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

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:

Results analysis stage

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

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

Notes:

General information about the trial

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

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.

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

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	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

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

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

Arm title	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^2 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).

Number of subjects in period 1	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)[1]

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

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups

Reporting group title	Eribulin mesylate

Reporting group description: -

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

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

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

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

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

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

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

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

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

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

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'.

Notes: