



Clinical trial results:

A Single Arm, Phase 2 Study of Ganetespib in Subjects with Advanced Non- Small-Cell Lung Cancer with Anaplastic Lymphoma Kinase Gene Rearrangement (ALK-Positive NSCLC)

Summary

EudraCT number	2012-000639-16
Trial protocol	GB ES
Global end of trial date	04 July 2014

Results information

Result version number	v1 (current)
This version publication date	02 April 2016
First version publication date	02 April 2016

Trial information

Trial identification

Sponsor protocol code	9090-09
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01562015
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Synta Pharmaceuticals Corp
Sponsor organisation address	45 Hartwell Avenue, Lexington, MA, United States, 02421
Public contact	VP Clinical Research, Synta Pharmaceuticals Corp, 001 781-541-7261,
Scientific contact	VP Clinical Research, Synta Pharmaceuticals Corp, 001 781-541-7261,

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	09 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	04 July 2014
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Determine the objective response rate (ORR) of ganetespib in subjects with advanced ALK-positive non-small-cell lung cancer (NSCLC)

Protection of trial subjects:

The informed consent document must be reviewed and approved by Synta or its designee and the investigative site IRB/IEC prior to the initiation of the study.

Prior to the start of any protocol-specific evaluations or screening procedures, the Investigator (or designated staff) will explain the nature of the study and its risks and benefits to the patient (or the patient's legal representative). Each patient will receive an informed consent document with patient information. Patients should be given ample time to read the information and the opportunity to ask questions. Informed consent must be obtained from each patient prior to performing any protocol-specific evaluations. One copy of the signed informed consent document will be given to the patient, and another will be retained by the Investigator.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 April 2012
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	Canada: 6
Country: Number of subjects enrolled	Serbia: 2
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	Bosnia and Herzegovina: 1
Worldwide total number of subjects	12
EEA total number of subjects	0

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)	6
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 264 patients were screened for possible inclusion in the study. Of these (and due to the rarity of the ALK rearrangement in the NSCLC population), 12 patients were enrolled at 7 study centers.

Period 1

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

Arms

Arm title	GanetespiB 200 mg/m ²
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Arm description:

Patients received single-agent ganetespiB 200 mg/m² once weekly for the first 3 weeks of 4-week treatment cycles (Days 1, 8, and 15 of each 28-day treatment cycle). The amount of ganetespiB was calculated based on the patient's body surface area (BSA), determined on Day 1 of each cycle. GanetespiB was administered via an approximately 1-hour peripheral intravenous (IV) infusion, under supervision of study personnel. Patients continued ganetespiB treatment until evidence of objective disease progression or symptomatic deterioration, occurrence of unacceptable toxicity, or withdrawal of consent, or early study termination.

Arm type	Experimental
Investigational medicinal product name	ganetespiB
Investigational medicinal product code	
Other name	STA-9090
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Single-agent ganetespiB 200 mg/m² once weekly for the first 3 weeks of 4-week treatment cycles (Days 1, 8, and 15 of each 28-day treatment cycle). The amount of ganetespiB was calculated based on the patient's body surface area (BSA), determined on Day 1 of each cycle. GanetespiB was administered via an approximately 1-hour peripheral intravenous (IV) infusion, under supervision of study personnel.

Number of subjects in period 1	GanetespiB 200 mg/m ²
Started	12
Completed	0
Not completed	12
Clinical progression	3
Consent withdrawn by subject	2
Symptomatic deterioration	2
Progressive disease	4
Sponsor decision	1

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period
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Reporting group description: -

Reporting group values	Treatment Period	Total	
Number of subjects	12	12	
Age categorical			
Units: Subjects			
Adults (18-64 years)	6	6	
From 65-84 years	6	6	
Age continuous			
Units: years			
arithmetic mean	58.8		
standard deviation	± 14.66	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	5	5	
Race			
Units: Subjects			
White/Caucasian	11	11	
Asian	1	1	
Smoking Status			
Units: Subjects			
Never Smoked	8	8	
Past Smoker	2	2	
Current Smoker	2	2	
Stage at Initial Diagnosis			
Units: Subjects			
Stage I/II	1	1	
Stage IIIA	0	0	
Stage IIIB	4	4	
Stage IV	7	7	
Stage at Study Entry			
Units: Subjects			
Stage IIIB	2	2	
Stage IV	10	10	
ECOG at Study Entry			
Eastern Cooperative Oncology Group (ECOG) Performance Status:			
0: Fully active			
1: Ambulatory, carry out work of a light or sedentary nature			
Units: Subjects			
0: Fully active	6	6	
1: Ambulatory, carry out light work	6	6	
Brain Metastasis			
Units: Subjects			
Yes	3	3	

No	9	9	
Liver Metastasis Units: Subjects			
Yes	4	4	
No	8	8	
Lung Metastasis Units: Subjects			
Yes	9	9	
No	3	3	
Lymph Nodes Metastasis Units: Subjects			
Yes	5	5	
No	7	7	
Bone Metastasis Units: Subjects			
Yes	4	4	
No	8	8	
Pleura Metastasis Units: Subjects			
Yes	5	5	
No	7	7	
Adrenal Metastasis Units: Subjects			
Yes	2	2	
No	10	10	
Weight Units: kg			
arithmetic mean	71.92		
standard deviation	± 12.719	-	
Body Surface Area (BSA) Units: m ²			
arithmetic mean	1.808		
standard deviation	± 0.199	-	
Number of Metastatic Sites Units: sites			
arithmetic mean	3.67		
standard deviation	± 2.188	-	
Baseline Total Tumor Burden Units: mm			
arithmetic mean	80.5		
standard deviation	± 37.876	-	

End points

End points reporting groups

Reporting group title	GanetespiB 200 mg/m ²
Reporting group description: Patients received single-agent ganetespiB 200 mg/m ² once weekly for the first 3 weeks of 4-week treatment cycles (Days 1, 8, and 15 of each 28-day treatment cycle). The amount of ganetespiB was calculated based on the patient's body surface area (BSA), determined on Day 1 of each cycle. GanetespiB was administered via an approximately 1-hour peripheral intravenous (IV) infusion, under supervision of study personnel. Patients continued ganetespiB treatment until evidence of objective disease progression or symptomatic deterioration, occurrence of unacceptable toxicity, or withdrawal of consent, or early study termination.	
Subject analysis set title	All Patients
Subject analysis set type	Full analysis
Subject analysis set description: Includes all 12 patients treated with ganetespiB 200 mg/m ² .	
Subject analysis set title	FISH Positive ALK Patients
Subject analysis set type	Per protocol
Subject analysis set description: Patients deemed positive anaplastic lymphoma kinase (ALK) by the Vysis fluorescence in situ hybridization (FISH) assay, which was performed on all tumor samples determined to be ALK-positive by a central laboratory using immunohistochemistry (IHC).	

Primary: Objective Response Rate

End point title	Objective Response Rate ^[1]
End point description: The primary endpoint of the study is objective response rate (ORR) which is the percentage of patients showing a complete or partial response. - Complete Response (CR): Disappearance (or normalization) of all target lesions. Any pathological lymph nodes (whether target or non-target) must have had reduction in SA to <10 mm. - Partial Response (PR): ≥30% decrease in the sum of diameters of target lesions compared to the baseline sum.	
End point type	Primary
End point timeframe: Week 6 - Week 92	
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: No statistics since the study populations were small due to early termination.	

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: percentage of patients				
number (confidence interval 95%)	8.3 (0.2 to 38.5)	12.5 (0.3 to 52.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Rate at 6 months

End point title	Progression Free Survival (PFS) Rate at 6 months
End point description: PFS means the patient was alive and progression free. Progression was the interval from the date of first dose until objective tumor progression per RECIST 1.1 or death from any cause, whichever occurred first.	
End point type	Secondary
End point timeframe: 6 months	

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: percentage of patients				
number (confidence interval 95%)	33.3 (9.9 to 65.1)	37.5 (8.5 to 75.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Rate at 12 Months

End point title	Progression Free Survival (PFS) Rate at 12 Months
End point description: PFS means the patient was alive and progression free. Progression was the interval from the date of first dose until objective tumor progression per RECIST 1.1 or death from any cause, whichever occurred first.	
End point type	Secondary
End point timeframe: 12 months	

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: percentage of patients				
number (confidence interval 95%)	16.7 (2.1 to 48.4)	12.5 (0.3 to 52.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival (PFS) Rate at 18 months

End point title	Progression Free Survival (PFS) Rate at 18 months
End point description: PFS means the patient was alive and progression free. Progression was the interval from the date of first dose until objective tumor progression per RECIST 1.1 or death from any cause, whichever occurred first.	
End point type	Secondary
End point timeframe: 18 months	

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: percentage of patients				
number (confidence interval 95%)	8.3 (0.2 to 38.5)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response
End point description: Duration of Response (DOR) was defined as the date of first documented objective response (complete response or partial response, whichever status is recorded first) to the earliest date that progressive disease is objectively documented. If progression has not been documented, a subject's duration of objective response will be censored at the date of last assessment.	
End point type	Secondary
End point timeframe: Week 6 - Week 92	

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[2]	0 ^[3]		
Units: weeks				
median (confidence interval 95%)	(to)	(to)		

Notes:

[2] - Data not analyzed because of the small number of patients.

[3] - Data not analyzed because of the small number of patients.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) and 1-Year OS

End point title	Overall Survival (OS) and 1-Year OS
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End point description:

Overall Survival (OS) was defined as the time from the first dose until death due to any cause. Subjects who are lost to follow-up were censored at the time of the last contact.

End point type	Secondary
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End point timeframe:

up to 2 years

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[4]	0 ^[5]		
Units: months				
median (confidence interval 95%)	(to)	(to)		

Notes:

[4] - Data not analyzed because of the small number of patients.

[5] - Data not analyzed because of the small number of patients.

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DSR) at Weeks 6 and 12

End point title	Disease Control Rate (DSR) at Weeks 6 and 12
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End point description:

The DCR was defined as the percentage of patients with best response of complete response, partial response, or stable disease, where the stable disease must have been for at least 6 or 12 weeks (according to modified RECIST 1.1).

- Complete Response (CR): Disappearance (or normalization) of all target lesions. Any pathological lymph nodes (whether target or non-target) must have had reduction in SA to <10 mm.

- Partial Response (PR): $\geq 30\%$ decrease in the sum of diameters of target lesions compared to the baseline sum.

- Stable Disease (SD): Neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD, taking as reference the smallest sum of diameters while on study.

End point type	Secondary
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End point timeframe:

Weeks 6 and 12

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	12	8		
Units: percentage of patients				
number (confidence interval 95%)				
Week 6	83.3 (51.6 to 97.9)	75 (34.9 to 96.8)		
Week 12	50 (21.1 to 78.9)	50 (15.7 to 84.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Tumor Size (CTS) at Weeks 6 and 12

End point title	Change in Tumor Size (CTS) at Weeks 6 and 12
End point description:	Change in Tumor Size (CTS) is measured from baseline to at least 6 weeks (CTS-6) or 12 weeks (CTS-12)
End point type	Secondary
End point timeframe:	Day 1 (baseline), Weeks 6 and 12

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[6]	0 ^[7]		
Units: mm				
arithmetic mean (standard deviation)	()	()		

Notes:

[6] - Data not analyzed because of the small number of patients.

[7] - Data not analyzed because of the small number of patients.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinically Relevant Improvement in Disease Symptoms Using Functional Assessment of Cancer Therapy - Lung (FACT-L)

End point title	Clinically Relevant Improvement in Disease Symptoms Using Functional Assessment of Cancer Therapy - Lung (FACT-L)
End point description:	The responses to the FACT-L were transformed and the LCS scores will be calculated. Subjects were rated as improved, no change, or worsened according to their scores compared with baseline. Missing data points were counted as no change in symptoms. Clinically relevant improvement, defined as 2-point improvement maintained for at least 21 days, were calculated.
End point type	Secondary

End point timeframe:

Day 1 (baseline) up to Week 92

End point values	All Patients	FISH Positive ALK Patients		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 ^[8]	0 ^[9]		
Units: percentage of patients				
number (confidence interval 95%)	(to)	(to)		

Notes:

[8] - Data not analyzed because of the small number of patients.

[9] - Data not analyzed because of the small number of patients.

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with Treatment-Emergent Adverse Events (AEs)

End point title	Participants with Treatment-Emergent Adverse Events (AEs)
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End point description:

At each summarization level, a patient is counted once if the patient reported one or more events. National Cancer Institute (NCI) Common Terminology Criteria (NCI-CTCAE V4) is a scale of the severity of the AE. CTCAE grade 3 is severe (the AE is intolerable and disrupts normal daily activities, may require additional therapy or hospitalization, and/or discontinuation of the study drug), and grade 4 is life threatening (the AE exposes the subject to risk of death at the time of the event; it does not refer to an event that may have caused death if the event was more severe).

End point type	Secondary
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End point timeframe:

Day 1 up to Week 92

End point values	Ganetespib 200 mg/m ²			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: participants				
>=1 AE	11			
>= 1 AE with CTCAE grade 3 or 4	7			
>=1 serious AE	4			
>=1 AE leading to dose reduction	0			
>=1 AE leading to delayed dose	3			
>=1 AE leading to study drug d/c	0			
>=1 serious AE leading to study drug	0			
>=1 SAE leading to hospitalization	3			
>=1 AE with outcome of death	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 to Week 92

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16.1
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Reporting groups

Reporting group title	Ganetespi 200 mg/m ²
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Reporting group description:

Patients received single-agent ganetespi 200 mg/m² once weekly for the first 3 weeks of 4-week treatment cycles (Days 1, 8, and 15 of each 28-day treatment cycle). The amount of ganetespi was calculated based on the patient's body surface area (BSA), determined on Day 1 of each cycle. Ganetespi was administered via an approximately 1-hour peripheral intravenous (IV) infusion, under supervision of study personnel. Patients continued ganetespi treatment until evidence of objective disease progression or symptomatic deterioration, occurrence of unacceptable toxicity, or withdrawal of consent, or early study termination.

Serious adverse events	Ganetespi 200 mg/m ²		
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 12 (33.33%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Sudden cardiac death			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Nausea			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Ganetespib 200 mg/m ²		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Cancer pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2		
Tumour pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Vascular disorders Flushing subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Hot flush subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Hypertension subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 4		
Fatigue subjects affected / exposed occurrences (all)	9 / 12 (75.00%) 12		
Feeling jittery subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 2		
Influenza like illness subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Infusion site reaction subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Non-cardiac chest pain subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 5		
Oedema peripheral			

subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2 1 / 12 (8.33%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Hiccups subjects affected / exposed occurrences (all) Productive cough subjects affected / exposed occurrences (all)	6 / 12 (50.00%) 7 1 / 12 (8.33%) 3 1 / 12 (8.33%) 1		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1 5 / 12 (41.67%) 7		
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all) Aspartate aminotransferase increased subjects affected / exposed occurrences (all) Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) Blood bilirubin increased subjects affected / exposed occurrences (all) Blood lactate dehydrogenase	2 / 12 (16.67%) 3 1 / 12 (8.33%) 1 4 / 12 (33.33%) 7 1 / 12 (8.33%) 1		

increased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Electrocardiogram T wave abnormal			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Lipase increased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Urine output decreased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Weight decreased			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Infusion related reaction			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Procedural pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Tachycardia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		

Dizziness subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 3		
Dysgeusia subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Headache subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3		
Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 10		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		
Vision blurred subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Gastrointestinal disorders Abdominal distension subjects affected / exposed occurrences (all)	2 / 12 (16.67%) 2		
Abdominal pain subjects affected / exposed occurrences (all)	3 / 12 (25.00%) 3		
Constipation subjects affected / exposed occurrences (all)	4 / 12 (33.33%) 5		
Diarrhoea subjects affected / exposed occurrences (all)	9 / 12 (75.00%) 92		
Dysphagia			

subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Gastrointestinal pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	7		
Stomatitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	3 / 12 (25.00%)		
occurrences (all)	8		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Dermatitis allergic			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Dry skin			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Erythema			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		

Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Urinary retention			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Bone pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Groin pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Spinal pain			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	3		
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Tooth infection			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	6 / 12 (50.00%)		
occurrences (all)	8		
Dehydration			
subjects affected / exposed	4 / 12 (33.33%)		
occurrences (all)	10		
Hyperglycaemia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	4		
Hyperkalaemia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	2		
Hypoalbuminaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	2		
Hypokalaemia			
subjects affected / exposed	1 / 12 (8.33%)		
occurrences (all)	1		
Hyponatraemia			
subjects affected / exposed	2 / 12 (16.67%)		
occurrences (all)	6		

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

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

An enrollment of 110 patients was planned; however, the study was terminated after 12 patients were enrolled due to the low level of clinical activity observed in these patients and the changing landscape for the treatment of this population.
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Notes: