysfunction | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 3 (33.33%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Amnesia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|-----------------------------|-----------------|----------------|------------------|
| Dizziness | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 3 (33.33%) | 18 / 84 (21.43%) |
| occurrences (all) | 1 | 1 | 25 |
| Dysgeusia | | | |
| subjects affected / exposed | 7 / 16 (43.75%) | 1 / 3 (33.33%) | 21 / 84 (25.00%) |
| occurrences (all) | 7 | 1 | 27 |
| Headache | | | |
| subjects affected / exposed | 9 / 16 (56.25%) | 0 / 3 (0.00%) | 11 / 84 (13.10%) |
| occurrences (all) | 11 | 0 | 13 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mental impairment | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Peroneal nerve palsy | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 3 (33.33%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 3 (33.33%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sedation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 3 (33.33%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|----------------------|---------------------|-------------------------|
| Hypoaesthesia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia subjects affected / exposed occurrences (all) | 4 / 16 (25.00%) 9 | 1 / 3 (33.33%) 5 | 37 / 84 (44.05%) 292 |
| Febrile neutropenia subjects affected / exposed occurrences (all) | 8 / 16 (50.00%) 9 | 0 / 3 (0.00%) 0 | 8 / 84 (9.52%) 8 |
| Leukocytosis subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 6 / 84 (7.14%) 6 |
| Leukopenia subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 3 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Lymphadenitis subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 2 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Neutropenia subjects affected / exposed occurrences (all) | 4 / 16 (25.00%) 8 | 2 / 3 (66.67%) 7 | 13 / 84 (15.48%) 38 |
| Spleen disorder subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Splenomegaly subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Thrombocytopenia subjects affected / exposed occurrences (all) | 3 / 16 (18.75%) 4 | 1 / 3 (33.33%) 2 | 26 / 84 (30.95%) 107 |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Eye disorders | | | |

| | | | |
|-----------------------------|-----------------|----------------|------------------|
| Diplopia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye haemorrhage | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Scleral pigmentation | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 6 / 16 (37.50%) | 1 / 3 (33.33%) | 14 / 84 (16.67%) |
| occurrences (all) | 7 | 1 | 15 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 7 / 84 (8.33%) |
| occurrences (all) | 1 | 0 | 8 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal haemorrhage | | | |

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|----------------------------------|------------------|----------------|------------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Angina bullosa haemorrhagica | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ascites | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 10 / 16 (62.50%) | 1 / 3 (33.33%) | 21 / 84 (25.00%) |
| occurrences (all) | 14 | 1 | 28 |
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 16 (62.50%) | 0 / 3 (0.00%) | 23 / 84 (27.38%) |
| occurrences (all) | 18 | 0 | 44 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 3 (33.33%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Faeces discoloured | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 3 (33.33%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |

| | | | |
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| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Haematemesis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 0 / 3 (0.00%) | 7 / 84 (8.33%) |
| occurrences (all) | 5 | 0 | 7 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Megacolon | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences (all) | 1 | 0 | 2 |
| Nausea | | | |
| subjects affected / exposed | 14 / 16 (87.50%) | 1 / 3 (33.33%) | 30 / 84 (35.71%) |
| occurrences (all) | 25 | 2 | 46 |
| Oral disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral mucosal blistering | | | |

| | | | |
|-----------------------------|-----------------|----------------|------------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proctalgia | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 2 / 3 (66.67%) | 0 / 84 (0.00%) |
| occurrences (all) | 11 | 2 | 0 |
| Tongue disorder | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tooth loss | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Toothache | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 1 / 3 (33.33%) | 18 / 84 (21.43%) |
| occurrences (all) | 11 | 1 | 29 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|----------------------|---------------------|----------------------|
| Hyperbilirubinaemia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 4 / 16 (25.00%) 4 | 2 / 3 (66.67%) 2 | 9 / 84 (10.71%) 9 |
| Decubitus ulcer subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Dermatitis acneiform subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Dry skin subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Ecchymosis subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Erythema subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | 0 / 3 (0.00%) 0 | 7 / 84 (8.33%) 8 |
| Macule subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Night sweats subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Pain of skin subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 84 (0.00%) 0 |
| Palmar erythema subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Panniculitis | | | |

| | | | |
|-----------------------------|-----------------|---------------|------------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 7 / 84 (8.33%) |
| occurrences (all) | 1 | 0 | 7 |
| Plantar erythema | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 0 / 3 (0.00%) | 6 / 84 (7.14%) |
| occurrences (all) | 4 | 0 | 9 |
| Pruritus allergic | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Purpura | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 11 / 84 (13.10%) |
| occurrences (all) | 4 | 0 | 11 |
| Rash macular | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin ulcer | | | |

| | | | |
|-----------------------------|-----------------|---------------|----------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 7 / 84 (8.33%) |
| occurrences (all) | 3 | 0 | 7 |
| Dysuria | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Haematuria | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proteinuria | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal cyst | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Renal failure | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary retention | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urinary incontinence | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 7 / 84 (8.33%) |
| occurrences (all) | 0 | 0 | 7 |

| | | | |
|---|------------------|----------------|------------------|
| Endocrine disorders | | | |
| Adrenal insufficiency | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypothyroidism | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 10 / 84 (11.90%) |
| occurrences (all) | 0 | 0 | 14 |
| Back pain | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 2 / 3 (66.67%) | 8 / 84 (9.52%) |
| occurrences (all) | 4 | 2 | 10 |
| Bone pain | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 0 / 3 (0.00%) | 2 / 84 (2.38%) |
| occurrences (all) | 4 | 0 | 4 |
| Joint effusion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 10 / 16 (62.50%) | 2 / 3 (66.67%) | 19 / 84 (22.62%) |
| occurrences (all) | 12 | 4 | 45 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 3 (33.33%) | 6 / 84 (7.14%) |
| occurrences (all) | 1 | 1 | 6 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 5 / 84 (5.95%) |
| occurrences (all) | 3 | 0 | 6 |
| Neck pain | | | |

| | | | |
|-----------------------------|-----------------|----------------|------------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Osteoarthritis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 1 / 3 (33.33%) | 15 / 84 (17.86%) |
| occurrences (all) | 4 | 1 | 19 |
| Pain in jaw | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Plantar fasciitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Candida infection | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|----------------------|--------------------|---------------------|
| Clostridium difficile colitis subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Clostridium difficile infection subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 2 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Device related infection subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Enterobacter bacteraemia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Enterocolitis bacterial subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Enterocolitis infectious subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Folliculitis subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Fungal infection subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Genital infection viral subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Onychomycosis subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |
| Otitis media subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 3 (0.00%) 0 | 0 / 84 (0.00%) 0 |

| | | | |
|-----------------------------------|-----------------|----------------|----------------|
| Pneumonia | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 8 / 84 (9.52%) |
| occurrences (all) | 2 | 0 | 9 |
| Pneumonia fungal | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pulmonary mycosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sepsis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 3 (33.33%) | 5 / 84 (5.95%) |
| occurrences (all) | 0 | 1 | 6 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 3 / 84 (3.57%) |
| occurrences (all) | 0 | 0 | 3 |

| | | | |
|------------------------------------|-----------------|----------------|------------------|
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 2 / 3 (66.67%) | 28 / 84 (33.33%) |
| occurrences (all) | 2 | 5 | 41 |
| Dehydration | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypernatraemia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 3 (33.33%) | 0 / 84 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 3 (0.00%) | 7 / 84 (8.33%) |
| occurrences (all) | 2 | 0 | 8 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hypokalaemia | | | |

| | | | |
|-----------------------------|-----------------|----------------|------------------|
| subjects affected / exposed | 6 / 16 (37.50%) | 0 / 3 (0.00%) | 12 / 84 (14.29%) |
| occurrences (all) | 6 | 0 | 18 |
| Hypomagnesaemia | | | |
| subjects affected / exposed | 4 / 16 (25.00%) | 0 / 3 (0.00%) | 8 / 84 (9.52%) |
| occurrences (all) | 4 | 0 | 11 |
| Hyponatraemia | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 1 / 3 (33.33%) | 10 / 84 (11.90%) |
| occurrences (all) | 6 | 2 | 28 |
| Hypophagia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 3 (0.00%) | 0 / 84 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| Non-serious adverse events | Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunoru bicin | Phase 1B: Glasdegib 200 mg + Cytarabine/Daunoru bicin | Phase 2 Unfit: LDAC alone |
|--|---|--|------------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 69 / 69 (100.00%) | 6 / 6 (100.00%) | 39 / 41 (95.12%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |

| | | | |
|---|------------------------|---------------------|-----------------------|
| Squamous cell carcinoma subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Vascular disorders | | | |
| Hypertension subjects affected / exposed occurrences (all) | 12 / 69 (17.39%) 14 | 1 / 6 (16.67%) 1 | 1 / 41 (2.44%) 1 |
| Hypotension subjects affected / exposed occurrences (all) | 14 / 69 (20.29%) 15 | 0 / 6 (0.00%) 0 | 4 / 41 (9.76%) 4 |
| Ischaemia subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Phlebitis subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Thrombophlebitis subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Venous thrombosis subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Pallor subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 3 / 41 (7.32%) 3 |
| Haematoma subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 2 / 41 (4.88%) 2 |
| General disorders and administration site conditions | | | |
| Asthenia subjects affected / exposed occurrences (all) | 8 / 69 (11.59%) 10 | 0 / 6 (0.00%) 0 | 8 / 41 (19.51%) 20 |
| Catheter site pain subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Catheter site swelling | | | |

| | | | |
|-----------------------------|------------------|----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest pain | | | |
| subjects affected / exposed | 9 / 69 (13.04%) | 2 / 6 (33.33%) | 1 / 41 (2.44%) |
| occurrences (all) | 9 | 2 | 1 |
| Chills | | | |
| subjects affected / exposed | 21 / 69 (30.43%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 30 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 25 / 69 (36.23%) | 2 / 6 (33.33%) | 8 / 41 (19.51%) |
| occurrences (all) | 37 | 3 | 11 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Generalised oedema | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hernia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Localised oedema | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mucosal inflammation | | | |
| subjects affected / exposed | 8 / 69 (11.59%) | 1 / 6 (16.67%) | 2 / 41 (4.88%) |
| occurrences (all) | 8 | 1 | 3 |
| Nodule | | | |

| | | | |
|--|------------------|----------------|-----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oedema | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 9 | 1 | 0 |
| Oedema peripheral | | | |
| subjects affected / exposed | 22 / 69 (31.88%) | 2 / 6 (33.33%) | 7 / 41 (17.07%) |
| occurrences (all) | 37 | 4 | 7 |
| Pain | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 0 / 6 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 6 | 0 | 3 |
| Performance status decreased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 34 / 69 (49.28%) | 1 / 6 (16.67%) | 9 / 41 (21.95%) |
| occurrences (all) | 52 | 3 | 11 |
| Thirst | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Catheter site erythema | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Catheter site haemorrhage | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Reproductive system and breast disorders | | | |

| | | | |
|---|------------------|----------------|------------------|
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vaginal haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vulvovaginal pruritus | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Atelectasis | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Cough | | | |
| subjects affected / exposed | 14 / 69 (20.29%) | 2 / 6 (33.33%) | 7 / 41 (17.07%) |
| occurrences (all) | 18 | 2 | 7 |
| Dysphonia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dyspnoea | | | |
| subjects affected / exposed | 13 / 69 (18.84%) | 2 / 6 (33.33%) | 11 / 41 (26.83%) |
| occurrences (all) | 14 | 2 | 11 |
| Dyspnoea exertional | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Epistaxis | | | |
| subjects affected / exposed | 11 / 69 (15.94%) | 1 / 6 (16.67%) | 6 / 41 (14.63%) |
| occurrences (all) | 13 | 1 | 7 |
| Hypoxia | | | |
| subjects affected / exposed | 8 / 69 (11.59%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Lung infiltration | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |

| | | | |
|-----------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 7 / 69 (10.14%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 12 / 69 (17.39%) | 2 / 6 (33.33%) | 0 / 41 (0.00%) |
| occurrences (all) | 12 | 3 | 0 |
| Pleural effusion | | | |
| subjects affected / exposed | 9 / 69 (13.04%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Pleuritic pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary fibrosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pulmonary oedema | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Respiratory failure | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Wheezing | | | |
| subjects affected / exposed | 7 / 69 (10.14%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| hiccups | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Psychiatric disorders | | | |

| | | | |
|------------------------------------|------------------|----------------|----------------|
| Agitation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 0 | 0 | 3 |
| Anxiety | | | |
| subjects affected / exposed | 15 / 69 (21.74%) | 1 / 6 (16.67%) | 4 / 41 (9.76%) |
| occurrences (all) | 17 | 1 | 4 |
| Apathy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Confusional state | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Depressed mood | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Depression | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 2 / 6 (33.33%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| Disorientation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 19 / 69 (27.54%) | 0 / 6 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 21 | 0 | 3 |
| Panic attack | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Delirium | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Hallucination | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Investigations | | | |
| Alanine aminotransferase increased | | | |

| | | | |
|--|------------------|----------------|----------------|
| subjects affected / exposed | 21 / 69 (30.43%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 26 | 1 | 0 |
| Amylase increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 17 / 69 (24.64%) | 1 / 6 (16.67%) | 1 / 41 (2.44%) |
| occurrences (all) | 23 | 1 | 1 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed | 13 / 69 (18.84%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 16 | 1 | 0 |
| Blood bilirubin increased | | | |
| subjects affected / exposed | 19 / 69 (27.54%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 35 | 0 | 0 |
| Blood creatinine increased | | | |
| subjects affected / exposed | 14 / 69 (20.29%) | 1 / 6 (16.67%) | 3 / 41 (7.32%) |
| occurrences (all) | 16 | 1 | 4 |
| Blood fibrinogen decreased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood magnesium decreased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood uric acid increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Chest X-ray abnormal | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eastern Cooperative Oncology Group performance status worsened | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Electrocardiogram QT prolonged | | | |

| | | | |
|---|------------------|----------------|-----------------|
| subjects affected / exposed | 7 / 69 (10.14%) | 1 / 6 (16.67%) | 1 / 41 (2.44%) |
| occurrences (all) | 15 | 1 | 1 |
| International normalised ratio increased | | | |
| subjects affected / exposed | 7 / 69 (10.14%) | 0 / 6 (0.00%) | 5 / 41 (12.20%) |
| occurrences (all) | 8 | 0 | 5 |
| Karnofsky scale worsened | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipase increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Liver function test increased | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lymphocyte count decreased | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 12 / 69 (17.39%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 14 | 0 | 1 |
| Platelet count decreased | | | |
| subjects affected / exposed | 18 / 69 (26.09%) | 0 / 6 (0.00%) | 4 / 41 (9.76%) |
| occurrences (all) | 47 | 0 | 24 |
| Weight decreased | | | |
| subjects affected / exposed | 9 / 69 (13.04%) | 1 / 6 (16.67%) | 1 / 41 (2.44%) |
| occurrences (all) | 12 | 1 | 1 |
| White blood cell count decreased | | | |
| subjects affected / exposed | 20 / 69 (28.99%) | 0 / 6 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 54 | 0 | 2 |
| Activated partial thromboplastin time prolonged | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Weight increased | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 4 / 69 (5.80%) 4 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| C-reactive protein increased subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 6 / 41 (14.63%) 9 |
| Injury, poisoning and procedural complications | | | |
| Contusion subjects affected / exposed occurrences (all) | 6 / 69 (8.70%) 7 | 0 / 6 (0.00%) 0 | 2 / 41 (4.88%) 2 |
| Fall subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 6 (16.67%) 1 | 1 / 41 (2.44%) 1 |
| Infusion related reaction subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Post procedural haemorrhage subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Procedural headache subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Skin abrasion subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Vascular access complication subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Cardiac disorders | | | |
| Angina pectoris subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Atrial fibrillation subjects affected / exposed occurrences (all) | 5 / 69 (7.25%) 6 | 0 / 6 (0.00%) 0 | 1 / 41 (2.44%) 1 |
| Diastolic dysfunction | | | |

| | | | |
|-------------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palpitations | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Sinus bradycardia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus tachycardia | | | |
| subjects affected / exposed | 7 / 69 (10.14%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 7 | 0 | 0 |
| Tachycardia | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Ventricular tachycardia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pericardial effusion | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Nervous system disorders | | | |
| Ageusia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Amnesia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Central nervous system lesion | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cognitive disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dizziness | | | |
| subjects affected / exposed | 12 / 69 (17.39%) | 2 / 6 (33.33%) | 4 / 41 (9.76%) |
| occurrences (all) | 15 | 2 | 5 |

| | | | |
|-----------------------------|------------------|----------------|-----------------|
| Dysgeusia | | | |
| subjects affected / exposed | 19 / 69 (27.54%) | 1 / 6 (16.67%) | 1 / 41 (2.44%) |
| occurrences (all) | 22 | 1 | 1 |
| Headache | | | |
| subjects affected / exposed | 22 / 69 (31.88%) | 2 / 6 (33.33%) | 5 / 41 (12.20%) |
| occurrences (all) | 34 | 2 | 5 |
| Lethargy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Memory impairment | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mental impairment | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Paraesthesia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Peroneal nerve palsy | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sedation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Syncope | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypoaesthesia | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |

| | | | |
|--------------------------------------|------------------|----------------|------------------|
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 28 / 69 (40.58%) | 1 / 6 (16.67%) | 17 / 41 (41.46%) |
| occurrences (all) | 54 | 1 | 62 |
| Febrile neutropenia | | | |
| subjects affected / exposed | 38 / 69 (55.07%) | 2 / 6 (33.33%) | 4 / 41 (9.76%) |
| occurrences (all) | 44 | 2 | 7 |
| Leukocytosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 0 | 0 | 2 |
| Leukopenia | | | |
| subjects affected / exposed | 9 / 69 (13.04%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 11 | 1 | 0 |
| Lymphadenitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Neutropenia | | | |
| subjects affected / exposed | 15 / 69 (21.74%) | 1 / 6 (16.67%) | 8 / 41 (19.51%) |
| occurrences (all) | 32 | 1 | 13 |
| Spleen disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Splenomegaly | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Thrombocytopenia | | | |
| subjects affected / exposed | 23 / 69 (33.33%) | 2 / 6 (33.33%) | 11 / 41 (26.83%) |
| occurrences (all) | 46 | 4 | 53 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Eye disorders | | | |
| Diplopia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Eye haemorrhage | | | |

| | | | |
|------------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Scleral pigmentation | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vision blurred | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Abdominal distension | | | |
| subjects affected / exposed | 10 / 69 (14.49%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Abdominal pain | | | |
| subjects affected / exposed | 20 / 69 (28.99%) | 0 / 6 (0.00%) | 4 / 41 (9.76%) |
| occurrences (all) | 24 | 0 | 4 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 0 | 1 |
| Anal fissure | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Angina bullosa haemorrhagica | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|----------------------------------|------------------|-----------------|-----------------|
| Ascites | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 32 / 69 (46.38%) | 3 / 6 (50.00%) | 6 / 41 (14.63%) |
| occurrences (all) | 39 | 3 | 7 |
| Diarrhoea | | | |
| subjects affected / exposed | 49 / 69 (71.01%) | 6 / 6 (100.00%) | 9 / 41 (21.95%) |
| occurrences (all) | 62 | 8 | 10 |
| Diverticulum | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dry mouth | | | |
| subjects affected / exposed | 10 / 69 (14.49%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 10 | 1 | 0 |
| Dyspepsia | | | |
| subjects affected / exposed | 12 / 69 (17.39%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 13 | 1 | 0 |
| Dysphagia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Faeces discoloured | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 2 / 6 (33.33%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 2 | 0 |
| Gingival bleeding | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |

| | | | |
|-----------------------------|------------------|----------------|-----------------|
| Gingival pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haematemesis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Haematochezia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoidal haemorrhage | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Haemorrhoids | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 2 / 6 (33.33%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 2 | 0 |
| Hiatus hernia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Megacolon | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mouth haemorrhage | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 0 / 6 (0.00%) | 4 / 41 (9.76%) |
| occurrences (all) | 6 | 0 | 4 |
| Nausea | | | |
| subjects affected / exposed | 40 / 69 (57.97%) | 3 / 6 (50.00%) | 5 / 41 (12.20%) |
| occurrences (all) | 70 | 4 | 6 |
| Oral disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral mucosal blistering | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Oral pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|--|------------------|----------------|----------------|
| Pancreatitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proctalgia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Retching | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Stomatitis | | | |
| subjects affected / exposed | 17 / 69 (24.64%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 20 | 0 | 0 |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tooth loss | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Toothache | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 25 / 69 (36.23%) | 4 / 6 (66.67%) | 4 / 41 (9.76%) |
| occurrences (all) | 36 | 5 | 4 |
| Mouth ulceration | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 0 | 0 | 3 |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |

| | | | |
|-----------------------------|------------------|----------------|----------------|
| Alopecia | | | |
| subjects affected / exposed | 16 / 69 (23.19%) | 2 / 6 (33.33%) | 0 / 41 (0.00%) |
| occurrences (all) | 19 | 2 | 0 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis acneiform | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 0 | 0 | 3 |
| Macule | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Night sweats | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 1 | 0 |
| Pain of skin | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Palmar erythema | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Panniculitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Petechiae | | | |
| subjects affected / exposed | 11 / 69 (15.94%) | 1 / 6 (16.67%) | 4 / 41 (9.76%) |
| occurrences (all) | 13 | 1 | 5 |

| | | | |
|-----------------------------|------------------|----------------|----------------|
| Plantar erythema | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pruritus | | | |
| subjects affected / exposed | 10 / 69 (14.49%) | 1 / 6 (16.67%) | 1 / 41 (2.44%) |
| occurrences (all) | 11 | 1 | 1 |
| Pruritus allergic | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Purpura | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rash | | | |
| subjects affected / exposed | 14 / 69 (20.29%) | 1 / 6 (16.67%) | 1 / 41 (2.44%) |
| occurrences (all) | 18 | 1 | 1 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash maculo-papular | | | |
| subjects affected / exposed | 9 / 69 (13.04%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 10 | 0 | 0 |
| Rash papular | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin disorder | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|-----------------------|---------------------|---------------------|
| Hyperhidrosis subjects affected / exposed occurrences (all) | 9 / 69 (13.04%) 9 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Renal and urinary disorders | | | |
| Acute kidney injury subjects affected / exposed occurrences (all) | 8 / 69 (11.59%) 10 | 2 / 6 (33.33%) 2 | 1 / 41 (2.44%) 1 |
| Dysuria subjects affected / exposed occurrences (all) | 4 / 69 (5.80%) 5 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Haematuria subjects affected / exposed occurrences (all) | 5 / 69 (7.25%) 5 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Pollakiuria subjects affected / exposed occurrences (all) | 4 / 69 (5.80%) 4 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Proteinuria subjects affected / exposed occurrences (all) | 4 / 69 (5.80%) 4 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Renal cyst subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Renal failure subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Urinary retention subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Urinary incontinence subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Endocrine disorders | | | |
| Adrenal insufficiency subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Hypothyroidism | | | |

| | | | |
|---|------------------|----------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 11 / 69 (15.94%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 13 | 1 | 0 |
| Back pain | | | |
| subjects affected / exposed | 12 / 69 (17.39%) | 1 / 6 (16.67%) | 3 / 41 (7.32%) |
| occurrences (all) | 14 | 1 | 3 |
| Bone pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 0 | 0 | 5 |
| Joint effusion | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle spasms | | | |
| subjects affected / exposed | 11 / 69 (15.94%) | 2 / 6 (33.33%) | 2 / 41 (4.88%) |
| occurrences (all) | 14 | 4 | 2 |
| Muscular weakness | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 7 / 69 (10.14%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 8 | 0 | 0 |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Myalgia | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Neck pain | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Osteoarthritis | | | |

| | | | |
|-------------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 9 / 69 (13.04%) | 3 / 6 (50.00%) | 2 / 41 (4.88%) |
| occurrences (all) | 12 | 3 | 2 |
| Pain in jaw | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Periarthritis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Plantar fasciitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Arthritis bacterial | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacteraemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Candida infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Clostridium difficile colitis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| | | | |
|---|---------------------|---------------------|---------------------|
| Clostridium difficile infection subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 1 / 6 (16.67%) 1 | 0 / 41 (0.00%) 0 |
| Device related infection subjects affected / exposed occurrences (all) | 5 / 69 (7.25%) 5 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Enterobacter bacteraemia subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Enterocolitis bacterial subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Enterocolitis infectious subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Folliculitis subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Fungal infection subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Genital infection viral subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Onychomycosis subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Otitis media subjects affected / exposed occurrences (all) | 0 / 69 (0.00%) 0 | 0 / 6 (0.00%) 0 | 0 / 41 (0.00%) 0 |
| Pneumonia subjects affected / exposed occurrences (all) | 6 / 69 (8.70%) 6 | 1 / 6 (16.67%) 1 | 3 / 41 (7.32%) 3 |

| | | | |
|------------------------------------|-----------------|----------------|-----------------|
| Pneumonia fungal | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 2 / 6 (33.33%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 2 | 0 |
| Pulmonary mycosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Sepsis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Staphylococcal bacteraemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 8 / 69 (11.59%) | 1 / 6 (16.67%) | 5 / 41 (12.20%) |
| occurrences (all) | 8 | 1 | 5 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 3 / 41 (7.32%) |
| occurrences (all) | 0 | 0 | 3 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |

| | | | |
|-----------------------------|------------------|----------------|-----------------|
| subjects affected / exposed | 26 / 69 (37.68%) | 2 / 6 (33.33%) | 5 / 41 (12.20%) |
| occurrences (all) | 33 | 2 | 9 |
| Dehydration | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 6 | 0 | 0 |
| Gout | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 6 / 69 (8.70%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 9 | 0 | 0 |
| Hypermagnesaemia | | | |
| subjects affected / exposed | 4 / 69 (5.80%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Hypernatraemia | | | |
| subjects affected / exposed | 5 / 69 (7.25%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 5 | 0 | 0 |
| Hyperphosphataemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 1 / 41 (2.44%) |
| occurrences (all) | 0 | 1 | 1 |
| Hypoalbuminaemia | | | |
| subjects affected / exposed | 18 / 69 (26.09%) | 2 / 6 (33.33%) | 0 / 41 (0.00%) |
| occurrences (all) | 24 | 2 | 0 |
| Hypocalcaemia | | | |
| subjects affected / exposed | 22 / 69 (31.88%) | 2 / 6 (33.33%) | 0 / 41 (0.00%) |
| occurrences (all) | 32 | 4 | 0 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypokalaemia | | | |
| subjects affected / exposed | 37 / 69 (53.62%) | 2 / 6 (33.33%) | 6 / 41 (14.63%) |
| occurrences (all) | 64 | 3 | 7 |
| Hypomagnesaemia | | | |

| | | | |
|-----------------------------|------------------|----------------|----------------|
| subjects affected / exposed | 20 / 69 (28.99%) | 1 / 6 (16.67%) | 2 / 41 (4.88%) |
| occurrences (all) | 23 | 1 | 2 |
| Hyponatraemia | | | |
| subjects affected / exposed | 23 / 69 (33.33%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 35 | 1 | 0 |
| Hypophagia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypophosphataemia | | | |
| subjects affected / exposed | 15 / 69 (21.74%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 21 | 0 | 0 |
| Hypovolaemia | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolic acidosis | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tumour lysis syndrome | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 0 / 69 (0.00%) | 1 / 6 (16.67%) | 0 / 41 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 13 / 69 (18.84%) | 0 / 6 (0.00%) | 0 / 41 (0.00%) |
| occurrences (all) | 16 | 0 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 15 May 2012 | <p>Inclusion criteria had been modified to provide clarification for the ECOG performance status requirement, age, and gender. The starting dose of PF 04449913 for the safety cohorts was 100 mg daily based on the data from the ongoing Phase 1 study in hematologic malignancies, and the potential dose levels were modified accordingly. For the Safety Cohorts, cumulative incidence of relapse (CIR), relapse free survival (RFS), event free survival (EFS), and cumulative incidence of death (CID) had been removed as secondary endpoints. For the Efficacy Expansion Cohorts, the following had been added as secondary endpoints: disease specific efficacy endpoints such as Morphologic Leukemia Free State, Partial Remission (PR), Partial Remission with incomplete blood count recovery (PRi), Minor Response (MR), Stable Disease (SD), Cytogenetic Complete Response (CRc), and Molecular Complete Response (CRm) for AML, and Hematologic Improvement (HI), marrow CR, Partial Remission (PR), Stable Disease (SD), and Partial or Complete Cytogenetic Response for MDS. Approximately 30 evaluable subjects from treatment arms PF 04449913 in combination with LDAC or decitabine were undergo additional ECG assessments as outlined in the Schedule of Activities. The schedule of PF 04449913 pharmacokinetic sample collection had also been modified. The Adverse Event reporting section had been updated due to alignment with the US Food and Drug Administration Final Rule (21 CFR Parts 312 and 320) and the European Union CT 3 Guidance (2011/C 172/01). Guidance on tumor lysis syndrome prophylaxis had been added. Clarification that subjects who received prior azacitidine treatment for their high risk MDS or AHD were eligible for Arm A only had been provided.</p> |
| 01 November 2012 | <p>The study design was modified and B1371003 had been a phase 1B/2 study. Requirement for safety and efficacy review of study results by an internal review committee (IOBU SDMC) had been introduced. The expansion cohort for the evaluation of PF 04449913 at the RP2D in combination with decitabine had been removed. Unfit subjects in phase 2 portion were randomized 2:1 (LDAC + PF 04449913: LDAC alone) and stratified based on prognosis (poor vs good/intermediate). Study objectives and endpoints had been updated and aligned with the Phase 1B/2 study design. The inclusion/exclusion criteria had been updated as followed: restriction of enrollment to subjects ≥ 55 years old in the phase 2 portion for unfit subjects, as the efficacy of the PF 04449913 + LDAC combination was evaluated in this subject population; requirement of known cytogenetic profile at study entry for enrollment in the phase 2 portion for unfit subjects; requirement of 2 negative pregnancy tests before starting study treatments for women of childbearing potential; clarification that no prior treatment with investigational agents for antecedent hematologic disease was allowed; explicit exclusion of subjects who showed recent or active suicidal ideation or behavior from enrollment. The number of required consolidation cycles for fit subjects had been updated from 4 to 2-4 depending on disease response. The dose modification criteria for PF 04449913 and backbone chemotherapy agents had been updated. Allowed concomitant medications (antimicrobial agents and doses) had been added. The treatment duration and withdrawal criteria for unfit subjects had been modified. The Adverse Event reporting section had been updated to clarify the expectation for reporting SAEs after the active safety reporting period.</p> |

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| 26 March 2014 | The RP2D for Phase 2 Fit and Phase 2 Unfit was confirmed as PF-04449913 100 mg QD. Exclusion criteria for prohibited concomitant medications (CYP3A4 inhibitors, narrow therapeutic index CYP3A4 substrates and P glycoprotein inhibitors/inducers) were removed. Transplant exclusion criteria were removed. A Prep B1 plasma sample was added at screening to be used for pharmacogenomic assessments. The schedule of events added creatine kinase at select timepoints. The bone marrow assessment schedule has clarified aspirate collection requirements, changed initial hematologic recovery bone marrow collection from 7 days to 14 days, and for Unfit subjects changed the timepoints to Cycle 3 Day 1 and every third cycle to better align with standard of care and removed the treatment duration criteria. For fit subjects Maintenance Day 15 visit was removed. Continuous PF 04449913 dosing during induction and/or consolidation cycles >28 days was clarified. Extended contraception use to 180 days after last dose of investigational products to align with the Summary of Product Characteristics (SPC) for cytarabine and daunorubicin. Concomitant medication restrictions were minimized and/or removed. The independent bone marrow pathology review was removed. The MDS response timeframe for Hematologic Improvement, and the AML response definitions for Minor Response and Treatment Failure, were clarified. Appendix 6 containing list of drugs with known risk of Torsade de Pointes was added. Appendix 7 containing list of strong and moderate CYP3A4/5 inhibitors was added. Appendix 8 containing list of strong and moderate CYP3A4/5 inducers was added. |
| 20 April 2015 | Eligibility criteria corrected an inconsistency for inclusion criteria #2 (Acute Promyelocytic Leukemia (APL) subjects with t(15;17) are excluded) and clarified prior treatments for exclusion criteria #14. Sections 5.3.7 and 7.1.6: Revised dosing modification guidelines for treatment-related QTcF prolongation. Phase 2 Unfit Schedule of Activities, Sections 7.5.1 and 7.6.1: Removed requirement for bone marrow biopsies, if this evaluation was not performed as standard of care (the requirement for bone marrow aspirates remains unchanged). Section 8 Adverse Event Reporting: text updated to align with revised protocol template. Section 15.1 Communication of Results by Pfizer: text updated to align with revised protocol template. Modified AML response criteria for CRi requirements. |
| 08 February 2016 | Phase 2 secondary endpoints cumulative incidence of relapse (CIR), relapse free survival (RFS), event free survival (EFS), cumulative incidence of death (CID), and hematologic improvement (MDS subjects only) were removed. Table 2 Schedule of Activities and sections 3 and 5 for Phase 2 Unfit subjects updated to include survival follow up requirement for randomized subjects that did not start treatment. Section 1.2.8.5 Summary of Benefit-Risk Assessment updated with information concerning QTc interval prolongation. Section 5.3.7.1 QTcF Interval Monitoring and Management added for monitoring of potential cardiovascular symptoms and guidance on the use of moderate/strong CYP3A4/5 inhibitors or drugs with a known risk of Torsade de pointes as concomitant therapy. Section 5.5 Concomitant Medications updated for consistency with the new safety monitoring guidance provided in Section 7.1.6 and Table 8. Section 7.1.6 Triplicate (12-Lead) added new safety guidance when moderate/strong CYP3A4/5 inhibitors or drugs with a known risk of Torsade de pointes were administered as concomitant therapy. Section 8.6.1 Protocol-Specified Serious Adverse Events updated to include SAE reporting of all cases of > Grade 2 mQTcF prolongation regardless of causality for up to 28 calendar days after the last dose of study drug administered. Section 9.3.2 removed secondary endpoints CIR, RFS, EFS, CID, and independent central review of bone marrow samples. Appendix 6, 7 and 8 replaced with new tables and updated source references. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported