Clinical trial results:
A Phase I/II, open-label multicenter study to determine safety, pharmacokinetics and efficacy of GMI-1271 in combination with chemotherapy in patients with acute myeloid leukemia

Summary

EudraCT number	2014-002448-42
Trial protocol	IE
Global end of trial date	15 May 2018

Results information

Result version number	v1 (current)
This version publication date	14 October 2021
First version publication date	14 October 2021

Trial information

Trial identification

Sponsor protocol code	GMI-1271-201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02306291
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlycoMimetics Inc.
Sponsor organisation address	9708 Medical Center Dr, Rockville, Maryland, United States, 20850
Public contact	Eric Feldman, GlycoMimetics Inc., +1 301-417-4269, efeldman@glycomimetics.com
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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	17 September 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the safety of uproleselan (GMI-1271) in combination with chemotherapy. The secondary objectives of the study were to characterize the pharmacokinetic (PK) profile of GMI-1271; to evaluate the efficacy of GMI-1271 in combination with chemotherapy (relapsed/refractory [R/R] subjects: MEC; treatment-naïve subjects: "7+3" cytarabine/idarubicin) as measured by overall response rate (ORR), i.e., complete response (CR) and CR with incomplete blood count recovery (CRi); to evaluate the Time to response (TTR), duration of response (DOR), event-free survival (EFS), and 6-month and 12-month Overall Survival (OS) probability.

Protection of trial subjects:

The study was conducted in accordance with the protocol and the ethical principles derived from the Declaration of Helsinki and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Guideline of GCP pertinent to the safety of trial subjects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 May 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Ireland: 3
Country: Number of subjects enrolled	Australia: 5
Country: Number of subjects enrolled	United States: 83
Worldwide total number of subjects	91
EEA total number of subjects	3

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	57
From 65 to 84 years	31
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

This multicenter study in the United States,Australia and Ireland started on 15 May 2015 and completed on 15 May 2018. Total 91 adult participants were enrolled in this 2 phase study with either relapsed/refractory (R/R) acute myeloid leukemia (AML) in >/=18 years or newly diagnosed AML in >/=60 years participants, of whom 7 completed the study.

Pre-assignment

Screening details:

Participants with R/R AML got Mitoxantrone,Etoposide and Cytarabine (MEC) chemotherapy with GMI-1271 (5,10,and 20 milligrams per kilogram (mg/kg) in Phase 1,and 10 mg/kg thereafter as recommended Phase 2 dose [RP2D]).Participants with newly diagnosed AML in Phase 2 got "7+3" cytarabine/idarubicin induction chemotherapy along with GMI-1271 10 mg/kg.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC

Arm description:

GMI-1271 5, 10, and 20 mg/kg in Dose-escalation of Phase 1 and GMI-1271 10 mg/kg as RP2D in combination with MEC chemotherapy regimen were given in induction of Phase 1 and both induction and consolidation cycles of Phase 2 until disease progression (PD), unacceptable toxicity or study drug discontinuation.GMI-1271 first dose was given intravenously (IV) on Day (d) 1, 24 hours (h) before first dose of either induction or consolidation cycles, then GMI-1271 was given every 12 h± 1 h on chemotherapy days, starting 2 hours before chemotherapy and additional 2 days following the last dose of chemotherapy in adult participants (>/=18 years) with R/R AML. Combination chemotherapy included: Mitoxantrone 10 milligrams per meter square per day (mg/m^2/d) IV over 15 to 20 minutes; Etoposide 100 mg/m^2/d IV over 60 minutes; and Cytarabine 1000 mg/m^2/d IV over 60 minutes for 5 days in induction (first course of treatment) and for 4 days in consolidation (second course of treatment).

Arm type	Experimental
Investigational medicinal product name	GMI-1271
Investigational medicinal product code	
Other name	Uproleselan
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

GMI-1271 was administered in Dose-escalation of Phase 1 in the induction of Phase 1 and both induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity, or study drug discontinuation as per the scheduled dosing regimen.

Investigational medicinal product name	Mitoxantrone
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Mitoxantrone was administered as part of MEC chemotherapy, given in induction of Phase 1 and both induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity, or study drug discontinuation as per the scheduled dosing regimen.

Investigational medicinal product name	Etoposide
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Etoposide was administered as part of MEC chemotherapy, given in induction of Phase 1 and both induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity, or study drug discontinuation as per the scheduled dosing regimen.

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Cytarabine was administered as part of MEC chemotherapy, given in induction of Phase 1 and both induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity, or study drug discontinuation as per the scheduled dosing regimen.

Arm title	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"

Arm description:

GMI-1271 10 mg/kg in combination with "7+3" Cytarabine/Idarubicin chemotherapy was given in induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity or study drug discontinuation.GMI-1271 10 mg/kg IV first dose was given on d1,24 hours(h) before first dose of either induction or consolidation chemotherapy,then GMI-1271 10 mg/kg was given every 12±1h on chemotherapy days,starting 2 h before chemotherapy and additional 2d following the last dose of chemotherapy in participants (>/=60 years) with newly diagnosed AML.Combination chemotherapy included:Cytarabine 200 mg/m^2 continuous infusion for 7d with idarubicin 12 mg/m^2 for 3d ("7+3") for 1 induction cycle (first treatment course);Cytarabine 200 mg/m^2 continuous infusion for 5d with idarubicin 12 mg/m^2 for 2d ("5+2") for reinduction;and either Cytarabine 2 g/m^2/d IV over 3h for 5 d or Cytarabine 1.5 g/m^2/d IV over 3h twice daily every other d (EOD) for up to 3 consolidation cycles during third treatment course

Arm type	Experimental
Investigational medicinal product name	GMI-1271
Investigational medicinal product code	
Other name	Uproleselan
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

GMI-1271 was administered in both induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity, or study drug discontinuation as per the scheduled dosing regimen.

Investigational medicinal product name	Cytarabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Cytarabine was administered as part of "7+3" Cytarabine/Idarubicin chemotherapy, given in both induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity, or study drug discontinuation as per the scheduled dosing regimen.

Investigational medicinal product name	Idarubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Idarubicin was administered as part of "7+3" Cytarabine/Idarubicin chemotherapy, given in both

induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity, or study drug discontinuation as per the scheduled dosing regimen.

Number of subjects in period 1	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"
Started	66	25
Completed	5	2
Not completed	61	23
Death	46	14
Not Specified	14	9
Non-compliance	1	-

Baseline characteristics

Reporting groups

Reporting group title	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC

Reporting group description:

GMI-1271 5, 10, and 20 mg/kg in Dose-escalation of Phase 1 and GMI-1271 10 mg/kg as RP2D in combination with MEC chemotherapy regimen were given in induction of Phase 1 and both induction and consolidation cycles of Phase 2 until disease progression (PD), unacceptable toxicity or study drug discontinuation.GMI-1271 first dose was given intravenously (IV) on Day (d) 1, 24 hours (h) before first dose of either induction or consolidation cycles, then GMI-1271 was given every 12 h± 1 h on chemotherapy days, starting 2 hours before chemotherapy and additional 2 days following the last dose of chemotherapy in adult participants (>/=18 years) with R/R AML. Combination chemotherapy included: Mitoxantrone 10 milligrams per meter square per day (mg/m^2/d) IV over 15 to 20 minutes; Etoposide 100 mg/m^2/d IV over 60 minutes; and Cytarabine 1000 mg/m^2/d IV over 60 minutes for 5 days in induction (first course of treatment) and for 4 days in consolidation (second course of treatment).

Reporting group title	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"

Reporting group description:

GMI-1271 10 mg/kg in combination with "7+3" Cytarabine/Idarubicin chemotherapy was given in induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity or study drug discontinuation.GMI-1271 10 mg/kg IV first dose was given on d1,24 hours(h) before first dose of either induction or consolidation chemotherapy,then GMI-1271 10 mg/kg was given every 12±1h on chemotherapy days,starting 2 h before chemotherapy and additional 2d following the last dose of chemotherapy in participants (>/=60 years) with newly diagnosed AML.Combination chemotherapy included:Cytarabine 200 mg/m^2 continuous infusion for 7d with idarubicin 12 mg/m^2 for 3d ("7+3") for 1 induction cycle (first treatment course);Cytarabine 200 mg/m^2 continuous infusion for 5d with idarubicin 12 mg/m^2 for 2d ("5+2") for reinduction;and either Cytarabine 2 g/m^2/d IV over 3h for 5 d or Cytarabine 1.5 g/m^2/d IV over 3h twice daily every other d (EOD) for up to 3 consolidation cycles during third treatment course

Reporting group values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	Total
Number of subjects	66	25	91
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)	49	8	57
From 65-84 years	15	16	31
85 years and over	2	1	3
Gender categorical Units: Subjects			
Female	25	11	36
Male	41	14	55
Race/Ethnicity Units: Subjects			
American Indian or Alaskan Native	0	0	0

Asian	0	0	0
Black or African American	5	1	6
Native Hawaiian or other Pacific Islander	1	0	1
White	53	20	73
Other	2	1	3
Not Reported or Missing	5	3	8
Region of Enrollment Units: Subjects			
United States	59	24	83
Ireland	3	0	3
Australia	4	1	5

End points

End points reporting groups

Reporting group title	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC

Reporting group description:

GMI-1271 5, 10, and 20 mg/kg in Dose-escalation of Phase 1 and GMI-1271 10 mg/kg as RP2D in combination with MEC chemotherapy regimen were given in induction of Phase 1 and both induction and consolidation cycles of Phase 2 until disease progression (PD), unacceptable toxicity or study drug discontinuation.GMI-1271 first dose was given intravenously (IV) on Day (d) 1, 24 hours (h) before first dose of either induction or consolidation cycles, then GMI-1271 was given every 12 h± 1 h on chemotherapy days, starting 2 hours before chemotherapy and additional 2 days following the last dose of chemotherapy in adult participants (>/=18 years) with R/R AML. Combination chemotherapy included: Mitoxantrone 10 milligrams per meter square per day (mg/m^2/d) IV over 15 to 20 minutes; Etoposide 100 mg/m^2/d IV over 60 minutes; and Cytarabine 1000 mg/m^2/d IV over 60 minutes for 5 days in induction (first course of treatment) and for 4 days in consolidation (second course of treatment).

Reporting group title	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + “7+3”

Reporting group description:

GMI-1271 10 mg/kg in combination with "7+3" Cytarabine/Idarubicin chemotherapy was given in induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity or study drug discontinuation.GMI-1271 10 mg/kg IV first dose was given on d1,24 hours(h) before first dose of either induction or consolidation chemotherapy,then GMI-1271 10 mg/kg was given every 12±1h on chemotherapy days,starting 2 h before chemotherapy and additional 2d following the last dose of chemotherapy in participants (>/=60 years) with newly diagnosed AML.Combination chemotherapy included:Cytarabine 200 mg/m^2 continuous infusion for 7d with idarubicin 12 mg/m^2 for 3d ("7+3") for 1 induction cycle (first treatment course);Cytarabine 200 mg/m^2 continuous infusion for 5d with idarubicin 12 mg/m^2 for 2d ("5+2") for reinduction;and either Cytarabine 2 g/m^2/d IV over 3h for 5 d or Cytarabine 1.5 g/m^2/d IV over 3h twice daily every other d (EOD) for up to 3 consolidation cycles during third treatment course

Subject analysis set title	Intent to treat (ITT)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

ITT population included all participants who received at least one infusion of GMI-1271.

Subject analysis set title	Safety population
Subject analysis set type	Safety analysis

Subject analysis set description:

Safety population included all participants who received at least one infusion of GMI-1271.

Subject analysis set title	Phase 1 and 2: Arm A + Arm B
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Combined analysis of both group (Relapsed/Refractory [Phase 1 and 2 Arm A]: GMI-1271 + MEC; Newly Diagnosed [Phase 2 Arm B]: GMI- 1271 10 mg/kg + “7+3”) sequences.

Subject analysis set title	Response population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Response population consists of the subset of the ITT population that achieved documented CR or CRi.

Subject analysis set title	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

GMI-1271 10 mg/kg in Dose-escalation of Phase 1 and then GMI-1271 10 mg/kg as RP2D in combination with MEC chemotherapy regimen were given in induction of Phase 1 and both induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity or study drug discontinuation. GMI-1271 first IV dose was given on d 1, 24 hours before first dose of either induction or consolidation cycles, then GMI-1271 was given every 12 hours ± 1 hour on chemotherapy days, starting 2 hours before chemotherapy and additional 2 days following the last dose of chemotherapy in adult participants (>/=18 years) with R/R AML. Combination chemotherapy included: Mitoxantrone 10 milligrams per meter square per day (mg/m^2/d) IV over 15 to 20 minutes; Etoposide 100 mg/m^2/d IV over 60

minutes; and Cytarabine 1000 mg/m^2/d IV over 60 minutes for 5 days in induction (first course of treatment) and for 4 days in consolidation (second course of treatment).

Primary: Number of Participants With Treatment-Emergent Adverse Events (AEs)

End point title	Number of Participants With Treatment-Emergent Adverse Events (AEs)[1]

End point description:

An AE was any untoward medical occurrence in a participant who received study drug, which does not necessarily have a causal relationship with this treatment. Treatment-emergent AEs (TEAEs) are defined as any event not present prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments. The safety population included all participants who received at least one infusion of GMI-1271.

End point type	Primary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not planned in the protocol for this measure thereby only descriptive analysis is reported.

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	66	25	54	
Units: subjects	66	25	54	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Treatment-Related AEs

End point title	Number of Participants With Treatment-Related AEs[2]

End point description:

An AE was any untoward medical occurrence in a participant who received study drug, which does not necessarily have a causal relationship with this treatment. Treatment-emergent AEs (TEAEs) are defined as any event not present prior to the initiation of the treatments or any event already present that worsens in either intensity or frequency following exposure to the treatments. A treatment-related AE is any untoward medical occurrence attributed to study drug in a participant who received study drug. The safety population included all participants who received at least one infusion of GMI-1271.

End point type	Primary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not planned in the protocol for this measure thereby only descriptive analysis is reported.

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	66	25	54	
Units: subjects	36	16	29	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Serious Adverse Events (SAEs)

End point title	Number of Participants With Serious Adverse Events (SAEs)[3]

End point description:

An SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; birth defect. The safety population included all participants who received at least one infusion of GMI-1271.

End point type	Primary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

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: Statistical analysis was not planned in the protocol for this measure thereby only descriptive analysis is reported.

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	66	25	54	
Units: subjects	23	9	18	

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With AEs According to Severity as Assessed by Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03

End point title	Number of Participants With AEs According to Severity as Assessed by Common Terminology Criteria for Adverse Events (CTCAE) Version 4.03[4]

End point description:

AE: Any untoward medical occurrence in a participant who received study drug, which does not necessarily have a causal relationship with this treatment.Severity of AE were graded in the following

categories per CTCAE grading criteria:1=mild (the AE was of little concern to the participants and was not expected to have any effect on the participant's health or well-being),2=moderate (the participant had enough discomfort to cause interference with or change in usual activities.The AE was of some concern to the participant's health or well-being and may have required medical intervention),3=severe(The participant was incapacitated and unable to work or participate in many or all usual activities.The AE was of definite concern to the participant and/or poses substantial risk to the participant's health or well-being.The event was likely to require medical intervention and/or close follow-up.),4=life threatening (Life-threatening consequences; urgent intervention indicated) and

End point type	Primary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Statistical analysis was not planned in the protocol for this measure thereby only descriptive analysis is reported.

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	66	25	54	
Units: subjects				
Mild	1	0	1	
Moderate	3	0	3	
Severe	19	8	15	
Life threatening	43	15	35	
Fatal	0	2	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve From Time Zero to Extrapolated Infinite Time (AUCinf)

End point title	Area Under the Curve From Time Zero to Extrapolated Infinite Time (AUCinf)

End point description:

AUCinf= Area under the plasma concentration versus time curve (AUC) from time zero (pre-dose) to extrapolated infinite time (0 - inf). It is obtained from AUC (0 - t) plus AUC (t - inf). The PK analysis population consists of all enrolled participants who have at least one infusion of GMI-1271 and one sample providing evaluable PK data.

End point type	Secondary

End point timeframe:

5 minutes(M) pre-dose,20 m,40 m,hours(H)1.5,3,6,12 post-dose on Days(D) 1,3,8(R/R AML participants[P]),and 10 (newly diagnosed AML P);12 H and 36 H post-last dose on D 9 and 10(R/R AML P);12 H and 36 H post-last dose on D 10 and 12 (newly diagnosed AML P)

End point values	Phase 1 and 2: Arm A + Arm B			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: day*micrograms/milliliters (day*mcg/mL)				
arithmetic mean (standard deviation)	5.95 (± 3.079)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Observed Plasma Concentration (Cmax) of GMI-1271

End point title	Maximum Observed Plasma Concentration (Cmax) of GMI-1271

End point description:

The PK analysis population consists of all enrolled participants who have at least one infusion of GMI-1271 and one sample providing evaluable PK data.

End point type	Secondary

End point timeframe:

5 minutes(M) pre-dose,20 m,40 m,hours(H)1.5,3,6,12 post-dose on Days(D) 1,3,8(R/R AML participants[P]),and 10 (newly diagnosed AML P);12 H and 36 H post-last dose on D 9 and 10(R/R AML P);12 H and 36 H post-last dose on D 10 and 12 (newly diagnosed AML P)

End point values	Phase 1 and 2: Arm A + Arm B			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: mcg/mL				
arithmetic mean (standard deviation)	78.94 (± 83.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Terminal Elimination Half-Life (t1/2) of GMI-1271

End point title	Terminal Elimination Half-Life (t1/2) of GMI-1271

End point description:

Terminal elimination half-life (t1/2) is the time measured for the plasma concentration to decrease by one half. The PK analysis population consists of all enrolled participants who have at least one infusion of GMI-1271 and one sample providing evaluable PK data.

End point type	Secondary

End point timeframe:

5 minutes(M) pre-dose,20 m,40 m,hours(H)1.5,3,6,12 post-dose on Days(D) 1,3,8(R/R AML participants[P]),and 10 (newly diagnosed AML P);12 H and 36 H post-last dose on D 9 and 10(R/R AML P);12 H and 36 H post-last dose on D 10 and 12 (newly diagnosed AML P)

End point values	Phase 1 and 2: Arm A + Arm B			
Subject group type	Subject analysis set			
Number of subjects analysed	59			
Units: days				
median (full range (min-max))	0.18 (0.0925 to 4.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

The percentage of participants who achieved a complete remission (CR) or complete remission with incomplete recovery (CRi). CR required the following criteria to be achieved prior to alternative therapy: Bone marrow blasts <5%; absolute neutrophil count (ANC) >/=1.0*109/L; and Platelets >/=100*109/L. CRi was defined as CR but failing to meet either platelet or ANC recovery. The Response population consists of the subset of the ITT population that achieved documented CR or CRi.

End point type	Secondary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	26	18	22	
Units: Percentage of subjects				
number (not applicable)				
Complete Remission (CR)	33	52	35	
Complete Remission with incomplete recovery (CRi)	6	20	6	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR is the time from date of first documented remission (first of CR or CRi) to the date of relapse or death from any cause, whichever occurs first. CR required the following criteria to be achieved prior to alternative therapy: Bone marrow blasts <5%; absolute neutrophil count (ANC) >/=1.0*109/L; and Platelets >/=100*109/L. CRi was defined as CR but failing to meet either platelet or ANC recovery. '99999' stands for data not available, as participants were still alive at the time of Database lock so this data was not collected. The Greenwood method was used to determine 90% confidence interval about median. The Response population consists of the subset of the ITT population that achieved documented CR or CRi.

End point type	Secondary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	26	18	22	
Units: Months				
median (confidence interval 90%)	8.7 (6.0 to 16.4)	10.5 (7.1 to 19.4)	9.5 (6.3 to 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Response (TTR)

End point title	Time To Response (TTR)

End point description:

TTR is the time from date of first dose to first documented remission (first of CR or CRi). CR required the following criteria to be achieved prior to alternative therapy: Bone marrow blasts <5%; absolute neutrophil count (ANC) >/=1.0*109/L; and Platelets >/=100*109/L. CRi was defined as CR but failing to meet either platelet or ANC recovery. Data for this outcome measure is not reported as TTR was omitted from the study objectives per the changes in the planned analysis of the study, and thereby not analyzed.

End point type	Secondary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[5]	0[6]		
Units: days				
median (full range (min-max))	(to)	(to)		

Notes:

[5] - TTR was not analyzed as per changes in the planned analysis.

[6] - TTR was not analyzed as per changes in the planned analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Event-free Survival (EFS)

End point title	Event-free Survival (EFS)

End point description:

EFS is the time from date of first dose of chemotherapy to the date of treatment failure, relapse, or death from any cause, whichever occurs first. The Greenwood method was used to determine 90% confidence interval about median. The ITT population included all participants who received at least one infusion of GMI-1271.

End point type	Secondary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	66	25	54	
Units: Months				
median (full range (min-max))	1.4 (1.3 to 1.8)	9.2 (3.3 to 12.2)	1.5 (1.3 to 1.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Probability of OS at 6 and 12 Months

End point title	Probability of OS at 6 and 12 Months

End point description:

OS is the time from date of first dose to the date of death from any cause. Percentage of participants with survival at 6 months and 12 months after the date of first dose of chemotherapy was reported. The Greenwood method was used to determine 90% confidence interval. The ITT population included all

participants who received at least one infusion of GMI-1271.

End point type	Secondary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	66	25	54	
Units: Percentage of subjects				
number (confidence interval 90%)				
At 6-months	56.06 (43.3 to 67.0)	76.00 (54.2 to 88.4)	57.41 (43.2 to 69.3)	
At 12-months	36.36 (25.0 to 47.8)	52.00 (31.2 to 69.2)	37.04 (24.4 to 49.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

OS is the time from date of first dose to the date of death from any cause. The Greenwood method was used to determine 90% confidence interval. '99999' stands for data not available, as participants were still alive at the time of Database lock so this data was not collected. The ITT population included all participants who received at least one infusion of GMI-1271.

End point type	Secondary

End point timeframe:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

End point values	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI- 1271 10 mg/kg + "7+3"	RP2D GMI-1271 10mg + MEC (Phase 1 and 2 Arm A)	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	66	25	54	
Units: months				
median (confidence interval 90%)	8.1 (5.7 to 10.7)	12.6 (10.3 to 99999)	8.8 (5.8 to 10.8)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to safety evaluation completion visit (30 days after the last dose of study drug)

Adverse event reporting additional description:

Safety population included all participants who received at least one infusion of GMI-1271.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC

Reporting group description:

GMI-1271 5, 10, and 20 mg/kg in Dose-escalation of Phase 1 and GMI-1271 10 mg/kg as RP2D in combination with MEC chemotherapy regimen were given in induction of Phase 1 and both induction and consolidation cycles of Phase 2 until disease progression (PD), unacceptable toxicity or study drug discontinuation.GMI-1271 first dose was given intravenously (IV) on Day (d) 1, 24 hours before first dose of either induction or consolidation cycles, then GMI-1271 was given every 12 hours ± 1 hour on chemotherapy days, starting 2 hours before chemotherapy and additional 2 days following the last dose of chemotherapy in adult participants (>/=18 years) with R/R AML. Combination chemotherapy included: Mitoxantrone 10 milligrams per meter square per day (mg/m^2/d) IV over 15 to 20 minutes; Etoposide 100 mg/m^2/d IV over 60 minutes; and Cytarabine 1000 mg/m^2/d IV over 60 minutes for 5 days in induction (first course of treatment) and for 4 days in consolidation (second course of treatment).

Reporting group title	Newly Diagnosed (Phase 2 Arm B): GMI-1271 10 mg/kg + "7+3"

Reporting group description:

GMI-1271 10 mg/kg in combination with "7+3" Cytarabine/Idarubicin chemotherapy was given in induction and consolidation cycles of Phase 2 until PD, unacceptable toxicity or study drug discontinuation.GMI-1271 10 mg/kg IV first dose was given on d1,24 hours(h) before first dose of either induction or consolidation chemotherapy,then GMI-1271 10 mg/kg was given every 12±1h on chemotherapy days,starting 2 h before chemotherapy and additional 2d following the last dose of chemotherapy in participants (>/=60 years) with newly diagnosed AML.Combination chemotherapy included:Cytarabine 200 mg/m^2 continuous infusion for 7d with idarubicin 12 mg/m^2 for 3d ("7+3") for 1 induction cycle (first treatment course);Cytarabine 200 mg/m^2 continuous infusion for 5d with idarubicin 12 mg/m^2 for 2d ("5+2") for reinduction;and either Cytarabine 2 g/m^2/d IV over 3h for 5 d or Cytarabine 1.5 g/m^2/d IV over 3h twice daily every other d (EOD) for up to 3 consolidation cycles during third treatment course

Serious adverse events	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI-1271 10 mg/kg + "7+3"	
Total subjects affected by serious adverse events			
subjects affected / exposed	23 / 66 (34.85%)	9 / 25 (36.00%)	
number of deaths (all causes)	0	2	
number of deaths resulting from adverse events	0	0	
Cardiac disorders			
Cardiac arrest			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	7 / 66 (10.61%)	2 / 25 (8.00%)	
occurrences causally related to treatment / all	0 / 11	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			

subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver disorder			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pulmonary oedema			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clostridial infection			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterobacter sepsis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 66 (4.55%)	2 / 25 (8.00%)	
occurrences causally related to treatment / all	1 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatococcal infection			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic mycosis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypernatraemia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Relapsed/Refractory (Phase 1 and 2 Arm A): GMI-1271 + MEC	Newly Diagnosed (Phase 2 Arm B): GMI-1271 10 mg/kg + "7+3"	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	66 / 66 (100.00%)	25 / 25 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Renal neoplasm			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Thyroid neoplasm			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Flushing			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Haematoma			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Hypertension			
subjects affected / exposed	6 / 66 (9.09%)	3 / 25 (12.00%)	
occurrences (all)	6	4	
Hypotension			
subjects affected / exposed	16 / 66 (24.24%)	5 / 25 (20.00%)	
occurrences (all)	16	5	
Orthostatic hypotension			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Peripheral venous disease			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Thrombophlebitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	8 / 66 (12.12%)	3 / 25 (12.00%)	
occurrences (all)	8	3	
Catheter site erythema			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Catheter site haematoma			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Catheter site haemorrhage			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Catheter site inflammation			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Catheter site pain			
subjects affected / exposed	1 / 66 (1.52%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Catheter site swelling			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Catheter site vesicles			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Chest discomfort			
subjects affected / exposed	1 / 66 (1.52%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Chest pain			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Chills			
subjects affected / exposed	23 / 66 (34.85%)	9 / 25 (36.00%)	
occurrences (all)	25	11	
Device leakage			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	2	
Fatigue			
subjects affected / exposed	30 / 66 (45.45%)	15 / 25 (60.00%)	
occurrences (all)	39	18	
Gait disturbance			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Generalised oedema			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Hypothermia			

subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Infusion site extravasation			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Infusion site reaction			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Injection site rash			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Localised oedema			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Nodule			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Non-cardiac chest pain			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Oedema			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Oedema peripheral			
subjects affected / exposed	19 / 66 (28.79%)	14 / 25 (56.00%)	
occurrences (all)	23	17	
Pain			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Peripheral swelling			
subjects affected / exposed	1 / 66 (1.52%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Pyrexia			

subjects affected / exposed	12 / 66 (18.18%)	11 / 25 (44.00%)	
occurrences (all)	16	13	
Thrombosis in device			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Immune system disorders			
Graft versus host disease			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hypogammaglobulinaemia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Gynaecomastia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Penile oedema			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Perineal pain			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Peyronie's disease			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Scrotal oedema			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Scrotal pain			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Testicular swelling			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vaginal haemorrhage			

subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Vaginal lesion			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal discomfort			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vulvovaginal pruritus			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Atelectasis			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	12 / 66 (18.18%)	5 / 25 (20.00%)	
occurrences (all)	12	5	
Dysphonia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Dyspnoea			
subjects affected / exposed	11 / 66 (16.67%)	6 / 25 (24.00%)	
occurrences (all)	11	6	
Dyspnoea exertional			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Epistaxis			
subjects affected / exposed	10 / 66 (15.15%)	7 / 25 (28.00%)	
occurrences (all)	12	7	
Hiccups			

subjects affected / exposed	1 / 66 (1.52%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Nasal congestion			
subjects affected / exposed	3 / 66 (4.55%)	2 / 25 (8.00%)	
occurrences (all)	3	2	
Nasal discomfort			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Nasal dryness			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Nasal ulcer			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Oropharyngeal pain			
subjects affected / exposed	9 / 66 (13.64%)	4 / 25 (16.00%)	
occurrences (all)	10	5	
Paranasal sinus discomfort			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Pharyngeal inflammation			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	2	
Pharyngeal oedema			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Pleural effusion			
subjects affected / exposed	7 / 66 (10.61%)	2 / 25 (8.00%)	
occurrences (all)	7	2	
Pleuritic pain			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Productive cough			
subjects affected / exposed	1 / 66 (1.52%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Pulmonary mass			

subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Pulmonary oedema			
subjects affected / exposed	5 / 66 (7.58%)	3 / 25 (12.00%)	
occurrences (all)	5	3	
Rales			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Respiratory distress			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Respiratory failure			
subjects affected / exposed	1 / 66 (1.52%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Rhinitis allergic			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Rhinorrhoea			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Sinus congestion			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Sneezing			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Tachypnoea			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Throat irritation			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Wheezing			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hypoxia			
subjects affected / exposed	10 / 66 (15.15%)	4 / 25 (16.00%)	
occurrences (all)	11	4	
Psychiatric disorders			
Abnormal dreams			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Agitation			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Anxiety			
subjects affected / exposed	7 / 66 (10.61%)	5 / 25 (20.00%)	
occurrences (all)	8	5	
Confusional state			
subjects affected / exposed	6 / 66 (9.09%)	6 / 25 (24.00%)	
occurrences (all)	7	6	
Delirium			
subjects affected / exposed	1 / 66 (1.52%)	4 / 25 (16.00%)	
occurrences (all)	1	4	
Depression			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Depression suicidal			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Frustration			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hallucination			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	

Insomnia			
subjects affected / exposed	21 / 66 (31.82%)	4 / 25 (16.00%)	
occurrences (all)	21	4	
Irritability			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Mental status changes			
subjects affected / exposed	1 / 66 (1.52%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Personality change			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Suicidal ideation			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Investigations			
Clostridium difficile infection			
subjects affected / exposed	4 / 66 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Alanine aminotransferase increased			
subjects affected / exposed	8 / 66 (12.12%)	1 / 25 (4.00%)	
occurrences (all)	9	2	
Aspartate aminotransferase increased			
subjects affected / exposed	5 / 66 (7.58%)	2 / 25 (8.00%)	
occurrences (all)	5	5	
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 66 (1.52%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Blood creatinine increased			
subjects affected / exposed	5 / 66 (7.58%)	0 / 25 (0.00%)	
occurrences (all)	7	0	
Blood fibrinogen decreased			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Blood lactate dehydrogenase increased			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Blood pressure increased			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Blood pressure orthostatic abnormal			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Body temperature increased			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Breath sounds abnormal			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Chest X-ray abnormal			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Ejection fraction decreased			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	6 / 66 (9.09%)	2 / 25 (8.00%)	
occurrences (all)	7	2	
Face and mouth X-ray abnormal			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Gastric occult blood positive			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Heart rate irregular			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
International normalised ratio			

increased			
subjects affected / exposed	4 / 66 (6.06%)	4 / 25 (16.00%)	
occurrences (all)	4	4	
Liver function test abnormal			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Lymphocyte count decreased			
subjects affected / exposed	4 / 66 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	8	1	
Neutrophil count decreased			
subjects affected / exposed	5 / 66 (7.58%)	5 / 25 (20.00%)	
occurrences (all)	12	8	
Oxygen saturation decreased			
subjects affected / exposed	2 / 66 (3.03%)	3 / 25 (12.00%)	
occurrences (all)	6	3	
Platelet count decreased			
subjects affected / exposed	12 / 66 (18.18%)	6 / 25 (24.00%)	
occurrences (all)	35	26	
Prothrombin time prolonged			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vitamin D decreased			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Weight decreased			
subjects affected / exposed	7 / 66 (10.61%)	0 / 25 (0.00%)	
occurrences (all)	7	0	
Weight increased			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
White blood cell count decreased			
subjects affected / exposed	7 / 66 (10.61%)	5 / 25 (20.00%)	
occurrences (all)	18	11	
White blood cell count increased			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	

Blood bilirubin increased			
subjects affected / exposed	2 / 66 (3.03%)	5 / 25 (20.00%)	
occurrences (all)	2	8	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Endotracheal intubation complication			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Eye contusion			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Feeding tube complication			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Head injury			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Infusion related reaction			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Laceration			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Periorbital haemorrhage			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Post procedural haematoma			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Post procedural haemorrhage			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Post procedural oedema			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Procedural haemorrhage			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	4 / 66 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Procedural site reaction			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Scratch			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Subcutaneous haematoma			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Transfusion reaction			
subjects affected / exposed	8 / 66 (12.12%)	2 / 25 (8.00%)	
occurrences (all)	11	3	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Atrioventricular block first degree			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Bradycardia			
subjects affected / exposed	8 / 66 (12.12%)	1 / 25 (4.00%)	
occurrences (all)	8	1	
Cardiac failure			
subjects affected / exposed	4 / 66 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	4	0	

Diastolic dysfunction			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Pericardial effusion			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Sinus bradycardia			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Sinus tachycardia			
subjects affected / exposed	4 / 66 (6.06%)	1 / 25 (4.00%)	
occurrences (all)	4	1	
Tachycardia			
subjects affected / exposed	7 / 66 (10.61%)	2 / 25 (8.00%)	
occurrences (all)	9	2	
Ventricular tachycardia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Lethargy			
subjects affected / exposed	2 / 66 (3.03%)	3 / 25 (12.00%)	
occurrences (all)	2	3	
Aphasia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Burning sensation			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Dizziness			
subjects affected / exposed	11 / 66 (16.67%)	3 / 25 (12.00%)	
occurrences (all)	12	3	
Dysarthria			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Dysgeusia			

subjects affected / exposed	6 / 66 (9.09%)	5 / 25 (20.00%)	
occurrences (all)	6	5	
Dyskinesia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Encephalopathy			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	17 / 66 (25.76%)	6 / 25 (24.00%)	
occurrences (all)	20	7	
Hypoaesthesia			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Mental impairment			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Parosmia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Partial seizures			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Sciatica			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Sinus headache			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Somnolence			

subjects affected / exposed	3 / 66 (4.55%)	3 / 25 (12.00%)	
occurrences (all)	4	3	
Syncope			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Tremor			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	20 / 66 (30.30%)	8 / 25 (32.00%)	
occurrences (all)	59	18	
Coagulopathy			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Eosinophilia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Febrile neutropenia			
subjects affected / exposed	34 / 66 (51.52%)	21 / 25 (84.00%)	
occurrences (all)	34	21	
Increased tendency to bruise			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Neutropenia			
subjects affected / exposed	11 / 66 (16.67%)	3 / 25 (12.00%)	
occurrences (all)	11	3	
Pancytopenia			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Thrombocytopenia			
subjects affected / exposed	23 / 66 (34.85%)	6 / 25 (24.00%)	
occurrences (all)	23	6	

Disseminated intravascular coagulation			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Cerumen impaction			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Ear discomfort			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Ear pain			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Ear pruritus			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Dry eye			
subjects affected / exposed	1 / 66 (1.52%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Erythema of eyelid			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Eye pain			
subjects affected / exposed	1 / 66 (1.52%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Eye swelling			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Ocular hyperaemia			

subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Ocular icterus			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Periorbital oedema			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Pupils unequal			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Retinal haemorrhage			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Vision blurred			
subjects affected / exposed	4 / 66 (6.06%)	4 / 25 (16.00%)	
occurrences (all)	4	4	
Visual impairment			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	4 / 66 (6.06%)	3 / 25 (12.00%)	
occurrences (all)	4	3	
Abdominal distension			
subjects affected / exposed	6 / 66 (9.09%)	8 / 25 (32.00%)	
occurrences (all)	6	8	
Abdominal pain			
subjects affected / exposed	17 / 66 (25.76%)	8 / 25 (32.00%)	
occurrences (all)	17	8	
Abdominal pain lower			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Abdominal pain upper			
subjects affected / exposed	5 / 66 (7.58%)	0 / 25 (0.00%)	
occurrences (all)	5	0	

Abdominal tenderness			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Anal fissure			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Anorectal discomfort			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Aphthous stomatitis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Ascites			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Cheilitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Coating in mouth			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Colitis			
subjects affected / exposed	5 / 66 (7.58%)	4 / 25 (16.00%)	
occurrences (all)	5	4	
Constipation			
subjects affected / exposed	26 / 66 (39.39%)	10 / 25 (40.00%)	
occurrences (all)	27	12	
Dental discomfort			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	45 / 66 (68.18%)	22 / 25 (88.00%)	
occurrences (all)	50	28	
Dry mouth			
subjects affected / exposed	3 / 66 (4.55%)	4 / 25 (16.00%)	
occurrences (all)	3	4	

Dyspepsia			
subjects affected / exposed	5 / 66 (7.58%)	2 / 25 (8.00%)	
occurrences (all)	5	2	
Dysphagia			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	3	2	
Enteritis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Enterocolitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Faeces discoloured			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Gastrointestinal disorder			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal oedema			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 66 (6.06%)	2 / 25 (8.00%)	
occurrences (all)	4	2	
Gingival pain			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Glossodynia			
subjects affected / exposed	4 / 66 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	4	0	

Haematemesis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Haematochezia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Haemorrhoids			
subjects affected / exposed	6 / 66 (9.09%)	2 / 25 (8.00%)	
occurrences (all)	6	2	
Hiatus hernia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Ileus			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Lip dry			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Lip haematoma			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Mouth ulceration			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Nausea			
subjects affected / exposed	41 / 66 (62.12%)	17 / 25 (68.00%)	
occurrences (all)	44	19	
Neutropenic colitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Odynophagia			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Oesophageal pain			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	

Oesophagitis			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Oral discomfort			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Oral disorder			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Oral mucosal blistering			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Oral pain			
subjects affected / exposed	5 / 66 (7.58%)	0 / 25 (0.00%)	
occurrences (all)	5	0	
Proctalgia			
subjects affected / exposed	0 / 66 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Retching			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Salivary hypersecretion			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Small intestinal obstruction			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Stomatitis			
subjects affected / exposed	18 / 66 (27.27%)	5 / 25 (20.00%)	
occurrences (all)	23	5	
Tongue dry			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Tongue ulceration			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	

Toothache			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	21 / 66 (31.82%)	11 / 25 (44.00%)	
occurrences (all)	23	12	
Catheter site pruritus			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Tongue discolouration			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hyperbilirubinaemia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Liver injury			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 66 (3.03%)	3 / 25 (12.00%)	
occurrences (all)	2	3	
Dermatitis acneiform			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Dermatitis bullous			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Drug eruption			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Blister			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Decubitus ulcer			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	4 / 66 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Ecchymosis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Hyperhidrosis			
subjects affected / exposed	1 / 66 (1.52%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Hypersensitivity vasculitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Macule			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Nail ridging			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Night sweats			
subjects affected / exposed	3 / 66 (4.55%)	2 / 25 (8.00%)	
occurrences (all)	3	2	
Palmar-plantar erythrodysaesthesia			

syndrome			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Papule			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Petechiae			
subjects affected / exposed	6 / 66 (9.09%)	2 / 25 (8.00%)	
occurrences (all)	6	3	
Pruritus			
subjects affected / exposed	7 / 66 (10.61%)	4 / 25 (16.00%)	
occurrences (all)	7	4	
Pruritus generalised			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Purpura			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Rash			
subjects affected / exposed	11 / 66 (16.67%)	8 / 25 (32.00%)	
occurrences (all)	11	13	
Rash erythematous			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Rash generalised			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Rash macular			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	4	1	
Rash maculo-papular			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	4	3	
Rash papular			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	

Rash pruritic			
subjects affected / exposed	1 / 66 (1.52%)	2 / 25 (8.00%)	
occurrences (all)	2	3	
Skin exfoliation			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Skin induration			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	2 / 66 (3.03%)	3 / 25 (12.00%)	
occurrences (all)	2	3	
Skin mass			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Skin ulcer			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Urticaria			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Palmar erythema			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Bladder spasm			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	5 / 66 (7.58%)	1 / 25 (4.00%)	
occurrences (all)	5	1	
Haematuria			

subjects affected / exposed	5 / 66 (7.58%)	3 / 25 (12.00%)	
occurrences (all)	5	3	
Micturition urgency			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Nocturia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	2	3	
Polyuria			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Proteinuria			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Renal failure acute			
subjects affected / exposed	9 / 66 (13.64%)	4 / 25 (16.00%)	
occurrences (all)	11	4	
Urinary incontinence			
subjects affected / exposed	6 / 66 (9.09%)	1 / 25 (4.00%)	
occurrences (all)	6	1	
Urinary retention			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 66 (12.12%)	2 / 25 (8.00%)	
occurrences (all)	8	2	
Back pain			
subjects affected / exposed	6 / 66 (9.09%)	2 / 25 (8.00%)	
occurrences (all)	7	3	
Bone pain			

subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Flank pain			
subjects affected / exposed	1 / 66 (1.52%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Fracture pain			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Groin pain			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Joint effusion			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Muscle twitching			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain			
subjects affected / exposed	5 / 66 (7.58%)	2 / 25 (8.00%)	
occurrences (all)	5	2	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	4 / 66 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Neck pain			

subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Pain in jaw			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Soft tissue necrosis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Infections and infestations			
Anal abscess			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Bacteraemia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Body tinea			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Catheter site cellulitis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Cellulitis			
subjects affected / exposed	5 / 66 (7.58%)	0 / 25 (0.00%)	
occurrences (all)	6	0	
Clostridium bacteraemia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 66 (1.52%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Device related infection			
subjects affected / exposed	4 / 66 (6.06%)	0 / 25 (0.00%)	
occurrences (all)	4	0	

Ecthyma			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Enterococcal bacteraemia			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Enterococcal infection			
subjects affected / exposed	2 / 66 (3.03%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Escherichia bacteraemia			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Escherichia sepsis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Folliculitis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Fungaemia			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Herpes dermatitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hordeolum			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Klebsiella bacteraemia			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Klebsiella sepsis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Lung infection			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	

Neutropenic sepsis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Onychomycosis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Oral candidiasis			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Periodontitis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Pneumonia			
subjects affected / exposed	2 / 66 (3.03%)	4 / 25 (16.00%)	
occurrences (all)	2	5	
Pneumonia legionella			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Pyelonephritis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Respiratory moniliasis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Sepsis			
subjects affected / exposed	6 / 66 (9.09%)	0 / 25 (0.00%)	
occurrences (all)	6	0	
Sinusitis			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Staphylococcal infection			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Streptococcal bacteraemia			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	

Tinea pedis			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Tooth abscess			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 66 (1.52%)	1 / 25 (4.00%)	
occurrences (all)	1	1	
Urinary tract infection			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Vaginal infection			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Vulvovaginal candidiasis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Alkalosis			
subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Decreased appetite			
subjects affected / exposed	27 / 66 (40.91%)	12 / 25 (48.00%)	
occurrences (all)	30	12	
Dehydration			
subjects affected / exposed	3 / 66 (4.55%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Fluid overload			
subjects affected / exposed	6 / 66 (9.09%)	4 / 25 (16.00%)	
occurrences (all)	6	4	
Fluid retention			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Hypercalcaemia			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Hyperglycaemia			
subjects affected / exposed	6 / 66 (9.09%)	0 / 25 (0.00%)	
occurrences (all)	8	0	
Hyperkalaemia			
subjects affected / exposed	2 / 66 (3.03%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Hypernatraemia			
subjects affected / exposed	2 / 66 (3.03%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Hypervolaemia			
subjects affected / exposed	0 / 66 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Hypoalbuminaemia			
subjects affected / exposed	5 / 66 (7.58%)	2 / 25 (8.00%)	
occurrences (all)	6	5	
Hypocalcaemia			
subjects affected / exposed	7 / 66 (10.61%)	5 / 25 (20.00%)	
occurrences (all)	8	7	
Hypokalaemia			
subjects affected / exposed	26 / 66 (39.39%)	10 / 25 (40.00%)	
occurrences (all)	27	12	
Hypomagnesaemia			
subjects affected / exposed	11 / 66 (16.67%)	4 / 25 (16.00%)	
occurrences (all)	13	4	
Hyponatraemia			
subjects affected / exposed	6 / 66 (9.09%)	1 / 25 (4.00%)	
occurrences (all)	7	2	
Hypophosphataemia			
subjects affected / exposed	9 / 66 (13.64%)	6 / 25 (24.00%)	
occurrences (all)	16	8	
Lactic acidosis			

subjects affected / exposed	1 / 66 (1.52%)	0 / 25 (0.00%)	
occurrences (all)	1	0	
Malnutrition			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Metabolic acidosis			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	
Tumour lysis syndrome			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Vitamin D deficiency			
subjects affected / exposed	3 / 66 (4.55%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Vitamin K deficiency			
subjects affected / exposed	0 / 66 (0.00%)	1 / 25 (4.00%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 October 2015	1) Updated the definitions of dose limiting toxicities (DLT). 2) Updated the criteria used for the determination if subjects were evaluable for DLT assessment.
29 January 2016	1) Included an optional second course of treatment to relapsed / refractory and treatment-naïve subjects. 2) Updated to Exclusion Criterion Number 9 to allow use of FLT3 inhibitors or TKI inhibitors (to avoid any drug-drug interactions such agents must have been discontinued 5 days before protocol treatment began).
02 August 2016	1) Allow optional 1 to 3 consolidation courses of cytarabine to be administered to subjects ≥60 years with newly diagnosed AML who met specific eligibility criteria. 2) Allow an additional 25 subjects be enrolled in the Phase II Arm A relapsed/refractory arm to obtain additional PK and safety data and gain experience with more than one course of uproleselan treatment for any subjects meeting criteria for continuation. 3) Allow collection of PK samples in all subjects enrolled in the study.
23 January 2017	1) Revised cytarabine consolidation review of first 3 subjects as discussed and agreed to by the DSMB. 2) Updated cytarabine consolidation eligibility, specifically direct bilirubin levels, to be consistent with enrollment eligibility requirements as discussed and agreed to by the DSMB.

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.

Due to changes in the planned analysis, TTR was not analyzed. Additionally, deaths due to AEs are reported in the adverse event section.

Notes: