Clinical trial results:
An open-label, Phase I/II trial to determine the maximum tolerated dose and investigate safety, pharmacokinetics and efficacy of BI 836858 in combination with decitabine in patients with acute myeloid leukemia

Summary

EudraCT number	2015-002892-30
Trial protocol	DE ES IT
Global end of trial date	16 January 2023

Results information

Result version number	v1 (current)
This version publication date	31 January 2024
First version publication date	31 January 2024

Trial information

Trial identification

Sponsor protocol code	1315.2

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02632721
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Straße, Ingelheim am Rhein, Germany, 55216
Public contact	Boehringer Ingelheim Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	Boehringer Ingelheim Call Center, Boehringer Ingelheim, 001 18002430127, clintriage.rdg@boehringer-ingelheim.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	24 February 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2023
Global end of trial reached?	Yes
Global end of trial date	16 January 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Phase I Dose Escalation: To determine the maximum tolerated dose (MTD) and the recommended dose for Phase I Extension (RExP1D) and to investigate the safety, pharmacokinetics, and efficacy of BI 836858 in combination with decitabine.
Phase I Extension: To collect additional data on safety, pharmacokinetics, and efficacy and to decide if the RExP1D would become the Recommended Phase II Dose (RP2D) of BI 836858 in combination with decitabine.

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All subjects were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all subjects was adhered to throughout the trial conduct.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 2
Country: Number of subjects enrolled	United States: 11
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Germany: 32
Worldwide total number of subjects	63
EEA total number of subjects	52

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)	7
From 65 to 84 years	54
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

This was an open-label, Phase I/II trial to determine the maximum tolerated dose and investigate safety, pharmacokinetics and efficacy of BI 836858 in combination with decitabine in patients with acute myeloid leukemia.

Pre-assignment

Screening details:

All subjects were screened for eligibility prior to participation in the trial. Subjects attended a specialist site which ensured that they (the subjects) strictly met all inclusion and none of the exclusion criteria. Subjects were not to be allocated to a treatment group if any of the entry criteria were violated.

Period 1

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

Blinding implementation details:

Open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase I dose escalation: BI 836858 20 mg + decitabine

Arm description:

20 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm type	Experimental
Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Investigational medicinal product name	BI836858
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

20 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm title	Phase I dose escalation: BI 836858 40 mg + decitabine

Arm description:

40 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm type	Experimental
Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Investigational medicinal product name	BI 836858
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

40 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm title	Phase I dose escalation: BI 836858 80 mg + decitabine

Arm description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm type	Experimental
Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Investigational medicinal product name	BI 836858
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion

Routes of administration	Intravenous use

Dosage and administration details:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm title	Phase I Extension A: BI 836858 80 mg + decitabine

Arm description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm type	Experimental
Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Investigational medicinal product name	BI 836858
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm title	Phase I Extension B: BI 836858 80 mg + decitabine

Arm description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 5 consecutive days (standard treatment) from Day 1 to 5 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Arm type	Experimental
Investigational medicinal product name	Decitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area

(BSA) of decitabine administered daily via intravenous infusion for 5 consecutive days (standard treatment) from Day 1 to 5 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Investigational medicinal product name	BI 836858
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 5 consecutive days (standard treatment) from Day 1 to 5 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Number of subjects in period 1[1]	Phase I dose escalation: BI 836858 20 mg + decitabine	Phase I dose escalation: BI 836858 40 mg + decitabine	Phase I dose escalation: BI 836858 80 mg + decitabine
Started	4	3	9
Completed	0	0	0
Not completed	4	3	9
Inadequate clinical condition	-	-	-
Dose limiting toxicity	-	-	-
Allergic reaction	-	-	-
Increase of white blood cell count	-	-	-
Refused to continue taking trial medication	-	1	1
Therapy refractory AML	-	-	-
Patient wish for other treatment	-	1	-
Relapsed Pneumonia	-	-	-
No meet eligibility	-	-	-
Adverse event, non-fatal	-	-	2
Receiving Decitabine locally	-	-	1
Allogeneic peripheral stem cell transplantation	-	-	1
Progressive disease	3	-	4
No benefit from study treatment	1	1	-

Number of subjects in period 1[1]	Phase I Extension A: BI 836858 80 mg + decitabine	Phase I Extension B: BI 836858 80 mg + decitabine
Started	15	18
Completed	1	2
Not completed	14	16
Inadequate clinical condition	-	1
Dose limiting toxicity	1	-

Allergic reaction	1	-
Increase of white blood cell count	-	1
Refused to continue taking trial medication	1	2
Therapy refractory AML	-	1
Patient wish for other treatment	-	-
Relapsed Pneumonia	-	1
No meet eligibility	-	1
Adverse event, non-fatal	5	3
Receiving Decitabine locally	-	-
Allogeneic peripheral stem cell transplantation	-	-
Progressive disease	6	5
No benefit from study treatment	-	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Worldwide 63 subjects were enrolled into the trial, whereof 49 subjects actually started in the trial.

Baseline characteristics

Reporting groups	
Reporting group title	Phase I dose escalation: BI 836858 20 mg + decitabine
Reporting group description:	
20 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).	
Reporting group title	Phase I dose escalation: BI 836858 40 mg + decitabine
Reporting group description:	
40 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).	
Reporting group title	Phase I dose escalation: BI 836858 80 mg + decitabine
Reporting group description:	
80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).	
Reporting group title	Phase I Extension A: BI 836858 80 mg + decitabine
Reporting group description:	
80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).	
Reporting group title	Phase I Extension B: BI 836858 80 mg + decitabine
Reporting group description:	
80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 5 consecutive days (standard treatment) from Day 1 to 5 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).	

Reporting group values	Phase I dose escalation: BI 836858 20 mg + decitabine	Phase I dose escalation: BI 836858 40 mg + decitabine	Phase I dose escalation: BI 836858 80 mg + decitabine
Number of subjects	4	3	9
Age categorical			
Treated set: The treated set includes all patients who have received at least one dose of study medication (BI 836858 and/or decitabine).			
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)	1	2	3
From 65-84 years	3	1	6
85 years and over	0	0	0
Age Continuous			
Treated set: The treated set includes all patients who have received at least one dose of study medication (BI 836858 and/or decitabine).			
Units: years			
arithmetic mean	72.0	52.3	66.3
standard deviation	± 11.34	± 27.61	± 13.02
Sex: Female, Male			
Treated set: The treated set includes all patients who have received at least one dose of study medication (BI 836858 and/or decitabine).			
Units: Participants			
Female	1	2	4
Male	3	1	5
Race (NIH/OMB)			
Treated set: The treated set includes all patients who have received at least one dose of study medication (BI 836858 and/or decitabine).			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	4	3	9
More than one race	0	0	0
Unknown or Not Reported	0	0	0

Reporting group values	Phase I Extension A: BI 836858 80 mg + decitabine	Phase I Extension B: BI 836858 80 mg + decitabine	Total
Number of subjects	15	18	49
Age categorical			
Treated set: The treated set includes all patients who have received at least one dose of study medication (BI 836858 and/or decitabine).			
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)	0	0	6
From 65-84 years	14	18	42
85 years and over	1	0	1
Age Continuous			
Treated set: The treated set includes all patients who have received at least one dose of study medication (BI 836858 and/or decitabine).			
Units: years			

arithmetic mean	74.9	76.6	
standard deviation	± 6.62	± 4.24	-

Sex: Female, Male			
Treated set: The treated set includes all patients who have received at least one dose of study medication (BI 836858 and/or decitabine).			
Units: Participants			
Female	7	6	20
Male	8	12	29
Race (NIH/OMB)			
Treated set: The treated set includes all patients who have received at least one dose of study medication (BI 836858 and/or decitabine).			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	15	18	49
More than one race	0	0	0
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	Phase I dose escalation: BI 836858 20 mg + decitabine

Reporting group description:

20 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Reporting group title	Phase I dose escalation: BI 836858 40 mg + decitabine

Reporting group description:

40 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Reporting group title	Phase I dose escalation: BI 836858 80 mg + decitabine

Reporting group description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Reporting group title	Phase I Extension A: BI 836858 80 mg + decitabine

Reporting group description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Reporting group title	Phase I Extension B: BI 836858 80 mg + decitabine

Reporting group description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 5 consecutive days (standard treatment) from Day 1 to 5 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Subject analysis set title	Phase I: BI 836858 + decitabine
Subject analysis set type	Full analysis

Subject analysis set description:

Comprises all dose cohorts during the Phase I dose escalation and extension parts. 20/40/80 milligram (mg) of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 (standard treatment: 5 consecutive days from Day 1 to 5) in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Primary: Phase I: Number of patients with dose limiting toxicity (DLT(s)) during first treatment cycle

End point title	Phase I: Number of patients with dose limiting toxicity (DLT(s)) during first treatment cycle[1]

End point description:

Number of patients with dose limiting toxicity (DLT(s)) for BI 836858 in combination with decitabine during first treatment cycle (Phase 1).

DLT was defined as any non-disease-related non-haematological adverse event (AE) of Common Terminology Criteria for Adverse Events (CTCAE) grade 3 or higher. Expected non-haematological disease-related AEs were not to be regarded as a DLT.

Bayesian logistic regression model (BLRM) with overdose control was used to determine the maximum tolerated dose (MTD), defined as highest dose with less than 25% risk of the true DLT rate being equal to or above 33%. Posterior probabilities of the DLT rate lying in the intervals [0.16, 0.33) (target dosing), and [0.33,1] (overdosing) are reported.
Treated set: All subjects who were documented to have received at least one dose of trial medication.

End point type	Primary

End point timeframe:

Up to 28 days (first treatment cycle).

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: Endpoint has been analyzed descriptively.

End point values	Phase I dose escalation: BI 836858 20 mg + decitabine	Phase I dose escalation: BI 836858 40 mg + decitabine	Phase I dose escalation: BI 836858 80 mg + decitabine	Phase I Extension A: BI 836858 80 mg + decitabine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4[2]	3[3]	9[4]	15
Units: Participants	0	0	0	1

Notes:

[2] - Probability of DLT rate in [0.16, 0.33) = 0.081; in [0.33,1] = 0.

[3] - Probability of DLT rate in [0.16, 0.33) = 0.028; in [0.33,1] = 0.

[4] - Probability of DLT rate in [0.16, 0.33) = 0.012; in [0.33,1] = 0.

End point values	Phase I Extension B: BI 836858 80 mg + decitabine			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Phase I: Maximum Tolerated Dose (MTD) of BI 836858 in combination with decitabine

End point title	Phase I: Maximum Tolerated Dose (MTD) of BI 836858 in combination with decitabine[5]

End point description:

The MTD of BI 836858 in combination with decitabine was estimated after the dose escalation part of the trial obtaining on the basis of DLTs observed during the first treatment cycle. However, for those patients who received more than one cycle of the combination treatment, all adverse events that constitute a DLT will be considered for re-estimation of the MTD based on the Bayesian logistic regression model (BLRM). MTD is defined as the highest dose of BI 836858 (in combination with decitabine) with less than 25% risk of the true DLT rate being above 33% during the MTD evaluation

period.

MTD evaluable set: All subjects who were entered, treated and completed first cycle of planned treatment or subjects received at least 2 doses of BI 836858 due to BI 836858-related toxicity but not replaced.
99999 = not applicable value.
No formal MTD was determined due to no DLTs were reported during dose escalation and only 2 DLTs were observed in the extension phase.

End point type	Primary

End point timeframe:

From first drug administration until end of treatment, up to 941 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: Endpoint has been analyzed descriptively.

End point values	Phase I: BI 836858 + decitabine			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: milligram	99999			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1: Number of patients with objective response (CR + CRi)

End point title	Phase 1: Number of patients with objective response (CR + CRi)

End point description:

Number of patients with objective response (Complete remission (CR) + complete remission with incomplete remission (CRi)).
CR was defined as bone marrow (BM) blasts < 5%; absence of blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count > 1.0 x 109/L [1,000/µL]; platelet count > 100 x 109/L [100,000/µL]; independence of red blood cells transfusions (no transfusion for 1 week prior to the assessment). No minimum duration of response is required.
CRi was defined as all CR criteria except for residual neutropenia (< 1.0 x 109/L [1,000/µL]) or thrombocytopenia (< 100 x 109/L [100,000/µL]).
Treated set: All subjects who were documented to have received at least one dose of trial medication.

End point type	Secondary

End point timeframe:

From start of treatment until the earliest of progression, death or end of trial, up to 971 days.

End point values	Phase I dose escalation: BI 836858 20 mg + decitabine	Phase I dose escalation: BI 836858 40 mg + decitabine	Phase I dose escalation: BI 836858 80 mg + decitabine	Phase I Extension A: BI 836858 80 mg + decitabine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	3	9	15
Units: Participants				
Objective response (CR + CRi)	2	0	6	7
Complete remission (CR)	1	0	1	3

Complete remission with incomplete recovery (CRi)	1	0	5	4

End point values	Phase I Extension B: BI 836858 80 mg + decitabine			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Participants				
Objective response (CR + CRi)	4			
Complete remission (CR)	3			
Complete remission with incomplete recovery (CRi)	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first administration of trial medication until 30 days of residual effect period after the last administration of trial medication, up to 971 days.

Adverse event reporting additional description:

Treated set: All subjects who were documented to have received at least one dose of trial medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Phase I dose escalation: BI 836858 20 mg + decitabine

Reporting group description:

20 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Reporting group title	Phase I dose escalation: BI 836858 40 mg + decitabine

Reporting group description:

40 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Reporting group title	Phase I Extension B: BI 836858 80 mg + decitabine

Reporting group description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 5 consecutive days (standard treatment) from Day 1 to 5 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Reporting group title	Phase I Extension A: BI 836858 80 mg + decitabine

Reporting group description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Reporting group title	Phase I dose escalation: BI 836858 80 mg + decitabine

Reporting group description:

80 milligram (mg) of concentrate for solution for infusion of BI 836858 were administered as single dose via rate-controlled intravenous infusion once per week in 28-day treatment cycle (i.e. on Days 1, 8, 15, and 22 of the 28-day treatment cycles), together with 20 mg/square meter (m2) body surface area (BSA) of decitabine administered daily via intravenous infusion for 10 consecutive days (intensive treatment) from Day 1 to 10 in each treatment cycle. The BI 836858 dose was diluted in 0.9% sodium chloride to have full volume of the diluted compound 250 milliliter (mL).

Serious adverse events	Phase I dose escalation: BI 836858 20 mg + decitabine	Phase I dose escalation: BI 836858 40 mg + decitabine	Phase I Extension B: BI 836858 80 mg + decitabine
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	3 / 3 (100.00%)	17 / 18 (94.44%)
number of deaths (all causes)	3	2	13
number of deaths resulting from adverse events	0	1	6
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	5 / 18 (27.78%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 3
Acute myeloid leukaemia recurrent			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic neoplasm			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (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
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (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
Mucosal inflammation			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (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
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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 fibrinogen decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
Subdural haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infusion related reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (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
Tibia fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (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			
Acute myocardial infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tachyarrhythmia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
Haemorrhage intracranial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglossal nerve paresis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial nerve disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (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
Subarachnoid haemorrhage			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intraventricular haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (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
Blood and lymphatic system disorders			
White blood cell disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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 neutropenia			
subjects affected / exposed	2 / 4 (50.00%)	2 / 3 (66.67%)	5 / 18 (27.78%)
occurrences causally related to treatment / all	1 / 4	0 / 3	4 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			

Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (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			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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 kidney injury			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (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
Infections and infestations			
Bacterial infection			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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 valve abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (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
Infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocarditis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
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			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	3 / 18 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	4 / 18 (22.22%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Tumour lysis syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1

Serious adverse events	Phase I Extension A:	Phase I dose	

	BI 836858 80 mg + decitabine	escalation: BI 836858 80 mg + decitabine	
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 15 (93.33%)	8 / 9 (88.89%)	
number of deaths (all causes)	11	5	
number of deaths resulting from adverse events	5	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant neoplasm progression			
subjects affected / exposed	5 / 15 (33.33%)	2 / 9 (22.22%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 1	
Acute myeloid leukaemia recurrent			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic neoplasm			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 15 (20.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal inflammation			

subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infiltration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood fibrinogen decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infusion related reaction			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Tachyarrhythmia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglossal nerve paresis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial nerve disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			

subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraventricular haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
White blood cell disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	5 / 15 (33.33%)	5 / 9 (55.56%)	
occurrences causally related to treatment / all	4 / 9	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			

Abdominal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 15 (13.33%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacterial infection			

subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 15 (0.00%)	2 / 9 (22.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve abscess			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Escherichia infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			

subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 1	
Pneumonia			
subjects affected / exposed	2 / 15 (13.33%)	3 / 9 (33.33%)	
occurrences causally related to treatment / all	0 / 3	1 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Septic shock			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Tumour lysis syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Phase I dose escalation: BI 836858 20 mg + decitabine	Phase I dose escalation: BI 836858 40 mg + decitabine	Phase I Extension B: BI 836858 80 mg + decitabine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	3 / 3 (100.00%)	18 / 18 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Anogenital warts			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Haematoma			
subjects affected / exposed	3 / 4 (75.00%)	0 / 3 (0.00%)	3 / 18 (16.67%)
occurrences (all)	5	0	5
Hypertension			
subjects affected / exposed	3 / 4 (75.00%)	2 / 3 (66.67%)	0 / 18 (0.00%)
occurrences (all)	6	3	0
Hypotension			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	1	3	2
Jugular vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Superficial vein thrombosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Thrombophlebitis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Venous thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Face oedema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Chills			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	0 / 18 (0.00%)
occurrences (all)	2	2	0
Asthenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	6
Catheter site pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Catheter site thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Chest pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Fatigue			
subjects affected / exposed	3 / 4 (75.00%)	2 / 3 (66.67%)	1 / 18 (5.56%)
occurrences (all)	5	6	1
Gait disturbance			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Treatment noncompliance			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Implant site pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Injection site reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Localised oedema			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Malaise			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Mucosal inflammation			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	4 / 18 (22.22%)
occurrences (all)	1	2	7
Oedema peripheral			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	6 / 18 (33.33%)
occurrences (all)	4	3	10
Pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Puncture site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	4 / 18 (22.22%)
occurrences (all)	4	3	8
Systemic inflammatory response			

syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
General physical health deterioration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Vessel puncture site pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vessel puncture site swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	0	1	2
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Vulvovaginal pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Penile haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pharyngeal erythema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Oropharyngeal pain			
subjects affected / exposed	3 / 4 (75.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	1
Nasal dryness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Lung infiltration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypoxia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Hiccups			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	4 / 18 (22.22%)
occurrences (all)	3	0	5
Dyspnoea exertional			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	2 / 4 (50.00%)	2 / 3 (66.67%)	2 / 18 (11.11%)
occurrences (all)	7	5	2
Cough			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	6
Atelectasis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pleurisy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Productive cough			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Tachypnoea			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	1	2	0
Wheezing			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pulmonary pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Confusional state			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Disorientation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	3 / 18 (16.67%)
occurrences (all)	1	0	3
Nervousness			

subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Sleep disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Restlessness			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Persistent depressive disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	5
Alanine aminotransferase increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Blood bilirubin increased			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	4
Lymphocyte count decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Blood creatinine increased			

subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	3	1	1
Blood fibrinogen decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood potassium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood sodium increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Blood urea increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood uric acid increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Cortisol decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Ejection fraction decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Gamma-glutamyltransferase increased			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	7
International normalised ratio increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Blood calcium decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neutrophil count decreased			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	2	8	33
Platelet count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	5 / 18 (27.78%)
occurrences (all)	7	6	21
Prothrombin time prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Prothrombin time shortened			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Weight increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
White blood cell count decreased			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	5 / 18 (27.78%)
occurrences (all)	1	3	36
White blood cell count increased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	2	0

Injury, poisoning and procedural complications			
Transplantation complication			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Transfusion reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Subcutaneous haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Skin laceration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Refractoriness to platelet transfusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Infusion related reaction			
subjects affected / exposed	3 / 4 (75.00%)	3 / 3 (100.00%)	11 / 18 (61.11%)
occurrences (all)	17	6	19
Fall			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	4 / 18 (22.22%)
occurrences (all)	4	0	12
Contusion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			

Atrial fibrillation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Atrioventricular block			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Cardiovascular disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Left ventricular dysfunction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Mitral valve incompetence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Sinus tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Supraventricular extrasystoles			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	2	0	2
Cardiovascular insufficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Facial paralysis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	8	4	1
Balance disorder			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	3 / 18 (16.67%)
occurrences (all)	3	0	3
Presyncope			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	3 / 18 (16.67%)
occurrences (all)	0	0	5
Tremor			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hypogeusia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypoglossal nerve paresis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Peripheral motor neuropathy			

subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Acquired antithrombin III deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	6 / 18 (33.33%)
occurrences (all)	10	3	63
Leukocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Thrombocytosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	5	2	30
Thrombocytopenia			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	3	0	32
Leukopenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Thrombotic microangiopathy			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Vertigo			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Vestibular disorder			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eye haematoma			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Eye haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	2	0	0
Eyelid bleeding			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Eyelid oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Macular oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vitreous floaters			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	3	1	4
Abdominal pain lower			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 4 (25.00%)	2 / 3 (66.67%)	2 / 18 (11.11%)
occurrences (all)	1	2	5
Anal incontinence			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	3 / 4 (75.00%)	2 / 3 (66.67%)	1 / 18 (5.56%)
occurrences (all)	8	6	3
Aphthous ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 4 (50.00%)	2 / 3 (66.67%)	6 / 18 (33.33%)
occurrences (all)	2	3	9
Diarrhoea			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	12	1	3
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	1	1	0
Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Glossodynia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	2 / 4 (50.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	1
Mouth haemorrhage			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Anal inflammation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Odynophagia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Oral discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Proctitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Rectal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Stomatitis			

subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	2	1	2
Toothache			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	3 / 4 (75.00%)	3 / 3 (100.00%)	2 / 18 (11.11%)
occurrences (all)	4	5	3
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Hepatotoxicity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	2
Decubitus ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Dermatitis allergic			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Petechiae			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pruritus			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	4
Purpura			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Rash			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	3 / 18 (16.67%)
occurrences (all)	1	1	4
Skin lesion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Urethral haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Renal haematoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Renal failure			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Pollakiuria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Oliguria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Nocturia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1

Micturition urgency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Incontinence			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Haematuria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	0	1	3
Back pain			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	2	1	2
Arthralgia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	2
Spinal pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	2	0	2
Osteoporosis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Neck pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Myopathy			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Muscular weakness			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	2	1	0
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Bronchitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Cerebral fungal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	1	1	1

Ecthyma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Endocarditis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Enterococcal infection			
subjects affected / exposed	1 / 4 (25.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	1	1	1
Herpes simplex viraemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	0	1	1
Intervertebral discitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	1 / 18 (5.56%)
occurrences (all)	2	1	1
Lip infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Skin candida			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	1	0	1
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	3 / 18 (16.67%)
occurrences (all)	0	0	3

Otitis media			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Oral infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	2 / 4 (50.00%)	1 / 3 (33.33%)	2 / 18 (11.11%)
occurrences (all)	2	1	2
Oral candidiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Nail infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	1	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
COVID-19			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0

Cellulitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	2 / 4 (50.00%)	2 / 3 (66.67%)	3 / 18 (16.67%)
occurrences (all)	7	6	3
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	2
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Folate deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Gout			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	6	0	1
Vitamin B12 deficiency			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	3 / 4 (75.00%)	1 / 3 (33.33%)	4 / 18 (22.22%)
occurrences (all)	4	1	6
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	0 / 18 (0.00%)
occurrences (all)	0	0	0
Hypervolaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 3 (33.33%)	0 / 18 (0.00%)
occurrences (all)	0	1	0
Hyperuricaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	1	0	2
Hyperphosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	1 / 18 (5.56%)
occurrences (all)	0	0	1
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 3 (0.00%)	2 / 18 (11.11%)
occurrences (all)	0	0	3

Non-serious adverse events	Phase I Extension A: BI 836858 80 mg + decitabine	Phase I dose escalation: BI 836858 80 mg + decitabine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 15 (100.00%)	9 / 9 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Anogenital warts			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Flushing			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Haematoma			
subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Hypertension			
subjects affected / exposed	4 / 15 (26.67%)	3 / 9 (33.33%)	
occurrences (all)	4	3	
Hypotension			
subjects affected / exposed	2 / 15 (13.33%)	2 / 9 (22.22%)	
occurrences (all)	2	2	
Jugular vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Phlebitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Superficial vein thrombosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Thrombophlebitis			
subjects affected / exposed	0 / 15 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Venous thrombosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Face oedema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	1 / 15 (6.67%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Asthenia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Catheter site pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Catheter site thrombosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Chest discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Chest pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Fatigue			
subjects affected / exposed	2 / 15 (13.33%)	3 / 9 (33.33%)	
occurrences (all)	3	3	
Gait disturbance			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Treatment noncompliance			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Implant site pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Inflammation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	

Injection site reaction				
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)		
occurrences (all)	1	0		
Localised oedema				
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)		
occurrences (all)	0	1		
Malaise				
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)		
occurrences (all)	0	0		
Mucosal inflammation				
subjects affected / exposed	3 / 15 (20.00%)	3 / 9 (33.33%)		
occurrences (all)	5	3		
Oedema peripheral				
subjects affected / exposed	7 / 15 (46.67%)	4 / 9 (44.44%)		
occurrences (all)	9	5		
Pain				
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)		
occurrences (all)	1	1		
Peripheral swelling				
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)		
occurrences (all)	0	1		
Puncture site pain				
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)		
occurrences (all)	1	0		
Pyrexia				
subjects affected / exposed	4 / 15 (26.67%)	2 / 9 (22.22%)		
occurrences (all)	4	5		
Systemic inflammatory response syndrome				
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)		
occurrences (all)	0	0		
General physical health deterioration				
subjects affected / exposed	2 / 15 (13.33%)	0 / 9 (0.00%)		
occurrences (all)	2	0		
Vessel puncture site pain				

subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Vessel puncture site swelling			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Illness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Penile haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	1 / 15 (6.67%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Pharyngeal erythema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Oropharyngeal pain			
subjects affected / exposed	1 / 15 (6.67%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Nasal dryness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			

subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Lung infiltration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hypoxia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hiccups			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	4 / 15 (26.67%)	1 / 9 (11.11%)	
occurrences (all)	4	1	
Dyspnoea exertional			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	0 / 15 (0.00%)	3 / 9 (33.33%)	
occurrences (all)	0	5	
Cough			
subjects affected / exposed	0 / 15 (0.00%)	6 / 9 (66.67%)	
occurrences (all)	0	8	
Atelectasis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Pleurisy			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Productive cough			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Tachypnoea			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Upper-airway cough syndrome			

subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Wheezing			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Pulmonary pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Confusional state			
subjects affected / exposed	2 / 15 (13.33%)	2 / 9 (22.22%)	
occurrences (all)	2	2	
Depression			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Disorientation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Hallucination			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Insomnia			
subjects affected / exposed	1 / 15 (6.67%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Nervousness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Sleep disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Restlessness			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	

Persistent depressive disorder			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	3 / 15 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	5	0	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 15 (13.33%)	0 / 9 (0.00%)	
occurrences (all)	6	0	
Blood bilirubin increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Lymphocyte count decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Blood creatinine increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Blood fibrinogen decreased			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Blood potassium decreased			

subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	4	0	
Blood sodium increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Blood urea increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Blood uric acid increased			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
C-reactive protein increased			
subjects affected / exposed	1 / 15 (6.67%)	2 / 9 (22.22%)	
occurrences (all)	2	3	
Cortisol decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Ejection fraction decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Gamma-glutamyltransferase increased			
subjects affected / exposed	3 / 15 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	10	0	
International normalised ratio increased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Blood calcium decreased			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	5	0	
Neutrophil count decreased			

subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	
occurrences (all)	14	19	
Platelet count decreased			
subjects affected / exposed	3 / 15 (20.00%)	4 / 9 (44.44%)	
occurrences (all)	16	62	
Prothrombin time prolonged			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Prothrombin time shortened			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Weight decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Weight increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
White blood cell count decreased			
subjects affected / exposed	2 / 15 (13.33%)	3 / 9 (33.33%)	
occurrences (all)	18	19	
White blood cell count increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Injury, poisoning and procedural complications			
Transplantation complication			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Transfusion reaction			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Subcutaneous haematoma			

subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Skin laceration			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Skin injury			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Skin abrasion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Refractoriness to platelet transfusion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Procedural pain			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Infusion related reaction			
subjects affected / exposed	8 / 15 (53.33%)	4 / 9 (44.44%)	
occurrences (all)	21	33	
Fall			
subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	
occurrences (all)	4	1	
Contusion			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Atrioventricular block			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Bradycardia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	

Cardiovascular disorder			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Left ventricular dysfunction			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Mitral valve incompetence			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Sinus tachycardia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Supraventricular extrasystoles			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Tachycardia			
subjects affected / exposed	0 / 15 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Cardiovascular insufficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Facial paralysis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	1 / 15 (6.67%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Balance disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Headache			

subjects affected / exposed	4 / 15 (26.67%)	0 / 9 (0.00%)	
occurrences (all)	5	0	
Presyncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Restless legs syndrome			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Somnolence			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Syncope			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Tremor			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hypogeusia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hypoglossal nerve paresis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Neuropathy peripheral			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Peripheral motor neuropathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Blood and lymphatic system disorders			
Acquired antithrombin III deficiency			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Anaemia			
subjects affected / exposed	4 / 15 (26.67%)	6 / 9 (66.67%)	
occurrences (all)	23	54	

Leukocytosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Thrombocytosis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Neutropenia			
subjects affected / exposed	3 / 15 (20.00%)	3 / 9 (33.33%)	
occurrences (all)	8	10	
Thrombocytopenia			
subjects affected / exposed	2 / 15 (13.33%)	2 / 9 (22.22%)	
occurrences (all)	8	13	
Leukopenia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Thrombotic microangiopathy			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Vertigo			
subjects affected / exposed	1 / 15 (6.67%)	2 / 9 (22.22%)	
occurrences (all)	1	2	
Vestibular disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Diplopia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Dry eye			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Eye haematoma			

subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Eye haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Eyelid bleeding			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Eyelid oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Macular oedema			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Vitreous floaters			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Abdominal discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Abdominal distension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Abdominal pain lower			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	2 / 15 (13.33%)	0 / 9 (0.00%)	
occurrences (all)	3	0	

Anal incontinence			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Nausea			
subjects affected / exposed	6 / 15 (40.00%)	2 / 9 (22.22%)	
occurrences (all)	7	4	
Aphthous ulcer			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	7 / 15 (46.67%)	4 / 9 (44.44%)	
occurrences (all)	7	7	
Diarrhoea			
subjects affected / exposed	4 / 15 (26.67%)	2 / 9 (22.22%)	
occurrences (all)	7	7	
Dyspepsia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Dysphagia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Glossodynia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Haematochezia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	

Haemorrhoids			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Mouth haemorrhage			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Anal inflammation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Odynophagia			
subjects affected / exposed	2 / 15 (13.33%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Oral discomfort			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Proctalgia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Proctitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Rectal haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Stomatitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Toothache			
subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	
occurrences (all)	2	1	
Vomiting			
subjects affected / exposed	5 / 15 (33.33%)	0 / 9 (0.00%)	
occurrences (all)	7	0	
Hepatobiliary disorders			
Cholelithiasis			

subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hepatotoxicity			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Skin and subcutaneous tissue disorders			
Acute febrile neutrophilic dermatosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Decubitus ulcer			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Erythema			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Dry skin			
subjects affected / exposed	1 / 15 (6.67%)	2 / 9 (22.22%)	
occurrences (all)	1	3	
Petechiae			
subjects affected / exposed	2 / 15 (13.33%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Pruritus			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Purpura			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Rash			
subjects affected / exposed	3 / 15 (20.00%)	3 / 9 (33.33%)	
occurrences (all)	4	4	
Skin lesion			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	

Urticaria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Urethral haemorrhage			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Renal haematoma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Renal failure			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Pollakiuria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Oliguria			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Nocturia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Micturition urgency			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Incontinence			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Haematuria			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Dysuria			

subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Urinary incontinence			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	3 / 15 (20.00%)	2 / 9 (22.22%)	
occurrences (all)	5	2	
Arthralgia			
subjects affected / exposed	4 / 15 (26.67%)	1 / 9 (11.11%)	
occurrences (all)	4	1	
Flank pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Spinal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Pain in extremity			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	4	
Osteoporosis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Neck pain			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Myopathy			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			

subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Muscular weakness			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	3	
Joint swelling			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Infections and infestations			
Bacterial infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Bronchitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Bronchopulmonary aspergillosis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Cerebral fungal infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Device related infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	2	
Ecthyma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Endocarditis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Enterococcal infection			
subjects affected / exposed	2 / 15 (13.33%)	1 / 9 (11.11%)	
occurrences (all)	2	1	

Herpes simplex viraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Intervertebral discitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Lip infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Skin candida			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	1 / 15 (6.67%)	1 / 9 (11.11%)	
occurrences (all)	1	1	
Otitis media			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Oral infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Oral herpes			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	

Oral candidiasis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Nasopharyngitis			
subjects affected / exposed	0 / 15 (0.00%)	2 / 9 (22.22%)	
occurrences (all)	0	2	
Nail infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Mucosal infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Localised infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Vaginal infection			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Urinary tract infection enterococcal			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
COVID-19			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Cellulitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Herpes zoster			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Cachexia			

subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Decreased appetite			
subjects affected / exposed	2 / 15 (13.33%)	3 / 9 (33.33%)	
occurrences (all)	2	4	
Dehydration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Folate deficiency			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hypercalcaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	1	0	
Hyperglycaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Vitamin B12 deficiency			
subjects affected / exposed	0 / 15 (0.00%)	1 / 9 (11.11%)	
occurrences (all)	0	1	
Hypophosphataemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hyponatraemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			

subjects affected / exposed	1 / 15 (6.67%)	3 / 9 (33.33%)	
occurrences (all)	1	6	
Hypocalcaemia			
subjects affected / exposed	3 / 15 (20.00%)	0 / 9 (0.00%)	
occurrences (all)	3	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 9 (0.00%)	
occurrences (all)	2	0	
Hypervolaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hyperuricaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hyperphosphataemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	
Hyperkalaemia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 9 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2016	The key changes to the original Clinical Trial Protocol (CTP) specified by Amendment 1 comprised clarifications and edits requested by the German Regulatory Authority.
09 June 2016	Changes specified by Amendment 2 comprised logistical or administrative aspects only.
16 December 2016	Changes specified by Amendment 3 comprised clarifications, corrections, further specification of dosing, and adjustments to the expected recruitment rate.
06 July 2017	Changes specified by Amendment 4 comprised clarifications, corrections, and addition of further Pharmacokinetic (PK), ADA (Anti-drug antibody), and biomarker sampling time points.
22 June 2018	Preliminary biomarker and Pharmacokinetic (PK) /Pharmacodynamic (PD) data from patients treated in 80 mg cohorts (Phase I Dose Escalation Cohort as well as Phase I Extension Cohort A) indicated that 80 mg might not be the optimal Recommended Phase II Dose (RP2D). It was therefore decided by the SMC and the Sponsor to include the option for further Dose Escalation cohorts to allow testing of higher doses of BI 836858 prior to starting the Phase II part of the trial (this further dose escalation was not performed due to trial termination). The benefit risk-assessment was also updated with new safety information and associated safety measures. Other changes specified by Amendment 5 comprised clarifications and corrections.
21 August 2019	After the Sponsor’s decision to discontinue development of BI 836858 and to stop further recruitment of patients into study 1315.2, trial participants still on treatment and with clinical benefit from BI 836858 and decitabine were offered to stay on treatment in this trial. With the aim to minimize the burden for trial participants, the mandatory protocol procedures were reduced for all patients in treatment cycles >7 (this included all 3 patients with ongoing treatment).

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.

Sponsor stopped development of the study drug before Phase II start. Phase II was not performed.

Notes: