Clinical trial results:
A Randomised, Double-Blind, Placebo-Controlled, Multicentre Phase II Study to Compare the Efficacy, Safety and Tolerability of Olaparib Versus Placebo When Given in Addition to Abiraterone Treatment in Patients With Metastatic Castrate-Resistant Prostate Cancer Who Have Received Prior Chemotherapy Containing Docetaxel

Summary

EudraCT number	2013-003520-37
Trial protocol	GB BE NL CZ ES IT FR
Global end of trial date	24 August 2023

Results information

Result version number	v1 (current)
This version publication date	26 November 2023
First version publication date	26 November 2023

Trial information

Trial identification

Sponsor protocol code	D081DC00008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01972217
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, MD 20878
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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	22 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	22 September 2017
Global end of trial reached?	Yes
Global end of trial date	24 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

In Part A, to assess the safety and tolerability of olaparib twice daily (bid) administration when given in addition to abiraterone and to recommend, by assessment of dose-limiting toxicities (DLTs) and other safety and tolerability data, a dose of olaparib for further study when given in addition to abiraterone. In Part B, to compare the efficacy of olaparib when given in addition to abiraterone, with placebo given in addition to abiraterone.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with International Council on Harmonisation/Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

Background therapy:

Patients received abiraterone 1000 milligrams (mg) once daily. Abiraterone is indicated in combination with prednisone or prednisolone 5 mg once daily for the treatment of patients with metastatic castrate-resistant prostate cancer (mCRPC).

Evidence for comparator: -

Actual start date of recruitment	01 April 2014
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: 24
Country: Number of subjects enrolled	United Kingdom: 27
Country: Number of subjects enrolled	Italy: 17
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Canada: 11
Country: Number of subjects enrolled	Czechia: 13
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Russian Federation: 31
Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	United States: 2
Worldwide total number of subjects	158
EEA total number of subjects	87

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)	42
From 65 to 84 years	114
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

In this 2-part study, patients with mCRPC were recruited at 41 sites in Europe, Russia and North America. Part A had 2 cohorts for olaparib dose selection when given with approved treatment abiraterone. Part B compared olaparib versus placebo both with abiraterone in post-chemotherapy mCRPC patients.

Pre-assignment

Screening details:

Patients dosed in open-label Part A could not participate in Part B which was a randomised, double-blind, placebo-controlled comparison of olaparib + abiraterone versus placebo + abiraterone in patients who had received prior chemotherapy containing docetaxel.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A Cohort 1: Olaparib 200 mg + abiraterone

Arm description:

Patients received olaparib 200 mg bid and abiraterone 1000 mg once daily. Patients were assessed at Weeks 1, 2 and 4, then every 4 weeks up to Week 52, and every 12 weeks thereafter.
Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Arm type	Experimental
Investigational medicinal product name	Olaparib
Investigational medicinal product code	AZD2281
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received 200 mg olaparib bid, administered as 2 x 100 mg tablets.

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

Dosage and administration details:

Patients received 5 mg prednisolone or prednisone once daily as indicated with abiraterone treatment for mCRPC.

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

Dosage and administration details:

Patients received 1000 mg abiraterone once daily, administered as 4 x 250 mg tablets.

Arm title	Part A Cohort 2: Olaparib 300 mg + abiraterone

Arm description:

If the combination of olaparib 200 mg + abiraterone 1000 mg was well tolerated (determined after a minimum of 14 days treatment in Cohort 1), patients were recruited into Cohort 2. Cohort 2 Group 1: patients received olaparib 300 mg bid alone for 3 to 7 days. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 5 days. Cohort 2 Group 2: patients received abiraterone 1000 mg once daily alone for 5 to 7 days. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 3 days.
Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Arm type	Experimental
Investigational medicinal product name	Olaparib
Investigational medicinal product code	AZD2281
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received 300 mg olaparib bid, administered as 3 x 100 mg tablets or 2 x 150 mg tablets.

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

Dosage and administration details:

Patients received 5 mg prednisolone or prednisone once daily as indicated with abiraterone treatment for mCRPC.

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

Dosage and administration details:

Patients received 1000 mg abiraterone once daily, administered as 4 x 250 mg tablets.

Arm title	Part B: Olaparib + abiraterone

Arm description:

Patients received the selected dose of olaparib 300 mg bid + abiraterone 1000 mg once daily. Patients were assessed every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Arm type	Experimental
Investigational medicinal product name	Olaparib
Investigational medicinal product code	AZD2281
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Patients received 300 mg olaparib bid, administered as 3 x 100 mg tablets or 2 x 150 mg tablets.

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

Dosage and administration details:

Patients received 5 mg prednisolone or prednisone once daily as indicated with abiraterone treatment for mCRPC.

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

Dosage and administration details:

Patients received 1000 mg abiraterone once daily, administered as 4 x 250 mg tablets.

Arm title	Part B: Placebo + abiraterone

Arm description:

Patients received placebo bid + abiraterone 1000 mg once daily. Patients were assessed every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

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

Dosage and administration details:

Patients received placebo to match olaparib 100 mg or 150 mg tablets.

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

Dosage and administration details:

Patients received 1000 mg abiraterone once daily, administered as 4 x 250 mg tablets.

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

Dosage and administration details:

Patients received 5 mg prednisolone or prednisone once daily as indicated with abiraterone treatment for mCRPC.

Number of subjects in period 1	Part A Cohort 1: Olaparib 200 mg + abiraterone	Part A Cohort 2: Olaparib 300 mg + abiraterone	Part B: Olaparib + abiraterone
Started	3	13	71
Completed	2	1	25
Not completed	1	12	46
Reason not recorded	-	-	1
Adverse event, non-fatal	-	1	-
Death	-	1	43
Condition under investigation worsened	1	9	-
Screen failure	-	-	-

Lost to follow-up	-	-	2
Withdrawal by patient	-	1	-

Number of subjects in period 1	Part B: Placebo + abiraterone
Started	71
Completed	24
Not completed	47
Reason not recorded	-
Adverse event, non-fatal	-
Death	44
Condition under investigation worsened	-
Screen failure	1
Lost to follow-up	1
Withdrawal by patient	1

Baseline characteristics

Reporting groups	
Reporting group title	Part A Cohort 1: Olaparib 200 mg + abiraterone
Reporting group description:	
Patients received olaparib 200 mg bid and abiraterone 1000 mg once daily. Patients were assessed at Weeks 1, 2 and 4, then every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.	
Reporting group title	Part A Cohort 2: Olaparib 300 mg + abiraterone
Reporting group description:	
If the combination of olaparib 200 mg + abiraterone 1000 mg was well tolerated (determined after a minimum of 14 days treatment in Cohort 1), patients were recruited into Cohort 2. Cohort 2 Group 1: patients received olaparib 300 mg bid alone for 3 to 7 days. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 5 days. Cohort 2 Group 2: patients received abiraterone 1000 mg once daily alone for 5 to 7 days. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 3 days. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.	
Reporting group title	Part B: Olaparib + abiraterone
Reporting group description:	
Patients received the selected dose of olaparib 300 mg bid + abiraterone 1000 mg once daily. Patients were assessed every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.	
Reporting group title	Part B: Placebo + abiraterone
Reporting group description:	
Patients received placebo bid + abiraterone 1000 mg once daily. Patients were assessed every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.	

Reporting group values	Part A Cohort 1: Olaparib 200 mg + abiraterone	Part A Cohort 2: Olaparib 300 mg + abiraterone	Part B: Olaparib + abiraterone
Number of subjects	3	13	71
Age Categorical Units: Subjects			
In Utero	0	0	0
Preterm newborn- gestational age < 37 wk	0	0	0
Newborns (0-27days)	0	0	0
Infants and toddlers (28days - 23months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
From 18 - 64 years	0	3	17
From 65 - 84 years	3	9	53
Over 85 years	0	1	1
Sex: Female, Male Units: Subjects			
Female	0	0	0
Male	3	13	71
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0

Asian	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	1
White	3	13	67
More than one race	0	0	0
Unknown or Not Reported	0	0	2
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	0	11
Not Hispanic or Latino	2	13	58
Unknown or Not Reported	0	0	2

Reporting group values	Part B: Placebo + abiraterone	Total	
Number of subjects	71	158	
Age Categorical Units: Subjects			
In Utero	0	0	
Preterm newborn- gestational age < 37 wk	0	0	
Newborns (0-27days)	0	0	
Infants and toddlers (28days - 23months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
From 18 - 64 years	22	42	
From 65 - 84 years	49	114	
Over 85 years	0	2	
Sex: Female, Male Units: Subjects			
Female	0	0	
Male	71	158	
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	
Asian	0	1	
Native Hawaiian or Other Pacific Islander	0	0	
Black or African American	1	2	
White	67	150	
More than one race	0	0	
Unknown or Not Reported	3	5	
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	5	17	
Not Hispanic or Latino	63	136	
Unknown or Not Reported	3	5	

End points

End points reporting groups

Reporting group title	Part A Cohort 1: Olaparib 200 mg + abiraterone

Reporting group description:

Patients received olaparib 200 mg bid and abiraterone 1000 mg once daily. Patients were assessed at Weeks 1, 2 and 4, then every 4 weeks up to Week 52, and every 12 weeks thereafter.
Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Reporting group title	Part A Cohort 2: Olaparib 300 mg + abiraterone

Reporting group description:

If the combination of olaparib 200 mg + abiraterone 1000 mg was well tolerated (determined after a minimum of 14 days treatment in Cohort 1), patients were recruited into Cohort 2. Cohort 2 Group 1: patients received olaparib 300 mg bid alone for 3 to 7 days. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 5 days. Cohort 2 Group 2: patients received abiraterone 1000 mg once daily alone for 5 to 7 days. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 3 days.
Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Reporting group title	Part B: Olaparib + abiraterone

Reporting group description:

Patients received the selected dose of olaparib 300 mg bid + abiraterone 1000 mg once daily. Patients were assessed every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Reporting group title	Part B: Placebo + abiraterone

Reporting group description:

Patients received placebo bid + abiraterone 1000 mg once daily. Patients were assessed every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Subject analysis set title	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received olaparib 300 mg bid alone for 3 to 7 days to determine the steady state PK profile for olaparib. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 5 days to determine the PK profiles of both olaparib and abiraterone.
Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Subject analysis set title	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patients received abiraterone 1000 mg once daily alone for 5 to 7 days to determine the steady state PK profile for abiraterone. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 3 days to determine the PK profiles of both olaparib and abiraterone.
Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Primary: Part A: Percentage of Patients Experiencing Adverse Events (AEs)

End point title	Part A: Percentage of Patients Experiencing Adverse Events (AEs)[1][2]

End point description:

The safety and tolerability of olaparib in combination with abiraterone was assessed during Part A of the study. The percentage of patients experiencing AEs, including information on seriousness, severity, study treatment relationship and those leading to discontinuation for all doses of olaparib and for abiraterone are presented. Severity of AEs was assessed using the National Cancer Institute (NCI) Common Terminology Criteria for Adverse events (CTCAE) v4.0. AEs were assigned to a Grade from 1 through 5 as follows: Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe or medically significant but not immediately life-threatening requiring hospitalisation; Grade 4: Life-threatening consequences; Grade 5: Death related to AE. 'c-r' = causally related 'discont' = discontinuation.
The Part A Safety analysis set consisted of all patients who received at least 1 dose of study treatment

in Part A.

End point type	Primary

End point timeframe:

Cohort 1 and 2: From Baseline in Part A (Day 1 for each cohort) up to 30 days following last dose of study treatment (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: Part A was a safety run where safety and tolerability were assessed. Thus, no statistical analyses was required.
[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: Part A was a safety run where safety and tolerability were assessed. Thus, no statistical analyses was required.

End point values	Part A Cohort 1: Olaparib 200 mg + abiraterone	Part A Cohort 2: Olaparib 300 mg + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	13		
Units: Percentage of patients				
number (not applicable)				
Any AE c-r to olaparib + abiraterone	66.7	46.2		
Any AE c-r to olaparib only	33.3	7.7		
Any AE c-r to abiraterone only	0	15.4		
Any AE CTCAE Grade 3 or higher	66.7	23.1		
Any AE CTCAE Grade 3 or higher c-r to olaparib	0	7.7		
Any AE CTCAE Grade 3 or higher c-r to abiraterone	0	7.7		
Any AE with outcome = death	0	0		
Any serious AE (SAE)	66.7	23.1		
Any SAE c-r to olaparib	0	0		
Any SAE c-r to abiraterone	0	0		
Any AE causing discont of olaparib	0	7.7		
Any AE causing discont c-r to olaparib	0	0		
Any AE causing discont c-r to abiraterone	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Part A: Number of Patients with DLTs

End point title	Part A: Number of Patients with DLTs[3][4]

End point description:

DLTs were assessed by a Safety Review Committee (SRC) after a minimum of 3 patients had received at least 14 days of treatment in Part A. A DLT was defined as any toxicity which was not a recognised AE of abiraterone or prednisolone, and was not attributable to the disease or disease-related processes under investigation, which occurred during a minimum period of 14 days treatment and which included: 1. haematological toxicity CTCAE v4.0 Grade 4 or higher present for more than 4 days (except anaemia); 2. non-haematological toxicity CTCAE v4.0 Grade 3 or higher including infection, corrected QT interval prolongation; 3. any other toxicity that was greater than that at baseline, was clinically significant and/or unacceptable, did not respond to supportive care, resulted in a disruption of dosing schedule of 7

days or more, or was judged to be a DLT by the SRC. A DLT excluded alopecia and isolated laboratory changes of any grade without clinical sequelae or clinical significance.

End point type	Primary

End point timeframe:

From Day 1 for Cohort 1 and from Day 4 for Cohort 2 up to 14 days treatment with olaparib + abiraterone for 3 patients.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Part A was a safety run where safety and tolerability were assessed. Thus, no statistical analyses was required.
[4] - 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: Part A was a safety run where safety and tolerability were assessed. Thus, no statistical analyses was required.

End point values	Part A Cohort 1: Olaparib 200 mg + abiraterone	Part A Cohort 2: Olaparib 300 mg + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	13		
Units: Patients				
number (not applicable)	2	4		

Statistical analyses

No statistical analyses for this end point

Primary: Part B: Percentage of Patients with Progression Events or Death (rPFS)

End point title	Part B: Percentage of Patients with Progression Events or Death (rPFS)[5]

End point description:

The efficacy of olaparib when given in combination with abiraterone was assessed by rPFS, defined as the time from randomisation to disease progression using RECIST version 1.1 (for soft tissue disease) and PCWG-2 (for bone disease) criteria, or death. Progression using RECIST 1.1 criteria was defined as at least 20% increase from baseline in the sum of diameters of target lesions, progression of existing non-target lesions, or the appearance of at least 1 new lesion. Progression using PCWG-2 criteria was determined if 2 or more new metastatic bone lesions were observed (with a total of at least 4 new lesions since baseline assessment if observed at the 12 week scan, or persistence of or increase in number of lesions if observed after the 12 week scan as determined by a confirmatory scan at least 6 weeks later or at next scheduled visit). The percentage of patients with progression events is presented overall and according to RECIST 1.1 and/or PCWG-2 criteria, or death.

End point type	Primary

End point timeframe:

From baseline, every 12 weeks up to Week 72, then every 24 weeks up to 24 months.

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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Percentage of patients				
number (not applicable)	64.8	76.1		

Statistical analyses

Statistical analysis title	Comparison of rPFS

Statistical analysis description:

The 1-sided p-value provides a test for rejecting the null hypothesis of no treatment effect versus the superiority alternative that patients on olaparib have a lower risk of progression compared with placebo.

Comparison groups	Part B: Olaparib + abiraterone v Part B: Placebo + abiraterone
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.651
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.438
upper limit	0.969

Primary: Part B: Median Radiological Progression-Free Survival (rPFS) Time

End point title	Part B: Median Radiological Progression-Free Survival (rPFS) Time[6][7]

End point description:

The efficacy of olaparib when given in combination with abiraterone was assessed by rPFS, defined as the time from randomisation to disease progression using Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1 (for soft tissue disease) and Prostate Cancer Working Group 2 (PCWG-2) (for bone disease) criteria, or death. Progression using RECIST 1.1 criteria was defined as at least 20% increase from baseline in the sum of diameters of target lesions, progression of existing non-target lesions, or the appearance of at least 1 new lesion. Progression using PCWG-2 criteria was determined if 2 or more new metastatic bone lesions were observed (with a total of at least 4 new lesions since baseline assessment if observed at the 12 week scan, or persistence of or increase in number of lesions if observed after the 12 week scan as determined by a confirmatory scan at least 6 weeks later or at next scheduled visit).

End point type	Primary

End point timeframe:

From baseline, every 12 weeks up to Week 72, then every 24 weeks up to 24 months.

Notes:

[6] - 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: Only the Median which is a descriptive measure was presented here. Hence, no statistical analysis is needed here.

[7] - 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: Only the Median which is a descriptive measure was presented here. Hence, no statistical analysis is needed here.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Months				
median (confidence interval 95%)	13.8 (10.8 to 20.4)	8.2 (5.5 to 9.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A Pharmacokinetics (PK): Olaparib Maximum Plasma Concentration at Steady State (Cmax,ss)

End point title	Part A Pharmacokinetics (PK): Olaparib Maximum Plasma Concentration at Steady State (Cmax,ss)

End point description:

Following multiple dosing to steady state of olaparib 300 mg bid, the Cohort 2 olaparib Cmax,ss is presented for olaparib monotherapy and for olaparib given in combination with abiraterone. Only patients with data available for analysis at each time point are presented.
The PK analysis set consisted of all patients who received at least 1 dose of olaparib per the protocol, for whom there was at least 1 reportable PK concentration and who had no important protocol deviations or AEs that impacted on PK on all PK sampling days.

End point type	Secondary

End point timeframe:

PK sampling for Cohort 2 Group 1 was between Days 3 and 7 for olaparib, and Days 4 and 8 for olaparib and abiraterone. PK sampling for Cohort 2 Group 2 was between Days 5 and 7 for abiraterone, and Days 6 and 8 for olaparib and abiraterone.

End point values	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6[8]		
Units: micrograms per millilitre (mcg/mL)				
geometric mean (geometric coefficient of variation)				
Olaparib alone (n=6, n=0)	7.781 (± 25.06)	9999999 (± 99999999)		
Olaparib + abiraterone (n=5, n=6)	6.504 (± 20.90)	7.724 (± 28.05)		

Notes:

[8] - Cohort 2 Group 2 did not receive olaparib alone.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A PK: Abiraterone Cmax,ss

End point title	Part A PK: Abiraterone Cmax,ss

End point description:

Following multiple dosing to steady state of abiraterone 1000 mg once daily, the Cohort 2 abiraterone Cmax,ss is presented for abiraterone monotherapy and for olaparib given in combination with abiraterone. Only patients with data available for analysis at each time point are presented.
The PK analysis set consisted of all patients who received at least 1 dose of olaparib per the protocol, for whom there was at least 1 reportable PK concentration and who had no important protocol deviations or AEs that impacted on PK on all PK sampling days.

End point type	Secondary

End point timeframe:

PK sampling for Cohort 2 Group 1 was between Days 3 and 7 for olaparib, and Days 4 and 8 for olaparib and abiraterone. PK sampling for Cohort 2 Group 2 was between Days 5 and 7 for abiraterone, and Days 6 and 8 for olaparib and abiraterone.

End point values	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6[9]	6		
Units: nanograms per millilitre (ng/mL)				
geometric mean (geometric coefficient of variation)				
Abiraterone alone (n=0, n=6)	99999999 (± 99999999)	145.8 (± 135.5)		
Olaparib + abiraterone (n=6, n=4)	130.7 (± 68.87)	86.12 (± 48.88)		

Notes:

[9] - Cohort 2 Group 1 did not receive abiraterone alone.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A PK: Abiraterone tmax,ss

End point title	Part A PK: Abiraterone tmax,ss

End point description:

Following multiple dosing to steady state of abiraterone 1000 mg once daily, the Cohort 2 abiraterone tmax,ss is presented for abiraterone monotherapy and for olaparib given in combination with abiraterone. Only patients with data available for analysis at each time point are presented.
The PK analysis set consisted of all patients who received at least 1 dose of olaparib per the protocol, for

whom there was at least 1 reportable PK concentration and who had no important protocol deviations or AEs that impacted on PK on all PK sampling days.

End point type	Secondary

End point timeframe:

PK sampling for Cohort 2 Group 1 was between Days 3 and 7 for olaparib, and Days 4 and 8 for olaparib and abiraterone. PK sampling for Cohort 2 Group 2 was between Days 5 and 7 for abiraterone, and Days 6 and 8 for olaparib and abiraterone.

End point values	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6[10]	6		
Units: Hours				
median (full range (min-max))				
Abiraterone alone (n=0, n=6)	99999999 (99999999 to 99999999)	2.525 (1.00 to 3.00)		
Olaparib + abiraterone (n=6, n=4)	3.000 (1.08 to 3.00)	2.500 (2.00 to 3.02)		

Notes:

[10] - Cohort 2 Group 1 did not receive abiraterone alone.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A PK Analysis: Olaparib Time to Reach Maximum Plasma Concentration at Steady State (tmax,ss)

End point title	Part A PK Analysis: Olaparib Time to Reach Maximum Plasma Concentration at Steady State (tmax,ss)

End point description:

Following multiple dosing to steady state of olaparib 300 mg bid, the Cohort 2 olaparib tmax,ss is presented for olaparib monotherapy and for olaparib given in combination with abiraterone. Only patients with data available for analysis at each time point are presented.
The PK analysis set consisted of all patients who received at least 1 dose of olaparib per the protocol, for whom there was at least 1 reportable PK concentration and who had no important protocol deviations or AEs that impacted on PK on all PK sampling days.

End point type	Secondary

End point timeframe:

PK sampling for Cohort 2 Group 1 was between Days 3 and 7 for olaparib, and Days 4 and 8 for olaparib and abiraterone. PK sampling for Cohort 2 Group 2 was between Days 5 and 7 for abiraterone, and Days 6 and 8 for olaparib and abiraterone.

End point values	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6[11]		
Units: Hours (h)				
median (full range (min-max))				
Olaparib alone (n=6, n=0)	2.000 (1.00 to 2.17)	99999999 (99999999 to 99999999)		
Olaparib + abiraterone (n=5, n=6)	2.080 (2.00 to 4.00)	2.000 (0.500 to 3.02)		

Notes:

[11] - Cohort 2 Group 2 did not receive olaparib alone.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A PK Analysis: Olaparib Minimum Plasma Concentration at Steady State (Cmin,ss)

End point title	Part A PK Analysis: Olaparib Minimum Plasma Concentration at Steady State (Cmin,ss)

End point description:

Following multiple dosing to steady state of olaparib 300 mg bid, the Cohort 2 olaparib Cmin,ss is presented for olaparib monotherapy and for olaparib given in combination with abiraterone. Only patients with data available for analysis at each time point are presented.
The PK analysis set consisted of all patients who received at least 1 dose of olaparib per the protocol, for whom there was at least 1 reportable PK concentration and who had no important protocol deviations or AEs that impacted on PK on all PK sampling days.

End point type	Secondary

End point timeframe:

PK sampling for Cohort 2 Group 1 was between Days 3 and 7 for olaparib, and Days 4 and 8 for olaparib and abiraterone. PK sampling for Cohort 2 Group 2 was between Days 5 and 7 for abiraterone, and Days 6 and 8 for olaparib and abiraterone.

End point values	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6[12]		
Units: mcg/mL				
geometric mean (geometric coefficient of variation)				
Olaparib alone (n=6, n=0)	1.264 (± 46.58)	99999999 (± 99999999)		
Olaparib + abiraterone (n=5, n=6)	0.9170 (± 31.56)	1.279 (± 65.36)		

Notes:

[12] - Cohort 2 Group 2 did not receive olaparib alone.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A PK Analysis: Olaparib Area Under the Plasma Concentration-Time Curve at Steady State (AUCss)

End point title	Part A PK Analysis: Olaparib Area Under the Plasma Concentration-Time Curve at Steady State (AUCss)

End point description:

Following multiple dosing to steady state of olaparib 300 mg bid, the Cohort 2 olaparib AUCss is presented for olaparib monotherapy and for olaparib given in combination with abiraterone. Only patients with data available for analysis at each time point are presented.
The PK analysis set consisted of all patients who received at least 1 dose of olaparib per the protocol, for whom there was at least 1 reportable PK concentration and who had no important protocol deviations or AEs that impacted on PK on all PK sampling days.

End point type	Secondary

End point timeframe:

PK sampling for Cohort 2 Group 1 was between Days 3 and 7 for olaparib, and Days 4 and 8 for olaparib and abiraterone. PK sampling for Cohort 2 Group 2 was between Days 5 and 7 for abiraterone, and Days 6 and 8 for olaparib and abiraterone.

End point values	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6	6[13]		
Units: mcg*h/mL				
geometric mean (geometric coefficient of variation)				
Olaparib alone (n=6, n=0)	45.27 (± 31.89)	99999999 (± 99999999)		
Olaparib + abiraterone (n=5, n=6)	40.83 (± 11.47)	49.51 (± 37.30)		

Notes:

[13] - Cohort 2 Group 2 did not receive olaparib alone.

Statistical analyses

No statistical analyses for this end point

Secondary: Part A PK: Abiraterone Cmin,ss

End point title	Part A PK: Abiraterone Cmin,ss

End point description:

Following multiple dosing to steady state of abiraterone 1000 mg once daily, the Cohort 2 abiraterone Cmin,ss is presented for abiraterone monotherapy and for olaparib given in combination with

abiraterone. Only patients with data available for analysis at each time point are presented.
The PK analysis set consisted of all patients who received at least 1 dose of olaparib per the protocol, for whom there was at least 1 reportable PK concentration and who had no important protocol deviations or AEs that impacted on PK on all PK sampling days.

End point type	Secondary

End point timeframe:

PK sampling for Cohort 2 Group 1 was between Days 3 and 7 for olaparib, and Days 4 and 8 for olaparib and abiraterone. PK sampling for Cohort 2 Group 2 was between Days 5 and 7 for abiraterone, and Days 6 and 8 for olaparib and abiraterone.

End point values	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6[14]	6		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Abiraterone alone (n=0, n=6)	99999999 (± 99999999)	8.376 (± 96.52)		
Olaparib + abiraterone (n=6, n=4)	7.983 (± 163.3)	6.358 (± 50.96)		

Notes:

[14] - Cohort 2 Group 1 did not receive abiraterone alone.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Patients Experiencing AEs

End point title	Part B: Percentage of Patients Experiencing AEs[15]

End point description:

The safety and tolerability of olaparib when given in combination with abiraterone was assessed during Part B of the study. The percentage of patients experiencing AEs, including information on seriousness, severity, study treatment relationship and those leading to discontinuation for all doses of olaparib and for abiraterone are presented. Severity of AEs was assessed using the NCI Common Terminology CTCAE v4.0. AEs were assigned to a Grade from 1 through 5 as follows: Grade 1: Mild; Grade 2: Moderate; Grade 3: Severe or medically significant but not immediately life-threatening requiring hospitalisation; Grade 4: Life-threatening consequences; Grade 5: Death related to AE. 'c-r' = causally related. 'discont' = discontinuation. 'ola/pla' = olaparib/placebo.
Part B safety analysis set consisted of all patients randomised into Part B of the study who received at least 1 dose of olaparib/placebo.

End point type	Secondary

End point timeframe:

From first dose of study treatment following randomisation in Part B up to 30 days following last dose of study treatment (up to approximately 3 years).

Notes:

[15] - 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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Percentage of patients				
number (not applicable)				
Any AE c-r to ola/pla + abiraterone	45.1	12.7		
Any AE c-r to ola/pla only	18.3	9.9		
Any AE c-r to abiraterone only	1.4	7.0		
Any AE CTCAE Grade 3 or higher	53.5	28.2		
Any AE CTCAE Grade 3 or higher c-r to ola/pla	23.9	5.6		
Any AE CTCAE Grade 3 or higher c-r to abiraterone	16.9	1.4		
Any AE with outcome = death	5.6	1.4		
Any AE with outcome = death c-r to ola/pla	1.4	0		
Any AE with outcome = death c-r to abiraterone	0	0		
Any SAE	35.2	19.7		
Any SAE c-r to ola/pla	9.9	1.4		
Any SAE c-r to abiraterone	5.6	0		
Any AE causing discont of ola/pla	29.6	9.9		
Any AE causing discont c-r to ola/pla	16.9	5.6		
Any AE causing discont c-r abiraterone	8.5	1.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Part A PK: Abiraterone AUCss

End point title	Part A PK: Abiraterone AUCss

End point description:

Following multiple dosing to steady state of abiraterone 1000 mg once daily, the Cohort 2 abiraterone AUCss is presented for abiraterone monotherapy and for olaparib given in combination with abiraterone. Only patients with data available for analysis at each time point are presented.
The PK analysis set consisted of all patients who received at least 1 dose of olaparib per the protocol, for whom there was at least 1 reportable PK concentration and who had no important protocol deviations or AEs that impacted on PK on all PK sampling days.

End point type	Secondary

End point timeframe:

PK sampling for Cohort 2 Group 1 was between Days 3 and 7 for olaparib, and Days 4 and 8 for olaparib and abiraterone. PK sampling for Cohort 2 Group 2 was between Days 5 and 7 for abiraterone, and Days 6 and 8 for olaparib and abiraterone.

End point values	Part A Cohort 2 Group 1: Olaparib, olaparib + abiraterone	Part A Cohort 2 Group 2: Abiraterone, olaparib + abiraterone		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	6[16]	6		
Units: ng*h/mL				
geometric mean (geometric coefficient of variation)				
Abiraterone alone (n=0, n=6)	99999999 (± 99999999)	825.5 (± 105.5)		
Olaparib + abiraterone (n=6, n=4)	718.9 (± 102.0)	524.6 (± 37.65)		

Notes:

[16] - Cohort 2 Group 1 did not receive abiraterone alone.

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Patients With PSA Responses

End point title	Part B: Percentage of Patients With PSA Responses[17]

End point description:

The percentages of patients with single visit responses and with confirmed responses are presented to assess the anti-tumour activity of olaparib when given in addition to abiraterone, compared with placebo given in addition to abiraterone. A single visit response was defined as any post-dose visit PSA level reduced by 50% or more compared with baseline. A confirmed response was defined as a reduction in PSA level of 50% or more on 2 consecutive occasions at least 4 weeks apart compared with baseline. Patients may have had more than 1 single visit response or confirmed response but were counted once. The Full analysis set consisted of all randomised patients in Part B, regardless of treatment actually received.

End point type	Secondary

End point timeframe:

From baseline, then every 4 weeks up to Week 52, and then every 12 weeks.

Notes:

[17] - 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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Percentage of patients				
number (confidence interval 80%)				
Single visit response	50.7 (43.10 to 58.31)	47.9 (40.29 to 55.49)		
Confirmed response	47.9 (40.29 to 55.49)	42.3 (34.74 to 49.77)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Median Best Percentage Change From Baseline in Prostate Specific Antigen (PSA) Levels

End point title	Part B: Median Best Percentage Change From Baseline in Prostate Specific Antigen (PSA) Levels[18]

End point description:

The median best percentage change from baseline in PSA levels was determined to assess the anti-tumour activity of olaparib when given in addition to abiraterone, compared with placebo given in addition to abiraterone. The best percentage change was defined as the biggest reduction in PSA level compared with baseline or smallest increase in the absence of a decrease.
The Full analysis set consisted of all randomised patients in Part B, regardless of treatment actually received. Only patients with data available for analysis are presented.

End point type	Secondary

End point timeframe:

From baseline, then every 4 weeks up to Week 52, and then every 12 weeks.

Notes:

[18] - 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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	68		
Units: Percentage change in PSA level				
median (full range (min-max))	-54.16 (-100.0 to 533.2)	-49.85 (-100.0 to 230.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Median Best Percentage Change From Baseline in Circulating Tumour Cell (CTC) Level

End point title	Part B: Median Best Percentage Change From Baseline in Circulating Tumour Cell (CTC) Level[19]

End point description:

The best percentage change from baseline in CTC levels was determined to assess the anti-tumour activity of olaparib when given in combination with abiraterone, compared with placebo given in addition to abiraterone. The best percentage change was defined as the biggest CTC level reduction compared with baseline or smallest increase in the absence of a decrease.
The Full analysis set consisted of all randomised patients in Part B, regardless of treatment actually received. Only patients with data available for analysis are presented.

End point type	Secondary

End point timeframe:

From baseline, then every 4 weeks up to Week 52, and then every 12 weeks.

Notes:

[19] - 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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	61		
Units: Percentage change in CTC level				
median (full range (min-max))	-1.0 (-478 to 613)	-1.0 (-1279 to 414)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part B: Percentage of Patients With At Least One Objective Response (Objective Response Rate [ORR])

End point title	Part B: Percentage of Patients With At Least One Objective Response (Objective Response Rate [ORR])[20]

End point description:

The overall radiological ORR was calculated to assess the anti-tumour activity of olaparib when given in combination with abiraterone, compared with placebo given in addition to abiraterone. The best overall ORR was defined as the percentage of patients with at least 1 visit response of complete response (CR) or partial response (PR) in soft tissue disease assessed by RECIST 1.1 and also bone scan status of non-progressive disease or non-evaluable for their bone scans assessed by PCWG-2. CR: Disappearance of all target lesions. Reduction of pathological lymph nodes to <10 millimetres. PR: At least a 30% decrease in the sum of diameters of target lesions from baseline. The percentage of patients with a response is presented.
The Full analysis set consisted of all randomised patients in Part B, regardless of treatment actually received, and only patients with measurable disease at baseline are included.

End point type	Secondary

End point timeframe:

From baseline, then every 4 weeks up to Week 52, and then every 12 weeks.

Notes:

[20] - 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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	38		
Units: Percentage of patients				
number (not applicable)	27.3	31.6		

Statistical analyses

Statistical analysis title	Comparison of ORR
Comparison groups	Part B: Olaparib + abiraterone v Part B: Placebo + abiraterone

Number of subjects included in analysis	71
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.309 [21]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.813
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.285
upper limit	2.261

Notes:

[21] - The p value was calculated with a 1-sided significance level of 2.5%.

Secondary: Part B: Median Overall Survival (OS)

End point title	Part B: Median Overall Survival (OS)[22]

End point description:

OS was determined to assess the efficacy of olaparib when given in addition to abiraterone, compared with placebo given in addition to abiraterone. OS was performed at the time of the analysis of rPFS, and the median OS, calculated using the Kaplan-Meier technique, is presented.
The Full analysis set consisted of all randomised patients in Part B, regardless of treatment actually received.

End point type	Secondary

End point timeframe:

From baseline, every 12 weeks up to Week 72, then every 24 weeks up to 24 months.

Notes:

[22] - 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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Months				
median (confidence interval 95%)	22.7 (17.4 to 29.4)	20.9 (17.6 to 26.3)		

Statistical analyses

Statistical analysis title	Comparison of OS
Comparison groups	Part B: Olaparib + abiraterone v Part B: Placebo + abiraterone

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.331 [23]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.911
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.384

Notes:

[23] - The p value was calculated with a 1-sided significance level of 2.5%.

Secondary: Median Time to First Subsequent Therapy (TFST) and Median Time to Second Subsequent Therapy (TSST)

End point title	Median Time to First Subsequent Therapy (TFST) and Median Time to Second Subsequent Therapy (TSST)[24]

End point description:

The TFST and TSST were determined to assess the anti-tumour activity of olaparib when given in combination with abiraterone, compared with placebo given in addition to abiraterone. TFST was defined as the time from randomisation to the earlier of first subsequent anti-cancer therapy start date following study treatment discontinuation, or death. TSST was defined as the time from randomisation to the earlier of the second subsequent anti-cancer therapy start date following study treatment discontinuation, or death.
The Full analysis set consisted of all randomised patients in Part B, regardless of treatment actually received.

End point type	Secondary

End point timeframe:

From randomisation until analysis cut-off date (up to approximately 3 years).

Notes:

[24] - 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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Months				
median (confidence interval 95%)				
TFST	13.5 (11.1 to 17.2)	9.7 (7.3 to 12.9)		
TSST	19.6 (16.5 to 25.1)	18.0 (16.9 to 20.6)		

Statistical analyses

Statistical analysis title	Comparison of TSST
Comparison groups	Part B: Olaparib + abiraterone v Part B: Placebo + abiraterone

Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.147 [25]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.809
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.545
upper limit	1.201

Notes:

[25] - The p value was calculated with a 1-sided significance level of 2.5%.

Statistical analysis title	Comparison of TFST
Comparison groups	Part B: Olaparib + abiraterone v Part B: Placebo + abiraterone
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.095 [26]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.781
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.54
upper limit	1.13

Notes:

[26] - The p value was calculated with a 1-sided significance level of 2.5%.

Secondary: Part B: Median Time to Second Progression or Death (PFS2)

End point title	Part B: Median Time to Second Progression or Death (PFS2)[27]

End point description:

The efficacy of olaparib when given in combination with abiraterone was assessed by PFS2, defined by local standard clinical practice and included objective radiological progression by RECIST 1.1 (soft tissue), symptomatic progression, rise in PSA level or death in the absence of overall progression.
The Full analysis set consisted of all randomised patients in Part B, regardless of treatment actually received.

End point type	Secondary

End point timeframe:

From randomisation until analysis cut-off date (up to approximately 3 years).

Notes:

[27] - 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: All arms are reported for this cohort/part.

End point values	Part B: Olaparib + abiraterone	Part B: Placebo + abiraterone		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71[28]	71		
Units: Months				
median (confidence interval 95%)	23.3 (17.4 to 99999999)	18.5 (16.1 to 23.8)		

Notes:

[28] - Too few patients with events to allow calculation of upper limit for 95% confidence interval.

Statistical analyses

Statistical analysis title	Comparison of PFS2
Comparison groups	Part B: Olaparib + abiraterone v Part B: Placebo + abiraterone
Number of subjects included in analysis	142
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.14 [29]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.788
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.511
upper limit	1.215

Notes:

[29] - The p value was calculated with a 1-sided significance level of 2.5%.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part A: From baseline (Day 1 for each cohort) up to 30 days following last dose of study treatment. Part B: From first dose of study treatment following randomisation up to 30 days following last dose of study treatment (up to approximately 3 years).

Adverse event reporting additional description:

The Part A Safety analysis set consisted of all patients who received at least 1 dose of study treatment in Part A.
Part B safety analysis set consisted of all patients randomised into Part B of the study who received at least 1 dose of olaparib/placebo.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Part A Cohort 1: Olaparib 200 mg + abiraterone

Reporting group description:

Patients received olaparib 200 mg bid and abiraterone 1000 mg once daily. Patients were assessed at Weeks 1, 2 and 4, then every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Reporting group title	Part A Cohort 2: Olaparib 300 mg + abiraterone

Reporting group description:

If the combination of olaparib 200 mg + abiraterone 1000 mg was well tolerated (determined after a minimum of 14 days treatment in Cohort 1), patients were recruited into Cohort 2. Cohort 2 Group 1: patients received olaparib 300 mg bid alone for 3 to 7 days. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 5 days. Cohort 2 Group 2: patients received abiraterone 1000 mg once daily alone for 5 to 7 days. Patients then received olaparib 300 mg bid and abiraterone 1000 mg once daily for at least 3 days. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Reporting group title	Part B: Olaparib + abiraterone

Reporting group description:

Patients received the selected dose of olaparib 300 mg bid + abiraterone 1000 mg once daily. Patients were assessed every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Reporting group title	Part B: Placebo + abiraterone

Reporting group description:

Patients received placebo bid + abiraterone 1000 mg once daily. Patients were assessed every 4 weeks up to Week 52, and every 12 weeks thereafter. Patients also received prednisone or prednisolone 5 mg bid in combination with the abiraterone treatment.

Serious adverse events	Part A Cohort 1: Olaparib 200 mg + abiraterone	Part A Cohort 2: Olaparib 300 mg + abiraterone	Part B: Olaparib + abiraterone
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 13 (23.08%)	25 / 71 (35.21%)
number of deaths (all causes)	0	1	43
number of deaths resulting from adverse events	0	0	1
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Internal haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral ischaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (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
General physical health deterioration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	2 / 71 (2.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Urinary tract stoma complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Patella fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (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			

Myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	2 / 71 (2.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Acute myocardial infarction			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	2 / 71 (2.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	5 / 71 (7.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Febrile neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
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			
Eye haemorrhage			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (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
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proctitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (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
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			

subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	4 / 71 (5.63%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mediastinitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (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
Pyelonephritis chronic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Bacterial infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	2 / 71 (2.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
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 tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	2 / 71 (2.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			

subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B: Placebo + abiraterone		
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 71 (19.72%)		
number of deaths (all causes)	45		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Squamous cell carcinoma of the tongue			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Internal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombosis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peripheral ischaemia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General physical health deterioration			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Interstitial lung disease			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Urinary tract stoma complication			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal fracture			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Patella fracture			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Myocardial infarction			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure chronic			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac failure			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute myocardial infarction			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombotic stroke			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ischaemic stroke				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Febrile neutropenia				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Eye haemorrhage				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Vomiting				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				

subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Renal failure				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Back pain				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Pneumonia				
subjects affected / exposed	3 / 71 (4.23%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Mediastinitis				
subjects affected / exposed	0 / 71 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 71 (1.41%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Cellulitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis chronic			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Bacterial infection			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bacteraemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Candida infection			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			

subjects affected / exposed	1 / 71 (1.41%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Part A Cohort 1: Olaparib 200 mg + abiraterone	Part A Cohort 2: Olaparib 300 mg + abiraterone	Part B: Olaparib + abiraterone
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)	7 / 13 (53.85%)	63 / 71 (88.73%)
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	3 / 71 (4.23%)
occurrences (all)	0	0	3
Hot flush			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	3 / 71 (4.23%)
occurrences (all)	1	1	3
Haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	4 / 71 (5.63%)
occurrences (all)	0	0	5
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	2 / 13 (15.38%)	3 / 71 (4.23%)
occurrences (all)	0	3	3
Oedema peripheral			

subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	14 / 71 (19.72%)
occurrences (all)	1	0	16
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	15 / 71 (21.13%)
occurrences (all)	1	1	16
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	16 / 71 (22.54%)
occurrences (all)	0	0	22
Pyrexia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	10 / 71 (14.08%)
occurrences (all)	1	0	11
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	2 / 71 (2.82%)
occurrences (all)	1	0	2
Pneumonitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	1	0	1
Nasal congestion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	10 / 71 (14.08%)
occurrences (all)	2	1	12
Cough			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	11 / 71 (15.49%)
occurrences (all)	0	2	17
Psychiatric disorders			
Euphoric mood			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	2 / 71 (2.82%)
occurrences (all)	1	0	2
Depressed mood			

subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Affect lability			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	6 / 71 (8.45%)
occurrences (all)	0	0	7
Investigations			
Blood urea increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	3	0	1
Blood potassium decreased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	2 / 71 (2.82%)
occurrences (all)	1	2	3
Blood glucose increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	3 / 71 (4.23%)
occurrences (all)	3	1	3
Blood calcium decreased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	1	0	1
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	1	0	1
Body temperature increased			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Electrocardiogram QT prolonged			

subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	2	0
Haemoglobin decreased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	2	0
Heart rate irregular			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Urine output increased			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	4 / 71 (5.63%)
occurrences (all)	0	0	4
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	3 / 71 (4.23%)
occurrences (all)	1	0	3
Fall			
subjects affected / exposed	2 / 3 (66.67%)	1 / 13 (7.69%)	5 / 71 (7.04%)
occurrences (all)	2	1	5
Humerus fracture			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Laceration			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	1 / 71 (1.41%)
occurrences (all)	2	1	1
Lower limb fracture			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Rib fracture			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Thermal burn			

subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Wound secretion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Tremor			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 71 (1.41%)
occurrences (all)	0	1	1
Headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	6 / 71 (8.45%)
occurrences (all)	1	0	9
Dysgeusia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	4 / 71 (5.63%)
occurrences (all)	0	0	5
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	4 / 71 (5.63%)
occurrences (all)	0	1	5
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	8 / 71 (11.27%)
occurrences (all)	0	1	8
Lymphopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 71 (1.41%)
occurrences (all)	0	2	1
Anaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	18 / 71 (25.35%)
occurrences (all)	0	1	23
Ear and labyrinth disorders			

Tympanic membrane perforation			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Cerumen impaction			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	1	1	0
Eyelid oedema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	4 / 71 (5.63%)
occurrences (all)	0	0	5
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	8 / 71 (11.27%)
occurrences (all)	1	0	9
Abdominal discomfort			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Dyspepsia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	1	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	1	0	1
Constipation			
subjects affected / exposed	1 / 3 (33.33%)	2 / 13 (15.38%)	17 / 71 (23.94%)
occurrences (all)	1	2	19
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)	3 / 13 (23.08%)	11 / 71 (15.49%)
occurrences (all)	4	3	17
Vomiting			
subjects affected / exposed	1 / 3 (33.33%)	2 / 13 (15.38%)	14 / 71 (19.72%)
occurrences (all)	4	3	26
Rectal haemorrhage			

subjects affected / exposed	2 / 3 (66.67%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	2	0	1
Nausea			
subjects affected / exposed	2 / 3 (66.67%)	2 / 13 (15.38%)	27 / 71 (38.03%)
occurrences (all)	5	2	42
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	4 / 71 (5.63%)
occurrences (all)	0	0	4
Frequent bowel movements			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Dysphagia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	5 / 71 (7.04%)
occurrences (all)	0	0	5
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Skin lesion			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Skin atrophy			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	1	0	1
Purpura			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	2 / 71 (2.82%)
occurrences (all)	1	0	2
Dry skin			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Blister			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0

Renal and urinary disorders			
Hypertonic bladder			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Urinary retention			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	2 / 71 (2.82%)
occurrences (all)	0	1	2
Pollakiuria			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	8 / 71 (11.27%)
occurrences (all)	1	1	8
Back pain			
subjects affected / exposed	3 / 3 (100.00%)	1 / 13 (7.69%)	17 / 71 (23.94%)
occurrences (all)	5	1	21
Bone pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	11 / 71 (15.49%)
occurrences (all)	0	1	12
Groin pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 71 (1.41%)
occurrences (all)	0	1	1
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	4 / 71 (5.63%)
occurrences (all)	0	1	4
Musculoskeletal chest pain			
subjects affected / exposed	2 / 3 (66.67%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	4	0	1
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	7 / 71 (9.86%)
occurrences (all)	0	0	8
Spinal pain			

subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	2 / 71 (2.82%)
occurrences (all)	0	1	2
Pain in extremity			
subjects affected / exposed	1 / 3 (33.33%)	2 / 13 (15.38%)	5 / 71 (7.04%)
occurrences (all)	2	3	6
Osteoporosis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Osteopenia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Neck pain			
subjects affected / exposed	0 / 3 (0.00%)	2 / 13 (15.38%)	2 / 71 (2.82%)
occurrences (all)	0	2	2
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Oral candidiasis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	2 / 71 (2.82%)
occurrences (all)	0	1	2
Lower respiratory tract infection			
subjects affected / exposed	2 / 3 (66.67%)	0 / 13 (0.00%)	0 / 71 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	4 / 71 (5.63%)
occurrences (all)	0	0	4
Furuncle			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Cellulitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	3	0
Arthritis infective			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0

Sinusitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	1	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	8 / 71 (11.27%)
occurrences (all)	0	0	10
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 13 (0.00%)	8 / 71 (11.27%)
occurrences (all)	0	0	9
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	12 / 71 (16.90%)
occurrences (all)	1	1	12
Fluid retention			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 3 (0.00%)	1 / 13 (7.69%)	1 / 71 (1.41%)
occurrences (all)	0	1	1
Hypocalcaemia			
subjects affected / exposed	1 / 3 (33.33%)	0 / 13 (0.00%)	1 / 71 (1.41%)
occurrences (all)	1	0	1
Hypokalaemia			
subjects affected / exposed	1 / 3 (33.33%)	1 / 13 (7.69%)	5 / 71 (7.04%)
occurrences (all)	3	3	7

Non-serious adverse events	Part B: Placebo + abiraterone		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	52 / 71 (73.24%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	5		
Hot flush			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Haematoma			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Peripheral swelling			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Oedema peripheral			
subjects affected / exposed	8 / 71 (11.27%)		
occurrences (all)	8		
Fatigue			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences (all)	11		
Asthenia			
subjects affected / exposed	10 / 71 (14.08%)		
occurrences (all)	11		
Pyrexia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Pneumonitis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Cough			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Psychiatric disorders			

Euphoric mood			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Depressed mood			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Affect lability			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Investigations			
Blood urea increased			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Blood potassium decreased			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	2		
Blood glucose increased			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Blood creatinine increased			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Blood calcium decreased			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Alanine aminotransferase increased			

subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Body temperature increased			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Haemoglobin decreased			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Heart rate irregular			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Urine output increased			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Fall			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	2		
Humerus fracture			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Laceration			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Lower limb fracture			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Rib fracture			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Thermal burn			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Wound secretion			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Arrhythmia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Tremor			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	7		
Dysgeusia			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Dizziness			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Lymphopenia			

subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Anaemia			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Tympanic membrane perforation			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Cerumen impaction			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Eye disorders			
Ocular hyperaemia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Eyelid oedema			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Abdominal discomfort			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Dyspepsia			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Abdominal pain upper			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Constipation			
subjects affected / exposed	8 / 71 (11.27%)		
occurrences (all)	10		
Diarrhoea			

subjects affected / exposed	8 / 71 (11.27%)		
occurrences (all)	11		
Vomiting			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences (all)	12		
Rectal haemorrhage			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	15 / 71 (21.13%)		
occurrences (all)	16		
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Frequent bowel movements			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Dysphagia			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Skin lesion			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Skin atrophy			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Purpura			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		

Dry skin			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Blister			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Hypertonic bladder			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Urinary retention			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Back pain			
subjects affected / exposed	14 / 71 (19.72%)		
occurrences (all)	18		
Bone pain			
subjects affected / exposed	9 / 71 (12.68%)		
occurrences (all)	9		
Groin pain			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Joint swelling			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Muscle spasms			
subjects affected / exposed	2 / 71 (2.82%)		
occurrences (all)	2		
Musculoskeletal chest pain			

subjects affected / exposed	5 / 71 (7.04%)		
occurrences (all)	7		
Musculoskeletal pain			
subjects affected / exposed	6 / 71 (8.45%)		
occurrences (all)	7		
Spinal pain			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Pain in extremity			
subjects affected / exposed	4 / 71 (5.63%)		
occurrences (all)	4		
Osteoporosis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Osteopenia			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Infections and infestations			
Sepsis			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		
Oral candidiasis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	2		
Lower respiratory tract infection			
subjects affected / exposed	3 / 71 (4.23%)		
occurrences (all)	3		
Gastroenteritis			
subjects affected / exposed	1 / 71 (1.41%)		
occurrences (all)	1		
Furuncle			
subjects affected / exposed	0 / 71 (0.00%)		
occurrences (all)	0		

Cellulitis subjects affected / exposed occurrences (all)	0 / 71 (0.00%) 0		
Arthritis infective subjects affected / exposed occurrences (all)	0 / 71 (0.00%) 0		
Sinusitis subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 1		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	3 / 71 (4.23%) 3		
Urinary tract infection subjects affected / exposed occurrences (all)	2 / 71 (2.82%) 2		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	5 / 71 (7.04%) 5		
Fluid retention subjects affected / exposed occurrences (all)	0 / 71 (0.00%) 0		
Hyperglycaemia subjects affected / exposed occurrences (all)	1 / 71 (1.41%) 2		
Hypocalcaemia subjects affected / exposed occurrences (all)	2 / 71 (2.82%) 2		
Hypokalaemia subjects affected / exposed occurrences (all)	4 / 71 (5.63%) 6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 August 2014	-Frequency of clinic visits increased to every 4 weeks for first 52 weeks. -Log rank test replaced Cox proportional hazrd model as primary analysis for time-to-event endpoints. -Inclusion of additional Eastern Cooperative Oncology Group assessments to Part B. -Removed text relating to a separate study for chemotherapy-naive CRPC patients as study was not planned; and text relating to closure of Part A database. -Amendment of text relating to Hy's law cases.
13 October 2015	-Secondary endpoints amended to include investigation of Ataxia telangiectasia mutated gene and Breast cancer gene mutations as candidate predictors of response to olaparib. -Changes to text relating to contraception during study. -Updated text regarding olaparib drug-drug interactions to reflect recent findings. -Added text to state once olaparib/placebo dose had been reduced, escalation was not permitted to clarify dose reduction management. -Text regarding olaparib anaemia management was updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

'99999999' in the end points section indicates data is not available.

Notes: