



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	04 March 2019

Results information

Result version number	v2 (current)
This version publication date	07 March 2020
First version publication date	29 December 2017
Version creation reason	

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 8007181021, 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	Final
Date of interim/final analysis	04 March 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 January 2017
Global end of trial reached?	Yes
Global end of trial date	04 March 2019
Was the trial ended prematurely?	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	2 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
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Arm title	Phase 1B: Glasdegib 100 mg + LDAC
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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
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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
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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 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.

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
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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
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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
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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
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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
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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
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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
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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	1	0	0
Not completed	16	6	4
Adverse event, serious fatal	15	6	4
Consent withdrawn by subject	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	6	2
Not completed	3	10	4
Adverse event, serious fatal	2	9	3
Consent withdrawn by subject	1	-	1
: 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	18	4	1
Not completed	53	84	43
Adverse event, serious fatal	46	76	39
Consent withdrawn by subject	3	3	1

: Randomized, not treated	2	4	3
Lost to follow-up	2	1	-

Baseline characteristics

Reporting groups

Reporting group title	Phase 1B: Glasdegib 100 mg + LDAC
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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
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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
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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
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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
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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
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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
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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
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	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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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)
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Subject analysis set type	Sub-group analysis
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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
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End points

End points reporting groups

Reporting group title	Phase 1B: Glasdegib 100 mg + LDAC
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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
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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
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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
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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
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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
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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
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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]}
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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 ≥ 3 non-hematologic toxicity, excluding Grade ≥ 3 infection, fever, infusion related AEs, electrolyte abnormalities and ALT/AST elevation that returned to Grade ≤ 1 or baseline within 7 days; (2) prolonged myelosuppression lasted longer than 42 days from the point of detection, defined as absolute neutrophil count $< 500/\text{mL}$ or platelet count $< 10 \times 10^9/\text{L}$ 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
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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: statistical analyses were not planned for this endpoint

[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]
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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
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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: statistical analyses were not planned for this endpoint

[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]
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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 for each subject. Full analysis set was used to analyze this end point, including all randomized subjects of Phase 2 Unfit arm.

End point type	Primary
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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	= 0.002 ^[12]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.569
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	0.441
upper limit	0.734

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 for each subject. 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)	37.8 (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]
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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 for each subject. 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
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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
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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
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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]
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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
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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	18.2 (12.9 to 23.5)	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	= 0.0112
Method	Cochran-Mantel-Haenszel
Parameter estimate	Odds ratio (OR)
Point estimate	4.2755
Confidence interval	
level	Other: 80 %
sides	2-sided
lower limit	1.3057
upper limit	13.9994

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)	5.1 (2.3 to 10.0)	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)	16.7 (11.3 to 23.4)	21.1 (12.7 to 31.9)	
CRc	35.9 (27.9 to 44.7)	11.5 (7.1 to 17.6)	0.0 (0.0 to 5.9)	
CRm	37.5 (29.4 to 46.2)	16.7 (11.3 to 23.4)	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]
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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
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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]
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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
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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 (AUCtau) 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 (AUCtau) of glasdegib in subjects receiving glasdegib and decitabine at Phase 1B on Cycle 1/Day 10 and Cycle 2/Day 1 ^[18]
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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
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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]
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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
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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/Da unorubicin	Phase 1B: Glasdegib 200 mg + Cytarabine/Da unorubicin		
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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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		
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	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
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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
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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)
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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
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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)			
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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)		
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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)
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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
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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)
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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
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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
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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
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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]
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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
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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]
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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
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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]
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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
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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]
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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
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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-1β	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]
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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
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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)
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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
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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)
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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
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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)
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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
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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
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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
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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]
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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
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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]
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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
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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
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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
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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
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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)
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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]
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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
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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]
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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
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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]
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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
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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)
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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
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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
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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
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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)
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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
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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
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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 \geq 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 \geq 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]
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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 \geq 500 msec; QTcF interval increase from baseline: <30 msec; QTcF interval increase from baseline: 30 to <60 msec; QTcF interval increase from baseline \geq 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
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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 \geq 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 \geq 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)
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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 and occurred within 28 days post last dose. 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
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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
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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 and occurred within 28 days post last dose. 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
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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]
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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 and occurred within 28 days post last dose. A 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
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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]
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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 and occurred within 28 days post last dose. 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
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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]
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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 and occurred within 28 days post last dose. 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
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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]
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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 and occurred within 28 days post last dose. 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
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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	68	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 21.1 coding dictionary was applied for all AE tables.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.1
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Reporting groups

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

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (16.67%)	1 / 4 (25.00%)
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 / 6 (0.00%)	0 / 4 (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%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Nodule			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (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%)	1 / 6 (16.67%)	0 / 4 (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
Asthenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (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%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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%)	1 / 6 (16.67%)	0 / 4 (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
Confusional state			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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%)	1 / 6 (16.67%)	0 / 4 (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
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin abrasion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (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 / 6 (0.00%)	0 / 4 (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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurotoxicity			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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%)	3 / 6 (50.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	2 / 3	1 / 3	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (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%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic colitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (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%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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%)	0 / 6 (0.00%)	1 / 4 (25.00%)
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	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (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 / 6 (0.00%)	0 / 4 (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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (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 / 6 (0.00%)	0 / 4 (0.00%)
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%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (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%)	1 / 6 (16.67%)	0 / 4 (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
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
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 / 6 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial sepsis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (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
Abdominal infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
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%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (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 / 6 (0.00%)	0 / 4 (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%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			

subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (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 / 6 (0.00%)	0 / 4 (0.00%)
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 200 mg + Decitabine	Phase 1B: Glasdegib 200 mg + Cytarabine/Daunoru bicin	Phase 1B: Glasdegib 100 mg + Cytarabine/Daunoru bicin
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 6 (50.00%)	10 / 16 (62.50%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 16 (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
Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Polyneuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyskinesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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	1 / 3 (33.33%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (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 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
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 sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridial sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
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 2 Fit: Glasdegib 100 mg + Cytarabine/Daunorubicin	Phase 2 Unfit: Glasdegib 100 mg + LDAC	Phase 2 Unfit: LDAC alone
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 69 (50.72%)	68 / 84 (80.95%)	32 / 41 (78.05%)
number of deaths (all causes)	5	26	17

number of deaths resulting from adverse events	5	26	17
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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 / 84 (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%)	1 / 84 (1.19%)	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
Hypertension			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	2 / 69 (2.90%)	10 / 84 (11.90%)	5 / 41 (12.20%)
occurrences causally related to treatment / all	0 / 2	0 / 10	0 / 5
deaths causally related to treatment / all	2 / 2	8 / 8	5 / 5
Fatigue			
subjects affected / exposed	0 / 69 (0.00%)	3 / 84 (3.57%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 3	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 / 84 (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 / 84 (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%)	3 / 84 (3.57%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	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
Oedema			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 69 (0.00%)	2 / 84 (2.38%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	2 / 2	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			

subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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 / 84 (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 / 84 (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 / 84 (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%)	1 / 84 (1.19%)	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
Pleural effusion			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Respiratory arrest			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	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
Psychiatric disorders			
Bipolar II disorder			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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%)	2 / 84 (2.38%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin abrasion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	2 / 69 (2.90%)	0 / 84 (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%)	1 / 84 (1.19%)	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
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Splenic rupture			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	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
Cardiac disorders			
Acute myocardial infarction subjects affected / exposed	1 / 69 (1.45%)	0 / 84 (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 / 84 (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%)	1 / 84 (1.19%)	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
Atrial fibrillation subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest subjects affected / exposed	0 / 69 (0.00%)	2 / 84 (2.38%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Cardiac failure subjects affected / exposed	0 / 69 (0.00%)	2 / 84 (2.38%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiogenic shock subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	2 / 84 (2.38%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	1 / 1
Tachyarrhythmia			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Ventricular fibrillation			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis			
subjects affected / exposed	1 / 69 (1.45%)	0 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 69 (1.45%)	4 / 84 (4.76%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Haemorrhage intracranial			
subjects affected / exposed	0 / 69 (0.00%)	3 / 84 (3.57%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	2 / 2	1 / 1
Peripheral sensorimotor neuropathy			

subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Cerebrovascular accident			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	14 / 69 (20.29%)	24 / 84 (28.57%)	7 / 41 (17.07%)
occurrences causally related to treatment / all	10 / 16	10 / 27	3 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Neutropenia			
subjects affected / exposed	2 / 69 (2.90%)	0 / 84 (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 / 84 (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%)	6 / 84 (7.14%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	6 / 8	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 / 84 (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 / 84 (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%)	1 / 84 (1.19%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytosis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Eye disorders			
Mydriasis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	2 / 84 (2.38%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Impaired gastric emptying			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic colitis			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	2 / 69 (2.90%)	0 / 84 (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 / 84 (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 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematemesis			

subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	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
Retroperitoneal haematoma			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	2 / 69 (2.90%)	0 / 84 (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 / 84 (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 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin toxicity			

subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	1 / 69 (1.45%)	3 / 84 (3.57%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 4	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 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 69 (1.45%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle spasms			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 69 (0.00%)	2 / 84 (2.38%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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%)	19 / 84 (22.62%)	7 / 41 (17.07%)
occurrences causally related to treatment / all	2 / 5	6 / 26	1 / 12
deaths causally related to treatment / all	1 / 1	9 / 9	3 / 3
Sepsis			
subjects affected / exposed	6 / 69 (8.70%)	3 / 84 (3.57%)	5 / 41 (12.20%)
occurrences causally related to treatment / all	5 / 7	2 / 3	1 / 8
deaths causally related to treatment / all	1 / 1	1 / 1	5 / 5
Skin infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 69 (1.45%)	0 / 84 (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
Septic shock			
subjects affected / exposed	1 / 69 (1.45%)	2 / 84 (2.38%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	1 / 1	1 / 1	1 / 1
Abscess			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Aspergillus infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 69 (1.45%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	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%)	1 / 84 (1.19%)	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
Herpes zoster			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Infected dermal cyst			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Influenza			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	1 / 41 (2.44%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media chronic			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Pneumonia fungal			

subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Pseudomembranous colitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	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
Septic encephalopathy			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urogenital infection bacterial			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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 / 84 (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
Clostridial sepsis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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
Abdominal infection			
subjects affected / exposed	0 / 69 (0.00%)	1 / 84 (1.19%)	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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperuricaemia			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	2 / 84 (2.38%)	0 / 41 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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%)	1 / 84 (1.19%)	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

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

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

subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Thrombophlebitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Venous thrombosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pallor			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 17 (17.65%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	3	2	1
Catheter site pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Catheter site swelling			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chills			

subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Fatigue			
subjects affected / exposed	6 / 17 (35.29%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	8	1	1
Gait disturbance			
subjects affected / exposed	0 / 17 (0.00%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	0	2	1
Generalised oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hernia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nodule			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Oedema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oedema peripheral			

subjects affected / exposed	5 / 17 (29.41%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	6	1	0
Pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Performance status decreased			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pyrexia			
subjects affected / exposed	5 / 17 (29.41%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	5	0	2
Thirst			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Catheter site erythema			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Catheter site haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Vaginal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			

Atelectasis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	4 / 17 (23.53%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	4	1	1
Dysphonia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Dyspnoea			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	2
Dyspnoea exertional			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Epistaxis			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	1	1	2
Hypoxia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	1
Lung infiltration			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pleural effusion			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Pleuritic pain			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0

Pulmonary fibrosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Respiratory failure			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Wheezing			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	1 / 17 (5.88%)	2 / 6 (33.33%)	0 / 4 (0.00%)
occurrences (all)	1	2	0
Apathy			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Confusional state			

subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	2	1	1
Depressed mood			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	2 / 17 (11.76%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	2	1	0
Disorientation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	2	0	2
Panic attack			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Amylase increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	2 / 17 (11.76%)	2 / 6 (33.33%)	1 / 4 (25.00%)
occurrences (all)	2	2	1
Blood fibrinogen decreased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Karnofsky scale worsened			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Liver function test increased			

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

subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Post procedural haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Procedural headache			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Vascular access complication			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Diastolic dysfunction			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sinus bradycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0

Ventricular tachycardia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Nervous system disorders			
Ageusia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 6 (0.00%) 0	1 / 4 (25.00%) 1
Amnesia subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 6 (16.67%) 1	0 / 4 (0.00%) 0
Central nervous system lesion subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 6 (16.67%) 1	0 / 4 (0.00%) 0
Cognitive disorder subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	2 / 6 (33.33%) 2	1 / 4 (25.00%) 1
Dysgeusia subjects affected / exposed occurrences (all)	4 / 17 (23.53%) 4	4 / 6 (66.67%) 4	1 / 4 (25.00%) 2
Headache subjects affected / exposed occurrences (all)	3 / 17 (17.65%) 3	1 / 6 (16.67%) 1	1 / 4 (25.00%) 1
Lethargy subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1	0 / 6 (0.00%) 0	0 / 4 (0.00%) 0
Memory impairment subjects affected / exposed occurrences (all)	0 / 17 (0.00%) 0	1 / 6 (16.67%) 1	1 / 4 (25.00%) 1
Mental impairment			

subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Sedation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Syncope			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 17 (17.65%)	1 / 6 (16.67%)	2 / 4 (50.00%)
occurrences (all)	9	2	3
Febrile neutropenia			
subjects affected / exposed	3 / 17 (17.65%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	3	0	0
Leukocytosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Leukopenia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Lymphadenitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Neutropenia			
subjects affected / exposed	7 / 17 (41.18%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	11	0	3
Spleen disorder			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Splenomegaly			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	6 / 17 (35.29%)	1 / 6 (16.67%)	2 / 4 (50.00%)
occurrences (all)	9	1	2
Lymphadenopathy			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Eye haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Scleral pigmentation			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			

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

Dyspepsia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	2 / 4 (50.00%)
occurrences (all)	0	0	3
Dysphagia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	1	0	1
Faeces discoloured			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	2	0	0
Gingival pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Haematemesis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

Hiatus hernia			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Megacolon			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	6 / 17 (35.29%)	4 / 6 (66.67%)	4 / 4 (100.00%)
occurrences (all)	10	5	6
Oral disorder			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Oral mucosal blistering			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Oral pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Pancreatitis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Proctalgia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	2 / 17 (11.76%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	4	0	0
Tongue disorder			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0

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

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

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

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

subjects affected / exposed	5 / 17 (29.41%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	6	3	0
Muscular weakness			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Neck pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Osteoarthritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	2	0	1
Pain in jaw			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Periarthritis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Plantar fasciitis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			

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

Fungal infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Genital infection viral			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Onychomycosis			
subjects affected / exposed	0 / 17 (0.00%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Otitis media			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Pneumonia fungal			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pulmonary mycosis			
subjects affected / exposed	1 / 17 (5.88%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Sepsis			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	2 / 17 (11.76%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	2	1	0

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

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

subjects affected / exposed	1 / 17 (5.88%)	1 / 6 (16.67%)	0 / 4 (0.00%)
occurrences (all)	1	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 17 (0.00%)	0 / 6 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1B: Glasdegib 200 mg + Decitabine	Phase 1B: Glasdegib 200 mg + Cytarabine/Daunoru bicin	Phase 1B: Glasdegib 100 mg + Cytarabine/Daunoru bicin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	6 / 6 (100.00%)	16 / 16 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	3 / 16 (18.75%)
occurrences (all)	1	1	3
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	4 / 16 (25.00%)
occurrences (all)	0	0	5
Ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Thrombophlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Pallor			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	2	0	1
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Catheter site swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 16 (0.00%)
occurrences (all)	0	2	0
Chills			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	5 / 16 (31.25%)
occurrences (all)	1	0	7
Fatigue			
subjects affected / exposed	2 / 3 (66.67%)	2 / 6 (33.33%)	6 / 16 (37.50%)
occurrences (all)	5	3	10
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hernia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Localised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Nodule			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	4
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Oedema peripheral			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	7 / 16 (43.75%)
occurrences (all)	1	4	8
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	4
Performance status decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	10 / 16 (62.50%)
occurrences (all)	0	3	15
Thirst			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Catheter site erythema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Catheter site haemorrhage subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Immune system disorders Hypersensitivity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Reproductive system and breast disorders Pelvic pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1
Vulvovaginal pruritus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 2
Respiratory, thoracic and mediastinal disorders Atelectasis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1	2 / 16 (12.50%) 2
Cough subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 6 (33.33%) 2	1 / 16 (6.25%) 1
Dysphonia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Dyspnoea subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 3	2 / 6 (33.33%) 2	3 / 16 (18.75%) 5
Dyspnoea exertional			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	3 / 16 (18.75%)
occurrences (all)	1	1	3
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Lung infiltration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 16 (6.25%)
occurrences (all)	0	3	2
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pleuritic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pulmonary fibrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Rhinorrhoea			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Sinus congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	3 / 16 (18.75%)
occurrences (all)	0	1	3
Apathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Depression			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Disorientation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	5 / 16 (31.25%)
occurrences (all)	0	0	5

Panic attack			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Delirium			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	4 / 16 (25.00%)
occurrences (all)	0	1	5
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	2 / 16 (12.50%)
occurrences (all)	0	1	3
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Blood fibrinogen decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Blood uric acid increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Chest X-ray abnormal			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Eastern Cooperative Oncology Group performance status worsened			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
International normalised ratio increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Karnofsky scale worsened			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	3
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	6
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
White blood cell count decreased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	4 / 16 (25.00%)
occurrences (all)	0	0	7
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Post procedural haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Procedural headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vascular access complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Diastolic dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tachycardia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Ventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Amnesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Central nervous system lesion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	1 / 16 (6.25%)
occurrences (all)	1	2	1
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	7 / 16 (43.75%)
occurrences (all)	1	1	7
Headache			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	9 / 16 (56.25%)
occurrences (all)	0	2	11
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mental impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Peroneal nerve palsy			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Sedation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Syncope			

subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	4 / 16 (25.00%)
occurrences (all)	5	1	9
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	8 / 16 (50.00%)
occurrences (all)	0	2	9
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	2 / 16 (12.50%)
occurrences (all)	0	1	3
Lymphadenitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Neutropenia			
subjects affected / exposed	2 / 3 (66.67%)	1 / 6 (16.67%)	4 / 16 (25.00%)
occurrences (all)	7	1	8
Spleen disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	3 / 16 (18.75%)
occurrences (all)	2	4	4
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

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

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Angina bullosa haemorrhagica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	10 / 16 (62.50%)
occurrences (all)	1	3	14
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	6 / 6 (100.00%)	10 / 16 (62.50%)
occurrences (all)	0	8	18
Diverticulum			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Dry mouth			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	4 / 16 (25.00%)
occurrences (all)	0	1	4
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Gingival pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Haematemesis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	4 / 16 (25.00%)
occurrences (all)	0	2	5
Hiatus hernia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Megacolon			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Mouth haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	14 / 16 (87.50%)
occurrences (all)	2	4	25
Oral disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Oral mucosal blistering			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	3
Pancreatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Retching			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Stomatitis			
subjects affected / exposed	2 / 3 (66.67%)	0 / 6 (0.00%)	5 / 16 (31.25%)
occurrences (all)	2	0	11
Tongue disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	4 / 6 (66.67%)	5 / 16 (31.25%)
occurrences (all)	1	5	11
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2	2 / 6 (33.33%) 2	4 / 16 (25.00%) 4
Decubitus ulcer subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Dermatitis acneiform subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1
Dry skin subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1	2 / 16 (12.50%) 2
Ecchymosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	2 / 16 (12.50%) 2
Macule subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Night sweats subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1	1 / 16 (6.25%) 1
Pain of skin subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Palmar erythema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Panniculitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Petechiae			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Plantar erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	4 / 16 (25.00%)
occurrences (all)	0	1	4
Pruritus allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	3 / 16 (18.75%)
occurrences (all)	0	1	4
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	4
Rash papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Skin disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	3 / 16 (18.75%)
occurrences (all)	0	2	3
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Renal cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	2 / 3 (66.67%)	1 / 6 (16.67%)	4 / 16 (25.00%)
occurrences (all)	2	1	4
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	4 / 16 (25.00%)
occurrences (all)	0	0	4
Joint effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	2 / 3 (66.67%)	2 / 6 (33.33%)	10 / 16 (62.50%)
occurrences (all)	4	4	12
Muscular weakness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	4
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	3 / 16 (18.75%)
occurrences (all)	0	1	3
Neck pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Osteoarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	4 / 16 (25.00%)
occurrences (all)	1	3	4
Pain in jaw			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Periarthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Spinal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Bronchiolitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Clostridium difficile colitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1	1 / 16 (6.25%) 1
Clostridium difficile infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 6 (16.67%) 1	2 / 16 (12.50%) 2
Device related infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1
Enterobacter bacteraemia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Enterocolitis bacterial subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1
Enterocolitis infectious subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1
Folliculitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1
Fungal infection subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1
Genital infection viral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Onychomycosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	0 / 16 (0.00%) 0
Otitis media subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 6 (0.00%) 0	1 / 16 (6.25%) 1

Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	2 / 16 (12.50%)
occurrences (all)	0	1	2
Pneumonia fungal			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 16 (6.25%)
occurrences (all)	0	2	1
Pulmonary mycosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Viral infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)	2 / 6 (33.33%)	2 / 16 (12.50%)
occurrences (all)	5	2	2
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Gout			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypermagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypernatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hyperphosphataemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	2 / 16 (12.50%)
occurrences (all)	1	1	2
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	2 / 16 (12.50%)
occurrences (all)	0	1	2
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	3 / 16 (18.75%)
occurrences (all)	0	2	3
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	5 / 16 (31.25%)
occurrences (all)	0	4	10
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hypokalaemia			

subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	6 / 16 (37.50%)
occurrences (all)	0	3	6
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	4 / 16 (25.00%)
occurrences (all)	0	2	4
Hyponatraemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	5 / 16 (31.25%)
occurrences (all)	2	1	6
Hypophagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 16 (18.75%)
occurrences (all)	0	0	4
Hypovolaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Metabolic acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Tumour lysis syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2 Fit: Glasdegib 100 mg + Cytarabine/Daunorubicin	Phase 2 Unfit: Glasdegib 100 mg + LDAC	Phase 2 Unfit: LDAC alone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	69 / 69 (100.00%)	82 / 84 (97.62%)	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 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Vascular disorders			
Hypertension subjects affected / exposed occurrences (all)	12 / 69 (17.39%) 14	6 / 84 (7.14%) 7	1 / 41 (2.44%) 1
Hypotension subjects affected / exposed occurrences (all)	14 / 69 (20.29%) 15	12 / 84 (14.29%) 13	4 / 41 (9.76%) 4
Ischaemia subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Phlebitis subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Thrombophlebitis subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Venous thrombosis subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Pallor subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	1 / 84 (1.19%) 1	3 / 41 (7.32%) 3
Haematoma subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	5 / 84 (5.95%) 7	2 / 41 (4.88%) 2
General disorders and administration site conditions			
Asthenia subjects affected / exposed occurrences (all)	8 / 69 (11.59%) 10	10 / 84 (11.90%) 16	8 / 41 (19.51%) 20
Catheter site pain subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Catheter site swelling			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	9 / 69 (13.04%)	9 / 84 (10.71%)	1 / 41 (2.44%)
occurrences (all)	9	9	1
Chills			
subjects affected / exposed	21 / 69 (30.43%)	5 / 84 (5.95%)	1 / 41 (2.44%)
occurrences (all)	30	5	1
Fatigue			
subjects affected / exposed	25 / 69 (36.23%)	26 / 84 (30.95%)	8 / 41 (19.51%)
occurrences (all)	37	71	11
Gait disturbance			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Generalised oedema			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hernia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation			
subjects affected / exposed	8 / 69 (11.59%)	6 / 84 (7.14%)	2 / 41 (4.88%)
occurrences (all)	8	10	3
Nodule			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	6 / 69 (8.70%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	9	0	0
Oedema peripheral			
subjects affected / exposed	22 / 69 (31.88%)	22 / 84 (26.19%)	7 / 41 (17.07%)
occurrences (all)	37	35	7
Pain			
subjects affected / exposed	6 / 69 (8.70%)	4 / 84 (4.76%)	3 / 41 (7.32%)
occurrences (all)	6	5	3
Performance status decreased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	34 / 69 (49.28%)	23 / 84 (27.38%)	9 / 41 (21.95%)
occurrences (all)	52	44	11
Thirst			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	6 / 69 (8.70%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	6	0	0
Catheter site haemorrhage			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal pruritus			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Cough			
subjects affected / exposed	14 / 69 (20.29%)	18 / 84 (21.43%)	7 / 41 (17.07%)
occurrences (all)	18	20	7
Dysphonia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	13 / 69 (18.84%)	21 / 84 (25.00%)	11 / 41 (26.83%)
occurrences (all)	14	36	11
Dyspnoea exertional			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	11 / 69 (15.94%)	7 / 84 (8.33%)	6 / 41 (14.63%)
occurrences (all)	13	11	7
Hypoxia			
subjects affected / exposed	8 / 69 (11.59%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	8	0	0
Lung infiltration			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			

subjects affected / exposed	7 / 69 (10.14%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	7	0	0
Oropharyngeal pain			
subjects affected / exposed	12 / 69 (17.39%)	9 / 84 (10.71%)	0 / 41 (0.00%)
occurrences (all)	12	9	0
Pleural effusion			
subjects affected / exposed	9 / 69 (13.04%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	10	0	0
Pleuritic pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pulmonary fibrosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pulmonary oedema			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Respiratory failure			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Sinus congestion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	7 / 69 (10.14%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	7	0	0
Hiccups			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Psychiatric disorders			

Agitation			
subjects affected / exposed	0 / 69 (0.00%)	3 / 84 (3.57%)	3 / 41 (7.32%)
occurrences (all)	0	5	3
Anxiety			
subjects affected / exposed	15 / 69 (21.74%)	3 / 84 (3.57%)	4 / 41 (9.76%)
occurrences (all)	17	3	4
Apathy			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	4 / 69 (5.80%)	7 / 84 (8.33%)	0 / 41 (0.00%)
occurrences (all)	4	7	0
Depressed mood			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Disorientation			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	19 / 69 (27.54%)	10 / 84 (11.90%)	2 / 41 (4.88%)
occurrences (all)	21	11	3
Panic attack			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Delirium			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Hallucination			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	21 / 69 (30.43%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	26	0	0
Amylase increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	17 / 69 (24.64%)	6 / 84 (7.14%)	1 / 41 (2.44%)
occurrences (all)	23	15	1
Blood alkaline phosphatase increased			
subjects affected / exposed	13 / 69 (18.84%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	16	0	0
Blood bilirubin increased			
subjects affected / exposed	19 / 69 (27.54%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	35	0	0
Blood creatinine increased			
subjects affected / exposed	14 / 69 (20.29%)	9 / 84 (10.71%)	3 / 41 (7.32%)
occurrences (all)	16	13	4
Blood fibrinogen decreased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (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 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	7 / 69 (10.14%)	7 / 84 (8.33%)	1 / 41 (2.44%)
occurrences (all)	15	11	1
International normalised ratio increased			

subjects affected / exposed	7 / 69 (10.14%)	3 / 84 (3.57%)	5 / 41 (12.20%)
occurrences (all)	8	3	5
Karnofsky scale worsened			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Liver function test increased			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased			
subjects affected / exposed	6 / 69 (8.70%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	9	0	0
Neutrophil count decreased			
subjects affected / exposed	12 / 69 (17.39%)	11 / 84 (13.10%)	1 / 41 (2.44%)
occurrences (all)	14	45	1
Platelet count decreased			
subjects affected / exposed	18 / 69 (26.09%)	14 / 84 (16.67%)	4 / 41 (9.76%)
occurrences (all)	47	148	24
Weight decreased			
subjects affected / exposed	9 / 69 (13.04%)	17 / 84 (20.24%)	1 / 41 (2.44%)
occurrences (all)	12	28	1
White blood cell count decreased			
subjects affected / exposed	20 / 69 (28.99%)	13 / 84 (15.48%)	2 / 41 (4.88%)
occurrences (all)	54	55	2
Activated partial thromboplastin time prolonged			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Weight increased			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 69 (0.00%)	6 / 84 (7.14%)	6 / 41 (14.63%)
occurrences (all)	0	10	9

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	6 / 69 (8.70%)	5 / 84 (5.95%)	2 / 41 (4.88%)
occurrences (all)	7	10	2
Fall			
subjects affected / exposed	0 / 69 (0.00%)	9 / 84 (10.71%)	1 / 41 (2.44%)
occurrences (all)	0	15	1
Infusion related reaction			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Post procedural haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Procedural headache			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Vascular access complication			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Atrial fibrillation			
subjects affected / exposed	5 / 69 (7.25%)	7 / 84 (8.33%)	1 / 41 (2.44%)
occurrences (all)	6	10	1
Diastolic dysfunction			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Palpitations			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Sinus bradycardia			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Sinus tachycardia			
subjects affected / exposed	7 / 69 (10.14%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	7	0	0
Tachycardia			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Ventricular tachycardia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Nervous system disorders			
Ageusia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Amnesia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Central nervous system lesion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	12 / 69 (17.39%)	18 / 84 (21.43%)	4 / 41 (9.76%)
occurrences (all)	15	25	5
Dysgeusia			
subjects affected / exposed	19 / 69 (27.54%)	21 / 84 (25.00%)	1 / 41 (2.44%)
occurrences (all)	22	27	1
Headache			
subjects affected / exposed	22 / 69 (31.88%)	11 / 84 (13.10%)	5 / 41 (12.20%)
occurrences (all)	34	13	5

Lethargy			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Memory impairment			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Mental impairment			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Peroneal nerve palsy			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Sedation			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	28 / 69 (40.58%)	37 / 84 (44.05%)	17 / 41 (41.46%)
occurrences (all)	54	318	62
Febrile neutropenia			
subjects affected / exposed	38 / 69 (55.07%)	8 / 84 (9.52%)	4 / 41 (9.76%)
occurrences (all)	44	8	7
Leukocytosis			

subjects affected / exposed	0 / 69 (0.00%)	6 / 84 (7.14%)	2 / 41 (4.88%)
occurrences (all)	0	6	2
Leukopenia			
subjects affected / exposed	9 / 69 (13.04%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	11	0	0
Lymphadenitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	15 / 69 (21.74%)	13 / 84 (15.48%)	8 / 41 (19.51%)
occurrences (all)	32	38	13
Spleen disorder			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Splenomegaly			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	23 / 69 (33.33%)	26 / 84 (30.95%)	11 / 41 (26.83%)
occurrences (all)	46	110	53
Lymphadenopathy			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Ocular hyperaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Photophobia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Scleral pigmentation subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Gastrointestinal disorders			
Abdominal discomfort subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Abdominal distension subjects affected / exposed occurrences (all)	10 / 69 (14.49%) 10	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Abdominal pain subjects affected / exposed occurrences (all)	20 / 69 (28.99%) 24	15 / 84 (17.86%) 17	4 / 41 (9.76%) 4
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	7 / 84 (8.33%) 8	1 / 41 (2.44%) 1
Anal fissure subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Anal haemorrhage subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Angina bullosa haemorrhagica subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Ascites subjects affected / exposed occurrences (all)	0 / 69 (0.00%) 0	0 / 84 (0.00%) 0	0 / 41 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	32 / 69 (46.38%) 39	21 / 84 (25.00%) 28	6 / 41 (14.63%) 7
Diarrhoea			

subjects affected / exposed	49 / 69 (71.01%)	24 / 84 (28.57%)	9 / 41 (21.95%)
occurrences (all)	62	49	10
Diverticulum			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	10 / 69 (14.49%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	10	0	0
Dyspepsia			
subjects affected / exposed	12 / 69 (17.39%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	13	0	0
Dysphagia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Gastritis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	6 / 69 (8.70%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	6	0	0
Gingival bleeding			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Gingival pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Haematochezia			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	5 / 69 (7.25%)	7 / 84 (8.33%)	0 / 41 (0.00%)
occurrences (all)	5	7	0
Hiatus hernia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Megacolon			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	5 / 69 (7.25%)	2 / 84 (2.38%)	4 / 41 (9.76%)
occurrences (all)	6	2	4
Nausea			
subjects affected / exposed	40 / 69 (57.97%)	30 / 84 (35.71%)	5 / 41 (12.20%)
occurrences (all)	70	46	6
Oral disorder			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Oral mucosal blistering			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Oral pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pancreatitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Retching			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	17 / 69 (24.64%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	20	0	0
Tongue disorder			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Tooth loss			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Vomiting			
subjects affected / exposed	25 / 69 (36.23%)	18 / 84 (21.43%)	4 / 41 (9.76%)
occurrences (all)	36	29	4
Mouth ulceration			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	3 / 41 (7.32%)
occurrences (all)	0	0	3
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hyperbilirubinaemia			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	16 / 69 (23.19%)	9 / 84 (10.71%)	0 / 41 (0.00%)
occurrences (all)	19	9	0
Decubitus ulcer			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 69 (0.00%)	7 / 84 (8.33%)	2 / 41 (4.88%)
occurrences (all)	0	9	3
Macule			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Pain of skin			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Palmar erythema			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Panniculitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	11 / 69 (15.94%)	7 / 84 (8.33%)	4 / 41 (9.76%)
occurrences (all)	13	7	5
Plantar erythema			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	10 / 69 (14.49%)	6 / 84 (7.14%)	1 / 41 (2.44%)
occurrences (all)	11	9	1
Pruritus allergic			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Purpura			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	14 / 69 (20.29%)	11 / 84 (13.10%)	1 / 41 (2.44%)
occurrences (all)	18	11	1
Rash macular			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	9 / 69 (13.04%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	10	0	0
Rash papular			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	9 / 69 (13.04%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	9	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	8 / 69 (11.59%)	7 / 84 (8.33%)	1 / 41 (2.44%)
occurrences (all)	10	8	1

Dysuria			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Haematuria			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Pollakiuria			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Proteinuria			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Renal cyst			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Renal failure			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 69 (0.00%)	7 / 84 (8.33%)	0 / 41 (0.00%)
occurrences (all)	0	7	0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hypothyroidism			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 69 (15.94%)	10 / 84 (11.90%)	0 / 41 (0.00%)
occurrences (all)	13	14	0
Back pain			

subjects affected / exposed	12 / 69 (17.39%)	9 / 84 (10.71%)	3 / 41 (7.32%)
occurrences (all)	14	12	3
Bone pain			
subjects affected / exposed	0 / 69 (0.00%)	2 / 84 (2.38%)	3 / 41 (7.32%)
occurrences (all)	0	4	5
Joint effusion			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	11 / 69 (15.94%)	19 / 84 (22.62%)	2 / 41 (4.88%)
occurrences (all)	14	46	2
Muscular weakness			
subjects affected / exposed	0 / 69 (0.00%)	6 / 84 (7.14%)	0 / 41 (0.00%)
occurrences (all)	0	6	0
Musculoskeletal pain			
subjects affected / exposed	7 / 69 (10.14%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	8	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	5 / 69 (7.25%)	5 / 84 (5.95%)	0 / 41 (0.00%)
occurrences (all)	5	6	0
Neck pain			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Osteoarthritis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	9 / 69 (13.04%)	15 / 84 (17.86%)	2 / 41 (4.88%)
occurrences (all)	12	20	2
Pain in jaw			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Periarthritis			

subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Plantar fasciitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Bacteraemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Bronchiolitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Cellulitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Enterobacter bacteraemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Enterocolitis bacterial			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Enterocolitis infectious			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Folliculitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Fungal infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Genital infection viral			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Onychomycosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Otitis media			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	6 / 69 (8.70%)	9 / 84 (10.71%)	3 / 41 (7.32%)
occurrences (all)	6	10	3
Pneumonia fungal			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Pulmonary mycosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Sepsis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0

Skin infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Staphylococcal infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Subcutaneous abscess			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	8 / 69 (11.59%)	5 / 84 (5.95%)	5 / 41 (12.20%)
occurrences (all)	8	6	5
Viral infection			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 69 (0.00%)	3 / 84 (3.57%)	3 / 41 (7.32%)
occurrences (all)	0	5	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	26 / 69 (37.68%)	29 / 84 (34.52%)	5 / 41 (12.20%)
occurrences (all)	33	44	9
Dehydration			
subjects affected / exposed	6 / 69 (8.70%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	6	0	0
Gout			
subjects affected / exposed	0 / 69 (0.00%)	5 / 84 (5.95%)	2 / 41 (4.88%)
occurrences (all)	0	6	2
Hyperkalaemia			

subjects affected / exposed	6 / 69 (8.70%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	9	0	0
Hypermagnesaemia			
subjects affected / exposed	4 / 69 (5.80%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	4	0	0
Hypernatraemia			
subjects affected / exposed	5 / 69 (7.25%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	5	0	0
Hyperphosphataemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 69 (0.00%)	7 / 84 (8.33%)	1 / 41 (2.44%)
occurrences (all)	0	8	1
Hypoalbuminaemia			
subjects affected / exposed	18 / 69 (26.09%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	24	0	0
Hypocalcaemia			
subjects affected / exposed	22 / 69 (31.88%)	5 / 84 (5.95%)	1 / 41 (2.44%)
occurrences (all)	32	5	1
Hypoglycaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hypokalaemia			
subjects affected / exposed	37 / 69 (53.62%)	13 / 84 (15.48%)	6 / 41 (14.63%)
occurrences (all)	64	19	7
Hypomagnesaemia			
subjects affected / exposed	20 / 69 (28.99%)	8 / 84 (9.52%)	2 / 41 (4.88%)
occurrences (all)	23	11	2
Hyponatraemia			
subjects affected / exposed	23 / 69 (33.33%)	10 / 84 (11.90%)	0 / 41 (0.00%)
occurrences (all)	35	36	0
Hypophagia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			

subjects affected / exposed	15 / 69 (21.74%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	21	0	0
Hypovolaemia			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Tumour lysis syndrome			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 69 (0.00%)	0 / 84 (0.00%)	0 / 41 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	13 / 69 (18.84%)	0 / 84 (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>

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