Clinical trial results:
A Phase 2 Efficacy and Safety Study of Niraparib in Men with Metastatic Castration- Resistant Prostate Cancer and DNA-Repair Anomalies

Summary

EudraCT number	2016-002057-38
Trial protocol	SE GB ES BE DK NL FR IT
Global end of trial date	16 August 2023

Results information

Result version number	v1 (current)
This version publication date	23 August 2024
First version publication date	23 August 2024

Trial information

Trial identification

Sponsor protocol code	64091742PCR2001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02854436
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International BV
Sponsor organisation address	Antwerpseweg 15-17, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen-Cilag International BV, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International BV, ClinicalTrialsEU@its.jnj.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	26 January 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this trial was to assess the efficacy of niraparib in subjects with measurable metastatic castration-resistant prostate cancer (mCRPC) and who had either biallelic deoxyribonucleic acid repair anomalies in breast cancer gene (BRCA; BRCA1 or BRCA2) or germline BRCA.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 August 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 31
Country: Number of subjects enrolled	Belgium: 18
Country: Number of subjects enrolled	Brazil: 12
Country: Number of subjects enrolled	Canada: 21
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	Spain: 39
Country: Number of subjects enrolled	France: 48
Country: Number of subjects enrolled	United Kingdom: 17
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Netherlands: 6
Country: Number of subjects enrolled	Russian Federation: 7
Country: Number of subjects enrolled	Sweden: 24
Country: Number of subjects enrolled	Taiwan: 9
Country: Number of subjects enrolled	United States: 45
Worldwide total number of subjects	289
EEA total number of subjects	136

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)	84
From 65 to 84 years	198
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

For long-term extension (LTE) phase, as pre planned in the protocol no efficacy analysis was performed. Due to change in the conduct of the study, no adverse events data were collected and thus no adverse event data were reported for the LTE phase.

Period 1

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

Arms

Arm title	Niraparib

Arm description:

Male subjects who were over the age of 18 years with metastatic castration-resistant prostate cancer (mCRPC) and deoxyribonucleic acid (DNA) repair anomalies and who had received prior taxane-based chemotherapy and androgen receptor (AR)-targeted therapy received once daily oral dose of 300 milligrams (mg) niraparib capsules starting Day 1 until disease progression, unacceptable toxicity, death, or termination of the study by the sponsor (up to 52 months). After completion of treatment phase, subjects were offered entry into the long-term extension (LTE) phase (which was planned as per protocol amendment 8, dated 17-Jul-2020) with a separate informed consent and to continue treatment per the investigator's discretion until no benefits from treatment or Sponsor's decision.

Arm type	Experimental
Investigational medicinal product name	JNJ-64091742
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received niraparib 300mg (3 capsule of 100 mg) once daily.

Number of subjects in period 1	Niraparib
Started	289
Completed	0
Not completed	289
Adverse event, serious fatal	208
Physician decision	6
Consent withdrawn by subject	24
Adverse event, non-fatal	1
Unspecified	45
Lost to follow-up	5

Baseline characteristics

Reporting groups	
Reporting group title	Niraparib

Reporting group description:

Male subjects who were over the age of 18 years with metastatic castration-resistant prostate cancer (mCRPC) and deoxyribonucleic acid (DNA) repair anomalies and who had received prior taxane-based chemotherapy and androgen receptor (AR)-targeted therapy received once daily oral dose of 300 milligrams (mg) niraparib capsules starting Day 1 until disease progression, unacceptable toxicity, death, or termination of the study by the sponsor (up to 52 months). After completion of treatment phase, subjects were offered entry into the long-term extension (LTE) phase (which was planned as per protocol amendment 8, dated 17-Jul-2020) with a separate informed consent and to continue treatment per the investigator's discretion until no benefits from treatment or Sponsor's decision.

Reporting group values	Niraparib	Total	
Number of subjects	289	289	
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	84	84	
From 65 to 84 years	198	198	
85 years and over	7	7	
Title for AgeContinuous			
Units: years			
arithmetic mean	68.8		
standard deviation	± 7.8	-	
Title for Gender			
Units: subjects			
Male	289	289	
Female	0	0	

End points

End points reporting groups

Reporting group title	Niraparib

Reporting group description:

Male subjects who were over the age of 18 years with metastatic castration-resistant prostate cancer (mCRPC) and deoxyribonucleic acid (DNA) repair anomalies and who had received prior taxane-based chemotherapy and androgen receptor (AR)-targeted therapy received once daily oral dose of 300 milligrams (mg) niraparib capsules starting Day 1 until disease progression, unacceptable toxicity, death, or termination of the study by the sponsor (up to 52 months). After completion of treatment phase, subjects were offered entry into the long-term extension (LTE) phase (which was planned as per protocol amendment 8, dated 17-Jul-2020) with a separate informed consent and to continue treatment per the investigator's discretion until no benefits from treatment or Sponsor's decision.

Primary: Objective Response Rate (ORR) for Subjects with Measurable Metastatic Castration-resistant Prostate Cancer (mCRPC) and Breast Cancer Gene (BRCA) Mutation

End point title	Objective Response Rate (ORR) for Subjects with Measurable Metastatic Castration-resistant Prostate Cancer (mCRPC) and Breast Cancer Gene (BRCA) Mutation[1]

End point description:

ORR defined as percentage of subjects with BRCA DNA-repair anomalies and measurable disease whose best response is either complete response (CR) or partial response (PR) per Response Evaluation Criteria in Solid Tumors (RECIST 1.1) and with no evidence of bone progression per Prostate Cancer Working Group 3 (PCWG3) criteria. Measurable intent to treat (ITT) population also referred to as efficacy analysis set included all subjects who received at least 1 dose of study drug and had BRCA (biallelic or germline DNA-repair anomalies) and measurable disease at baseline.

End point type	Primary

End point timeframe:

Up to 52 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: No inferential statistics was done. Only descriptive statistics was performed.

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	76			
Units: percentage of subjects				
number (confidence interval 95%)	34.2 (23.7 to 46.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate for Subjects with Measurable Metastatic Castration-resistant Prostate Cancer (mCRPC) and Non-Breast Cancer Gene (BRCA) Mutation

End point title	Objective Response Rate for Subjects with Measurable Metastatic Castration-resistant Prostate Cancer (mCRPC) and

	Non-Breast Cancer Gene (BRCA) Mutation

End point description:

ORR defined as percentage of subjects with BRCA deoxyribonucleic acid (DNA)-repair anomalies and measurable disease whose best response is either CR or PR per RECIST 1.1 and with no evidence of bone progression per PCWG3 criteria. Measurable ITT analysis set included all subjects who received at least 1 dose of study drug and had non-BRCA (biallelic DNA-repair anomaly) and measurable disease at baseline.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: percentage of subjects				
number (confidence interval 95%)	10.6 (3.5 to 23.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Circulating Tumor Cells (CTC) Response Rate

End point title	Circulating Tumor Cells (CTC) Response Rate

End point description:

CTC response rate was defined as the percentage of subjects with CTC equals to (=) 0 per 7.5 millilitres (mL) blood at 8 weeks post-baseline in subjects with baseline CTC greater than (>) 0. ITT analysis set included all subjects who received at least 1 dose of study drug. Here 'N' (number of subjects analysed) specifies the subjects with baseline CTC (per 7.5 mL blood) > 0. Here, 'n' (number analysed) specifies the number of subjects evaluated for specific categories.

End point type	Secondary

End point timeframe:

At 8 weeks post-baseline

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	202			
Units: percentage of subjects				
number (not applicable)				
BRCA (n=131) Non-BRCA (n=71)	23.7 8.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as time from enrollment to death from any cause. ITT analysis set included subjects who had received at least 1 dose of study drug. Here, 'n' (number analysed) specifies the number of subjects evaluated for specific categories.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: months				
median (confidence interval 95%)				
BRCA (n=142) Non-BRCA (n=81)	13.01 (11.04 to 14.29) 9.63 (8.05 to 13.44)			

Statistical analyses

No statistical analyses for this end point

Secondary: Radiographic Progression-Free Survival (rPFS)

End point title	Radiographic Progression-Free Survival (rPFS)

End point description:

rPFS was defined as time from enrollment to radiographic progression or death from any cause, whichever occurred first. Radiographic progression was evaluated per RECIST 1.1 criteria for soft tissue disease and per PCWG3 criteria for bone disease. ITT analysis set included subjects who had received at least 1 dose of study drug. Here, 'n' (number analysed) specifies the number of subjects evaluated for specific categories.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: months				
median (confidence interval 95%)				
BRCA (n= 142)	8.08 (5.55 to 8.38)			
Non-BRCA (n=81)	3.71 (1.97 to 5.49)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Radiographic Progression

End point title	Time to Radiographic Progression

End point description:

Time to radiographic progression is defined as time from enrollment to radiographic progression or death due to disease progression, whichever occurs first. Disease progression was defined as at least a 20 percent (%) increase in the sum of diameters of target lesions, taking as reference the smallest sum on study (this includes the baseline sum if that was smallest on study). In addition to the relative increase of 20%, the sum must also demonstrate an absolute increase of at least 5 mm. The appearance of one or more new lesions was also considered progression. ITT analysis set included subjects who had received at least 1 dose of study drug. Here, 'n' (number analysed) specifies the number of subjects evaluated for specific categories.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: months				
median (confidence interval 95%)				
BRCA (n=142)	8.08 (5.75 to 8.97)			
Non-BRCA (n=81)	3.78 (2.00 to 5.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Prostate-Specific Antigen (PSA) Progression

End point title	Time to Prostate-Specific Antigen (PSA) Progression

End point description:

Time to PSA progression was defined as time from enrollment to the first date of documented PSA progression based on PCWG3 criteria. A subjects was considered to have a PSA progression if the PSA level had a 25 percent (%) or greater increase from nadir and an absolute increase of 2 nanograms per millilitre (ng/mL) or more, which was confirmed by a second value obtained in 3 or more weeks. ITT analysis set included subjects who had received at least 1 dose of study drug. Here, 'n' (number analysed) specifies the number of subjects evaluated for specific categories.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: months				
median (confidence interval 95%)				
BRCA (n=142)	5.13 (4.60 to 5.59)			
Non-BRCA (n=81)	3.65 (2.83 to 3.71)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Symptomatic Skeletal Event (SSE)

End point title	Time to Symptomatic Skeletal Event (SSE)

End point description:

Time to SSE was defined as the time from enrollment to first occurrence of one of the following symptomatic skeletal events: tumor-related spinal cord compression, radiation to bone to relieve skeletal symptoms, surgery to bone or need for tumor-related orthopedic surgical intervention, symptomatic or pathologic fracture. ITT analysis set included subjects who had received at least 1 dose of study drug. Here, 'n' (number analysed) specifies the number of subjects evaluated for specific categories. Here, 99999 indicates that upper limit of 95% confidence interval (CI) was not estimable due to less number of events.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	223			
Units: months				
median (confidence interval 95%)				
BRCA (n=142)	13.80 (10.41 to 99999)			

Non-BRCA (n=81)	10.35 (8.18 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response

End point title	Duration of Objective Response

End point description:

Duration of objective response is defined as time from CR or PR to radiographic progression of disease, unequivocal clinical progression or death, whichever occurs first. Unequivocal clinical progression defined as one or more of following: 1) deterioration in Eastern Cooperative Oncology Group Performance Status (ECOG PS) to Grade 3 or higher; 2) initiated any of following because of tumor progression (even in absence of radiographic evidence of disease): alternative anticancer therapy for prostate cancer, radiation therapy, surgical interventions for complications due to tumor progression. Measurable ITT responder analysis set included all subjects who received at least 1 dose of study drug, responded to it and have BRCA or non-BRCA and measurable disease at baseline. Here, 'n' (number analysed) specifies the number of subjects evaluated for specificed categories. Here, '99999' indicates that upper limit of 95% CI was not estimable due to less number of events.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: months				
median (confidence interval 95%)				
BRCA (n=26)	5.55 (3.91 to 7.20)			
non-BRCA (n=5)	5.16 (2.14 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events (AEs)

End point title	Number of Subjects with Adverse Events (AEs)

End point description:

An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/ biological agent under study. Safety analysis set included all subjects who received at least 1 dose of study drug.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	289			
Units: Subjects	288			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Worst Toxicity Grades for Clinical Laboratory Tests based on National Cancer Institute - Common Terminology Criteria for Adverse Events (NCI-CTCAE)

End point title	Number of Subjects with Worst Toxicity Grades for Clinical Laboratory Tests based on National Cancer Institute - Common Terminology Criteria for Adverse Events (NCI-CTCAE)

End point description:

Number of subjects with worst toxicity grades for clinical laboratory tests (chemistry and hematology) based on NCI-CTCAE were reported. The chemistry laboratory parameters were: alanine aminotransferase (ALT) increased, alkaline phosphatase (AP) increased, aspartate aminotransferase (AST) increased, blood bilirubin increased, creatinine increased, gamma glutamyl transferase (GGT) increased and the hematology parameters were: hemoglobin increased, lymphocyte count increased. Grading was done as: Grade 1 (=mild), Grade 2 (=moderate), Grade 3 (=severe) and Grade 4 (=potentially life-threatening). Safety analysis set included all subjects who received at least 1 dose of study drug and with at least one postbaseline assessment for the specific lab test within the time period. Here, 'n' (number analysed) specifies the number of subjects evaluated for specified categories.

End point type	Secondary

End point timeframe:

Up to 52 months

End point values	Niraparib			
Subject group type	Reporting group			
Number of subjects analysed	283			
Units: subjects				
ALT increased (Grade 1 or 2) (n=283)	67			
ALT increased (Grade 3 or 4) (n=283)	4			
AP increased (Grade 1 or 2) (n=283)	102			
AP increased (Grade 3 or 4) (n=283)	7			
AST increased (Grade 1 or 2) (n=283)	70			
AST increased (Grade 3 or 4) (n=283)	4			
Blood bilirubin increased (Grade 1 or 2) (n=283)	9			
Blood bilirubin increased (Grade 3 or 4) (n=283)	2			

Creatinine increased (Grade 1 or 2) (n=283)	45			
Creatinine increased (Grade 3 or 4) (n=283)	2			
GGT increased (Grade 1 or 2) (n=282)	105			
GGT increased (Grade 3 or 4) (n=282)	14			
Hemoglobin increased (Grade 1 or 2) (n=283)	0			
Hemoglobin increased (Grade 3 or 4) (n=283)	0			
Lymphocyte count increased (Grade 1 or 2) (n=283)	6			
Lymphocyte count increased (Grade 3 or 4) (n=283)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 52 months.

Adverse event reporting additional description:

Safety analysis set included all subjects who received at least 1 dose of study drug. Due to change in the conduct of the study, no adverse events data were collected and thus no adverse event data were reported for the LTE phase.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Niraparib

Reporting group description:

Male Subjects who were over the age of 18 years with metastatic castration-resistant prostate cancer (mCRPC) and deoxyribonucleic acid (DNA) repair anomalies and who had received prior taxane-based chemotherapy and androgen receptor (AR)-targeted therapy received once daily oral dose of 300 milligrams (mg) niraparib capsules starting Day 1 until disease progression, unacceptable toxicity, death, or termination of the study by the sponsor (up to 52 months). After completion of treatment phase, subjects were offered entry into the long-term extension (LTE) phase (which was planned as per protocol amendment 8, dated 17-Jul-2020) with a separate informed consent and to continue treatment per the investigator's discretion until no benefits from treatment or Sponsor's decision.

Serious adverse events	Niraparib		
Total subjects affected by serious adverse events			
subjects affected / exposed	134 / 289 (46.37%)		
number of deaths (all causes)	208		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal Cell Carcinoma			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Stromal Tumour			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases to Meninges			

subjects affected / exposed	3 / 289 (1.04%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Prostate Cancer Metastatic				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 2			
Tumour Pain				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Deep Vein Thrombosis				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Embolism				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Phlebitis				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Systemic Inflammatory Response Syndrome				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Pyrexia			
subjects affected / exposed	4 / 289 (1.38%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Performance Status Decreased			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	2 / 289 (0.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Non-Cardiac Chest Pain			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General Physical Health Deterioration			
subjects affected / exposed	8 / 289 (2.77%)		
occurrences causally related to treatment / all	1 / 8		
deaths causally related to treatment / all	0 / 4		
Facial Pain			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	4 / 289 (1.38%)		
occurrences causally related to treatment / all	2 / 5		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	4 / 289 (1.38%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			

Prostatitis				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute Respiratory Failure				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic Obstructive Pulmonary Disease				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung Disorder				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary Embolism				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory Distress				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Psychiatric disorders			
Confusional State			
subjects affected / exposed	2 / 289 (0.69%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood Calcium Increased			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood Creatinine Increased			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Electrocardiogram QT Prolonged			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Extradural Haematoma			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Femur Fracture			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head Injury			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hip Fracture			

subjects affected / exposed	2 / 289 (0.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Spinal Fracture			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis Radiation			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Ventricular Tachycardia			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac Failure Congestive			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Cardiac Failure			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Cardiac Arrest			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Atrial Fibrillation			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Altered State of Consciousness				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cauda Equina Syndrome				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular Accident				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	6 / 289 (2.08%)			
occurrences causally related to treatment / all	1 / 6			
deaths causally related to treatment / all	0 / 0			
Ischaemic Stroke				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Monoparesis				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Nerve Compression				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Neuropathy Peripheral				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paraparesis				

subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal Cord Compression				
subjects affected / exposed	6 / 289 (2.08%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Transient Ischaemic Attack				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Neutropenia				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	17 / 289 (5.88%)			
occurrences causally related to treatment / all	17 / 18			
deaths causally related to treatment / all	0 / 0			
Febrile Neutropenia				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Anaemia				

subjects affected / exposed	13 / 289 (4.50%)			
occurrences causally related to treatment / all	8 / 15			
deaths causally related to treatment / all	0 / 1			
Leukopenia				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Vomiting				
subjects affected / exposed	7 / 289 (2.42%)			
occurrences causally related to treatment / all	6 / 8			
deaths causally related to treatment / all	0 / 0			
Volvulus				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Small Intestinal Obstruction				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal Haemorrhage				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	5 / 289 (1.73%)			
occurrences causally related to treatment / all	5 / 6			
deaths causally related to treatment / all	0 / 0			
Lower Gastrointestinal Haemorrhage				

subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inflammatory Bowel Disease				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal Haemorrhage				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	5 / 289 (1.73%)			
occurrences causally related to treatment / all	2 / 8			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acute Abdomen				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal Pain				

subjects affected / exposed	4 / 289 (1.38%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	2 / 289 (0.69%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	6 / 289 (2.08%)		
occurrences causally related to treatment / all	2 / 8		
deaths causally related to treatment / all	0 / 1		
Renal Impairment			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Retention			
subjects affected / exposed	2 / 289 (0.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 289 (1.04%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Back Pain			
subjects affected / exposed	7 / 289 (2.42%)		
occurrences causally related to treatment / all	0 / 7		
deaths causally related to treatment / all	0 / 0		
Bone Pain			
subjects affected / exposed	3 / 289 (1.04%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Joint Effusion				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Muscular Weakness				
subjects affected / exposed	3 / 289 (1.04%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal Pain				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Myalgia				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in Extremity				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in Jaw				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pathological Fracture				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Septic Shock				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Skin Infection				

subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Spinal Cord Infection			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	3 / 289 (1.04%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	5 / 289 (1.73%)		
occurrences causally related to treatment / all	2 / 7		
deaths causally related to treatment / all	1 / 2		
Pyelonephritis Acute			
subjects affected / exposed	2 / 289 (0.69%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia Haemophilus			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	4 / 289 (1.38%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Pneumocystis Jirovecii Pneumonia			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			

subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Neutropenic Sepsis				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Malaria				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower Respiratory Tract Infection				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Infected Lymphocele				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Herpes Zoster				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Escherichia Urinary Tract Infection				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abscess Jaw				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal Infection				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	2 / 289 (0.69%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	1 / 1			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	4 / 289 (1.38%)			
occurrences causally related to treatment / all	3 / 5			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypocalcaemia				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hypokalaemia				
subjects affected / exposed	1 / 289 (0.35%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				

subjects affected / exposed	2 / 289 (0.69%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hypophosphataemia			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hypovolaemia			
subjects affected / exposed	1 / 289 (0.35%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Niraparib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	280 / 289 (96.89%)		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	17 / 289 (5.88%)		
occurrences (all)	25		
Aspartate Aminotransferase Increased			
subjects affected / exposed	20 / 289 (6.92%)		
occurrences (all)	27		
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	26 / 289 (9.00%)		
occurrences (all)	35		
Electrocardiogram QT Prolonged			
subjects affected / exposed	17 / 289 (5.88%)		
occurrences (all)	23		
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	25 / 289 (8.65%)		
occurrences (all)	38		
Weight Decreased			

subjects affected / exposed	50 / 289 (17.30%)		
occurrences (all)	61		
Vascular disorders			
Hot Flush			
subjects affected / exposed	17 / 289 (5.88%)		
occurrences (all)	19		
Hypertension			
subjects affected / exposed	34 / 289 (11.76%)		
occurrences (all)	47		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	17 / 289 (5.88%)		
occurrences (all)	18		
Dizziness			
subjects affected / exposed	19 / 289 (6.57%)		
occurrences (all)	20		
Headache			
subjects affected / exposed	30 / 289 (10.38%)		
occurrences (all)	40		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	154 / 289 (53.29%)		
occurrences (all)	472		
Leukopenia			
subjects affected / exposed	27 / 289 (9.34%)		
occurrences (all)	57		
Lymphopenia			
subjects affected / exposed	24 / 289 (8.30%)		
occurrences (all)	42		
Neutropenia			
subjects affected / exposed	54 / 289 (18.69%)		
occurrences (all)	114		
Thrombocytopenia			
subjects affected / exposed	94 / 289 (32.53%)		
occurrences (all)	270		
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	45 / 289 (15.57%)		
occurrences (all)	73		
Fatigue			
subjects affected / exposed	105 / 289 (36.33%)		
occurrences (all)	163		
Oedema Peripheral			
subjects affected / exposed	41 / 289 (14.19%)		
occurrences (all)	48		
Pyrexia			
subjects affected / exposed	17 / 289 (5.88%)		
occurrences (all)	19		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	23 / 289 (7.96%)		
occurrences (all)	28		
Constipation			
subjects affected / exposed	98 / 289 (33.91%)		
occurrences (all)	125		
Diarrhoea			
subjects affected / exposed	48 / 289 (16.61%)		
occurrences (all)	66		
Dry Mouth			
subjects affected / exposed	20 / 289 (6.92%)		
occurrences (all)	20		
Dyspepsia			
subjects affected / exposed	21 / 289 (7.27%)		
occurrences (all)	24		
Nausea			
subjects affected / exposed	167 / 289 (57.79%)		
occurrences (all)	256		
Stomatitis			
subjects affected / exposed	19 / 289 (6.57%)		
occurrences (all)	28		
Vomiting			

subjects affected / exposed	109 / 289 (37.72%)		
occurrences (all)	175		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	39 / 289 (13.49%)		
occurrences (all)	50		
Cough			
subjects affected / exposed	17 / 289 (5.88%)		
occurrences (all)	21		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	24 / 289 (8.30%)		
occurrences (all)	28		
Musculoskeletal and connective tissue disorders			
Pain in Extremity			
subjects affected / exposed	30 / 289 (10.38%)		
occurrences (all)	35		
Musculoskeletal Pain			
subjects affected / exposed	29 / 289 (10.03%)		
occurrences (all)	37		
Bone Pain			
subjects affected / exposed	30 / 289 (10.38%)		
occurrences (all)	42		
Arthralgia			
subjects affected / exposed	43 / 289 (14.88%)		
occurrences (all)	76		
Back Pain			
subjects affected / exposed	59 / 289 (20.42%)		
occurrences (all)	78		
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	93 / 289 (32.18%)		
occurrences (all)	130		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2016	The purpose of the study amendment was the overall reason for the amendment is to address feedback from FDA received 5 July 2016. ECG monitoring at every cycle was added due to FDA concern regarding higher ECG abnormalities in the elderly population. FDA recommendation that toxicities which have not resolved within 21 days should undergo dose reduction or discontinuation. FDA recommendation that a hematologist must be consulted in the event of greater than (>) 1 transfusion or that did not recover to Grade 1 or less after 28 days.
25 January 2017	The purpose of the study amendment was primary endpoint of the study was amended to comply with feedback from health authorities. The primary endpoint was changed from a composite endpoint to objective response rate (ORR). With this change, the subject population for the primary analysis will include only subjects with measurable disease. Subjects with non-measurable disease will still be included in the study to increase the size of the safety database and assess the activity of niraparib in this population.
04 October 2017	The purpose of the study amendment was to include additional cardiac monitoring to better understand the cardiovascular effect of niraparib monotherapy in the prostate cancer population. This additional safety monitoring is precautionary only and is not indicative of a known cardiac signal for niraparib. An ITT Population was also added to allow for all subjects with biallelic DNA-repair anomalies to be analyzed separately for efficacy. Other minor changes (ie, removal of pharmacodynamics sampling and updates to the inclusion/exclusion criteria) are also included in this amendment.
20 March 2018	The purpose of the study amendment was to improve the subject selection criteria based on using an enhanced biomarker assay and the corresponding statistical analysis plan, to remove Holter monitoring, and other minor changes throughout the protocol.
30 November 2018	The purpose of the study amendment was based on the updated safety information of niraparib with more subjects exposed to drug and to be consistent with clinical practice of physicians, changes were made to inclusion/exclusion criteria and other study-related procedures throughout the protocol.
20 June 2019	The purpose of the study amendment was to modify and clarify the protocol's inclusion and exclusion criteria to align with current clinical practice for the treatment of patients with metastatic prostate cancer based on protocol steering committee feedback and to reflect the characteristics of the third line mCRPC population.
30 October 2019	The purpose of the study amendment was to allow subjects with local germline pathogenic results for Breast Cancer gene 1 (BRCA1) or Breast Cancer gene 2 (BRCA2) DNA-repair defects (DRD) to enter the trial given the high likelihood of biallelic mutations.
17 April 2020	The purpose of the study amendment was to provide study-related guidance during the global coronavirus (COVID-19) pandemic. For health and safety reasons, subjects may not be able to come to the study site for scheduled procedures.
17 July 2020	The purpose of the study amendment was (1) to add a Long-term Extension Phase, (2) to include subjects who have germline pathogenic Non-Breast Cancer Gene 1 or Breast Cancer gene 2 (BRCA1 or BRCA2) mutations in the efficacy analyses, and (3) to provide updated patient enrollment recruitment requirements.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported