



Clinical trial results:

A Phase 2, Open-Label, Single-Arm Study of Pamiparib (BGB-290) for the Treatment of Patients with Metastatic Castration-Resistant Prostate Cancer (mCRPC) with Homologous Recombination Deficiency (HRD)

Summary

EudraCT number	2018-002587-28
Trial protocol	GB ES
Global end of trial date	02 September 2020

Results information

Result version number	v1
This version publication date	18 August 2021
First version publication date	18 August 2021

Trial information

Trial identification

Sponsor protocol code	BGB-290-202
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03712930
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BeiGene, Ltd
Sponsor organisation address	BeiGene, Ltd., c/o BeiGene USA, Inc. 2955 Campus Drive, Suite 200 San Mateo, California , United States, 94403
Public contact	BeiGene DDT Call Center, BeiGene, 1 877-828-5568, clinicaltrials@beigene.com
Scientific contact	clinicaltrials@beigene.com, BeiGene, 1 877-828-5568, clinicaltrials@beigene.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	11 November 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 August 2020
Global end of trial reached?	Yes
Global end of trial date	02 September 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of pamiparib in patients with metastatic castration-resistant prostate cancer (mCRPC) positive for circulating tumor cells (CTC) with homologous recombination deficiency (CTC-HRD-positive; per Epic Sciences assay), as per Prostate Cancer Clinical Trials Working Group [PCWG3] criteria.

Protection of trial subjects:

This trial was designed and monitored in accordance with Sponsor procedures, which comply with the ethical principles of GCP as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki.

The IEC/IRB-approved ICF was signed and dated by the subject or the subject's legally authorized representative before his or her participation in the study. A copy of each signed ICF was provided to the subject or the subject's legally authorized representative. All signed and dated ICFs were retained in each patient's study file or in the site file. For any updated or revised ICFs, written informed consent was obtained using the IEC/IRB-approved updated/revised ICFs for continued participation in the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 February 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	United States: 6
Country: Number of subjects enrolled	Spain: 1
Worldwide total number of subjects	13
EEA total number of subjects	1

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)	4
From 65 to 84 years	9
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Eighteen subjects were screened; 5 subjects failed screening and 13 subjects were dosed.

Pre-assignment

Screening details:

All subjects enrolled had unknown BRCA1/2 status at study entry and were assigned to cohorts 1B or 2B; there were no subjects known to be BRCA1/2 positive at enrollment.

Period 1

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

Arms

Arm title	Pamiparib
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Arm description:

Participants received 60 mg pamiparib orally twice daily

Arm type	Experimental
Investigational medicinal product name	Pamiparib
Investigational medicinal product code	
Other name	BGB-290
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

60 mg pamiparib capsule orally twice daily

Number of subjects in period 1	Pamiparib
Started	13
Completed	0
Not completed	13
Physician decision	1
Death	7
Progressive Disease	2
Study terminated by sponsor	3

Baseline characteristics

Reporting groups

Reporting group title	Overall
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Reporting group description: -

Reporting group values	Overall	Total	
Number of subjects	13	13	
Age categorical			
Units: Subjects			
Adults (18-64 years)	4	4	
From 65 to 84 years	9	9	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	69.3		
standard deviation	± 9.49	-	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	13	13	

End points

End points reporting groups

Reporting group title	Pamiparib
Reporting group description:	
Participants received 60 mg pamiparib orally twice daily	

Primary: Objective Response Rate (ORR) Determined by Independent Central Review

End point title	Objective Response Rate (ORR) Determined by Independent Central Review ^[1]
End point description:	
ORR is the percentage of participants with a best objective response of complete response (CR) or partial response (PR) confirmed at a subsequent timepoint ≥ 4 weeks later by an Independent Review Committee (IRC)	
End point type	Primary
End point timeframe:	
An average of 1 year	

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: This study stopped prematurely and only 13 subjects enrolled. No summary statistics are available given the limited data from the small number of evaluable patients and individual patient data are also not presented to protect the privacy of the individuals.

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[2]			
Units: Number				

Notes:

[2] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Primary: Prostate-Specific Antigen (PSA) Response Rate

End point title	Prostate-Specific Antigen (PSA) Response Rate ^[3]
End point description:	
PSA response rate is defined as the percentage of participants with PSA decline $\geq 50\%$ from baseline [confirmed by a second PSA value ≥ 3 weeks later] for CTC-HRD-positive patients with or without measurable disease	
End point type	Primary
End point timeframe:	
An average of 1 year	

Notes:

[3] - 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: This study stopped prematurely and only 13 subjects enrolled. No summary statistics are available given the limited data from the small number of evaluable patients and individual patient data

are also not presented to protect the privacy of the individuals.

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[4]			
Units: Number				

Notes:

[4] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response

End point title	Duration of Response
End point description: DOR is defined as the time from the date of the earliest documented CR or PR (that is subsequently confirmed) to radiographic disease progression or death due to any cause, whichever occurs first	
End point type	Secondary
End point timeframe: An average of 1 year	

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[5]			
Units: Months				

Notes:

[5] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate by Investigator

End point title	Objective Response Rate by Investigator
End point description: ORR is the percentage of participants with a best objective response of complete response (CR) or partial response (PR) confirmed at a subsequent timepoint ≥ 4 weeks later by the investigator	
End point type	Secondary
End point timeframe: An average of 1 year	

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[6]			
Units: Percentage of participants				

Notes:

[6] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Objective Response

End point title	Time to Objective Response
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End point description:

Time to objective response is defined as the time from the date of the first dose of study drug to the first documented confirmed response of CR or PR assessed by the investigator and summarized for participants who have achieved a confirmed objective response.

End point type	Secondary
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End point timeframe:

An average of 1 year

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[7]			
Units: Months				

Notes:

[7] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate

End point title	Clinical Benefit Rate
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End point description:

Clinical benefit rate is defined as the percentage of participants with a documented confirmed CR, PR, or stable disease

End point type	Secondary
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End point timeframe:

An average of 1 year

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[8]			
Units: Percentage of participants				

Notes:

[8] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PSA Response

End point title	Time to PSA Response
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End point description:

Time to PSA response is defined as the time from the date of the first dose of study drug to the first PSA decline $\geq 50\%$ that is subsequently confirmed. Assessments are summarized for participants who have achieved a confirmed PSA response.

End point type	Secondary
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End point timeframe:

An average of 1 year

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[9]			
Units: Months				

Notes:

[9] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of PSA Response

End point title	Duration of PSA Response
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End point description:

Duration of PSA response is defined as the time from the date of the earliest documented PSA response (that is subsequently confirmed) to PSA progression or death due to any cause, whichever occurs first. PSA progression is defined as a $\geq 25\%$ increase in PSA with an absolute increase of $\geq 2 \mu\text{g/L}$ above the nadir (or above the baseline for patients with no PSA decline after 12 weeks), confirmed by a second value ≥ 3 weeks later. The nadir is defined as the lowest value at or after baseline

End point type	Secondary
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End point timeframe:

An average of 1 year

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[10]			
Units: Months				

Notes:

[10] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PSA Progression

End point title	Time to PSA Progression
End point description:	
Time to PSA progression is defined as the time from the date of the first dose of study drug to a $\geq 25\%$ increase in PSA with an absolute increase of ≥ 2 ng/mL above the nadir [or above the baseline for participants with no PSA decline after 12 weeks], confirmed by a second value ≥ 3 weeks later	
End point type	Secondary
End point timeframe:	
An average of 1 year	

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[11]			
Units: Months				

Notes:

[11] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Symptomatic Skeletal Event

End point title	Time to Symptomatic Skeletal Event
End point description:	
Time to symptomatic skeletal event is defined as time from the date of the first dose of study drug to the first symptomatic fracture, radiation or surgery to bone, or spinal cord compression	
End point type	Secondary
End point timeframe:	
An average of 1 year	

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[12]			
Units: Months				

Notes:

[12] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Radiographic Progression-Free Survival

End point title	Radiographic Progression-Free Survival
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End point description:

Radiographic progression-free survival is defined as the time from the date of the first dose of study drug to radiographic disease progression by IRC or death due to any cause, whichever occurs first.

End point type	Secondary
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End point timeframe:

An average of 1 year

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[13]			
Units: Months				

Notes:

[13] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)
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End point description:

Overall survival is defined as the time from the date of the first dose of study drug to death due to any cause.

End point type	Secondary
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End point timeframe:

An average of 2 years

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	0 ^[14]			
Units: Months				

Notes:

[14] - Study stopped prematurely. No summary statistics available due to limited data from low enrollment.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Treatment-Emergent Adverse Events graded according to National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE)Version 4.03

End point title	Number of Participants with Treatment-Emergent Adverse Events graded according to National Cancer Institute-Common Terminology Criteria for Adverse Events (NCI-CTCAE)Version 4.03
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End point description:

End point type	Secondary
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End point timeframe:

From the date of first Pamiparib dose until 30 days after the last dose or initiation of new anti-cancer therapy, whichever occurs first. (approximately 13 months)

End point values	Pamiparib			
Subject group type	Reporting group			
Number of subjects analysed	13			
Units: Number				
Participants with at Least One TEAE	13			
Grade 3 or Higher	11			
Serious	6			
Leading to Death	1			
Leading to Treatment Discontinuation	3			
Leading to Dose Modification	11			
Leading to Dose Interruption	9			
Leading to Dose Reduction	5			
Treatment Related TEAEs	11			
Treatment Related Grade 3 or Higher	7			
Treatment Related Serious	1			
Treatment Related Leading to Death	0			
Treatment Related Leading to Discontinuation	3			
Treatment Related Leading to Dose Modification	7			
Treatment Related Leading to Dose Interruption	6			
Treatment Related Leading to Dose Reduction	3			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the date of first Pamiparib dose until 30 days after the last dose or initiation of new anti-cancer therapy, whichever occurs first. (approximately 13 months)

Adverse event reporting additional description:

Safety Analysis Set (SAF): included all subjects enrolled in the study who received any dose of pamiparib. The Safety Analysis Set was used for all safety analyses.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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Reporting groups

Reporting group title	Pamiparib
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Reporting group description:

Participants received 60 mg pamiparib orally twice daily

Serious adverse events	Pamiparib		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 13 (46.15%)		
number of deaths (all causes)	9		
number of deaths resulting from adverse events	1		
Nervous system disorders			
Hemiparesis			
subjects affected / exposed	1 / 13 (7.69%)		
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	2 / 13 (15.38%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Peripheral swelling			
subjects affected / exposed	1 / 13 (7.69%)		
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	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile neutropenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory failure			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ureteric obstruction			
subjects affected / exposed	1 / 13 (7.69%)		
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	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Oesophageal candidiasis			
subjects affected / exposed	1 / 13 (7.69%)		
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 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pamiparib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	13 / 13 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 13 (38.46%)		
occurrences (all)	5		
Asthenia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	2		
Reproductive system and breast			

disorders			
Pelvic pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	2		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Investigations			
Weight decreased			
subjects affected / exposed	3 / 13 (23.08%)		
occurrences (all)	4		
Blood alkaline phosphatase increased			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Blood creatinine increased			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	3		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Blood lactate dehydrogenase increased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Platelet count decreased			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Dysgeusia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Headache			

subjects affected / exposed occurrences (all) Taste disorder subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all) Leukopenia subjects affected / exposed occurrences (all)	7 / 13 (53.85%) 11 2 / 13 (15.38%) 4 2 / 13 (15.38%) 2 1 / 13 (7.69%) 1		
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1		
Eye disorders Dry eye subjects affected / exposed occurrences (all) Orbital oedema subjects affected / exposed occurrences (all)	1 / 13 (7.69%) 1 1 / 13 (7.69%) 1		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Vomiting	7 / 13 (53.85%) 8 4 / 13 (30.77%) 4		

subjects affected / exposed	4 / 13 (30.77%)		
occurrences (all)	4		
Abdominal pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Dry mouth			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Rectal haemorrhage			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Rectal tenesmus			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Back pain			

subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Myalgia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Infections and infestations			
Urinary tract infection			
subjects affected / exposed	2 / 13 (15.38%)		
occurrences (all)	2		
Oral candidiasis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	6 / 13 (46.15%)		
occurrences (all)	6		
Dehydration			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Hypocalcaemia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	2		
Hypophosphataemia			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		
Malnutrition			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 October 2018	To incorporate additional changes based on feedback from the United States Food and Drug Administration (US FDA) To incorporate changes per BeiGene protocol template for better consistency across multiple studies Minor editorial and formatting changes have been made to enhance clarity and readability;

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
27 May 2020	Due to changes in standard of care for mCRPC, slow enrollment and lack of responses in this heavily pretreated patient population, the study was terminated.	-

Notes:

Limitations and caveats

None reported