Clinical trial results:
Talapro-1: A Phase 2, Open-Label, Response Rate Study of Talazoparib in Men with DNA Repair Defects and Metastatic Castration-Resistant Prostate Cancer Who Previously Received Taxane-Based Chemotherapy and Progressed on at Least 1 Novel Hormonal Agent (Enzalutamide And/or Abiraterone Acetate/Prednisone)

Summary

EudraCT number	2016-002036-32
Trial protocol	DE NL ES FR BE GB AT DK HU IT
Global end of trial date	31 March 2023

Results information

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

Trial information

Trial identification

Sponsor protocol code	C3441006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03148795
WHO universal trial number (UTN)	-
Other trial identifiers	MDV3800-06: Other ID

Notes:

Sponsors

Sponsor organisation name	Pfizer Inc.
Sponsor organisation address	235 E 42nd Street, New York, United States, NY 10017
Public contact	Pfizer Inc., Pfizer ClinicalTrials.gov Call Center, 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com
Scientific contact	Pfizer ClinicalTrials.gov Call Center, Pfizer Inc., 001 8007181021, ClinicalTrials.gov_Inquiries@pfizer.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	04 July 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy, of single agent talazoparib in Deoxyribonucleic acid damage repair (DDR) + Metastatic castration-resistant prostate cancer (mCRPC) as measured by best objective response rate (ORR).

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and in compliance with all International Conference on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. All the local regulatory requirements pertinent to safety of trial subjects were followed.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 July 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 11
Country: Number of subjects enrolled	Germany: 6
Country: Number of subjects enrolled	Brazil: 1
Country: Number of subjects enrolled	French Guiana: 22
Country: Number of subjects enrolled	Hungary: 3
Country: Number of subjects enrolled	Italy: 23
Country: Number of subjects enrolled	Belgium: 12
Country: Number of subjects enrolled	Spain: 5
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Netherlands: 15
Country: Number of subjects enrolled	Korea, Republic of: 1
Country: Number of subjects enrolled	Poland: 1
Country: Number of subjects enrolled	United Kingdom: 7
Country: Number of subjects enrolled	United States: 16
Worldwide total number of subjects	127
EEA total number of subjects	69

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)	39
From 65 to 84 years	88
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subjects with measurable soft tissue disease as per RECIST 1.1 and progressive metastatic castration-resistant prostate cancer (CRPC) and DNA damage repair deficiencies, previously received 1 to 2 taxane-based chemotherapy and progressed on at least 1 line of novel hormonal therapy (enzalutamide and/or abiraterone acetate/prednisone) were enrolled.

Period 1

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

Arms

Arm title	Talazoparib

Arm description:

Subjects received talazoparib 1 milligram per day (mg/day) orally until radiographic progression that was determined by independent central review, unacceptable toxicity, withdrawal of consent, or death. Talazoparib was continued upon disease progression only if, in the opinion of the investigator the subject was clinically benefitting, no new concurrent systemic therapy was initiated, and the sponsor was notified. Maximum duration of treatment was approximately 36 months.

Arm type	Experimental
Investigational medicinal product name	Talazoparib
Investigational medicinal product code	
Other name	PF-06944076
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Subjects received talazoparib 1 milligram per day (mg/day).

Number of subjects in period 1	Talazoparib
Started	127
Completed	126
Not completed	1
Progressive Disease	1

Baseline characteristics

Reporting groups	
Reporting group title	Talazoparib

Reporting group description:

Subjects received talazoparib 1 milligram per day (mg/day) orally until radiographic progression that was determined by independent central review, unacceptable toxicity, withdrawal of consent, or death. Talazoparib was continued upon disease progression only if, in the opinion of the investigator the subject was clinically benefitting, no new concurrent systemic therapy was initiated, and the sponsor was notified. Maximum duration of treatment was approximately 36 months.

Reporting group values	Talazoparib	Total	
Number of subjects	127	127	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	39	39	
From 65-84 years	88	88	
85 years and over	0	0	
Age Continuous Units: Years			
arithmetic mean	68.16		
standard deviation	± 8.02	-	
Sex: Female, Male Units: Subjects			
Female	0	0	
Male	127	127	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	4	4	
Not Hispanic or Latino	106	106	
Unknown or Not Reported	17	17	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	3	3	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	4	4	
White	110	110	
More than one race	0	0	
Unknown or Not Reported	10	10	

End points

End points reporting groups

Reporting group title	Talazoparib

Reporting group description:

Subjects received talazoparib 1 milligram per day (mg/day) orally until radiographic progression that was determined by independent central review, unacceptable toxicity, withdrawal of consent, or death. Talazoparib was continued upon disease progression only if, in the opinion of the investigator the subject was clinically benefitting, no new concurrent systemic therapy was initiated, and the sponsor was notified. Maximum duration of treatment was approximately 36 months.

Primary: Best Objective Response Rate (ORR)

End point title	Best Objective Response Rate (ORR)[1]

End point description:

Best ORR was defined as the percentage of subjects with best overall soft tissue response of complete response (CR) or partial response (PR) as per RECIST1.1 by an independent central review. RECIST 1.1 criteria, CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than 10 millimeter (mm). Disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (less than 10 mm short axis); PR: at least 30 percent (%) decrease in sum of diameters of target lesions taking as reference baseline sum diameters. DDR deficient measurable disease population included all enrolled subjects who had measurable soft tissue disease at screening by investigator assessment, had DDR deficiencies likely to sensitize to PARP inhibitor therapy, and received at least 1 dose of talazoparib.

End point type	Primary

End point timeframe:

From first dose of study drug to best overall soft tissue response CR or PR (maximum duration of 25 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 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.

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: Percentage of subjects				
number (confidence interval 95%)	29.8 (21.2 to 39.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Prostate-Specific Antigen (PSA) Response of Greater Than or Equal to (>=) 50 Percentage (%)

End point title	Percentage of Subjects With Prostate-Specific Antigen (PSA) Response of Greater Than or Equal to (>=) 50 Percentage (%)

End point description:

Percentage of subjects with PSA response of >= 50% was reported in this outcome measure. PSA

response was calculated as a decline from baseline PSA (ng/mL) by at least 50% measured by central laboratory. Final analyses for this endpoint was till the cutoff date 04 September 2020. DDR deficient measurable disease population included all enrolled subjects who had measurable soft tissue disease at screening by investigator assessment, had DDR deficiencies likely to sensitize to PARP inhibitor therapy, and received at least 1 dose of talazoparib. Here ''Number of subjects analyzed'' signifies number of subjects evaluable data for this endpoint.

End point type	Secondary

End point timeframe:

From the date of first dose of study treatment until confirmed PSA progression or start of new anticancer treatment given after the first dose of study treatment (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: Percentage of subjects				
number (confidence interval 95%)	45.8 (35.6 to 56.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR)

End point title	Duration of Response (DOR)

End point description:

DOR was defined as the time from the first objective evidence of soft tissue response (CR or PR, whichever is earlier) per RECIST 1.1 and no evidence of confirmed bone disease progression per PCWG3 to the date of first objective evidence of radiographic progression or death due to any cause without evidence of radiographic progression, whichever occurs first. RECIST 1.1 criteria, CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than 10 mm. Disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (less than 10 mm short axis); PR: at least 30 % decrease in sum of diameters of target lesions taking as reference baseline sum diameters. DDR deficient measurable disease population evaluated. 99999 indicates Upper limit of 95% confidence interval (CI) was not estimable as there were less number of subjects with an event.

End point type	Secondary

End point timeframe:

From the first objective evidence of soft tissue response (CR or PR, whichever is earlier) to radiographic progression or death due to any cause without evidence of radiographic progression, whichever occurs first (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Months				
median (confidence interval 95%)	12.8 (6.5 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Conversion of Circulating Tumor Cell (CTC) Count

End point title	Percentage of Subjects With Conversion of Circulating Tumor Cell (CTC) Count

End point description:

Percentage of subjects with conversion of CTC count was defined as percentage of subjects with a CTC count >= 5 CTC per 7.5 milliliter (mL) of blood at baseline that decreased to < 5 CTC per 7.5 mL of blood any time on study. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects with a baseline CTC assessment and at least 1 post-baseline CTC assessment from the DDR deficient measurable disease population. Subjects with a CTC count <5 per 7.5 mL of blood at baseline were not analyzed for this conversion endpoint. Here, "Number of subjects analyzed'' signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to anytime on study during final analyses (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	33			
Units: Percentage of subjects				
number (confidence interval 95%)	63.6 (45.1 to 79.6)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Objective Response

End point title	Time to Objective Response

End point description:

Time to objective response was defined as the time from first dose of talazoparib to the first objective evidence of soft tissue response with no evidence of confirmed bone disease progression on bone scan per prostate cancer working Group 3 (PCWG3). Soft tissue response is defined as a best overall response of CR or PR per RECIST 1.1 by independent central review. RECIST 1.1 criteria, CR: disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) must have reduction in short axis to less than 10 mm. Disappearance of all non-target lesions and normalization of tumor marker level. All lymph nodes must be non-pathological in size (less than 10 mm short axis); PR: at least 30 % decrease in sum of diameters of target lesions taking as reference baseline sum diameters. DDR deficient measurable disease population evaluated.

End point type	Secondary

End point timeframe:

From first dose of study drug to first objective response (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: Months				
median (full range (min-max))	3.4 (1.6 to 7.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: : Percentage of Subjects With Baseline CTC Count <5 CTC Showed Increased CTC Counts at any Time on Study

End point title	: Percentage of Subjects With Baseline CTC Count <5 CTC Showed Increased CTC Counts at any Time on Study

End point description:

Percentage of subjects with CTC count <5 CTC per 7.5 mL of blood at baseline those who showed an increased CTC count, compared to baseline, any time on study was reported in this study. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects with a baseline CTC assessment and at least 1 post-baseline CTC assessment from the DDR deficient measurable disease population. Here, "Number of subjects analyzed'' signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to anytime on study during final analyses (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	29			
Units: Percentage of subjects				
number (confidence interval 95%)	37.9 (20.7 to 57.7)			

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 the time from first dose of study treatment to the date of PSA progression, which was subsequently confirmed. The time from first dose of talazoparib to the date that a >=25% increase in PSA with an absolute increase of ≥2micogram per liter (2 nanogram per mL) above the nadir (or baseline for subjects with no PSA decline) was documented, confirmed by a second consecutive PSA value obtained >=3 weeks (21 days) later. Kaplan-Meier method was used for analysis. Final analyses for this endpoint was till the cutoff date 04 September 2020. DDR deficient measurable disease population included all enrolled subjects who had measurable soft tissue disease at screening by investigator assessment, had DDR deficiencies likely to sensitize to PARP inhibitor therapy, and received at least 1 dose of talazoparib.

End point type	Secondary

End point timeframe:

From the date of first dose of study treatment until confirmed PSA progression or start of new anticancer treatment given after the first dose of study treatment (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: Months				
median (confidence interval 95%)	9.2 (5.6 to 11.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With a Null CTC Count

End point title	Percentage of Subjects With a Null CTC Count

End point description:

Percentage of subjects with a null CTC count was defined as percentage of subjects with CTC count >=1 CTC per 7.5 mL of blood at baseline that decreased to CTC = 0 per 7.5 mL of blood any time on study. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects with a baseline CTC assessment and at least 1 post-baseline CTC assessment from the DDR deficient measurable disease population. Subjects with a CTC count 0 per 7.5 mL of blood at baseline were not analyzed for this endpoint. Here, "Number of subjects analyzed'' signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline to anytime on study during final analyses (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Percentage of subjects				
number (confidence interval 95%)	53.3 (37.9 to 68.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Radiographic Progression-Free Survival (PFS)

End point title	Radiographic Progression-Free Survival (PFS)

End point description:

Radiographic PFS was defined as the time from date of first dose of talazoparib to first objective evidence of radiographic progression as assessed in soft tissue per modified RECIST 1.1 or confirmed progression in bone per PCWG3 guidelines by independent central review or death without documented radiographic progression, whichever occurs first. DDR deficient measurable disease population included all enrolled subjects who had measurable soft tissue disease at screening by investigator assessment, had DDR deficiencies likely to sensitize to PARP inhibitor therapy, and received at least 1 dose of talazoparib.

End point type	Secondary

End point timeframe:

From date of first dose of study drug to first objective evidence of radiographic progression or death without documented radiographic progression, whichever occurs first (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: Months				
median (confidence interval 95%)	5.6 (3.7 to 8.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS was defined as the time from start date (the date of first dose of treatment) to the date of death due to any cause. Subjects who had not died were censored at the date of last contact. Kaplan-Meier method was used for analysis. Final analyses for this endpoint was till the cutoff date 31 March 2023. DDR deficient measurable disease population included all enrolled subjects who had measurable soft tissue disease at screening by investigator assessment, had DDR deficiencies likely to sensitize to PARP inhibitor therapy, and received at least 1 dose of talazoparib.

End point type	Secondary

End point timeframe:

From first dose of study treatment up to death due to any cause during study or date of last contact (approximately 36 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	104			
Units: Months				
median (confidence interval 95%)	16.9 (13.0 to 20.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment Emergent Adverse Events (TEAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a subjects who received study drug without regard to possibility of causal relationship. AEs included both serious AEs and all non-serious AEs. Treatment-emergent are events between first dose of study drug and up to 28 days after last dose that were absent before treatment or that worsened relative to pretreatment state. Safety population included all subjects who received at least 1 dose of talazoparib including subjects enrolled prior to amendment 3 with non-measurable disease and/or with DDR deficiencies, which may sensitize the tumor to PARP inhibition as assessed using an expanded DDR gene panel.

End point type	Secondary

End point timeframe:

First dose of study drug up to 28 days after last dose of study drug (study treatment was approximately for 36 months, safety follow up to approximately 37 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Subjects	125			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Permanent Treatment Discontinuation Due to Adverse Events

End point title	Number of Subjects With Permanent Treatment Discontinuation Due to Adverse Events

End point description:

Treatment discontinuation was defined as permanent cessation of study drug treatment administration. Safety population included all subjects who received at least 1 dose of talazoparib including subjects

enrolled prior to amendment 3 with non-measurable disease and/or with DDR deficiencies, which may sensitize the tumor to PARP inhibition as assessed using an expanded DDR gene panel.

End point type	Secondary

End point timeframe:

During study treatment (approximately up to 36 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Subjects	21			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Significant Abnormalities in Vital Signs

End point title	Number of Subjects With Clinically Significant Abnormalities in Vital Signs

End point description:

Vital sign abnormalities criteria included: 1) Systolic blood pressure (SBP) in millimeters of mercury (mmHg): absolute result (AR) greater than (>) 180 mmHg and increase from baseline (IFB) greater than or equal to (>=) 40 mmHg or AR < 90 mmHg and decrease from baseline (DFB) > 30 mmHg; 2) Diastolic blood pressure (DBP) (mmHg): AR > 110 mmHg and IFB >= 30 mmHg or AR < 50 mmHg and DFB > 20 mmHg or >= 20 mmHg IFB; 3) Heart rate in beats per minutes (bpm): AR < 50 bpm and DFB > 20 bpm or AR > 120 bpm and IFB > 30 bpm; Weight in kilogram: > 10% DFB. Safety population evaluated. Here, “Number of Subjects Analyzed” signifies subjects evaluable for this endpoint and "n” signifies those subjects who were evaluable at specified rows.

End point type	Secondary

End point timeframe:

During study treatment (approximately up to 36 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: Subjects				
SBP: AR >180 mmHg & IFB >=40 mmHg,n=125	0			
SBP: AR <90 mmHg & DFB >30 mmHg, n=125	0			
DBP: AR >110mmHg & IFB >=30mmHg, n=125	0			
DBP: AR <50 mmHg & DFB >20 mmHg, n=125	0			
DBP: >= 20 mmHg IFB, n=125	17			
Heart rate: AR < 50bpm & DFB >20bpm, n=125	0			

Heart rate: AR >120 bpm & IFB >30 bpm, n=125	2			
Weight: > 10% DFB, n=124	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Shift in Laboratory Parameter Values (Hematology) From Grade less than equal to (<=) 2 at Baseline to Grade 3 or 4 Post-baseline

End point title	Number of Subjects With Shift in Laboratory Parameter Values (Hematology) From Grade less than equal to (<=) 2 at Baseline to Grade 3 or 4 Post-baseline

End point description:

Hematology parameters included anemia, hemoglobin increased, lymphocyte count decreased, lymphocyte count increased, neutrophil count decreased, platelet count decreased, Leukocytosis and white blood cell decreased. Severity was graded as Grade 1: asymptomatic or mild symptoms, clinical or diagnostic observations only, intervention not indicated; Grade 2: moderate, minimal, local or non-invasive intervention indicated, limiting age-appropriate instrumental activities of daily life (ADL); Grade 3: severe or medically significant but not immediately life-threatening, hospitalization or prolongation of existing hospitalization indicated, disabling, limiting self-care ADL; Grade 4: life-threatening consequence, urgent intervention indicated; Grade 5: death related to AE. Safety population evaluated. Here, "Number of Subjects Analyzed" signifies subjects evaluable for this endpoint. "n" signifies subjects evaluable at specific rows.

End point type	Secondary

End point timeframe:

During study treatment (approximately up to 36 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	125			
Units: Subjects				
Anemia, n=125	30			
Hemoglobin increased, n=125	1			
Lymphocyte count decreased, n=125	23			
Lymphocyte count increased, n=125	0			
Neutrophil count decreased, n=125	11			
Platelet count decreased, n=125	3			
White blood cell decreased, n=125	5			
Leukocytosis, n=125	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Shift in Laboratory Parameter Values

(Chemistry) From Grade <=2 at Baseline to Grade 3 or 4 Post-baseline

End point title	Number of Subjects With Shift in Laboratory Parameter Values (Chemistry) From Grade <=2 at Baseline to Grade 3 or 4 Post-baseline

End point description:

Parameters: alanine aminotransferase (AT) increased (inc), alkaline phosphatase inc, aspartate AT inc, blood bilirubin inc, chronic kidney disease, creatinine inc, gamma-glutamyl transferase (GGT) inc, hypercalcemia, hyperglycemia, hyperkalemia, hypermagnesemia, hypocalcemia, hyponatremia, hypoglycemia, hypokalemia, hypomagnesemia, hypernatremia, hypoalbuminemia, hypophosphatemia. Grade(G)1: asymptomatic or mild symptoms, clinical or diagnostic observations only, intervention not indicated; G2:moderate, minimal, local or noninvasive intervention indicated, limiting age-appropriate instrumental ADL; G3:severe or medically significant but not immediately life-threatening, hospitalization or prolongation of existing hospitalization indicated, disabling, limiting self-care ADL; G4:life-threatening consequence, urgent intervention indicated; G5: death related to AEs. Safety set used. "Number of Subjects Analyzed": subjects evaluable for endpoint; "n": subjects evaluable at specific rows.

End point type	Secondary

End point timeframe:

During study treatment (approximately up to 36 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	126			
Units: Subjects				
Alanine aminotransferase increased, n=126	0			
Alkaline phosphatase increased, n=126	9			
Aspartate aminotransferase increased, n=126	0			
Blood bilirubin increased, n=126	0			
Chronic kidney disease, n=126	2			
Creatinine increased, n=126	1			
GGT increased, n=53	3			
Hypercalcemia, n=126	0			
Hyperglycemia, n=126	5			
Hyperkalemia, n=126	4			
Hypermagnesemia, n=126	1			
Hypernatremia, n=126	0			
Hypoalbuminemia, n=126	0			
Hypocalcemia, n=126	4			
Hypoglycemia, n=126	0			
Hypokalemia, n=126	0			
Hypomagnesemia, n=126	1			
Hyponatremia, n=126	3			
Hypophosphatemia, n=126	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Dose Modification

End point title	Number of Subjects With Dose Modification

End point description:

Number of subjects with dose modification due to adverse events was reported. Safety population included all subjects who received at least 1 dose of talazoparib including subjects enrolled prior to amendment 3 with non-measurable disease and/or with DDR deficiencies, which may sensitize the tumor to PARP inhibition as assessed using an expanded DDR gene panel.

End point type	Secondary

End point timeframe:

During study treatment (approximately up to 36 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	127			
Units: Subjects	37			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Deterioration in Pain Symptom Scores

End point title	Time to Deterioration in Pain Symptom Scores

End point description:

Time deterioration is based on BPI-SF question 3: "Please rate your pain by marking the box beside the number that best describes your pain at its worst in the last 24 hours." Pain intensity was to be answered on a range of 0 to 10, where 0 corresponded to no pain and 10 worst pain. Time to this event is defined as the time from the date of first dose of study treatment to onset of pain progression, where pain progression is defined as a 2-point or more increase from baseline in the question 3 score. Kaplan-Meier method was used for analysis. Average of all assessments visits is reported in this endpoint. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects from the DDR deficient measurable disease population with a baseline PRO assessment and at least 1 post-baseline PRO assessment prior to the end of treatment.

End point type	Secondary

End point timeframe:

Baseline till final analysis (maximum duration of 25 months)

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Months				
median (confidence interval 95%)	99999 (99999 to 99999)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Subjects Reported Pain Scores per BPI-SF Question 3 Through Final Analysis

End point title	Change From Baseline in Subjects Reported Pain Scores per BPI-SF Question 3 Through Final Analysis

End point description:

BPI-SF:11-item self-report questionnaire, assessed severity and impact of pain on daily functions. BPI-SF have 4 questions to assess pain intensity (worst, least, average, right now) and 7 questions to assess impact of pain on daily functions (general activity, mood, walking ability, normal work, relations with other people, sleep, enjoyment of life). Each question is answered on a scale from 0 (No pain) to 10 (Pain as bad as you can imagine). Measure can be scored by item, lower scores = less pain or pain interference. BPI-SF question 3 was related to subjects experiencing worst pain in last 24 hours, score range 0 to 10, large values = worse outcomes. Final analysis for this endpoint was till the cutoff date 04 September 2020. DDR deficient measurable disease population evaluated. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table; however, may not have evaluable data for every row. "n" signifies subjects evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 3, 5, 7, 9, 13, 17, 21, 25, 37, 49, 61, 73, 85, Follow-up Visit (28 days after last dose) [maximum duration of 25 months]

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 1, n=0	99999 (± 99999)			
Change at Week 3, n=70	-0.51 (± 2.04)			
Change at Week 5, n=72	-1.39 (± 2.55)			
Change at Week 7, n=61	-1.20 (± 2.89)			
Change at Week 9, n=63	-1.25 (± 2.38)			
Change at Week 13, n=55	-0.85 (± 2.51)			
Change at Week 17, n=54	-1.06 (± 2.73)			
Change at Week 21, n=44	-0.89 (± 2.77)			
Change at Week 25, n=44	-1.14 (± 3.14)			
Change at Week 37, n=27	-1.00 (± 2.30)			
Change at Week 49, n=17	-1.53 (± 3.50)			
Change at Week 61, n=12	-2.50 (± 3.42)			
Change at Week 73, n=5	-2.80 (± 5.17)			
Change at Week 85, n=2	-5.50 (± 3.54)			
Change at Follow-up, n=24	-0.25 (± 3.21)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in European Quality of Life 5-Domain 5-Level Scale (EQ-5D-5L) Visual Analogue Scores (VAS)

End point title	Change From Baseline in European Quality of Life 5-Domain 5-Level Scale (EQ-5D-5L) Visual Analogue Scores (VAS)

End point description:

The EQ-5D VAS score was a subjects rated questionnaire where subjects rated how they felt at assessment visit on a vertical VAS that ranged from 0 (worst imaginable health state) to 100 (best imaginable health state), with higher scores indicating a better health condition. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects from the DDR deficient measurable disease population with a baseline PRO assessment and at least 1 post-baseline PRO assessment prior to the end of treatment. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table; however, may not have evaluable data for every row. Here, "n" signifies number of subjects evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 3, 5,7, 9, 13, 17, 21, 25, 37, 49, 61, 73, 85, 97, Follow-up Visit (28 days after last dose) [maximum duration of 25 months]

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Change at Week 1, n=0	99999 (± 99999)			
Change at Week 3, n=89	4.16 (± 17.25)			
Change at Week 5, n=93	4.44 (± 17.26)			
Change at Week 7, n=84	6.61 (± 17.20)			
Change at Week 9, n=88	6.18 (± 20.21)			
Change at Week 13, n=71	7.68 (± 16.85)			
Change at Week 17, n=73	7.84 (± 19.40)			
Change at Week 21, n=62	6.63 (± 19.26)			
Change at Week 25, n=59	5.34 (± 21.50)			
Change at Week 37, n=37	4.65 (± 19.01)			
Change at Week 49, n=23	8.96 (± 17.55)			
Change at Week 61, n=16	12.75 (± 19.02)			
Change at Week 73, n=8	1.25 (± 24.89)			
Change at Week 85, n=4	11.50 (± 25.01)			
Change at Week 97, n=1	17.00 (± 99999)			
Change at Follow-up, n=30	-2.87 (± 21.55)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 5 Response Levels for EQ-5D-5L Mobility

Domain	
End point title	Number of Subjects With 5 Response Levels for EQ-5D-5L Mobility Domain

End point description:

EQ-5D-5L: subjects rated assessed level of current health using 5 domains: mobility, self-care, usual activities, pain and discomfort, anxiety, and depression. EQ-5D mobility domain had 5 responses: no problem, slight problem, moderate problem, severe problem and extreme problem. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects from the DDR deficient measurable disease population with a baseline PRO assessment and at least 1 post-baseline PRO assessment prior to the end of treatment. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table; however, may not have evaluable data for every row. Here, "n" signifies number of subjects evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 3, 5,7, 9, 13, 17, 21, 25, 37, 49, 61, 73, 85, 97, Follow-up Visit (28 days after last dose) [maximum duration of 25 months]

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Subjects				
Week 1, No Problem, n=96	30			
Week 3, No Problem, n=90	36			
Week 5, No Problem, n=95	36			
Week 7, No Problem, n=86	37			
Week 9, No Problem, n=90	38			
Week 13, No Problem, n=73	28			
Week 17, No Problem, n=74	30			
Week 21, No Problem, n=63	30			
Week 25, No Problem, n=59	29			
Week 37, No Problem, n=37	16			
Week 49, No Problem, n=23	10			
Week 61, No Problem, n=16	7			
Week 73, No Problem, n=8	4			
Week 85, No Problem, n=4	2			
Week 97, No Problem, n=1	1			
Follow-up, No Problem, n=30	11			
Week 1, Slight Problem, n=96	29			
Week 3, Slight Problem, n=90	23			
Week 5, Slight Problem, n=95	29			
Week 7, Slight Problem, n=86	24			
Week 9, Slight Problem, n=90	26			
Week 13, Slight Problem, n=73	26			
Week 17, Slight Problem, n=74	28			
Week 21, Slight Problem, n=63	15			
Week 25, Slight Problem, n=59	14			
Week 37, Slight Problem, | n=37	14			
Week 49, Slight Problem, | n=23	7			
Week 61, Slight Problem, n=16	5			
Week 73, Slight Problem, n=8	2			
Week 85, Slight Problem, n=4	2			

Week 97, Slight Problem, n=1	0			
Follow-up, Slight Problem, n=30	8			
Week 1, Moderate Problem, n=96	25			
Week 3, Moderate Problem, n=90	20			
Week 5, Moderate Problem, n=95	23			
Week 7, Moderate Problem, n=86	22			
Week 9, Moderate Problem, n=90	20			
Week 13, Moderate Problem, n=73	12			
Week 17, Moderate Problem, n=74	14			
Week 21, Moderate Problem, n=63	15			
Week 25, Moderate Problem, n=59	13			
Week 37, Moderate Problem, n=37	4			
Week 49, Moderate Problem, n=23	5			
Week 61, Moderate Problem, n=16	3			
Week 73, Moderate Problem, n=8	2			
Week 85, Moderate Problem, n=4	0			
Week 97, Moderate Problem, n=1	0			
Follow-up, Moderate Problem, n=30	6			
Week 1, Severe Problem, n=96	12			
Week 3, Severe Problem, n=90	10			
Week 5, Severe Problem, n=95	6			
Week 7, Severe Problem, n=86	3			
Week 9, Severe Problem, n=90	4			
Week 13, Severe Problem, n=73	5			
Week 17, Severe Problem, n=74	1			
Week 21, Severe Problem, n=63	3			
Week 25, Severe Problem, n=59	3			
Week 37, Severe Problem, n=37	3			
Week 49, Severe Problem, n=23	1			
Week 61, Severe Problem, n=16	1			
Week 73, Severe Problem, n=8	0			
Week 85, Severe Problem, n=4	0			
Week 97, Severe Problem, n=1	0			
Follow-up, Severe Problem, n=30	5			
Week 1, Extreme Problem, n=96	0			
Week 3, Extreme Problem, n=90	1			
Week 5, Extreme Problem, n=95	1			
Week 7, Extreme Problem, n=86	0			
Week 9, Extreme Problem, n=90	2			
Week 13, Extreme Problem, n=73	2			
Week 17, Extreme Problem, n=74	1			
Week 21, Extreme Problem, n=63	0			
Week 25, Extreme Problem, n=59	0			
Week 37, Extreme Problem, n=37	0			
Week 49, Extreme Problem, n=23	0			
Week 61, Extreme Problem, n=16	0			
Week 73, Extreme Problem, n=8	0			
Week 85, Extreme Problem, n=4	0			
Week 97, Extreme Problem, n=1	0			
Follow-up, Extreme Problem, n=30	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 5 Response Levels for EQ-5D-5L Self-Care Domain

End point title	Number of Subjects With 5 Response Levels for EQ-5D-5L Self-Care Domain

End point description:

EQ-5D-5L: subjects rated assessed level of current health using 5 domains: mobility, self-care, usual activities, pain and discomfort, anxiety, and depression. EQ-5D self-care domain had 5 responses: no problem, slight problem, moderate problem, severe problem and extreme problem. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects from the DDR deficient measurable disease population with a baseline PRO assessment and at least 1 post-baseline PRO assessment prior to the end of treatment. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table; however, may not have evaluable data for every row. Here, "n" signifies number of subjects evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 3, 5,7, 9, 13, 17, 21, 25, 37, 49, 61, 73, 85, 97, Follow-up Visit (28 days after last dose) [maximum duration of 25 months]

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Subjects				
Week 1, No Problem, n=95	65			
Week 3, No Problem, n=90	63			
Week 5, No Problem, n=95	62			
Week 7, No Problem, n=85	59			
Week 9, No Problem, n=90	64			
Week 13, No Problem, n=73	51			
Week 17, No Problem, n=74	55			
Week 21, No Problem, n=63	44			
Week 25, No Problem, n=59	39			
Week 37, No Problem, n=37	25			
Week 49, No Problem, n=23	18			
Week 61, No Problem, n=16	11			
Week 73, No Problem, n=8	7			
Week 85, No Problem, n=4	4			
Week 97, No Problem, n=1	1			
Follow-up, No Problem, n=30	19			
Week 1, Slight Problem, n=95	18			
Week 3, Slight Problem, n=90	17			
Week 5, Slight Problem, n=95	20			

Week 7, Slight Problem, n=85	14			
Week 9, Slight Problem, n=90	15			
Week 13, Slight Problem, n=73	14			
Week 17, Slight Problem, n=74	13			
Week 21, Slight Problem, n=63	12			
Week 25, Slight Problem, n=59	13			
Week 37, Slight Problem, n=37	10			
Week 49, Slight Problem, n=23	4			
Week 61, Slight Problem, n=16	5			
Week 73, Slight Problem, n=8	1			
Week 85, Slight Problem, n=4	0			
Week 97, Slight Problem, n=1	0			
Follow-up Slight Problem, n=30	3			
Week 1, Moderate Problem, n=95	9			
Week 3, Moderate Problem, n=90	8			
Week 5, Moderate Problem, n=95	12			
Week 7, Moderate Problem, n=85	12			
Week 9, Moderate Problem, n=90	8			
Week 13, Moderate Problem, n=73	3			
Week 17, Moderate Problem, n=74	4			
Week 21, Moderate Problem, n=63	5			
Week 25, Moderate Problem, n=59	7			
Week 37, Moderate Problem, n=37	2			
Week 49, Moderate Problem, n=23	1			
Week 61, Moderate Problem, n=16	0			
Week 73, Moderate Problem, n=8	0			
Week 85, Moderate Problem, n=4	0			
Week 97, Moderate Problem, n=1	0			
Follow-up, Moderate Problem, n=30	7			
Week 1, Severe Problem, n=95	3			
Week 3, Severe Problem, n=90	2			
Week 5, Severe Problem, n=95	1			
Week 7, Severe Problem, n=85	0			
Week 9, Severe Problem, n=90	2			
Week 13, Severe Problem, n=73	4			
Week 17, Severe Problem, n=74	2			
Week 21, Severe Problem, n=63	2			
Week 25, Severe Problem, n=59	0			
Week 37, Severe Problem, n=37	0			
Week 49, Severe Problem, n=23	0			
Week 61, Severe Problem, n=16	0			
Week 73, Severe Problem, n=8	0			
Week 85, Severe Problem, n=4	0			
Week 97, Severe Problem, n=1	0			
Follow-up, Severe Problem, n=30	1			
Week 1, Extreme Problem, n=95	0			
Week 3, Extreme Problem, n=90	0			
Week 5, Extreme Problem, n=95	0			
Week 7, Extreme Problem, n=85	0			
Week 9, Extreme Problem, n=90	1			
Week 13, Extreme Problem, n=73	1			
Week 17, Extreme Problem, n=74	0			

Week 21, Extreme Problem, n=63	0			
Week 25, Extreme Problem, n=59	0			
Week 37, Extreme Problem, n=37	0			
Week 49, Extreme Problem, n=23	0			
Week 61, Extreme Problem, n=16	0			
Week 73, Extreme Problem, n=8	0			
Week 85, Extreme Problem, n=4	0			
Week 97, Extreme Problem, n=1	0			
Follow-up, Extreme Problem, n=30	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 5 Response Levels for EQ-5D-5L Usual Activity Domain

End point title	Number of Subjects With 5 Response Levels for EQ-5D-5L Usual Activity Domain

End point description:

EQ-5D-5L: subjects rated assessed level of current health using 5 domains: mobility, self-care, usual activities, pain and discomfort, anxiety, and depression. EQ-5D usual activities domain had 5 responses: no problem, slight problem, moderate problem, severe problem and extreme problem. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects from the DDR deficient measurable disease population with a baseline PRO assessment and at least 1 post-baseline PRO assessment prior to the end of treatment. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table; however, may not have evaluable data for every row. Here, "n" signifies number of subjects evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 3, 5,7, 9, 13, 17, 21, 25, 37, 49, 61, 73, 85, 97, Follow-up Visit (28 days after last dose) [maximum duration of 25 months]

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Subjects				
Week 1, No Problem, n=96	33			
Week 3, No Problem, n=90	33			
Week 5, No Problem, n=95	36			
Week 7, No Problem, n=85	34			
Week 9, No Problem, n=90	41			
Week 13, No Problem, n=73	36			
Week 17, No Problem, n=74	36			
Week 21, No Problem, n=63	35			
Week 25, No Problem, n=59	29			
Week 37, No Problem, n=37	17			
Week 49, No Problem, n=23	11			
Week 61, No Problem, n=16	8			
Week 73, No Problem, n=8	6			

Week 85, No Problem, n=4	2			
Week 97, No Problem, n=1	1			
Follow-up, No Problem, n=30	10			
Week 1, Slight Problem, n=96	30			
Week 3, Slight Problem, n=90	26			
Week 5, Slight Problem, n=95	30			
Week 7, Slight Problem, n=85	24			
Week 9, Slight Problem, n=90	26			
Week 13, Slight Problem, n=73	22			
Week 17, Slight Problem, n=74	21			
Week 21, Slight Problem, n=63	13			
Week 25, Slight Problem, n=59	12			
Week 37, Slight Problem, n=37	10			
Week 49, Slight Problem, n=23	5			
Week 61, Slight Problem, n=16	4			
Week 73, Slight Problem, n=8	0			
Week 85, Slight Problem, n=4	2			
Week 97, Slight Problem, n=1	0			
Follow-up, Slight Problem, n=30	10			
Week 1, Moderate Problem, n=96	19			
Week 3, Moderate Problem, n=90	22			
Week 5, Moderate Problem, n=95	21			
Week 7, Moderate Problem, n=85	22			
Week 9, Moderate Problem, n=90	15			
Week 13, Moderate Problem, n=73	10			
Week 17, Moderate Problem, n=74	14			
Week 21, Moderate Problem, n=63	12			
Week 25, Moderate Problem, n=59	12			
Week 37, Moderate Problem, n=37	7			
Week 49, Moderate Problem, n=23	6			
Week 61, Moderate Problem, n=16	3			
Week 73, Moderate Problem, n=8	2			
Week 85, Moderate Problem, n=4	0			
Week 97, Moderate Problem, n=1	0			
Follow-up, Moderate Problem, n=30	5			
Week 1, Severe Problem, n=96	10			
Week 3, Severe Problem, n=90	8			
Week 5, Severe Problem, n=95	4			
Week 7, Severe Problem, n=85	3			
Week 9, Severe Problem, n=90	5			
Week 13, Severe Problem, n=73	2			
Week 17, Severe Problem, n=74	2			
Week 21, Severe Problem, n=63	2			
Week 25, Severe Problem, n=59	6			
Week 37, Severe Problem, n=37	3			
Week 49, Severe Problem, n=23	1			
Week 61, Severe Problem, n=16	1			
Week 73, Severe Problem, n=8	0			
Week 85, Severe Problem, n=4	0			
Week 97, Severe Problem, n=1	0			
Follow-up, Severe Problem, n=30	5			
Week 1, Extreme Problem, n=96	4			

Week 3, Extreme Problem, n=90	1			
Week 5, Extreme Problem, n=95	4			
Week 7, Extreme Problem, n=85	2			
Week 9, Extreme Problem, n=90	3			
Week 13, Extreme Problem, n=73	3			
Week 17, Extreme Problem, n=74	1			
Week 21, Extreme Problem, n=63	1			
Week 25, Extreme Problem, n=59	0			
Week 37, Extreme Problem, n=37	0			
Week 49, Extreme Problem, n=23	0			
Week 61, Extreme Problem, n=16	0			
Week 73, Extreme Problem, n=8	0			
Week 85, Extreme Problem, n=4	0			
Week 97, Extreme Problem, n=1	0			
Follow-up, Extreme Problem, n=30	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 5 Response Levels for EQ-5D-5L Pain and Discomfort Domain

End point title	Number of Subjects With 5 Response Levels for EQ-5D-5L Pain and Discomfort Domain

End point description:

EQ-5D-5L: subjects rated assessed level of current health using 5 domains: mobility, self-care, usual activities, pain and discomfort, anxiety, and depression. EQ-5D pain and discomfort domain had 5 responses: no problem, slight problem, moderate problem, severe problem and extreme problem. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects from the DDR deficient measurable disease population with a baseline PRO assessment and at least 1 post-baseline PRO assessment prior to the end of treatment. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table; however, may not have evaluable data for every row. Here, "n" signifies number of subjects evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 3, 5,7, 9, 13, 17, 21, 25, 37, 49, 61, 73, 85, 97, Follow-up Visit (28 days after last dose) [maximum duration of 25 months]

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Subjects				
Week 1, No Problem, n=96	15			
Week 3, No Problem, n=90	25			
Week 5, No Problem, n=95	30			
Week 7, No Problem, n=85	26			
Week 9, No Problem, n=90	34			
Week 13, No Problem, n=73	23			
Week 17, No Problem, n=74	27			

Week 21, No Problem, n=63	24			
Week 25, No Problem, n=59	22			
Week 37, No Problem, n=37	12			
Week 49, No Problem, n=23	11			
Week 61, No Problem, n=16	6			
Week 73, No Problem, n=8	2			
Week 85, No Problem, n=4	2			
Week 9, No Problem, n=1	0			
Follow-up, No Problem, n=30	9			
Week 1, Slight Problem, n=96	35			
Week 3, Slight Problem, n=90	25			
Week 5, Slight Problem, n=95	27			
Week 7, Slight Problem, n=85	32			
Week 9, Slight Problem, n=90	29			
Week 13, Slight Problem, n=73	33			
Week 17, Slight Problem, n=74	25			
Week 21, Slight Problem, n=63	19			
Week 25, Slight Problem, n=59	17			
Week 37, Slight Problem, n=37	12			
Week 49, Slight Problem, n=23	3			
Week 61, Slight Problem, n=16	5			
Week 73, Slight Problem, n=8	4			
Week 85, Slight Problem, n=4	2			
Week 97, Slight Problem, n=1	1			
Follow-up, Slight Problem, n=30	8			
Week 1, Moderate Problem, n=96	30			
Week 3, Moderate Problem, n=90	32			
Week 5, Moderate Problem, n=95	29			
Week 7, Moderate Problem, n=85	23			
Week 9, Moderate Problem, n=90	21			
Week 13, Moderate Problem, n=73	12			
Week 17, Moderate Problem, n=74	17			
Week 21, Moderate Problem, n=63	17			
Week 25, Moderate Problem, n=59	17			
Week 37, Moderate Problem, n=37	10			
Week 49, Moderate Problem, n=23	7			
Week 61, Moderate Problem, n=16	5			
Week 73, Moderate Problem, n=8	1			
Week 85, Moderate Problem, n=4	0			
Week 97, Moderate Problem, n=1	0			
Follow-up, Moderate Problem, n=30	9			
Week 1, Severe Problem, n=96	16			
Week 3, Severe Problem, n=90	8			
Week 5, Severe Problem, n=95	9			
Week 7, Severe Problem, n=85	4			
Week 9, Severe Problem, n=90	6			
Week 13, Severe Problem, n=73	3			
Week 17, Severe Problem, n=74	5			
Week 21, Severe Problem, n=63	2			
Week 25, Severe Problem, n=59	3			
Week 37, Severe Problem, n=37	3			
Week 49, Severe Problem, n=23	2			

Week 61, Severe Problem, n=16	0			
Week 73, Severe Problem, n=8	1			
Week 85, Severe Problem, n=4	0			
Week 97, Severe Problem, n=1	0			
Follow-up, Severe Problem, n=30	4			
Week 1, Extreme Problem, n=96	0			
Week 3, Extreme Problem, n=90	0			
Week 5, Extreme Problem, n=95	0			
Week 7, Extreme Problem, n=85	0			
Week 9, Extreme Problem, n=90	0			
Week 13, Extreme Problem, n=73	2			
Week 17, Extreme Problem, n=74	0			
Week 21, Extreme Problem, n=63	1			
Week 25, Extreme Problem, n=59	0			
Week 37, Extreme Problem, n=37	0			
Week 49, Extreme Problem, n=23	0			
Week 61, Extreme Problem, n=16	0			
Week 73, Extreme Problem, n=8	0			
Week 85, Extreme Problem, n=4	0			
Week 97, Extreme Problem, n=1	0			
Follow-up, Extreme Problem, n=30	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With 5 Response Levels for EQ-5D-5L Anxiety and Depression Domain

End point title	Number of Subjects With 5 Response Levels for EQ-5D-5L Anxiety and Depression Domain

End point description:

EQ-5D-5L: subjects rated assessed level of current health using 5 domains: mobility, self-care, usual activities, pain and discomfort, anxiety, and depression. EQ-5D anxiety and depression domain had 5 responses: no problem, slight problem, moderate problem, severe problem and extreme problem. Final analyses for this endpoint was till the cutoff date 04 September 2020. All subjects from the DDR deficient measurable disease population with a baseline PRO assessment and at least 1 post-baseline PRO assessment prior to the end of treatment. All subjects reported under 'Number of Subjects Analyzed' contributed data to the table; however, may not have evaluable data for every row. Here, "n" signifies number of subjects evaluable for specified time points.

End point type	Secondary

End point timeframe:

Baseline, Week 1, 3, 5,7, 9, 13, 17, 21, 25, 37, 49, 61, 73, 85, 97, Follow-up Visit (28 days after last dose) [maximum duration of 25 months]

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	97			
Units: Subjects				
Week 1, No Problem, n=96	48			
Week 3, No Problem, n=90	45			
Week 5, No Problem, n=95	43			
Week 7, No Problem, n=85	45			
Week 9, No Problem, n=90	49			
Week 13, No Problem, n=73	40			
Week 17, No Problem, n=74	40			
Week 21, No Problem, n=63	41			
Week 25, No Problem, n=59	29			
Week 37, No Problem, n=37	20			
Week 49, No Problem, n=23	12			
Week 61, No Problem, n=16	8			
Week 73, No Problem, n=8	4			
Week 85, No Problem, n=4	2			
Week 97, No Problem, n=1	1			
Follow-up, No Problem, n=30	16			
Week 1, Slight Problem, n=96	30			
Week 3, Slight Problem, n=90	27			
Week 5, Slight Problem, n=95	35			
Week 7, Slight Problem, n=85	30			
Week 9, Slight Problem, n=90	27			
Week 13, Slight Problem, n=73	23			
Week 17, Slight Problem, n=74	21			
Week 21, Slight Problem, n=63	15			
Week 25, Slight Problem, n=59	24			
Week 37, Slight Problem, n=37	14			
Week 49, Slight Problem, n=23	9			
Week 61, Slight Problem, n=16	8			
Week 73, Slight Problem, n=8	3			
Week 85, Slight Problem, n=4	2			
Week 97, Slight Problem, n=1	0			
Follow-up, Slight Problem, n=30	6			
Week 1, Moderate Problem, n=96	18			
Week 3, Moderate Problem, n=90	17			
Week 5, Moderate Problem, n=95	16			
Week 7, Moderate Problem, n=85	7			
Week 9, Moderate Problem, n=90	12			
Week 13, Moderate Problem, n=73	6			
Week 17, Moderate Problem, n=74	12			
Week 21, Moderate Problem, n=63	7			
Week 25, Moderate Problem, n=59	4			
Week 37, Moderate Problem, n=37	3			
Week 49, Moderate Problem, n=23	2			
Week 61, Moderate Problem, n=16	0			
Week 73, Moderate Problem, n=8	1			
Week 85, Moderate Problem, n=4	0			
Week 97, Moderate Problem, n=1	0			

Follow-up, Moderate Problem, n=30	5			
Week 1, Severe Problem, n=96	0			
Week 3, Severe Problem, n=90	1			
Week 5, Severe Problem, n=95	0			
Week 7, Severe Problem, n=85	2			
Week 9, Severe Problem, n=90	1			
Week 13, Severe Problem, n=73	2			
Week 17, Severe Problem, n=74	0			
Week 21, Severe Problem, n=63	0			
Week 25, Severe Problem, n=59	2			
Week 37, Severe Problem, n=37	0			
Week 49, Severe Problem, n=23	0			
Week 61, Severe Problem, n=16	0			
Week 73, Severe Problem, n=8	0			
Week 85, Severe Problem, n=4	0			
Week 97, Severe Problem, n=1	0			
Follow-up, Severe Problem, n=30	3			
Week 1, Extreme Problem, n=96	0			
Week 3, Extreme Problem, n=90	0			
Week 5, Extreme Problem, n=95	1			
Week 7, Extreme Problem, n=85	1			
Week 9, Extreme Problem, n=90	1			
Week 13, Extreme Problem, n=73	2			
Week 17, Extreme Problem, n=74	1			
Week 21, Extreme Problem, n=63	0			
Week 25, Extreme Problem, n=59	0			
Week 37, Extreme Problem, n=37	0			
Week 49, Extreme Problem, n=23	0			
Week 61, Extreme Problem, n=16	0			
Week 73, Extreme Problem, n=8	0			
Week 85, Extreme Problem, n=4	0			
Week 97, Extreme Problem, n=1	0			
Follow-up, Extreme Problem, n=30	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Pre-dose Plasma Concentration (Ctrough) of Talazoparib

End point title	Pre-dose Plasma Concentration (Ctrough) of Talazoparib

End point description:

Ctrough was defined as pre-dose plasma concentration during dosing and observed directly from data. Pharmacokinetic (PK) population included all subjects from the safety population who had at least 1 reportable drug concentration data point. Here, “Number of Subjects Analyzed” signifies subjects evaluable for this endpoint and "n” signifies subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

Pre-dose at Week 1, 5, 9 and 13

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: nanograms per milliliter				
geometric mean (geometric coefficient of variation)				
At Week 1, n=92	2631.898 (± 23.2043)			
At Week 5, n=82	4748.147 (± 63.2488)			
At Week 9, n=71	4213.250 (± 52.8028)			
At Week 13, n=55	4378.123 (± 47.5360)			

Statistical analyses

No statistical analyses for this end point

Secondary: Post-dose Plasma Concentration (Ctrough) of Talazoparib

End point title	Post-dose Plasma Concentration (Ctrough) of Talazoparib

End point description:

Plasma concentration was measured 2 hours after dosing and observed directly from data. PK population included all subjects from the safety population who had at least 1 reportable drug concentration data point. Here, “Number of Subjects Analyzed” signifies subjects evaluable for this endpoint and "n” signifies subjects evaluable at specified time points.

End point type	Secondary

End point timeframe:

2 hours post-dose at Week 1 and 5

End point values	Talazoparib			
Subject group type	Reporting group			
Number of subjects analysed	31			
Units: nanograms per milliliter				
geometric mean (geometric coefficient of variation)				
At week 1, n=25	2289.540 (± 51.0724)			
At Week 5, n=31	10713.918 (± 49.4248)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs and Non-SAEs: Baseline up to 28 days after last dose of study drug (maximum up to 37 months); All-cause mortality: During study included safety follow up and beyond that (approximately 69 months of study)

Adverse event reporting additional description:

Same event may appear as both an AE and serious adverse event (SAE). However, what is presented are distinct events. An event may be categorized as serious in 1 subject and as non-serious in another, or a subject may have experienced both a serious and non-serious event. Safety population set was analyzed.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Talazoparib

Reporting group description:

Subjects received talazoparib 1 milligram per day (mg/day) orally until radiographic progression that was determined by independent central review, unacceptable toxicity, withdrawal of consent, or death. Talazoparib was continued upon disease progression only if, in the opinion of the investigator the subjects was clinically benefitting, no new concurrent systemic therapy was initiated, and the sponsor was notified. Maximum duration of treatment was approximately 36 months.

Serious adverse events	Talazoparib		
Total subjects affected by serious adverse events			
subjects affected / exposed	51 / 127 (40.16%)		
number of deaths (all causes)	45		
number of deaths resulting from adverse events	11		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma of colon			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			

subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Neoplasm progression				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pancreatic carcinoma				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to spine				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Hypotension				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Disease progression				
subjects affected / exposed	5 / 127 (3.94%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 5			
General physical health deterioration				
subjects affected / exposed	2 / 127 (1.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			

Pain				
subjects affected / exposed	2 / 127 (1.57%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	2 / 127 (1.57%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Penile pain				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Pulmonary embolism				
subjects affected / exposed	9 / 127 (7.09%)			
occurrences causally related to treatment / all	1 / 9			
deaths causally related to treatment / all	0 / 1			
Dyspnoea				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Asthma				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Platelet count decreased				
subjects affected / exposed	2 / 127 (1.57%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
White blood cell count decreased				

subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
SARS-CoV-2 test positive			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Subdural haematoma			
subjects affected / exposed	2 / 127 (1.57%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Overdose			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardio-respiratory arrest			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Hemianopia			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Hypoaesthesia				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paraesthesia				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	1 / 127 (0.79%)			
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	9 / 127 (7.09%)			
occurrences causally related to treatment / all	7 / 10			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				
subjects affected / exposed	1 / 127 (0.79%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Inguinal hernia			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dysuria			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Pain in extremity			
subjects affected / exposed	2 / 127 (1.57%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bursitis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	4 / 127 (3.15%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			

subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neutropenic sepsis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Parotitis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	4 / 127 (3.15%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	1 / 127 (0.79%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	3 / 127 (2.36%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	2 / 127 (1.57%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Talazoparib		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	120 / 127 (94.49%)		
Vascular disorders			
Hot flush			
subjects affected / exposed	12 / 127 (9.45%)		
occurrences (all)	13		
Hypertension			
subjects affected / exposed	7 / 127 (5.51%)		
occurrences (all)	9		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	32 / 127 (25.20%)		
occurrences (all)	62		
Pyrexia			
subjects affected / exposed	10 / 127 (7.87%)		
occurrences (all)	18		
Oedema peripheral			
subjects affected / exposed	23 / 127 (18.11%)		
occurrences (all)	32		
Fatigue			
subjects affected / exposed	28 / 127 (22.05%)		
occurrences (all)	39		
Chest pain			
subjects affected / exposed	9 / 127 (7.09%)		
occurrences (all)	11		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	10 / 127 (7.87%)		
occurrences (all)	10		
Dyspnoea			
subjects affected / exposed	17 / 127 (13.39%)		
occurrences (all)	22		
Psychiatric disorders			

Insomnia subjects affected / exposed occurrences (all)	8 / 127 (6.30%) 10		
Investigations Lymphocyte count decreased subjects affected / exposed occurrences (all)	11 / 127 (8.66%) 25		
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	8 / 127 (6.30%) 10		
Alanine aminotransferase increased subjects affected / exposed occurrences (all)	7 / 127 (5.51%) 7		
White blood cell count decreased subjects affected / exposed occurrences (all)	13 / 127 (10.24%) 32		
Weight decreased subjects affected / exposed occurrences (all)	7 / 127 (5.51%) 7		
Platelet count decreased subjects affected / exposed occurrences (all)	27 / 127 (21.26%) 80		
Neutrophil count decreased subjects affected / exposed occurrences (all)	22 / 127 (17.32%) 43		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	9 / 127 (7.09%) 9		
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all)	8 / 127 (6.30%) 8		
Dizziness subjects affected / exposed occurrences (all)	15 / 127 (11.81%) 20		

Paraesthesia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	8 / 127 (6.30%) 12 9 / 127 (7.09%) 11		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	67 / 127 (52.76%) 208		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	27 / 127 (21.26%) 29 22 / 127 (17.32%) 28 45 / 127 (35.43%) 65 16 / 127 (12.60%) 17		
Renal and urinary disorders Haematuria subjects affected / exposed occurrences (all)	8 / 127 (6.30%) 10		
Musculoskeletal and connective tissue disorders Pain in extremity subjects affected / exposed occurrences (all) Bone pain subjects affected / exposed occurrences (all) Back pain	13 / 127 (10.24%) 17 9 / 127 (7.09%) 12		

subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all)	19 / 127 (14.96%) 31 19 / 127 (14.96%) 30		
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Urinary tract infection subjects affected / exposed occurrences (all)	 8 / 127 (6.30%) 8 10 / 127 (7.87%) 15		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 38 / 127 (29.92%) 57		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 March 2017	Safety related updates included: - Increased the frequency of clinical laboratory tests after week 25 from every 12 weeks to every 8 weeks for increased patient safety and consistency across talazoparib studies. - Added guidance for dose modification of talazoparib and updates talazoparib product information for increased patient safety and consistency across talazoparib studies.
15 November 2018	The primary purpose of this Amendment is to address updated information reported in the August 2018 version of the Talazoparib Investigator's Brochure. In addition, guidance for talazoparib dose modifications due to adverse events was updated to align with the Risk Management Committee (RMC) recommendations and the proposed regional labels. Changes included: • Extension of the time required, for contraceptive use and for patients to refrain from sperm donation, from 105 days to 4 months. • Clarification/changes regarding prior and concomitant medications. • Clarifications to responses to adverse events, including talazoparib dose modifications. • Updated safety and efficacy data from clinical studies in patients that have taken talazoparib. • Updated pharmacokinetics data. • Update to the benefits and risks assessment. • The section pertaining to medication errors was updated to address talazoparib overdose.
22 September 2022	Safety related updates included: Talazoparib Benefits and Risks Assessment section was amended with updated information reported in the May 2021 version of the Talazoparib Investigator's Brochure.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported