

**Clinical trial results:**

A PHASE 1/2 STUDY TO INVESTIGATE THE SAFETY, PHARMACOKINETICS AND EFFICACY OF EDO-S101, A FIRST-IN-CLASS ALKYLATING HISTONE DEACETYLASE INHIBITION (HDACI) FUSION MOLECULE, IN PATIENTS WITH ADVANCED SOLID TUMORS. SUB-STUDY TO CHARACTERIZE THE EFFECTS OF TINOSTAMUSTINE AT A DOSE OF 60 MG/M2 ADMINISTERED DURING A 60-MINUTE INFUSION ON CARDIAC REPOLARIZATION IN PATIENTS WITH ADVANCED SOLID TUMORS. SUB-STUDY TO CHARACTERIZE THE EFFECTS OF TINOSTAMUSTINE AT A DOSE OF 80 MG/M2 ADMINISTERED DURING A 80-MINUTE INFUSION ON CARDIAC REPOLARIZATION IN PATIENTS WITH ADVANCED SOLID TUMORS

Summary

EudraCT number	2020-004246-11
Trial protocol	NL IT
Global end of trial date	29 March 2023

Results information

Result version number	v1 (current)
This version publication date	14 July 2024
First version publication date	14 July 2024

Trial information**Trial identification**

Sponsor protocol code	EDO-S101-1002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03345485
WHO universal trial number (UTN)	-
Other trial identifiers	IND: 125180

Notes:

Sponsors

Sponsor organisation name	Mundipharma Research Limited
Sponsor organisation address	Cambridge Science Park, Milton Road, Cambridge , United Kingdom, CB4 0AB
Public contact	Elizabeth Chong, Mundipharma Research Limited, 0044 01223 424900, elizabeth.chong@mundipharma-rd.eu
Scientific contact	Elizabeth Chong, Mundipharma Research Limited, 0044 01223 424900, elizabeth.chong@mundipharma-rd.eu

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	29 March 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 July 2022
Global end of trial reached?	Yes
Global end of trial date	29 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Phase 1: To determine the safety, tolerability, maximum tolerated dose (MTD), and recommended phase 2 dose (RP2D) of tinostamustine as a single agent in subjects with solid tumours who have progressed after at least one (1) line of therapy and no other standard therapy with proven clinical benefit is available.

Phase 2: To determine the objective response rate (ORR) of any duration, plus the rate of subjects with stable disease (SD) of at least 12-week duration at a dose of 80 mg/m² administered over 1 hour on Day 1 and Day 15 of each 4-week treatment cycle.

Substudies: To characterize the effect of tinostamustine at a dose of 60 or 80 mg/m² on cardiac repolarization (QTcF) and other electrocardiogram (ECG) parameters in 6 -12 subjects with solid tumours who have progressed after at least 1 line of therapy and for whom no other standard therapy with proven clinical benefit is available.

Protection of trial subjects:

The study protocol was approved by relevant regulatory authorities and ethics committees, and clinical trial agreements signed prior to site initiation and activation.

All amendments were submitted for relevant approvals before implementation.

Only site staff who were delegated by the Principal investigator on the study delegation log and had received training could work on the study. Potential subjects were provided with the ethics approved informed consent form and had the opportunity to discuss the study with delegated investigators before providing consent to take part.

Only subjects who meet the eligible criteria were enrolled.

The protocol included numerous safety assessments including physical examinations, measurement of vital signs, hematology and clinical chemistry tests, urinalysis, assessment of ECOG performance status and cardiac monitoring.

Subjects had to agree to follow contraception requirements, and women of child-bearing potential are required to undergo pregnancy test with negative test results prior to every treatment.

Subjects were asked about any adverse events (AE) and use of concomitant medications including herbal supplements, vitamins and minerals, and all were recorded in the study database.

Beyond cycle 1 day 1, the re-treatment criteria must be met.

During treatment, subjects will be closely monitored for any QTc prolongations. Additional ECGs are taken if the QTcF value is >500ms or represents an increase >60ms from baseline. If the average QTcF is grade 3 or higher, tinostamustine infusion must be stopped and QTcF prolongation reported as a serious adverse event.

All AEs must be reported from the time of ICF signature through the point of tinostamustine discontinuation, and followed to resolution or stabilization of event.

Tinostamustine must be stored at 2 to 8°C in a secure area with access limited to the Investigator and authorized site staff, and with appropriate temperature monitoring.

Background therapy: -

Evidence for comparator:

There is no comparator in this study.

Actual start date of recruitment	18 October 2017
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Long term follow-up planned	No
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Independent data monitoring committee (IDMC) involvement?	No
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Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 1
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Country: Number of subjects enrolled	Italy: 5
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Country: Number of subjects enrolled	Canada: 7
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Country: Number of subjects enrolled	United States: 58
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Worldwide total number of subjects	71
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EEA total number of subjects	6
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Notes:

Subjects enrolled per age group

In utero	0
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Preterm newborn - gestational age < 37 wk	0
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Newborns (0-27 days)	0
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Infants and toddlers (28 days-23 months)	0
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Children (2-11 years)	0
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Adolescents (12-17 years)	0
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Adults (18-64 years)	48
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From 65 to 84 years	23
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85 years and over	0
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Subject disposition

Recruitment

Recruitment details:

P1: First Subject First Dose: 08-Nov-2017; Date of last subject enrolled: 11-Oct-2018

P2: First Subject First Dose: 26-Dec-2018; Date of last subject enrolled: 14-Dec-2021

SS1: First Subject First Dose: 09-June-2020; Date of last subject enrolled: 08-Oct-2020

SS2: First Subject First Dose: 30-Dec-2021; Date of last subject enrolled: 30-June-2022

Pre-assignment

Screening details:

Adults with histologically confirmed diagnosis of advanced or metastatic solid tumors, disease should have progressed during or following at least 1 previous line of therapy and no other standard therapy with proven clinical benefit is available or recommended based on the investigator's individual risk-benefit assessment for the patient.

Period 1

Period 1 title	Tinostamustine treatment
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 1 - 60mg/m ² (30 Min). Cohort 1

Arm description:

This is dose level 1 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 60mg/m² administered i.v. over 30min on D1 and D15 of each 4-week cycle.

The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.

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

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C.

Tinostamustine as a single agent was administered at doses of 60mg/m² by intravenous infusion over 30 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Phase 1 - 80mg/m ² (30 Min). Cohort 2
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Arm description:

This is dose level 2 of the dose escalation phase (Phase 1) of the study.

Tinostamustine at dose of 80mg/m² administered i.v. over 30min on D1 and D15 of each 4-week cycle.

The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.

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

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C. Tinostamustine as a single agent administered at doses of 80mg/m² by intravenous infusion over 30 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Phase 1 - 100mg/m ² (30 Min). Cohort 3.
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Arm description:

This is dose level 3 of the dose escalation phase (Phase 1) of the study.

Tinostamustine at dose of 100mg/m² administered i.v. over 30min on D1 and D15 of each 4-week cycle.

In the 30-minute infusion study drug dosing had to be delayed in subsequent cycles due to thrombocytopenia, which was associated with an extremely high C_{max} of Tinostamustine. To ensure that subjects continue the study treatment safely, the Sponsor decided to stop the investigation of the 30-minute infusion time and open cohorts with the 60-minute infusion in 3 subjects with relapse/refractory solid tumors.

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

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C. Tinostamustine as a single agent was administered at doses of 100mg/m² by intravenous infusion over 30 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Phase 1 - 60mg/m ² (60 Min). Cohort 4
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Arm description:

This is dose level 4 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 60mg/m² administered i.v. over 60min on D1 and D15 of each 4-week cycle.

The decision to escalate to the nextdose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.

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

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C. Tinostamustine as a single agent was administered at doses of 60mg/m² by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Phase 1 - 80mg/m ² (60 Min). Cohort 5
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Arm description:

This is dose level 5 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 80mg/m² administered i.v. over 60min on D1 and D15 of each 4-week cycle. The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.

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

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C. Tinostamustine as a single agent was administered at doses of 80mg/m² by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Phase 1 - 100mg/m ² (60 Min). Cohort 6
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Arm description:

This is dose level 6 of the dose escalation phase (Phase 1) of the study. DLT of electrocardiogram QTc prolongation occurred 1 patient. Considering the DLT observed in this cohort and the rapid occurrence of treatment-induced thrombocytopenia (not meeting the DLT definitions), the SRC concluded as follows: The dose of 100 mg/m² was determined the MAD. The dose level of 80 mg/m² given i.v. over 60 minutes was determined to be the MTD The dose level of 80 mg/m² given i.v. over 60 minutes on Day 1 and Day 15 of each 4-week treatment cycle was determined to be the RP2D.

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

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C. Tinostamustine as a single agent was administered at doses of 100mg/m² by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) coho
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Arm description:

Tinostamustine at dose of 80mg/m² administered i.v. over 60min on D1 and D15 of each 4-week cycle.

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

Dosage and administration details:

Tinostamustine as a single agent was administered at doses of 80mg/m² by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort
Arm description: Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.	
Arm type	Experimental
Investigational medicinal product name	Tinostamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion, Powder for injection
Routes of administration	Intravenous use
Dosage and administration details: Tinostamustine as a single agent was administered at doses of 80mg/m2 by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.	
Arm title	Phase 2 Relapsed/refractory Triple Negative breast Cancer
Arm description: Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.	
Arm type	Experimental
Investigational medicinal product name	Tinostamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion, Powder for injection
Routes of administration	Intravenous use
Dosage and administration details: Tinostamustine as a single agent was administered at doses of 80mg/m2 by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.	
Arm title	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
Arm description: Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.	
Arm type	Experimental
Investigational medicinal product name	Tinostamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion, Powder for injection
Routes of administration	Intravenous use
Dosage and administration details: Tinostamustine as a single agent was administered at doses of 80mg/m2 by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.	
Arm title	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort
Arm description: Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.	
Arm type	Experimental
Investigational medicinal product name	Tinostamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion, Powder for injection
Routes of administration	Intravenous use
Dosage and administration details: Tinostamustine as a single agent was administered at doses of 80mg/m2 by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.	
Arm title	Sub study 1 (SS1)

Arm description:

Tinostamustine at dose of 60mg/m² administered i.v. over 60min on D1 and D15 of each 4-week cycle.

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

Dosage and administration details:

Tinostamustine as a single agent was administered at doses of 60mg/m² by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Substudy 2 (SS2)
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Arm description:

Tinostamustine at dose of 80mg/m² administered i.v. over 80min on D1 and D15 of each 4-week cycle.

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

Dosage and administration details:

Tinostamustine as a single agent was administered at doses of 80mg/m² by intravenous infusion over 80 minutes on Days (D) 1 and 15 of each 28-day cycle.

Number of subjects in period 1	Phase 1 - 60mg/m ² (30 Min). Cohort 1	Phase 1 - 80mg/m ² (30 Min). Cohort 2	Phase 1 - 100mg/m ² (30 Min). Cohort 3.
Started	3	3	3
Completed	3	3	3
Not completed	0	0	0
Do not have a post-dose tumour assessment	-	-	-

Number of subjects in period 1	Phase 1 - 60mg/m ² (60 Min). Cohort 4	Phase 1 - 80mg/m ² (60 Min). Cohort 5	Phase 1 - 100mg/m ² (60 Min). Cohort 6
Started	3	8	2
Completed	3	8	2
Not completed	0	0	0
Do not have a post-dose tumour assessment	-	-	-

Number of subjects in period 1	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) coho	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer
Started	4	10	4
Completed	3	8	4
Not completed	1	2	0
Do not have a post-dose tumour assessment	1	2	-

Number of subjects in period 1	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort	Sub study 1 (SS1)
	Started	12	6
Completed	12	4	3
Not completed	0	2	3
Do not have a post-dose tumour assessment	-	2	3

Number of subjects in period 1	Substudy 2 (SS2)
Started	7
Completed	4
Not completed	3
Do not have a post-dose tumour assessment	3

Period 2

Period 2 title	PK cohorts
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Phase 2 all cohorts
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tinostamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion, Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C. Tinostamustine as a single agent was administered at doses of 80mg/m² by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Substudy 1
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tinostamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion, Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C. Tinostamustine as a single agent was administered at doses of 60mg/m² by intravenous infusion over 60 minutes on Days (D) 1 and 15 of each 28-day cycle.

Arm title	Substudy 2
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Tinostamustine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for concentrate for solution for infusion, Powder for injection
Routes of administration	Intravenous use

Dosage and administration details:

Tinostamustine powder for injection 100 mg reconstituted with 20 mL of 0.9% saline and then immediately further diluted with 0.9% saline to a final volume of 50 mL. The diluted solution is stored in infusion container (bottle or bag) for a maximum of 10 hours, of which a maximum of 4 hours may be at room temperature including duration of infusion, with the remaining storage period at 2 to 8°C. Tinostamustine as a single agent was administered at doses of 80mg/m² by intravenous infusion over 80 minutes on Days (D) 1 and 15 of each 28-day cycle.

Number of subjects in period 2^[1]	Phase 2 all cohorts	Substudy 1	Substudy 2
Started	36	6	7
Completed	31	3	4
Not completed	5	3	3
Do not have a post-dose tumour assessment	5	3	3

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: A separate period is entered in order for group results to be provided for PK endpoints. In phase 2 of the study, all patients receive study drug at the same dose with same infusion duration, hence PK data are analysed together.

Baseline characteristics

Reporting groups

Reporting group title	Phase 1 - 60mg/m2 (30 Min). Cohort 1
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Reporting group description:

This is dose level 1 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 60mg/m2 administered i.v. over 30min on D1 and D15 of each 4-week cycle. The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.

Reporting group title	Phase 1 - 80mg/m2 (30 Min). Cohort 2
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Reporting group description:

This is dose level 2 of the dose escalation phase (Phase 1) of the study.

Tinostamustine at dose of 80mg/m2 administered i.v. over 30min on D1 and D15 of each 4-week cycle.

The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.

Reporting group title	Phase 1 - 100mg/m2 (30 Min). Cohort 3.
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Reporting group description:

This is dose level 3 of the dose escalation phase (Phase 1) of the study.

Tinostamustine at dose of 100mg/m2 administered i.v. over 30min on D1 and D15 of each 4-week cycle.

In the 30-minute infusion study drug dosing had to be delayed in subsequent cycles due to thrombocytopenia, which was associated with an extremely high Cmax of Tinostamustine. To ensure that subjects continue the study treatment safely, the Sponsor decided to stop the investigation of the 30-minute infusion time and open cohorts with the 60-minute infusion in 3 subjects with relapse/refractory solid tumors.

Reporting group title	Phase 1 - 60mg/m2 (60 Min). Cohort 4
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Reporting group description:

This is dose level 4 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 60mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle. The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.

Reporting group title	Phase 1 - 80mg/m2 (60 Min). Cohort 5
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Reporting group description:

This is dose level 5 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle. The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.

Reporting group title	Phase 1 - 100mg/m2 (60 Min). Cohort 6
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Reporting group description:

This is dose level 6 of the dose escalation phase (Phase 1) of the study. DLT of electrocardiogram QTc prolongation occurred 1 patient. Considering the DLT observed in this cohort and the rapid occurrence of treatment-induced thrombocytopenia (not meeting the DLT definitions), the SRC concluded as follows: The dose of 100 mg/m2 was determined the MAD. The dose level of 80 mg/m2 given i.v. over 60 minutes was determined to be the MTD. The dose level of 80 mg/m2 given i.v. over 60 minutes on Day 1 and Day 15 of each 4-week treatment cycle was determined to be the RP2D.

Reporting group title	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) coho
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Phase 2 Relapsed/refractory Triple Negative breast Cancer
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Sub study 1 (SS1)
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Reporting group description:

Tinostamustine at dose of 60mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Substudy 2 (SS2)
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 80min on D1 and D15 of each 4-week cycle.

Reporting group values	Phase 1 - 60mg/m2 (30 Min). Cohort 1	Phase 1 - 80mg/m2 (30 Min). Cohort 2	Phase 1 - 100mg/m2 (30 Min). Cohort 3.
Number of subjects	3	3	3
Age categorical			
Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics			
Units: Subjects			
Adults (18-64 years)	1	1	2
From 65-74	2	2	1
75 years and over	0	0	0
Gender categorical			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			
Female	2	1	2
Male	1	2	1
Ethnicity			
Unit of measure: participants			
Units: Subjects			
Hispanic or Latino	1	0	0
Not Hispanic or Latino	2	3	3
Unknown or Not Reported	0	0	0
Race			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			
Asian	0	1	2
Black or African American	0	0	0
White	3	2	1

Height at Screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: centimetre			
median	166.6	171.5	165.5
full range (min-max)	158 to 176	166 to 183	148 to 183
Weight at Screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: kilogram(s)			
median	75.3	95.8	75.3
full range (min-max)	46 to 102	84 to 98	67 to 84
BMI at screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: kilogra			
median	31.620	28.610	27.775
full range (min-max)	30.36 to 32.88	28.53 to 35.41	24.96 to 30.59
Reporting group values	Phase 1 - 60mg/m ² (60 Min). Cohort 4	Phase 1 - 80mg/m ² (60 Min). Cohort 5	Phase 1 - 100mg/m ² (60 Min). Cohort 6
Number of subjects	3	8	2
Age categorical			
Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics			
Units: Subjects			
Adults (18-64 years)	3	4	2
From 65-74	0	4	0
75 years and over	0	0	0
Gender categorical			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			
Female	2	4	2
Male	1	4	0
Ethnicity			
Unit of measure: participants			
Units: Subjects			
Hispanic or Latino	2	1	0
Not Hispanic or Latino	1	7	2
Unknown or Not Reported	0	0	0
Race			

Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			
Asian	0	2	0
Black or African American	0	0	0
White	3	6	2
Height at Screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: centimetre			
median	154.9	161.8	164.8
full range (min-max)	154 to 178	156 to 198	161 to 169
Weight at Screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: kilogram(s)			
median	95.4	69.3	87.6
full range (min-max)	84 to 102	45 to 112	70 to 106
BMI at screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: kilogra			
median	35.460	21.920	32.675
full range (min-max)	30.11 to 42.34	18.19 to 36.19	24.40 to 40.95
Reporting group values	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) coho	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer
Number of subjects	4	10	4
Age categoral			
Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics			
Units: Subjects			
Adults (18-64 years)	2	8	2
From 65-74	2	2	1
75 years and over	0	0	1
Gender categoral			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			

Female	2	6	4
Male	2	4	0

Ethnicity			
Unit of measure: participants			
Units: Subjects			
Hispanic or Latino	0	2	0
Not Hispanic or Latino	4	7	4
Unknown or Not Reported	0	1	0

Race

Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.

Units: Subjects			
Asian	0	2	0
Black or African American	0	0	1
White	4	8	3

Height at Screening

Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.

Units: centimetre			
median	163	166.1	158.2
full range (min-max)	156 to 185	155 to 177	152 to 168

Weight at Screening

Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.

Units: kilogram(s)			
median	54.5	71.8	58.1
full range (min-max)	52 to 130	42 to 142	48 to 85

BMI at screening

Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.

Units: kilogra			
median	21.485	24.060	24.005
full range (min-max)	19.67 to 37.95	17.36 to 50.82	19.70 to 30.22

Reporting group values	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort	Sub study 1 (SS1)
Number of subjects	12	6	6
Age categorical			

Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics

Units: Subjects			
Adults (18-64 years)	8	3	6
From 65-74	3	3	0
75 years and over	1	0	0
Gender categorical			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			
Female	12	6	5
Male	0	0	1
Ethnicity			
Unit of measure: participants			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	12	6	4
Unknown or Not Reported	0	0	2
Race			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			
Asian	2	2	1
Black or African American	0	0	0
White	10	4	5
Height at Screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: centimetre			
median	159.1	160.4	166.7
full range (min-max)	152 to 170	155 to 164	151 to 183
Weight at Screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: kilogram(s)			
median	65.0	59.7	93.1
full range (min-max)	50 to 96	54 to 86	65 to 142
BMI at screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: kilogra			
median	25.505	23.255	32.880
full range (min-max)	20.98 to 38.28	20.69 to 34.10	23.23 to 50.99

Reporting group values	Substudy 2 (SS2)	Total	
Number of subjects	7	71	
Age categorical			
Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics			
Units: Subjects			
Adults (18-64 years)	6	48	
From 65-74	0	20	
75 years and over	1	3	
Gender categorical			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			
Female	4	52	
Male	3	19	
Ethnicity			
Unit of measure: participants			
Units: Subjects			
Hispanic or Latino	0	6	
Not Hispanic or Latino	7	62	
Unknown or Not Reported	0	3	
Race			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: Subjects			
Asian	0	12	
Black or African American	1	2	
White	6	57	
Height at Screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: centimetre			
median	166.4		
full range (min-max)	156 to 183	-	
Weight at Screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.			
Units: kilogram(s)			
median	72.5		
full range (min-max)	55 to 105	-	
BMI at screening			
Demographics and baseline characteristics are summarised for Safety Population. Demographic			

information included age, sex, ethnicity, race, height, weight and BMI. Demographics and baseline characteristics were summarised descriptively. Subject demographics (sex, ethnicity, race, and age category) were presented using discrete summary statistics. Age, height, weight and BMI were presented using continuous summary statistics.

Units: kilogra			
median	23.590		
full range (min-max)	20.76 to 40.06	-	

End points

End points reporting groups

Reporting group title	Phase 1 - 60mg/m2 (30 Min). Cohort 1
Reporting group description: This is dose level 1 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 60mg/m2 administered i.v. over 30min on D1 and D15 of each 4-week cycle. The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.	
Reporting group title	Phase 1 - 80mg/m2 (30 Min). Cohort 2
Reporting group description: This is dose level 2 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 80mg/m2 administered i.v. over 30min on D1 and D15 of each 4-week cycle. The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.	
Reporting group title	Phase 1 - 100mg/m2 (30 Min). Cohort 3.
Reporting group description: This is dose level 3 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 100mg/m2 administered i.v. over 30min on D1 and D15 of each 4-week cycle. In the 30-minute infusion study drug dosing had to be delayed in subsequent cycles due to thrombocytopenia, which was associated with an extremely high Cmax of Tinostamustine. To ensure that subjects continue the study treatment safely, the Sponsor decided to stop the investigation of the 30-minute infusion time and open cohorts with the 60-minute infusion in 3 subjects with relapse/refractory solid tumors.	
Reporting group title	Phase 1 - 60mg/m2 (60 Min). Cohort 4
Reporting group description: This is dose level 4 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 60mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle. The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.	
Reporting group title	Phase 1 - 80mg/m2 (60 Min). Cohort 5
Reporting group description: This is dose level 5 of the dose escalation phase (Phase 1) of the study. Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle. The decision to escalate to the next dose level occurred after all 3 subjects completed the Dose-limiting toxicity (DLT) observation time and were evaluated for safety and toxicity.	
Reporting group title	Phase 1 - 100mg/m2 (60 Min). Cohort 6
Reporting group description: This is dose level 6 of the dose escalation phase (Phase 1) of the study. DLT of electrocardiogram QTc prolongation occurred 1 patient. Considering the DLT observed in this cohort and the rapid occurrence of treatment-induced thrombocytopenia (not meeting the DLT definitions), the SRC concluded as follows: The dose of 100 mg/m2 was determined the MAD. The dose level of 80 mg/m2 given i.v. over 60 minutes was determined to be the MTD The dose level of 80 mg/m2 given i.v. over 60 minutes on Day 1 and Day 15 of each 4-week treatment cycle was determined to be the RP2D.	
Reporting group title	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) coho
Reporting group description: Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.	
Reporting group title	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort
Reporting group description: Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.	
Reporting group title	Phase 2 Relapsed/refractory Triple Negative breast Cancer

Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Sub study 1 (SS1)
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Reporting group description:

Tinostamustine at dose of 60mg/m2 administered i.v. over 60min on D1 and D15 of each 4-week cycle.

Reporting group title	Substudy 2 (SS2)
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Reporting group description:

Tinostamustine at dose of 80mg/m2 administered i.v. over 80min on D1 and D15 of each 4-week cycle.

Reporting group title	Phase 2 all cohorts
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Reporting group description: -

Reporting group title	Substudy 1
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Reporting group description: -

Reporting group title	Substudy 2
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Reporting group description: -

Primary: Clinical Benefit Response Rate in Selected Solid Tumor Cohorts on Phase 2

End point title	Clinical Benefit Response Rate in Selected Solid Tumor Cohorts on Phase 2 ^{[1][2]}
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End point description:

The Clinical Benefit Response Rate is calculated as the number of patients with Clinical Benefit Response divided by number of patients in the FAS (in the respective cohort).

End point type	Primary
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End point timeframe:

Over complete study

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: Due to the nature of the phase 1/2 study, no statistical analysis was to be performed other than summary statistics

[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: This study is designed into various phases. This is not an end point in Phase 1 or for the sub-studies.

End point values	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) cohort	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	4	12
Units: percent				
number (confidence interval 90%)				
Clinical Benefit Response Rate (CR+PR+durable SD)	0 (0 to 52.7)	40 (15.0 to 69.6)	50.0 (9.8 to 90.2)	50.0 (24.5 to 75.5)

End point values	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: percent				
number (confidence interval 90%)				
Clinical Benefit Response Rate (CR+PR+durable SD)	50.0 (15.3 to 84.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Highest Change From Baseline in QTcF in Sub-studies

End point title	Highest Change From Baseline in QTcF in Sub-studies ^{[3][4]}
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End point description:

QTcF: corrected QT interval [QTc] using Fridericia's formula) and other electrocardiogram (ECG) parameters in subjects with solid tumours who have progressed after at least 1 line of therapy and for whom no other standard therapy with proven clinical benefit is available.

Within each cycle a Change from baseline (CfB) is calculated for QTcF relative to the baseline value of day 1 of the cycle. QTcF CfB= QTcF Post-dose value - QTcF pre-dose value of D1 ECG Parameters: 4-hours ECG holter monitoring in C1 and ECGs during EDO-S101 administration.

Continuous variables the mean and standard deviation are presented together with the total number of observations and the number of missing and non-missing values.

End point type	Primary
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End point timeframe:

QTcF change from baseline over all cycles.

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: Due to the nature of the phase 1/2 study, no statistical analysis was to be performed other than summary statistics

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

Justification: This study is designed into various phases. This end-point is only applicable to the sub-studies.

End point values	Sub study 1 (SS1)	Substudy 2 (SS2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: msec				
arithmetic mean (standard deviation)	53.33 (± 23.777)	33.24 (± 12.588)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with treatment-related adverse events as assessed by CTCAE V4.03 on Phase 1

End point title	Number of participants with treatment-related adverse events as assessed by CTCAE V4.03 on Phase 1 ^{[5][6]}
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End point description:

All TEAEs were reported from the first dose of study drug through the time of study drug discontinuation (at any time or Day 28 of the last treatment Cycle). All treatment-related TEAEs were followed until resolution or stabilization. For the purpose of regulatory reporting requirements, causal relationships of definite, probable, and possible were considered treatment-related.

Number of patients experiencing treatment-related adverse events (TEAE) as assessed by CTCAE v4.03. (June 2010).

End point type	Primary
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End point timeframe:

From start treatment until end of treatment

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: Due to the nature of the phase 1/2 study, no statistical analysis was to be performed other than summary statistics

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

Justification: This study is designed into various phases.

This end point is a primary endpoint in phase 1, but a secondary endpoint in phase 2 and substudies, hence they are reported separately.

End point values	Phase 1 - 60mg/m ² (30 Min). Cohort 1	Phase 1 - 80mg/m ² (30 Min). Cohort 2	Phase 1 - 100mg/m ² (30 Min). Cohort 3.	Phase 1 - 60mg/m ² (60 Min). Cohort 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	3
Units: number of participants				
Investigations	3	3	3	3
Gastrointestinal disorders	3	3	2	1
Blood and lymphatic system disorders	1	3	2	3
General disorders and administration site condition	1	2	2	2
Nervous system disorders	1	1	2	1
Skin and subcutaneous tissue disorders	1	2	1	1
Metabolism and nutrition disorders	1	0	0	1
Injury, poisoning and procedural complications	0	1	0	0
Respiratory, thoracic and mediastinal disorders	0	0	1	0
Cardiac disorders	0	0	0	0
Musculoskeletal and connective tissue disorders	0	0	0	0
Vascular disorders	0	0	0	1

End point values	Phase 1 - 80mg/m ² (60 Min). Cohort 5	Phase 1 - 100mg/m ² (60 Min). Cohort 6		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	2		
Units: number of participants				
Investigations	6	2		
Gastrointestinal disorders	8	2		
Blood and lymphatic system disorders	4	1		
General disorders and administration site conditio	5	1		
Nervous system disorders	3	2		
Skin and subcutaneous tissue disorders	2	0		
Metabolism and nutrition disorders	3	1		
Injury, poisoning and procedural complications	1	0		
Respiratory, thoracic and mediastinal disorders	1	0		
Cardiac disorders	1	0		
Musculoskeletal and connective tissue disorders	1	0		
Vascular disorders	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Safety Population With Treatment-related Adverse Events on Phase 2 and Sub Studies

End point title	Safety Population With Treatment-related Adverse Events on Phase 2 and Sub Studies ^[7]
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End point description:

Number of patients experiencing treatment-related adverse events (TEAE) as assessed by CTCAE v4.03, June 2010, with the exception that assessment of QTc prolongations constituting adverse events (AEs) of special interest were based on NCI CTCAE version 5.0, November 2017.

All subjects who received at least 1 dose of study treatment were included in the Safety Population. Safety analyses were performed on data from all subjects in the Safety Population.

End point type	Secondary
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End point timeframe:

P2: A single dose of 80 mg/m² over 60 min of EDO-101 on D1 and D15 of each four (4) week treatment cycle. SS: A single dose of 60 mg/m² over 60 min of EDO-101. SS2: A single dose of 80 mg/m² over 80 min of EDO-101 on D1 and D15 in cycle 1.

Notes:

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

Justification: This study is designed into various phases.

This end point is a primary endpoint in phase 1, but a secondary endpoint in phase 2 and substudies, hence they are reported separately.

End point values	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) cohort	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	4	12

Units: Patients				
Gastrointestinal disorders	2	4	3	12
Investigations	3	3	2	8
Blood and lymphatic system disorders	2	4	2	7
General disorders and administration site conditio	2	3	1	9
Metabolism and nutrition disorders	1	1	1	4
Nervous system disorders	2	2	0	3
Skin and subcutaneous tissue disorders	1	3	0	4
Musculoskeletal and connective tissue disorders	1	1	0	1
Respiratory, thoracic and mediastinal disorders	1	1	1	0
Vascular disorders	0	2	0	2
Cardiac disorders	0	0	1	1
Injury, poisoning and procedural complications	1	0	1	1
Infections and infestations	0	1	0	0

End point values	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort	Sub study 1 (SS1)	Substudy 2 (SS2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: Patients				
Gastrointestinal disorders	4	2	2	
Investigations	5	3	2	
Blood and lymphatic system disorders	3	3	3	
General disorders and administration site conditio	5	2	1	
Metabolism and nutrition disorders	3	1	0	
Nervous system disorders	3	1	0	
Skin and subcutaneous tissue disorders	1	0	0	
Musculoskeletal and connective tissue disorders	0	1	1	
Respiratory, thoracic and mediastinal disorders	1	1	0	
Vascular disorders	1	0	0	
Cardiac disorders	1	0	0	
Injury, poisoning and procedural complications	0	0	0	
Infections and infestations	0	0	2	

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of stable disease (SD) that persists for at least 4 months in

selected solid tumor cohorts on Sub studies

End point title	Duration of stable disease (SD) that persists for at least 4 months in selected solid tumor cohorts on Sub studies ^[8]
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End point description:

Duration of SD, was defined as the number of days between the date of the first dose of treatment and the first date of disease progression or death.

SD was regarded as durable if, after observing SD, the first observation of progression disease was at least 84 days after the start of study treatment.

End point type	Secondary
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End point timeframe:

Every 2 cycles until end of treatment

Notes:

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

Justification: This study is designed into various phases. This end-point is only applicable to the sub-studies.

End point values	Sub study 1 (SS1)	Substudy 2 (SS2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	1		
Units: participants				
<84 days	0	0		
≥84 days	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR) and the clinical benefit rate (CBR) that persists for at least four (4) months in selected solid tumor cohorts on Sub studies

End point title	Objective Response Rate (ORR) and the clinical benefit rate (CBR) that persists for at least four (4) months in selected solid tumor cohorts on Sub studies ^[9]
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End point description:

Every 2 cycles until end of treatment

End point type	Secondary
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End point timeframe:

To determine the objective response rate (ORR), the clinical benefit rate (CBR [CR, PR plus SD]), and Duration of SD on Sub Studies.

SD was regarded as durable if, after observing SD, the first observation of PD was at least 84 days after 1st dose.

Notes:

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

Justification: This study is designed into various phases. This end-point is only applicable to the sub-studies.

End point values	Sub study 1 (SS1)	Substudy 2 (SS2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	7		
Units: day				
least squares mean (confidence interval 90%)				
Objective Response Rate	16.7 (0.9 to 58.2)	0 (0 to 34.8)		
Clinical Benefit Response	50.0 (15.3 to 84.7)	14.3 (0.7 to 52.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: To Determine the Duration of Response (DoR) time for Phase 2 and Sub Studies

End point title	To Determine the Duration of Response (DoR) time for Phase 2 and Sub Studies ^[10]
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End point description:

To Determine the Duration of Response (DoR) time for Phase 2 and Sub Studies

End point type	Secondary
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End point timeframe:

Date of the first tumor response assessment with an Investigator's Overall Response of CR or PR (whichever status is recorded first) until the date of progression or death.

Notes:

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

Justification: This study is designed into various phases. DoR time is not one of the endpoints in phase 1.

End point values	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) cohort	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	4	12
Units: day				
number (not applicable)	0	51	0	52

End point values	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort	Sub study 1 (SS1)	Substudy 2 (SS2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: day				

number (not applicable)	0	734	0	
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Statistical analyses

No statistical analyses for this end point

Secondary: To Determine the Overall Survival (OS) Time for Phase 2 and Sub Studies

End point title	To Determine the Overall Survival (OS) Time for Phase 2 and Sub Studies ^[11]
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End point description:

Phase 2: To determine the overall survival (OS) time for subjects with solid tumours

SS1: To determine the overall survival (OS) time for subjects who received 60 mg/m² of EDO-S101 during a 60-minute Infusion.

SS2: To determine the overall survival (OS) time for subjects who received 80 mg/m² of EDO-S101 during a 80-minute Infusion.

NOTE: 999999 is entered for data not presented or not estimable

End point type	Secondary
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End point timeframe:

On Day 1 and 15 of each 4-week treatment cycle.

Notes:

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

Justification: This study is designed into various phases. OS is not one of the endpoints in phase 1.

End point values	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) cohort	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	4	12
Units: day				
median (inter-quartile range (Q1-Q3))	114.5 (88.5 to 150.0)	346.5 (167.0 to 650.0)	218.5 (92.5 to 999999)	261.0 (121.0 to 1260.0)

End point values	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort	Sub study 1 (SS1)	Substudy 2 (SS2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: day				
median (inter-quartile range (Q1-Q3))	127.0 (68.0 to 1058.0)	177.0 (78.0 to 784.0)	139.0 (130.0 to 999999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) in Phase 2 and Sub Studies

End point title	Maximum Plasma Concentration (Cmax) in Phase 2 and Sub Studies
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End point description:

Cmax (Maximum Plasma Concentration) of EDO-S101 and 2 metabolites M2 and M8.

*999999 is entered where data field could not be calculated due to insufficient data.

End point type	Secondary
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End point timeframe:

Blood samples were collected over a period of 24hr (phase 2 and sub-study 1) and 30hr (sub-study 2) on Cycle 1 Day 1 and Day 15.

End point values	Phase 2 all cohorts	Substudy 1	Substudy 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	6	7	
Units: nanogram(s)/millilitre				
geometric mean (geometric coefficient of variation)				
EDO-S101 concentration, Cycle 1 D1	1620 (\pm 43.3)	1150 (\pm 15.8)	1210 (\pm 11.3)	
EDO-S101 concentration, Cycle 1 D15	1540 (\pm 41.5)	999 (\pm 38.6)	1040 (\pm 21.2)	
M2 metabolite concentration, Cycle 1 D1	1.92 (\pm 77.9)	2.18 (\pm 65.4)	2.32 (\pm 65.5)	
M2 metabolite concentration, Cycle 1 D15	1.98 (\pm 63.3)	2.31 (\pm 105)	2.91 (\pm 999999)	
M8 metabolite concentration, Cycle 1 D1	47.7 (\pm 50.2)	37.4 (\pm 17.0)	27.0 (\pm 36.5)	
M8 metabolite concentration, Cycle 1 D15	49.8 (\pm 43.7)	31.2 (\pm 46.3)	24.6 (\pm 33.3)	

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Time for Phase 2 and Sub Studies

End point title	Progression Free Survival (PFS) Time for Phase 2 and Sub Studies ^[12]
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End point description:

PFS was defined as the number of days between the date of the first dose of treatment and the first date of disease progression or death.

Phase 2: To determine the PFS time for subjects who received 80 mg/m² over 60-minute of EDO-S101

infusion.

SS1: To determine the PFS time for subjects who received 60 mg/m² over 60-minute of EDO-S101 infusion.

SS2: To determine the PFS time for subjects who received 80 mg/m² over 80-minute of EDO-S101 infusion.

End point type	Secondary
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End point timeframe:

Date of the first dose of treatment and the first date of disease progression or death.

Notes:

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

Justification: This study is designed into various phases. PFS is not one of the endpoints in phase 1.

End point values	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) cohort	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	10	4	12
Units: day				
median (inter-quartile range (Q1-Q3))	54.0 (51.0 to 74.0)	56.0 (52.0 to 236.0)	85.0 (58.0 to 310.0)	63.0 (46.5 to 97.0)

End point values	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort	Sub study 1 (SS1)	Substudy 2 (SS2)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	7	
Units: day				
median (inter-quartile range (Q1-Q3))	87.0 (52.0 to 107.0)	177.0 (78.0 to 784.0)	65.0 (42.0 to 131.0)	

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Curve [AUC(0-t)] in Phase 2 and Sub Studies.

End point title	Area Under the Curve [AUC(0-t)] in Phase 2 and Sub Studies.
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End point description:

All enrolled subjects in the Safety Population with at least 1 quantifiable pre-dose and 1 quantifiable post-dose PK plasma concentration in Cycle 1 were included in the PK Population. PK analyses were performed using the PK population. 48 subjects of the Safety Population were included in the PK Population.

*999999 is entered for those fields where a value cannot be calculated due to insufficient data.

End point type	Secondary
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End point timeframe:

Blood samples were collected over a period of 24hr (phase 2 and sub-study 1) and 30hr (sub-study 2) on Cycle 1 Day 1 and Day 15.

End point values	Phase 2 all cohorts	Substudy 1	Substudy 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	6	7	
Units: ng.h/mL				
geometric mean (geometric coefficient of variation)				
EDO-S101 concentration, Cycle 1 D1	1490 (\pm 40.9)	938 (\pm 41.9)	1680 (\pm 22.6)	
EDO-S101 concentration, Cycle 1 D15	1520 (\pm 41.7)	943 (\pm 53.7)	1390 (\pm 28.7)	
M2 metabolite concentration, Cycle 1 D1	0.865 (\pm 248)	5.19 (\pm 420)	12.4 (\pm 1430)	
M2 metabolite concentration, Cycle 1 D15	1.32 (\pm 163)	2.32 (\pm 9060)	48.6 (\pm 999999)	
M8 metabolite concentration, Cycle 1 D1	47.7 (\pm 48.3)	36.0 (\pm 80.5)	54.4 (\pm 61.2)	
M8 metabolite concentration, Cycle 1 D15	53.3 (\pm 44.8)	40.9 (\pm 94.1)	35.2 (\pm 33.7)	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Tmax in in Phase 2 and Sub Studies.

End point title	Summary of Tmax in in Phase 2 and Sub Studies.
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End point description:

All enrolled subjects in the Safety Population with at least 1 quantifiable pre-dose and 1 quantifiable post-dose PK plasma concentration in Cycle 1 were included in the PK Population. PK analyses were performed using the PK population. 48 subjects of the Safety Population were included in the PK Population.

*999999 is entered for those fields where a value cannot be calculated due to insufficient data

End point type	Secondary
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End point timeframe:

Blood samples were collected over a period of 24hr (phase 2 and sub-study 1) and 30hr (sub-study 2) on Cycle 1 Day 1 and Day 15.

End point values	Phase 2 all cohorts	Substudy 1	Substudy 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	6	7	
Units: hours				
median (full range (min-max))				
EDO-S101 concentration, Cycle 1 D1	0.750 (0.250 to 1.25)	0.750 (0.250 to 0.750)	1 (0.750 to 1.33)	

EDO-S101 concentration, Cycle 1 D15	0.750 (0 to 1.25)	0.750 (0.5 to 0.750)	0.875 (0.167 to 1.33)	
M2 metabolite concentration, Cycle 1 D1	1.00 (0.25 to 2.00)	1 (0.250 to 6)	1.58 (0.750 to 24)	
M2 metabolite concentration, Cycle 1 D15	1.00 (0 to 6)	1 (0.250 to 24)	3.50 (3.50 to 3.50)	
M8 metabolite concentration, Cycle 1 D1	0.750 (0.250 to 1.50)	0.750 (0.250 to 1)	1 (1 to 1.33)	
M8 metabolite concentration, Cycle 1 D15	0.750 (0 to 1.25)	0.750 (0.500 to 0.750)	1.33 (1 to 1.33)	

Statistical analyses

No statistical analyses for this end point

Secondary: Clearance of Tinostamustine and Metabolites in Phase 2 and Substudies

End point title	Clearance of Tinostamustine and Metabolites in Phase 2 and Substudies
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End point description:

All enrolled subjects in the Safety Population with at least 1 quantifiable pre-dose and 1 quantifiable post-dose PK plasma concentration in Cycle 1 were included in the PK Population. PK analyses were performed using the PK population. 48 subjects of the Safety Population were included in the PK Population.

*999999 is entered for those fields where a value cannot be calculated due to insufficient data

End point type	Secondary
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End point timeframe:

Blood samples were collected over a period of 24hr (phase 2 and sub-study 1) and 30hr (sub-study 2) on Cycle 1 Day 1 and Day 15.

End point values	Phase 2 all cohorts	Substudy 1	Substudy 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	6	7	
Units: mL/h/m ²				
geometric mean (geometric coefficient of variation)				
EDO-S101 concentration, Cycle 1 D1	50800 (± 41.1)	69800 (± 48.7)	56000 (± 23.9)	
EDO-S101 concentration, Cycle 1 D15	53600 (± 45.2)	89600 (± 19.5)	49600 (± 58.3)	
M2 metabolite concentration, Cycle 1 D1	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)	
M2 metabolite concentration, Cycle 1 D15	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)	
M8 metabolite concentration, Cycle 1 D1	999999 (± 999999)	2410000 (± 54.2)	2270000 (± 22.4)	
M8 metabolite concentration, Cycle 1 D15	999999 (± 999999)	1240000 (± 14.8)	1740000 (± 40.8)	

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Half-life of Tinostamustine in Phase 2 and Substudies

End point title	Summary of Half-life of Tinostamustine in Phase 2 and Substudies
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End point description:

All enrolled subjects in the Safety Population with at least 1 quantifiable pre-dose and 1 quantifiable post-dose PK plasma concentration in Cycle 1 were included in the PK Population. PK analyses were performed using the PK population. 48 subjects of the Safety Population were included in the PK Population.

*999999 is entered for those fields where a value cannot be calculated due to insufficient data

End point type	Secondary
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End point timeframe:

Blood samples were collected over a period of 24hr (phase 2 and sub-study 1) and 30hr (sub-study 2) on Cycle 1 Day 1 and Day 15.

End point values	Phase 2 all cohorts	Substudy 1	Substudy 2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	35	6	7	
Units: Hour				
geometric mean (geometric coefficient of variation)				
EDO-S101 concentration, Cycle 1 D1	0.70 (± 54)	0.919 (± 38)	2.14 (± 185)	
EDO-S101 concentration, Cycle 1 D15	0.704 (± 51.2)	0.678 (± 45.8)	4.03 (± 2150)	
M2 metabolite concentration, Cycle 1 D1	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)	
M2 metabolite concentration, Cycle 1 D15	999999 (± 999999)	999999 (± 999999)	999999 (± 999999)	
M8 metabolite concentration, Cycle 1 D1	0.414 (± 49)	0.602 (± 30.2)	1.22 (± 96.8)	
M8 metabolite concentration, Cycle 1 D15	4.43 (± 553)	2.30 (± 153)	2.48 (± 99.7)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All TEAEs occurring during the course of the study.

Adverse event reporting additional description:

Number of patients experiencing treatment-related adverse events (TEAE) as assessed by CTCAE v4.03, June 2010, with the exception that assessment of QTc prolongations constituting adverse events (AEs) of special interest were based on NCI CTCAE version 5.0, November 2017.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.0
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Reporting groups

Reporting group title	Phase 1 - 60mg/m2 (30 Min) Cohort 1
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Reporting group description:

Patients who received 60mg/m2 over 30 minutes infusion time of EDO-S101

Reporting group title	Phase 1 - 80mg/m2 (30 Min) Cohort 2
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Reporting group description:

Patients who received 80mg/m2 over 30 minutes infusion time of EDO-S101

Reporting group title	Phase 1 - 100mg/m2 (30 Min) Cohort 3
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Reporting group description:

Patients who received 100mg/m2 over 30 minutes infusion time of EDO-S101

Reporting group title	Phase 1 - 60mg/m2 (60 Min). Cohort 4
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Reporting group description:

Patients who received 60mg/m2 over 60 minutes infusion time of EDO-S101

Reporting group title	Phase 1 - 80mg/m2 (60 Min) Cohort 5
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Reporting group description:

Patients who received who 80mg/m2 over 60 minutes infusion time of EDO-S101

Reporting group title	Phase 1 - 100mg/m2 (60 Min). Cohort 6
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Reporting group description:

Patients who received who 100mg/m2 over 60 minutes infusion time of EDO-S101

Reporting group title	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) coho
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Reporting group description:

Patient with relapsed/refractory SCLC who received 80mg/m2 over 60 minutes infusion time of EDO-S101

Reporting group title	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort
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Reporting group description:

Patient with relapsed/refractory STS who received 80mg/m2 over 60 minutes infusion time of EDO-S101

Reporting group title	Phase 2 Relapsed/refractory Triple Negative breast Cancer
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Reporting group description:

Patient with relapsed/refractory TNBC who received 80mg/m2 over 60 minutes infusion time of EDO-S101

Reporting group title	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort
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Reporting group description: -

Reporting group title	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort
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Reporting group description:

Patient with relapsed/refractory OC who received 80mg/m2 over 60 minutes infusion time of EDO-S101

Reporting group title	Sub study 1 (SS1)
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Reporting group description:

Patients who received 60mg/m2 over 60 minutes infusion time of EDO-S101

Reporting group title	Sub study 2 (SS2)
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Reporting group description:

Patients who received 80mg/m2 over 80 minutes infusion time of EDO-S101

Serious adverse events	Phase 1 - 60mg/m2 (30 Min) Cohort 1	Phase 1 - 80mg/m2 (30 Min) Cohort 2	Phase 1 - 100mg/m2 (30 Min) Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	2 / 3 (66.67%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sarcoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Lymphocyte count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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

Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 perforation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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 / 3 (0.00%)	0 / 3 (0.00%)
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			

Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
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	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (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			

Failure to thrive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1 - 60mg/m ² (60 Min). Cohort 4	Phase 1 - 80mg/m ² (60 Min) Cohort 5	Phase 1 - 100mg/m ² (60 Min). Cohort 6
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	5 / 8 (62.50%)	2 / 2 (100.00%)
number of deaths (all causes)	1	2	0
number of deaths resulting from adverse events	1	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sarcoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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 pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (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	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (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			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (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
Generalised oedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (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
Pyrexia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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 / 8 (0.00%)	0 / 2 (0.00%)
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 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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			
Lymphocyte count decreased			
subjects affected / exposed	1 / 3 (33.33%)	3 / 8 (37.50%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	1 / 1	4 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Platelet count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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			
Infusion related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery thrombosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (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

Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (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			
Syncope			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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			
Thrombocytopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (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
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			

subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (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
Fistula of small intestine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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 perforation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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 / 8 (0.00%)	0 / 2 (0.00%)
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%)	1 / 8 (12.50%)	0 / 2 (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
Urinary tract obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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			

Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (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
Pyelonephritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
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			

Failure to thrive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) coho	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	6 / 10 (60.00%)	1 / 4 (25.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sarcoma			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pleural effusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pneumothorax			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Platelet count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery thrombosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tachycardia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic ascites			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Urinary tract obstruction			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			

Flank pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall abscess			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

Failure to thrive			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort	Sub study 1 (SS1)
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 12 (58.33%)	4 / 6 (66.67%)	6 / 6 (100.00%)
number of deaths (all causes)	1	0	1
number of deaths resulting from adverse events	1	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sarcoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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 pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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			
Multiple organ dysfunction syndrome			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (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
Generalised oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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			
Lymphocyte count decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (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

Platelet count decreased			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transaminases increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (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
White blood cell count decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (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
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Coronary artery thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Tachycardia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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			
Syncope			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	2 / 2	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 6 (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
Abdominal pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (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
Ascites			

subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fistula of small intestine			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Haemorrhagic ascites			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Intestinal perforation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intra-abdominal haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (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 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract obstruction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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			

Flank pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal wall abscess			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Sepsis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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			

Failure to thrive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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	Sub study 2 (SS2)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Sarcoma			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Generalised oedema			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoxia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary alveolar haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Lymphocyte count decreased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Platelet count decreased subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Electrocardiogram QT prolonged subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transaminases increased subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
White blood cell count decreased subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Infusion related reaction subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac arrest subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery thrombosis subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Tachycardia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Syncope			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ascites			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fistula of small intestine			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic ascites			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intestinal perforation			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intra-abdominal haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract obstruction			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			

Flank pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal wall abscess			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Failure to thrive			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase 1 - 60mg/m2 (30 Min) Cohort 1	Phase 1 - 80mg/m2 (30 Min) Cohort 2	Phase 1 - 100mg/m2 (30 Min) Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Phlebitis superficial			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Sinus operation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	2 / 3 (66.67%)	2 / 3 (66.67%)
occurrences (all)	1	4	2
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	2
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Administration site irritation			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Administration site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Catheter site related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injection site discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Mucosal dryness			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Mucosal inflammation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Oedema subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Reproductive system and breast disorders Female genital tract fistula subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Haemoptysis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Anticipatory anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Mental status changes subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Investigations			
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 3 (66.67%) 5	1 / 3 (33.33%) 3
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 2
Blood creatinine increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Blood bilirubin increased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Activated partial thromboplastin time prolonged subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0

Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory rate increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Compression fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Radiation necrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stoma site haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pericardial effusion			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	3	2	1
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ataxia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Sciatica subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	3 / 3 (100.00%) 7	3 / 3 (100.00%) 6
Leukopenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Lymphopenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Hypereosinophilic syndrome subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Cyclic neutropenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Otorrhoea subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Eye disorders			
Eye swelling subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Exophthalmos			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vision blurred			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dental caries			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Large intestinal obstruction subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Proctalgia subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Retching subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Stomatitis subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Flatulence subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Food poisoning subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry mouth subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Dyspepsia subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Abdominal distension subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1

Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	2	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Skin ulcer subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Swelling face subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Hydronephrosis subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pain in extremity subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Arthralgia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Muscular weakness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Neck pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abscess neck			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Clostridium difficile infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Corona virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enterobacter bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nail infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pelvic abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Rhinitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Hypokalaemia			
subjects affected / exposed	2 / 3 (66.67%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	4	1	1
Dehydration			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hypomagnesaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Hyponatraemia			
subjects affected / exposed	2 / 3 (66.67%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	3	0	0
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Acidosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1 - 60mg/m ² (60 Min). Cohort 4	Phase 1 - 80mg/m ² (60 Min) Cohort 5	Phase 1 - 100mg/m ² (60 Min). Cohort 6
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	8 / 8 (100.00%)	2 / 2 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Phlebitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hot flush			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Phlebitis superficial subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Surgical and medical procedures Sinus operation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
General disorders and administration site conditions			
Fatigue subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4	6 / 8 (75.00%) 14	1 / 2 (50.00%) 1
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	2 / 8 (25.00%) 2	0 / 2 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0
Infusion site pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	1 / 2 (50.00%) 1
Chills subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Non-cardiac chest pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0
Face oedema subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0
Influenza like illness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0
Pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Administration site irritation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Administration site pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Catheter site hypersensitivity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Catheter site related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Early satiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gait disturbance			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Infusion site discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion site erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infusion site reaction			

subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Injection site discomfort subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Mucosal dryness subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0
Mucosal inflammation subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Oedema subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Reproductive system and breast disorders Female genital tract fistula subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1	2 / 8 (25.00%) 2	0 / 2 (0.00%) 0
Dyspnoea exertional			

subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Rhinitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Sinus pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 3 (33.33%)	2 / 8 (25.00%)	2 / 2 (100.00%)
occurrences (all)	1	2	2
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0

Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Anticipatory anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Mental status changes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Investigations			
Neutrophil count decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences (all)	0	2	3
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood bilirubin increased			
subjects affected / exposed	0 / 3 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	2	2	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	1	0	1
International normalised ratio increased			

subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
C-reactive protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Respiratory rate increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Weight increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	3	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Compression fracture			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Radiation necrosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Stoma site haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal injury			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pericardial effusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Supraventricular tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 3 (33.33%)	2 / 8 (25.00%)	1 / 2 (50.00%)
occurrences (all)	1	2	1
Dysgeusia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Dizziness			
subjects affected / exposed	1 / 3 (33.33%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	1	2	0
Paraesthesia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences (all)	0	1	1
Hypoaesthesia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ataxia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Balance disorder			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	2	0	0
Cerebral haemorrhage			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Sciatica			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 3 (100.00%)	3 / 8 (37.50%)	1 / 2 (50.00%)
occurrences (all)	16	6	1
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypereosinophilic syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Cyclic neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Otorrhoea			

subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0
Eye disorders			
Eye swelling subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Exophthalmos subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 2	0 / 2 (0.00%) 0
Diplopia subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0
Retinal detachment subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	1 / 8 (12.50%) 1	0 / 2 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Dental caries subjects affected / exposed occurrences (all)	0 / 3 (0.00%) 0	0 / 8 (0.00%) 0	0 / 2 (0.00%) 0
Enteritis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gingival bleeding			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Haematochezia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Large intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Proctalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Retching			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Dry mouth			

subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences (all)	1	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3 (33.33%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	1	2	0
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	2	0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences (all)	0	2	1
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Alopecia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Skin discolouration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	2	1	0
Pain in extremity			

subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	3	1	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Arthritis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Groin pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Synovial cyst			

subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Abscess neck			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Corona virus infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Enterobacter bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Lung infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Nail infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	1 / 2 (50.00%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Pelvic abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	3 / 8 (37.50%)	1 / 2 (50.00%)
occurrences (all)	1	3	1
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences (all)	1	1	1
Dehydration			
subjects affected / exposed	0 / 3 (0.00%)	3 / 8 (37.50%)	0 / 2 (0.00%)
occurrences (all)	0	5	0
Hypomagnesaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	1	1	0
Hypoalbuminaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 8 (12.50%)	1 / 2 (50.00%)
occurrences (all)	3	1	2
Hyponatraemia			

subjects affected / exposed	1 / 3 (33.33%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	1	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 8 (25.00%)	0 / 2 (0.00%)
occurrences (all)	0	4	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Acidosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 8 (12.50%)	0 / 2 (0.00%)
occurrences (all)	0	1	0
Hypoglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			
subjects affected / exposed	0 / 3 (0.00%)	0 / 8 (0.00%)	0 / 2 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2 Relapsed/refractory Small Cell Lung Cancer (SCLC) coho	Phase 2 Relapsed/refractory Soft Tissue Sarcoma (STS) cohort	Phase 2 Relapsed/refractory Triple Negative breast Cancer
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 4 (100.00%)	10 / 10 (100.00%)	4 / 4 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flushing			

subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Phlebitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Hot flush			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Phlebitis superficial			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Surgical and medical procedures			
Sinus operation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 4 (25.00%)	4 / 10 (40.00%)	1 / 4 (25.00%)
occurrences (all)	2	5	2
Oedema peripheral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Infusion site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chills			

subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Face oedema			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Administration site irritation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Administration site pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Catheter site hypersensitivity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Catheter site related reaction			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Early satiety			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Gait disturbance subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Infusion site discomfort subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Infusion site erythema subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Infusion site reaction subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Injection site discomfort subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Mucosal dryness subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Mucosal inflammation subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Oedema subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 2	0 / 4 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Reproductive system and breast disorders			

Female genital tract fistula subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Dyspnoea exertional subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Oropharyngeal pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Haemoptysis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Atelectasis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Epistaxis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Nasal congestion subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Pneumonitis			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	1 / 4 (25.00%) 1
Productive cough subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Sinus pain subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Insomnia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	1 / 4 (25.00%) 1
Depression subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Anticipatory anxiety subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Mental status changes subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Investigations			
Neutrophil count decreased subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Weight decreased			

subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood bilirubin increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Alanine aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Respiratory rate increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Weight increased			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Compression fracture			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Radiation necrosis			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Stoma site haemorrhage			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Vulvovaginal injury			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Cardiac disorders			
Palpitations			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Pericardial effusion			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Supraventricular tachycardia			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Nervous system disorders			
Headache			
subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	3 / 10 (30.00%) 3	0 / 4 (0.00%) 0
Dysgeusia			
subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Dizziness			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Ataxia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Balance disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Cerebral haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 4 (25.00%)	2 / 10 (20.00%)	2 / 4 (50.00%)
occurrences (all)	1	4	3
Leukopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Lymphopenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypereosinophilic syndrome			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Cyclic neutropenia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Otorrhoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Exophthalmos			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Vision blurred			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Diplopia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Retinal detachment			

subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain lower subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Dental caries subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	1 / 4 (25.00%) 1
Enteritis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Gingival bleeding subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Gingival pain subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 1	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Haematochezia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	1 / 10 (10.00%) 1	0 / 4 (0.00%) 0
Large intestinal obstruction subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Proctalgia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Retching subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Toothache subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0

Stomatitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Abdominal distension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Constipation			
subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences (all)	1	1	1
Diarrhoea			
subjects affected / exposed	1 / 4 (25.00%)	1 / 10 (10.00%)	2 / 4 (50.00%)
occurrences (all)	1	2	3
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Rash maculo-papular			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 4 (0.00%)	2 / 10 (20.00%)	0 / 4 (0.00%)
occurrences (all)	0	2	0
Alopecia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dermatitis acneiform			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Dry skin			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Rash erythematous			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin discolouration			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Swelling face			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Urticaria			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	3	0

Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hydronephrosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	2
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	2 / 4 (50.00%)
occurrences (all)	0	1	4
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Neck pain			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	4	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Arthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Groin pain			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	1 / 4 (25.00%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Abscess neck			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Chronic sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Corona virus infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Enterobacter bacteraemia subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Herpes zoster subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Lung infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Nail infection subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Oral herpes subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Pelvic abscess subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Rhinitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	0 / 4 (0.00%) 0	0 / 10 (0.00%) 0	0 / 4 (0.00%) 0
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	1 / 4 (25.00%) 2	1 / 10 (10.00%) 1	1 / 4 (25.00%) 1
Hypokalaemia			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Dehydration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	1 / 4 (25.00%)
occurrences (all)	0	1	1
Hypomagnesaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypocalcaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	1 / 10 (10.00%)	0 / 4 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Acidosis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Hypoglycaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0
Vitamin D deficiency			

subjects affected / exposed	0 / 4 (0.00%)	0 / 10 (0.00%)	0 / 4 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 2 Relapsed/refractory Ovarian Cancer (OC) cohort	Phase 2 Relapsed/refractory Endometrial Cancer (EC) cohort	Sub study 1 (SS1)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 12 (100.00%)	6 / 6 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Flushing			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Phlebitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hot flush			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	2
Lymphoedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Phlebitis superficial			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Surgical and medical procedures			
Sinus operation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	3 / 12 (25.00%)	5 / 6 (83.33%)	1 / 6 (16.67%)
occurrences (all)	6	8	1
Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Asthenia			
subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	7	0	0
Infusion site pain			
subjects affected / exposed	0 / 12 (0.00%)	3 / 6 (50.00%)	0 / 6 (0.00%)
occurrences (all)	0	4	0
Chills			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Face oedema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Peripheral swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Administration site irritation			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Administration site pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Catheter site hypersensitivity			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Catheter site related reaction subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Chest discomfort subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Chest pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Early satiety subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gait disturbance subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Infusion site discomfort subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Infusion site erythema subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Infusion site reaction subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injection site discomfort subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Mucosal dryness subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Mucosal inflammation subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Oedema			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Catheter site pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Reproductive system and breast disorders Female genital tract fistula subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Pelvic pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Vaginal haemorrhage subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1
Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	1 / 6 (16.67%) 3
Oropharyngeal pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1
Haemoptysis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Atelectasis			

subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nasal congestion			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pneumonitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinus pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anticipatory anxiety			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Mental status changes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Neutrophil count decreased			

subjects affected / exposed	3 / 12 (25.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	8	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 12 (16.67%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	3	2	1
Blood creatinine increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Weight decreased			
subjects affected / exposed	1 / 12 (8.33%)	2 / 6 (33.33%)	1 / 6 (16.67%)
occurrences (all)	1	2	1
Blood bilirubin increased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Alanine aminotransferase increased			
subjects affected / exposed	2 / 12 (16.67%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
International normalised ratio increased			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
C-reactive protein increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Respiratory rate increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Weight increased subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1
Compression fracture subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Radiation necrosis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Stoma site haemorrhage subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vulvovaginal injury subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Cardiac disorders			
Palpitations subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Pericardial effusion subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Supraventricular tachycardia			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Nervous system disorders			
Headache			
subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3	2 / 6 (33.33%) 2	0 / 6 (0.00%) 0
Dysgeusia			
subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	2 / 6 (33.33%) 2	0 / 6 (0.00%) 0
Dizziness			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	1 / 6 (16.67%) 1
Paraesthesia			
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Disturbance in attention			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hypoaesthesia			
subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Peripheral sensory neuropathy			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Ataxia			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Balance disorder			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Cerebral haemorrhage			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Neuropathy peripheral			
subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0

Sciatica subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	5 / 12 (41.67%) 7	4 / 6 (66.67%) 15	2 / 6 (33.33%) 6
Leukopenia subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Lymphopenia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 4	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hypereosinophilic syndrome subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Cyclic neutropenia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Otorrhoea subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Eye disorders			
Eye swelling subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Exophthalmos subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Conjunctival haemorrhage			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vision blurred subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Diplopia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Retinal detachment subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gastrointestinal disorders			
Abdominal pain lower subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Abdominal pain upper subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dental caries subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Enteritis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gingival bleeding subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gingival pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Haematochezia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Large intestinal obstruction subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0

Proctalgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Retching			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Toothache			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Stomatitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Food poisoning			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Abdominal distension			
subjects affected / exposed	2 / 12 (16.67%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	3	2	0
Gastroesophageal reflux disease			
subjects affected / exposed	0 / 12 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Constipation			
subjects affected / exposed	5 / 12 (41.67%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	8	1	2

Diarrhoea subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 4	2 / 6 (33.33%) 3	1 / 6 (16.67%) 1
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin and subcutaneous tissue disorders Rash maculo-papular subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 4	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Night sweats subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Alopecia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dermatitis acneiform subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dry skin subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Rash erythematous subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin discolouration subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Skin ulcer			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Swelling face subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Urticaria subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Hydronephrosis subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3	2 / 6 (33.33%) 4	1 / 6 (16.67%) 1
Pain in extremity subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	3 / 6 (50.00%) 3	1 / 6 (16.67%) 1
Arthralgia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 3	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Muscle spasms subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Muscular weakness subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Musculoskeletal pain			

subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Myalgia			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Arthritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Groin pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Limb discomfort			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Synovial cyst			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Abscess neck			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Candida infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Chronic sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Clostridium difficile infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Corona virus infection			
subjects affected / exposed	1 / 12 (8.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Enterobacter bacteraemia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Herpes zoster			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lung infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nail infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pelvic abscess			
subjects affected / exposed	0 / 12 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Rhinitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

Sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	2 / 12 (16.67%)	4 / 6 (66.67%)	0 / 6 (0.00%)
occurrences (all)	3	4	0
Hypokalaemia			
subjects affected / exposed	2 / 12 (16.67%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	5	3	2
Dehydration			
subjects affected / exposed	1 / 12 (8.33%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	1	1
Hypomagnesaemia			
subjects affected / exposed	4 / 12 (33.33%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	7	1	1
Hypoalbuminaemia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	0 / 12 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	3	0
Hypocalcaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Acidosis			

subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hyperuricaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hypoglycaemia subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vitamin D deficiency subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1

Non-serious adverse events	Sub study 2 (SS2)		
Total subjects affected by non-serious adverse events subjects affected / exposed	6 / 7 (85.71%)		
Vascular disorders			
Hypotension subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Flushing subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Phlebitis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Hot flush subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Hypertension subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Lymphoedema subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Phlebitis superficial			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Surgical and medical procedures Sinus operation subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Asthenia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Infusion site pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Face oedema subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Influenza like illness subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Peripheral swelling			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Administration site irritation subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Administration site pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Catheter site hypersensitivity subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Catheter site related reaction subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Chest discomfort subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Chest pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Early satiety subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Gait disturbance subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Infusion site discomfort subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Infusion site erythema subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Infusion site reaction subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Injection site discomfort			

<p>subjects affected / exposed occurrences (all)</p> <p>Mucosal dryness subjects affected / exposed occurrences (all)</p> <p>Mucosal inflammation subjects affected / exposed occurrences (all)</p> <p>Oedema subjects affected / exposed occurrences (all)</p> <p>Catheter site pain subjects affected / exposed occurrences (all)</p>	<p>0 / 7 (0.00%) 0</p>		
<p>Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)</p>	<p>0 / 7 (0.00%) 0</p>		
<p>Reproductive system and breast disorders Female genital tract fistula subjects affected / exposed occurrences (all)</p> <p>Pelvic pain subjects affected / exposed occurrences (all)</p> <p>Vaginal haemorrhage subjects affected / exposed occurrences (all)</p>	<p>0 / 7 (0.00%) 0</p> <p>0 / 7 (0.00%) 0</p> <p>0 / 7 (0.00%) 0</p>		
<p>Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)</p> <p>Dyspnoea exertional subjects affected / exposed occurrences (all)</p> <p>Oropharyngeal pain</p>	<p>2 / 7 (28.57%) 2</p> <p>0 / 7 (0.00%) 0</p>		

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Haemoptysis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Rhinitis allergic subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Atelectasis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Epistaxis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Nasal congestion subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Pneumonitis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Productive cough subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Sinus pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Insomnia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Depression subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		

Anticipatory anxiety subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Mental status changes subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Investigations			
Neutrophil count decreased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Blood creatinine increased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Weight decreased subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 2		
Blood bilirubin increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
International normalised ratio increased subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Activated partial thromboplastin time			

prolonged			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 7 (14.29%)		
occurrences (all)	1		
Breath sounds abnormal			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
C-reactive protein increased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Respiratory rate increased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Compression fracture			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Radiation necrosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Stoma site haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vulvovaginal injury			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Cardiac disorders			

Palpitations			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Pericardial effusion			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Supraventricular tachycardia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dysgeusia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Disturbance in attention			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Ataxia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Balance disorder			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Cerebral haemorrhage subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Neuropathy peripheral subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Sciatica subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Leukopenia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Lymphopenia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Hypereosinophilic syndrome subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Cyclic neutropenia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Ear and labyrinth disorders			
Ear pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Otorrhoea subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Tinnitus			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Eye disorders			
Eye swelling			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Exophthalmos			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Conjunctival haemorrhage			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vision blurred			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Diplopia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Retinal detachment			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain lower			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Abdominal pain upper			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dental caries			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Enteritis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gingival bleeding			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Gingival pain			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Haematochezia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Large intestinal obstruction			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Proctalgia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Retching			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Abdominal discomfort			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Food poisoning			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dyspepsia			

subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Abdominal distension subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Constipation subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Diarrhoea subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Hepatobiliary disorders Hyperbilirubinaemia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Skin and subcutaneous tissue disorders Rash maculo-papular subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Pruritus subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Rash subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Night sweats subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Alopecia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Dermatitis acneiform			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Dry skin subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Rash erythematous subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Skin discolouration subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Skin ulcer subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Swelling face subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Urticaria subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Hydronephrosis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2		
Pain in extremity subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Arthralgia			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Muscle spasms subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Muscular weakness subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Neck pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Musculoskeletal pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Myalgia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Arthritis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Groin pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Joint swelling subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Limb discomfort subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Musculoskeletal chest pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Synovial cyst subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Infections and infestations			

Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Tooth infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Abscess neck subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Candida infection subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Chronic sinusitis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Clostridium difficile infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Corona virus infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Enterobacter bacteraemia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Gastroenteritis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Herpes zoster subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1		
Infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		
Lung infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0		

Nail infection			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Pelvic abscess			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Rhinitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypomagnesaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypoalbuminaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hyponatraemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			

subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hyperkalaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypophosphataemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Acidosis			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Hypoglycaemia			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		
Vitamin D deficiency			
subjects affected / exposed	0 / 7 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 October 2018	<p>Amendment 1: Protocol version 4.0</p> <p>Reason for Changes: Added the RP2D determined in Phase 1 and Updated the Phase 2 sections in the protocol.</p> <p>Description of Changes: Clarified Phase 2 primary objective and efficacy evaluation time points. Added a fifth subject cohort (endometrial cancer) and eligibility requirements. Clarified that treatment could continue until progression, intolerable toxicity, or until CR has been achieved. Changed patient eligibility to allow recovery to \leq Grade 2 for neuropathy or other endocrinopathies from prior treatment. Clarified the inclusion eligibility for GIST subjects Added allopurinol as a prohibitive medication. Pre-treatment with allopurinol was contraindicated. Changed drug preparation instructions to reflect new, higher concentration of the drug product. Added window of +5 minutes to drug infusion duration.</p>
04 February 2019	<p>Amendment 2: Protocol version 5.0</p> <p>Reason for changes: Updated the Phase 2 sections in the protocol.</p> <p>Description of Changes: Added a statement (underline text) to the inclusion criteria: Must have received at least one line of chemotherapy and no other standard therapy with proven clinical benefit is available or recommended based on the Investigator's individual risk-benefit assessment for the subject. Clarified for TNBC subjects that HER2 negative needed to be proven by immunohistochemistry or in situ hybridization per ASCO-CAP guidelines. Clarified the timing of the pre-dose ECG assessment and the pre-dose PK sample collection. Clarified Phase 2 criteria for subjects to receive subsequent treatment after Cycle 1, and the option to dose reduce in case of safety concerns. Clarified that a second serotonin 5-HT3 receptor antagonist, granisetron (Kytril), was acceptable for the prophylaxis of delayed nausea and vomiting</p>
28 January 2020	<p>Amendment 3: Protocol version 6.0</p> <p>Reason for Changes: Updated the Phase 2 sections in the protocol. Implemented Risk Mitigation Measures related to possible QTc prolongations.</p> <p>Description of Changes: Limited study treatment to a maximum of 12 cycles. Implemented strict guidelines on methods of contraception for subjects of childbearing potential. Specified that the subject population eligible for the study were subjects who have been progressing or relapsing after their previous treatment. Specified that the subject could withdraw from study for any reason. Specified that the Sponsor would continuously assess the benefit-risk ratio for subject safety and discontinue treatment if deemed necessary. Specified that a separate ICF was needed for gene expression sample collection. Specified that blood samples for laboratory tests were needed to be taken before the start of study drug administration. Clarified reporting of TEAEs, SAEs and Suspected Unexpected Serious Adverse Reactions.</p>

08 April 2020	<p>Amendment 4: Protocol version 6.2.</p> <p>Reason for Changes: Requested by the FDA.</p> <p>Description of Changes: Created a separate protocol for Sub-study 1 to characterize the effect of tinostamustine 60 mg/m² infused over 60 minutes on cardiac repolarization (QTc) and other ECG parameters.</p>
05 September 2020	<p>Amendment 5: Protocol version 7.0.</p> <p>Description of Changes: Added centres in Europe. Each cohort could treat an additional 19 subjects (29 in total) if there was evidence of 2 successes in that cohort. Dose reduction to 60 mg/m² in case of safety concerns. Allowed to reintroduce the initial dose if toxicity issues were resolved and specified that a subject must be withdrawn if she/he did not tolerate the reduced dose. Clarifications to the general inclusion criteria for phase 1 and phase 2 of the trial. Clarifications to cohort specific eligibility criteria. Clarifications to the schedule of assessments. Guidance on IMP administration. Clarifications on reporting of AEs, SAEs and pregnancies.</p>
27 September 2020	<p>Amendment 6: Protocol version 7.1.</p> <p>Reason for Changes: Updated the Phase 2 sections in the protocol.</p> <p>Description of Changes: Added "Life expectancy > 3 months" to the inclusion criteria. Exclude subjects being treated with valproic acid from the study. Excluded MMT from the study. Deleted the paragraph on replacement of subjects Specified that serum potassium and magnesium should be at least at the LLN before the start of study drug infusion. Specified that clinically significant laboratory findings must be recorded as AEs. Specified that PD itself and death from PD should not be recorded as an AE.</p>
22 March 2021	<p>Amendment 7: Protocol version 7.2.</p> <p>Reason for Changes: Followed the Clinical Trials Facilitation group's guidance, which was updated in September 2020, on contraception to be used for investigational drugs that have demonstrated genotoxicity.</p> <p>Description of Changes: Contraceptive measures for women of childbearing potential were extended from 90 days to 6 months after the last study drug administration.</p>

02 April 2021	<p>Amendment 8: Protocol version 8.0.</p> <p>Reason for Changes: Updated the Phase 2 sections in the protocol.</p> <p>Description of Changes: Noted the halting the recruitment into the cohorts for TNBC and endometrial cancer. Update the washout period of previous anticancer therapies from 3 weeks to 28 days. Updated the washout period of other investigational agents from 30 days or 5 half-lives to 28 days prior to first dose of tinostamustine. Update the allowable elapsed time since prior treatment from at least 3 weeks to at least 28 days. Added that platelets must be $\geq 100,000$ μL without platelet transfusion within the 14 days before Day 1 of Cycle 1. Updated the allowable window for the collection of blood samples on Days 1 and 15 from ± 2 days to -2 days. Updated the allowable window for the collection of the 60-minute PK sample from ± 5 minutes to -5 minutes Clarified that all PK sample times should be calculated from the start of the tinostamustine infusion. Updated the storage instructions for the diluted solution of study drug, in line with the latest Investigator's Brochure dated 19 March 2021. Updated the criteria for continuing study drug to reduce the rate of thrombocytopenia leading to study discontinuation. Clarified the allowable supportive care for subjects.</p>
10 May 2021	<p>Amendment 9: Protocol version 8.1.</p> <p>Reason for Changes: Corrected changes erroneously made in Protocol Version 8.0.</p> <p>Description of Changes: Corrected to revert the removal of the relapsed/refractory TNBC and relapsed/refractory endometrial cancer cohorts from the safety analysis.</p>
12 July 2021	<p>Amendment 10: Protocol version 6.3.</p> <p>Reason for Changes: Completed Sub-study 1 safely.</p> <p>Description of Changes: Created a separate protocol for Sub-study 2 to characterize the effect of tinostamustine 80 mg/m² infused over 80 minutes on cardiac repolarization (QTc) and other ECG parameters. Updated some sections to be aligned with the latest protocol for Phase 2 (version 8.1). Amended the wording of the secondary objective to state more clearly 'determine plasma concentrations.' Removed the exploratory objective for gene expression analysis as tumour samples were not collected in Sub-study 2. Allowed additional subjects to be recruited up to 12 in total. Amended the stopping rules to be more specific and to separate stopping rules for individual subject's treatment and those for the whole study. Clarified that the subject should stay in the unit until the QTcF decreased to $\leq 450\text{ms}$. Amended the timepoints for Holter readings and PK sampling to include more timepoints during study drug infusion and to align with a change in infusion duration of 80 minutes</p>

11 August 2021	<p>Amendment 11: Protocol version 6.4.</p> <p>Reason for Change: Requested by the FDA.</p> <p>Description of Changes: Amended the stopping rules as per the following FDA comments: Add to the study stopping rules that for any treatment-related death, the study would be stopped. Add that for a specified rate or number of Grade 3 or higher QT prolongation (i.e. 2 subjects), the study would be stopped. Add to the dose modification guidelines, that for Grade 4 non-haematologic toxicity, the subject would be discontinued from further treatment.</p>
18 August 2021	<p>Amendment 12: Protocol version 6.5.</p> <p>Reason for Changes: Requested by the FDA.</p> <p>Description of Changes: Amended the inclusion criteria as per the following FDA comments: Revise the renal function inclusion criterion to specify creatinine clearance (CLcr) is utilized rather than serum creatinine and specify a consistent and appropriately validated prediction equation in adults is used for the estimation of eGFR (e.g., Cockcroft-Gault for CLcr or Modification of Diet in Renal Disease method). Revise the hepatic function inclusion criterion for total bilirubin to be expressed as multiples of ULN.</p>
14 February 2023	<p>Amendment 13: Protocol version 6.7</p> <p>Reason for Changes: Updated the protocol for Sub-study 2.</p> <p>Description of Changes: Changed the follow-up overall survival period to a maximum of 12 months.</p>

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
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04 June 2019	<p>QTc prolongation was noted in separate study with Tinostamustin administered at high dose (180 or 220mg/m² over 1hr). Although the QTc prolongations were transient and asymptomatic, the Sponsor terminated the EDO-S101-1004 study and decided not to pursue further development of high-dose tinostamustine. The Sponsor decided to conduct an in-depth analysis of clinically relevant ECG findings and a consequential benefit-risk assessment. Subject recruitment in the US sites for the EDO-S101-1002 study (this phase 1/2 study) was set on hold as a consequence of the Partial Clinical Hold Letter issued by the Food and Drug Administration (FDA) on 03 June 2019. The FDA requested that the Sponsor perform additional studies to better characterise the effect of tinostamustine on cardiac repolarization (QTc). After the benefit-risk assessment, the protocol was amended to include more intense ECG and PK collection in order to allow a precise characterization of the effects of tinostamustine on QTc and other ECG parameters, at the dosages being investigated for the treatment of solid tumours. QTc prolongations were also defined as AEs of special interest. Consequently, 2 sub-studies were planned for and conducted. The hold was lifted in the US for the 60mg/m² over 60min substudy 1 and 80mg/m² over 80min. The phase 2 of the study could be carried out in non-US sites.</p>	09 April 2020
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Notes:

Limitations and caveats

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

No applicable

Notes: