Clinical trial results:
A Multicenter, Open-Label Trial of Belinostat in Patients with Relapsed or Refractory Peripheral T-Cell Lymphoma

Summary

EudraCT number	2008-005843-40
Trial protocol	DK FR IT NL BE DE ES HU SK PL GB
Global end of trial date	27 October 2014

Results information

Result version number	v2 (current)
This version publication date	27 January 2017
First version publication date	11 November 2016
Version creation reason	• Changes to summary attachments Replacing draft results provided in attachments (Study report and Investigator's Brochure) by final consolidated results (Full Data Set). Deleting the investigator's brochure and study report attachments from version 1.

Trial information

Trial identification

Sponsor protocol code	PXD101-CLN-19

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00865969
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Spectrum Pharmaceuticals
Sponsor organisation address	157 Technology Drive, Irvine, United States, 92618
Public contact	Clinical Operations, Spectrum Pharmaceuticals, clinicaltrialinquiries@sppirx.com
Scientific contact	Clinical Operations, Spectrum Pharmaceuticals, clinicaltrialinquiries@sppirx.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 December 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 October 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to determine the objective response rate in patients with peripheral T cell lymphoma who are treated with belinostat monotherapy.

Protection of trial subjects:

Informed Consent Form was used to ensure all participation is voluntary and study subjects are aware of their right, including personal health information privacy. Clinical monitoring visits were conducted throughout the life of study to ensure study patient safety are continuously monitored and protected. The assigned medical monitor also reviewed the data on frequent basis to ensure that all safety data are adequately monitored and issues addressed timely.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 December 2008
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	Netherlands: 10
Country: Number of subjects enrolled	Israel: 4
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	United States: 37
Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	South Africa: 3
Country: Number of subjects enrolled	Poland: 8
Country: Number of subjects enrolled	Slovakia: 2
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Belgium: 11
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Hungary: 11
Country: Number of subjects enrolled	Italy: 3
Worldwide total number of subjects	129
EEA total number of subjects	78

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)	67
From 65 to 84 years	62
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Patients with relapsed or refractory T-Cell lymphoma must sign consent and meet all Inclusion/Exclusion criteria

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Belinostat

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Belinostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

1000 mg/m2 of Belinostat administered as a 30 minutes IV infusion on days 1-5 of every 3-week cycle

Number of subjects in period 1	Belinostat
Started	129
Completed	129

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	129	129	
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			
median	63		
full range (min-max)	29 to 81	-	
Gender categorical Units: Subjects			
Female	60	60	
Male	69	69	
Disease Stage at Entry Units: Subjects			
Stage IA	6	6	
Stage IIA	8	8	
Stage IIIA	26	26	
Stage IVA	38	38	
Stage IIB	4	4	
Stage IIIB	19	19	
Stage IVB	26	26	
Unknown	2	2	
Height Units: cm			
arithmetic mean	167.6		
standard deviation	± 10.1	-	
Weight Units: kg			
arithmetic mean	74.9		
standard deviation	± 18.6	-	

End points

End points reporting groups

Reporting group title	Belinostat

Reporting group description: -

Primary: Objective Response Rate

End point title	Objective Response Rate[1]

End point description:

Overall study duration from first dose until 2 years after the first dose. Objective response rate was defined as the percentage of patients with a complete response or a partial response according to IWG criteria. Response was assessed on the basis of clinical and radiological criteria. In addition to the primary analysis of response by central radiographic and clinical review by the IRC, the response assessment was also determined by the local Investigators. As pre-defined, the primary endpoint analysis for this study was based on the IRC assessment of response.

End point type	Primary

End point timeframe:

24 months

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: Descriptive statistics for these endpoints

End point values	Belinostat			
Subject group type	Reporting group			
Number of subjects analysed	120[2]			
Units: Percentage				
number (confidence interval 95%)	25.8 (18.3 to 34.6)			

Notes:

[2] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Response

End point title	Time to Response

End point description:

End point type	Secondary

End point timeframe:

24 months

End point values	Belinostat			
Subject group type	Reporting group			
Number of subjects analysed	120[3]			
Units: Weeks				
median (full range (min-max))	5.6 (4.3 to 50.4)			

Notes:

[3] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response

End point description:

The Duration of Response was assessed by IWG criteria per the IRC and estimated by the Kaplan-Meier method. The median Duration of Response for the Efficacy Analysis Dataset, was assessed by IRC using IWG criteria and based on 31 responding patients.

End point type	Secondary

End point timeframe:

24 months

End point values	Belinostat			
Subject group type	Reporting group			
Number of subjects analysed	120[4]			
Units: Months				
median (confidence interval 95%)	13.6 (4.5 to 29.4)			

Notes:

[4] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Progression

End point title	Time to Progression

End point description:

End point type	Secondary

End point timeframe:

24 months

End point values	Belinostat			
Subject group type	Reporting group			
Number of subjects analysed	120[5]			
Units: Months				
median (confidence interval 95%)	2 (1.5 to 2.8)			

Notes:

[5] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

End point type	Secondary

End point timeframe:

24 months

End point values	Belinostat			
Subject group type	Reporting group			
Number of subjects analysed	120[6]			
Units: Months				
median (confidence interval 95%)	1.6 (1.4 to 2.7)			

Notes:

[6] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

End point type	Secondary

End point timeframe:

24 months

End point values	Belinostat			
Subject group type	Reporting group			
Number of subjects analysed	120[7]			
Units: Months				
median (confidence interval 95%)	7.9 (6.1 to 13.9)			

Notes:

[7] - Efficacy Analysis Dataset= pts received at least 1 dose of Belinostat & confirmed PTCL diagnosis

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

25 months. Patients must be carefully monitored for all adverse events that occur from the time Informed Consent is obtained until 30 days after the last study drug administration.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	Full Patient Population

Reporting group description:

Overall description of adverse events in CLN-19 trial.

Serious adverse events	Full Patient Population		
Total subjects affected by serious adverse events			
subjects affected / exposed	61 / 129 (47.29%)		
number of deaths (all causes)	14		
number of deaths resulting from adverse events	14		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour associated fever			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tumour haemorrhage			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	3 / 129 (2.33%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Hypotension			

subjects affected / exposed	2 / 129 (1.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Extremity necrosis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Iliac artery occlusion			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vasculitis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Venous thrombosis limb			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Central venous catheterisation			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	6 / 129 (4.65%)		
occurrences causally related to treatment / all	4 / 8		
deaths causally related to treatment / all	0 / 0		

Multi-organ disorder			
subjects affected / exposed	3 / 129 (2.33%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 3		
Fatigue			
subjects affected / exposed	2 / 129 (1.55%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chills			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Disease progression			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Euthanasia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
General physical health deterioration			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Malaise			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			

subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	3 / 129 (2.33%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Alveolitis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Chylothorax			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
hypoxia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary haemorrhage			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pulmonary mass			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Anxiety				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Impaired self-care				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Blood creatinine increased				
subjects affected / exposed	3 / 129 (2.33%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
Alanine aminotransferase increased				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gamma-glutamyltransferase increased				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Injury, poisoning and procedural complications			
Lower limb fracture			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple fractures			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac failure			
subjects affected / exposed	2 / 129 (1.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Atrial fibrillation			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 129 (2.33%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Thrombocytopenia			
subjects affected / exposed	3 / 129 (2.33%)		
occurrences causally related to treatment / all	5 / 5		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			

subjects affected / exposed	2 / 129 (1.55%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Autoimmune haemolytic anaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemolytic anaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Splenomegaly			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Toxic cataract			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hepatobiliary disorders			

Hepatic failure			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Hyperbilirubinaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Actinic keratosis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain of skin			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Urosepsis			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthralgia			

subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	10 / 129 (7.75%)			
occurrences causally related to treatment / all	2 / 10			
deaths causally related to treatment / all	0 / 1			
Infection				
subjects affected / exposed	4 / 129 (3.10%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	3 / 129 (2.33%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	2 / 129 (1.55%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchitis bacterial				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchopneumopathy				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				

subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Endocarditis				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal fungal infection				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pharyngitis				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Septic shock				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 129 (0.78%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Tumour lysis syndrome				
subjects affected / exposed	2 / 129 (1.55%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Decreased appetite				

subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 129 (0.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Full Patient Population		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	125 / 129 (96.90%)		
Investigations			
Blood lactate dehydrogenase increased			
subjects affected / exposed	20 / 129 (15.50%)		
occurrences (all)	45		
Electrocardiogram QT prolonged			
subjects affected / exposed	15 / 129 (11.63%)		
occurrences (all)	46		
Aspartate aminotransferase increased			

subjects affected / exposed occurrences (all)	11 / 129 (8.53%) 20		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	9 / 129 (6.98%) 29		
Blood creatinine increased subjects affected / exposed occurrences (all)	8 / 129 (6.20%) 16		
Platelet count decreased subjects affected / exposed occurrences (all)	8 / 129 (6.20%) 16		
Weight decreased subjects affected / exposed occurrences (all)	8 / 129 (6.20%) 8		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	7 / 129 (5.43%) 12		
Vascular disorders Hypotension subjects affected / exposed occurrences (all)	13 / 129 (10.08%) 26		
Phlebitis subjects affected / exposed occurrences (all)	12 / 129 (9.30%) 23		
Flushing subjects affected / exposed occurrences (all)	9 / 129 (6.98%) 11		
Hypertension subjects affected / exposed occurrences (all)	7 / 129 (5.43%) 8		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	19 / 129 (14.73%) 20		
Dizziness			

subjects affected / exposed	13 / 129 (10.08%)		
occurrences (all)	26		
Neuropathy peripheral			
subjects affected / exposed	9 / 129 (6.98%)		
occurrences (all)	9		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	47 / 129 (36.43%)		
occurrences (all)	76		
Pyrexia			
subjects affected / exposed	45 / 129 (34.88%)		
occurrences (all)	98		
Oedema Peripheral			
subjects affected / exposed	27 / 129 (20.93%)		
occurrences (all)	34		
Chills			
subjects affected / exposed	21 / 129 (16.28%)		
occurrences (all)	23		
Infusion site pain			
subjects affected / exposed	18 / 129 (13.95%)		
occurrences (all)	31		
Asthenia			
subjects affected / exposed	12 / 129 (9.30%)		
occurrences (all)	14		
Pain			
subjects affected / exposed	12 / 129 (9.30%)		
occurrences (all)	12		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	41 / 129 (31.78%)		
occurrences (all)	132		
Thrombocytopenia			
subjects affected / exposed	21 / 129 (16.28%)		
occurrences (all)	73		
Leukopenia			

subjects affected / exposed	13 / 129 (10.08%)		
occurrences (all)	36		
Neutropenia			
subjects affected / exposed	13 / 129 (10.08%)		
occurrences (all)	39		
Lymphopenia			
subjects affected / exposed	11 / 129 (8.53%)		
occurrences (all)	91		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	55 / 129 (42.64%)		
occurrences (all)	130		
Vomiting			
subjects affected / exposed	37 / 129 (28.68%)		
occurrences (all)	95		
Constipation			
subjects affected / exposed	29 / 129 (22.48%)		
occurrences (all)	37		
Diarrhoea			
subjects affected / exposed	28 / 129 (21.71%)		
occurrences (all)	44		
Abdominal pain			
subjects affected / exposed	14 / 129 (10.85%)		
occurrences (all)	17		
Abdominal pain upper			
subjects affected / exposed	7 / 129 (5.43%)		
occurrences (all)	9		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	29 / 129 (22.48%)		
occurrences (all)	34		
Cough			
subjects affected / exposed	25 / 129 (19.38%)		
occurrences (all)	27		
Oropharyngeal pain			

subjects affected / exposed occurrences (all)	8 / 129 (6.20%) 10		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Night sweats subjects affected / exposed occurrences (all) Hyperhidrosis subjects affected / exposed occurrences (all)	 26 / 129 (20.16%) 36 21 / 129 (16.28%) 39 8 / 129 (6.20%) 11 7 / 129 (5.43%) 8		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all)	 9 / 129 (6.98%) 11 7 / 129 (5.43%) 8		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all)	 11 / 129 (8.53%) 20 9 / 129 (6.98%) 13		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Bronchitis subjects affected / exposed occurrences (all)	 10 / 129 (7.75%) 12 9 / 129 (6.98%) 15		

Nasopharyngitis			
subjects affected / exposed	7 / 129 (5.43%)		
occurrences (all)	8		
Sinusitis			
subjects affected / exposed	7 / 129 (5.43%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	19 / 129 (14.73%)		
occurrences (all)	23		
Hypokalaemia			
subjects affected / exposed	17 / 129 (13.18%)		
occurrences (all)	45		
Hyperglycaemia			
subjects affected / exposed	12 / 129 (9.30%)		
occurrences (all)	36		
Hypoalbuminaemia			
subjects affected / exposed	10 / 129 (7.75%)		
occurrences (all)	16		
Hypomagnesaemia			
subjects affected / exposed	9 / 129 (6.98%)		
occurrences (all)	18		
Hyperuricaemia			
subjects affected / exposed	8 / 129 (6.20%)		
occurrences (all)	37		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported