Clinical trial results:
TRITON3: A Multicenter, Randomized, Open-label Phase 3 Study of Rucaparib Versus Physician's Choice of Therapy for Patients with Metastatic Castration-resistant Prostate Cancer Associated with Homologous Recombination Deficiency

Summary

EudraCT number	2016-003163-20
Trial protocol	GB IE BE ES DK DE IT
Global end of trial date	08 August 2024

Results information

Result version number	v1 (current)
This version publication date	23 August 2025
First version publication date	23 August 2025

Trial information

Trial identification

Sponsor protocol code	CO-338-063

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02975934
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	pharmaand GmbH
Sponsor organisation address	Taborstraße 1, Wien, Austria, 1020
Public contact	Medical Information Department, pharmaand GmbH, +43 13560006, medinfo@pharmaand.com
Scientific contact	Medical Information Department, pharmaand GmbH, +43 13560006, medinfo@pharmaand.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	08 August 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 August 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of rucaparib versus physician’s choice of treatment based on independent radiology review (IRR) of radiographic progression free survival (rPFS) in metastatic castration-resistant prostate cancer (mCRPC) participants with homologous recombination deficiency (HRD) who progressed on prior androgen receptor (AR)-directed therapy and had not yet received chemotherapy in the castration-resistant setting.

Protection of trial subjects:

The study was conducted in accordance with the protocol and applicable standard operating procedures (SOPs); and in compliance with the Declaration of Helsinki, the International Council on Harmonisation Guidelines for Good Clinical Practice, and regulatory requirements as applicable.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 June 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: 13
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Canada: 60
Country: Number of subjects enrolled	Denmark: 11
Country: Number of subjects enrolled	France: 36
Country: Number of subjects enrolled	Germany: 12
Country: Number of subjects enrolled	Ireland: 27
Country: Number of subjects enrolled	Israel: 11
Country: Number of subjects enrolled	Italy: 15
Country: Number of subjects enrolled	Spain: 52
Country: Number of subjects enrolled	United Kingdom: 56
Country: Number of subjects enrolled	United States: 107
Worldwide total number of subjects	405
EEA total number of subjects	158

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)	116
From 65 to 84 years	273
85 years and over	16

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were randomized to receive rucaparib or physician’s choice of docetaxel or AR-directed therapy (abiraterone acetate or enzalutamide, whichever the participant had not yet received).

Period 1

Period 1 title	Treatment Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Rucaparib

Arm description:

Oral rucaparib (monotherapy).

Arm type	Experimental
Investigational medicinal product name	Rucaparib
Investigational medicinal product code	CO-338
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rucaparib was administered daily.

Arm title	Abiraterone Acetate or Enzalutamide or Docetaxel

Arm description:

Oral abiraterone acetate (monotherapy, given in combination with prednisone). Oral enzalutamide (monotherapy). Intravenous docetaxel (monotherapy, given in combination with prednisone or prednisolone).

Arm type	Active comparator
Investigational medicinal product name	Abiraterone acetate
Investigational medicinal product code	
Other name	Zytiga
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Abiraterone acetate was administered daily.

Investigational medicinal product name	Enzalutamide
Investigational medicinal product code	
Other name	Xtandi
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Enzalutamide was administered daily.

Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	Taxotere

Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

Docetaxel was administered daily.

Number of subjects in period 1	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel
Started	270	135
Received at least 1 dose of study drug	270	130
Safety Population	270	130
Completed	270	130
Not completed	0	5
Never initiated study drug	-	5

Period 2

Period 2 title	Cross-Over Phase
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Rucaparib (Cross-Over Phase)

Arm description:

Oral rucaparib (monotherapy).

Rucaparib: Rucaparib was administered daily. Participants from the Abiraterone Acetate/Enzalutamide/Docetaxel arm who completed the Treatment Phase and radiographically progressed by IRR received rucaparib treatment during the Cross-Over Phase.

After analysis of the primary endpoint, investigator-assessed radiographic disease progression was used for cross-over eligibility evaluation.

Arm type	Experimental
Investigational medicinal product name	Rucaparib
Investigational medicinal product code	CO-338
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Rucaparib was administered daily.

Number of subjects in period 2[1]	Rucaparib (Cross-Over Phase)
Started	70
Received at least 1 dose of study drug	70
Safety Population	70
Completed	70

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Not all participants who completed Period 1 proceeded to Period 2.

Baseline characteristics

Reporting groups	
Reporting group title	Rucaparib
Reporting group description:	
Oral rucaparib (monotherapy).	
Reporting group title	Abiraterone Acetate or Enzalutamide or Docetaxel
Reporting group description:	
Oral abiraterone acetate (monotherapy, given in combination with prednisone). Oral enzalutamide (monotherapy). Intravenous docetaxel (monotherapy, given in combination with prednisone or prednisolone).	

Reporting group values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel	Total
Number of subjects	270	135	405
Age categorical Units: Subjects			
<=18 years	0	0	0
Between 18 and 65 years	84	32	116
>=65 years	186	103	289
Age continuous Units: years			
median	70	71	
full range (min-max)	45 to 90	47 to 92	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	270	135	405
Ethnicity Units: Subjects			
Hispanic or Latino	3	4	7
Not Hispanic or Latino	216	103	319
Unknown or Not Reported	51	28	79
Race Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	4	1	5
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	10	4	14
White	199	103	302
More than one race	3	0	3
Unknown or Not Reported	53	27	80
Region of Enrollment Units: Subjects			
North America	111	56	167
Europe	141	73	214
Australia	10	3	13
Israel	8	3	11

Eastern Cooperative Oncology Group (ECOG) Performance Status (at Stratification)			
ECOG Performance Status Scale. ECOG 0 = Fully active, able to carry on all pre-disease performance without restriction. ECOG 1 = Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature (for example, light house work or office work).			
Units: Subjects			
ECOG 0	132	68	200
ECOG 1	138	67	205
Gene Alteration (at stratification)			
BRCA1 = Breast Cancer 1 Gene BRCA2 = Breast Cancer 2 Gene ATM = Ataxia Telangiectasia Mutated Serine/Threonine Kinase			
Units: Subjects			
BRCA1	29	15	44
BRCA2	172	86	258
ATM	69	34	103
Prior Therapies for Castration-resistant Prostate Cancer (CRPC) Units: Subjects			
0 therapy	48	26	74
≥1 therapy	222	109	331
Gleason score ≥8 at diagnosis Units: Subjects			
Gleason score ≥8	173	96	269
Gleason score <8	97	39	136
Measurable Disease per IRR Units: Subjects			
Yes	106	55	161
No	164	80	244
Baseline prostate specific antigen (PSA) Units: nanograms (ng)/milliliter (mL)			
median	26.9	28.8	
full range (min-max)	0.1 to 1247	0 to 1039	-

End points

End points reporting groups

Reporting group title	Rucaparib
Reporting group description:	
Oral rucaparib (monotherapy).	
Reporting group title	Abiraterone Acetate or Enzalutamide or Docetaxel
Reporting group description:	
Oral abiraterone acetate (monotherapy, given in combination with prednisone). Oral enzalutamide (monotherapy). Intravenous docetaxel (monotherapy, given in combination with prednisone or prednisolone).	
Reporting group title	Rucaparib (Cross-Over Phase)
Reporting group description:	
Oral rucaparib (monotherapy). Rucaparib: Rucaparib was administered daily. Participants from the Abiraterone Acetate/Enzalutamide/Docetaxel arm who completed the Treatment Phase and radiographically progressed by IRR received rucaparib treatment during the Cross-Over Phase. After analysis of the primary endpoint, investigator-assessed radiographic disease progression was used for cross-over eligibility evaluation.	

Primary: rPFS by IRR in Participants With a Breast Cancer Gene (BRCA) Alteration

End point title	rPFS by IRR in Participants With a Breast Cancer Gene (BRCA) Alteration
End point description:	
rPFSirr was defined as time from randomization to the first objective evidence of radiographic progression, or death due to any cause (whichever occurred first). Radiographic disease progression included confirmed soft tissue disease progression and confirmed bone disease progression per modified Response Evaluation Criteria in Solid Tumors (RECIST) Version 1.1 (≥20% increase in sum of the longest diameter [LD] of target lesions or appearance of ≥1 new extra-skeletal lesions and/or unequivocal progression of existing nontarget lesions) or progression by bone determined by Prostate Cancer Working Group 3 (PCWG3) criteria (≥2 new lesions appearing during the first 12-week flare window followed by 2 additional new lesions in confirmatory scan appearing after 12-week flare window; or after the 12-week flare window, ≥2 new lesions relative to the first post-treatment scan confirmed on a subsequent scan). Intent-to-treat (ITT) Population with BRCA mutated mCRPC.	
End point type	Primary
End point timeframe:	
From enrollment to primary completion of study (Total follow-up was up to approximately 4 years)	

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	101		
Units: months				
median (confidence interval 95%)	11.2 (9.2 to 13.8)	6.4 (5.4 to 8.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Rucaparib v Abiraterone Acetate or Enzalutamide or Docetaxel
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.69

Primary: rPFS by IRR in Participants With a BRCA or ATM Alteration Combined

End point title	rPFS by IRR in Participants With a BRCA or ATM Alteration Combined

End point description:

rPFSirr was defined as time from randomization to the first objective evidence of radiographic progression, or death due to any cause (whichever occurred first). Radiographic disease progression included confirmed soft tissue disease progression and confirmed bone disease progression per modified RECIST Version 1.1 (≥20% increase in sum of the LD of target lesions or appearance of ≥1 new extra-skeletal lesions and/or unequivocal progression of existing nontarget lesions) or progression by bone determined by PCWG3 criteria (≥2 new lesions appearing during first 12-week flare window followed by 2 additional new lesions in the confirmatory scan appearing after the 12-week flare window; or after the 12-week flare window, ≥2 new lesions relative to the first post-treatment scan confirmed on a subsequent scan). ITT Population included all randomized participants (participants with BRCA mutated mCRPC and participants with ATM mutated mCRPC).

End point type	Primary

End point timeframe:

From enrollment to primary completion of study (Total follow-up was up to approximately 4 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	270	135		
Units: months				
median (confidence interval 95%)	10.2 (8.3 to 11.2)	6.4 (5.6 to 8.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Rucaparib v Abiraterone Acetate or Enzalutamide or Docetaxel
Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	0.8

Secondary: Overall Survival (OS) in Participants With a BRCA Alteration

End point title	Overall Survival (OS) in Participants With a BRCA Alteration
End point description:	
The OS time was calculated as the time from randomization to death (by any cause) +1 day. Participants who did not die were censored on the date the participant was last known to be alive. ITT Population with BRCA mutated mCRPC.	
End point type	Secondary
End point timeframe:	
From enrollment to completion of study (up to approximately 7 years)	

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	101		
Units: months				
median (confidence interval 95%)	23.2 (19.1 to 25.2)	21.2 (18.0 to 23.1)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Rucaparib v Abiraterone Acetate or Enzalutamide or Docetaxel
Number of subjects included in analysis	302
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5044
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.2

Secondary: OS in Participants With a BRCA or ATM Alteration Combined

End point title	OS in Participants With a BRCA or ATM Alteration Combined

End point description:

The OS time was calculated as the time from randomization to death (by any cause) +1 day. Participants who did not die were censored on the date the participants was last known to be alive. ITT Population included all randomized participants (participants with BRCA mutated mCRPC and participants with ATM mutated mCRPC).

End point type	Secondary

End point timeframe:

From enrollment to completion of study (up to approximately 7 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	270	135		
Units: months				
median (confidence interval 95%)	22.8 (19.0 to 24.2)	21.7 (18.9 to 23.3)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Rucaparib v Abiraterone Acetate or Enzalutamide or Docetaxel

Number of subjects included in analysis	405
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9368
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.26

Secondary: Objective Response Rate (ORR) by IRR in Participants With a BRCA Alteration

End point title	Objective Response Rate (ORR) by IRR in Participants With a BRCA Alteration

End point description:

ORR was defined as the percentage of participants with a confirmed best response of Complete Response (CR) or Partial Response (PR) in participants with measurable disease at study entry. Modified RECIST Version 1.1 criteria was used to determine ORR (that is, CR or PR by IRR assessment and no progression in bone per PCWG3 by IRR assessment). CR was disappearance of all target and non-target lesions; any pathological lymph nodes (whether target or non-target) must have reduction in short axis to <10 millimeters (mm). PR was at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum of diameters. ITT Population with BRCA mutated mCRPC and measurable disease at baseline.

End point type	Secondary

End point timeframe:

From enrollment to primary completion of study (Total follow-up was up to approximately 4 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	82	41		
Units: participants	37	7		

Statistical analyses

No statistical analyses for this end point

Secondary: ORR by IRR in Participants With a BRCA or ATM Alteration Combined

End point title	ORR by IRR in Participants With a BRCA or ATM Alteration Combined

End point description:

ORR was defined as the percentage of participants with a confirmed best response of CR or PR in participants with measurable disease at study entry. Modified RECIST Version 1.1 criteria was used to

determine ORR (that is, CR or PR by IRR assessment and no progression in bone per PCWG3 by IRR assessment). CR was disappearance of all target and non-target lesions; any pathological lymph nodes (whether target or non-target) must have had reduction in short axis to <10 mm. PR was at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum of diameters. ITT Population included all randomized participants (participants with BRCA mutated mCRPC and participants with ATM mutated mCRPC) with measurable disease at baseline.

End point type	Secondary

End point timeframe:

From enrollment to primary completion of study (Total follow-up was up to approximately 4 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	55		
Units: participants	37	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) by IRR in Participants With a BRCA Alteration

End point title	Duration of Response (DOR) by IRR in Participants With a BRCA Alteration

End point description:

DOR was defined as the time from the first confirmed response (CR or PR by modified RECIST Version 1.1 in participants with nodal or visceral ± nodal disease) until the first date that Progressive Disease (PD) (using the same criteria) was documented. ITT Population with BRCA mutated mCRPC and measurable disease at baseline. ‘Overall number of participants analyzed’ = participants with objective response. '9999' signifies 'the upper limit of the confidence interval (CI) is inestimable likely due to the small number of participants in this treatment group'.

End point type	Secondary

End point timeframe:

From enrollment to primary completion of study (Total follow-up was up to approximately 4 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	7		
Units: months				
median (confidence interval 95%)	7.4 (6.4 to 12.7)	7.4 (3.5 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: DOR by IRR in Participants With a BRCA or ATM Alteration Combined

End point title	DOR by IRR in Participants With a BRCA or ATM Alteration Combined

End point description:

DOR was defined as the time from the first confirmed response (CR or PR by modified RECIST Version 1.1 in participants with nodal or visceral ± nodal disease) until the first date that PD (using the same criteria) was documented. ITT Population included all randomized participants (participants with BRCA mutated mCRPC and participants with ATM mutated mCRPC) with measurable disease at baseline. 'Overall number of participants analyzed' = participants with objective response.

End point type	Secondary

End point timeframe:

From enrollment to primary completion of study (Total follow-up was up to approximately 4 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37	9		
Units: months				
median (confidence interval 95%)	7.4 (6.4 to 12.7)	7.4 (3.5 to 14.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: PSA Response in Participants With a BRCA Alteration

End point title	PSA Response in Participants With a BRCA Alteration

End point description:

Confirmed PSA response was defined as ≥ 50% reduction in PSA from baseline on at least two assessments conducted at least 3 weeks apart. PSA response was calculated for all participants with PSA values at baseline and at least one post-baseline assessment. PSA was assessed by a local laboratory. ITT Population with BRCA mutated mCRPC.

End point type	Secondary

End point timeframe:

From enrollment to primary completion of study (up to approximately 5 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	101		
Units: percentage of participants				
number (not applicable)	54.7	26.7		

Statistical analyses

No statistical analyses for this end point

Secondary: PSA Response in Participants With a BRCA or ATM Alteration Combined

End point title	PSA Response in Participants With a BRCA or ATM Alteration Combined

End point description:

Confirmed PSA response was defined as ≥ 50% reduction in PSA from baseline on at least two assessments conducted at least 3 weeks apart. PSA response was calculated for all participants with PSA values at baseline and at least one post-baseline assessment. PSA was assessed by a local laboratory. ITT Population included all randomized participants (participants with BRCA mutated mCRPC and participants with ATM mutated mCRPC).

End point type	Secondary

End point timeframe:

From enrollment to primary completion of study (up to approximately 5 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	270	135		
Units: percentage of participants				
number (not applicable)	41.9	26.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) by IRR at 6 Months in Participants With a BRCA Alteration

End point title	Clinical Benefit Rate (CBR) by IRR at 6 Months in Participants With a BRCA Alteration

End point description:

Defined as the percentage of participants with a CR, PR, and stable disease (SD) according to modified RECIST Version 1.1 with no progression in bone per PCWG3 criteria. The Safety Population included all participants with BRCA mutated mCRPC who received at least one dose of protocol-specified treatment and had 6 months of follow-up prior to the data cutoff.

End point type	Secondary

End point timeframe:

From enrollment to 6 months

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	200	97		
Units: percentage of participants				
number (not applicable)	63.0	22.7		

Statistical analyses

No statistical analyses for this end point

Secondary: CBR by IRR at 6 Months in Participants With a BRCA or ATM Alteration Combined

End point title	CBR by IRR at 6 Months in Participants With a BRCA or ATM Alteration Combined

End point description:

Defined as the percentage of participants with a CR, PR, and SD, according to Modified RECIST Version 1.1 with no progression in bone per PCWG3 Criteria. The Safety Population included all participants who received at least one dose of protocol-specified treatment and had 6 months of follow-up prior to the data cutoff.

End point type	Secondary

End point timeframe:

From enrollment to 6 months

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	269	130		
Units: percentage of participants				
number (not applicable)	57.6	25.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PSA Progression in Participants With a BRCA Alteration

End point title	Time to PSA Progression in Participants With a BRCA Alteration

End point description:

Time to PSA progression was defined as the time from randomization to the date that a ≥ 25% increase and absolute increase of ≥ 2 ng/mL above the nadir (or baseline value for participants who did not have a decline in PSA). The increase was confirmed by a second consecutive assessment conducted at least 3 weeks later. ITT Population with BRCA mutated mCRPC.

End point type	Secondary

End point timeframe:

From enrollment to primary completion of study (up to approximately 5 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	201	101		
Units: months				
median (confidence interval 95%)	6.6 (5.9 to 7.7)	3.8 (3.1 to 4.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PSA Progression in Participants With a BRCA or ATM Alteration Combined

End point title	Time to PSA Progression in Participants With a BRCA or ATM Alteration Combined

End point description:

Time to PSA progression was defined as the time from randomization to the date that a ≥ 25% increase and absolute increase of ≥ 2 ng/mL above the nadir (or baseline value for participants who did not have a decline in PSA). The increase was confirmed by a second consecutive assessment conducted at least 3 weeks later. ITT Population included all randomized participants (participants with BRCA mutated mCRPC and participants with ATM mutated mCRPC).

End point type	Secondary

End point timeframe:

From enrollment to primary completion of study (up to approximately 5 years)

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	270	135		
Units: months				
median (confidence interval 95%)	5.7 (4.6 to 6.5)	3.6 (3.5 to 4.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient-reported Outcome (PRO) in Participants With a BRCA Alteration: Functional Assessment of Cancer Therapy–Prostate (FACT-P)

End point title	Change From Baseline in Patient-reported Outcome (PRO) in Participants With a BRCA Alteration: Functional Assessment of Cancer Therapy–Prostate (FACT-P)

End point description:

Changes in health and pain status from baseline to Week 25 using: FACT-P total score (on a scale of 0 to 156 where a higher score is better quality of life). The greater the decrease in score (that is, more negative) from baseline to Week 25 the greater the decrease in health status. Assessments completed during screening, at study treatment visits (Day 1, Day 15, Day 29, Day 43, Day 57, and every 29 days thereafter), during the Treatment Phase, the Treatment Discontinuation Visit, and during the Follow-up Phase. ITT Population with BRCA mutated mCRPC. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From enrollment to up to approximately 25 weeks

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	35		
Units: units on a scale				
least squares mean (standard error)	-0.8 (± 1.13)	-3.9 (± 2.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in PRO in Participants With a BRCA Alteration: Brief Pain Inventory–Short Form (BPI-SF)

End point title	Change from Baseline in PRO in Participants With a BRCA Alteration: Brief Pain Inventory–Short Form (BPI-SF)

End point description:

Changes in health and pain status from baseline to week 25 using BPI-SF questionnaire (on a scale of 1 to 10, from mild to severe, for pain and pain-interference scores). A decrease indicates less severe pain/interference. Assessments completed during screening, at study treatment visits (Day 1, Day 15, Day 29, Day 43, Day 57, and every 29 days thereafter), during the Treatment Phase, the Treatment Discontinuation Visit, and during the Follow-up Phase. ITT Population with BRCA mutated mCRPC. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure. 'n' = participants evaluable for specified category.

End point type	Secondary

End point timeframe:

From enrollment to up to approximately 25 weeks

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	32		
Units: units on a scale				
arithmetic mean (standard error)				
BPI-SF Pain Score (n=133,32)	-0.32 (± 0.139)	0.14 (± 0.285)		
BPI-SF Interference Score (n=130,31)	-0.28 (± 0.147)	0.65 (± 0.302)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PRO in Participants With a BRCA Alteration: EuroQol 5 Dimensions 5 Level Questionnaire (EQ-5D-5L)

End point title	Change From Baseline in PRO in Participants With a BRCA Alteration: EuroQol 5 Dimensions 5 Level Questionnaire (EQ-5D-5L)

End point description:

Changes in health and pain status from baseline to Week 25 using EuroQol-5D-5L Visual Analogue Scale (VAS); on a scale from 100 to 0, from best to worst health status). The greater the increase in score (including more negative) from baseline to Week 25 the greater the increase in health status. Assessments completed during screening, at study treatment visits (Day 1, Day 15, Day 29, Day 43, Day 57, and every 29 days thereafter), during the Treatment Phase, the Treatment Discontinuation Visit, and during the Follow-up Phase. ITT Population with BRCA mutated mCRPC. Here, 'Overall number of participants analyzed' = participants evaluable for this outcome measure.

End point type	Secondary

End point timeframe:

From enrollment to up to approximately 25 weeks

End point values	Rucaparib	Abiraterone Acetate or Enzalutamide or Docetaxel		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	36		
Units: units on a scale				
least squares mean (standard error)	2.4 (± 1.23)	1.8 (± 2.39)		

Statistical analyses

No statistical analyses for this end point

Secondary: Trough Plasma Pharmacokinetic (PK) (Cmin) of Rucaparib Based on Sparse Sampling

End point title	Trough Plasma Pharmacokinetic (PK) (Cmin) of Rucaparib Based on Sparse Sampling[1]

End point description:

Mean trough PK plasma concentration over time in the safety population with at least one PK sample collected at timepoints Week 5, 9, 13 and 17; only Week 5 data presented. Safety Population with at least 1 PK sample collected.

End point type	Secondary

End point timeframe:

From enrollment to Week 5 of dosing

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint is reporting statistics for the specified arm only.

End point values	Rucaparib			
Subject group type	Reporting group			
Number of subjects analysed	228			
Units: ng/mL				
median (full range (min-max))	1310 (5.5 to 4180)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug through 28 days after receiving the last dose of study drug (approximately 7 years). The Safety Population included all participants who received at least 1 dose of study drug.

Adverse event reporting additional description:

SAEs and AEs were assessed in the Safety Population. After 28 days following last dose of study drug, only SAEs assessed as potentially related to study drug are reported. Events of progression of the participant's underlying cancer, and progression of disease leading to death are not reported as an AE or SAE.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	Rucaparib (Treatment Phase)

Reporting group description:

Oral rucaparib (monotherapy).

Reporting group title	Abiraterone Acetate/Enzalutamide/Docetaxel (Treatment Phase)

Reporting group description:

Oral abiraterone acetate (monotherapy, given in combination with prednisone). Oral enzalutamide (monotherapy). Intravenous docetaxel (monotherapy, given in combination with prednisone or prednisolone).

Reporting group title	Rucaparib (Cross-over Phase)

Reporting group description:

Oral rucaparib (monotherapy). Rucaparib: Rucaparib was administered daily. Participants from the Abiraterone Acetate/Enzalutamide/Docetaxel arm who completed the Treatment Phase and radiographically progressed by IRR received rucaparib treatment during the Cross-Over Phase.

After analysis of the primary endpoint, investigator-assessed radiographic disease progression was used for cross-over eligibility evaluation.

Serious adverse events	Rucaparib (Treatment Phase)	Abiraterone Acetate/Enzalutamide/Docetaxel (Treatment Phase)	Rucaparib (Cross-over Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	81 / 270 (30.00%)	36 / 130 (27.69%)	18 / 70 (25.71%)
number of deaths (all causes)	6	3	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung neoplasm malignant			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			

subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm of eyelid			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic malignant melanoma			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal squamous cell carcinoma			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 270 (0.00%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis superficial			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Fatigue			
subjects affected / exposed	1 / 270 (0.37%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Systemic inflammatory response syndrome			

subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchopneumopathy			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cough			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 270 (0.00%)	2 / 130 (1.54%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	5 / 270 (1.85%)	4 / 130 (3.08%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Blood bilirubin increased			
subjects affected / exposed	0 / 270 (0.00%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blood creatinine increased			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haemorrhage			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 270 (0.37%)	1 / 130 (0.77%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Angina pectoris			
subjects affected / exposed	3 / 270 (1.11%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 270 (0.37%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 270 (0.00%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular fibrillation			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			

subjects affected / exposed	1 / 270 (0.37%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paralysis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuralgia			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 270 (0.00%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sacral radiculopathy			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	0 / 270 (0.00%)	2 / 130 (1.54%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			

subjects affected / exposed	2 / 270 (0.74%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	9 / 270 (3.33%)	0 / 130 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	8 / 9	0 / 0	3 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia			
subjects affected / exposed	1 / 270 (0.37%)	8 / 130 (6.15%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 1	11 / 11	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leukopenia			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic haematoma			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 270 (0.00%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Retinal detachment			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 270 (0.37%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	3 / 270 (1.11%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal fistula			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal perforation			

subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophagitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal haemorrhage			
subjects affected / exposed	0 / 270 (0.00%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 270 (0.37%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholangitis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			

subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic cirrhosis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatotoxicity			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	8 / 270 (2.96%)	0 / 130 (0.00%)	2 / 70 (2.86%)
occurrences causally related to treatment / all	4 / 9	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 270 (0.37%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 270 (0.00%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue			

disorders			
Back pain			
subjects affected / exposed	1 / 270 (0.37%)	2 / 130 (1.54%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Compartment syndrome			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	2 / 270 (0.74%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 270 (0.00%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Blastocystis infection			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	3 / 270 (1.11%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 270 (0.00%)	2 / 130 (1.54%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter infection			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermo-hypodermitis			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			

subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	8 / 270 (2.96%)	1 / 130 (0.77%)	3 / 70 (4.29%)
occurrences causally related to treatment / all	0 / 8	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	2 / 270 (0.74%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella bacteraemia			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	2 / 270 (0.74%)	2 / 130 (1.54%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			

subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	7 / 270 (2.59%)	1 / 130 (0.77%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	2 / 10	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection bacterial			
subjects affected / exposed	0 / 270 (0.00%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	3 / 270 (1.11%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 270 (0.37%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	5 / 270 (1.85%)	0 / 130 (0.00%)	1 / 70 (1.43%)
occurrences causally related to treatment / all	0 / 5	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	1 / 270 (0.37%)	1 / 130 (0.77%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			

subjects affected / exposed	2 / 270 (0.74%)	0 / 130 (0.00%)	0 / 70 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Rucaparib (Treatment Phase)	Abiraterone Acetate/Enzalutamide/Docetaxel (Treatment Phase)	Rucaparib (Cross-over Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	270 / 270 (100.00%)	127 / 130 (97.69%)	67 / 70 (95.71%)
Vascular disorders			
Hot flush			
subjects affected / exposed	17 / 270 (6.30%)	3 / 130 (2.31%)	3 / 70 (4.29%)
occurrences (all)	18	5	3
Hypertension			
subjects affected / exposed	18 / 270 (6.67%)	11 / 130 (8.46%)	5 / 70 (7.14%)
occurrences (all)	36	16	15
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	58 / 270 (21.48%)	20 / 130 (15.38%)	9 / 70 (12.86%)
occurrences (all)	136	36	12
Fatigue			
subjects affected / exposed	117 / 270 (43.33%)	63 / 130 (48.46%)	23 / 70 (32.86%)
occurrences (all)	203	123	41
Oedema peripheral			
subjects affected / exposed	55 / 270 (20.37%)	21 / 130 (16.15%)	14 / 70 (20.00%)
occurrences (all)	70	29	15
Pyrexia			
subjects affected / exposed	15 / 270 (5.56%)	7 / 130 (5.38%)	6 / 70 (8.57%)
occurrences (all)	17	11	6
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	27 / 270 (10.00%)	17 / 130 (13.08%)	8 / 70 (11.43%)
occurrences (all)	28	17	10
Dyspnoea			

subjects affected / exposed	45 / 270 (16.67%)	15 / 130 (11.54%)	6 / 70 (8.57%)
occurrences (all)	66	21	6
Pulmonary embolism			
subjects affected / exposed	6 / 270 (2.22%)	7 / 130 (5.38%)	1 / 70 (1.43%)
occurrences (all)	6	7	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	22 / 270 (8.15%)	14 / 130 (10.77%)	2 / 70 (2.86%)
occurrences (all)	23	16	2
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	67 / 270 (24.81%)	3 / 130 (2.31%)	19 / 70 (27.14%)
occurrences (all)	146	3	44
Aspartate aminotransferase increased			
subjects affected / exposed	65 / 270 (24.07%)	4 / 130 (3.08%)	20 / 70 (28.57%)
occurrences (all)	120	5	46
Blood alkaline phosphatase increased			
subjects affected / exposed	17 / 270 (6.30%)	2 / 130 (1.54%)	2 / 70 (2.86%)
occurrences (all)	19	2	3
Blood bilirubin increased			
subjects affected / exposed	13 / 270 (4.81%)	1 / 130 (0.77%)	7 / 70 (10.00%)
occurrences (all)	43	1	17
Blood creatinine increased			
subjects affected / exposed	55 / 270 (20.37%)	6 / 130 (4.62%)	8 / 70 (11.43%)
occurrences (all)	97	8	10
Lymphocyte count decreased			
subjects affected / exposed	11 / 270 (4.07%)	7 / 130 (5.38%)	4 / 70 (5.71%)
occurrences (all)	27	10	9
Neutrophil count decreased			
subjects affected / exposed	17 / 270 (6.30%)	5 / 130 (3.85%)	4 / 70 (5.71%)
occurrences (all)	64	5	11
Platelet count decreased			
subjects affected / exposed	29 / 270 (10.74%)	0 / 130 (0.00%)	4 / 70 (5.71%)
occurrences (all)	103	0	20
Weight decreased			

subjects affected / exposed	40 / 270 (14.81%)	15 / 130 (11.54%)	10 / 70 (14.29%)
occurrences (all)	65	21	18
White blood cell count decreased			
subjects affected / exposed	18 / 270 (6.67%)	3 / 130 (2.31%)	7 / 70 (10.00%)
occurrences (all)	52	7	27
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	11 / 270 (4.07%)	7 / 130 (5.38%)	1 / 70 (1.43%)
occurrences (all)	11	7	1
Fall			
subjects affected / exposed	15 / 270 (5.56%)	6 / 130 (4.62%)	3 / 70 (4.29%)
occurrences (all)	22	7	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	37 / 270 (13.70%)	11 / 130 (8.46%)	6 / 70 (8.57%)
occurrences (all)	44	12	6
Dysgeusia			
subjects affected / exposed	45 / 270 (16.67%)	18 / 130 (13.85%)	7 / 70 (10.00%)
occurrences (all)	48	22	8
Headache			
subjects affected / exposed	31 / 270 (11.48%)	9 / 130 (6.92%)	5 / 70 (7.14%)
occurrences (all)	42	10	6
Neuropathy peripheral			
subjects affected / exposed	9 / 270 (3.33%)	18 / 130 (13.85%)	1 / 70 (1.43%)
occurrences (all)	9	20	1
Peripheral sensory neuropathy			
subjects affected / exposed	8 / 270 (2.96%)	11 / 130 (8.46%)	2 / 70 (2.86%)
occurrences (all)	8	16	2
Taste disorder			
subjects affected / exposed	7 / 270 (2.59%)	7 / 130 (5.38%)	2 / 70 (2.86%)
occurrences (all)	7	8	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	121 / 270 (44.81%)	24 / 130 (18.46%)	26 / 70 (37.14%)
occurrences (all)	435	30	90
Neutropenia			

subjects affected / exposed	17 / 270 (6.30%)	6 / 130 (4.62%)	4 / 70 (5.71%)
occurrences (all)	37	6	5
Thrombocytopenia			
subjects affected / exposed	24 / 270 (8.89%)	0 / 130 (0.00%)	6 / 70 (8.57%)
occurrences (all)	44	0	8
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	21 / 270 (7.78%)	10 / 130 (7.69%)	3 / 70 (4.29%)
occurrences (all)	23	11	6
Abdominal pain upper			
subjects affected / exposed	15 / 270 (5.56%)	3 / 130 (2.31%)	3 / 70 (4.29%)
occurrences (all)	15	4	3
Constipation			
subjects affected / exposed	76 / 270 (28.15%)	19 / 130 (14.62%)	12 / 70 (17.14%)
occurrences (all)	101	23	16
Diarrhoea			
subjects affected / exposed	85 / 270 (31.48%)	36 / 130 (27.69%)	10 / 70 (14.29%)
occurrences (all)	118	49	11
Dyspepsia			
subjects affected / exposed	18 / 270 (6.67%)	5 / 130 (3.85%)	0 / 70 (0.00%)
occurrences (all)	25	6	0
Nausea			
subjects affected / exposed	137 / 270 (50.74%)	25 / 130 (19.23%)	26 / 70 (37.14%)
occurrences (all)	222	44	41
Stomatitis			
subjects affected / exposed	12 / 270 (4.44%)	10 / 130 (7.69%)	0 / 70 (0.00%)
occurrences (all)	20	15	0
Vomiting			
subjects affected / exposed	65 / 270 (24.07%)	11 / 130 (8.46%)	12 / 70 (17.14%)
occurrences (all)	98	16	25
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 270 (1.85%)	26 / 130 (20.00%)	2 / 70 (2.86%)
occurrences (all)	5	28	2
Dry skin			

subjects affected / exposed	23 / 270 (8.52%)	10 / 130 (7.69%)	2 / 70 (2.86%)
occurrences (all)	24	12	2
Photosensitivity reaction			
subjects affected / exposed	27 / 270 (10.00%)	0 / 130 (0.00%)	6 / 70 (8.57%)
occurrences (all)	39	0	7
Pruritus			
subjects affected / exposed	22 / 270 (8.15%)	5 / 130 (3.85%)	2 / 70 (2.86%)
occurrences (all)	24	9	2
Rash			
subjects affected / exposed	19 / 270 (7.04%)	4 / 130 (3.08%)	5 / 70 (7.14%)
occurrences (all)	27	4	6
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	15 / 270 (5.56%)	8 / 130 (6.15%)	4 / 70 (5.71%)
occurrences (all)	17	9	4
Urinary retention			
subjects affected / exposed	5 / 270 (1.85%)	1 / 130 (0.77%)	5 / 70 (7.14%)
occurrences (all)	5	1	7
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	52 / 270 (19.26%)	28 / 130 (21.54%)	9 / 70 (12.86%)
occurrences (all)	69	41	11
Back pain			
subjects affected / exposed	65 / 270 (24.07%)	26 / 130 (20.00%)	13 / 70 (18.57%)
occurrences (all)	97	31	19
Bone pain			
subjects affected / exposed	15 / 270 (5.56%)	4 / 130 (3.08%)	3 / 70 (4.29%)
occurrences (all)	19	4	3
Muscular weakness			
subjects affected / exposed	13 / 270 (4.81%)	4 / 130 (3.08%)	4 / 70 (5.71%)
occurrences (all)	15	4	6
Musculoskeletal chest pain			
subjects affected / exposed	16 / 270 (5.93%)	6 / 130 (4.62%)	6 / 70 (8.57%)
occurrences (all)	20	8	7
Musculoskeletal pain			

subjects affected / exposed	26 / 270 (9.63%)	11 / 130 (8.46%)	5 / 70 (7.14%)
occurrences (all)	29	15	5
Myalgia			
subjects affected / exposed	14 / 270 (5.19%)	9 / 130 (6.92%)	1 / 70 (1.43%)
occurrences (all)	15	10	1
Pain in extremity			
subjects affected / exposed	34 / 270 (12.59%)	14 / 130 (10.77%)	8 / 70 (11.43%)
occurrences (all)	48	18	17
Infections and infestations			
COVID-19			
subjects affected / exposed	16 / 270 (5.93%)	5 / 130 (3.85%)	3 / 70 (4.29%)
occurrences (all)	17	5	3
Urinary tract infection			
subjects affected / exposed	20 / 270 (7.41%)	3 / 130 (2.31%)	7 / 70 (10.00%)
occurrences (all)	29	3	11
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	99 / 270 (36.67%)	29 / 130 (22.31%)	18 / 70 (25.71%)
occurrences (all)	139	43	27
Dehydration			
subjects affected / exposed	9 / 270 (3.33%)	3 / 130 (2.31%)	4 / 70 (5.71%)
occurrences (all)	9	4	4
Hypertriglyceridaemia			
subjects affected / exposed	17 / 270 (6.30%)	4 / 130 (3.08%)	3 / 70 (4.29%)
occurrences (all)	51	5	16
Hypokalaemia			
subjects affected / exposed	12 / 270 (4.44%)	10 / 130 (7.69%)	2 / 70 (2.86%)
occurrences (all)	16	17	2
Hypophosphataemia			
subjects affected / exposed	19 / 270 (7.04%)	7 / 130 (5.38%)	2 / 70 (2.86%)
occurrences (all)	34	13	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 December 2017	It included following changes: - Updated the inclusion criterion for renal function to remove the requirement for serum creatinine ≤1.5 * upper limit of normal (ULN), as glomerular filtration rate (calculated by Cockcroft-Gault) was considered a more appropriate measure (age corrected) for older participants. - Added details and updates to the description of modified RECIST response evaluation and to the PCWG3 criteria for confirmation of disease progression in bone. - Updated version of the EQ-5D-5L Health Questionnaire provided to clarify version to be used in this study. - Clarification that progressive disease was not an adverse event. - Provided requirements on age of archival tissue for homologous recombination repair (HRR) gene testing to improve the probability of satisfactory testing results. Additionally, reinforced that if archival tissue testing in Pre-screening failed, that participant should provide tissue during Screening.
19 June 2018	It included following changes: - Agents that target the AR pathway that were given for metastatic hormone-sensitive prostate cancer and for non-metastatic castrate-resistant cancer were now considered to meet prior AR-therapy requirements. - Implemented a stand-alone Pre-Screening Phase for the confirmation of deleterious BRCA1/2 and ATM gene mutation in tumor tissue. - Allowed participants to be eligible if they had received radiation therapy within 14 days prior to enrolment, since the use of palliative radiotherapy for treatment of bony metastases was allowed during the study, and since separate eligibility criteria required recovery from any toxicities related to prior treatment. - Included clarifications in dose modification that investigators might judge when participants should resume study drug cases of disease-related anemia. - Re-treatment criteria had been integrated with dose modification guidelines.
27 August 2020	It included following changes: - To achieve a better understanding of whether there was a relationship between pneumonitis and rucaparib treatment, Clovis was designating pneumonitis as an adverse events of special interests (AESI) to gather information on all reported cases. - Updated the interval after the last dose of study drug for which men must use contraceptive measures or abstinence or refrain from donating semen, including the specifications for female partners of the men in the study. The interval changed from 6 months to 3 months and was correspond with the latest approved Investigator’s Brochure and product information. - There was clarification throughout the protocol that participants in the Cross-over Phase will not be evaluated by IRR, just by investigator assessment of radiography, and that the interval to initiate treatment with rucaparib in the Cross-over Phase might be >28 days, with sponsor approval. - Clarified that participants might be permitted to cross over to rucaparib treatment if intervening systemic anticancer therapy was administered urgently after Treatment of Physician’s Choice. - Decreased the acceptable level of hemoglobin from ≥10 grams (g)/deciliter (dL) to ≥9 g/dL as part of a participant having adequate bone marrow function to be eligible to cross over from the comparator Treatment of Physician’s Choice to rucaparib. - Changes were made in relation to removing timepoints for collection of blood samples that were not needed for the analysis of circulating cell-free tumor deoxyribonucleic acid (ctDNA).

18 February 2022	Amendment 4 replaced Amendment 3 of the study CO-338-063 protocol, globally, including the Germany-specific version. Significant changes are summarized as follows: • Statistical analyses in the amendment were revised to align with the SAP and following consultation with the FDA. Changes incorporated in the amendment included: • Elevating the OS endpoint to the first secondary endpoint in the step-down analysis procedure. • Adding the Haybittle-Peto stopping rule to adjust for multiple OS analyses since OS data at the time of the primary PFS analysis are anticipated to be immature. A final OS analysis will be performed when these data are mature. • Clarifying the official statistical test used in the hierarchical testing of PFS and OS will be the log-rank test. • Removing the DOR and PSA endpoints from the step-down procedure. The revised step-down procedure will include rPFS by central IRR, OS, then ORR. • Incorporating description of adjustment to eliminate small stratification analyses (eg, < 5 patients). • Clarifying that the ORR endpoint will be analyzed using a CMH test. • Clarified that rPFS assessments specifically by IRR would be removed after patient data unblinding for the primary endpoint analysis, to facilitate subsequent analyses and long-term follow-up of patients using rPFS assessed by investigator only. Radiographic scans would no longer be necessary and did not need to be submitted for IRR after unblinding patient data. • Clarified that after the analysis of the primary endpoint was completed, for patients remaining on TPC, the eligibility for cross over (to rucaparib) would be determined by radiographic progression as assessed by the investigator and scans no longer needed to be read by IRR. • Revised the End-of-Study language. • Aligned the contraceptive measures with the current version of the rucaparib IB. • Clarified the collection of pneumonitis and similar events if they occur after the 28-day safety follow-up period.
27 November 2023	Amendment 5 updated the Study Responsibility and Sponsorship from Clovis Oncology to pharmaand GmbH and Removal of the requirement to collect the following research samples as the primary analysis has been conducted: Biomarker Analysis – ctDNA/genomic DNA from Blood, Pharmacokinetics Evaluation and Post-progression Tumor Biopsy (Optional).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported