

**Clinical trial results:****An Open-Label, Multi-Center, Expanded Access Program With Eribulin for the Treatment of Advanced Breast Cancer Refractory to All Other Commercially Available Therapies****Summary**

EudraCT number	2009-017671-22
Trial protocol	BE
Global end of trial date	10 November 2014

**Results information**

Result version number	v1 (current)
This version publication date	05 November 2016
First version publication date	05 November 2016

**Trial information****Trial identification**

Sponsor protocol code	E7389-G000-398
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**Additional study identifiers**

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01240421
WHO universal trial number (UTN)	-

Notes:

**Sponsors**

Sponsor organisation name	Eisai
Sponsor organisation address	100 Tice Boulevard, Woodcliff Lake, United States, 07677
Public contact	Eisai Call Center, Eisai Inc., 888 422-4743,
Scientific contact	Eisai Call Center, Eisai Inc., 888 422-4743,

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:

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**Results analysis stage**

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Analysis stage	Final
Date of interim/final analysis	23 April 2015
Is this the analysis of the primary completion data?	No

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Global end of trial reached?	Yes
Global end of trial date	10 November 2014
Was the trial ended prematurely?	No

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Notes:

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**General information about the trial**

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Main objective of the trial:

To provide eribulin to patients with advanced breast cancer who have no further treatment options and therapy is requested by an investigator

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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 Conference 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 Conference on Harmonisation 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.
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Background therapy: -

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Evidence for comparator: -

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Actual start date of recruitment	06 August 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

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Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

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Country: Number of subjects enrolled	Belgium: 141
Country: Number of subjects enrolled	France: 261
Country: Number of subjects enrolled	Canada: 104
Worldwide total number of subjects	506
EEA total number of subjects	402

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Notes:

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**Subjects enrolled per age group**

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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)	385
From 65 to 84 years	121
85 years and over	0

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## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Of the 508 participants enrolled into the study, 2 participants did not receive any study drug, 414 participants completed the Treatment Phase, and 92 participants discontinued the study prior to the clinical or radiological evidence of progression.

### Period 1

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

### Arms

<b>Arm title</b>	Eribulin
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Eribulin mesylate
Investigational medicinal product code	E7389
Other name	Halaven
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous bolus use

Dosage and administration details:

Eribulin mesylate at a dose of 1.4 mg/m<sup>2</sup> was administered as a 2 to 5 minute intravenous (IV) bolus on Days 1 and 8 of a 21-day cycle. If desired, the dose was diluted in up to 100 mL of normal saline for injection (an aqueous solution of 0.9% weight per volume (w/v) of sodium chloride).

<b>Number of subjects in period 1</b>	Eribulin
Started	506
Completed	414
Not completed	92
Participant choice	17
Consent withdrawn by subject	14
Adverse event, non-fatal	53
Not specified	8

## Baseline characteristics

### Reporting groups

Reporting group title	Overall Period
Reporting group description: -	

Reporting group values	Overall Period	Total	
Number of subjects	506	506	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	56.7		
standard deviation	± 10.84	-	
Gender categorical Units: Subjects			
Female	506	506	
Male	0	0	

## End points

### End points reporting groups

Reporting group title	Eribulin
Reporting group description:	-

### Primary: Overview of Treatment-Emergent Adverse Events (TEAEs)

End point title	Overview of Treatment-Emergent Adverse Events (TEAEs) <sup>[1]</sup>
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End point description:

General safety was assessed by monitoring all adverse events (AEs) and serious adverse events (SAEs), regular monitoring of hematology and blood chemistry, regular measurement of vital signs, and the performance of physical examinations and other safety assessments. Descriptive statistics were used to summarize the frequency, and listings indicated severity, duration, and relationship to treatment for all AEs occurring after initiation of treatment. TEAEs were defined as AEs that had an onset date, or a worsening in severity from baseline (pre-treatment), on or after the first dose of study drug up to the last visit, or 30 days following the last dose of study drug. AEs were graded in severity according to Common Terminology Criteria for Adverse Events (CTCAE). Participants with multiple CTCAE grades were counted in their highest grade. Treatment-related AEs were considered by the investigator to be possible or probably related to study drug.

End point type	Primary
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End point timeframe:

From date of administration of first dose up to 30 days after the last dose, or each participant, or up to approximately 2 years and 4 months per overall study duration.

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 analyses were performed for this data.

End point values	Eribulin			
Subject group type	Reporting group			
Number of subjects analysed	506			
Units: Percentage of participants				
number (not applicable)				
All TEAEs	98.6			
Treatment-related TEAEs	94.9			
TEAEs with CTCAE grade 3	40.7			
TEAEs with CTCAE grade 4	18.4			
TEAEs with CTCAE grade 5 (Deaths)	2.8			
Serious TEAEs	27.7			
TEAEs leading to study drug withdrawal	8.9			
TEAEs leading to study drug dose reduction	29.2			
TEAEs leading to study drug interruption	27.7			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From date of administration of first dose up to 30 days after the last dose, or each participant, or up to approximately 2 years and 4 months per overall study duration.

Adverse event reporting additional description:

Treatment-emergent adverse events (TEAEs) and serious TEAEs were collected and reported. Safety analysis set included all participants who received at least one dose of study drug. AEs were graded using Common Terminology Criteria for Adverse Events (CTCAE) version 4.03.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	17.1
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### Reporting groups

Reporting group title	Eribulin mesylate
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Reporting group description: -

<b>Serious adverse events</b>	Eribulin mesylate		
Total subjects affected by serious adverse events			
subjects affected / exposed	140 / 506 (27.67%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Lymphangiosis carcinomatosa			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metastases to central nervous system			
subjects affected / exposed	3 / 506 (0.59%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metastases to meninges			

subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Metastases to skin</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Metastatic pain</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Paraneoplastic syndrome</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Skin neoplasm bleeding</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Vascular disorders</b>			
<b>Deep vein thrombosis</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Lymphoedema</b>			
subjects affected / exposed	3 / 506 (0.59%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Surgical and medical procedures</b>			
<b>Tumour excision</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>General disorders and administration</b>			

site conditions				
Asthenia				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Axillary pain				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device malfunction				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Disease progression				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Euthanasia				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
General physical health deterioration				
subjects affected / exposed	15 / 506 (2.96%)			
occurrences causally related to treatment / all	2 / 20			
deaths causally related to treatment / all	1 / 5			
Malaise				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Mucosal inflammation				

subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	13 / 506 (2.57%)		
occurrences causally related to treatment / all	6 / 16		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cough			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	17 / 506 (3.36%)		
occurrences causally related to treatment / all	2 / 17		
deaths causally related to treatment / all	0 / 0		
Laryngeal dyspnoea			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lung disorder			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pleural effusion			

subjects affected / exposed	8 / 506 (1.58%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
<b>Pneumothorax</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Pulmonary embolism</b>			
subjects affected / exposed	5 / 506 (0.99%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 1		
<b>Respiratory failure</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
<b>Psychiatric disorders</b>			
<b>Confusional state</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Delirium</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Mental disorder</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Mental status changes</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Investigations</b>			

Alanine aminotransferase increased subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood creatinine increased subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ejection fraction decreased subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Liver function test abnormal subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutrophil count decreased subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Oxygen saturation decreased subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications Fall subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Femur fracture			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Radiation sickness syndrome			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Left ventricular dysfunction			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sinus tachycardia			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Brain oedema				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebellar syndrome				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coma				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	3 / 506 (0.59%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	2 / 506 (0.40%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	1 / 506 (0.20%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				

subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hepatic encephalopathy</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Intracranial pressure increased</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Peripheral sensorimotor neuropathy</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Somnolence</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Blood and lymphatic system disorders</b>			
<b>Anemia</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Disseminated intravascular coagulation</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Febrile neutropenia</b>			
subjects affected / exposed	26 / 506 (5.14%)		
occurrences causally related to treatment / all	25 / 26		
deaths causally related to treatment / all	0 / 0		
<b>Neutropenia</b>			

subjects affected / exposed	12 / 506 (2.37%)		
occurrences causally related to treatment / all	15 / 15		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	6 / 506 (1.19%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal obstruction			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			

subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Nausea</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Oesophagitis</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Small intestinal obstruction</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Stomatitis</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Subileus</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Hepatobiliary disorders</b>			
<b>Cholecystitis</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hepatic failure</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
<b>Hepatic pain</b>			

subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 506 (0.99%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Bone pain			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Flank pain			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Musculoskeletal chest pain			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neck pain			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	5 / 506 (0.99%)		
occurrences causally related to treatment / all	2 / 6		
deaths causally related to treatment / all	0 / 0		
Spinal pain			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Enterococcal sepsis			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Erysipelas			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Lobar pneumonia			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Lung infection			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumocystis jirovecii pneumonia			

subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Pneumonia</b>			
subjects affected / exposed	6 / 506 (1.19%)		
occurrences causally related to treatment / all	4 / 6		
deaths causally related to treatment / all	0 / 0		
<b>Sepsis</b>			
subjects affected / exposed	4 / 506 (0.79%)		
occurrences causally related to treatment / all	2 / 4		
deaths causally related to treatment / all	0 / 0		
<b>Septic shock</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
<b>Staphylococcal skin infection</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Tonsillitis</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Urinary tract infection</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Metabolism and nutrition disorders</b>			
<b>Decreased appetite</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Dehydration</b>			

subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
<b>Diabetes mellitus</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hypercalcaemia</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
<b>Hyperkalaemia</b>			
subjects affected / exposed	1 / 506 (0.20%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
<b>Hyponatraemia</b>			
subjects affected / exposed	2 / 506 (0.40%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Eribulin mesylate		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	490 / 506 (96.84%)		
<b>Investigations</b>			
Gamma-glutamyltransferase increased			
subjects affected / exposed	30 / 506 (5.93%)		
occurrences (all)	44		
<b>Nervous system disorders</b>			
Dysgeusia			
subjects affected / exposed	33 / 506 (6.52%)		
occurrences (all)	44		
Headache			

subjects affected / exposed occurrences (all)	54 / 506 (10.67%) 73		
Neuropathy peripheral subjects affected / exposed occurrences (all)	109 / 506 (21.54%) 179		
Paraesthesia subjects affected / exposed occurrences (all)	50 / 506 (9.88%) 61		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	35 / 506 (6.92%) 49		
<b>Blood and lymphatic system disorders</b>			
Anaemia subjects affected / exposed occurrences (all)	98 / 506 (19.37%) 170		
Leukopenia subjects affected / exposed occurrences (all)	42 / 506 (8.30%) 96		
Lymphopenia subjects affected / exposed occurrences (all)	34 / 506 (6.72%) 61		
Neutropenia subjects affected / exposed occurrences (all)	191 / 506 (37.75%) 429		
Thrombocytopenia subjects affected / exposed occurrences (all)	35 / 506 (6.92%) 60		
<b>General disorders and administration site conditions</b>			
Asthenia subjects affected / exposed occurrences (all)	187 / 506 (36.96%) 293		
Fatigue subjects affected / exposed occurrences (all)	158 / 506 (31.23%) 223		
Mucosal inflammation			

subjects affected / exposed occurrences (all)	30 / 506 (5.93%) 33		
Oedema peripheral subjects affected / exposed occurrences (all)	42 / 506 (8.30%) 46		
Pyrexia subjects affected / exposed occurrences (all)	84 / 506 (16.60%) 127		
Eye disorders Lacrimation increased subjects affected / exposed occurrences (all)	39 / 506 (7.71%) 53		
Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all)	40 / 506 (7.91%) 45		
Abdominal pain upper subjects affected / exposed occurrences (all)	39 / 506 (7.71%) 41		
Constipation subjects affected / exposed occurrences (all)	107 / 506 (21.15%) 135		
Diarrhoea subjects affected / exposed occurrences (all)	91 / 506 (17.98%) 122		
Nausea subjects affected / exposed occurrences (all)	151 / 506 (29.84%) 206		
Stomatitis subjects affected / exposed occurrences (all)	52 / 506 (10.28%) 63		
Vomiting subjects affected / exposed occurrences (all)	74 / 506 (14.62%) 90		
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	53 / 506 (10.47%) 66		
Dyspnoea subjects affected / exposed occurrences (all)	79 / 506 (15.61%) 100		
Skin and subcutaneous tissue disorders Alopecia subjects affected / exposed occurrences (all)	212 / 506 (41.90%) 243		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	53 / 506 (10.47%) 76		
Back pain subjects affected / exposed occurrences (all)	37 / 506 (7.31%) 41		
Bone pain subjects affected / exposed occurrences (all)	35 / 506 (6.92%) 42		
Muscle spasms subjects affected / exposed occurrences (all)	32 / 506 (6.32%) 39		
Myalgia subjects affected / exposed occurrences (all)	66 / 506 (13.04%) 87		
Pain in extremity subjects affected / exposed occurrences (all)	30 / 506 (5.93%) 33		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	86 / 506 (17.00%) 106		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 April 2011	The purpose of the amendment was to support the use of eribulin on a compassionate use basis prior to regulatory approval in Canada.

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

Age is not available for 13 participants. Since the mean age was 56.7 years, these participants were added to the 18-64 years age category in 'Age group breakdown for trial'.
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Notes: