Clinical trial results:
A Randomized (1:1), Double-blind, Multi-center, Placebo Controlled Study Evaluating Intensive Chemotherapy With or Without Glasdegib (Pf-04449913) or Azacitidine (AZA) With or Without Glasdegib in Patients With Previously Untreated Acute Myeloid Leukemia

Summary

EudraCT number	2017-002822-19
Trial protocol	FR GB CZ SE BE PL ES DE IT RO
Global end of trial date	02 December 2022

Results information

Result version number	v2 (current)
This version publication date	17 December 2023
First version publication date	04 August 2021
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	B1371019

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03416179
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, 10017
Public contact	Pfizer ClinicalTrials.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	02 December 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 December 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate that glasdegib is superior to placebo in combination with azacitidine (non-intensive study) or cytarabine and daunorubicin (intensive study) in prolonging overall survival (OS) in subjects with untreated acute myeloid leukemia (AML). To monitor the safety and tolerability of the investigational drugs in participants continuing study intervention from this study and participants originating from Study B1371012.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Council for Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 April 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	5 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 21
Country: Number of subjects enrolled	Belgium: 3
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	China: 72
Country: Number of subjects enrolled	Czechia: 61
Country: Number of subjects enrolled	France: 30
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 37
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Italy: 22
Country: Number of subjects enrolled	Japan: 86
Country: Number of subjects enrolled	Korea, Republic of: 29
Country: Number of subjects enrolled	Poland: 25
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 33
Country: Number of subjects enrolled	Spain: 73

Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	Taiwan: 19
Country: Number of subjects enrolled	United Kingdom: 22
Country: Number of subjects enrolled	United States: 143
Country: Number of subjects enrolled	Austria: 16
Country: Number of subjects enrolled	Mexico: 4
Worldwide total number of subjects	743
EEA total number of subjects	295

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)	318
From 65 to 84 years	410
85 years and over	15

Subject disposition

Recruitment

Recruitment details:

Study evaluated glasdegib in intensive(INT)&non-intensive(NINT)chemotherapy patients.INT study: Glasdegib in combination with cytarabine & daunorubicin for treating adults with previously untreated AML. Eligible NINT cohort subjects enrolled in B1371019(NCT03416179) &B1371012(NCT02367456) study were included in an open-label continuation study.

Pre-assignment

Screening details:

NI study:Glasdegib in combination with azacitidine for treatment of adults with previously untreated AML who were not candidates for intensive induction chemotherapy.Open-label extension study:Eligible NINT cohort subjects enrolled in B1371019(NCT03416179)& B1371012(NCT02367456)study eligible subjects were included in an open-label extension study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator

Arms

Are arms mutually exclusive?	Yes
Arm title	Intensive Study: Glasdegib + Cytarabine + Daunorubicin

Arm description:

Subjects received 28 days induction therapy: Cytarabine 100 milligram per square meter (mg/m^2) intravenous (IV) daily for 7 days + daunorubicin 60 mg/m^2 daily IV for 3 days. Depending on bone marrow blast or investigator judgement subjects had second induction to receive either same therapy or cytarabine 100 mg/m^2 IV daily for 5 days + daunorubicin 60 mg/m^2 IV daily for 2 days. Subjects with less than (<) 5 percentage (%) bone marrow blasts entered consolation phase: treated with either or both of: 1) Cytarabine 1 to 3 gm/m^2 IV for adults greater than or equal to (>=) 60 to <60 years twice daily on Days 1, 3, 5 for 4 cycle (1 cycle=28 days) or cytarabine per local prescribing information. 2) Received HSCT per local standard of care. Subjects received Glasdegib 100 mg tablet per oral (PO) once a day (QD) from Day 1 up to 28 days in both induction and until 2 consecutive CR MRD-negative, whichever came first.

Arm type	Experimental
Investigational medicinal product name	Glasdegib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Glasdegib 100 mg tablet orally (PO) once daily (QD) from Day 1 of chemotherapy up to 28 days in both induction and up to 2 years post randomization or until 2 consecutive (complete remission) CR MRD-negative central laboratory results, whichever came first.

Investigational medicinal product name	Daunorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received daunorubicin 60 mg/m^2 daily IV for 3 days. If >=5% bone marrow blast or investigator judgement for < 5% bone marrow blasts then received daunorubicin 60 mg/m^2 IV daily for 2 days or daunorubicin 60 mg/m^2 IV daily for 3 days.

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Cytarabine 100 mg/m^2 daily by IV infusion for 7 days. If greater than or equals to (>=) 5 percent (%) bone marrow blast or investigator judgement for less than (<) 5% bone marrow blasts then subjects received either option 1: cytarabine 100 mg/m^2 IV daily for 5 days or option 2: cytarabine 100 mg/m^2 IV daily for 7 days.

Arm title	Intensive Study: Placebo + Cytarabine + Daunorubicin

Arm description:

Subjects received 28 days induction therapy: Cytarabine 100 mg/m^2 IV daily for 7 days + daunorubicin 60 mg/m^2 daily IV for 3 days. Depending on bone marrow blast or investigator judgement subjects had second induction to receive either same therapy or cytarabine 100 mg/m^2 IV daily for 5 days + daunorubicin 60 mg/m^2 IV daily for 2 days. Subjects with <5% bone marrow blasts entered consolation phase: treated with either or both of: 1) Cytarabine 1 to 3 gm/m^2 IV for adults >= 60 to <60 years twice daily on Days 1, 3, 5 for 4 cycle (1 cycle=28 days) or cytarabine per local prescribing information. 2) Received HSCT per local standard of care. Subjects received Glasdegib matched placebo tablet PO QD from Day 1 up to 28 days in both induction and until 2 consecutive CR MRD-negative, whichever came first.

Arm type	Placebo
Investigational medicinal product name	Glasdegib matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received Glasdegib 100 mg matching placebo tablet PO QD from Day 1 of chemotherapy up to 28 days in both induction and up to 2 years post randomization or until 2 consecutive CR MRD-negative central laboratory results, whichever came first.

Investigational medicinal product name	Daunorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received daunorubicin 60 mg/m^2 daily IV for 3 days. If >=5% bone marrow blast or investigator judgement for < 5% bone marrow blasts then received daunorubicin 60 mg/m^2 IV daily for 2 days or daunorubicin 60 mg/m^2 IV daily for 3 days.

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received Cytarabine 100 mg/m^2 daily by IV infusion for 7 days. If >=5% bone marrow blast or investigator judgement for <5% bone marrow blasts then subjects received either option 1: cytarabine 100 mg/m^2 IV daily for 5 days or option 2: cytarabine 100 mg/m^2 IV daily for 7 days.

Arm title	Non-intensive Study: Glasdegib + Azacitidine

Arm description:

Subjects received chemotherapy with azacitidine 75 mg/m^2 subcutaneous (SC) injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, subject refusal or death, whichever occurred first. Subjects also received glasdegib 100 mg PO QD from Day 1 of chemotherapy until clinical benefit or disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first. Eligible subjects underwent hematopoietic stem cell transplantation (HSCT) per local standard of care and received glasdegib unless 2 consecutive

negative minimal residual disease (MRD) assessments.

Arm type	Experimental
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, patient refusal or death, whichever occurred first.

Investigational medicinal product name	Glasdegib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received glasdegib 100 mg PO QD from Day 1 of chemotherapy and continued if subject's demonstrated reasonable evidence of clinical benefit or until disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first.

Arm title	Non-intensive Study: Placebo + Azacitidine

Arm description:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, subjects refusal or death, whichever occurred first. Subjects also received glasdegib 100 mg tablet matching placebo PO QD from Day 1 of chemotherapy until clinical benefit or disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first. Eligible subjects underwent HSCT per local standard of care and glasdegib matching placebo unless 2 consecutive negative MRD assessments.

Arm type	Placebo
Investigational medicinal product name	Azacitidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, patient refusal or death, whichever occurred first.

Investigational medicinal product name	Glasdegib matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received glasdegib 100 mg matching placebo PO QD from Day 1 of chemotherapy and continued if subject's demonstrated reasonable evidence of clinical benefit or until disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first.

Arm title	Open Label Extension: Glasdegib + Azacitidine

Arm description:

Subjects received glasdegib 100 mg tablet PO QD in combination with azacitidine 75 mg/ m^2/day as SC injection or IV infusion for 7 days every 28 days. Treatment continued until objective disease progression or relapse, death, unacceptable toxicity, or participant refusal, whichever occurred first. Participants were followed up for 28 days after end of study treatment.

Arm type	Experimental

Investigational medicinal product name	Azactidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, patient refusal or death, whichever occurred first.

Investigational medicinal product name	Glasdegib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received glasdegib 100 mg PO QD from Day 1 of chemotherapy and continued if subject's demonstrated reasonable evidence of clinical benefit or until disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first.

Arm title	Open Label Extension: Placebo + Azacitidine

Arm description:

Subjects received placebo matched to Glasdegib in combination with azacitidine 75mg/m^2/day SC or IV for 7 days every 28 days. Treatment continued until objective disease progression or relapse, death, unacceptable toxicity, or participant refusal, whichever occurred first. Participants were followed up for 28 days after end of study treatment.

Arm type	Placebo
Investigational medicinal product name	Azactidine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, patient refusal or death, whichever occurred first.

Investigational medicinal product name	Glasdegib matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received glasdegib 100 mg matching placebo PO QD from Day 1 of chemotherapy and continued if subject's demonstrated reasonable evidence of clinical benefit or until disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first.

Number of subjects in period 1	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin	Non-intensive Study: Glasdegib + Azacitidine
Started	201	203	163
Completed	0	0	0
Not completed	201	203	163
Adverse event, serious fatal	67	60	96

Consent withdrawn by subject	13	19	5
Death	-	-	-
Ongoing	121	123	62
Unspecified	-	1	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Non-intensive Study: Placebo + Azacitidine	Open Label Extension: Glasdegib + Azacitidine	Open Label Extension: Placebo + Azacitidine
Started	162	9	5
Completed	0	4	1
Not completed	162	5	4
Adverse event, serious fatal	88	-	-
Consent withdrawn by subject	6	-	-
Death	-	1	-
Ongoing	66	-	-
Unspecified	-	4	4
Lost to follow-up	2	-	-

Baseline characteristics

Reporting groups

Reporting group title	Intensive Study: Glasdegib + Cytarabine + Daunorubicin

Reporting group description:

Subjects received 28 days induction therapy: Cytarabine 100 milligram per square meter (mg/m^2) intravenous (IV) daily for 7 days + daunorubicin 60 mg/m^2 daily IV for 3 days. Depending on bone marrow blast or investigator judgement subjects had second induction to receive either same therapy or cytarabine 100 mg/m^2 IV daily for 5 days + daunorubicin 60 mg/m^2 IV daily for 2 days. Subjects with less than (<) 5 percentage (%) bone marrow blasts entered consolation phase: treated with either or both of: 1) Cytarabine 1 to 3 gm/m^2 IV for adults greater than or equal to (>=) 60 to <60 years twice daily on Days 1, 3, 5 for 4 cycle (1 cycle=28 days) or cytarabine per local prescribing information. 2) Received HSCT per local standard of care. Subjects received Glasdegib 100 mg tablet per oral (PO) once a day (QD) from Day 1 up to 28 days in both induction and until 2 consecutive CR MRD-negative, whichever came first.

Reporting group title	Intensive Study: Placebo + Cytarabine + Daunorubicin

Reporting group description:

Subjects received 28 days induction therapy: Cytarabine 100 mg/m^2 IV daily for 7 days + daunorubicin 60 mg/m^2 daily IV for 3 days. Depending on bone marrow blast or investigator judgement subjects had second induction to receive either same therapy or cytarabine 100 mg/m^2 IV daily for 5 days + daunorubicin 60 mg/m^2 IV daily for 2 days. Subjects with <5% bone marrow blasts entered consolation phase: treated with either or both of: 1) Cytarabine 1 to 3 gm/m^2 IV for adults >= 60 to <60 years twice daily on Days 1, 3, 5 for 4 cycle (1 cycle=28 days) or cytarabine per local prescribing information. 2) Received HSCT per local standard of care. Subjects received Glasdegib matched placebo tablet PO QD from Day 1 up to 28 days in both induction and until 2 consecutive CR MRD-negative, whichever came first.

Reporting group title	Non-intensive Study: Glasdegib + Azacitidine

Reporting group description:

Subjects received chemotherapy with azacitidine 75 mg/m^2 subcutaneous (SC) injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, subject refusal or death, whichever occurred first. Subjects also received glasdegib 100 mg PO QD from Day 1 of chemotherapy until clinical benefit or disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first. Eligible subjects underwent hematopoietic stem cell transplantation (HSCT) per local standard of care and received glasdegib unless 2 consecutive negative minimal residual disease (MRD) assessments.

Reporting group title	Non-intensive Study: Placebo + Azacitidine

Reporting group description:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, subjects refusal or death, whichever occurred first. Subjects also received glasdegib 100 mg tablet matching placebo PO QD from Day 1 of chemotherapy until clinical benefit or disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first. Eligible subjects underwent HSCT per local standard of care and glasdegib matching placebo unless 2 consecutive negative MRD assessments.

Reporting group title	Open Label Extension: Glasdegib + Azacitidine

Reporting group description:

Subjects received glasdegib 100 mg tablet PO QD in combination with azacitidine 75 mg/ m^2/day as SC injection or IV infusion for 7 days every 28 days. Treatment continued until objective disease progression or relapse, death, unacceptable toxicity, or participant refusal, whichever occurred first. Participants were followed up for 28 days after end of study treatment.

Reporting group title	Open Label Extension: Placebo + Azacitidine

Reporting group description:

Subjects received placebo matched to Glasdegib in combination with azacitidine 75mg/m^2/day SC or IV for 7 days every 28 days. Treatment continued until objective disease progression or relapse, death, unacceptable toxicity, or participant refusal, whichever occurred first. Participants were followed up for 28 days after end of study treatment.

Reporting group values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin	Non-intensive Study: Glasdegib + Azacitidine
Number of subjects	201	203	163
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	144	141	16
From 65-84 years	57	61	142
85 years and over	0	1	5
Age Continuous Units: years			
arithmetic mean	56.55	55.38	73.19
standard deviation	± 12.60	± 13.61	± 7.17
Sex: Female, Male Units: subjects			
Female	71	97	97
Male	130	106	66
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	66	57	51
Black or African American	3	3	1
White	110	123	97
More than one race	1	0	0
Unknown or Not Reported	20	20	14
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	19	12	12
Not Hispanic or Latino	166	171	140
Unknown or Not Reported	16	20	11

Reporting group values	Non-intensive Study: Placebo + Azacitidine	Open Label Extension: Glasdegib + Azacitidine	Open Label Extension: Placebo + Azacitidine
Number of subjects	162	9	5
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0

Adults (18-64 years)	17	0	0
From 65-84 years	136	9	5
85 years and over	9	0	0
Age Continuous			
Units: years			
arithmetic mean	73.14	72.33	76.80
standard deviation	± 6.82	± 3.94	± 5.26
Sex: Female, Male			
Units: subjects			
Female	89	3	3
Male	73	6	2
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	44	1	0
Black or African American	7	0	1
White	99	5	4
More than one race	0	0	0
Unknown or Not Reported	12	3	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	16	1	1
Not Hispanic or Latino	139	7	4
Unknown or Not Reported	7	1	0

Reporting group values	Total		
Number of subjects	743		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	318		
From 65-84 years	410		
85 years and over	15		
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Units: subjects			
Female	360		
Male	383		
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1		
Asian	219		

Black or African American	15		
White	438		
More than one race	1		
Unknown or Not Reported	69		
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	61		
Not Hispanic or Latino	627		
Unknown or Not Reported	55		

End points

End points reporting groups

Reporting group title	Intensive Study: Glasdegib + Cytarabine + Daunorubicin

Reporting group description:

Subjects received 28 days induction therapy: Cytarabine 100 milligram per square meter (mg/m^2) intravenous (IV) daily for 7 days + daunorubicin 60 mg/m^2 daily IV for 3 days. Depending on bone marrow blast or investigator judgement subjects had second induction to receive either same therapy or cytarabine 100 mg/m^2 IV daily for 5 days + daunorubicin 60 mg/m^2 IV daily for 2 days. Subjects with less than (<) 5 percentage (%) bone marrow blasts entered consolation phase: treated with either or both of: 1) Cytarabine 1 to 3 gm/m^2 IV for adults greater than or equal to (>=) 60 to <60 years twice daily on Days 1, 3, 5 for 4 cycle (1 cycle=28 days) or cytarabine per local prescribing information. 2) Received HSCT per local standard of care. Subjects received Glasdegib 100 mg tablet per oral (PO) once a day (QD) from Day 1 up to 28 days in both induction and until 2 consecutive CR MRD-negative, whichever came first.

Reporting group title	Intensive Study: Placebo + Cytarabine + Daunorubicin

Reporting group description:

Subjects received 28 days induction therapy: Cytarabine 100 mg/m^2 IV daily for 7 days + daunorubicin 60 mg/m^2 daily IV for 3 days. Depending on bone marrow blast or investigator judgement subjects had second induction to receive either same therapy or cytarabine 100 mg/m^2 IV daily for 5 days + daunorubicin 60 mg/m^2 IV daily for 2 days. Subjects with <5% bone marrow blasts entered consolation phase: treated with either or both of: 1) Cytarabine 1 to 3 gm/m^2 IV for adults >= 60 to <60 years twice daily on Days 1, 3, 5 for 4 cycle (1 cycle=28 days) or cytarabine per local prescribing information. 2) Received HSCT per local standard of care. Subjects received Glasdegib matched placebo tablet PO QD from Day 1 up to 28 days in both induction and until 2 consecutive CR MRD-negative, whichever came first.

Reporting group title	Non-intensive Study: Glasdegib + Azacitidine

Reporting group description:

Subjects received chemotherapy with azacitidine 75 mg/m^2 subcutaneous (SC) injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, subject refusal or death, whichever occurred first. Subjects also received glasdegib 100 mg PO QD from Day 1 of chemotherapy until clinical benefit or disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first. Eligible subjects underwent hematopoietic stem cell transplantation (HSCT) per local standard of care and received glasdegib unless 2 consecutive negative minimal residual disease (MRD) assessments.

Reporting group title	Non-intensive Study: Placebo + Azacitidine

Reporting group description:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, subjects refusal or death, whichever occurred first. Subjects also received glasdegib 100 mg tablet matching placebo PO QD from Day 1 of chemotherapy until clinical benefit or disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first. Eligible subjects underwent HSCT per local standard of care and glasdegib matching placebo unless 2 consecutive negative MRD assessments.

Reporting group title	Open Label Extension: Glasdegib + Azacitidine

Reporting group description:

Subjects received glasdegib 100 mg tablet PO QD in combination with azacitidine 75 mg/ m^2/day as SC injection or IV infusion for 7 days every 28 days. Treatment continued until objective disease progression or relapse, death, unacceptable toxicity, or participant refusal, whichever occurred first. Participants were followed up for 28 days after end of study treatment.

Reporting group title	Open Label Extension: Placebo + Azacitidine

Reporting group description:

Subjects received placebo matched to Glasdegib in combination with azacitidine 75mg/m^2/day SC or IV for 7 days every 28 days. Treatment continued until objective disease progression or relapse, death, unacceptable toxicity, or participant refusal, whichever occurred first. Participants were followed up for 28 days after end of study treatment.

Primary: Intensive Study: Overall Survival (OS)

End point title	Intensive Study: Overall Survival (OS)[1]

End point description:

OS was defined as the time from the date of randomisation to the date of death due to any cause. Subjects last known to be alive were to be censored at the date of last contact. Full Analysis (FA) set included all randomised subjects. Here, '99999 =Upper limit of 95 % CI was not estimable due to low number of subjects with events.'

End point type	Primary

End point timeframe:

Baseline up to 25 months

Notes:

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

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	203		
Units: Months				
median (confidence interval 95%)	17.3 (15.2 to 18.5)	20.4 (17.6 to 99999)		

Statistical analyses

Statistical analysis title	Glasdegib Vs Placebo

Statistical analysis description:

Hazard ratio based on Cox proportional hazards model; under proportional hazards, hazard ratio less than (<) 1 indicated a reduction in hazard rate in favor of Glasdegib 100 mg PO + Cytarabine 100 mg/m^2 IV + Daunorubicin 60 mg/m^2 compared to Placebo + Cytarabine 100 mg/m^2 IV + Daunorubicin 60 mg/m^2.

Comparison groups	Intensive Study: Glasdegib + Cytarabine + Daunorubicin v Intensive Study: Placebo + Cytarabine + Daunorubicin
Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6579
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.755
upper limit	1.532

Primary: Non-intensive Study: OS

End point title	Non-intensive Study: OS[2]

End point description:

OS was defined as the time from date of first study treatment to date of death from any cause. Subject's last known to be alive were to be censored at the date of last contact. FA set included all randomised subjects.

End point type	Primary

End point timeframe:

Baseline up to 25 months

Notes:

[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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Months				
median (confidence interval 95%)	10.3 (7.7 to 12.4)	10.6 (8.4 to 13.3)		

Statistical analyses

Statistical analysis title	Glasdegib Vs Placebo

Statistical analysis description:

Hazard ratio based on Cox proportional hazards model; under proportional hazards, hazard ratio < 1 indicates a reduction in hazard rate in favor of Glasdegib 100 mg PO QD + Azacitidine compared to Placebo + Azacitidine

Comparison groups	Non-intensive Study: Glasdegib + Azacitidine v Non-intensive Study: Placebo + Azacitidine
Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5955
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.775
upper limit	1.388

Primary: Open Label Extension: Number of Subjects With Treatment Emergent Adverse Event (AE) and Treatment Related AE

End point title	Open Label Extension: Number of Subjects With Treatment Emergent Adverse Event (AE) and Treatment Related AE[3][4]

End point description:

An AE was any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. An AE was considered treatment emergent if the event occurred during the on-treatment period (regardless of if it was seen prior to the start of treatment). An AE was considered treatment related as assigned by the investigator.

End point type	Primary

End point timeframe:

From initiation of study treatment to study completion from 17-May-2021 to 02-Dec-2022 (approximately 565 days)

Notes:

[3] - 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: No statistical analysis was planned

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

End point values	Open Label Extension: Glasdegib + Azacitidine	Open Label Extension: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	5		
Units: Subjects				
Treatment emergent AE	7	4		
Treatment related AE	5	4		

Statistical analyses

No statistical analyses for this end point

Primary: Open Label Extension: Number of Subjects With Treatment Emergent Serious Adverse Events (SAE) and Treatment Related SAEs

End point title	Open Label Extension: Number of Subjects With Treatment Emergent Serious Adverse Events (SAE) and Treatment Related SAEs[5][6]

End point description:

A SAE was defined as any untoward medical occurrence that, at any dose that resulted in death; was life-threatening, required inpatient hospitalisation or prolongation of existing hospitalisation, resulted in persistent disability/incapacity, was a congenital anomaly/birth defect or other medical events as per investigator’s judgement. A SAE was considered treatment emergent if the event occurred during the on-treatment period (regardless of if it was seen prior to the start of treatment). A SAE was considered treatment related as assigned by the investigator.

End point type	Primary

End point timeframe:

From initiation of study treatment to study completed from 17-May-2021 to 02-Dec-2022 (approximately 565 days)

Notes:

[5] - 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: No statistical analysis was planned

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

End point values	Open Label Extension: Glasdegib + Azacitidine	Open Label Extension: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	5		
Units: Subjects				
Treatment emergent SAEs	2	1		
Treatment related SAEs	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Percentage of Subjects who Improved in Fatigue Score Measured by the MDASI-AML/MDS Questionnaire at Week 12

End point title	Non-intensive Study: Percentage of Subjects who Improved in Fatigue Score Measured by the MDASI-AML/MDS Questionnaire at Week 12[7]

End point description:

MDASI-AML/MDS: consists of 23 items, 13-item core cancer symptoms (pain, fatigue, nausea, disturbed sleep, distress, shortness of breath, problem remembering, lack of appetite, drowsiness, dry mouth, sadness, vomiting, and numbness), 4-item AML/MDS specific symptoms (malaise, diarrhea, muscle weakness, and skin problems), and 6 areas of interference (general activity, mood, work, walking, relations with other people, and enjoyment of life). “Fatigue” was measured at the subjects’ worst level in last 24 hours by asking subjects to respond to each item on an 0-10 numeric rating scale (NRS), where 0 = “not present” and 10 = “as bad as you can imagine”. Percentage of subjects who had improvement in "fatigue" symptoms reported in this end point. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Post-baseline up to Week 12

Notes:

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

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Units on a scale				
number (confidence interval 95%)	11.66 (6.73 to 16.58)	15.43 (9.87 to 21.00)		

Statistical analyses

Statistical analysis title	Glasdegib vs Placebo
Comparison groups	Non-intensive Study: Glasdegib + Azacitidine v Non-intensive Study: Placebo + Azacitidine

Number of subjects included in analysis	325
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.8359
Method	Mantel-Haenszel

Secondary: Percentage of Subjects who Improved in Fatigue Score Measured by the MD Anderson Symptom Inventory -Acute Myelogenous Leukemia/Myelodysplastic Syndrome (MDASI-AML/MDS) Questionnaire

End point title	Percentage of Subjects who Improved in Fatigue Score Measured by the MD Anderson Symptom Inventory -Acute Myelogenous Leukemia/Myelodysplastic Syndrome (MDASI-AML/MDS) Questionnaire[8]

End point description:

MDASI-AML/MDS: consists of 23 items, 13-item core cancer symptoms (pain, fatigue, nausea, disturbed sleep, distress, shortness of breath, problem remembering, lack of appetite, drowsiness, dry mouth, sadness, vomiting, and numbness), 4-item AML/MDS specific symptoms (malaise, diarrhea, muscle weakness, and skin problems), and 6 areas of interference (general activity, mood, work, walking, relations with other people, and enjoyment of life). “Fatigue” was measured at the subjects’ worst level in last 24 hours by asking subjects to respond to each item on an 0-10 numeric rating scale (NRS), where 0 = “not present” and 10 = “as bad as you can imagine”. Percentage of subjects who had improvement in "fatigue" symptoms reported in this end point. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Post-baseline up to Week 8

Notes:

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

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	203		
Units: Percentage of participants				
number (confidence interval 95%)	17.41 (12.17 to 22.66)	17.24 (12.05 to 22.44)		

Statistical analyses

Statistical analysis title	Glasdegib vs Placebo
Comparison groups	Intensive Study: Glasdegib + Cytarabine + Daunorubicin v Intensive Study: Placebo + Cytarabine + Daunorubicin

Number of subjects included in analysis	404
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5095
Method	Mantel-Haenszel

Secondary: Intensive Study: Percentage of Subjects With Complete Remission Without Negative Minimal Residual Disease (CRMRD-neg)

End point title	Intensive Study: Percentage of Subjects With Complete Remission Without Negative Minimal Residual Disease (CRMRD-neg)[9]

End point description:

Complete remission (CR) was defined based on 2017 European LeukemiaNet (ELN) recommendations. CR: Bone marrow blasts <5 percentage (%); absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count (ANC) greater than equal to (>=) 1.0*10^9/Liter (L); platelet count >=100*10^9/L. CRMRD-neg: CR with negativity for a genetic marker by reverse transcription quantitative polymerase chain reaction (RT-qPCR), or CR with negativity by Multiparameter Flow Cytometry (MFC). Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

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

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	203		
Units: Percentage of subjects				
number (confidence interval 95%)	5.0 (2.4 to 9.0)	5.4 (2.7 to 9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Percentage of Subjects With Complete Remission With Incomplete Hematologic Recovery (CRi)

End point title	Intensive Study: Percentage of Subjects With Complete Remission With Incomplete Hematologic Recovery (CRi)[10]

End point description:

CR was defined based on 2017 ELN recommendations. CR: MRD (positive or unknown), bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC less than (<) 1.0*10^9/L; platelet count <100 × 10^9/L. CRi (included CR [includes CRMRD-neg]): not qualifying for CR, neutropenia <1.0*10^9/L or platelets <100*10^9, absence of extramedullary disease, and absence of blasts with Auer rods. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

[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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	203		
Units: Percentage of subjects				
number (confidence interval 95%)	1.5 (0.3 to 4.3)	5.4 (2.7 to 9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Percentage of Subjects With CR Including CRMRD-neg

End point title	Non-intensive Study: Percentage of Subjects With CR Including CRMRD-neg[11]

End point description:

CR was defined based on 2017 ELN recommendations. CR: Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC >=1.0*10^9/L; platelet count >=100*10^9/L. CRMRDneg: CR with negativity for a genetic marker by RT-qPCR, or CR with negativity by MFC. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Percentage of subjects				
number (confidence interval 95%)	19.6 (13.8 to 26.6)	13.0 (8.2 to 19.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Percentage of Subjects With CR Including CRMRD-neg

End point title	Intensive Study: Percentage of Subjects With CR Including CRMRD-neg[12]

End point description:

CR was defined based on 2017 ELN recommendations. CR: Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC >=1.0*10^9/L; platelet count >=100*10^9/L. CRMRDneg: CR with negativity for a genetic marker by RT-qPCR, or CR with negativity by MFC. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

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

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	203		
Units: Percentage of subjects				
number (confidence interval 95%)	49.3 (42.1 to 56.4)	47.3 (40.3 to 54.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Percentage of Subjects With CRMRD-neg

End point title	Non-intensive Study: Percentage of Subjects With CRMRD-

End point description:

CR was defined based on 2017 ELN recommendations. CR: Bone marrow blasts <5 %; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC >= 1.0*10^9/L; platelet count >=100*10^9/L. CRMRD-neg: CR with negativity for a genetic marker by RT-qPCR, or CR with negativity by MFC. Full analysis set included all randomised subjects. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Percentage of subjects				
number (confidence interval 95%)	1.8 (0.4 to 5.3)	0.6 (0.0 to 3.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Percentage of Subjects With CRi

End point title	Non-intensive Study: Percentage of Subjects With CRi[14]

End point description:

CR was defined based on 2017 ELN recommendations. CR: MRD (positive or unknown), bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC <1.0*10^9/L; platelet count <100*10^9/L. CRi (included CR [includes CRMRD-neg]): not qualifying for CR, neutrophil <0.5*10^9/L or platelets <50*10^9/L, absence of extramedullary disease, and absence of blasts with Auer rods. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Percentage of subjects				
number (confidence interval 95%)	2.5 (0.7 to 6.2)	4.9 (2.2 to 9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Percentage of Subjects With Morphologic Leukemia-free State (MLFS)

End point title	Intensive Study: Percentage of Subjects With Morphologic Leukemia-free State (MLFS)[15]

End point description:

MLFS was defined based on 2017 ELN recommendations. MLFS: MRD (positive or unknown), bone marrow blasts <5%, no hematologic recovery required, marrow should not be aplastic, at least 200 cells enumerated or cellularity absence of extramedullary disease >=10%, and absence of blasts with Auer

rods. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	203		
Units: Percentage of subjects				
number (confidence interval 95%)	1.5 (0.3 to 4.3)	2.0 (0.5 to 5.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Percentage of Subjects With MLFS

End point title	Non-intensive Study: Percentage of Subjects With MLFS[16]

End point description:

MLFS was defined based on 2017 ELN recommendations. MLFS: MRD (positive or unknown), bone marrow blasts <5%, no hematologic recovery required, marrow should not be aplastic, at least 200 cells enumerated or cellularity absence of extramedullary disease >=10%, and absence of blasts with Auer rods. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Percentage of subjects				
number (confidence interval 95%)	3.1 (1.0 to 7.0)	0.6 (0.0 to 3.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Percentage of Subjects With Partial Remission (PR)

End point title	Intensive Study: Percentage of Subjects With Partial Remission (PR)[17]

End point description:

PR was defined based on 2017 ELN recommendations. PR: MRD (positive or unknown); bone marrow blasts – decrease to 5-25% and decrease of pre-treatment bone marrow blast percentage by at least 50%; neutrophil count >=1.0*10^9/L; and platelets count >=100*10^9/L. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	203		
Units: Percentage of subjects				
number (confidence interval 95%)	5.0 (2.4 to 9.0)	4.4 (2.0 to 8.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Duration of Response (DoRi)

End point title	Intensive Study: Duration of Response (DoRi)[18]

End point description:

DoRi: only defined for subjects who have ever achieved CRi or better (included CR as well) on study as the time from date of first achieving CRi or better to the date of relapse after CRi or better or death due to any cause. CRi: not qualifying for CR, neutropenia (neutrophils <1.0*10^9/L) or platelets <100*10^9/L, absence of extramedullary disease, and absence of blasts with Auer rods. Subjects last known to be alive who were free from relapse after CRi or better were censored at the date of last disease assessment that verifies their status. DORi was not analysed as the intensive cohort ended in futility. Subjects ended study intervention early and were not followed for the remainder of the study.

End point type	Secondary

End point timeframe:

From date of first achieving CRi or better to the date of relapse after CRi or better or death due to any cause (maximum up to 2 years)

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	0[20]		
Units: Months				
arithmetic mean (standard deviation)	()	()		

Notes:

[19] - DORi was not analysed as the intensive cohort ended in futility.

[20] - DORi was not analysed as the intensive cohort ended in futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Percentage of Subjects With PR

End point title	Non-intensive Study: Percentage of Subjects With PR[21]

End point description:

PR was defined based on 2017 ELN recommendations. PR: MRD (positive or unknown); bone marrow blasts – decrease to 5-25% and decrease of pre-treatment bone marrow blast percentage by at least 50%; neutrophil count >=1.0*10^9/L; and platelets count >=100*10^9/L. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Percentage of subjects				
number (confidence interval 95%)	2.5 (0.7 to 6.2)	4.9 (2.2 to 9.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Percentage of Subjects With Complete Remission With Partial Hematologic Recovery (CRh)

End point title	Non-intensive Study: Percentage of Subjects With Complete Remission With Partial Hematologic Recovery (CRh)[22]

End point description:

CRh: MRD (positive or unknown); bone marrow blasts <5%; assessed in non-intensive chemotherapy study only, not qualifying for CR, ie, both neutrophil >=0.5*10^9/L and platelets >=50*10^9/L must be met, but does not satisfy both Neutrophils >=1*10^9/L and Platelets >=100*10^9/L at the same

time; absence of extramedullary disease; and absence of blasts with Auer rods. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Percentage of subjects				
number (confidence interval 95%)	3.1 (1.0 to 7.0)	3.1 (1.0 to 7.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Time to Response

End point title	Non-intensive Study: Time to Response[23]

End point description:

TTRi: Subjects who achieved CRi or better, as the time from the date of randomisation to the first documentation of response (CRi or better). TTRh: Subjects who achieved CRh or better, as the time from the date of randomisation to the first documentation of response (CRh or better). CRi: not qualifying for CR, neutrophil <0.5*10^9/L or platelets <50*10^9/L, absence of extramedullary disease, and absence of blasts with Auer rods. CRh: MRD (positive or unknown); bone marrow blasts <5%; assessed in non-intensive chemotherapy study only, not qualifying for CR, ie, both neutrophil >=0.5*10^9/L and platelets >=50*10^9/L must be met, but does not satisfy both Neutrophils >=1*10^9/L and Platelets >=100*10^9/L at the same time; absence of extramedullary disease; and absence of blasts with Auer rods. Full analysis set included all randomised subjects.

End point type	Secondary

End point timeframe:

From the date of randomisation to the first documentation of response (CRi/CRh or better) (maximum up to 3 years)

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	163	162		
Units: Months				
arithmetic mean (standard deviation)				

TTRi	4.057 (± 1.9532)	4.093 (± 2.1809)		
TTRh	4.334 (± 1.8853)	4.146 (± 2.1540)		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: DoRi

End point title	Non-intensive Study: DoRi[24]

End point description:

Dori: Subjects who ever achieved CRi or better (included CR,CRh) on study as time from date of first achieving CRi or better to date of relapse after CRi or better or death due to any cause. DoRh: Subjects ever achieved CRh or better (included CR) on study as time from date of first achieving CRh or better to date of disease progression, or relapse after CRh or better,or death due to any cause. CRi: not qualifying for CR,neutrophil(N)<0.5*10^9/L or platelets (P)<50*10^9, absence of extramedullary disease and blasts with Auer rods. CRh: MRD (positive or unknown); bone marrow blasts <5%; assessed in non-intensive chemotherapy study only, not qualifying for CR, ie, both N >=0.5*10^9/L, P >=50*10^9/L must be met, but does not satisfy both N >=1*10^9/L and P>=100*10^9/L at same time; absence of extramedullary disease and blasts with Auer rods. DORi not analysed as intensive cohort ended in futility. Subjects ended study intervention early and were not followed for remainder of study.

End point type	Secondary

End point timeframe:

From date of first achieving CRi/CRh or better to the date of relapse/disease progression after CRi/CRh or better or death due to any cause (maximum up to 3 years)

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[25]	0[26]		
Units: Months				
number (confidence interval 95%)	(to)	(to)		

Notes:

[25] - DORi was not analysed as the intensive cohort ended in futility.

[26] - DORi was not analysed as the intensive cohort ended in futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: MDASI-AML/MDS Score

End point title	Intensive Study: MDASI-AML/MDS Score[27]

End point description:

MDASI-AML/MDS: consists of 23 items,13-item core cancer symptoms(pain, fatigue, nausea, disturbed sleep, distress, shortness of breath, problem remembering, lack of appetite, drowsiness, dry mouth, sadness, vomiting, numbness), 4-item AML/MDS specific symptoms(malaise, diarrhea, muscle

weakness,skin problems), and 6 areas of interference (general activity, mood, work, walking, relations with other people, enjoyment of life). The 13 core symptoms and 6 core interference items had highest frequency and/or severity in subjects with various cancers and treatment types. It was measured at severity of symptoms and related interference at their worst level in last 24 hours by asking subjects to respond to each item on an 0-10 NRS,where 0 = "not present" or "did not interfere" and 10 = "worst" or "interfered completely". MDASI-AML/MDS score was not analysed as intensive cohort terminated because of futility. Subjects ended study intervention early and were not followed up as planned.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[28]	0[29]		
Units: Units on a scale				
number (confidence interval 95%)	(to)	(to)		

Notes:

[28] - MDASI-AML/MDS score was not analysed as intensive cohort terminated because of futility.

[29] - MDASI-AML/MDS score was not analysed as intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: MDASI-AML/MDS Score

End point title	Non-intensive Study: MDASI-AML/MDS Score[30]

End point description:

MDASI-AML/MDS: consists of 23 items, 13-item core cancer symptoms (pain, fatigue, nausea, disturbed sleep, distress, shortness of breath, problem remembering, lack of appetite, drowsiness, dry mouth, sadness, vomiting,numbness), 4-item AML/MDS specific symptoms (malaise, diarrhea, muscle weakness,skin problems), and 6 areas of interference (general activity, mood, work, walking, relations with other people, enjoyment of life). The 13 core symptoms and 6 core interference items had highest frequency and/or severity in subjects with various cancers and treatment types. It was measured at severity of symptoms and related interference at their worst level in last 24 hours by asking subjects to respond to each item on an 0-10 NRS,where 0 = "not present" or "did not interfere" and 10 = "worst" or "interfered completely". MDASI-AML/MDS score was not analysed as non-intensive cohort terminated because of futility. Subjects ended study intervention early and were not followed up as planned.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[31]	0[32]		
Units: Units on a scale				
number (confidence interval 95%)	(to)	(to)		

Notes:

[31] - MDASI-AML/MDS score was not analysed as non-intensive cohort terminated because of futility.

[32] - MDASI-AML/MDS score was not analysed as non-intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: EFS

End point title	Non-intensive Study: EFS[33]

End point description:

EFS: Time from the date of randomisation to the date of TF, relapse from CR, or death from any cause, whichever comes first. TF was defined as failure to achieve CR during the induction cycle (including the re-induction cycle if there is one) and the event date for TF is the day of randomisation. CR was defined based on 2017 ELN recommendations. CR: Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC >=1.0*10^9/L; platelet count >=100*10^9/L. Subjects ended study intervention early and were not followed for the remainder of the study.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of TF, relapse from CR, or death from any cause, whichever comes first (maximum up to 3 years)

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[34]	0[35]		
Units: Months				
number (confidence interval 95%)	(to)	(to)		

Notes:

[34] - EFS was not analysed as the non-intensive cohort ended in futility.

[35] - EFS was not analysed as the non-intensive cohort ended in futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Event-free Survival (EFS)

End point title	Intensive Study: Event-free Survival (EFS)[36]

End point description:

EFS: Time from the date of randomisation to the date of treatment failure (TF), relapse from CR, or death from any cause, whichever comes first. TF was defined as failure to achieve CR during the

induction cycle (including the re-induction cycle if there is one) and the event date for TF is the day of randomisation. CR was defined based on 2017 ELN recommendations. CR: Bone marrow blasts <5%; absence of circulating blasts and blasts with Auer rods; absence of extramedullary disease; ANC >=1.0*10^9/L; platelet count >=100*10^9/L. Subjects ended study intervention early and were not followed for the remainder of the study.

End point type	Secondary

End point timeframe:

From the date of randomisation to the date of TF, relapse from CR, or death from any cause, whichever comes first (maximum up to 2 years)

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[37]	0[38]		
Units: Months				
number (confidence interval 95%)	(to)	(to)		

Notes:

[37] - EFS was not analysed as the intensive cohort ended in futility.

[38] - EFS was not analysed as the intensive cohort ended in futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Patients Global Impression of Symptoms (PGIS)

End point title	Intensive Study: Patients Global Impression of Symptoms (PGIS)[39]

End point description:

PGIS: is a single 1-item questionnaire designed to assess subject's overall impression of disease severity at a given point in time. It uses a 4-point Likert scale as follows: In the last 24 hours, my leukemia symptoms are: 1-"absent (no symptoms)", 2-"mild", 3-" moderate", 4="severe". PGIS was not analysed as intensive cohort terminated because of futility. Subjects ended study intervention early and were not followed up as planned.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[40]	0[41]		
Units: Units on a scale				

number (confidence interval 95%)	(to)	(to)		

Notes:

[40] - PGIS was not analysed as intensive cohort terminated because of futility.

[41] - PGIS was not analysed as intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: EQ-VAS

End point title	Non-intensive Study: EQ-VAS[42]

End point description:

EQ-5D-5L: brief, self-administered, validated, reliable generic health status instrument developed by EuroQoL group. It consists of EQ-5D descriptive system and a VAS, EQ-VAS. EQ VAS records respondent's self-rated health on a 20-cm vertical, VAS from 0 (worst imaginable health state) to 100 (best imaginable health state). EQ-VAS was not analysed as non-intensive cohort terminated because of futility. Subjects ended study intervention early and were not followed up as planned.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

Notes:

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

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[43]	0[44]		
Units: Units on a scale				
number (confidence interval 95%)	(to)	(to)		

Notes:

[43] - EQ-VAS was not analysed as non-intensive cohort terminated because of futility.

[44] - EQ-VAS was not analysed as non-intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: EuroQoL Visual Analogue Scale (EQ-VAS)

End point title	Intensive Study: EuroQoL Visual Analogue Scale (EQ-VAS)[45]

End point description:

EQ-5D-5L: brief, self-administered, validated, reliable generic health status instrument developed by EuroQoL group. It consists of EQ-5D descriptive system and a VAS, EQ-VAS. EQ VAS records respondent's self-rated health on a 20-cm vertical, VAS from 0 (worst imaginable health state) to 100 (best imaginable health state). EQ-VAS was not analysed as intensive cohort terminated because of futility. Subjects ended study intervention early and were not followed up as planned.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[46]	0[47]		
Units: Units on a scale				
number (confidence interval 95%)	(to)	(to)		

Notes:

[46] - EQ-VAS was not analysed as intensive cohort terminated because of futility.

[47] - EQ-VAS was not analysed as intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: EQ-5D-5L Score

End point title	Non-intensive Study: EQ-5D-5L Score[48]

End point description:

EQ-5D-5L: brief, self-administered, validated, reliable generic health status instrument developed by EuroQoL Group. Consists of EQ-5D descriptive system and VAS, EuroQoL (EQ)-VAS. EQ-5D: descriptive system measures subject's health state on 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). Subject to indicate his/her health state by rating each dimension on 5-level scale (1=no problem, 5=extreme problem). Rating resulted in 1-digit number expressing level selected for that dimension. Digits for 5 dimensions were combined in 5-digit number describing respondent's health state. EQ-5D index scores ranges= 0 (worst health state) to1 (perfect health). EQ-5D-5L score was not analysed as non-intensive cohort terminated because of futility. Subjects ended study intervention early and were not followed up as planned.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[49]	0[50]		
Units: Units on a scale				
number (confidence interval 95%)	(to)	(to)		

Notes:

[49] - EQ-5D-5L score was not analysed as non-intensive cohort terminated because of futility.

[50] - EQ-5D-5L score was not analysed as non-intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: EQ-5D-5L Score

End point title	Intensive Study: EQ-5D-5L Score[51]

End point description:

EQ-5D-5L:brief,self-administered,validated,reliable generic health status instrument developed by EuroQoL(EQ)Group.Consists of EQ-5D descriptive system and visual analogue scale(VAS),EQ-VAS.EQ-5D:Measures subject's health state on 5-dimensions(mobility,self-care,usual activities,pain/discomfort,anxiety/depression).Health state indicated by rating each dimension on 5-level scale(1=no problem,5=extreme problem).Rating resulted in1-digit number expressing level selected for that dimension.Digits for 5 dimensions were combined in 5-digit number describing subject's health state. EQ-5D index scores ranges=0 (worst health state) to 1(perfect health). EQ-5D-5L score not analysed as intensive cohort ended in futility. Subjects ended study intervention early and not followed for remainder of study. EQ-5D-5L score was not analysed as intensive cohort terminated because of futility. Subjects ended study intervention early and were not followed up as planned.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[52]	0[53]		
Units: Units on a scale				
number (confidence interval 95%)	(to)	(to)		

Notes:

[52] - EQ-5D-5L score was not analysed as intensive cohort terminated because of futility.

[53] - EQ-5D-5L score was not analysed as intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: PGIC

End point title	Non-intensive Study: PGIC[54]

End point description:

PGIC: a single-item questionnaire designed to assess the subject's overall sense of whether there has been a change since starting treatment as rated on a 7-point Likert scale anchored by (1) 'very much improved' to (7) 'very much worse', with (4) =' no change'. The PGIC is a measure of "subject rating of global improvement and satisfaction with treatment". PGIC was not analysed as non-intensive cohort terminated because of futility. Subjects ended study intervention early and were not followed up as planned.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

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: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[55]	0[56]		
Units: Units on a scale				
number (confidence interval 95%)	(to)	(to)		

Notes:

[55] - PGIC was not analysed as non-intensive cohort terminated because of futility.

[56] - PGIC was not analysed as non-intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) Graded by NCI CTCAE v.4.03

End point title	Intensive Study: Number of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) Graded by NCI CTCAE v.4.03[57]

End point description:

AE: any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. SAE: any AE, regardless of dose, that led to death; was life-threatening; required hospitalisation or prolonged hospitalisation; led to persistent or significant incapacity or led to congenital anomaly or birth defect. AEs and SAEs based on NCI CTCAE v.4.03 has been reported in this endpoint. Grade 3=severe adverse event, Grade 4= life threatening consequences; urgent intervention indicated, Grade 5= death related to adverse event. Safety Analysis (SA) set included all subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

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: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	201		
Units: Subjects				
AEs	196	198		
SAEs	86	92		
Grade 3 or 4 AE	161	149		
Grade 5 AE	5	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: PGIS

End point title	Non-intensive Study: PGIS[58]

End point description:

PGIS: is a single 1-item questionnaire designed to assess subject's overall impression of disease severity at a given point in time. It uses a 4-point Likert scale as follows: In the last 24 hours, symptoms are: 1-"absent (no symptoms)", 2-"mild", 3-" moderate", 4="severe". The non-intensive cohort was terminated because of futility. Subjects ended study intervention early and were not followed up as planned. Hence, PGIS was not collected, analyzed and reported.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

Notes:

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

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[59]	0[60]		
Units: Percentage of participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[59] - PGIS was not analysed as non-intensive cohort terminated because of futility.

[60] - PGIS was not analysed as non-intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Participants Global Impression of Change (PGIC)

End point title	Intensive Study: Participants Global Impression of Change (PGIC)[61]

End point description:

PGIC: a single-item questionnaire designed to assess the participant's overall sense of whether there has been a change since starting treatment as rated on a 7-point Likert scale anchored by (1) 'very much improved' to (7) 'very much worse', with (4) =' no change'. The PGIC is a measure of "participant rating of global improvement and satisfaction with treatment". The intensive cohort was terminated because of futility. Subjects ended study intervention early and were not followed up as planned. Hence, PGIC was not collected, analysed and reported.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

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

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[62]	0[63]		
Units: Percentage of Participants				
number (confidence interval 95%)	(to)	(to)		

Notes:

[62] - PGIC was not analysed as intensive cohort terminated because of futility.

[63] - PGIC was not analysed as intensive cohort terminated because of futility.

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Number of Subjects With AEs and SAEs Graded by NCI CTCAE v.4.03

End point title	Non-intensive Study: Number of Subjects With AEs and SAEs Graded by NCI CTCAE v.4.03[64]

End point description:

AE: any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. SAE: any AE, regardless of dose, that led to death; was life-threatening; required hospitalisation or prolonged hospitalisation; led to persistent or significant incapacity or led to congenital anomaly or birth defect. AEs and SAEs based on NCI CTCAE v.4.03 has been reported in this endpoint. Grade 3=severe adverse event, Grade 4= life threatening consequences; urgent intervention indicated, Grade 5= death related to adverse event. SA set included all subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

Notes:

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

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	160		
Units: Subjects				
AEs	161	158		
SAEs	117	124		
Grade 3 or 4 AE	106	100		
Grade 5 AE	50	52		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Number of Subjects With Treatment Related AEs and SAEs Graded by NCI CTCAE v.4.03

End point title	Intensive Study: Number of Subjects With Treatment Related AEs and SAEs Graded by NCI CTCAE v.4.03[65]

End point description:

AE: any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. SAE: any AE, regardless of dose, that led to death; was life-threatening; required hospitalisation or prolonged hospitalisation; led to persistent or significant incapacity or led to congenital anomaly or birth defect. AEs and SAEs based on NCI CTCAE v.4.03 has been reported in this endpoint. Grade 3=severe adverse event, Grade 4= life threatening consequences; urgent intervention indicated, Grade 5= death related to adverse event. SA set included all subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

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

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	201		
Units: Subjects				
Treatment related AEs	181	188		
Treatment related SAEs	48	60		
Grade 3 or 4 AE	161	149		
Grade 5 AE	5	8		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Number of Subjects With Shift From Baseline in Hematological Laboratory Abnormalities Graded by NCI CTCAE v.4.03

End point title	Intensive Study: Number of Subjects With Shift From Baseline in Hematological Laboratory Abnormalities Graded by NCI CTCAE v.4.03[66]

End point description:

Hematology laboratory test included: anemia(A), hemoglobin(H) increased, international normalized ratio (INR) increased, lymphocyte(L) count decreased, lymphocyte count increased, neutrophil(N) count decreased, platelet(P) count decreased, and white blood cell(WBC) decreased. Laboratory results were categorically summarised according to the NCI-CTCAE criteria v4.03. Grade (G) 1= mild; G2= moderate; G 3= severe and G 4= life-threatening or disabling. Number of subjects with shift from baseline(B) for hematology laboratory test were assessed. Only those laboratory test parameters in which at least 1 subject had data were reported. SA set included all subjects who received at least one dose of study drug. Here, "Overall Number of Subjects Analyzed" signifies subjects evaluable for this endpoint and "Number Analyzed" signifies subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

[66] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	197		
Units: Subjects				
A:Missing(B)toG3/4(CTCAEG)n=196,197	0	2		
A:G<=2BtoG<=2(CTCAE G)n=196,197	27	14		
A:G<=2 B to G3/4(CTCAE G)n=196,197	113	103		
A:G3/4 B toG<=2(CTCAEG)n=196,197	4	5		
A:G3/4 B toG3/4(CTCAE G)n=196,197	52	73		
H inc:Missing B to G<=2 (CTCAE G),n=196,197	0	2		
H inc:G<=2(B G to G<=2 (CTCAE G) n=196,197	194	194		
H inc:G<=2 (B G)to G3/4 (CTCAE G)n=196,197	2	1		
INR inc G<=2 (B G) to G<=2 (CTCAE G) n=3,1	3	1		
Lcount dec Missing (BG) to G<=2CTCAE n=193,193	0	2		
Lcount dec:Missing (B G) to G3/4 (CTCAEG)n=193,193	0	4		
Lcount dec:G<=2(B) to G<=2(CTCAEG),n=193,193	21	26		
Lcount dec:G<=2(B G) to G3/4(CTCAE G)n=193,193	160	152		
Lcount dec:G3/4 (B G)to G<=2(CTCAEG)n=193,193	1	0		
Lcount dec:G3/4(B G)to G3/4 (CTCAEG)n=193,193	11	9		
Lcount inc:Missing(B G)toG <=2(CTCAEG)n=193,193	0	6		
Lcount inc.G<=2(B G)toG<=2 (CTCAEG),n=193,193	185	180		
Lcount dec:G<=2 (B G) to G3/4(CTCAEG) n=193,193	6	4		
Lcount inc:G3/4(B G) toG<=2 (CTCAEG) n=193,193	1	3		
Lcount inc G3/4 (B G)to G3/4 (CTCAEG) n=193,193	1	0		
Ncount dec Missing (B G) toG3/4(CTCAEG) n=194,193	0	4		
Ncount dec:G<=2(B G) toG<=2(CTCAE G) n=194,193	4	2		
N count dec:G<=2 (B G) to G3/4 (CTCAEG) n=194,193	85	79		
N count dec:G3/4 (B G) to G<=2 (CTCAEG) n=194,193	0	2		
N count dec:G3/4 (B G) to G3/4 (CTCAEG) n=194,193	105	106		

Pcount dec:Missing (BG)to G3/4 (CTCAEG)n=196,197	1	2		
P count dec:G<=2 (B G) to G3/4 (CTCAE G) n=196,197	98	100		
P count dec:G3/4 (B G) to G3/4 (CTCAE G) n=196,197	97	95		
WBC dec: Missing (B G) to G 3/4(CTCAE G) n=196,197	1	4		
WBC dec:G<=2 (B G) to G<=2 (CTCAE G) n=196,197	3	2		
WBC dec G<=2(B G) to G 3/4(CTCAE G) n=196,197	155	156		
WBC dec:G3/4(B G) to G3/4(CTCAE G) n=196,197	37	35		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Number of Subjects With Treatment Related AEs and SAEs Graded by NCI CTCAE v.4.03

End point title	Non-intensive Study: Number of Subjects With Treatment Related AEs and SAEs Graded by NCI CTCAE v.4.03[67]

End point description:

AE: any untoward medical occurrence in subject who received study drug without regard to possibility of causal relationship. SAE: any AE, regardless of dose, that led to death; was life-threatening; required hospitalisation or prolonged hospitalisation; led to persistent or significant incapacity or led to congenital anomaly or birth defect. AEs and SAEs based on NCI CTCAE v.4.03 has been reported in this endpoint. Grade 3=severe adverse event, Grade 4= life threatening consequences; urgent intervention indicated, Grade 5= death related to adverse event. SA set included all subjects who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

Notes:

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

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	160		
Units: Subjects				
Treatment related AEs	133	123		
Treatment related SAEs	45	37		
Grade 3 or 4 AE	97	72		
Grade 5 AE	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Number of Subjects With Shift From Baseline in Hematological Laboratory Abnormalities Graded by NCI CTCAE v.4.03

End point title	Non-intensive Study: Number of Subjects With Shift From Baseline in Hematological Laboratory Abnormalities Graded by NCI CTCAE v.4.03[68]

End point description:

Hematology laboratory test included: anemia, hemoglobin increased, INR increased, lymphocyte count decreased, lymphocyte count increased, neutrophil count decreased, platelet count decreased, and white blood cell decreased. Laboratory results were categorically summarized according to the NCI-CTCAE criteria v4.03. Grade 1= mild; Grade 2= moderate; Grade 3= severe and Grade 4= life-threatening or disabling. Number of subjects with shift from baseline for hematology laboratory test were assessed. Only those laboratory test parameters in which at least 1 subject had data were reported. SA set included all participants who received at least one dose of study drug. Here, "Number of Subjects Analysed" signifies participants evaluable for this outcome measure and "Number Analyzed" signifies subjects evaluable for specified rows.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

Notes:

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

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	160		
Units: Subjects				
Anemia:G<=2(BG)to G<=2(CTCAE G)n=160,160	29	41		
A:G<=2 (B G) to G3/4 (CTCAE G) n=160,160	97	87		
A:G3/4(BG)toG<=2(CTCAE G)n=160,160	5	1		
Anemia:G3/4 (BG) to G3/4 (CTCAE G)n=160,160	29	31		
H inc: G<=2 (BG) to G<=2 (CTCAEG)n=160,160	160	159		
H inc: G<=2 (BG) to G3/4 (CTCAE G)n=160,160	0	1		
L count dec:Missing(BG) to G<=2 (CTCAE G)n=159,160	2	0		
L count dec:Missing(BG) to G3/4 (CTCAE G)n=159,160	1	0		
L count dec:G<=2 (BG) to G<=2 (CTCAE G)n=159,160	96	89		
L count dec:G<=2 (BG) to G3/4 (CTCAE G)n=159,160	51	54		
L count dec:G3/4(BG) to G<=2 (CTCAE G)n=159,160	2	4		
L count dec:G3/4 (BG) to G3/4 (CTCAE G)n=159,160	7	13		
L count inc:Missing(BG) to G<=2 (CTCAE G)n=159,160	3	0		

L count inc:G<=2 (BG) to G<=2 (CTCAE G)n=159,160	147	157		
L count inc:G<=2 (BG) to G3/4 (CTCAE G)n=159,160	7	3		
L count dec:G3/4 (BG) to G3/4 (CTCAEG)n=159,160	2	0		
Ncount dec:Missing(BG)to G3/4 (CTCAE G)n=159,160	4	0		
N count dec:G<=2 (BG) to G<=2 (CTCAE G)n=159,160	13	22		
N count dec:G<=2 (BG) to G3/4 (CTCAE G) n=159,160	48	40		
N count dec: G3/4 (BG) to G<=2 (CTCAE G) n=159,160	2	1		
N count dec: G3/4 (BG) to G3/4 (CTCAE G)n=160,160	92	97		
P count dec:G<=2 (BG) to G<=2 (CTCAE G)n=160,160	21	28		
P count dec:G<=2 (BG) to G3/4 (CTCAE G)n=160,160	55	64		
P count dec:G3/4 (BG) to G<=2 (CTCAE G)n=160,160	1	0		
P count dec:G3/4 (BG) to G3/4 (CTCAE G)n=160,160	83	68		
WBC dec:Missing (BG) to G<=2 (CTCAE G)n=160,159	1	0		
WBC dec:Missing(BG) to G3/4 (CTCAE G) n=160,159	1	0		
WBC dec:G<=2 (BG) to G<=2 (CTCAE G)n=160,159	43	48		
WBC dec:G<=2 (BG) to G3/4 (CTCAE G)n=160,159	70	62		
WBC dec:G3/4 (BG) to G<=2 (CTCAE G)n=160,159	0	1		
WBC dec:G3/4 (BG) to G3/4 (CTCAE G)n=160,159	45	48		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Number of Subjects With Shift From Baseline in Chemistry Laboratory Abnormalities Graded by NCI CTCAE v.4.03

End point title	Intensive Study: Number of Subjects With Shift From Baseline in Chemistry Laboratory Abnormalities Graded by NCI CTCAE v.4.03[69]

End point description:

Chemistry laboratory test included:alanine aminotransferase(ALT)increased(inc),alkaline phosphatase(ALP)inc,aspartate aminotransferase(AST)inc,blood bilirubin(bil) inc,chronic kidney disease(CKD),creatine phosphokinase(CPK)inc,creatinine inc,gamma glutamyl transferase(GGT)inc,hypercalcemia, hyperglycemia,hyperkalemia,hypermagnesemia(hypermag),hypernatremia,hypoalbuminemia(hypoalb),hypocalcemia,hypoglycemia, hypokalemia,hypomagnesemia(hypomag),hyponatremia,hypophosphatemia(hypophos).Results were summarised according to NCI-CTCAE criteria v4.03.Grade1=mild;Grade2=moderate;Grade3=severe;Grade 4=life-threatening or disabling.Number of subjects with shift from baseline for chemistry laboratory test were assessed.Only those lab test parameters in which at least 1 subject had data is reported.SA set=subjects who received at least one

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

[69] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	198		
Units: Subjects				
ALT inc:Missing (BG) to G<=2 (CTCAE G)n=193,198	1	1		
ALT inc:G<=2 (BG) to G<=2 (CTCAE G)n=193,198	175	184		
ALT inc:G<=2 (BG) to G3/4 (CTCAE G)n=193,198	16	13		
ALT inc:G3/4 (BG) to G<=2 (CTCAE G)n=193,198	1	0		
ALP inc:Missing(BG) to G<=2 (CTCAE G)n=191,198	2	3		
ALP inc:G<=2 (BG) to G<=2 (CTCAE G)n=191,198	187	192		
ALP inc:G<=2 (BG) to G3/4 (CTCAE G)n=191,198	2	3		
AST inc:Missing (BG) to G<=2 (CTCAE G)n=193,198	5	2		
AST inc:Missing (BG) to G3/4 (CTCAE G)n=193,198	0	1		
AST inc: G<=2 (BG) to G<=2 (CTCAE G)n=193,198	173	186		
AST inc: G<=2 (BG) to G3/4 (CTCAE G)n=193,198	15	9		
Blood Bil inc:Missing (BG)toG<=2(CTCAE G)n=192,198	0	3		
Blood bil inc:G<=2(BG) to G<=2 (CTCAE G)n=192,198	184	189		
Blood bil inc:G<=2(BG) to G3/4 (CTCAE G)n=192,198	8	5		
Blood bil inc:G3/4 (BG) to G3/4 (CTCAE G)n=192,198	0	1		
CKD: Missing (BG) to G<=2(CTCAE G)n=195,198	4	5		
CKD:G<=2 (BG) to G<=2 (CTCAE G)n=195,198	182	188		
CKD:G<=2 (BG) to G3/4 (CTCAE G)n=195,198	8	4		
CKD:G3/4 (BG) to G<=2 (CTCAE G)n=195,198	1	0		
CKD: G3/4 (BG) to G3/4 (CTCAE G)n=195,198	0	1		
CPK inc:Missing(BG)toG<=2 (CTCAE G)n=183,185	20	19		
CPK inc:G<=2(BG)to G<=2 (CTCAE G)n=183,185	161	166		

CPK inc:G<=2 (BG) to G3/4 (CTCAE G)n=183,185	2	0		
Creatinine inc:G<=2(BG)toG<=2 (CTCAE G)n=195,198	188	192		
Creatinine inc:G<=2 (BG)toG3/4 (CTCAEG)n=195,198	7	6		
GGT inc:Missing(BG) to G<=2 (CTCAEG)n=13,20	5	7		
GGT inc:Missing (BG) to G3/4 (CTCAE G)n=13,20	8	11		
GGT inc:G<=2 (BG) to G3/4 (CTCAE G)n=13,20	0	2		
Hypercalcemia:Missing(BG)to G<=2 (CTCAEG)n=192,197	1	5		
Hypercalcemia:G<=2(BG)toG<=2 (CTCAEG)n=192,197	191	192		
Hyperglycemia:Missing(BG)toG<=2 (CTCAEG)n=194,198	1	3		
Hyperglycemia:G<=2(BG)to G<=2 (CTCAEG)n=194,198	174	183		
Hyperglycemia:G<=2(BG)toG3/4 (CTCAEG)n=194,198	15	10		
Hyperglycemia:G3/4(BG) toG<=2 (CTCAEG)n=194,198	2	1		
Hyperglycemia:G3/4(BG)toG3/4 (CTCAEG)n=194,198	2	1		
Hyperkalemia:G<=2 (BG) to G<=2 (CTCAEG)n=196,198	194	194		
Hyperkalemia:G<=2(BG)toG3/4 (CTCAEG)n=196,198	2	3		
Hyperkalemia:G3/4(BG) to G<=2 (CTCAE G)n=196,198	0	1		
Hypermag:Missing(BG)to G<=2(CTCAEG)n=193,192	2	4		
Hypermag:Missing(BG) to G3/4 (CTCAEG)n=193,192	0	1		
Hypernatremia:G<=2 (BG) to G<=2 (CTCAEG)n=193,192	190	184		
Hypernatremia:G<=2(BG) to G3/4 (CTCAEG)n=193,192	1	2		
Hypernatremia:G3/4(BG) to G<=2 (CTCAEG)n=193,192	0	1		
Hypo alb:Missing(BG) to G<=2(CTCAEG)n=192,198	0	3		
Hypo alb:Missing(BG)to G3/4(CTCAEG)n=192,198	1	1		
Hypo alb:G<=2(BG)to G<=2 (CTCAEG)n=192,198	185	185		
Hypo alb:G<=2(BG)to G3/4 (CTCAE G)n=192,198	5	8		
Hypo alb:G3/4(BG) toG3/4 (CTCAEG)n=192,198	1	1		
Hypocalcemia:Missing(BG)toG<=2 (CTCAEG)n=192,197	1	5		
Hypocalcemia:G<=2(BG) to G<=2 (CTCAEG)n=192,197	190	189		
Hypocalcemia:G<=2(BG)to G3/4 (CTCAEG)n=192,197	1	3		
Hypoglycemia:Missing(BG) to G<=2 (CTCAEG)n=194,198	1	3		
Hypoglycemia:G<=2(BG) to G<=2 (CTCAEG)n=194,198	193	194		

Hypoglycemia:G<=2(BG)to G3/4 (CTCAEG)n=194,198	0	1		
Hypokalemia:G<=2(BG) to G<=2 (CTCAEG)n=196,198	155	159		
Hypokalemia:G<=2(BG) to G3/4 (CTCAEG)n=196,198	41	37		
Hypokalemia:G3/4(BG)to G<=2 (CTCAEG)n=196,198	0	2		
Hypomag:Missing(BG)to G<=2(CTCAEG)n=193,192	2	5		
Hypomag:G<=2(BG) to G<=2 (CTCAEG)n=193,192	190	187		
Hypomag:G<=2(BG) toG3/4 (CTCAEG)n=193,192	1	0		
Hyponatremia:G<=2(BG)to G<=2(CTCAEG)n=196,198	177	188		
Hyponatremia:G<=2(BG)to G3/4 (CTCAEG)n=196,198	17	8		
Hyponatremia:G3/4(BG) to G<=2 (CTCAEG)n=196,198	1	1		
Hyponatremia:G3/4(BG) to G3/4 (CTCAEG)n=196,198	1	1		
Hypophos:Missing(BG)to G<=2(CTCAEG)n=193,193	3	3		
Hypophos:Missing (BG) to G3/4 (CTCAEG)n=193,193	1	1		
Hypophos:G<=2 (BG) toG<=2 (CTCAEG)n=193,193	153	153		
Hypophos:G<=2 (BG) to G3/4 (CTCAEG)n=193,193	33	33		
Hypophos:G3/4 (BG) to G<=2 (CTCAEG)n=193,193	0	2		
Hypophos: G3/4 (BG) to G3/4 (CTCAEG)n=193,193	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Number of Subjects With Shift From Baseline in Chemistry Laboratory Abnormalities Graded by NCI CTCAE v.4.03

End point title	Non-intensive Study: Number of Subjects With Shift From Baseline in Chemistry Laboratory Abnormalities Graded by NCI CTCAE v.4.03[70]

End point description:

Chemistry laboratory test included: alanine ALT increased, ALP increased, AST increased, blood bilirubin increased, chronic kidney disease, CPK increased, creatinine increased, GGT increased, hypercalcemia, hyperglycemia, hyperkalemia, hypermagnesemia, hypernatremia, hypoalbuminemia, hypocalcemia, hypoglycemia, hypokalemia, hypomagnesemia, hyponatremia, hypophosphatemia. Results were categorically summarised according to NCI-CTCAE criteria v4.03.Grade1=mild;Grade2=moderate;Grade3=severe;Grade 4=life-threatening or disabling.Number of subjects with shift from baseline for chemistry laboratory test were assessed.Only those lab test parameters in which at least 1 subject had data is reported.SA set=subjects who received at least one dose of study drug.Here,''Number of Subjects Analysed"=subjects evaluable for this end point;"Number Analysed"=subjects evaluable for specific time points.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

Notes:

[70] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	160	160		
Units: Subjects				
ALT inc:Missing (BG) to G<=2 (CTCAE G)n=160,160	2	0		
ALT inc:G<=2 (BG) to G<=2 (CTCAE G)n=160,160	152	154		
ALT inc:G<=2 (BG) to G3/4 (CTCAE G)n=160,160	6	6		
ALT inc:G3/4 (BG) to G<=2 (CTCAE G)n=160,160	0	0		
ALP inc:Missing(BG) to G<=2 (CTCAE G)n=159,159	0	1		
ALP inc:G<=2 (BG) to G<=2 (CTCAE G)n=159,159	159	157		
ALP inc:G<=2 (BG) to G3/4 (CTCAE G)n=159,159	0	1		
AST inc:Missing (BG) to G<=2 (CTCAE G)n=159,160	3	0		
AST inc: G<=2 (BG) to G<=2 (CTCAE G)n=159,160	152	156		
AST inc: G<=2 (BG) to G3/4 (CTCAE G)n=159,160	4	4		
Blood Bil inc:Missing (BG)toG<=2(CTCAE G)n=160,160	157	159		
CKD: Missing (BG) to G<=2(CTCAE G)n=160,160	2	1		
CKD:G<=2 (BG) to G<=2 (CTCAE G)n=160,160	130	134		
CKD:G<=2 (BG) to G3/4 (CTCAE G)n=160,160	28	23		
CKD: G3/4 (BG) to G3/4 (CTCAE G)n=160,160	0	2		
CPK inc:Missing(BG)toG<=2 (CTCAE G)n=157,157	9	8		
CPK inc:G<=2 (BG) to G3/4 (CTCAE G)n=157,157	1	2		
Creatinine inc:G<=2(BG)toG<=2 (CTCAE G)n=160,160	153	155		
Creatinine inc:G<=2 (BG)toG3/4 (CTCAEG)n=160,160	7	5		
GGT inc:Missing(BG) to G<=2 (CTCAEG)n=8,8	3	5		
GGT inc:Missing (BG) to G3/4 (CTCAE G)n=8,8	4	3		
GGT inc:G<=2 (BG) to G3/4 (CTCAE G)n=8,8	1	0		
Hypercalcemia:Missing(BG)to G<=2 (CTCAEG)n=158,160	2	2		
Hypercalcemia:G<=2(BG)toG<=2 (CTCAEG)n=158,160	156	158		

Hyperglycemia:Missing(BG)toG<=2 (CTCAEG)n=160,160	2	4		
Hyperglycemia:G<=2(BG)to G<=2 (CTCAEG))n=160,160	147	136		
Hyperglycemia:G<=2(BG)toG3/4 (CTCAEG)n=160,160	8	14		
Hyperglycemia:G3/4(BG) toG<=2 (CTCAEG)n=160,160	2	2		
Hyperkalemia:Missing(BG) to G<=2 (CTCAEG)n=159,160	2	0		
Hyperkalemia:G<=2 (BG) to G<=2 (CTCAEG)n=159,160	155	157		
Hyperkalemia:G<=2(BG)toG3/4 (CTCAEG)n=159,160	2	3		
Hyperkalemia:G3/4(BG) to G<=2 (CTCAE G)n=159,160	0	0		
Hyperkalemia:G3/4(BG)to G3/4 (CTCAEG)n=159,160	0	0		
Hypermag:Missing(BG)to G<=2(CTCAEG)n=159,160	2	4		
Hypermag:G<=2(BG) to G<=2 (CTCAEG)n=159,160	155	154		
Hypermag:G<=2(BG) to G3/4 (CTCAEG)n=159,160	2	2		
Hypernatremia:G<=2 (BG) to G<=2 (CTCAEG)n=160,160	158	159		
Hypernatremia:G<=2(BG) to G3/4 (CTCAEG)n=160,160	2	1		
Hypo alb:Missing(BG) to G<=2(CTCAEG)n= 159,160	2	0		
Hypo alb:G<=2(BG)to G<=2 (CTCAEG)n=159,160	151	157		
Hypo alb:G<=2(BG)to G3/4 (CTCAE G)n=159,160	6	3		
Hypocalcemia:Missing(BG)toG<=2 (CTCAEG)n=158,160	2	2		
Hypocalcemia:G<=2(BG) to G<=2 (CTCAEG)n=158,160	154	155		
Hypocalcemia:G<=2(BG)to G3/4 (CTCAEG)n=158,160	1	3		
Hypocalcemia:G3/4 (BG) to G3/4 (CTCAEG)n=158,160	0	0		
Hypoglycemia:Missing(BG) to G<=2 (CTCAEG)n=160,160	2	4		
Hypoglycemia:G<=2(BG) to G<=2 (CTCAEG)n=160,160	155	156		
Hypoglycemia:G<=2(BG)to G3/4 (CTCAEG)n=160,160	3	0		
Hypokalemia:Missing(BG) to G<=2 (CTCAEG)n=159,160	2	0		
Hypokalemia:G<=2(BG) to G<=2 (CTCAEG)n=159,160	129	139		
Hypokalemia:G<=2(BG) to G3/4 (CTCAEG)n=159,160	23	15		
Hypokalemia:G3/4(BG)to G<=2 (CTCAEG)n=159,160	1	2		
Hypokalemia:G3/4(BG) to G3/4 (CTCAEG)n=159,160	4	4		
Hypomag:Missing(BG)to G<=2(CTCAEG)n=159,160	2	4		
Hypomag:G<=2(BG) to G<=2 (CTCAEG)n=159,160	151	153		

Hypomag:G<=2(BG) toG3/4 (CTCAEG)n=159,160	6	2		
Hypomag:G3/4(BG) to G<=2 (CTCAEG)n=159,160	0	1		
Hyponatremia:G<=2(BG)to G<=2(CTCAEG)n=160,160	135	142		
Hyponatremia:G<=2(BG)to G3/4 (CTCAEG)n=160,160	24	15		
Hyponatremia:G3/4(BG) to G<=2 (CTCAEG)n=160,160	0	1		
Hyponatremia:G3/4(BG) to G3/4 (CTCAEG)n=160,160	1	2		
Hypophos:Missing(BG)to G<=2(CTCAEG)n=158,160	3	2		
Hypophos:Missing (BG) to G3/4 (CTCAEG)n=158,160	1	0		
Hypophos:G<=2 (BG) toG<=2 (CTCAEG)n=158,160	141	138		
Hypophos:G<=2 (BG) to G3/4 (CTCAEG)n=158,160	12	17		
Hypophos:G3/4 (BG) to G<=2 (CTCAEG)n=158,160	0	1		
Hypophos: G3/4 (BG) to G3/4 (CTCAEG)n=158,160	1	2		
Blood bil inc:G<=2(BG)toG3/4 (CTCAEG),n=160,160	3	1		
CPK inc:G<=2(BG)toG<=2(CTCAE G),n=157,157	147	147		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Number of Subjects With Shift From Baseline in Coagulation Laboratory Abnormalities Graded by NCI CTCAE v.4.03

End point title	Intensive Study: Number of Subjects With Shift From Baseline in Coagulation Laboratory Abnormalities Graded by NCI CTCAE v.4.03[71]

End point description:

Coagulation laboratory test included: activated partial thromboplastin time (APTT) prolonged, and INR increased. Laboratory results were categorically summarized according to the NCI-CTCAE criteria v4.03. Grade 0= no abnormality; Grade 1= mild; Grade 2= moderate; Grade 3= severe and Grade 4= life-threatening or disabling. Number of participants with shift from baseline for coagulation were assessed. Only those laboratory test parameters in which at least 1 subject had data were reported. SA set included all participants who received at least one dose of study drug. Here, "Overall Number of Subjects Analysed" signifies subjects evaluable for this end point and "Number Analysed" signifies subjects evaluable for specific time points.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

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

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	11		
Units: Subjects				
APTT prolonged: Missing (BG) to G0 (CTCAE G)n=4,9	1	0		
APTT prolonged: Missing (BG) to G1 (CTCAEG)n=4,9	0	1		
APTT prolonged:G0 (BG) to Grade 0 (CTCAEG)n=4,9	0	4		
APTT prolonged:G0(BG) to G1 (CTCAEG)n=4,9	1	2		
APTT prolonged:G0 (BG) to G2 (CTCAEG)n=4,9	0	1		
APTT prolonged: G0 (BG) to G3 (CTCAEG)n=4,9	1	0		
APTT prolonged:G1(BG) to G1 (CTCAEG)n=4,9	1	1		
INR increased:Missing(BG) toG0 (CTCAEG)n=6,11	1	1		
INR increased:Missing(BG) toG1(CTCAEG)n=6,11	0	1		
INR increased:Missing(BG) to G2 (CTCAEG)n=6,11	1	0		
INR increased: G0 (BG) to G0 (CTCAEG)n=6,11	0	2		
INR increased: G0 (BG) to G1 (CTCAEG)n=6,11	1	0		
INR increased: G0 (BG) to G2 (CTCAEG)n=6,11	1	1		
INR increased: G0 (BG) to G3 (CTCAEG)n=6,11	0	1		
INR increased: G1 (BG) to G0 (CTCAEG)n=6,11	0	1		
INR increased: G1 (BG) to G1 (CTCAEG)n=6,11	0	3		
INR increased: G1 (BG) to G2 (CTCAEG)n=6,11	1	1		
INR increased: G1 (BG) to G3 (CTCAEG)n=6,11	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Number of Subjects With Shift From Baseline in Coagulation Laboratory Abnormalities Graded by NCI CTCAE v.4.03

End point title	Non-intensive Study: Number of Subjects With Shift From Baseline in Coagulation Laboratory Abnormalities Graded by NCI CTCAE v.4.03[72]

End point description:

Coagulation laboratory test included: APTT prolonged, and INR increased. Laboratory results were categorically summarized according to the NCI-CTCAE criteria v4.03. Grade 0= no abnormality; Grade 1= mild; Grade 2= moderate; Grade 3= severe and Grade 4= life-threatening or disabling. Number of

participants with shift from baseline for coagulation were assessed. Only those laboratory test parameters in which at least 1 subject had data were reported. SA set included all participants who received at least one dose of study drug. Here, "Overall Number of Subjects Analysed" signifies subjects evaluable for this end point and "Number Analysed" signifies subjects evaluable for specific time points.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

Notes:

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

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	13		
Units: Subjects				
APTT prolonged:Missing(BG) toG0 (CTCAEG)n=17,12	1	0		
APTT prolonged:G0 (BG) to Grade 0 (CTCAEG)n=17,12	8	5		
APTT prolonged:G0(BG) to G1 (CTCAEG)n=17,12	5	7		
APTT prolonged: G1 (BG) to G0 (CTCAEG)n=17,12	1	0		
APTT prolonged:G1(BG) to G1 (CTCAEG)n=17,12	1	0		
APTT prolonged: G2 (BG) to G1 (CTCAEG)n=17,12	1	0		
INR increased:Missing(BG) toG0 (CTCAEG)n=17,13	1	0		
INR increased: G0 (BG) to G0 (CTCAEG)n=17,13	4	5		
INR increased: G0 (BG) to G1 (CTCAEG)n=17,13	6	4		
INR increased: G0 (BG) to G2 (CTCAEG)n=17,13	1	2		
INR increased: G0 (BG) to G3 (CTCAEG)n=17,13	1	0		
INR increased: G1 (BG) to G1 (CTCAEG)n=17,13	1	1		
INR increased: G1 (BG) to G2 (CTCAEG)n=17,13	2	0		
INR increased: G3 (BG) to G1 (CTCAEG)n=17,13	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Plasma Trough Concentration (Ctrough) of Glasdegib

End point title	Intensive Study: Plasma Trough Concentration (Ctrough) of Glasdegib[73]

End point description:

Ctrough of Glasdegib was measured in nanogram per milliliter (ng/mL). Analysis population included all subjects who were treated and who had at least 1 value of analyte concentration of Glasdegib available. Here, "Overall Number of Subjects Analysed" signifies subjects evaluable for this end point and "Number Analysed" signifies subjects evaluable for specific time points.

End point type	Secondary

End point timeframe:

Induction, Day 10 +/-1: pre-dose, 1, 4 hour; Consolidation phase, Day 1: pre-dose, 1, 4 hour

Notes:

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

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin			
Subject group type	Reporting group			
Number of subjects analysed	123			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Induction Day 10, n=81	413.54 (± 125)			
Consolidation 1, Day 1, n=33	245.48 (± 80)			
Consolidation 2, Day 1, n=41	259.79 (± 122)			

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Ctrough of Glasdegib

End point title	Non-intensive Study: Ctrough of Glasdegib[74]

End point description:

Ctrough of Glasdegib was measured in ng/mL. Analysis population included all subjects who were treated and who had at least 1 value of analyte concentration of Glasdegib available. Here, "Overall Number of Subjects Analysed" signifies subjects evaluable for this end point and "Number Analysed" signifies subjects evaluable for specific time points. SA set included all participants who received at least one dose of study drug.

End point type	Secondary

End point timeframe:

Pre-dose: Cycle 1 Day 15 and Cycle 2 Day 1

Notes:

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

End point values	Non-intensive Study: Glasdegib + Azacitidine			
Subject group type	Reporting group			
Number of subjects analysed	53			
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Day 15, n=34	565.44 (± 126)			
Cycle 2 Day 1, n=37	472.42 (± 122)			

Statistical analyses

No statistical analyses for this end point

Secondary: Intensive Study: Number of Subjects With Shift From Baseline in Corrected QT (QTc) Interval

End point title	Intensive Study: Number of Subjects With Shift From Baseline in Corrected QT (QTc) Interval[75]

End point description:

Triplicate 12-lead Electrocardiogram (ECG) measurements (each recording separated by approximately 2 minutes) were performed and average was calculated. The time corresponding to beginning of depolarization to repolarization of the ventricles (QT interval) was adjusted for RR interval using QT and RR from each ECG by Fridericia's formula (QTcF = QT divided by cube root of RR) and by Bazette's formula (QTcB = QT divided by square root of RR). Participants with maximum increase from baseline of <=450 to >500 msec (post-baseline[PB]) were summarized. Number of participants with shift from baseline for QTc were assessed. Only those QTc parameters in which at least 1 subject had data were reported. Here, "Overall Number of Subjects Analysed" signifies subjects evaluable for this end point and "Number Analysed" signifies subjects evaluable for specific time points.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 2 years

Notes:

[75] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is reporting statistics for the arms specified

End point values	Intensive Study: Glasdegib + Cytarabine + Daunorubicin	Intensive Study: Placebo + Cytarabine + Daunorubicin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	188	189		
Units: Subjects				
QTcB:<=450ms(B) to <=450 msec(PB),n=188,188	51	71		
QTcB:<=450ms(B)to >450-<=480 msec(PB),n=188,188	64	63		
QTcB:<=450ms(B)to >480-<=500 msec(PB),n=188,188	18	11		
QTcB:<=450ms(B)to >500msec (PB),n=188,188	11	6		

QTcB:>450-<=480ms(B)to<=450ms(PB),n=188,18	2	3		
QTcB:>450-<=480ms(B)to >450-<=480ms(PB),n=188,188	20	17		
QTcB:>450-<=480ms(B)to >480-<=500ms(PB),n=188,188	16	10		
QTcB:>450-<=480ms(B)to >500ms(PB),n=188,188	1	5		
QTcB:>480-<=500ms(B)to >450-<=480ms(PB),n=188,188	1	0		
QTcB:>480-<=500ms(B)to >480-<=500ms(PB), n=188,188	2	1		
QTcB:>480-<=500ms(B)to >500 ms(PB),n=188,188	1	0		
QTcB:>500ms(B)to >500ms(PB),n=188,188	1	1		
QTcF:<=450ms(B)to <=450ms(PB), n=187,189	116	132		
QTcF:<=450ms(B)to >450-<=480ms(PB),n=187,189	50	39		
QTcF:<=450ms(B)to >480-<=500ms(PB),n=187,189	8	10		
QTcF:<=450ms(B)to >500ms(PB),n=187,189	5	0		
QTcF:>450-<=480ms(B)to <=450 ms(PB),n=187,189	2	1		
QTcF:>450-<=480ms(B)to >450-<=480ms(PB),n=187,189	5	5		
QTcF:>450-<=480ms(B)to >500 ms(PB),n=187,189	1	1		
QTcF:>480-<=500ms(B)to >480-<=500ms(PB),n=187,189	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Non-intensive Study: Number of Subjects With Shift From Baseline in QTc Interval

End point title	Non-intensive Study: Number of Subjects With Shift From Baseline in QTc Interval[76]

End point description:

Triplicate 12-lead ECG measurements (each recording separated by approximately 2 minutes) were performed and average was calculated. The time corresponding to beginning of depolarization to repolarization of the ventricles (QT interval) was adjusted for RR interval using QT and RR from each ECG by Fridericia's formula (QTcF = QT divided by cube root of RR) and by Bazette's formula (QTcB = QT divided by square root of RR). Subjects with maximum increase from baseline of <=450 to >500 msec (post-baseline) were summarized. Number of subjects with shift from baseline for QTc were assessed. Only those QTc parameters in which at least 1 subjects had data were reported. SA set included all participants who received at least one dose of study drug. Here, "Overall Number of Participants Analyzed" signifies participants evaluable for this outcome measure and "Number Analyzed" signifies participants evaluable for specific time points.

End point type	Secondary

End point timeframe:

Day 1 up to maximum of 3 years

Notes:

[76] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: The endpoint is reporting statistics for the arms specified

End point values	Non-intensive Study: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	158	155		
Units: Subjects				
QTcB:<=450ms(B) to <=450 msec(PB),n=158,155	48	58		
QTcB:<=450ms(B)to >450-<=480 msec(PB), n=158,155	53	43		
QTcB:<=450ms(B)to >480-<=500 msec(PB),n=158,155	6	11		
QTcB:<=450ms(B)to>500msec (PB),n=158,155	7	3		
QTcB:>450-<=480ms(B)to<=450 ms(PB),n=158,155	0	1		
QTcB:>450-<=480ms(B)to >450-<=480ms(PB),n=158,155	20	22		
QTcB:>450-<=480ms(B)to>480-<=500ms(PB),n=158,155	13	8		
QTcB:>450-<=480ms(B)to>500 ms(PB),n=158,155	5	3		
QTcB:>480-<=500ms(B)to>450-<=480ms(PB),n=158,155	1	2		
QTcB:>480-<=500ms(B)to>480-<=500ms(PB),n=158,155	3	1		
QTcB:>480-<=500ms(B)to>500 ms(PB),n=158,155	2	3		
QTcF:<=450ms(B)to <=450ms(PB),n=155,155	100	104		
QTcF:<=450ms(B)to >450-<=480ms(PB),n=155,155	39	36		
QTcF:<=450ms(B)to >480-<=500ms(PB),n=155,155	7	0		
QTcF:<=450ms(B)to >500ms(PB),n=155,155	1	1		
QTcF:>450ms(B)to <=480 ms(PB),n=155,155	0	1		
QTcF:>480ms(B)to <500ms(post baseline), n=155,155	5	8		
QTcF:>480ms(B)to <=500ms(PB),n=155,155	1	4		
QTcF:>450ms(B)to >=480ms(PB),n=155,155	1	1		
QTcF:>450ms(B)to<500ms(PB),n=155,155	1	0		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Intensive study: Day 1 up to maximum of 2 years; non-intensive study: Day 1 up to maximum of 3 years; Open-label extension (OLE) study: Up to approximately 565 days

Adverse event reporting additional description:

Same event may appear as both an AE and SAE.However,what is presented are distinct events.Events may be serious in one subject and non-serious in other or both serious&non-serious in a subject.Safety analysis set included all subjects who received at least one dose of study drug.MedDRA23.1 was used for INT and NINT and 25.1 for OLE cohort.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Non-intensive Study: Glasdegib + Azacitidine

Reporting group description:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, subject refusal or death, whichever occurred first. Subjects also received glasdegib 100 mg orally PO QD from Day 1 of chemotherapy until clinical benefit or disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first. Eligible subjects underwent HSCT per local standard of care and received glasdegib up to 2 years following randomization unless 2 consecutive negative MRD assessments. Subjects were followed up for first 2 years from last dose of drug and had long term follow-up for survival for up to 5 years from randomization of last subject in study, or until death, or consent withdrawal.

Reporting group title	Intensive Study: Placebo + Cytarabine + Daunorubicin

Reporting group description:

Subjects received 28 days induction therapy: Cytarabine 100 mg/m^2 IV daily for 7 days + daunorubicin 60 mg/m^2 daily IV for 3 days. Depending on bone marrow blast or investigator judgement subjects had second induction to receive either same therapy or cytarabine 100 mg/m^2 IV daily for 5 days + daunorubicin 60 mg/m^2 IV daily for 2 days. Subjects with <5% bone marrow blasts entered consolation phase: treated with either or both of: 1) Cytarabine 1 to 3 gm/m^2 IV for adults >= 60 to <60 years twice daily on Days 1, 3, 5 for 4 cycle (1 cycle=28 days) or cytarabine per local prescribing information. 2) Received HSCT per local standard of care. Subjects received Glasdegib matched placebo tablet PO QD from Day 1 up to 28 days in both induction and up to 2 years post randomization or until 2 consecutive CR MRD-negative, whichever came first. FU was up to 2 years from last dose and long term survival FU from last subject randomized up to 5 years or until death or consent withdrawal.

Reporting group title	Intensive Study: Glasdegib + Cytarabine + Daunorubicin

Reporting group description:

Subjects received 28 days induction therapy: Cytarabine 100 mg/m^2 IV daily for 7 days + daunorubicin 60 mg/m^2 daily IV for 3 days. Depending on bone marrow blast or investigator judgement subjects had second induction to receive either same therapy or cytarabine 100 mg/m^2 IV daily for 5 days + daunorubicin 60 mg/m^2 IV daily for 2 days. Subjects with <5% bone marrow blasts entered consolation phase: treated with either or both of: 1) Cytarabine 1 to 3 gm/m^2 IV for adults >= 60 to <60 years twice daily on Days 1, 3, 5 for 4 cycle (1 cycle=28 days) or cytarabine per local prescribing information. 2) Received HSCT per local standard of care. Subjects received Glasdegib 100 mg tablet PO QD from Day 1 up to 28 days in both induction and up to 2 years post randomization or until 2 consecutive CR MRD-negative, whichever came first. FU was up to 2 years from last dose and long term survival FU from last subject randomized up to 5 years or until death or consent withdrawal.

Reporting group title	Open Label Extension: Placebo + Azacitidine

Reporting group description:

Participants received placebo matched to Glasdegib in combination with azacitidine 75mg/m^2/day SC or IV for 7 days every 28 days. Treatment continued until objective disease progression or relapse, death, unacceptable toxicity, or participant refusal, whichever occurred first. Participants were followed up for 28 days after end of study treatment.

Reporting group title	Open Label Extension: Glasdegib + Azacitidine

Reporting group description:

Participants received glasdegib 100 milligrams (mg) tablet per oral (PO) once a day (QD) in combination with azacitidine 75 mg per meter squared (m^2)/day as subcutaneous (SC) injection or intravenous (IV) infusion for 7 days every 28 days. Treatment continued until objective disease progression or relapse, death, unacceptable toxicity, or participant refusal, whichever occurred first. Participants were followed up for 28 days after end of study treatment.

Reporting group title	Non-intensive Study: Placebo + Azacitidine

Reporting group description:

Subjects received chemotherapy with azacitidine 75 mg/m^2 SC injection or IV infusion from Day 1 up to Day 7 of each cycle (28 day) and continued for at least 6 cycles or until unacceptable toxicity, subjects refusal or death, whichever occurred first. Subjects also received glasdegib 100 mg tablet matching placebo PO QD from Day 1 of chemotherapy until clinical benefit or disease progression, unacceptable toxicity, consent withdrawal, or death, whichever occurred first. Eligible subjects underwent HSCT per local standard of care and glasdegib matching placebo up to 2 years following randomization unless 2 consecutive negative MRD assessments. Subjects were followed up for first 2 years from last dose of drug and had long term follow-up for survival for up to 5 years from randomization of last subject in study, or until death, or consent withdrawal.

Serious adverse events	Non-intensive Study: Glasdegib + Azacitidine	Intensive Study: Placebo + Cytarabine + Daunorubicin	Intensive Study: Glasdegib + Cytarabine + Daunorubicin
Total subjects affected by serious adverse events			
subjects affected / exposed	110 / 162 (67.90%)	91 / 201 (45.27%)	85 / 198 (42.93%)
number of deaths (all causes)	96	60	67
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Differentiation syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 neoplasm	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm prostate	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Neoplasm progression	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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			
Deep vein thrombosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Hypotension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 1	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Orthostatic hypotension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Aneurysm ruptured	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Axillary vein thrombosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Thrombosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Circulatory collapse	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
General disorders and administration site conditions			
Pyrexia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	9 / 162 (5.56%)	6 / 201 (2.99%)	4 / 198 (2.02%)
occurrences causally related to treatment / all	3 / 10	3 / 6	1 / 4
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Multiple organ dysfunction syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 0
Disease progression	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	14 / 162 (8.64%)	4 / 201 (1.99%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 15	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Malaise	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Non-cardiac chest pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Sudden death	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Death	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	4 / 162 (2.47%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 0
Asthenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue inflammation	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Graft versus host disease in skin	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease in gastrointestinal tract	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Hypersensitivity	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Cytokine release syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	3 / 162 (1.85%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Respiratory failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	4 / 201 (1.99%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
Hypoxia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	2 / 201 (1.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infiltration	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Acute respiratory failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	3 / 201 (1.49%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	1 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary alveolar haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Pulmonary haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary oedema	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 aspiration	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Oropharyngeal pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Psychiatric disorders			
Confusional state	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adjustment disorder with depressed mood	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Investigations			
Blood creatinine increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Electrocardiogram QT prolonged	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	5 / 162 (3.09%)	8 / 201 (3.98%)	13 / 198 (6.57%)
occurrences causally related to treatment / all	3 / 5	8 / 10	9 / 15
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Blood alkaline phosphatase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	2 / 201 (1.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	1 / 2	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	2 / 201 (1.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	3 / 201 (1.49%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 0	3 / 4	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood lactate dehydrogenase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Gamma-glutamyltransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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

Neutrophil count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
SARS-CoV-2 test positive	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electroencephalogram abnormal	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Creatinine renal clearance decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
C-reactive protein increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Injury, poisoning and procedural complications			
Fall	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Femoral neck fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Subdural haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Transfusion reaction	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Cardiac disorders			
Cardiac failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Cardiac failure acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac arrest	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial fibrillation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	3 / 198 (1.52%)
occurrences causally related to treatment / all	0 / 1	0 / 1	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure congestive	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Intracardiac mass	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Cardiomyopathy	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Left ventricular dysfunction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Myocardial infarction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Myocardial ischaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiorenal syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Bradycardia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 flutter	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Cardiopulmonary failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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			
Epilepsy	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage intracranial	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	2 / 201 (1.00%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 1	1 / 2	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Syncope	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Seizure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Encephalopathy	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Cerebral infarction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	0 / 198 (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
Central nervous system lesion	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Somnolence	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Partial seizures	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Blood and lymphatic system disorders			
Febrile neutropenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	24 / 162 (14.81%)	17 / 201 (8.46%)	18 / 198 (9.09%)
occurrences causally related to treatment / all	14 / 33	22 / 23	20 / 26
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	5 / 162 (3.09%)	1 / 201 (0.50%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	1 / 6	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Thrombocytopenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	3 / 201 (1.49%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 4	28 / 28	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic necrosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukocytosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Vision blurred	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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			
Colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	4 / 162 (2.47%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	1 / 5	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	2 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	3 / 162 (1.85%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Gastrointestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	3 / 198 (1.52%)
occurrences causally related to treatment / all	0 / 3	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Haematemesis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Intestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Large intestine perforation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower gastrointestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Upper gastrointestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Rectal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Enteritis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Anal fistula	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterocolitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	0 / 198 (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
Abdominal distension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Anal fissure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Intra-abdominal haematoma	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	0 / 198 (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
Nausea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Mechanical ileus	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Gastrointestinal perforation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Glossitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids thrombosed	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	0 / 198 (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
Hepatobiliary disorders			
Cholecystitis acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Hyperbilirubinaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Cholelithiasis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Hepatitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Bile duct stone	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Cholangitis acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Dermatitis exfoliative generalised	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Drug eruption	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	3 / 201 (1.49%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Haematuria	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	0 / 198 (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
Chronic kidney disease	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Osteoarthritis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Synovitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue necrosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Infections and infestations			
Clostridium difficile colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterobacter bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	0 / 198 (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
Bronchopulmonary aspergillosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 2	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	3 / 162 (1.85%)	2 / 201 (1.00%)	4 / 198 (2.02%)
occurrences causally related to treatment / all	1 / 4	0 / 2	5 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	3 / 198 (1.52%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	3 / 162 (1.85%)	2 / 201 (1.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 6	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	26 / 162 (16.05%)	11 / 201 (5.47%)	15 / 198 (7.58%)
occurrences causally related to treatment / all	9 / 38	3 / 13	9 / 22
deaths causally related to treatment / all	0 / 9	0 / 1	0 / 5
Perirectal abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	1 / 201 (0.50%)	0 / 198 (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
Septic shock	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	4 / 162 (2.47%)	4 / 201 (1.99%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	3 / 7	4 / 4	1 / 2
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0
Sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	13 / 162 (8.02%)	13 / 201 (6.47%)	15 / 198 (7.58%)
occurrences causally related to treatment / all	5 / 18	10 / 14	12 / 26
deaths causally related to treatment / all	1 / 6	0 / 2	0 / 5
Pseudomembranous colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia fungal	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	2 / 201 (1.00%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	1 / 2	3 / 3	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	9 / 162 (5.56%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	3 / 13	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorectal infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Atypical pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Bacterial sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Brain abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Clostridium colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Clostridial sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Device related bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Escherichia sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Diarrhoea infectious	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Disseminated varicella zoster virus infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Enterococcal bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	2 / 198 (1.01%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes zoster	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Herpes ophthalmic	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Fungal infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Pulmonary tuberculosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Pseudomonal bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	3 / 198 (1.52%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethritis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	1 / 198 (0.51%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Candida sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
COVID-19	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Herpes dermatitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 skin ulcer	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Lower respiratory tract infection bacterial	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Liver abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Klebsiella bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Otitis media acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periodontitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Post procedural infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 staphylococcal	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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 sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Subdiaphragmatic abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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
Suspected COVID-19	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic mycosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Wound infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	3 / 162 (1.85%)	1 / 201 (0.50%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	3 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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
Hyperglycaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	1 / 201 (0.50%)	0 / 198 (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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	0 / 198 (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
Hyperkalaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 162 (1.23%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 162 (0.62%)	0 / 201 (0.00%)	0 / 198 (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

Serious adverse events	Open Label Extension: Placebo + Azacitidine	Open Label Extension: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 5 (20.00%)	2 / 9 (22.22%)	118 / 160 (73.75%)
number of deaths (all causes)	0	0	88
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Differentiation syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal neoplasm	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Neoplasm prostate	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasm progression	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Vascular disorders			
Deep vein thrombosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Orthostatic hypotension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aneurysm ruptured	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Axillary vein thrombosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous thrombosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 ischaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Circulatory collapse	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			
Pyrexia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	11 / 160 (6.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 14
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple organ dysfunction syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disease progression	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	22 / 160 (13.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 22
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chills	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	3 / 160 (1.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Death	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Asthenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue inflammation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Graft versus host disease in skin	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease in gastrointestinal tract	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Graft versus host disease	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cytokine release syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			
Dyspnoea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Epistaxis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 infiltration	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory distress syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 alveolar haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 oedema	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	3 / 160 (1.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			
Confusional state	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adjustment disorder with depressed mood	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hallucination	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			

Blood creatinine increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	3 / 160 (1.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	5 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 alkaline phosphatase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 bilirubin increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 lactate dehydrogenase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase	Additional description: MedDRA 25.1 was used for open label extension cohort.		

increased			
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SARS-CoV-2 test positive	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Electroencephalogram abnormal	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Creatinine renal clearance decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
C-reactive protein increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural complication	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tooth fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transfusion reaction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			
Cardiac failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Atrial fibrillation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocarditis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracardiac mass	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiomyopathy	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Left ventricular dysfunction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 ischaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiorenal syndrome	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiopulmonary failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (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
Nervous system disorders			
Epilepsy	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carotid artery stenosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Central nervous system lesion	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial aneurysm	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Partial seizures	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 5 (20.00%)	1 / 9 (11.11%)	18 / 160 (11.25%)
occurrences causally related to treatment / all	0 / 1	0 / 1	6 / 27
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Anaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	5 / 160 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic necrosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			
Vision blurred	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			

Colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Constipation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Diverticulum intestinal haemorrhagic	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Gastrointestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haematemesis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Intestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Large intestine perforation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper gastrointestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric ulcer	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 distension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fissure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haematoma	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical ileus	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal perforation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glossitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids thrombosed	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperbilirubinaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug-induced liver injury	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bile duct stone	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis exfoliative generalised	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			
Myalgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Synovitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue necrosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			
Clostridium difficile colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopulmonary aspergillosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	4 / 160 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	7 / 160 (4.38%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis infective	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	5 / 160 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	5 / 160 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	35 / 160 (21.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	9 / 49
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 9
Perirectal abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	5 / 160 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	7 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 3
Sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	9 / 160 (5.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 13
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 4
Pseudomembranous colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
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 fungal	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	3 / 160 (1.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	4 / 160 (2.50%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anorectal infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atypical pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 infectious	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 varicella zoster virus infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterococcal bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 ophthalmic	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 tuberculosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethritis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (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
COVID-19	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes dermatitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infected skin ulcer	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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 acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periodontitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	2 / 160 (1.25%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
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 staphylococcal	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdiaphragmatic abscess	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suspected COVID-19	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic mycosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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			
Decreased appetite	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
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	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	3 / 160 (1.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Failure to thrive	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Hyponatraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypophosphataemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	1 / 160 (0.63%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
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	Non-intensive Study: Glasdegib + Azacitidine	Intensive Study: Placebo + Cytarabine + Daunorubicin	Intensive Study: Glasdegib + Cytarabine + Daunorubicin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	153 / 162 (94.44%)	195 / 201 (97.01%)	194 / 198 (97.98%)
Vascular disorders			
Hypotension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	17 / 201 (8.46%)	18 / 198 (9.09%)
occurrences (all)	0	23	19
Hypertension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	25 / 201 (12.44%)	10 / 198 (5.05%)
occurrences (all)	0	39	15
General disorders and administration site conditions			
Fatigue	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	13 / 162 (8.02%)	32 / 201 (15.92%)	31 / 198 (15.66%)
occurrences (all)	17	47	53
Oedema peripheral	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	11 / 162 (6.79%)	32 / 201 (15.92%)	25 / 198 (12.63%)
occurrences (all)	13	43	36
Pyrexia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	41 / 162 (25.31%)	84 / 201 (41.79%)	84 / 198 (42.42%)
occurrences (all)	68	169	194
Asthenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	15 / 162 (9.26%)	11 / 201 (5.47%)	15 / 198 (7.58%)
occurrences (all)	24	14	21
Chills	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	11 / 201 (5.47%)	20 / 198 (10.10%)
occurrences (all)	0	17	25
Mucosal inflammation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	7 / 201 (3.48%)	12 / 198 (6.06%)
occurrences (all)	0	9	16
Non-cardiac chest pain	Additional description: General disorders and administration site conditions		
subjects affected / exposed	0 / 162 (0.00%)	8 / 201 (3.98%)	13 / 198 (6.57%)
occurrences (all)	0	10	16
Oedema	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	19 / 201 (9.45%)	9 / 198 (4.55%)
occurrences (all)	0	22	17
Injection site reaction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	11 / 162 (6.79%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	42	0	0
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	10 / 162 (6.17%)	23 / 201 (11.44%)	23 / 198 (11.62%)
occurrences (all)	10	25	28
Dyspnoea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	11 / 162 (6.79%)	23 / 201 (11.44%)	15 / 198 (7.58%)
occurrences (all)	11	25	18
Epistaxis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	8 / 162 (4.94%)	20 / 201 (9.95%)	19 / 198 (9.60%)
occurrences (all)	16	25	21
Oropharyngeal pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	19 / 201 (9.45%)	19 / 198 (9.60%)
occurrences (all)	0	21	23
Psychiatric disorders			
Insomnia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	12 / 162 (7.41%)	30 / 201 (14.93%)	27 / 198 (13.64%)
occurrences (all)	15	37	29
Investigations			
Alanine aminotransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	13 / 162 (8.02%)	53 / 201 (26.37%)	39 / 198 (19.70%)
occurrences (all)	27	138	104
Aspartate aminotransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	10 / 162 (6.17%)	41 / 201 (20.40%)	30 / 198 (15.15%)
occurrences (all)	17	83	51
Blood creatinine increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	20 / 162 (12.35%)	13 / 201 (6.47%)	18 / 198 (9.09%)
occurrences (all)	34	20	24
Electrocardiogram QT prolonged	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	20 / 162 (12.35%)	20 / 201 (9.95%)	21 / 198 (10.61%)
occurrences (all)	28	35	30
Neutrophil count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	22 / 162 (13.58%)	49 / 201 (24.38%)	56 / 198 (28.28%)
occurrences (all)	129	317	308
Platelet count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	30 / 162 (18.52%)	73 / 201 (36.32%)	77 / 198 (38.89%)
occurrences (all)	155	504	627
Weight decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	34 / 162 (20.99%)	22 / 201 (10.95%)	21 / 198 (10.61%)
occurrences (all)	63	32	37
White blood cell count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	17 / 162 (10.49%)	53 / 201 (26.37%)	63 / 198 (31.82%)
occurrences (all)	114	495	454
Gamma-glutamyltransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	10 / 162 (6.17%)	22 / 201 (10.95%)	12 / 198 (6.06%)
occurrences (all)	19	75	36
Blood bilirubin increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 162 (0.00%)	13 / 201 (6.47%)	25 / 198 (12.63%)
occurrences (all)	0	34	62
Lymphocyte count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	21 / 201 (10.45%)	19 / 198 (9.60%)
occurrences (all)	0	111	133
Blood alkaline phosphatase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	13 / 201 (6.47%)	14 / 198 (7.07%)
occurrences (all)	0	21	26
C-reactive protein increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	7 / 162 (4.32%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	13	0	0
Injury, poisoning and procedural complications			
Fall	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	10 / 162 (6.17%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	19	0	0
Cardiac disorders			
Sinus tachycardia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	7 / 201 (3.48%)	11 / 198 (5.56%)
occurrences (all)	0	7	13
Nervous system disorders			
Headache	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	4 / 162 (2.47%)	47 / 201 (23.38%)	39 / 198 (19.70%)
occurrences (all)	4	62	56
Dizziness	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	9 / 162 (5.56%)	18 / 201 (8.96%)	23 / 198 (11.62%)
occurrences (all)	9	26	32
Dysgeusia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	37 / 162 (22.84%)	20 / 201 (9.95%)	39 / 198 (19.70%)
occurrences (all)	41	21	48
Paraesthesia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	11 / 198 (5.56%)
occurrences (all)	0	0	11
Carotid arteriosclerosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			

Anaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	73 / 162 (45.06%)	97 / 201 (48.26%)	101 / 198 (51.01%)
occurrences (all)	217	530	553
Febrile neutropenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	22 / 162 (13.58%)	96 / 201 (47.76%)	97 / 198 (48.99%)
occurrences (all)	32	152	134
Neutropenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	35 / 162 (21.60%)	43 / 201 (21.39%)	41 / 198 (20.71%)
occurrences (all)	130	180	96
Thrombocytopenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	37 / 162 (22.84%)	52 / 201 (25.87%)	52 / 198 (26.26%)
occurrences (all)	152	324	271
Leukopenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	11 / 162 (6.79%)	13 / 201 (6.47%)	10 / 198 (5.05%)
occurrences (all)	52	65	34
Eye disorders			
Retinal detachment	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	12 / 162 (7.41%)	29 / 201 (14.43%)	31 / 198 (15.66%)
occurrences (all)	13	38	37
Constipation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	58 / 162 (35.80%)	61 / 201 (30.35%)	71 / 198 (35.86%)
occurrences (all)	90	87	96
Diarrhoea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	36 / 162 (22.22%)	88 / 201 (43.78%)	96 / 198 (48.48%)
occurrences (all)	49	133	141
Haemorrhoids	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	8 / 162 (4.94%)	19 / 201 (9.45%)	13 / 198 (6.57%)
occurrences (all)	11	21	13
Nausea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	55 / 162 (33.95%)	106 / 201 (52.74%)	110 / 198 (55.56%)
occurrences (all)	96	181	169
Vomiting	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	35 / 162 (21.60%)	40 / 201 (19.90%)	57 / 198 (28.79%)
occurrences (all)	47	57	77
Proctalgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	6 / 201 (2.99%)	14 / 198 (7.07%)
occurrences (all)	0	7	15
Abdominal pain upper	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	9 / 201 (4.48%)	12 / 198 (6.06%)
occurrences (all)	0	12	12
Dyspepsia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	5 / 201 (2.49%)	12 / 198 (6.06%)
occurrences (all)	0	5	13
Stomatitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	41 / 201 (20.40%)	29 / 198 (14.65%)
occurrences (all)	0	55	45
Colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
Colitis ulcerative	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
Inguinal hernia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	11 / 162 (6.79%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	18	0	0
Skin and subcutaneous tissue disorders			
Alopecia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	20 / 162 (12.35%)	26 / 201 (12.94%)	22 / 198 (11.11%)
occurrences (all)	22	29	26
Rash	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	10 / 162 (6.17%)	51 / 201 (25.37%)	46 / 198 (23.23%)
occurrences (all)	12	80	70
Pruritus	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	8 / 162 (4.94%)	11 / 201 (5.47%)	12 / 198 (6.06%)
occurrences (all)	8	19	12
Dry skin	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	10 / 201 (4.98%)	13 / 198 (6.57%)
occurrences (all)	0	12	13
Petechiae	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	11 / 201 (5.47%)	8 / 198 (4.04%)
occurrences (all)	0	11	10
Rash maculo-papular	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	21 / 201 (10.45%)	21 / 198 (10.61%)
occurrences (all)	0	30	26
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	11 / 162 (6.79%)	14 / 201 (6.97%)	17 / 198 (8.59%)
occurrences (all)	13	16	23
Back pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	7 / 162 (4.32%)	17 / 201 (8.46%)	22 / 198 (11.11%)
occurrences (all)	8	18	24
Muscle spasms	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	28 / 162 (17.28%)	3 / 201 (1.49%)	20 / 198 (10.10%)
occurrences (all)	44	3	31
Myalgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	11 / 201 (5.47%)	15 / 198 (7.58%)
occurrences (all)	0	12	27
Joint swelling	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Urinary tract infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	16 / 162 (9.88%)	11 / 201 (5.47%)	5 / 198 (2.53%)
occurrences (all)	24	12	5
Pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	19 / 162 (11.73%)	33 / 201 (16.42%)	32 / 198 (16.16%)
occurrences (all)	27	53	44
Upper respiratory tract infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	12 / 162 (7.41%)	11 / 201 (5.47%)	9 / 198 (4.55%)
occurrences (all)	14	16	13
Bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	11 / 201 (5.47%)	16 / 198 (8.08%)
occurrences (all)	0	14	20
Corynebacterium bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
SARS-CoV-2 test positive	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
Epstein-Barr virus infection reactivation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	0 / 201 (0.00%)	0 / 198 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	45 / 162 (27.78%)	41 / 201 (20.40%)	52 / 198 (26.26%)
occurrences (all)	55	68	67
Hyperglycaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	5 / 162 (3.09%)	10 / 201 (4.98%)	10 / 198 (5.05%)
occurrences (all)	5	17	12
Hypoalbuminaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	11 / 162 (6.79%)	30 / 201 (14.93%)	32 / 198 (16.16%)
occurrences (all)	28	57	78
Hypocalcaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	10 / 162 (6.17%)	17 / 201 (8.46%)	25 / 198 (12.63%)
occurrences (all)	25	37	41
Hypokalaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	35 / 162 (21.60%)	83 / 201 (41.29%)	76 / 198 (38.38%)
occurrences (all)	65	217	200
Hypomagnesaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	11 / 162 (6.79%)	24 / 201 (11.94%)	29 / 198 (14.65%)
occurrences (all)	17	49	52
Hyponatraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	16 / 162 (9.88%)	15 / 201 (7.46%)	24 / 198 (12.12%)
occurrences (all)	21	23	34
Hypophosphataemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	10 / 162 (6.17%)	44 / 201 (21.89%)	42 / 198 (21.21%)
occurrences (all)	21	84	88
Hyperuricaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 162 (0.00%)	9 / 201 (4.48%)	13 / 198 (6.57%)
occurrences (all)	0	28	20

Non-serious adverse events	Open Label Extension: Placebo + Azacitidine	Open Label Extension: Glasdegib + Azacitidine	Non-intensive Study: Placebo + Azacitidine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 5 (60.00%)	6 / 9 (66.67%)	149 / 160 (93.13%)
Vascular disorders			
Hypotension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Hypertension	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	23 / 160 (14.38%)
occurrences (all)	0	0	32
Oedema peripheral	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	18 / 160 (11.25%)
occurrences (all)	1	0	25
Pyrexia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	39 / 160 (24.38%)
occurrences (all)	0	0	65
Asthenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	18 / 160 (11.25%)
occurrences (all)	0	0	40
Chills	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Mucosal inflammation	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain	Additional description: General disorders and administration site conditions		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Oedema	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Injection site reaction	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	7 / 160 (4.38%)
occurrences (all)	0	0	19
Respiratory, thoracic and mediastinal disorders			
Cough	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	20 / 160 (12.50%)
occurrences (all)	0	0	26
Dyspnoea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	18 / 160 (11.25%)
occurrences (all)	0	0	25
Epistaxis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	10 / 160 (6.25%)
occurrences (all)	0	0	14
Oropharyngeal pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	8 / 160 (5.00%)
occurrences (all)	0	0	13
Investigations			
Alanine aminotransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	11 / 160 (6.88%)
occurrences (all)	0	0	20
Aspartate aminotransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	9 / 160 (5.63%)
occurrences (all)	0	0	20
Blood creatinine increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	13 / 160 (8.13%)
occurrences (all)	0	0	15
Electrocardiogram QT prolonged	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	19 / 160 (11.88%)
occurrences (all)	0	0	33
Neutrophil count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	22 / 160 (13.75%)
occurrences (all)	0	0	153
Platelet count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	26 / 160 (16.25%)
occurrences (all)	1	0	162
Weight decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	19 / 160 (11.88%)
occurrences (all)	0	0	36
White blood cell count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	18 / 160 (11.25%)
occurrences (all)	0	0	143
Gamma-glutamyltransferase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	8 / 160 (5.00%)
occurrences (all)	0	0	13
Blood bilirubin increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count decreased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	9 / 160 (5.63%)
occurrences (all)	0	2	20
Injury, poisoning and procedural complications			

Fall	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	10 / 160 (6.25%)
occurrences (all)	0	1	11
Cardiac disorders			
Sinus tachycardia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	9 / 160 (5.63%)
occurrences (all)	0	0	20
Dizziness	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	14 / 160 (8.75%)
occurrences (all)	0	0	24
Dysgeusia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	8 / 160 (5.00%)
occurrences (all)	0	0	8
Paraesthesia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Carotid arteriosclerosis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	70 / 160 (43.75%)
occurrences (all)	0	2	335
Febrile neutropenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	20 / 160 (12.50%)
occurrences (all)	0	0	37
Neutropenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	2 / 5 (40.00%)	4 / 9 (44.44%)	30 / 160 (18.75%)
occurrences (all)	3	14	120
Thrombocytopenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	32 / 160 (20.00%)
occurrences (all)	0	2	123
Leukopenia	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	4 / 160 (2.50%)
occurrences (all)	0	0	10
Eye disorders			
Retinal detachment	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Abdominal pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	10 / 160 (6.25%)
occurrences (all)	0	0	12
Constipation	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	50 / 160 (31.25%)
occurrences (all)	0	0	69
Diarrhoea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	31 / 160 (19.38%)
occurrences (all)	0	4	46
Haemorrhoids	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	10 / 160 (6.25%)
occurrences (all)	0	0	10
Nausea	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	44 / 160 (27.50%)
occurrences (all)	0	0	70
Vomiting	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	32 / 160 (20.00%)
occurrences (all)	0	1	44
Proctalgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Dyspepsia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Stomatitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Colitis	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Colitis ulcerative	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Inguinal hernia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Hepatobiliary disorders			
Hyperbilirubinaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Alopecia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	3 / 160 (1.88%)
occurrences (all)	0	1	3
Rash	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	13 / 160 (8.13%)
occurrences (all)	0	0	16
Pruritus	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	9 / 160 (5.63%)
occurrences (all)	0	0	9
Dry skin	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Petechiae	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	11 / 160 (6.88%)
occurrences (all)	0	1	20
Back pain	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	1 / 5 (20.00%)	0 / 9 (0.00%)	12 / 160 (7.50%)
occurrences (all)	1	0	15
Muscle spasms	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	4 / 160 (2.50%)
occurrences (all)	0	0	4
Myalgia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Joint swelling	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Urinary tract infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	9 / 160 (5.63%)
occurrences (all)	0	0	11
Pneumonia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	15 / 160 (9.38%)
occurrences (all)	0	0	19
Upper respiratory tract infection	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	11 / 160 (6.88%)
occurrences (all)	0	0	11
Bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0
Corynebacterium bacteraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
SARS-CoV-2 test positive	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Epstein-Barr virus infection reactivation	Additional description: MedDRA 25.1 was used for open label extension cohort.		

subjects affected / exposed	0 / 5 (0.00%)	1 / 9 (11.11%)	0 / 160 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	21 / 160 (13.13%)
occurrences (all)	0	0	32
Hyperglycaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	9 / 160 (5.63%)
occurrences (all)	0	0	19
Hypoalbuminaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	13 / 160 (8.13%)
occurrences (all)	0	0	28
Hypocalcaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	13 / 160 (8.13%)
occurrences (all)	0	0	32
Hypokalaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	22 / 160 (13.75%)
occurrences (all)	0	0	42
Hypomagnesaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	5 / 160 (3.13%)
occurrences (all)	0	0	6
Hyponatraemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	9 / 160 (5.63%)
occurrences (all)	0	0	19
Hypophosphataemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	15 / 160 (9.38%)
occurrences (all)	0	0	30
Hyperuricaemia	Additional description: MedDRA 25.1 was used for open label extension cohort.		
subjects affected / exposed	0 / 5 (0.00%)	0 / 9 (0.00%)	0 / 160 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 November 2017	In schedule of activities of Intenstive study, pregnancy testing added for Day 1 of each Consolidation Cycle with single-agent cytarabine and Day 1 of each cycle where single-agent glasdegib/placebo administered to ensure appropriate safety monitoring.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Inadvertently 1 subject was enrolled twice into the study resulting in enrollment number as 744. However, a total of 743 subject were randomized and received treatment in the study.

Notes: