Clinical trial results:
A Phase 2 Study of Hsp90 Inhibitor AT13387 Alone or in Combination with Abiraterone Acetate in the Treatment of Castration-Resistant Prostate Cancer (CRPC) no Longer Responding to Abiraterone

Summary

EudraCT number	2012-001574-28
Trial protocol	GB ES
Global end of trial date	17 July 2014

Results information

Result version number	v1 (current)
This version publication date	15 February 2018
First version publication date	15 February 2018

Trial information

Trial identification

Sponsor protocol code	AT13387-04

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	IND number: 101124

Notes:

Sponsors

Sponsor organisation name	Astex Pharmaceuticals, Inc.
Sponsor organisation address	4420 Rosewood Drive, Suite 200, Pleasanton, CA, United States, 94588
Public contact	Ross Ezzati, Medpace Inc, +1 51357999912072, r.ezzati@medpace.com
Scientific contact	Ross Ezzati, Medpace Inc, +1 51357999912072, r.ezzati@medpace.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	30 October 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 July 2014
Global end of trial reached?	Yes
Global end of trial date	17 July 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Part A:
To assess the safety and tolerability (incidence and severity of adverse events [AEs]) of the combination of onalespib (AT13387) and abiraterone acetate and to select the most promising treatment regimen for the combination in subjects with castration-resistant prostate cancer (CRPC) who are no longer responding to treatment with abiraterone acetate alone, based on the overall assessment of safety and antitumor activity.

Part B:
To assess and compare the antitumor activity (response rate per the Prostate Cancer Working Group 2 [PCWG2] recommendations) between single-agent AT13387 and the combination of AT13387 and abiraterone acetate in subjects who are no longer responding to treatment with abiraterone acetate alone.

Part A of the study was completed; however, Part B was not performed.

Protection of trial subjects:

The study was conducted in accordance with the International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) guidelines; the US 21 Code of Federal Regulations (CFR) Parts 11, 50, 54, 56, and 312; any other applicable local regulatory requirements; and the principles enunciated in the Declaration of Helsinki.

The ICF(s) used for each study centre complied with the Declaration of Helsinki, federal regulations (US 21 CFR Part 50 and other national requirements), and ICH GCP guidelines and was approved by the sponsor and the investigator's IRB/IEC. The investigator, or a person delegated by the investigator, explained the medical aspects of the study, including the nature of the study and the treatment, its purpose, the procedures involved, and the potential benefits and risks. After having been informed that participation was voluntary and that subjects may withdraw from the study at any time, without prejudice, each subject signed the IRB/IEC-approved ICF prior to undergoing any study specific procedures and enrollment in the study.

Background therapy:

Subjects were randomised to receive 1 of 2 different regimens of onalespib in combination with abiraterone acetate 1000 mg orally (PO) once daily and prednisone or prednisolone 5 mg PO twice daily.

Evidence for comparator:

Not applicable.

Actual start date of recruitment	17 December 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	United States: 25

Country: Number of subjects enrolled	Canada: 4
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 19
Worldwide total number of subjects	49
EEA total number of subjects	20

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)	14
From 65 to 84 years	32
85 years and over	3

Subject disposition

Recruitment

Recruitment details:

A total of 22 principal investigators at 33 study centres (21 in the US, 10 in the UK, 1 in Canada, and 1 in Spain) enrolled subjects in this study. The first subject was dosed with onalespib on 09 January 2013 and the last subject completed dosing on 17 July 2014.

Pre-assignment

Screening details:

A total of 90 subjects were screened for enrolment in the study. Of these, 41 were screen failures, 49 were enrolled, and 48 were treated.

A subject who was randomised but not treated was excluded from the summary statistics.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Regimen 1 (once weekly)

Arm description:

Regimen 1: onalespib given as a 1-hr intravenous (IV) infusion at a starting dose of 220 mg/square metre once weekly for 3 weeks in a 4-week cycle. Subjects also received abiraterone acetate 1000 mg (four 250 mg tablets) and prednisone or prednisolone (5 mg twice daily).

Arm type	Experimental
Investigational medicinal product name	Onalespib
Investigational medicinal product code	AT13387
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Starting dose of 220 mg/square metre on Days 1, 8, and 15 for 3 weeks in a 4-week cycle. Administered by intravenous infusion.

Arm title	Regimen 2 (twice weekly)

Arm description:

Regimen 2: onalespib administered as a 1-hr IV infusion at a starting dose of 120 mg/square metre on Day 1 and Day 2 weekly for 3 weeks in a 4-week cycle. Subjects also received abiraterone acetate 1000 mg (four 250 mg tablets) and prednisone or prednisolone (5 mg twice daily).

Arm type	Experimental
Investigational medicinal product name	Onalespib
Investigational medicinal product code	AT13387
Other name	
Pharmaceutical forms	Powder for solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Starting dose of 120 mg/square metre on Day 1 and Day 2 weekly for 3 weeks in a 4-week cycle. Administered by intravenous infusion.

Number of subjects in period 1[1]	Regimen 1 (once weekly)	Regimen 2 (twice weekly)
Started	23	25
Completed	0	0
Not completed	23	25
Sponsor decision to close study	7	5
Consent withdrawn by subject	1	2
Death	12	14
Study discontinued	3	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One subject was enrolled but not treated; therefore this subject was not included in summary statistics for the study.

Baseline characteristics

Reporting groups	
Reporting group title	Regimen 1 (once weekly)
Reporting group description:	
Regimen 1: onalespib given as a 1-hr intravenous (IV) infusion at a starting dose of 220 mg/square metre once weekly for 3 weeks in a 4-week cycle. Subjects also received abiraterone acetate 1000 mg (four 250 mg tablets) and prednisone or prednisolone (5 mg twice daily).	
Reporting group title	Regimen 2 (twice weekly)
Reporting group description:	
Regimen 2: onalespib administered as a 1-hr IV infusion at a starting dose of 120 mg/square metre on Day 1 and Day 2 weekly for 3 weeks in a 4-week cycle. Subjects also received abiraterone acetate 1000 mg (four 250 mg tablets) and prednisone or prednisolone (5 mg twice daily).	

Reporting group values	Regimen 1 (once weekly)	Regimen 2 (twice weekly)	Total
Number of subjects	23	25	48
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	71.3	68	
standard deviation	± 8.4	± 8.3	-
Gender categorical			
All the subjects participated in the trial were males.			
Units: Subjects			
Female	0	0	0
Male	23	25	48
Ethnicity			
Units: Subjects			
Hispanic or Latino	0	1	1
Not Hispanic or Latino	23	24	47

End points

End points reporting groups

Reporting group title	Regimen 1 (once weekly)

Reporting group description:

Regimen 1: onalespib given as a 1-hr intravenous (IV) infusion at a starting dose of 220 mg/square metre once weekly for 3 weeks in a 4-week cycle. Subjects also received abiraterone acetate 1000 mg (four 250 mg tablets) and prednisone or prednisolone (5 mg twice daily).

Reporting group title	Regimen 2 (twice weekly)

Reporting group description:

Regimen 2: onalespib administered as a 1-hr IV infusion at a starting dose of 120 mg/square metre on Day 1 and Day 2 weekly for 3 weeks in a 4-week cycle. Subjects also received abiraterone acetate 1000 mg (four 250 mg tablets) and prednisone or prednisolone (5 mg twice daily).

Primary: Safety and tolerability

End point title	Safety and tolerability[1]

End point description:

Adverse events (AEs) were monitored throughout subject treatment cycles and follow-up. AE severity was classified according to the National Cancer Institute Common Terminology Criteria for Adverse Events.

End point type	Primary

End point timeframe:

Duration of the study.

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: For safety and tolerability, descriptive statistics only are reported for this endpoint.

End point values	Regimen 1 (once weekly)	Regimen 2 (twice weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: Number of subjects				
Subjects with any AE	23	25		
Subjects with any Grade≥3 AE	15	14		
Subjects with AE leading to discontinuation	9	7		
Subjects with any serious AE	8	7		
Subjects with serious AE leading to death	2	0		
Other subjects with serious AE	6	7		

Statistical analyses

No statistical analyses for this end point

Primary: Response Rate (Any response)

End point title	Response Rate (Any response)[2]

End point description:

Subjects with response by Response Evaluation Criteria in Solid Tumors (RECIST) v1.1, prostate specific antigen (PSA), or circulating tumor cells (CTC) conversion at Week 12 were considered responders. Response rate was based on number of subjects in the efficacy analysis data set.

End point type	Primary

End point timeframe:

The time frame was up to 12 weeks.

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No subjects in either treatment regimen experienced any response according to trial criteria, and thus no statistical analysis is reported.

End point values	Regimen 1 (once weekly)	Regimen 2 (twice weekly)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	25		
Units: Number of subjects				
Any response	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were recorded on scheduled study days and at study follow-up.

Adverse event reporting additional description:

Note: For non-serious adverse events, the table below depicts at least one occurrence/preferred term/subject. The actual number of occurrences/preferred term/subject are higher in some of the cases.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Regimen 1 (once weekly)

Reporting group description:

Regimen 1: onalespib given as a 1-hr intravenous (IV) infusion at a starting dose of 220 mg/square metre once weekly for 3 weeks in a 4-week cycle. Subjects also received abiraterone acetate 1000 mg (four 250 mg tablets) and prednisone or prednisolone (5 mg twice daily).

Reporting group title	Regimen 2 (twice weekly)

Reporting group description:

Regimen 2: onalespib administered as a 1-hr IV infusion at a starting dose of 120 mg/square metre on Day 1 and Day 2 weekly for 3 weeks in a 4-week cycle. Subjects also received abiraterone acetate 1000 mg (four 250 mg tablets) and prednisone or prednisolone (5 mg twice daily).

Serious adverse events	Regimen 1 (once weekly)	Regimen 2 (twice weekly)	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 23 (34.78%)	7 / 25 (28.00%)	
number of deaths (all causes)	12	14	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Death			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Investigations			
Troponin I increased			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			

subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haematoma			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Spinal cord compression			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	2 / 23 (8.70%)	3 / 25 (12.00%)	
occurrences causally related to treatment / all	2 / 2	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nausea			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Proctalgia			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Arthritis bacterial			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 23 (0.00%)	1 / 25 (4.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 23 (4.35%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 23 (8.70%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Regimen 1 (once weekly)	Regimen 2 (twice weekly)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	23 / 23 (100.00%)	25 / 25 (100.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 23 (8.70%)	2 / 25 (8.00%)	
occurrences (all)	2	2	
Flushing			
subjects affected / exposed	1 / 23 (4.35%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Hypotension			

subjects affected / exposed	1 / 23 (4.35%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	16 / 23 (69.57%)	18 / 25 (72.00%)	
occurrences (all)	16	18	
Infusion site pain			
subjects affected / exposed	4 / 23 (17.39%)	3 / 25 (12.00%)	
occurrences (all)	4	3	
Oedema peripheral			
subjects affected / exposed	2 / 23 (8.70%)	4 / 25 (16.00%)	
occurrences (all)	2	4	
Pyrexia			
subjects affected / exposed	3 / 23 (13.04%)	3 / 25 (12.00%)	
occurrences (all)	3	3	
Asthenia			
subjects affected / exposed	3 / 23 (13.04%)	2 / 25 (8.00%)	
occurrences (all)	3	2	
Chills			
subjects affected / exposed	0 / 23 (0.00%)	4 / 25 (16.00%)	
occurrences (all)	0	4	
Infusion site reaction			
subjects affected / exposed	0 / 23 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Injection site pain			
subjects affected / exposed	2 / 23 (8.70%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 23 (17.39%)	5 / 25 (20.00%)	
occurrences (all)	4	5	
Dyspnoea			
subjects affected / exposed	3 / 23 (13.04%)	2 / 25 (8.00%)	
occurrences (all)	3	2	
Increased upper airway secretion			

subjects affected / exposed	0 / 23 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	4 / 23 (17.39%)	5 / 25 (20.00%)	
occurrences (all)	4	5	
Abnormal dreams			
subjects affected / exposed	0 / 23 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Investigations			
Weight decreased			
subjects affected / exposed	3 / 23 (13.04%)	6 / 25 (24.00%)	
occurrences (all)	3	6	
Aspartate aminotransferase increased			
subjects affected / exposed	4 / 23 (17.39%)	1 / 25 (4.00%)	
occurrences (all)	4	1	
Alanine aminotransferase increased			
subjects affected / exposed	2 / 23 (8.70%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 23 (8.70%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Electrocardiogram QT prolonged			
subjects affected / exposed	2 / 23 (8.70%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Blood potassium decreased			
subjects affected / exposed	0 / 23 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 23 (8.70%)	3 / 25 (12.00%)	
occurrences (all)	2	3	
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 23 (21.74%)	5 / 25 (20.00%)	
occurrences (all)	5	5	

Headache			
subjects affected / exposed	4 / 23 (17.39%)	5 / 25 (20.00%)	
occurrences (all)	4	5	
Dysgeusia			
subjects affected / exposed	3 / 23 (13.04%)	4 / 25 (16.00%)	
occurrences (all)	3	4	
Hypoaesthesia			
subjects affected / exposed	2 / 23 (8.70%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 23 (13.04%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 23 (26.09%)	6 / 25 (24.00%)	
occurrences (all)	6	6	
Eye disorders			
Dry eye			
subjects affected / exposed	2 / 23 (8.70%)	3 / 25 (12.00%)	
occurrences (all)	2	3	
Photopsia			
subjects affected / exposed	2 / 23 (8.70%)	3 / 25 (12.00%)	
occurrences (all)	2	3	
Visual impairment			
subjects affected / exposed	1 / 23 (4.35%)	3 / 25 (12.00%)	
occurrences (all)	1	3	
Vision blurred			
subjects affected / exposed	0 / 23 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	21 / 23 (91.30%)	24 / 25 (96.00%)	
occurrences (all)	21	24	
Nausea			
subjects affected / exposed	10 / 23 (43.48%)	15 / 25 (60.00%)	
occurrences (all)	10	15	
Vomiting			

subjects affected / exposed	7 / 23 (30.43%)	10 / 25 (40.00%)	
occurrences (all)	7	10	
Constipation			
subjects affected / exposed	8 / 23 (34.78%)	7 / 25 (28.00%)	
occurrences (all)	8	7	
Dry mouth			
subjects affected / exposed	5 / 23 (21.74%)	6 / 25 (24.00%)	
occurrences (all)	5	6	
Abdominal pain			
subjects affected / exposed	1 / 23 (4.35%)	5 / 25 (20.00%)	
occurrences (all)	1	5	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 23 (13.04%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Erythema			
subjects affected / exposed	2 / 23 (8.70%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	5 / 23 (21.74%)	2 / 25 (8.00%)	
occurrences (all)	5	2	
Nocturia			
subjects affected / exposed	0 / 23 (0.00%)	3 / 25 (12.00%)	
occurrences (all)	0	3	
Urinary retention			
subjects affected / exposed	2 / 23 (8.70%)	0 / 25 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	5 / 23 (21.74%)	7 / 25 (28.00%)	
occurrences (all)	5	7	
Arthralgia			
subjects affected / exposed	6 / 23 (26.09%)	4 / 25 (16.00%)	
occurrences (all)	6	4	
Muscular weakness			

subjects affected / exposed	5 / 23 (21.74%)	3 / 25 (12.00%)	
occurrences (all)	5	3	
Pain in extremity			
subjects affected / exposed	5 / 23 (21.74%)	2 / 25 (8.00%)	
occurrences (all)	5	2	
Muscle spasms			
subjects affected / exposed	1 / 23 (4.35%)	4 / 25 (16.00%)	
occurrences (all)	1	4	
Musculoskeletal pain			
subjects affected / exposed	4 / 23 (17.39%)	0 / 25 (0.00%)	
occurrences (all)	4	0	
Groin pain			
subjects affected / exposed	2 / 23 (8.70%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Musculoskeletal chest pain			
subjects affected / exposed	3 / 23 (13.04%)	0 / 25 (0.00%)	
occurrences (all)	3	0	
Myalgia			
subjects affected / exposed	0 / 23 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	3 / 23 (13.04%)	3 / 25 (12.00%)	
occurrences (all)	3	3	
Oral candidiasis			
subjects affected / exposed	1 / 23 (4.35%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	13 / 23 (56.52%)	16 / 25 (64.00%)	
occurrences (all)	13	16	
Hypokalaemia			
subjects affected / exposed	7 / 23 (30.43%)	3 / 25 (12.00%)	
occurrences (all)	7	3	
Dehydration			

subjects affected / exposed	4 / 23 (17.39%)	2 / 25 (8.00%)	
occurrences (all)	4	2	
Hypocalcaemia			
subjects affected / exposed	3 / 23 (13.04%)	1 / 25 (4.00%)	
occurrences (all)	3	1	
Hypophosphataemia			
subjects affected / exposed	0 / 23 (0.00%)	2 / 25 (8.00%)	
occurrences (all)	0	2	

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