Clinical trial results:
A Phase 1b/2, Multicenter, Open-label, Dose-escalation and Confirmation Study of Eribulin in Combination with Capecitabine

Summary

EudraCT number	2009-011217-24
Trial protocol	GB BG
Global end of trial date	13 October 2015

Results information

Result version number	v1 (current)
This version publication date	04 December 2020
First version publication date	04 December 2020

Trial information

Trial identification

Sponsor protocol code	E7389-E044-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01323530
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Ltd.
Sponsor organisation address	Mosquito Way, Hatfield, Hertfordshire, United Kingdom, AL10 9SN UK
Public contact	Eisai Medical Information, Eisai Inc., +1 888-274-2378, esi_oncmedinfo@eisai.com
Scientific contact	Eisai Medical Information, Eisai Inc., +1 888-274-2378, esi_oncmedinfo@eisai.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	13 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary purpose of the study is to determine the maximum tolerated dose (MTD) and dose-limiting toxicities (DLTs) of eribulin mesilate when administered in combination with capecitabine in two different dosing schedules in subjects with advanced and/or metastatic cancer in Dose Escalation Cohorts (Phase 1b), and to evaluate the activity of the combination of eribulin mesilate and capecitabine when administered in the selected schedule at the MTD (determined during dose escalation) in female subjects with advanced and/or metastatic breast cancer (Phase 2).

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following:
- Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008).
- International Council on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.
- Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312.
- European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states.
- Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan’s GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 January 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 47
Country: Number of subjects enrolled	Bulgaria: 6
Country: Number of subjects enrolled	Russian Federation: 23
Worldwide total number of subjects	76
EEA total number of subjects	53

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	61
From 65 to 84 years	15
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 13 investigative sites in Bulgaria, Russia, and United Kingdom from 26 January 2010 to 13 October 2015.

Pre-assignment

Screening details:

In Phase 1b (Dose Escalation Phase), a total of 43 subjects with solid tumors were screened, of which 9 were screen failures and 34 received study treatment, and in Phase 2 (Dose Confirmation Phase), a total of 54 female subjects with breast cancer were screened, of which 12 were screen failures and 42 received study treatment.

Period 1

Period 1 title	Phase 1b (Dose Escalation Phase)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)

Arm description:

Subjects received eribulin mesilate 1.2 milligrams per square meter (mg/m^2), injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of progressive disease (PD), undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Arm type	Experimental
Investigational medicinal product name	Eribulin mesilate
Investigational medicinal product code	E7389
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received eribulin mesilate 1.2 mg/m^2, injection, intravenously, once, on Day 1 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Arm title	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)

Arm description:

Subjects received eribulin mesilate 1.6 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Arm type	Experimental
Investigational medicinal product name	Eribulin mesilate
Investigational medicinal product code	E7389
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received eribulin mesilate 1.6 mg/m^2, injection, intravenously, once, on Day 1 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Arm title	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)

Arm description:

Subjects received eribulin mesilate 2.0 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Arm type	Experimental
Investigational medicinal product name	Eribulin mesilate
Investigational medicinal product code	E7389
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received eribulin mesilate 2.0 mg/m^2, injection, intravenously, once, on Day 1 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Arm title	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)

Arm description:

Subjects received eribulin mesilate 0.7 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Arm type	Experimental
Investigational medicinal product name	Eribulin mesilate
Investigational medicinal product code	E7389
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received eribulin mesilate 0.7 mg/m^2, injection, intravenously, once, on Days 1 and 8 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Arm title	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)

Arm description:

Subjects received eribulin mesilate 1.1 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Arm type	Experimental
Investigational medicinal product name	Eribulin mesilate
Investigational medicinal product code	E7389
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received eribulin mesilate 1.1 mg/m^2, injection, intravenously, once, on Days 1 and 8 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical

conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Arm title	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)

Arm description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Arm type	Experimental
Investigational medicinal product name	Eribulin mesilate
Investigational medicinal product code	E7389
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Number of subjects in period 1	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)
Started	8	6	5
Completed	5	4	4
Not completed	3	2	1
Adverse event, serious fatal	2	-	-
Consent withdrawn by subject	1	1	1
Clinical Progression	-	1	-

Number of subjects in period 1	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)
Started	3	6	6
Completed	3	3	3
Not completed	0	3	3
Adverse event, serious fatal	-	-	2
Consent withdrawn by subject	-	2	-
Clinical Progression	-	1	1

Period 2

Period 2 title	Phase 2 (Dose-confirmation Phase)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Phase 2: Eribulin mesilate 1.4 mg/m^2

Arm description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 2.

Arm type	Experimental
Investigational medicinal product name	Eribulin mesilate
Investigational medicinal product code	E7389
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 2.

Investigational medicinal product name	Capecitabine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 2.

Number of subjects in period 2	Phase 2: Eribulin mesilate 1.4 mg/m^2
Started	42
Completed	25
Not completed	17
Adverse event, serious fatal	2
Consent withdrawn by subject	8
Development of bladder cancer	1
Investigators decision	3
Clinical Progression	3

Baseline characteristics

Reporting groups[1]

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.2 milligrams per square meter (mg/m^2), injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of progressive disease (PD), undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.6 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 2.0 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 0.7 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.1 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.
Justification: The baseline period is the Dose-escalation Phase with 34 subjects. The baseline characteristics for remaining 42 subjects in Dose-confirmation Phase is reported using subject analysis set.

Reporting group values	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)
Number of subjects	8	6	5
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	4	3
From 65-84 years	1	2	2
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	6	0	3
Male	2	6	2
Race Units: Subjects			
White	8	6	5
Black or African American	0	0	0
Ethinicity Units: Subjects			
Non Hispanic or Latino	8	6	5

Reporting group values	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)
Number of subjects	3	6	6
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	5	3
From 65-84 years	1	1	3
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	2	3	5
Male	1	3	1
Race Units: Subjects			
White	3	6	6
Black or African American	0	0	0

Ethinicity Units: Subjects			
Non Hispanic or Latino	3	6	6

Reporting group values	Total		
Number of subjects	34		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	24		
From 65-84 years	10		
85 years and over	0		
Gender categorical Units: Subjects			
Female	19		
Male	15		
Race Units: Subjects			
White	34		
Black or African American	0		
Ethinicity Units: Subjects			
Non Hispanic or Latino	34		

Subject analysis sets

Subject analysis set title	Phase 2: Eribulin mesilate 1.4 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 2.

Reporting group values	Phase 2: Eribulin mesilate 1.4 mg/m^2		
Number of subjects	42		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		

Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	37		
From 65-84 years	5		
85 years and over	0		
Gender categorical Units: Subjects			
Female	42		
Male	0		
Race Units: Subjects			
White	41		
Black or African American	1		
Ethinicity Units: Subjects			
Non Hispanic or Latino	42		

End points reporting groups

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.2 milligrams per square meter (mg/m^2), injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of progressive disease (PD), undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.6 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 2.0 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 0.7 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.1 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Reporting group title	Phase 2: Eribulin mesilate 1.4 mg/m^2

Reporting group description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit

continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 2.

Subject analysis set title	Phase 2: Eribulin mesilate 1.4 mg/m^2
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 2.

Primary: Phase 1b: Number of Subjects with DLTs as per National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (NCI CTCAE v3.0)

End point title	Phase 1b: Number of Subjects with DLTs as per National Cancer Institute Common Terminology Criteria for Adverse Events version 3.0 (NCI CTCAE v3.0)[1]

End point description:

DLTs per NCI CTCAE v3.0 were defined as:1)Neutropenia Grade 4 that lasted 7 days, 2) Neutropenia Grade 3 or 4 complicated by fever or infection(absolute neutrophil count[ANC] less than 1.0*10^9/liter [L], fever of 38.5 degree celsius [°C]), 3)Thrombocytopenia Grade 4, 4)Thrombocytopenia Grade 3 complicated by bleeding or requiring platelet or blood transfusion, 5)Non-hematological toxicity Grade 3 or higher(excluding Grade 3 nausea, and Grade 3 or 4 vomiting or diarrhea in subjects who had not received optimal treatment with antiemetic or antidiarrheal medication; excluding laboratory abnormalities without clinical symptoms),6) Delayed recovery from treatment-related toxicity resulting in dose delay greater than 14 days,7)Failure to administer at least 75 percent(%) planned drugs during Cycle 1 as result of Grade 2 or higher treatment-related toxicity that constituted increase of at least 2 grades from baseline. Safety set: subjects who received drug, had 1 postdose safety assessment.

End point type	Primary

End point timeframe:

Cycle 1 (21 days)

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	6	5	3
Units: subjects	1	1	2	0

End point values	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: subjects	1	1		

Statistical analyses

No statistical analyses for this end point

Primary: Phase 2: Objective Response Rate (ORR)

End point title	Phase 2: Objective Response Rate (ORR)[2]

End point description:

ORR was defined as the percentage of subjects who had either a confirmed complete response (CR) or partial response (PR). ORR was assessed based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v 1.1). CR was defined as disappearance of all target lesions. All pathological lymph nodes (whether target or non-target) must have a reduction in their short axis to less than (<) 10 millimeter (mm). PR was defined as at least a 30 percent (%) decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum of the longest diameter. ORR was summarized using the Clopper-Pearson method. The Dose-confirmation full analysis set included all subjects who enrolled in the Dose-confirmation Cohort (Phase 2) and received at least 1 dose of drug.

End point type	Primary

End point timeframe:

From the first dose of study drug until PD or up to 30 days after the last dose of study treatment

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive data was planned to be analysed for this endpoint.

End point values	Phase 2: Eribulin mesilate 1.4 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (confidence interval 95%)	42.9 (27.7 to 59.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Time to Response

End point title	Phase 2: Time to Response

End point description:

Time to response (CR or PR) was defined as the time from the first dose until first documented evidence of CR or PR (whichever status was recorded first). Time to response was assessed based on RECIST v 1.1. CR was defined as disappearance of all target lesions. All pathological lymph nodes (whether target or non-target) must have a reduction in their short axis to less than 10 mm. PR was defined as at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum of the longest diameter. Time to response was summarized using the Kaplan-Meier method. The Dose-confirmation full analysis set included all subjects who enrolled in the Dose-confirmation Cohort (Phase 2) and received at least 1 dose of drug. Here "subjects analysed" signifies subjects who had CR

or PR.

End point type	Secondary

End point timeframe:

From the first dose of study drug treatment start date until date of first documented evidence of CR or PR or up to 30 days after the last dose of study treatment

End point values	Phase 2: Eribulin mesilate 1.4 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: days				
median (confidence interval 95%)	44.0 (42.0 to 84.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Response (DOR)

End point title	Phase 2: Duration of Response (DOR)

End point description:

DOR: time from first documented evidence of CR or PR until first documented sign of PD or death. DOR was assessed based on RECIST v 1.1. CR: disappearance of all target lesions. All pathological lymph nodes (whether target/non-target) must have a reduction in their short axis to >10 mm. PR: at least a 30% decrease in sum of longest diameter of target lesions, taking as reference the baseline sum of longest diameter. PD: at least a 20% increase in sum of diameters of target lesions, taking as reference smallest sum on study (this includes baseline sum if that is smallest on study). DOR was summarized using Kaplan-Meier method. The Dose-confirmation full analysis set included all subjects who enrolled in Dose-confirmation Cohort (Phase 2) and received at least 1 dose of drug. Here "subjects analysed" signifies subjects who had CR or PR. Here, 99999 means that upper limit of 95% confidence interval (CI) was not estimable due to an insufficient number of events.

End point type	Secondary

End point timeframe:

From date of the first CR or PR until the date of first documentation of PD or death or up to 30 days after the last dose of study treatment

End point values	Phase 2: Eribulin mesilate 1.4 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: days				
median (confidence interval 95%)	261.0 (161.0 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Stable Disease (SD) Rate

End point title	Phase 2: Stable Disease (SD) Rate

End point description:

SD rate was defined as the percentage of subjects with a SD that lasted for a minimum of 5 weeks. SD rate was assessed based on RECIST version 1.1. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study. PR: at least a 30% decrease in sum of longest diameter of target lesions, taking as reference the baseline sum of longest diameter. PD: at least a 20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study (this includes baseline sum if that is the smallest on study). The Dose-confirmation full analysis set included all subjects who enrolled in the Dose-confirmation Cohort (Phase 2) and received at least 1 dose of drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug until PD or up to 30 days after the last dose of study treatment

End point values	Phase 2: Eribulin mesilate 1.4 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (not applicable)	38.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 1b and Phase 2: Percentage of Subjects with Non-CR/Non-PD

End point title	Phase 1b and Phase 2: Percentage of Subjects with Non-CR/Non-PD

End point description:

Non-CR/Non-PD was for subjects who had non-target disease only (minimum duration from randomization to Non-CR/Non-PD >=7 weeks) and assessed by investigator based on RECIST v1.1. Non-CR/Non-PD: persistence of one or more non-target lesions, maintenance of tumor marker level above the normal limits. Full Analysis Set included all subjects who were enrolled and received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug until PD or up to 30 days after the last dose of study treatment

End point values	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	6	5	3
Units: percentage of subjects				
number (not applicable)	0	0	0	0

End point values	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)	Phase 2: Eribulin mesilate 1.4 mg/m^2	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	42	
Units: percentage of subjects				
number (not applicable)	16.7	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Duration of Stable Disease (SD)

End point title	Phase 2: Duration of Stable Disease (SD)

End point description:

Duration of SD was measured from date of the first dose until progression. Duration of SD was assessed based on RECIST v1.1. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study. PR: at least a 30% decrease in sum of longest diameter of target lesions, taking as reference the baseline sum of longest diameter. PD: at least a 20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study (this includes baseline sum if that is the smallest on study). Duration of SD was summarized using the Kaplan-Meier method. The Dose-confirmation full analysis set included all subjects who enrolled in the Dose-confirmation Cohort (Phase 2) and received at least 1 dose of drug. Here "subjects analysed" signifies subjects who had SD.

End point type	Secondary

End point timeframe:

From the first dose of study drug until PD or 30 days after the last dose of study treatment

End point values	Phase 2: Eribulin mesilate 1.4 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	16			
Units: days				
median (confidence interval 95%)	162.0 (91.0 to 330.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Disease Control Rate (DCR)

End point title	Phase 2: Disease Control Rate (DCR)

End point description:

DCR:percentage of subjects with a confirmed CR, PR, or SD divided by number of subjects in analysis set. DCR was assessed by an investigator based on RECIST v1.1. CR: disappearance of all target lesions. All pathological lymph nodes (whether target or non-target) must have reduction in their short axis to <10 mm. PR: at least 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum of the longest diameter. SD: neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum diameters while on study. PD: at least 20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study (this includes baseline sum if that is the smallest on study). DCR was summarized using the Clopper-Pearson method. The Dose-confirmation full analysis set included all subjects who enrolled in the Dose-confirmation Cohort (Phase 2) and received at least 1 dose of drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug until PD or 30 days after the last dose of study treatment

End point values	Phase 2: Eribulin mesilate 1.4 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (confidence interval 95%)	81.0 (65.9 to 91.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Clinical Benefit Rate (CBR)

End point title	Phase 2: Clinical Benefit Rate (CBR)

End point description:

CBR:percentage of subjects with confirmed CR, PR, or SD of at least 6 months duration(durable SD)

divided by number of subjects in analysis set. CBR was determined by an investigator based on RECIST v1.1. CR:disappearance of all target lesions. All pathological lymph nodes(whether target or non-target)must have reduction in their short axis to <10 mm. PR:at least 30% decrease in sum of longest diameter of target lesions,taking as reference baseline sum of the longest diameter.SD:neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD,taking as reference the smallest sum diameters while on study.PD:at least 20% increase in sum of diameters of target lesions,taking as reference the smallest sum on study(this includes baseline sum if that is the smallest on study).CBR was summarized using the Clopper-Pearson method. Dose-confirmation full analysis set: all subjects who enrolled in the Dose-confirmation Cohort (Phase 2) and received at least 1 dose of drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug until PD or 30 days after the last dose of study treatment

End point values	Phase 2: Eribulin mesilate 1.4 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: percentage of subjects				
number (confidence interval 95%)	57.1 (41.0 to 72.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Phase 2: Progression-free Survival (PFS)

End point title	Phase 2: Progression-free Survival (PFS)

End point description:

PFS was defined as the time from the first dose date until PD or death due to any cause. PFS was determined by an investigator based on RECIST v1.1. PD: at least a 20% increase in sum of diameters of target lesions, taking as reference the smallest sum on study (this includes baseline sum if that is the smallest on study). PFS was summarized using the Kaplan-Meier method. The Dose-confirmation full analysis set included all subjects who enrolled in the Dose-confirmation Cohort (Phase 2) and received at least 1 dose of drug.

End point type	Secondary

End point timeframe:

From the first dose of study drug until PD or death due to any cause or 30 days after the last dose of study treatment

End point values	Phase 2: Eribulin mesilate 1.4 mg/m^2			
Subject group type	Reporting group			
Number of subjects analysed	42			
Units: days				
median (confidence interval 95%)	219.0 (138.0			

to 330.0)

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From date of first dose up to 30 days after the last dose of study treatment

Adverse event reporting additional description:

The safety set included the group of subjects who received study drug and had at least 1 post dose safety assessment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.2 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.6 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 2.0 mg/m^2, injection, intravenously, once, on Day 1 and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 1).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 0.7 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.1 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Reporting group title	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)

Reporting group description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or

until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 1b (Schedule 2).

Reporting group title	Phase 2: Eribulin mesilate 1.4 mg/m^2

Reporting group description:

Subjects received eribulin mesilate 1.4 mg/m^2, injection, intravenously, once, on Days 1 and 8, and capecitabine 1000 mg/m^2, tablets, orally, twice daily from Day 1 to 14 in each 21-day treatment cycle for as long as the treatment was clinically appropriate according to the judgment of the investigator or until the occurrence of PD, undue toxicity, the presence of other medical conditions that prohibit continuation of therapy, pregnancy, a delay of more than 14 days in starting the next cycle during Phase 2.

Serious adverse events	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)	4 / 6 (66.67%)	1 / 5 (20.00%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Ascites			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Electrocardiogram QT prolongation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Spinal Cord Compression			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (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
Heparin-induced Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 6 (33.33%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 6 (33.33%)	1 / 5 (20.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal Ischaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestine obstruction			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary Embolism			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 6 (50.00%)	4 / 6 (66.67%)
number of deaths (all causes)	0	1	2
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Ascites			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic pain			
subjects affected / exposed	0 / 3 (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 / 3 (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			
Electrocardiogram QT prolongation			
subjects affected / exposed	0 / 3 (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			
Spinal Cord Compression			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	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
Heparin-induced Thrombocytopenia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 6 (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
Neutropenia			
subjects affected / exposed	0 / 3 (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
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 3 (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
Oedema peripheral			

subjects affected / exposed	0 / 3 (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 / 3 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 3 (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
Nausea			
subjects affected / exposed	0 / 3 (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
Vomiting			
subjects affected / exposed	0 / 3 (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
Abdominal Pain			
subjects affected / exposed	0 / 3 (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
Diarrhoea			
subjects affected / exposed	0 / 3 (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
Intestinal Ischaemia			

subjects affected / exposed	0 / 3 (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
Small intestine obstruction			
subjects affected / exposed	0 / 3 (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	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	1 / 3 (33.33%)	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
Pleural effusion			
subjects affected / exposed	0 / 3 (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
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Device related infection			

subjects affected / exposed	0 / 3 (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
Infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (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
Neutropenic sepsis			
subjects affected / exposed	0 / 3 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			
subjects affected / exposed	0 / 3 (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
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 3 (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	Phase 2: Eribulin mesilate 1.4 mg/m^2		
Total subjects affected by serious adverse events			
subjects affected / exposed	10 / 42 (23.81%)		
number of deaths (all causes)	3		
number of deaths resulting from	1		

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Ascites			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastatic pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tumour pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Investigations			
Electrocardiogram QT prolongation			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	5 / 8		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Spinal Cord Compression			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Heparin-induced Thrombocytopenia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenia			

subjects affected / exposed	2 / 42 (4.76%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Oedema peripheral			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		

Abdominal Pain				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal Ischaemia				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Small intestine obstruction				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Dyspnoea				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary Embolism				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Pleural effusion				
subjects affected / exposed	1 / 42 (2.38%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Confusional State				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	0 / 42 (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 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral Infection			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Phase 1b (Schedule 1): Eribulin mesilate (1.2 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (1.6 mg/m^2)	Phase 1b (Schedule 1): Eribulin mesilate (2.0 mg/m^2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 8 (87.50%)	6 / 6 (100.00%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	4
Vascular disorders			
Hypotension			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Lymphoedema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	2 / 5 (40.00%)
occurrences (all)	2	1	7
Asthenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Pain			

subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Catheter site erythema			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Catheter site related reaction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Influenza like illness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vaginal haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 8 (25.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	3	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	2 / 8 (25.00%)	2 / 6 (33.33%)	2 / 5 (40.00%)
occurrences (all)	2	2	2
Epistaxis			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haemoptysis			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rales			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Throat tightness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Wheezing			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Parasomnia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			

subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Cardiac Murmur			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram Abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram T Wave Abnormal			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Soft tissue injury			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Tooth fracture			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	0	1	2
Nervous system disorders			
Lethargy			
subjects affected / exposed	2 / 8 (25.00%)	4 / 6 (66.67%)	2 / 5 (40.00%)
occurrences (all)	3	7	4
Peripheral sensory neuropathy			

subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	3 / 8 (37.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	3	0	0
Neurotoxicity			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	5	0
Ageusia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Paraesthesia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	2	4	0
Leukopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Thrombocytopenia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0

Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye pain			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Visual impairment			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	4 / 8 (50.00%)	4 / 6 (66.67%)	4 / 5 (80.00%)
occurrences (all)	5	9	6
Diarrhoea			
subjects affected / exposed	6 / 8 (75.00%)	3 / 6 (50.00%)	1 / 5 (20.00%)
occurrences (all)	7	3	5
Stomatitis			
subjects affected / exposed	3 / 8 (37.50%)	3 / 6 (50.00%)	0 / 5 (0.00%)
occurrences (all)	4	6	0
Abdominal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	0 / 8 (0.00%)	3 / 6 (50.00%)	3 / 5 (60.00%)
occurrences (all)	0	5	6
Constipation			
subjects affected / exposed	2 / 8 (25.00%)	2 / 6 (33.33%)	2 / 5 (40.00%)
occurrences (all)	2	3	3
Dyspepsia			
subjects affected / exposed	0 / 8 (0.00%)	2 / 6 (33.33%)	1 / 5 (20.00%)
occurrences (all)	0	2	2
Abdominal discomfort			

subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Abdominal pain upper			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal tenderness			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dry mouth			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lip pain			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Paraesthesia oral			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rectal haemorrhage			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	7	0	0
Toothache			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 8 (25.00%)	2 / 6 (33.33%)	3 / 5 (60.00%)
occurrences (all)	2	2	3
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	1 / 8 (12.50%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	1	5	0
Dry skin			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Erythema			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pruritus			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Rash macular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash maculo-papular			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Skin mass			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Plantar Erythema			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			

Chromaturia			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Dysuria			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urine flow decreased			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 8 (25.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Pain in extremity			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	3
Joint swelling			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Myalgia			

subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	1 / 5 (20.00%)
occurrences (all)	0	4	3
Neck pain			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	2 / 8 (25.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Cellulitis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Localised infection			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	1 / 8 (12.50%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Tooth infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Urinary tract infection			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Vulvovaginal candidiasis			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 8 (0.00%)	1 / 6 (16.67%)	5 / 5 (100.00%)
occurrences (all)	0	1	6
Hypomagnesaemia			
subjects affected / exposed	0 / 8 (0.00%)	0 / 6 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Phase 1b (Schedule 2): Eribulin mesilate (0.7 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.1 mg/m^2)	Phase 1b (Schedule 2): Eribulin mesilate (1.4 mg/m^2)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	6 / 6 (100.00%)	6 / 6 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphoedema			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	5	1
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	0	1	3
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	3
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Catheter site erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Catheter site related reaction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chest discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vaginal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Oropharyngeal pain			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Dyspnoea			

subjects affected / exposed	2 / 3 (66.67%)	2 / 6 (33.33%)	1 / 6 (16.67%)
occurrences (all)	3	2	3
Epistaxis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	3	2
Haemoptysis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rales			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Throat tightness			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Wheezing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Depressed mood			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Parasomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Investigations			
Alanine aminotransferase increased			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood lactate dehydrogenase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cardiac Murmur			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Electrocardiogram Abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Electrocardiogram T Wave Abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Soft tissue injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Lethargy			
subjects affected / exposed	2 / 3 (66.67%)	4 / 6 (66.67%)	4 / 6 (66.67%)
occurrences (all)	5	22	15
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	0	0	2
Headache			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Neurotoxicity			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Ageusia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	1 / 6 (16.67%)
occurrences (all)	0	11	1
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	5 / 6 (83.33%)
occurrences (all)	0	3	19
Leukopenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Anaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	2	0	1
Thrombocytopenia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Lacrimation increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Eye pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Visual impairment			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	4
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	3 / 6 (50.00%)	6 / 6 (100.00%)
occurrences (all)	4	15	24
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	3 / 6 (50.00%)	4 / 6 (66.67%)
occurrences (all)	6	6	13
Stomatitis			
subjects affected / exposed	0 / 3 (0.00%)	2 / 6 (33.33%)	4 / 6 (66.67%)
occurrences (all)	0	3	6
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	3 / 6 (50.00%)	6 / 6 (100.00%)
occurrences (all)	0	7	18
Constipation			

subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	3	0	3
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	3	2
Abdominal discomfort			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	2	0
Abdominal tenderness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dry mouth			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Lip pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Paraesthesia oral			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Rectal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Toothache			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 3 (33.33%)	3 / 6 (50.00%)	2 / 6 (33.33%)
occurrences (all)	1	3	3
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	11	0
Dry skin			
subjects affected / exposed	1 / 3 (33.33%)	2 / 6 (33.33%)	0 / 6 (0.00%)
occurrences (all)	1	2	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Night sweats			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	1	1	0
Rash macular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Skin mass			

subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Plantar Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dysuria			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Urine flow decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	3
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	2
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal chest pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	0	1	1
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Localised infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	3 / 6 (50.00%)
occurrences (all)	0	0	3
Vulvovaginal candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	1 / 6 (16.67%)	3 / 6 (50.00%)
occurrences (all)	2	2	3
Hypomagnesaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Non-serious adverse events	Phase 2: Eribulin mesilate 1.4 mg/m^2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	39 / 42 (92.86%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypotension			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Lymphoedema			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	16		
Fatigue			

subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	10		
Asthenia			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	6		
Oedema peripheral			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Catheter site erythema			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Catheter site related reaction			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Chest discomfort			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Influenza like illness			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Vaginal haemorrhage			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	4 / 42 (9.52%) 5		
Oropharyngeal pain subjects affected / exposed occurrences (all)	4 / 42 (9.52%) 4		
Dyspnoea subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 4		
Epistaxis subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1		
Haemoptysis subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Rales subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1		
Throat tightness subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Wheezing subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 6		
Anxiety subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1		
Depressed mood			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Parasomnia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	15		
Blood lactate dehydrogenase increased			
subjects affected / exposed	6 / 42 (14.29%)		
occurrences (all)	9		
Weight decreased			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	7		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	7		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Cardiac Murmur			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Electrocardiogram Abnormal			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Electrocardiogram T Wave Abnormal			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Soft tissue injury			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Tooth fracture			

subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Cardiac disorders Palpitations subjects affected / exposed occurrences (all)	 0 / 42 (0.00%) 0		
Nervous system disorders Lethargy subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Neurotoxicity subjects affected / exposed occurrences (all) Ageusia subjects affected / exposed occurrences (all) Dysgeusia subjects affected / exposed occurrences (all) Dizziness subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all)	 8 / 42 (19.05%) 66 8 / 42 (19.05%) 21 4 / 42 (9.52%) 7 3 / 42 (7.14%) 3 0 / 42 (0.00%) 0 1 / 42 (2.38%) 3 2 / 42 (4.76%) 3 0 / 42 (0.00%) 0		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all) Leukopenia	 34 / 42 (80.95%) 238 		

subjects affected / exposed	20 / 42 (47.62%)		
occurrences (all)	73		
Anaemia			
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	24		
Thrombocytopenia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	5		
Lymphadenopathy			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Eye disorders			
Lacrimation increased			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Eye pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	12 / 42 (28.57%)		
occurrences (all)	28		
Diarrhoea			
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	30		
Stomatitis			
subjects affected / exposed	8 / 42 (19.05%)		
occurrences (all)	35		
Abdominal pain			

subjects affected / exposed	6 / 42 (14.29%)			
occurrences (all)	7			
Vomiting				
subjects affected / exposed	6 / 42 (14.29%)			
occurrences (all)	9			
Constipation				
subjects affected / exposed	4 / 42 (9.52%)			
occurrences (all)	6			
Dyspepsia				
subjects affected / exposed	3 / 42 (7.14%)			
occurrences (all)	3			
Abdominal discomfort				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Abdominal pain lower				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Abdominal pain upper				
subjects affected / exposed	2 / 42 (4.76%)			
occurrences (all)	2			
Abdominal tenderness				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Dry mouth				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Dysphagia				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Lip pain				
subjects affected / exposed	0 / 42 (0.00%)			
occurrences (all)	0			
Paraesthesia oral				

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Rectal haemorrhage			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Toothache			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	15 / 42 (35.71%)		
occurrences (all)	26		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	11 / 42 (26.19%)		
occurrences (all)	19		
Dry skin			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Erythema			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Night sweats			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Rash macular			

subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Rash maculo-papular			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Skin mass			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Plantar Erythema			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Chromaturia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Dysuria			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Urine flow decreased			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 42 (11.90%)		
occurrences (all)	7		
Pain in extremity			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	4		
Arthralgia			
subjects affected / exposed	3 / 42 (7.14%)		
occurrences (all)	3		
Joint swelling			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	4		
Muscle spasms			

subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	2		
Muscular weakness			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	2 / 42 (4.76%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 42 (9.52%)		
occurrences (all)	8		
Cellulitis			
subjects affected / exposed	0 / 42 (0.00%)		
occurrences (all)	0		
Localised infection			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Lower respiratory tract infection			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	1		
Oral candidiasis			
subjects affected / exposed	1 / 42 (2.38%)		
occurrences (all)	3		

Oral herpes subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2		
Tooth infection subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 42 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 4		
Vulvovaginal candidiasis subjects affected / exposed occurrences (all)	1 / 42 (2.38%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	3 / 42 (7.14%) 6		
Hypomagnesaemia subjects affected / exposed occurrences (all)	2 / 42 (4.76%) 2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 December 2010	Protocol Amendment 1: The main purpose of this amendment was to remove randomization from the study design for the Dose Escalation Cohorts (Phase 1b) as it was considered to be impractical and unnecessary for a Phase 1b study.
21 June 2011	Protocol Amendment 2: The main purpose of this amendment was to change the study design to include only 1 treatment arm in the Dose-Confirmation (Phase 2) part of the study. It was decided that the observed and tolerated dose levels in Schedule 2 could provide a better dose intensity than even the highest dose level in Schedule 1; therefore, only the MTD determined during Schedule 2 was selected for further exploration. As a result of this, the term "Randomized" was deleted from the title of the study; to delete Holter monitoring and revise the timing of the postdose electrocardiogram (ECG) for subjects included in the Dose Confirmation Cohort. The postdose 12-lead safety ECG time point was revised in accordance with the updated PK information available for eribulin; to delete an Exclusion Criterion based on new study results showing that no drug–drug interactions were expected with CYP 3A4 inhibitors, substrates, or inducers.
16 June 2014	Protocol Amendment 3: The main purpose of Amendment 3 was to reduce the frequency of tumor assessments for subjects (Dose-Confirmation Cohort, Extension Phase only) who had been in the study for 12 months or longer. This reduced the radiation risk for these subjects, as well as risks associated with the administration of contrast dye at the time of tumor assessments.
18 August 2015	Protocol Amendment 4: The main purpose of Amendment 4 was to further reduce the frequency of tumor assessments for subjects (Extension Phase only) who had been in the study for 12 months or longer. This further reduced the radiation risk for these subjects, as well as risks associated with the administration of contrast dye at the time of tumor assessments.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported