Clinical trial results:
TRITON2: A Multicenter, Open-label Phase 2 Study of Rucaparib in Patients with Metastatic Castration-resistant Prostate Cancer Associated with Homologous Recombination Deficiency

Summary

EudraCT number	2016-003162-13
Trial protocol	GB IE ES BE DK FR IT
Global end of trial date	27 July 2021

Results information

Result version number	v1 (current)
This version publication date	29 May 2022
First version publication date	29 May 2022

Trial information

Trial identification

Sponsor protocol code	CO-338-052

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02952534
WHO universal trial number (UTN)	-
Other trial identifiers	IND : 129,840

Notes:

Sponsors

Sponsor organisation name	Clovis Oncology, Inc.
Sponsor organisation address	5500 Flatiron Parkway, Suite 100, Boulder, CO, United States, 80301
Public contact	Dr Lindsey Rolfe, Clovis Oncology, Inc., +44 1223 3645500, lrolfe@clovisoncology.com
Scientific contact	Dr Lindsey Rolfe, Clovis Oncology, Inc., +44 1223 3645500, lrolfe@clovisoncology.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	27 July 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 July 2021
Global end of trial reached?	Yes
Global end of trial date	27 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of rucaparib based on the response rate in metastatic castration-resistant prostate cancer (mCRPC) patients with homologous recombination deficiency (HRD) who progressed on AR-targeted therapy (abiraterone acetate, enzalutamide, apalutamide or investigational AR-targeted agent) and taxane-based chemotherapy in the castration resistant setting

Protection of trial subjects:

Safety was assessed by evaluating hematology, biochemistry, urinalysis, vital signs, and changes in physical examination, and by monitoring the incidence, severity, and relationship of adverse events to rucaparib. Safety data was periodically reviewed by a Data Monitoring Committee (DMC). The DMC was comprised of study investigators and sponsor representatives.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 29
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Belgium: 10
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 25
Country: Number of subjects enrolled	Germany: 20
Country: Number of subjects enrolled	Ireland: 12
Country: Number of subjects enrolled	Italy: 9
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	United States: 113
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Australia: 25
Worldwide total number of subjects	277
EEA total number of subjects	110

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)	65
From 65 to 84 years	205
85 years and over	7

Subject disposition

Recruitment

Recruitment details:

A total of 277 patients were recruited from 102 sites across 12 countries.

Pre-assignment

Screening details:

After providing consent to participate, patients with a deleterious BRCA1/2, ATM, or other HRR gene mutation underwent Screening assessments within 28 days prior to the first dose of rucaparib.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	BRCA Mutation

Arm description:

Patients with a deleterious BRCA (breast cancer susceptibility gene) mutation detected in their tumor.

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

Dosage and administration details:

All patients received open-label oral rucaparib 600 mg BID in continuous 28-day cycles. Patients were to take rucaparib with or without food.

Arm title	ATM Mutation

Arm description:

Patients with a deleterious ATM (ataxia telangiectasia mutated serine/threonine kinase) mutation detected in their tumor.

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

Dosage and administration details:

All patients received open-label oral rucaparib 600 mg BID in continuous 28-day cycles. Patients were to take rucaparib with or without food.

Arm title	CDK12 Mutation

Arm description:

Patients with a deleterious CDK12 (Cyclin-dependent kinase 12) mutation detected in their tumor.

Arm type	Experimental

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

Dosage and administration details:

All patients received open-label oral rucaparib 600 mg BID in continuous 28-day cycles. Patients were to take rucaparib with or without food.

Arm title	CHEK2 Mutation

Arm description:

Patients with a deleterious CHEK2 (Checkpoint Kinase 2) mutation detected in their tumor.

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

Dosage and administration details:

All patients received open-label oral rucaparib 600 mg BID in continuous 28-day cycles. Patients were to take rucaparib with or without food.

Arm title	Other Gene Mutation

Arm description:

Patients with other deleterious HRR (homologous recombination repair) gene mutation detected in their tumor.

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

Dosage and administration details:

All patients received open-label oral rucaparib 600 mg BID in continuous 28-day cycles. Patients were to take rucaparib with or without food.

Number of subjects in period 1	BRCA Mutation	ATM Mutation	CDK12 Mutation
Started	172	59	14
Completed	172	59	14

Number of subjects in period 1	CHEK2 Mutation	Other Gene Mutation
Started	7	25
Completed	7	25

Baseline characteristics

Reporting groups	
Reporting group title	BRCA Mutation
Reporting group description:	
Patients with a deleterious BRCA (breast cancer susceptibility gene) mutation detected in their tumor.	
Reporting group title	ATM Mutation
Reporting group description:	
Patients with a deleterious ATM (ataxia telangiectasia mutated serine/threonine kinase) mutation detected in their tumor.	
Reporting group title	CDK12 Mutation
Reporting group description:	
Patients with a deleterious CDK12 (Cyclin-dependent kinase 12) mutation detected in their tumor.	
Reporting group title	CHEK2 Mutation
Reporting group description:	
Patients with a deleterious CHEK2 (Checkpoint Kinase 2) mutation detected in their tumor.	
Reporting group title	Other Gene Mutation
Reporting group description:	
Patients with other deleterious HRR (homologous recombination repair) gene mutation detected in their tumor.	

Reporting group values	BRCA Mutation	ATM Mutation	CDK12 Mutation
Number of subjects	172	59	14
Age categorical Units: Subjects			
Adults (18-64 years)	39	8	9
From 65-84 years	128	51	5
85 years and over	5	0	0
Age continuous Units: years			
median	72	73	64
full range (min-max)	49 to 88	51 to 84	49 to 79
Gender categorical Units: Subjects			
Female	0	0	0
Male	172	59	14
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	0	0
Native Hawaiian or Other Pacific Islander	1	0	0
Black or African American	8	3	1
White	127	43	6
More than one race	0	0	0
Unknown or Not Reported	33	13	7

Reporting group values	CHEK2 Mutation	Other Gene Mutation	Total
Number of subjects	7	25	277

Age categorical Units: Subjects			
Adults (18-64 years)	3	6	65
From 65-84 years	2	19	205
85 years and over	2	0	7
Age continuous Units: years			
median	65	70	
full range (min-max)	60 to 86	57 to 83	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	7	25	277
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	1	1	5
Native Hawaiian or Other Pacific Islander	0	0	1
Black or African American	0	4	16
White	5	17	198
More than one race	0	0	0
Unknown or Not Reported	1	3	57

End points

End points reporting groups

Reporting group title	BRCA Mutation
Reporting group description:	
Patients with a deleterious BRCA (breast cancer susceptibility gene) mutation detected in their tumor.	
Reporting group title	ATM Mutation
Reporting group description:	
Patients with a deleterious ATM (ataxia telangiectasia mutated serine/threonine kinase) mutation detected in their tumor.	
Reporting group title	CDK12 Mutation
Reporting group description:	
Patients with a deleterious CDK12 (Cyclin-dependent kinase 12) mutation detected in their tumor.	
Reporting group title	CHEK2 Mutation
Reporting group description:	
Patients with a deleterious CHEK2 (Checkpoint Kinase 2) mutation detected in their tumor.	
Reporting group title	Other Gene Mutation
Reporting group description:	
Patients with other deleterious HRR (homologous recombination repair) gene mutation detected in their tumor.	

Primary: Confirmed Objective Response Rate (ORR) by Gene in Patients With Measurable Disease at Baseline Per Central Independent Radiology Review (IRR)

End point title	Confirmed Objective Response Rate (ORR) by Gene in Patients With Measurable Disease at Baseline Per Central Independent Radiology Review (IRR)[1]

End point description:

The primary efficacy endpoint is confirmed radiographic ORR by central IRR. ORR is defined as the percentage of patients with a confirmed CR (complete response) or PR (partial response) by mRECIST (modified Response Evaluation Criteria in Solid Tumors) v1.1/PCWG3 (Prostate Cancer Working Group 3) criteria. The confirmed response is defined as a CR or PR on subsequent tumor assessment at least 28 days after first response documentation in the absence of confirmed progression in bone. CR is 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 mm. PR is at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum diameters.

End point type	Primary

End point timeframe:

Assessments every 8 weeks from study day 1 for the first 24 weeks, and then every 12 weeks until disease progression, death, or initiation of subsequent treatment. Total follow-up was up to approximately 3 years.

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 formal statistical analyses are done for single arm studies. We present confidence intervals for ORR.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	81	23	8	4
Units: Percentage of Patients				
number (confidence interval 95%)	45.7 (34.6 to 57.1)	0.0 (0.0 to 14.8)	0.0 (0.0 to 36.9)	0.0 (0.0 to 60.2)

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percentage of Patients				
number (confidence interval 95%)	41.2 (18.4 to 67.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Confirmed Objective Response Rate (ORR) by Gene in Patients With Measurable Disease at Baseline Per Investigator (INV)

End point title	Confirmed Objective Response Rate (ORR) by Gene in Patients With Measurable Disease at Baseline Per Investigator (INV)

End point description:

A supportive efficacy endpoint is confirmed radiographic ORR by INV. ORR is defined as the percentage of patients with a confirmed CR (complete response) or PR (partial response) by mRECIST (modified Response Evaluation Criteria in Solid Tumors) v1.1/PCWG3 (Prostate Cancer Working Group 3) criteria. The confirmed response is defined as a CR or PR on subsequent tumor assessment at least 28 days after first response documentation in the absence of confirmed progression in bone. CR is 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 mm. PR is at least a 30% decrease in the sum of the diameters of target lesions, taking as reference the baseline sum of diameters.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from study day 1 for the first 24 weeks, and then every 12 weeks until disease progression, death, or initiation of subsequent treatment. Total follow-up was up to approximately 3 years.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	87	21	9	4
Units: Percentage of Patients				
number (confidence interval 95%)	48.3 (37.4 to 59.2)	9.5 (1.2 to 30.4)	0.0 (0.0 to 33.6)	25.0 (0.6 to 80.6)

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: Percentage of Patients				
number (confidence interval 95%)	41.2 (18.4 to			

67.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) by Gene in Patients With Confirmed Response Per Central Independent Radiology Review (IRR)

End point title	Duration of Response (DOR) by Gene in Patients With Confirmed Response Per Central Independent Radiology Review (IRR)[2]

End point description:

A secondary efficacy endpoint is DOR by central IRR. The DOR is defined as the time from the date that a confirmed response per modified RECIST Version 1.1/PCWG3 is first reported to the time that progressive disease (PD) is first documented. Progressive disease is defined using RECIST v1.1, as at least a 20% increase in the sum of the diameters of target lesions, or an unequivocal increase in non-target lesions, or the appearance of new lesions. PCWG3 criteria is used to document evidence of disease progression in bone lesions.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from study day 1 for the first 24 weeks, and then every 12 weeks until disease progression, death, or initiation of subsequent treatment. Total follow-up was up to approximately 3 years.

Notes:

[2] - 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: There were no patients with confirmed response by IRR in the ATM, CDK12 and CHEK2 arms.

End point values	BRCA Mutation	Other Gene Mutation		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	37[3]	7[4]		
Units: months				
median (confidence interval 95%)	15.5 (6.4 to 36.2)	22.1 (10.1 to 31.4)		

Notes:

[3] - Upper confidence interval not available due to insufficient number of patients so max 36.2 is noted.

[4] - Upper confidence interval not available due to insufficient number of patients so max 31.4 is noted.

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DOR) by Gene in Patients With Confirmed Response Per Investigator

End point title	Duration of Response (DOR) by Gene in Patients With Confirmed Response Per Investigator[5]

End point description:

A secondary efficacy endpoint is DOR as assessed by the investigator. The DOR is defined as the time from the date that a confirmed response per modified RECIST Version 1.1/PCWG3 is first reported to the time that progressive disease (PD) is first documented. Progressive disease is defined using RECIST v1.1, as at least a 20% increase in the sum of the diameters of target lesions, or an unequivocal

in non-target lesions, or the appearance of new lesions. PCWG3 criteria is used to document evidence of disease progression in bone lesions.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from study day 1 for the first 24 weeks, and then every 12 weeks until disease progression, death, or initiation of subsequent treatment. Total follow-up was up to approximately 3 years.

Notes:

[5] - 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: There were no patients with confirmed response by investigator in the CDK12 arm.

End point values	BRCA Mutation	ATM Mutation	CHEK2 Mutation	Other Gene Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	2	1[6]	7[7]
Units: Months				
median (confidence interval 95%)	6.6 (5.6 to 11.6)	7.5 (4.6 to 10.4)	16.6 (16.6 to 16.6)	18.4 (10.1 to 31.4)

Notes:

[6] - There is only 1 responder in this group with DOR of 16.6 months.

[7] - Upper confidence interval not available due to insufficient number of patients so max 31.4 is noted.

Statistical analyses

No statistical analyses for this end point

Secondary: Confirmed PSA Response (≥ 50% Decrease) by Gene as Assessed by Local Laboratory

End point title	Confirmed PSA Response (≥ 50% Decrease) by Gene as Assessed by Local Laboratory

End point description:

A secondary endpoint is confirmed PSA (prostate-specific antigen) response (≥ 50% reduction) as assessed by local laboratory. Confirmed PSA response is analyzed for all patients who had PSA value at baseline and is defined as the percentage of patients having 2 consecutive PSA values (at least 3 weeks apart) that are at least 50% lower than baseline and that occur prior to PSA progression. PSA progression is defined as a ≥ 25% increase and absolute increase of ≥ 2 ng/mL above the nadir in PSA.

End point type	Secondary

End point timeframe:

PSA assessments were done at baseline, Week 5, Week 9, every 4 weeks thereafter, and at Treatment Discontinuation. Total follow-up was up to approximately 39 months.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	59	14	7
Units: Percentage of Patients				
number (confidence interval 95%)	53.5 (45.7 to 61.1)	3.4 (0.4 to 11.7)	7.1 (0.2 to 33.9)	14.3 (0.4 to 57.9)

End point values	Other Gene			

	Mutation			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percentage of Patients				
number (confidence interval 95%)	36.0 (18.0 to 57.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Confirmed PSA Response (≥ 90% Decrease) by Gene as Assessed by Local Laboratory

End point title	Confirmed PSA Response (≥ 90% Decrease) by Gene as Assessed by Local Laboratory

End point description:

A secondary endpoint is confirmed PSA (prostate-specific antigen) response (≥ 90% reduction) as assessed by local laboratory. Confirmed PSA response is analyzed for all patients who had PSA value at baseline and is defined as the percentage of patients having 2 consecutive PSA values (at least 3 weeks apart) that are at least 90% lower than baseline and that occur prior to PSA progression. PSA progression is defined as a ≥ 25% increase and absolute increase of ≥ 2 ng/mL above the nadir in PSA.

End point type	Secondary

End point timeframe:

PSA assessments were done at baseline, Week 5, Week 9, every 4 weeks thereafter, and at Treatment Discontinuation. Total follow-up was up to approximately 39 months.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	59	14	7
Units: Percentage of Patients				
number (confidence interval 95%)	19.8 (14.1 to 26.5)	0 (0 to 0)	0 (0 to 0)	14.3 (0.4 to 57.9)

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: Percentage of Patients				
number (confidence interval 95%)	16.0 (4.5 to 36.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Radiologic Progression-free Survival (rPFS) by Gene in All Patients Per Central Independent Radiology Review (IRR)

End point title	Radiologic Progression-free Survival (rPFS) by Gene in All Patients Per Central Independent Radiology Review (IRR)

End point description:

A secondary efficacy endpoint is Radiologic Progression-free Survival (rPFS) assessed by IRR. rPFS is defined as the time from first dose of rucaparib to the date of first objective evidence of radiographic progression (soft tissue or bone lesion) or death due to any cause, whichever occurs first, plus 1 day. Radiographic disease progression includes confirmed bone disease progression and soft tissue disease progression adjudicated by IRR using the PCWG3 guidelines for bone disease and modified RECIST Version1.1 for soft tissue disease.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from study day 1 for the first 24 weeks, and then every 12 weeks until disease progression, death, or initiation of subsequent treatment. Total follow-up was up to approximately 3 years.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	59	14	7[8]
Units: months				
median (confidence interval 95%)	10.7 (8.7 to 13.2)	5.3 (3.7 to 8.9)	3.7 (1.9 to 8.3)	9.4 (2.1 to 24.8)

Notes:

[8] - Upper confidence interval not available due to insufficient number of patients so max 24.8 is noted.

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: months				
median (confidence interval 95%)	11.6 (5.1 to 25.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Radiologic Progression-free Survival (rPFS) by Gene in All Patients Per Investigator

End point title	Radiologic Progression-free Survival (rPFS) by Gene in All Patients Per Investigator

End point description:

A secondary efficacy endpoint is Radiologic Progression-free Survival (rPFS) assessed by Investigator. rPFS is defined as the time from first dose of rucaparib to the date of first objective evidence of radiographic progression (soft tissue or bone lesion) or death due to any cause, whichever occurs first, plus 1 day. Radiographic disease progression includes confirmed bone disease progression and soft tissue disease progression using the PCWG3 guidelines for bone disease and modified RECIST Version

1.1 for soft tissue disease.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from study day 1 for the first 24 weeks, and then every 12 weeks until disease progression, death, or initiation of subsequent treatment. Total follow-up was up to approximately 3 years.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	59	14	7
Units: months				
median (confidence interval 95%)	9.6 (8.2 to 11.2)	7.8 (4.2 to 10.6)	3.7 (1.9 to 8.1)	3.5 (2.1 to 11.2)

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: months				
median (confidence interval 95%)	11.6 (5.8 to 22.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS) by Gene

End point title	Overall Survival (OS) by Gene

End point description:

A secondary efficacy endpoint is Overall Survival (OS). OS is defined as the date from first dose of rucaparib to the date of death due to any cause, +1 day.

End point type	Secondary

End point timeframe:

From date of first dose until event, loss to follow-up, withdrawal of consent, or study closure

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	59	14	7
Units: months				
median (confidence interval 95%)	17.2 (14.8 to 20.0)	14.6 (12.0 to 19.0)	13.9 (6.8 to 18.6)	11.1 (3.5 to 26.7)

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	25[9]			
Units: months				
median (confidence interval 95%)	11.6 (8.9 to 34.9)			

Notes:

[9] - Upper confidence interval not available due to insufficient number of patients so max 34.9 is noted.

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) by Gene Per Central Independent Radiology Review (IRR)

End point title	Clinical Benefit Rate (CBR) by Gene Per Central Independent Radiology Review (IRR)

End point description:

A secondary efficacy endpoint is Clinical Benefit Rate (CBR) assessed by IRR. CBR is defined as the number of patients without radiographic progression (defined by modified RECIST Version 1.1/ PCWG3 criteria) who were continuing with study drug treatment through the given time interval divided by the number of patients who had the given amount of follow-up. Clinical benefit rates are summarized at 6 and 12 months.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from study day 1 for the first 24 weeks, and then every 12 weeks until disease progression, death, or initiation of subsequent treatment. Total follow-up was up to approximately 3 years.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	59	14	7
Units: participants				
6 months	100	10	2	2
12 months	36	3	0	1

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: participants				
6 months	13			
12 months	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Clinical Benefit Rate (CBR) by Gene Per Investigator

End point title	Clinical Benefit Rate (CBR) by Gene Per Investigator

End point description:

A secondary efficacy endpoint is Clinical Benefit Rate (CBR) assessed by Investigator. CBR is defined as the number of patients without radiographic progression (defined by modified RECIST Version 1.1/ PCWG3 criteria) who were continuing with study drug treatment through the given time interval divided by the number of patients who had the given amount of follow-up. Clinical benefit rates are summarized at 6 and 12 months.

End point type	Secondary

End point timeframe:

Assessments every 8 weeks from study day 1 for the first 24 weeks, and then every 12 weeks until disease progression, death, or initiation of subsequent treatment. Total follow-up was up to approximately 3 years.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	59	14	7
Units: participants				
6 months	103	17	3	2
12 months	39	6	1	1

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: participants				
6 months	14			
12 months	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PSA Progression by Gene

End point title	Time to PSA Progression by Gene

End point description:

A secondary efficacy endpoint is time to PSA progression. Time to PSA progression is defined as the time from first dose of rucaparib to the date that a ≥ 25% increase and absolute increase of ≥ 2 ng/mL above the nadir (or baseline if there was no PSA decline after baseline) in PSA was measured, plus 1 day. The increase must be confirmed by a second consecutive assessment conducted at least 3 weeks later (unless the PSA progression occurred at the last recorded PSA assessment). If confirmed, the date used for time of PSA progression is the earlier of the 2 PSA dates.

End point type	Secondary

End point timeframe:

PSA assessments were done at baseline, Week 5, Week 9, every 4 weeks thereafter, and at Treatment Discontinuation. Total follow-up was up to approximately 39 months.

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	172	59	14	7[10]
Units: months				
median (confidence interval 95%)	6.5 (5.7 to 7.5)	3.1 (2.8 to 3.7)	3.5 (2.8 to 4.6)	5.6 (2.8 to 24.9)

Notes:

[10] - Upper confidence interval not available due to insufficient number of patients so max 24.9 is noted.

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	25			
Units: months				
median (confidence interval 95%)	5.3 (3.0 to 9.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Steady State Trough (Cmin) Level Rucaparib Concentrations

End point title	Steady State Trough (Cmin) Level Rucaparib Concentrations

End point description:

Trough (Cmin) concentrations of rucaparib are summarized for all patients with at least one PK sample collected. The absolute values of rucaparib plasma concentration at each time point are presented by gene.

End point type	Secondary

End point timeframe:

Participants were assessed at Study Day 29, Day 57, Day 85 and Day 113

End point values	BRCA Mutation	ATM Mutation	CDK12 Mutation	CHEK2 Mutation
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	101[11]	51[12]	14[13]	5[14]
Units: ng/mL				
median (standard deviation)				
Day 29	1539.565 (± 966.2604)	1605.002 (± 856.2478)	1639.357 (± 1428.5691)	1286.998 (± 1138.2119)
Day 57	1578.353 (± 1057.8049)	1600.380 (± 1198.3899)	1405.167 (± 806.4642)	1841.667 (± 2106.3362)
Day 85	1308.704 (± 693.6717)	1505.400 (± 802.0812)	1699.700 (± 991.9922)	815.500 (± 557.9073)
Day 113	1533.690 (± 889.6130)	1515.300 (± 1291.8497)	1520.700 (± 884.1374)	728.000 (± 469.5189)

Notes:

[11] - Day 29 = 101 pts, Day 57 = 85, Day 85 = 71, Day 113 = 60

[12] - Day 29 = 48 pts, Day 57 = 38, Day 85 = 30, Day 113 = 22

[13] - Day 29 = 14 pts, Day 57 = 12, Day 85 = 10, Day 113 = 10

[14] - Day 29 = 5 pts, Day 57 = 3, Day 85 = 2, Day 113 = 2

End point values	Other Gene Mutation			
Subject group type	Reporting group			
Number of subjects analysed	13[15]			
Units: ng/mL				
median (standard deviation)				
Day 29	1189.845 (± 748.3045)			
Day 57	1792.499 (± 1672.7732)			
Day 85	2255.889 (± 1831.9626)			
Day 113	1433.875 (± 637.4535)			

Notes:

[15] - Day 29 = 13 pts, Day 57 = 11, Day 85 = 9, Day 113 = 8

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were reported from date of first dose of study drug until 28 days after last dose of study drug, approximately 4.5 years.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	All patients

Reporting group description:

All patients received open-label oral rucaparib 600 mg BID (twice a day) in continuous 28-day cycles.

Serious adverse events	All patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	96 / 277 (34.66%)		
number of deaths (all causes)	8		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bladder cancer			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic lymphocytic leukaemia			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Vascular disorders			
Embolism			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	1 / 277 (0.36%)		
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	2 / 277 (0.72%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Fatigue			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Non-cardiac chest pain			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pain			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Psychiatric disorders			
Confusional state			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood creatinine increased			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Fall			

subjects affected / exposed	2 / 277 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative respiratory failure				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract stoma complication				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	3 / 277 (1.08%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	3 / 277 (1.08%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				

subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery occlusion				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Torsade de pointes				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Ventricular tachycardia				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cerebellar infarction				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cerebrovascular accident				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dysarthria				

subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ischaemic stroke			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sacral radiculopathy			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Spinal cord compression			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	2 / 3		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	14 / 277 (5.05%)			
occurrences causally related to treatment / all	17 / 19			
deaths causally related to treatment / all	0 / 0			
Anaemia of malignant disease				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Aplastic anaemia				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Leukopenia				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Neutropenia				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancytopenia				
subjects affected / exposed	2 / 277 (0.72%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				

subjects affected / exposed	3 / 277 (1.08%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal ischaemia				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Mechanical ileus				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	2 / 277 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				

subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	3 / 277 (1.08%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	7 / 277 (2.53%)		
occurrences causally related to treatment / all	3 / 7		
deaths causally related to treatment / all	0 / 0		
Haematuria			
subjects affected / exposed	6 / 277 (2.17%)		
occurrences causally related to treatment / all	1 / 7		
deaths causally related to treatment / all	0 / 0		
Hydronephrosis			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary retention			
subjects affected / exposed	3 / 277 (1.08%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Muscular weakness				
subjects affected / exposed	2 / 277 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				
subjects affected / exposed	2 / 277 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	5 / 277 (1.81%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Spinal pain				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess oral				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related infection				

subjects affected / exposed	2 / 277 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Fournier's gangrene				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Haemophilus infection				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infective exacerbation of chronic obstructive airways disease				
subjects affected / exposed	2 / 277 (0.72%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Legionella infection				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Paraspinal abscess				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	6 / 277 (2.17%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 1			
Pneumonia legionella				

subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonia staphylococcal				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	4 / 277 (1.44%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	4 / 277 (1.44%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	4 / 277 (1.44%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	1 / 277 (0.36%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				

subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Electrolyte imbalance			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Failure to thrive			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	2 / 277 (0.72%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	1 / 277 (0.36%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	2 / 277 (0.72%)		
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	All patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	274 / 277 (98.92%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	20 / 277 (7.22%)		
occurrences (all)	26		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	50 / 277 (18.05%)		
occurrences (all)	100		
Fatigue			
subjects affected / exposed	131 / 277 (47.29%)		
occurrences (all)	249		
Oedema peripheral			
subjects affected / exposed	50 / 277 (18.05%)		
occurrences (all)	58		
Pyrexia			
subjects affected / exposed	16 / 277 (5.78%)		
occurrences (all)	23		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	33 / 277 (11.91%)		
occurrences (all)	36		
Dyspnoea			
subjects affected / exposed	40 / 277 (14.44%)		
occurrences (all)	66		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	18 / 277 (6.50%)		
occurrences (all)	20		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	72 / 277 (25.99%)		
occurrences (all)	120		
Aspartate aminotransferase increased			

subjects affected / exposed occurrences (all)	71 / 277 (25.63%) 106		
Blood alkaline phosphatase increased subjects affected / exposed occurrences (all)	18 / 277 (6.50%) 30		
Blood creatinine increased subjects affected / exposed occurrences (all)	51 / 277 (18.41%) 76		
Platelet count decreased subjects affected / exposed occurrences (all)	32 / 277 (11.55%) 112		
Weight decreased subjects affected / exposed occurrences (all)	45 / 277 (16.25%) 64		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)	19 / 277 (6.86%) 31		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	54 / 277 (19.49%) 71		
Dysgeusia subjects affected / exposed occurrences (all)	32 / 277 (11.55%) 41		
Headache subjects affected / exposed occurrences (all)	28 / 277 (10.11%) 30		
Neuropathy peripheral subjects affected / exposed occurrences (all)	14 / 277 (5.05%) 17		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	130 / 277 (46.93%) 460		
Neutropenia			

subjects affected / exposed	20 / 277 (7.22%)		
occurrences (all)	63		
Thrombocytopenia			
subjects affected / exposed	33 / 277 (11.91%)		
occurrences (all)	92		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	17 / 277 (6.14%)		
occurrences (all)	19		
Constipation			
subjects affected / exposed	76 / 277 (27.44%)		
occurrences (all)	107		
Diarrhoea			
subjects affected / exposed	66 / 277 (23.83%)		
occurrences (all)	100		
Dyspepsia			
subjects affected / exposed	18 / 277 (6.50%)		
occurrences (all)	23		
Nausea			
subjects affected / exposed	140 / 277 (50.54%)		
occurrences (all)	231		
Vomiting			
subjects affected / exposed	70 / 277 (25.27%)		
occurrences (all)	114		
Skin and subcutaneous tissue disorders			
Dry skin			
subjects affected / exposed	18 / 277 (6.50%)		
occurrences (all)	20		
Photosensitivity reaction			
subjects affected / exposed	19 / 277 (6.86%)		
occurrences (all)	22		
Rash			
subjects affected / exposed	22 / 277 (7.94%)		
occurrences (all)	27		
Renal and urinary disorders			

Haematuria			
subjects affected / exposed	24 / 277 (8.66%)		
occurrences (all)	46		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	44 / 277 (15.88%)		
occurrences (all)	65		
Back pain			
subjects affected / exposed	51 / 277 (18.41%)		
occurrences (all)	74		
Bone pain			
subjects affected / exposed	18 / 277 (6.50%)		
occurrences (all)	26		
Muscular weakness			
subjects affected / exposed	17 / 277 (6.14%)		
occurrences (all)	21		
Musculoskeletal chest pain			
subjects affected / exposed	14 / 277 (5.05%)		
occurrences (all)	17		
Musculoskeletal pain			
subjects affected / exposed	34 / 277 (12.27%)		
occurrences (all)	41		
Myalgia			
subjects affected / exposed	14 / 277 (5.05%)		
occurrences (all)	16		
Pain in extremity			
subjects affected / exposed	33 / 277 (11.91%)		
occurrences (all)	49		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	20 / 277 (7.22%)		
occurrences (all)	24		
Urinary tract infection			
subjects affected / exposed	39 / 277 (14.08%)		
occurrences (all)	60		
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	96 / 277 (34.66%)		
occurrences (all)	137		
Dehydration			
subjects affected / exposed	15 / 277 (5.42%)		
occurrences (all)	22		
Hypocalcaemia			
subjects affected / exposed	21 / 277 (7.58%)		
occurrences (all)	35		
Hypophosphataemia			
subjects affected / exposed	27 / 277 (9.75%)		
occurrences (all)	44		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 October 2016	Added monitoring and management guidelines for anemia and MDS/AML because these events were reported with rucaparib as with other PARP inhibitors. Added language describing when treatment beyond radiographic progression may be appropriate. Added study drug interruption and discontinuation criteria for cases of DILI per Hy's Law. Clarified that bone scans were to be performed at each time of disease assessment, in addition to CT/MRI, to follow PCWG3 guidelines.
12 December 2017	Updated the inclusion criterion for renal function. Updated inclusion criterion 11 to avoid exposure of the partners of male patients to semen containing rucaparib. Included and emphasized specific warnings and protection measures regarding photosensitivity. Updated precautions related to concomitant medications, particularly for CYP drugs.
12 June 2018	Agents that target the AR pathway that are given for metastatic hormone-sensitive prostate cancer and for non-metastatic CRPC were now considered to meet prior AR-directed therapy requirements. Removed collection of blood samples for CTC analysis as exploratory analysis indicated an overall lack of feasibility.
24 August 2020	The sponsor designated pneumonitis as an AESI in response to a request from the US FDA. Updated the interval from 6 months to 3 months after the last dose of study drug for which men must use contraceptive measures or abstinence or refrain from donating semen.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported