



Clinical trial results:

A Phase 1b/2 Study of Entospletinib (GS-9973) Monotherapy and in Combination with Chemotherapy in Patients with Acute Myeloid Leukemia (AML)

Summary

EudraCT number	2016-003353-16
Trial protocol	DE
Global end of trial date	21 February 2019

Results information

Result version number	v2 (current)
This version publication date	29 November 2019
First version publication date	17 October 2019
Version creation reason	<ul style="list-style-type: none">• Correction of full data setUpdated timeframe and description for endpoints.

Trial information

Trial identification

Sponsor protocol code	GS-US-339-1559
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02343939
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Gilead Sciences
Sponsor organisation address	333 Lakeside Drive, Foster City, CA, United States, 94404
Public contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.com
Scientific contact	Gilead Clinical Study Information Center, Gilead Sciences, GileadClinicalTrials@gilead.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	21 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 September 2018
Global end of trial reached?	Yes
Global end of trial date	21 February 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

This study will evaluate the efficacy, safety, and tolerability of entospletinib (ENTO) when administered as monotherapy or in combination with chemotherapy in adults with acute myeloid leukemia (AML).

Protection of trial subjects:

The protocol and consent/assent forms were submitted by each investigator to a duly constituted Independent Ethics Committee (IEC) or Institutional Review Board (IRB) for review and approval before study initiation. All revisions to the consent/assent forms (if applicable) after initial IEC/IRB approval were submitted by the investigator to the IEC/IRB for review and approval before implementation in accordance with regulatory requirements.

This study was conducted in accordance with recognized international scientific and ethical standards, including but not limited to the International Conference on Harmonization guideline for Good Clinical Practice (ICH GCP) and the original principles embodied in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 July 2015
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	United States: 133
Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Germany: 5
Worldwide total number of subjects	148
EEA total number of subjects	5

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)	56
From 65 to 84 years	83
85 years and over	9

Subject disposition

Recruitment

Recruitment details:

Participants were enrolled at study sites in the United States, Canada, and Germany. The first participant was screened on 01 July 2015.

Pre-assignment

Screening details:

233 participants were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin

Arm description:

Participants received ENTO 200 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (during induction chemotherapy).

Arm type	Experimental
Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Arm title	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin
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Arm description:

Phase1b/2: Participants received ENTO 400 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (induction chemotherapy).

Phase 2 only: Participants who achieved a CR/CRi and did not require or could not proceed to allogeneic stem cell transplantation (SCT) were offered post-remission chemotherapy (cytarabine 3 g/m² intravenously every 12 hours on Days 1, 3, and 5 or 1 g/m² intravenously once daily on Days 1-5) in combination with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for at least 3 and up to 4 cycles. Participants who maintained a CR/CRi after 3 or 4 cycles were offered maintenance therapy with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for up to 12 cycles.

Arm type	Experimental
Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Arm title	Group B Phase 1b ENTO 200 mg + Decitabine
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Arm description:

Participants received ENTO 200 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 200 mg as monotherapy after completing 2 maintenance cycles.

Arm type	Experimental
Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Arm title	Group B Phase 1b ENTO 400 mg + Decitabine
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Arm description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Arm type	Experimental
Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Arm title	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)
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Arm description:

As part of the safety run-in, participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m² intravenously on Days 1-7 of a 28-day cycle (Cycle 1). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Arm type	Experimental
Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Arm title	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
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Arm description:

Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle

0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Arm type	Experimental
Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Arm title	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
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Arm description:

Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m² intravenously on Days 1-7 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Arm type	Experimental
Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Arm title	Group C Phase 1b/2 ENTO 400 mg
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Arm description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Arm type	Experimental
Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Arm title	Group C Phase 1b ENTO 800 mg
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Arm description:

Participants received ENTO 800 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Arm type	Experimental
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Investigational medicinal product name	Entospletinib
Investigational medicinal product code	
Other name	GS-9973, ENTO
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Tablet(s) administered orally every 12 hours

Number of subjects in period 1^[1]	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Started	3	50	5
Completed	0	2	0
Not completed	3	48	5
Consent withdrawn by subject	3	6	1
Adverse Event	-	-	-
Death	-	15	4
Treatment Failure	-	-	-
Study terminated by sponsor	-	27	-
Investigator's discretion	-	-	-

Number of subjects in period 1^[1]	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
Started	6	8	17
Completed	0	0	0
Not completed	6	8	17
Consent withdrawn by subject	2	2	-
Adverse Event	-	-	1
Death	2	5	11
Treatment Failure	-	-	-
Study terminated by sponsor	1	1	5
Investigator's discretion	1	-	-

Number of subjects in period 1^[1]	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)	Group C Phase 1b/2 ENTO 400 mg	Group C Phase 1b ENTO 800 mg
Started	14	35	7
Completed	0	0	0
Not completed	14	35	7
Consent withdrawn by subject	-	8	6
Adverse Event	-	-	-
Death	8	22	1

Treatment Failure	2	1	-
Study terminated by sponsor	3	4	-
Investigator's discretion	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: Three participants who were enrolled but not treated are not included in the subject disposition table.

Baseline characteristics

Reporting groups

Reporting group title	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin
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Reporting group description:

Participants received ENTO 200 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (during induction chemotherapy).

Reporting group title	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin
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Reporting group description:

Phase1b/2: Participants received ENTO 400 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (induction chemotherapy).

Phase 2 only: Participants who achieved a CR/CRi and did not require or could not proceed to allogeneic stem cell transplantation (SCT) were offered post-remission chemotherapy (cytarabine 3 g/m² intravenously every 12 hours on Days 1, 3, and 5 or 1 g/m² intravenously once daily on Days 1-5) in combination with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for at least 3 and up to 4 cycles. Participants who maintained a CR/CRi after 3 or 4 cycles were offered maintenance therapy with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for up to 12 cycles.

Reporting group title	Group B Phase 1b ENTO 200 mg + Decitabine
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Reporting group description:

Participants received ENTO 200 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 200 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 1b ENTO 400 mg + Decitabine
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Reporting group description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)
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Reporting group description:

As part of the safety run-in, participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m² intravenously on Days 1-7 of a 28-day cycle (Cycle 1). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
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Reporting group description:

Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles).

Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
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Reporting group description:

Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m² intravenously on Days 1-7 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group C Phase 1b/2 ENTO 400 mg
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Reporting group description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Reporting group title	Group C Phase 1b ENTO 800 mg
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Reporting group description:

Participants received ENTO 800 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Reporting group values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Number of subjects	3	50	5
Age categorical Units: Subjects			
< 65 Years	3	32	0
≥ 65 years	0	18	5
Gender categorical Units: Subjects			
Female	1	21	2
Male	2	29	3
Ethnicity Units: Subjects			
Hispanic or Latino	0	2	0
Not Hispanic or Latino	3	48	5
Not Permitted	0	0	0
Race Units: Subjects			
White/Caucasian	3	44	3
Black or African American	0	5	2
Asian	0	0	0
Other	0	1	0
Not Permitted	0	0	0

Reporting group values	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
Number of subjects	6	8	17

Age categorical Units: Subjects			
< 65 Years	1	1	1
≥ 65 years	5	7	16
Gender categorical Units: Subjects			
Female	2	2	7
Male	4	6	10
Ethnicity Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	6	7	15
Not Permitted	0	1	2
Race Units: Subjects			
White/Caucasian	6	6	14
Black or African American	0	1	0
Asian	0	0	0
Other	0	0	0
Not Permitted	0	1	3

Reporting group values	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)	Group C Phase 1b/2 ENTO 400 mg	Group C Phase 1b ENTO 800 mg
Number of subjects	14	35	7
Age categorical Units: Subjects			
< 65 Years	0	17	0
≥ 65 years	14	18	7
Gender categorical Units: Subjects			
Female	3	18	5
Male	11	17	2
Ethnicity Units: Subjects			
Hispanic or Latino	0	2	0
Not Hispanic or Latino	13	33	7
Not Permitted	1	0	0
Race Units: Subjects			
White/Caucasian	11	31	7
Black or African American	1	2	0
Asian	0	1	0
Other	1	1	0
Not Permitted	1	0	0

Reporting group values	Total		
Number of subjects	145		
Age categorical Units: Subjects			
< 65 Years	55		

≥ 65 years	90		
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Gender categorical Units: Subjects			
Female	61		
Male	84		
Ethnicity Units: Subjects			
Hispanic or Latino	4		
Not Hispanic or Latino	137		
Not Permitted	4		
Race Units: Subjects			
White/Caucasian	125		
Black or African American	11		
Asian	1		
Other	3		
Not Permitted	5		

End points

End points reporting groups

Reporting group title	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin
Reporting group description:	
Participants received ENTO 200 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m ² on Days 1-7 and daunorubicin 60 mg/m ² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (during induction chemotherapy).	
Reporting group title	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin
Reporting group description:	
Phase 1b/2: Participants received ENTO 400 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m ² on Days 1-7 and daunorubicin 60 mg/m ² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (induction chemotherapy). Phase 2 only: Participants who achieved a CR/CRi and did not require or could not proceed to allogeneic stem cell transplantation (SCT) were offered post-remission chemotherapy (cytarabine 3 g/m ² intravenously every 12 hours on Days 1, 3, and 5 or 1 g/m ² intravenously once daily on Days 1-5) in combination with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for at least 3 and up to 4 cycles. Participants who maintained a CR/CRi after 3 or 4 cycles were offered maintenance therapy with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for up to 12 cycles.	
Reporting group title	Group B Phase 1b ENTO 200 mg + Decitabine
Reporting group description:	
Participants received ENTO 200 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with decitabine 20 mg/m ² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 200 mg as monotherapy after completing 2 maintenance cycles.	
Reporting group title	Group B Phase 1b ENTO 400 mg + Decitabine
Reporting group description:	
Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m ² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.	
Reporting group title	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)
Reporting group description:	
As part of the safety run-in, participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m ² intravenously on Days 1-7 of a 28-day cycle (Cycle 1). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.	
Reporting group title	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
Reporting group description:	
Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m ² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles).	

Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
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Reporting group description:

Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m² intravenously on Days 1-7 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group C Phase 1b/2 ENTO 400 mg
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Reporting group description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Reporting group title	Group C Phase 1b ENTO 800 mg
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Reporting group description:

Participants received ENTO 800 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Subject analysis set title	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Participants received ENTO 200 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (during induction chemotherapy).

Subject analysis set title	Group A Phase 1b ENTO 400 mg + Cytarabine + Daunorubicin
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (during induction chemotherapy).

Subject analysis set title	Group A Phase 2 ENTO 400 mg + Cytarabine + Daunorubicin
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (induction chemotherapy). Participants who achieved a CR/CRi and did not require or could not proceed to allogeneic stem cell transplantation (SCT) were offered post-remission chemotherapy (cytarabine 3 g/m² intravenously every 12 hours on Days 1, 3, and 5 or 1 g/m² intravenously once daily on Days 1-5) in combination with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for at least 3 and up to 4 cycles. Participants who maintained a CR/CRi after 3 or 4 cycles were offered maintenance therapy with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for up to 12 cycles.

Subject analysis set title	Group B Phase 1b ENTO 200 mg + Decitabine
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Subject analysis set type	Sub-group analysis
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Subject analysis set description:

Participants received ENTO 200 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 200 mg as monotherapy after completing 2 maintenance cycles.

Subject analysis set title	Group B Phase 1b ENTO 400 mg + Decitabine
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Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m ² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.	
Subject analysis set title	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
As part of the safety run-in, participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m ² intravenously on Days 1-7 of a 28-day cycle (Cycle 1). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.	
Subject analysis set title	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m ² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.	
Subject analysis set title	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m ² intravenously on Days 1-7 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.	
Subject analysis set title	Group C Phase 1b ENTO 400 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.	
Subject analysis set title	Group C Phase 1b ENTO 800 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants received ENTO 800 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.	
Subject analysis set title	Group C Phase 2 ENTO 400 mg (Cohort C1A - R/R AML)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Participants with relapsed/refractory (R/R) acute myeloid leukemia (AML) received ENTO 400 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study	

termination by sponsor.

Subject analysis set title	Group C Phase 2 ENTO 400 mg (Cohort C2 - MLL)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants R/R AML with mixed-lineage leukemia (MLL) received ENTO 400 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Subject analysis set title	Group C Phase 2 ENTO 400 mg (Cohort C3 - Untreated AML)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants with previously untreated AML who were unfit for chemotherapy or hypomethylating agents or refused chemotherapy or hypomethylating agent received ENTO 400 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Primary: Percentage of Participants Experiencing Dose Limiting Toxicities (DLTs)

End point title	Percentage of Participants Experiencing Dose Limiting Toxicities (DLTs) ^{[1][2]}
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End point description:

DLTs refer to toxicities experienced during the first 28 days of study treatment that have been judged to be clinically significant and related to study treatment. DLT assessment was applicable only for Phase 1b and Phase 2 safety run-in participants. The DLT Analysis Set included all participants who received 21 days of ENTO (applicable to all groups) and all doses of cytarabine and daunorubicin in Group A Phase 1b, decitabine in Group B Phase 1b, or azacitidine in Group B Phase 2 safety run-in during the DLT assessment window; or experienced a DLT during the DLT assessment window.

End point type	Primary
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End point timeframe:

Group A: Cycle 0 Day 1 to Cycle 2 Day 28; Group B: Cycle 0 Day 1 to Cycle 1 Day 28; Group C: Cycle 1 Day 1 to Cycle 1 Day 28 (Cycle length: for Cycle 0 = 14 days, for all other cycles = 28 days)

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: No statistical comparison was planned or performed.

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

Justification: The endpoint was planned to include data only for the specified arms.

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine	Group B Phase 1b ENTO 400 mg + Decitabine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	3	6
Units: Percentage of Participants				
number (not applicable)	0.0	0.0	0.0	16.7

End point values	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group C Phase 1b/2 ENTO 400 mg	Group C Phase 1b ENTO 800 mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	6	
Units: Percentage of Participants				

number (not applicable)	0.0	0.0	16.7	
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Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Morphologic Complete Remission (CR) at the End of Induction

End point title	Percentage of Participants With Morphologic Complete Remission (CR) at the End of Induction ^[3]
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End point description:

Clinical response was assessed according to the International Working Group criteria (Cheson 2003). Morphologic CR included CR and cytogenetic CR (CRc). CR required all of the following: < 5% blasts in bone marrow aspirate; Neutrophils \geq 1,000/microliter (mCL); Platelets \geq 100,000/mCL; No extramedullary disease; No blasts with Auer rods detected; and Independent of transfusions. CRc, in addition to CR criteria, required reversion to a normal karyotype with an abnormal karyotype at the time of diagnosis. The Full Analysis Set included all participants who received at least 1 dose of study drug with treatment designated according to the planned treatment.

End point type	Primary
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End point timeframe:

At the end of induction (Group A: up to end of Cycle 2; Group B: up to end of Cycle 4) (cycle length = up to 28 days); Group C: From Day 1 until meeting the criteria for study treatment discontinuation (up to approximately 3 years)

Notes:

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

Justification: No statistical comparison was planned or performed.

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b ENTO 400 mg + Cytarabine + Daunorubicin	Group A Phase 2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	9	41	5
Units: Percentage of Participants				
number (confidence interval 95%)	66.7 (9.4 to 99.2)	66.7 (29.9 to 92.5)	46.3 (30.7 to 62.6)	0.0 (0.0 to 52.2)

End point values	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	17	14
Units: Percentage of Participants				
number (confidence interval 95%)	16.7 (0.4 to 64.1)	25.0 (3.2 to 65.1)	0.0 (0.0 to 19.5)	7.1 (0.2 to 33.9)

End point values	Group C Phase 1b ENTO 400 mg	Group C Phase 1b ENTO 800 mg	Group C Phase 2 ENTO 400 mg (Cohort C1A - R/R AML)	Group C Phase 2 ENTO 400 mg (Cohort C2 - MLL)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	6	13
Units: Percentage of Participants				
number (confidence interval 95%)	0.0 (0.0 to 41.0)	0.0 (0.0 to 41.0)	0.0 (0.0 to 45.9)	15.4 (1.9 to 45.4)

End point values	Group C Phase 2 ENTO 400 mg (Cohort C3 - Untreated AML)			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: Percentage of Participants				
number (confidence interval 95%)	11.1 (0.3 to 48.2)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With Composite Complete Remission at the End of Induction

End point title	Percentage of Participants With Composite Complete Remission at the End of Induction ^[4]
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End point description:

Clinical response was assessed according to the International Working Group criteria (Cheson 2003). Composite complete remission included CR, CRc, and morphologic complete remission with incomplete blood count recovery (CRi). CR required all of the following: < 5% blasts in bone marrow aspirate; Neutrophils \geq 1,000/mcL; Platelets \geq 100,000/mcL; No extramedullary disease; No blasts with Auer rods detected; and Independent of transfusions. CRc, in addition to CR criteria, required reversion to a normal karyotype with an abnormal karyotype at the time of diagnosis. CRi required all of the CR criteria except the criterion of neutrophils and platelets. Participants in the Full Analysis Set were analyzed.

End point type	Primary
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End point timeframe:

At the end of induction (Group A: up to end of Cycle 2; Group B: up to end of Cycle 4) (cycle length = up to 28 days); Group C: From Day 1 until meeting the criteria for study treatment discontinuation (up to approximately 3 years)

Notes:

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

Justification: No statistical comparison was planned or performed.

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b ENTO 400 mg + Cytarabine + Daunorubicin	Group A Phase 2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	9	41	5
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (29.2 to 100)	77.8 (40 to 97.2)	65.9 (49.4 to 79.9)	40.0 (5.3 to 85.3)

End point values	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	17	14
Units: Percentage of Participants				
number (confidence interval 95%)	50.0 (11.8 to 88.2)	25.0 (3.2 to 65.1)	23.5 (6.8 to 49.9)	14.3 (1.8 to 42.8)

End point values	Group C Phase 1b ENTO 400 mg	Group C Phase 1b ENTO 800 mg	Group C Phase 2 ENTO 400 mg (Cohort C1A - R/R AML)	Group C Phase 2 ENTO 400 mg (Cohort C2 - MLL)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	6	13
Units: Percentage of Participants				
number (confidence interval 95%)	14.3 (0.4 to 57.9)	0.0 (0.0 to 41.0)	0.0 (0.0 to 45.9)	15.4 (1.9 to 45.4)

End point values	Group C Phase 2 ENTO 400 mg (Cohort C3 - Untreated AML)			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: Percentage of Participants				
number (confidence interval 95%)	11.1 (0.3 to 48.2)			

Statistical analyses

Primary: Percentage of Participants With Overall Response at the End of Induction

End point title	Percentage of Participants With Overall Response at the End of Induction ^[5]
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End point description:

Clinical response was assessed according to the International Working Group criteria (Cheson 2003). Overall response included CR, CRc, CRi, and partial remission (PR). CR required all of the following: < 5% blasts in bone marrow aspirate; Neutrophils \geq 1,000/mcL; Platelets \geq 100,000/mcL; No extramedullary disease; No blasts with Auer rods detected; and Independent of transfusions. CRc, in addition to CR criteria, required reversion to a normal karyotype with an abnormal karyotype at the time of diagnosis. CRi required all of the CR criteria except the criterion of neutrophils and platelets. PR required all of the following: \geq 50% decrease in blasts in bone marrow aspirate to a range of 5% to 25%; Neutrophils \geq 1,000/mcL; Platelets \geq 100,000/mcL; Independent of transfusions; and A value of \leq 5% blasts was also considered a PR if Auer rods were detected. Participants in the Full Analysis Set were analyzed.

End point type	Primary
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End point timeframe:

At the end of induction (Group A: up to end of Cycle 2; Group B: up to end of Cycle 4) (cycle length = up to 28 days); Group C: From Day 1 until meeting the criteria for study treatment discontinuation (up to approximately 3 years)

Notes:

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

Justification: No statistical comparison was planned or performed.

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b ENTO 400 mg + Cytarabine + Daunorubicin	Group A Phase 2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	9	41	5
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (29.2 to 100)	77.8 (40 to 97.2)	70.7 (54.5 to 83.9)	40.0 (5.3 to 85.3)

End point values	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	17	14
Units: Percentage of Participants				
number (confidence interval 95%)	50.0 (11.8 to 88.2)	25.0 (3.2 to 65.1)	23.5 (6.8 to 49.9)	14.3 (1.8 to 42.8)

End point values	Group C Phase 1b ENTO 400 mg	Group C Phase 1b ENTO 800 mg	Group C Phase 2 ENTO 400 mg (Cohort C1A - R/R AML)	Group C Phase 2 ENTO 400 mg (Cohort C2 - MLL)
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Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	6	13
Units: Percentage of Participants				
number (confidence interval 95%)	14.3 (0.4 to 57.9)	0.0 (0 to 41)	0.0 (0 to 45.9)	15.4 (1.9 to 45.4)

End point values	Group C Phase 2 ENTO 400 mg (Cohort C3 - Untreated AML)			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: Percentage of Participants				
number (confidence interval 95%)	11.1 (0.3 to 48.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Exposure of Entospletinib

End point title	Duration of Exposure of Entospletinib
End point description: The Safety Analysis Set included all participants who received at least 1 dose of study drug.	
End point type	Secondary
End point timeframe: First dose date up to approximately 3 years	

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine	Group B Phase 1b ENTO 400 mg + Decitabine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	50	5	6
Units: weeks				
median (full range (min-max))	8.6 (6.1 to 10.0)	7.1 (0.9 to 72.9)	13.7 (1.6 to 50.9)	15.4 (1.9 to 58.9)

End point values	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)	Group C Phase 1b/2 ENTO 400 mg
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Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	17	14	35
Units: weeks				
median (full range (min-max))	10.1 (1.3 to 39.4)	13.9 (1.9 to 40.0)	10.1 (0.9 to 47.0)	4.4 (1.4 to 15.6)

End point values	Group C Phase 1b ENTO 800 mg			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: weeks				
median (full range (min-max))	7.6 (2.0 to 9.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Event Free Survival (EFS)

End point title	Event Free Survival (EFS)
End point description:	
EFS was defined as the time interval from the start of the study therapy until the date of treatment failure, acute myeloid leukemia (AML) relapse, or death from any cause, whichever occurred first. Participants who received other anti-cancer therapy (prior to the event if any) were censored. Median EFS was analyzed using Kaplan-Meier (KM) method. Participants in the Full Analysis Set were analyzed. 999 = not reached due to low number of participants with an event.	
End point type	Secondary
End point timeframe:	
First dose date up to approximately 38 months	

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b ENTO 400 mg + Cytarabine + Daunorubicin	Group A Phase 2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	9	41	5
Units: months				
median (confidence interval 95%)	999 (999 to 999)	1.9 (0.9 to 1.9)	9.0 (2.3 to 999)	2.2 (0.5 to 4.7)

End point values	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
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		In)		
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	17	14
Units: months				
median (confidence interval 95%)	2.9 (1.1 to 7.7)	2.3 (0.5 to 9.0)	3.2 (0.5 to 4.2)	2.4 (2.1 to 3.9)

End point values	Group C Phase 1b ENTO 400 mg	Group C Phase 1b ENTO 800 mg	Group C Phase 2 ENTO 400 mg (Cohort C1A - R/R AML)	Group C Phase 2 ENTO 400 mg (Cohort C2 - MLL)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	6	13
Units: months				
median (confidence interval 95%)	1.8 (0.9 to 1.9)	1.8 (0.5 to 1.9)	1.0 (0.7 to 2.8)	1.0 (0.8 to 2.7)

End point values	Group C Phase 2 ENTO 400 mg (Cohort C3 - Untreated AML)			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: months				
median (confidence interval 95%)	1.7 (0.8 to 1.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)
End point description:	
OS was defined as the time interval from the start of the study therapy to death from any cause. Median OS was analyzed using KM method. Participants in the Full Analysis Set were analyzed. 999 = not reached due to low number of participants with an event.	
End point type	Secondary
End point timeframe:	
First dose date up to approximately 38 months	

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b ENTO 400 mg + Cytarabine + Daunorubicin	Group A Phase 2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	3	9	41	5
Units: months				
median (confidence interval 95%)	37.1 (9.1 to 999)	34.1 (1.2 to 999)	999 (16.8 to 999)	3.2 (0.8 to 12.7)

End point values	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	17	14
Units: months				
median (confidence interval 95%)	5.3 (2.4 to 999)	6.9 (1.4 to 999)	7.3 (2.4 to 999)	6.2 (3.2 to 10.2)

End point values	Group C Phase 1b ENTO 400 mg	Group C Phase 1b ENTO 800 mg	Group C Phase 2 ENTO 400 mg (Cohort C1A - R/R AML)	Group C Phase 2 ENTO 400 mg (Cohort C2 - MLL)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	7	7	6	13
Units: months				
median (confidence interval 95%)	5.9 (0.9 to 6.3)	5.6 (0.5 to 8.4)	8.2 (0.7 to 24.3)	7.9 (3.3 to 11.9)

End point values	Group C Phase 2 ENTO 400 mg (Cohort C3 - Untreated AML)			
Subject group type	Subject analysis set			
Number of subjects analysed	9			
Units: months				
median (confidence interval 95%)	2.2 (1.0 to 4.7)			

Statistical analyses

Secondary: Percentage of Participants Experiencing Treatment-Emergent Adverse Events

End point title	Percentage of Participants Experiencing Treatment-Emergent Adverse Events
End point description: Participants in the Safety Analysis Set were analyzed.	
End point type	Secondary
End point timeframe: First dose date up to the last dose date plus 30 days (maximum: 18 months)	

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine	Group B Phase 1b ENTO 400 mg + Decitabine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	50	5	6
Units: Percentage of Participants				
number (not applicable)	100.0	100.0	100.0	100.0

End point values	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)	Group C Phase 1b/2 ENTO 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	17	14	35
Units: Percentage of Participants				
number (not applicable)	100.0	100.0	100.0	100.0

End point values	Group C Phase 1b ENTO 800 mg			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of Participants				
number (not applicable)	100.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants Who Experienced Laboratory Abnormalities

End point title	Percentage of Participants Who Experienced Laboratory Abnormalities
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End point description:

Treatment-emergent laboratory abnormalities were defined as values that increase at least one toxicity grade from baseline. The most severe graded abnormality from all tests was counted for each participant. Participants in the Safety Analysis Set who had non-missing postbaseline value prior to or on the last dosing date plus 30 days were analyzed.

End point type	Secondary
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End point timeframe:

First dose date up to the last dose date plus 30 days (maximum: 18 months)

End point values	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine	Group B Phase 1b ENTO 400 mg + Decitabine
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	50	5	6
Units: Percentage of Participants				
number (not applicable)				
Any Laboratory Abnormality	100	100	100	100
Grade 3 or 4 Laboratory Abnormalities	100	98.0	100	100

End point values	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)	Group C Phase 1b/2 ENTO 400 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	17	14	35
Units: Percentage of Participants				
number (not applicable)				
Any Laboratory Abnormality	100	94.1	100	100
Grade 3 or 4 Laboratory Abnormalities	85.7	94.1	92.9	82.9

End point values	Group C Phase 1b ENTO 800 mg			
Subject group type	Reporting group			
Number of subjects analysed	7			
Units: Percentage of Participants				
number (not applicable)				
Any Laboratory Abnormality	100			
Grade 3 or 4 Laboratory Abnormalities	85.7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

- All-Cause Mortality: First dose date up to approximately 38 months.
- Adverse Events: First dose date up to the last dose date plus 30 days (maximum: 18 months)

Adverse event reporting additional description:

The Safety Analysis Set included all participants who received at least 1 dose of study drug.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin
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Reporting group description:

Participants received ENTO 200 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (during induction chemotherapy).

Reporting group title	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin
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Reporting group description:

Phase1b/2: Participants received ENTO 400 mg tablet orally every 12 hours on Days 1 to 14 (Cycle 0) (monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with chemotherapy (cytarabine 100 mg/m² on Days 1-7 and daunorubicin 60 mg/m² on Days 1-3 intravenously) for up to two 14-day cycles (Cycles 1 and 2) (induction chemotherapy).

Phase 2 only: Participants who achieved a CR/CRi and did not require or could not proceed to allogeneic stem cell transplantation (SCT) were offered post-remission chemotherapy (cytarabine 3 g/m² intravenously every 12 hours on Days 1, 3, and 5 or 1 g/m² intravenously once daily on Days 1-5) in combination with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for at least 3 and up to 4 cycles. Participants who maintained a CR/CRi after 3 or 4 cycles were offered maintenance therapy with ENTO 400 mg tablet orally every 12 hours on Days 1-28 of each 28-day cycle for up to 12 cycles.

Reporting group title	Group B Phase 1b ENTO 200 mg + Decitabine
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Reporting group description:

Participants received ENTO 200 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 200 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 200 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 1b ENTO 400 mg + Decitabine
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Reporting group description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28) (induction chemotherapy). Participants who achieved a CR/CRi received SCT (if eligible) per investigator's discretion; other participants were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)
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Reporting group description:

As part of the safety run-in, participants received ENTO 400 mg tablet orally every 12 hours on Days 1-14 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in

combination with azacitidine 75 mg/m² intravenously on Days 1-7 of a 28-day cycle (Cycle 1). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
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Reporting group description:

Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with decitabine 20 mg/m² intravenously on Days 1-10 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with decitabine on Days 1-5 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to decitabine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)
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Reporting group description:

Participants were randomized to receive ENTO 400 mg tablet orally every 12 hours on Days 1-5 (Cycle 0) (during monotherapy lead-in), followed by ENTO 400 mg tablet orally every 12 hours in combination with azacitidine 75 mg/m² intravenously on Days 1-7 of every 28-day cycle for 2 cycles (or up to 4 cycles for participants with persistent disease after Cycle 2 Day 28). Participants who were not eligible for SCT were offered maintenance therapy with ENTO every 12 hours on Days 1-28 in combination with azacitidine on Days 1-7 of every 28-day cycle for at least 2 cycles (maximum up to 12 cycles). Participants who were intolerant to azacitidine were offered maintenance therapy with ENTO 400 mg as monotherapy after completing 2 maintenance cycles.

Reporting group title	Group C Phase 1b/2 ENTO 400 mg
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Reporting group description:

Participants received ENTO 400 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Reporting group title	Group C Phase 1b ENTO 800 mg
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Reporting group description:

Participants received ENTO 800 mg tablet orally every 12 hours on Days 1-28 of every 28-day cycle until treatment failure, start of new therapy, unacceptable toxicity, withdrawal of consent, withdrawal from study by investigator, or study termination by sponsor.

Serious adverse events	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	23 / 50 (46.00%)	5 / 5 (100.00%)
number of deaths (all causes)	2	21	5
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			

subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
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	0 / 3 (0.00%)	1 / 50 (2.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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

Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
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 consolidation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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

Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
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 chronic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
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 / 3 (0.00%)	0 / 50 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuromyopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Transient ischaemic attack			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	13 / 50 (26.00%)	4 / 5 (80.00%)
occurrences causally related to treatment / all	0 / 0	11 / 16	5 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			

subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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
Oesophagitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photosensitivity reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (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
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	2 / 5 (40.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anal abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis staphylococcal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal infection			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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
Vascular device infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			

subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (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
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)	7 / 8 (87.50%)	11 / 17 (64.71%)
number of deaths (all causes)	4	5	12
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thyroid cancer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (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
Thrombosis			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (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
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (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
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (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
Catheter site haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
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 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hypoxia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (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
Lung consolidation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
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 alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural			

complications			
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac failure chronic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
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 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuromyopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	4 / 6 (66.67%)	3 / 8 (37.50%)	8 / 17 (47.06%)
occurrences causally related to treatment / all	5 / 7	3 / 4	8 / 14
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
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 haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photosensitivity reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Lung infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Anal abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis staphylococcal			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enteritis infectious			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (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
Escherichia sepsis			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Gout			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (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

Serious adverse events	Group B Phase 2	Group C Phase 1b/2	Group C Phase 1b
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	ENTO 400 mg + Azacitidine (Randomized)	ENTO 400 mg	ENTO 800 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 14 (50.00%)	19 / 35 (54.29%)	4 / 7 (57.14%)
number of deaths (all causes)	11	30	6
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia recurrent			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Thyroid cancer			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (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
Hypotension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
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	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (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
Non-cardiac chest pain			

subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Catheter site haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
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 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Hypoxia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
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 consolidation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pleural effusion			

subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
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 alkaline phosphatase increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (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

Angina pectoris			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
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 chronic			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Haemorrhage intracranial			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cognitive disorder			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuromyopathy			

subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	5 / 35 (14.29%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Haematemesis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (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
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Colitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematochezia			

subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal ischaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestine perforation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctalgia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Stomatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Photosensitivity reaction			

subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
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 haemorrhage			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Musculoskeletal and connective tissue disorders			
Muscular weakness			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 14 (14.29%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	2 / 7 (28.57%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Device related infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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

Bacteraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Anal abscess			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Bacterial infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (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
Cellulitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Cellulitis staphylococcal			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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 infectious			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			

subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Mucosal infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Otitis media			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (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
Staphylococcal sepsis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular device infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour lysis syndrome			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (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
Gout			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Group A Phase 1b ENTO 200 mg + Cytarabine + Daunorubicin	Group A Phase 1b/2 ENTO 400 mg + Cytarabine + Daunorubicin	Group B Phase 1b ENTO 200 mg + Decitabine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	50 / 50 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	7 / 50 (14.00%)	0 / 5 (0.00%)
occurrences (all)	1	8	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	12 / 50 (24.00%)	0 / 5 (0.00%)
occurrences (all)	0	12	0
Haematoma			

subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Embolism			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Orthostatic hypotension			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	2 / 3 (66.67%)	29 / 50 (58.00%)	2 / 5 (40.00%)
occurrences (all)	3	35	2
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	14 / 50 (28.00%)	3 / 5 (60.00%)
occurrences (all)	1	16	3
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	9 / 50 (18.00%)	0 / 5 (0.00%)
occurrences (all)	0	12	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	8 / 50 (16.00%)	0 / 5 (0.00%)
occurrences (all)	0	9	0
Mucosal inflammation			
subjects affected / exposed	0 / 3 (0.00%)	10 / 50 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	10	1
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	7 / 50 (14.00%)	0 / 5 (0.00%)
occurrences (all)	0	7	0
Chest pain			

subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Catheter site erythema			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Malaise			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Catheter site pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Catheter site rash			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Catheter site dermatitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Device related thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	20 / 50 (40.00%)	2 / 5 (40.00%)
occurrences (all)	0	23	2
Cough			
subjects affected / exposed	0 / 3 (0.00%)	18 / 50 (36.00%)	1 / 5 (20.00%)
occurrences (all)	0	21	1
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	10 / 50 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	16	1
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	10 / 50 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	12	0
Hypoxia			
subjects affected / exposed	0 / 3 (0.00%)	11 / 50 (22.00%)	0 / 5 (0.00%)
occurrences (all)	0	11	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	7 / 50 (14.00%)	1 / 5 (20.00%)
occurrences (all)	0	8	1
Pleural effusion			

subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Pulmonary oedema			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	1 / 5 (20.00%)
occurrences (all)	0	3	1
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Rhinorrhoea			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Sinus pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Dyspnoea exertional			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rales			

subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hiccups			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lung infiltration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hyposecretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rhonchi			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	16 / 50 (32.00%)	2 / 5 (40.00%)
occurrences (all)	0	16	2
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	7 / 50 (14.00%)	1 / 5 (20.00%)
occurrences (all)	0	8	1
Confusional state			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	1 / 5 (20.00%)
occurrences (all)	0	6	1
Delirium			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0

Depression			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Hallucination			
subjects affected / exposed	1 / 3 (33.33%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Apathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Suicidal ideation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	26 / 50 (52.00%)	3 / 5 (60.00%)
occurrences (all)	0	38	3
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	18 / 50 (36.00%)	2 / 5 (40.00%)
occurrences (all)	0	25	2
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	16 / 50 (32.00%)	2 / 5 (40.00%)
occurrences (all)	0	24	2
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	12 / 50 (24.00%)	0 / 5 (0.00%)
occurrences (all)	0	12	0
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	6 / 50 (12.00%)	1 / 5 (20.00%)
occurrences (all)	0	9	1
Alanine aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	8 / 50 (16.00%)	0 / 5 (0.00%)
occurrences (all)	0	13	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	8 / 50 (16.00%)	0 / 5 (0.00%)
occurrences (all)	0	11	0
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Weight decreased			
subjects affected / exposed	1 / 3 (33.33%)	2 / 50 (4.00%)	1 / 5 (20.00%)
occurrences (all)	1	2	1
Ejection fraction decreased			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 50 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Weight increased			
subjects affected / exposed	2 / 3 (66.67%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Troponin I increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	2 / 5 (40.00%)
occurrences (all)	0	2	2
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	1 / 5 (20.00%)
occurrences (all)	0	4	1
Lipase increased			

subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
White blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Amylase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Body temperature increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Blood creatinine decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 50 (0.00%) 0	0 / 5 (0.00%) 0
Chest X-ray abnormal subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 50 (0.00%) 0	0 / 5 (0.00%) 0
Spleen palpable subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 50 (0.00%) 0	0 / 5 (0.00%) 0
Ultrasound liver abnormal subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 50 (0.00%) 0	0 / 5 (0.00%) 0
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 50 (4.00%) 3	1 / 5 (20.00%) 1
Fall subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	6 / 50 (12.00%) 7	0 / 5 (0.00%) 0
Infusion related reaction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 50 (4.00%) 2	0 / 5 (0.00%) 0
Transfusion reaction subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 50 (2.00%) 1	0 / 5 (0.00%) 0
Eye contusion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 50 (0.00%) 0	0 / 5 (0.00%) 0
Skin abrasion subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 50 (2.00%) 1	0 / 5 (0.00%) 0
Limb injury subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 50 (0.00%) 0	0 / 5 (0.00%) 0
Pelvic fracture			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular access complication			
subjects affected / exposed	1 / 3 (33.33%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	7 / 50 (14.00%)	1 / 5 (20.00%)
occurrences (all)	0	7	1
Sinus tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	6 / 50 (12.00%)	0 / 5 (0.00%)
occurrences (all)	0	7	0
Sinus bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Angina pectoris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Diastolic dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Nervous system disorders			
Headache			
subjects affected / exposed	1 / 3 (33.33%)	20 / 50 (40.00%)	2 / 5 (40.00%)
occurrences (all)	1	29	2
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	14 / 50 (28.00%)	0 / 5 (0.00%)
occurrences (all)	0	17	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	11 / 50 (22.00%)	0 / 5 (0.00%)
occurrences (all)	0	12	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Tremor			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Depressed level of consciousness			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Amnesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Encephalopathy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Lethargy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Parosmia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cerebrovascular accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 3 (66.67%)	36 / 50 (72.00%)	1 / 5 (20.00%)
occurrences (all)	2	53	3
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	24 / 50 (48.00%)	3 / 5 (60.00%)
occurrences (all)	0	28	3
Leukocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pancytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hypoacusis			

subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	10 / 50 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	10	0
Dry eye			
subjects affected / exposed	1 / 3 (33.33%)	4 / 50 (8.00%)	0 / 5 (0.00%)
occurrences (all)	1	4	0
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Scleral hyperaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Optic nerve cupping			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ulcerative keratitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 3 (100.00%)	34 / 50 (68.00%)	4 / 5 (80.00%)
occurrences (all)	4	49	4
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	34 / 50 (68.00%)	1 / 5 (20.00%)
occurrences (all)	2	55	1
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	20 / 50 (40.00%)	3 / 5 (60.00%)
occurrences (all)	1	28	3
Vomiting			
subjects affected / exposed	2 / 3 (66.67%)	16 / 50 (32.00%)	0 / 5 (0.00%)
occurrences (all)	2	28	0
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	13 / 50 (26.00%)	0 / 5 (0.00%)
occurrences (all)	2	15	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	8 / 50 (16.00%)	1 / 5 (20.00%)
occurrences (all)	0	8	1
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	7 / 50 (14.00%)	0 / 5 (0.00%)
occurrences (all)	0	7	0
Haemorrhoids			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	8 / 50 (16.00%)	0 / 5 (0.00%)
occurrences (all)	0	8	0
Oral pain			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3 (33.33%)	6 / 50 (12.00%)	1 / 5 (20.00%)
occurrences (all)	1	7	1
Abdominal pain upper			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Angina bullosa haemorrhagica			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Colitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Mouth ulceration			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Anal incontinence			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Lip pain			

subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Mouth haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Anal ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Small intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Tongue ulceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Colitis ischaemic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Enterocolitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Faecaloma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ileus			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Intestinal dilatation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pancreatic disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)	21 / 50 (42.00%)	1 / 5 (20.00%)
occurrences (all)	1	27	2
Petechiae			
subjects affected / exposed	1 / 3 (33.33%)	4 / 50 (8.00%)	0 / 5 (0.00%)
occurrences (all)	1	4	0
Pruritus			
subjects affected / exposed	1 / 3 (33.33%)	7 / 50 (14.00%)	0 / 5 (0.00%)
occurrences (all)	1	7	0
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	6 / 50 (12.00%)	0 / 5 (0.00%)
occurrences (all)	0	6	0
Rash			

subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Erythema			
subjects affected / exposed	1 / 3 (33.33%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Photosensitivity reaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Drug eruption			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hyperhidrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain of skin			
subjects affected / exposed	1 / 3 (33.33%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rash papular			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 3 (0.00%)	8 / 50 (16.00%)	0 / 5 (0.00%)
occurrences (all)	0	8	0
Haematuria			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	2 / 5 (40.00%)
occurrences (all)	0	5	2
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Nephrolithiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Back pain			
subjects affected / exposed	1 / 3 (33.33%)	6 / 50 (12.00%)	0 / 5 (0.00%)
occurrences (all)	1	6	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	7 / 50 (14.00%)	1 / 5 (20.00%)
occurrences (all)	0	8	1
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	6 / 50 (12.00%)	0 / 5 (0.00%)
occurrences (all)	0	6	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Myositis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vertebral lesion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	11 / 50 (22.00%)	1 / 5 (20.00%)
occurrences (all)	0	12	1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	1 / 5 (20.00%)
occurrences (all)	0	4	1
Device related infection			
subjects affected / exposed	1 / 3 (33.33%)	9 / 50 (18.00%)	1 / 5 (20.00%)
occurrences (all)	1	11	1
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	5 / 50 (10.00%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Mucosal infection			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			

subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Folliculitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Otitis externa			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Soft tissue infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Staphylococcal infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Atypical pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Bacterial infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Bacterial sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Corona virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Enterococcal bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Leptotrichia infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Mycobacterium avium complex infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Perirectal abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tinea cruris			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 3 (0.00%)	22 / 50 (44.00%)	2 / 5 (40.00%)
occurrences (all)	0	25	2
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	10 / 50 (20.00%)	1 / 5 (20.00%)
occurrences (all)	0	15	1
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	7 / 50 (14.00%)	1 / 5 (20.00%)
occurrences (all)	0	7	1
Hyponatraemia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	1 / 5 (20.00%)
occurrences (all)	0	4	1
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	4 / 50 (8.00%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	3 / 50 (6.00%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hypermagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	10	0
Hyperphosphataemia			

subjects affected / exposed	0 / 3 (0.00%)	1 / 50 (2.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fluid overload			
subjects affected / exposed	0 / 3 (0.00%)	2 / 50 (4.00%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Hypercalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypervolaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypophagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 50 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group B Phase 1b ENTO 400 mg + Decitabine	Group B Phase 2 ENTO 400 mg + Azacitidine (Safety Run-In)	Group B Phase 2 ENTO 400 mg + Decitabine (Randomized)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	7 / 8 (87.50%)	17 / 17 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Vascular disorders			

Hypotension			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	4 / 17 (23.53%)
occurrences (all)	0	3	6
Hypertension			
subjects affected / exposed	3 / 6 (50.00%)	0 / 8 (0.00%)	3 / 17 (17.65%)
occurrences (all)	3	0	3
Haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	2 / 17 (11.76%)
occurrences (all)	0	1	3
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Embolism			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Hot flush			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	3 / 6 (50.00%)	4 / 8 (50.00%)	6 / 17 (35.29%)
occurrences (all)	3	4	9
Fatigue			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	9 / 17 (52.94%)
occurrences (all)	1	2	10
Pyrexia			
subjects affected / exposed	2 / 6 (33.33%)	2 / 8 (25.00%)	2 / 17 (11.76%)
occurrences (all)	2	2	3
Chills			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	5
Mucosal inflammation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	2
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Malaise			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	2
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Catheter site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Catheter site rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Injection site erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Catheter site dermatitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Device related thrombosis			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
General physical health deterioration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Performance status decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	3 / 6 (50.00%)	2 / 8 (25.00%)	5 / 17 (29.41%)
occurrences (all)	3	2	6
Cough			
subjects affected / exposed	4 / 6 (66.67%)	3 / 8 (37.50%)	5 / 17 (29.41%)
occurrences (all)	4	4	5
Epistaxis			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	3 / 17 (17.65%)
occurrences (all)	3	0	3
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	3 / 17 (17.65%)
occurrences (all)	0	0	4
Hypoxia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Nasal congestion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	1	0	2
Pleural effusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	3 / 17 (17.65%)
occurrences (all)	0	0	3
Productive cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pulmonary oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rhinitis allergic			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Haemoptysis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dyspnoea exertional			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Pulmonary hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rales			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hiccups			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Lung infiltration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Paranasal sinus hyposecretion			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Rhonchi			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	2 / 17 (11.76%)
occurrences (all)	1	1	2
Anxiety			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1

Confusional state			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	2 / 17 (11.76%)
occurrences (all)	0	1	2
Delirium			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	2
Depression			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hallucination			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Mental status changes			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	2 / 17 (11.76%)
occurrences (all)	0	1	2
Restlessness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Apathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Suicidal ideation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	3 / 6 (50.00%)	3 / 8 (37.50%)	5 / 17 (29.41%)
occurrences (all)	3	3	7
White blood cell count decreased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	7 / 17 (41.18%)
occurrences (all)	2	3	12
Neutrophil count decreased			
subjects affected / exposed	2 / 6 (33.33%)	2 / 8 (25.00%)	4 / 17 (23.53%)
occurrences (all)	2	3	4
Blood bilirubin increased			

subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	5 / 17 (29.41%)
occurrences (all)	0	3	7
Blood creatinine increased			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	1 / 17 (5.88%)
occurrences (all)	1	1	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	0 / 17 (0.00%)
occurrences (all)	0	4	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	1 / 17 (5.88%)
occurrences (all)	0	4	1
Lymphocyte count decreased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	4 / 17 (23.53%)
occurrences (all)	1	2	4
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	3 / 17 (17.65%)
occurrences (all)	0	0	3
Ejection fraction decreased			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	0 / 17 (0.00%)
occurrences (all)	1	2	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	3 / 17 (17.65%)
occurrences (all)	0	0	3
International normalised ratio increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	3
Weight increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Troponin I increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	3
White blood cell count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Amylase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Lymphocyte count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
C-reactive protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Troponin increased			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Blood creatinine decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Blood phosphorus increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Chest X-ray abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Spleen palpable			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Ultrasound liver abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	4 / 17 (23.53%)
occurrences (all)	0	0	5
Infusion related reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Transfusion reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eye contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Limb injury			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pelvic fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Vascular access complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	3 / 17 (17.65%)
occurrences (all)	0	1	3
Sinus tachycardia			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	2 / 17 (11.76%)
occurrences (all)	2	1	3
Sinus bradycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Supraventricular tachycardia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Angina pectoris			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Arrhythmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Bradycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Diastolic dysfunction subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 3	0 / 8 (0.00%) 0	3 / 17 (17.65%) 3
Dizziness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Dysgeusia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	3 / 8 (37.50%) 3	2 / 17 (11.76%) 2
Paraesthesia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Tremor subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Depressed level of consciousness subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	0 / 17 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Amnesia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Encephalopathy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Lethargy subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Neuropathy peripheral			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Parosmia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Somnolence			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Cerebrovascular accident			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	3 / 6 (50.00%)	2 / 8 (25.00%)	2 / 17 (11.76%)
occurrences (all)	3	2	3
Anaemia			
subjects affected / exposed	1 / 6 (16.67%)	2 / 8 (25.00%)	5 / 17 (29.41%)
occurrences (all)	4	2	8
Leukocytosis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Thrombocytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Lymphadenopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pancytopenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	2	0	2
Hypoacusis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Tinnitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	2
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dry eye			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Eye pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Scleral hyperaemia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Eye haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Eye oedema			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Optic nerve cupping			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Periorbital oedema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Ulcerative keratitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	4 / 6 (66.67%) 5	4 / 8 (50.00%) 4	5 / 17 (29.41%) 6
Diarrhoea subjects affected / exposed occurrences (all)	3 / 6 (50.00%) 4	3 / 8 (37.50%) 4	9 / 17 (52.94%) 16
Constipation subjects affected / exposed occurrences (all)	4 / 6 (66.67%) 4	6 / 8 (75.00%) 7	10 / 17 (58.82%) 13
Vomiting subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 8 (12.50%) 1	6 / 17 (35.29%) 9
Abdominal pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Stomatitis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	4 / 17 (23.53%) 5
Abdominal distension subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 2	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	3 / 17 (17.65%) 3
Dyspepsia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 8 (25.00%) 2	0 / 17 (0.00%) 0
Oral pain subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	2 / 17 (11.76%) 4
Gastrooesophageal reflux disease			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	4 / 17 (23.53%)
occurrences (all)	1	0	4
Dry mouth			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	2 / 8 (25.00%)	1 / 17 (5.88%)
occurrences (all)	0	2	1
Gingival bleeding			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rectal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Angina bullosa haemorrhagica			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Colitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Proctalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Anal incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Haemorrhoidal haemorrhage			

subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Lip pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Mouth haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Anal ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Small intestinal obstruction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Tongue ulceration			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Ascites			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Colitis ischaemic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Enterocolitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Faecaloma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Ileus			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Intestinal dilatation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Pancreatic disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Salivary hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	3 / 6 (50.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	3	0	0
Petechiae			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	3
Pruritus			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Alopecia			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Skin ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dry skin			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Photosensitivity reaction			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Drug eruption			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Rash macular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Dermal cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Ecchymosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Pain of skin			

subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Skin lesion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	2 / 17 (11.76%)
occurrences (all)	0	1	2
Haematuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	1 / 17 (5.88%)
occurrences (all)	1	1	1
Pollakiuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Nephrolithiasis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Renal cyst			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	2	0	1
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	3
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	4 / 17 (23.53%)
occurrences (all)	1	1	5
Myalgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	3 / 17 (17.65%)
occurrences (all)	0	0	4
Bone pain			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Myositis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Vertebral lesion			

subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Infections and infestations			
Lung infection			
subjects affected / exposed	2 / 6 (33.33%)	1 / 8 (12.50%)	1 / 17 (5.88%)
occurrences (all)	2	1	1
Urinary tract infection			
subjects affected / exposed	1 / 6 (16.67%)	3 / 8 (37.50%)	0 / 17 (0.00%)
occurrences (all)	1	3	0
Device related infection			
subjects affected / exposed	2 / 6 (33.33%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	2	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Mucosal infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	1 / 6 (16.67%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	1	1	0
Clostridium difficile colitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Oral candidiasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Sepsis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	1	0	1

Clostridium difficile infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Folliculitis subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Bacteraemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Candida infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Otitis externa subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Skin infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	2 / 17 (11.76%) 3
Soft tissue infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	0 / 17 (0.00%) 0
Staphylococcal infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Abdominal infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	0 / 17 (0.00%) 0
Atypical pneumonia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Bacterial infection subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0
Bacterial sepsis subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	0 / 17 (0.00%) 0

Chronic sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Corona virus infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Enterococcal bacteraemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Leptotrichia infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Mycobacterium avium complex infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Perirectal abscess			
subjects affected / exposed	1 / 6 (16.67%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Postoperative wound infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Staphylococcal skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Tinea cruris			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	3 / 8 (37.50%) 3	6 / 17 (35.29%) 7
Hypokalaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 3	3 / 17 (17.65%) 5
Hypomagnesaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	2 / 17 (11.76%) 6
Hyponatraemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	0 / 8 (0.00%) 0	4 / 17 (23.53%) 9
Hypophosphataemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	3 / 17 (17.65%) 3
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1	1 / 8 (12.50%) 1	1 / 17 (5.88%) 1
Hyperkalaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Hypoalbuminaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	3 / 17 (17.65%) 4
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 2	0 / 17 (0.00%) 0
Dehydration subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	2 / 8 (25.00%) 2	2 / 17 (11.76%) 2
Hypermagnesaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	0 / 8 (0.00%) 0	1 / 17 (5.88%) 1
Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 6 (0.00%) 0	1 / 8 (12.50%) 1	3 / 17 (17.65%) 3

Hyperphosphataemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	1 / 17 (5.88%)
occurrences (all)	0	1	1
Hypoglycaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	2 / 17 (11.76%)
occurrences (all)	0	0	2
Fluid overload			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hypercalcaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	0 / 17 (0.00%)
occurrences (all)	0	0	0
Hypernatraemia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Hypervolaemia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Hypophagia			
subjects affected / exposed	0 / 6 (0.00%)	1 / 8 (12.50%)	0 / 17 (0.00%)
occurrences (all)	0	1	0
Metabolic acidosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1
Vitamin D deficiency			
subjects affected / exposed	0 / 6 (0.00%)	0 / 8 (0.00%)	1 / 17 (5.88%)
occurrences (all)	0	0	1

Non-serious adverse events	Group B Phase 2 ENTO 400 mg + Azacitidine (Randomized)	Group C Phase 1b/2 ENTO 400 mg	Group C Phase 1b ENTO 800 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	33 / 35 (94.29%)	7 / 7 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Vascular disorders			
Hypotension			
subjects affected / exposed	5 / 14 (35.71%)	6 / 35 (17.14%)	1 / 7 (14.29%)
occurrences (all)	11	8	1
Hypertension			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Haematoma			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Deep vein thrombosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Embolism			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Orthostatic hypotension			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Oedema peripheral			
subjects affected / exposed	4 / 14 (28.57%)	4 / 35 (11.43%)	3 / 7 (42.86%)
occurrences (all)	5	4	3
Fatigue			
subjects affected / exposed	6 / 14 (42.86%)	10 / 35 (28.57%)	3 / 7 (42.86%)
occurrences (all)	6	10	3
Pyrexia			
subjects affected / exposed	1 / 14 (7.14%)	5 / 35 (14.29%)	0 / 7 (0.00%)
occurrences (all)	1	5	0
Chills			
subjects affected / exposed	5 / 14 (35.71%)	4 / 35 (11.43%)	0 / 7 (0.00%)
occurrences (all)	5	4	0
Mucosal inflammation			

subjects affected / exposed	1 / 14 (7.14%)	4 / 35 (11.43%)	0 / 7 (0.00%)
occurrences (all)	1	4	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Chest pain			
subjects affected / exposed	2 / 14 (14.29%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	3	4	0
Catheter site erythema			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Asthenia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Catheter site pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Catheter site rash			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	2 / 14 (14.29%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Catheter site dermatitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Device related thrombosis			

subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
General physical health deterioration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Injection site pain			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Performance status decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Scrotal oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	4 / 14 (28.57%)	10 / 35 (28.57%)	1 / 7 (14.29%)
occurrences (all)	4	10	1
Cough			
subjects affected / exposed	5 / 14 (35.71%)	5 / 35 (14.29%)	0 / 7 (0.00%)
occurrences (all)	6	5	0
Epistaxis			
subjects affected / exposed	2 / 14 (14.29%)	7 / 35 (20.00%)	0 / 7 (0.00%)
occurrences (all)	2	7	0
Oropharyngeal pain			
subjects affected / exposed	1 / 14 (7.14%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	1	3	0
Hypoxia			

subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Nasal congestion			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Pleural effusion			
subjects affected / exposed	2 / 14 (14.29%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Productive cough			
subjects affected / exposed	2 / 14 (14.29%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Pulmonary oedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 14 (0.00%)	3 / 35 (8.57%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Wheezing			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Atelectasis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Haemoptysis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Dyspnoea exertional			

subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences (all)	2	0	1
Pulmonary hypertension			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Rales			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Respiratory failure			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hiccups			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lung infiltration			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Paranasal sinus hyposecretion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhonchi			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 14 (28.57%)	7 / 35 (20.00%)	0 / 7 (0.00%)
occurrences (all)	4	8	0
Anxiety			
subjects affected / exposed	0 / 14 (0.00%)	3 / 35 (8.57%)	0 / 7 (0.00%)
occurrences (all)	0	3	0

Confusional state			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Delirium			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Depression			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Hallucination			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Restlessness			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Apathy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Suicidal ideation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Investigations			
Platelet count decreased			
subjects affected / exposed	7 / 14 (50.00%)	9 / 35 (25.71%)	1 / 7 (14.29%)
occurrences (all)	10	10	1
White blood cell count decreased			
subjects affected / exposed	5 / 14 (35.71%)	4 / 35 (11.43%)	1 / 7 (14.29%)
occurrences (all)	11	4	1
Neutrophil count decreased			
subjects affected / exposed	2 / 14 (14.29%)	6 / 35 (17.14%)	2 / 7 (28.57%)
occurrences (all)	5	6	2
Blood bilirubin increased			

subjects affected / exposed	4 / 14 (28.57%)	3 / 35 (8.57%)	0 / 7 (0.00%)
occurrences (all)	7	3	0
Blood creatinine increased			
subjects affected / exposed	7 / 14 (50.00%)	2 / 35 (5.71%)	2 / 7 (28.57%)
occurrences (all)	13	2	3
Alanine aminotransferase increased			
subjects affected / exposed	1 / 14 (7.14%)	4 / 35 (11.43%)	2 / 7 (28.57%)
occurrences (all)	7	4	2
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 14 (14.29%)	3 / 35 (8.57%)	1 / 7 (14.29%)
occurrences (all)	6	3	1
Lymphocyte count decreased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	1 / 7 (14.29%)
occurrences (all)	0	1	2
Weight decreased			
subjects affected / exposed	2 / 14 (14.29%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	3	1	0
Ejection fraction decreased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 14 (7.14%)	2 / 35 (5.71%)	1 / 7 (14.29%)
occurrences (all)	2	2	1
International normalised ratio increased			
subjects affected / exposed	2 / 14 (14.29%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Weight increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Troponin I increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Blood creatine phosphokinase increased			

subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
White blood cell count increased			
subjects affected / exposed	1 / 14 (7.14%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Amylase increased			
subjects affected / exposed	4 / 14 (28.57%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	7	0	0
Lymphocyte count increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	2 / 14 (14.29%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Bilirubin conjugated increased			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Body temperature increased			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Troponin increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood creatinine decreased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Chest X-ray abnormal			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Spleen palpable			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Ultrasound liver abnormal			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 14 (7.14%)	4 / 35 (11.43%)	1 / 7 (14.29%)
occurrences (all)	1	4	1
Fall			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Infusion related reaction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Transfusion reaction			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Eye contusion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Limb injury			

subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pelvic fracture			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vascular access complication			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	3 / 14 (21.43%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	3	1	0
Sinus tachycardia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Sinus bradycardia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Tachycardia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Palpitations			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Angina pectoris			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Arrhythmia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Diastolic dysfunction subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Nervous system disorders			
Headache subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2	6 / 35 (17.14%) 6	2 / 7 (28.57%) 2
Dizziness subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	5 / 35 (14.29%) 5	0 / 7 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 4	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Paraesthesia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	3 / 35 (8.57%) 4	0 / 7 (0.00%) 0
Tremor subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	2 / 35 (5.71%) 2	0 / 7 (0.00%) 0
Depressed level of consciousness subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 35 (2.86%) 1	0 / 7 (0.00%) 0
Syncope subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Amnesia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Encephalopathy subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Lethargy subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Neuropathy peripheral			

subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Parosmia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Somnolence			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Cerebrovascular accident			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	4 / 14 (28.57%)	8 / 35 (22.86%)	0 / 7 (0.00%)
occurrences (all)	4	12	0
Anaemia			
subjects affected / exposed	6 / 14 (42.86%)	10 / 35 (28.57%)	3 / 7 (42.86%)
occurrences (all)	10	11	3
Leukocytosis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Thrombocytopenia			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	2	3	0
Lymphadenopathy			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Neutropenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pancytopenia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			

subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Hypoacusis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Vision blurred			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dry eye			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Eye pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Scleral hyperaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Eye haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Optic nerve cupping			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Periorbital oedema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1

Ulcerative keratitis subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Gastrointestinal disorders			
Nausea subjects affected / exposed occurrences (all)	7 / 14 (50.00%) 9	15 / 35 (42.86%) 15	2 / 7 (28.57%) 3
Diarrhoea subjects affected / exposed occurrences (all)	4 / 14 (28.57%) 9	14 / 35 (40.00%) 14	4 / 7 (57.14%) 4
Constipation subjects affected / exposed occurrences (all)	9 / 14 (64.29%) 14	3 / 35 (8.57%) 4	0 / 7 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	5 / 14 (35.71%) 7	8 / 35 (22.86%) 9	1 / 7 (14.29%) 2
Abdominal pain subjects affected / exposed occurrences (all)	4 / 14 (28.57%) 4	4 / 35 (11.43%) 4	0 / 7 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2	6 / 35 (17.14%) 6	1 / 7 (14.29%) 1
Abdominal distension subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2	2 / 35 (5.71%) 2	1 / 7 (14.29%) 1
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	3 / 35 (8.57%) 3	0 / 7 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	1 / 35 (2.86%) 1	0 / 7 (0.00%) 0
Oral pain subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 35 (2.86%) 1	0 / 7 (0.00%) 0
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Dry mouth			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Dysphagia			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Gingival bleeding			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	2	0
Rectal haemorrhage			
subjects affected / exposed	2 / 14 (14.29%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Angina bullosa haemorrhagica			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Colitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Mouth ulceration			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	3 / 14 (21.43%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	4	0	0
Anal incontinence			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Flatulence			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Haemorrhoidal haemorrhage			

subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Lip pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Mouth haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Abdominal pain lower			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Anal ulcer			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Small intestinal obstruction			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Tongue ulceration			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Ascites			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Colitis ischaemic			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Enterocolitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Faecaloma			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hiatus hernia			

subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Ileus			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Intestinal dilatation			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Intra-abdominal haematoma			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pancreatic disorder			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Regurgitation			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 14 (7.14%)	8 / 35 (22.86%)	1 / 7 (14.29%)
occurrences (all)	1	8	1
Petechiae			
subjects affected / exposed	2 / 14 (14.29%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Pruritus			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Alopecia			

subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Rash			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Skin ulcer			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dry skin			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Erythema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Photosensitivity reaction			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Drug eruption			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rash macular			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Dermal cyst			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pain of skin			

subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rash papular			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 14 (21.43%)	3 / 35 (8.57%)	0 / 7 (0.00%)
occurrences (all)	3	3	0
Haematuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Urinary retention			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pollakiuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Micturition urgency			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Nephrolithiasis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal cyst			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 14 (0.00%)	6 / 35 (17.14%)	1 / 7 (14.29%)
occurrences (all)	0	6	1
Arthralgia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Pain in extremity			
subjects affected / exposed	1 / 14 (7.14%)	3 / 35 (8.57%)	1 / 7 (14.29%)
occurrences (all)	1	3	1
Myalgia			
subjects affected / exposed	0 / 14 (0.00%)	4 / 35 (11.43%)	0 / 7 (0.00%)
occurrences (all)	0	4	0
Muscular weakness			
subjects affected / exposed	2 / 14 (14.29%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	2	1	0
Bone pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Groin pain			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal discomfort			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Myositis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vertebral lesion			

subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Infections and infestations			
Lung infection			
subjects affected / exposed	0 / 14 (0.00%)	3 / 35 (8.57%)	0 / 7 (0.00%)
occurrences (all)	0	3	0
Urinary tract infection			
subjects affected / exposed	3 / 14 (21.43%)	3 / 35 (8.57%)	0 / 7 (0.00%)
occurrences (all)	3	4	0
Device related infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 14 (7.14%)	3 / 35 (8.57%)	0 / 7 (0.00%)
occurrences (all)	1	5	0
Mucosal infection			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile colitis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Oral candidiasis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Sepsis			
subjects affected / exposed	1 / 14 (7.14%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	1	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 14 (0.00%)	2 / 35 (5.71%)	0 / 7 (0.00%)
occurrences (all)	0	2	0

Clostridium difficile infection subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Folliculitis subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	2 / 35 (5.71%) 2	0 / 7 (0.00%) 0
Bacteraemia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Candida infection subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Otitis externa subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	2 / 35 (5.71%) 2	0 / 7 (0.00%) 0
Skin infection subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Soft tissue infection subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Staphylococcal infection subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Abdominal infection subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Atypical pneumonia subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Bacterial infection subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 2	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Bacterial sepsis subjects affected / exposed occurrences (all)	0 / 14 (0.00%) 0	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0

Chronic sinusitis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Corona virus infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Enterococcal bacteraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Leptotrichia infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Mycobacterium avium complex infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Perirectal abscess			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Postoperative wound infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Staphylococcal skin infection			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Tinea cruris			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			

Decreased appetite subjects affected / exposed occurrences (all)	6 / 14 (42.86%) 8	7 / 35 (20.00%) 7	1 / 7 (14.29%) 1
Hypokalaemia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 3	4 / 35 (11.43%) 5	1 / 7 (14.29%) 1
Hypomagnesaemia subjects affected / exposed occurrences (all)	4 / 14 (28.57%) 6	3 / 35 (8.57%) 3	1 / 7 (14.29%) 1
Hyponatraemia subjects affected / exposed occurrences (all)	5 / 14 (35.71%) 8	2 / 35 (5.71%) 2	0 / 7 (0.00%) 0
Hypophosphataemia subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 2	4 / 35 (11.43%) 4	1 / 7 (14.29%) 1
Hyperglycaemia subjects affected / exposed occurrences (all)	2 / 14 (14.29%) 3	1 / 35 (2.86%) 1	1 / 7 (14.29%) 1
Hyperkalaemia subjects affected / exposed occurrences (all)	5 / 14 (35.71%) 7	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Hypoalbuminaemia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 9	1 / 35 (2.86%) 2	0 / 7 (0.00%) 0
Hyperuricaemia subjects affected / exposed occurrences (all)	3 / 14 (21.43%) 6	1 / 35 (2.86%) 1	1 / 7 (14.29%) 1
Dehydration subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	0 / 35 (0.00%) 0	0 / 7 (0.00%) 0
Hypermagnesaemia subjects affected / exposed occurrences (all)	4 / 14 (28.57%) 4	1 / 35 (2.86%) 1	0 / 7 (0.00%) 0
Hypocalcaemia subjects affected / exposed occurrences (all)	1 / 14 (7.14%) 1	1 / 35 (2.86%) 2	0 / 7 (0.00%) 0

Hyperphosphataemia			
subjects affected / exposed	2 / 14 (14.29%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	1 / 7 (14.29%)
occurrences (all)	3	0	1
Fluid overload			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypercalcaemia			
subjects affected / exposed	2 / 14 (14.29%)	1 / 35 (2.86%)	0 / 7 (0.00%)
occurrences (all)	5	1	0
Hypernatraemia			
subjects affected / exposed	1 / 14 (7.14%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Hypervolaemia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hypophagia			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Metabolic acidosis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 14 (0.00%)	0 / 35 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 January 2015	<ul style="list-style-type: none">- Increased the blood volume collected due to additional tube needed for biomarker testing- Added saliva sampling to serve as a source of DNA for whole exome sequencing to assess for germline mutations
12 May 2015	<ul style="list-style-type: none">- Clarified the use and timing of bone marrow biopsy and aspirate samples- Removed optional buccal swab- Removed pharmacodynamics basophil activation test (BAT) assay collection for Groups A and B- Specified that blood and bone marrow biomarker samples were stored for optional future research- Clarified dosing delay and dose modification language
24 November 2015	<ul style="list-style-type: none">- Updated DLT assessment windows- Included new information on concomitant medications with ENTO- Added contraindicated medications and additional creatine phosphokinase (CPK) monitoring- Added left ventricular ejection fraction inclusion criterion and included ECHO or MUGA at screening (all groups) and prior to re-induction (Group A only)- Extended the screening window for bone marrow biopsy and aspirate to 21 days- Added BAT assay sample time points for Group C at end of subsequent cycles and at End of Study and specified that BAT assay samples were only collected during the escalation phase- Updated Appendix 4 to align with standard protocol template- Aligned Appendix 5 with the International Working Group criteria- Updated and clarified the criteria for discontinuation of study treatment- Incorporated changes from Administrative Amendment dated 02 July 2015

05 August 2016	<ul style="list-style-type: none"> - Stated that the recommended Phase 2 dose (RP2D) was ENTO 400 mg and included the rationale for the dose selection - Removed the ENTO 800 mg dose level for Groups A and B - Increased the participant number to approximately 40 in Phase 2 for each of Groups A and B and approximately 75 for Group C - Added Group A postinduction cycles to evaluate ENTO in combination with cytarabine followed by ENTO monotherapy maintenance cycles in the dose expansion - Added a Group B safety run-in and DLT assessment of 6 participants to evaluate the safety of ENTO in combination with azacitidine prior to enrollment of the expansion cohort - Added a Group B arm in the dose expansion to evaluate ENTO in combination with azacitidine - Separated Group C relapsed/refractory and previously untreated participants into subcohorts for the dose expansion - Added a cohort C1B safety run-in and DLT assessment to evaluate ENTO in combination with mitoxantrone, etoposide, and cytarabine (MEC) - Updated the primary endpoints and objectives to include combinations with azacitidine and MEC - Updated and added schedule of assessment tables for all groups to include updated dose escalation assessments and dose expansion assessments - Added intensive PK sample collection to Group A on Cycle 1 Day 7 and to Cohort C1B on Cycle 1 Day 5 - Added disease assessment to the Group A and B Cycle 0 Day 14 bone marrow assessment - Updated Group A-specific inclusion and exclusion Criterion 1 to remove the age limit and to allow favorable risk AML participants - Updated Group C-specific inclusion criteria to include criteria that must have been met to be eligible for each subcohort - Updated the study discontinuation criteria to clarify the criterion that applied only to Group C and moved Group B language from criterion to the applicable sections - Updated Appendix 5 and Appendix 6 - Added Appendix 7 (defined MRD level) and new references
14 February 2017	<ul style="list-style-type: none"> - Updated the ENTO formulation composition, strength, and color per manufacturing changes - Added an exploratory optional biopsy to all groups' study designs - Removed minimal residual disease (MRD) treatment criteria from the protocol - Clarified CR criteria - Clarified morphologic leukemia-free state criteria - Updated PK collection schedule for Groups A and C - Updated study procedures tables for all groups - Specified "Dose Escalation" and "Dose Expansion" as well as "Phase 1b" and "Phase 2" throughout the protocol, as needed - Updated relapse-free survival criteria - Add dose modification guidelines for toxicities on various study treatments - Updated prohibited medication requirements per current drug and safety data - Added new serum chemistry requirement for beta-2 microglobulin
04 August 2017	<ul style="list-style-type: none"> - Ascertained the benefit of a 5-day ENTO lead-in - Evaluated responses in specific risk groups of AML (< 60 years of age versus ≥ 60 years of age; de novo versus secondary AML) - Confirmed the overall response rate in Group A to enable planning of a global Phase 3 study - Cohort C1B was removed due to the lack of responses in the relapsed/refractory AML population. However, due to the most encouraging results in the MLL cohort, the development of ENTO in the relapsed/refractory setting concentrated on the MLL subsets. - Remove references to ENTO 100 mg - Incorporated German-specific requirements - Updated introduction to AML to align with ENTO Investigator's Brochure Edition 8 - Added flow cytometry to determine blast percentage - Removed postinduction and replaced with postremission - Identified cohorts closed to enrollment - Emphasized participants were to be followed for survival

15 February 2018	<ul style="list-style-type: none"> - Removed Cohort A1 as interim analysis of Phase 1 and 2 Group A participants led to a CR rate no better than historical controls and this did not support enrollment to an AML study in "all comers AML" randomized to ENTO versus placebo plus cytarabine and daunorubicin (7+3). - Closed Group C3 screening due to the low enrollment rate of Group C3, lack of responses to ENTO monotherapy both during the lead-in period in Group A subjects and in all but one subject in C3, and the evolving treatment landscape for AML. Screening and enrollment activities were discontinued. - Removed all references to "placebo-to-match" and its formulation as only Cohort A1 involved treatment with a placebo. - Added note to indicate Group B Phase 1b enrollment completion. - Updated total subject number from 270 to 190 throughout the protocol to reflect removal of Cohort A1 (n = 80) - Renamed Drug Safety and Public Health (DSPH), a department at Gilead Sciences, to Pharmacovigilance and Epidemiology (PVE) effective December 1, 2017
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
21 November 2018	Study was terminated by sponsor due to lack of response to ENTO monotherapy and the evolving treatment landscape for acute myeloid leukemia.	-

Notes:

Limitations and caveats

None reported