Clinical trial results:
TOPARP: Phase II Trial of Olaparib in Patients with Advanced Castration Resistant Prostate Cancer.

Summary

EudraCT number	2011-000601-49
Trial protocol	GB
Global end of trial date	17 September 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025
Summary attachment (see zip file)	DNA-Repair Defects and Olaparib in Metastatic Prostate Cancer (Mateo 2015 - DNA Repair Defects and Olaparib in Metastatic Prostate Cancer - NEJM.pdf) DNA Repair Defects and Olaparib in Metastatic Prostate Cancer - Appendix (Mateo 2015 - Appendix - DNA Repair Defects and Olaparib in Metastatic Prostate Cancer - NEJM.pdf) Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial (TOPARP-B Lancet Oncology Mateo Porta et al - final citation 202001.pdf) Olaparib in patients with metastatic castration-resistant prostate cancer with DNA repair gene aberrations (TOPARP-B): a multicentre, open-label, randomised, phase 2 trial - Supplementary Materials (Supplementary Material - final.pdf)

Trial information

Trial identification

Sponsor protocol code	ICR-CTSU/2011/10030

Additional study identifiers

ISRCTN number	ISRCTN15124653
ClinicalTrials.gov id (NCT number)	NCT01682772
WHO universal trial number (UTN)	-
Other trial identifiers	ICR/RMH CCR Number: 3592, CR UK Reference Number: CRUK/C12540/A12354, REC Reference Number: 11/LO/2019

Notes:

Sponsors

Sponsor organisation name	The Institute of Cancer Research
Sponsor organisation address	15 Cotswold Road, London, United Kingdom,
Public contact	TOPARP Trial Manager, Institute of Cancer Research - Clinical Trials and Statistics Unit, TOPARP-icrctsu@icr.ac.uk
Scientific contact	TOPARP Trial Manager, Institute of Cancer Research - Clinical Trials and Statistics Unit, TOPARP-icrctsu@icr.ac.uk
Sponsor organisation name	The Royal Marsden Hospital NHS Foundation Trust
Sponsor organisation address	Downs Rd, Sutton, United Kingdom,
Public contact	TOPARP Trial Manager, The Royal Marsden Hospital NHS Foundation Trust, TOPARP-icrctsu@icr.ac.uk

Scientific contact	TOPARP Trial Manager, The Royal Marsden Hospital NHS Foundation Trust, TOPARP-icrctsu@icr.ac.uk

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	17 September 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 August 2021
Global end of trial reached?	Yes
Global end of trial date	17 September 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the activity of olaparib in patients with advanced prostate cancer who have progressed following one or two chemotherapy regimens including docetaxel.

Protection of trial subjects:

Patients were followed closely for any signs of adverse events of study treatment and the study protocol contains guidance for investigators on how to manage the adverse effects that were expected. The expected adverse effects were also listed in the patient information sheet. Patients had regular blood tests to ensure the safety of patients.

Patients were given a verbal explanation of the TOPARP trial and were offered the patient information sheet and any additional information about clinical trials and alternative treatments that would normally be offered to take home and discuss with friends and family. Patients were usually given at least 24 hours to consider the trial information and those who agreed to trial entry were asked to sign the consent form prior to any study specific procedures. The Principal Investigator at each site was responsible for ensuring written informed consent was obtained for each patient. This trial was overseen by an Independent Data Monitoring Committee, which would stop the study if there was any cause of concern with respect to patient safety and patients' oncologists would be notified immediately if this was the case.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 April 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 148
Worldwide total number of subjects	148
EEA total number of subjects	0

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)	50
From 65 to 84 years	97
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

TOPARP-A: 50 patients recruited from 04/07/2012 to 22/09/2014, across 8 UK centres.
TOPARP-B: 98 patients recruited from 01/04/2015 to 30/08/2015, across 17 UK centres.

Pre-assignment

Screening details:

TOPARP-A screening: 88 patients assessed for eligibility, 38 excluded from trial entry (37 did not meet inclusion criteria; 1 fractured hip during screening).
TOPARP-B screening: Of the 592 patients with at least one sample good enough for analysis, 161 were had alterations in any DNA defect repair gene. Of these, 98 DDRm patients were randomised.

Period 1

Period 1 title	TOPARP-A and TOPARP-B trial entry (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	TOPARP-A: Olaparib 400mg

Arm description:

Patients receive single agent olaparib at a dose of 400 mg twice daily, continuously on a 28-day cycle. Olaparib will be administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason.

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

Dosage and administration details:

400mg orally, BID

Arm title	TOPARP-B: Olaparib 300mg

Arm description:

Patients randomised to receive 300mg twice daily, continuously on a 28-day cycle. Olaparib is administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason. Patients randomised to the 300mg group are offered the option of dose escalation to 400mg twice daily.

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

Dosage and administration details:

400mg orally, BID

Investigational medicinal product name	Olaparib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

300mg orally, BID

Arm title	TOPARP-B: Olaparib 400mg

Arm description:

Patients randomised to receive 400mg twice daily, continuously on a 28-day cycle. Olaparib is administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason.

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

Dosage and administration details:

Olaparib 400mg orally, BID

Number of subjects in period 1	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg
Started	50	49	49
Completed	49	49	49
Not completed	1	0	0
Patient choice	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	TOPARP-A: Olaparib 400mg
Reporting group description:	
Patients receive single agent olaparib at a dose of 400 mg twice daily, continuously on a 28-day cycle. Olaparib will be administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason.	
Reporting group title	TOPARP-B: Olaparib 300mg
Reporting group description:	
Patients randomised to receive 300mg twice daily, continuously on a 28-day cycle. Olaparib is administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason. Patients randomised to the 300mg group are offered the option of dose escalation to 400mg twice daily.	
Reporting group title	TOPARP-B: Olaparib 400mg
Reporting group description:	
Patients randomised to receive 400mg twice daily, continuously on a 28-day cycle. Olaparib is administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason.	

Reporting group values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg
Number of subjects	50	49	49
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	18	19	13
From 65-84 years	32	29	36
85 years and over	0	1	0
Age continuous Units: years			
median	67.5	67.3	67.6
inter-quartile range (Q1-Q3)	60.6 to 72.2	61.2 to 72.1	63.2 to 72.7
Gender categorical Units: Subjects			
Female	0	0	0
Male	50	49	49
Primary tumour stage at diagnosis Units: Subjects			
T0	3	1	4
T1	1	3	3
T2	10	25	26
T3	21	8	7
T4	8	12	8

Unknown	7	0	1
Lymphadenopathy at diagnosis Units: Subjects			
N0	19	17	22
N1	15	17	16
N2	1	1	0
Unknown / NX	15	14	11
Metastatic disease at diagnosis Units: Subjects			
Yes	23	24	25
No	27	24	21
Not available	0	1	3
Lung metastases at diagnosis Units: Subjects			
Yes	0	1	1
No	23	23	24
No metastatic disease at diagnosis	27	25	24
Lymph nodes metastases at diagnosis Units: Subjects			
Yes	9	14	10
No	14	10	15
No metastatic disease at diagnosis	27	25	24
Liver metastases at diagnosis Units: Subjects			
Yes	2	1	1
No	21	23	24
No metastatic disease at diagnosis	27	25	24
Bone metastases at diagnosis Units: Subjects			
Yes	22	19	22
No	1	5	3
No metastatic disease at diagnosis	27	25	24
Gleason score at diagnosis Units: Subjects			
Score=5	1	1	0
Score=6	0	0	3
Score=7	12	3	12
Score=8	14	8	6
Score=9	15	28	22
Score=10	1	6	1
Unknown	7	3	5
Neuroendocrine features present at diagnosis Units: Subjects			
Yes	1	1	1
No	44	47	43
Unknown	5	1	5
Diagnosis of small cell prostate cancer Units: Subjects			
Yes	1	0	3
No	43	49	42

Unknown	6	0	4
Method of progression at trial entry Units: Subjects			
PSA only	12	15	12
Radiographic (with or without PSA progression)	38	34	37
RECIST measurable disease at trial entry Units: Subjects			
Target lesions (TOPARP-A)	32	0	0
Non-target lesions only (TOPARP-A)	10	0	0
No target or non-target lesions (TOPARP-A)	8	0	0
Bone lesions only (TOPARP-B)	0	5	5
Non-measurable disease only +/ bone (TOPARP-B)	0	5	8
Measurable disease +/ bone (TOPARP-B)	0	39	36
ECOG performance status at trial entry Units: Subjects			
Status 0	9	12	15
Status 1	35	32	25
Status 2	6	5	9
Received prior regimens for CRPC Units: Subjects			
2 regimens	3	0	0
3 regimens	7	0	0
>=4 regimens	40	0	0
Not reported (TOPARP-B)	0	49	49
DNA damage response aberration subgroup: BRCA1/2 Units: Subjects			
Yes	16	15	17
No	33	34	32
Unknown	1	0	0
DNA damage response aberration subgroup: ATM Units: Subjects			
Yes	5	10	11
No	44	39	38
Unknown	1	0	0
DNA damage response aberration subgroup: CDK12 Units: Subjects			
Yes	0	15	6
No	49	34	43
Unknown	1	0	0
DNA damage response aberration subgroup: PALB2 Units: Subjects			
Yes	1	3	4
No	48	46	45
Unknown	1	0	0
Previous treatments for prostate cancer:			

Radical radiotherapy Units: Subjects			
Yes	18	22	21
No	32	27	28
Previous treatments for prostate cancer: Prostatectomy Units: Subjects			
Yes	7	7	6
No	43	42	43
Previous treatments for prostate cancer: Transurethral resection of the prostate Units: Subjects			
Yes	2	7	5
No	48	42	44
Previous treatments for prostate cancer: Abiraterone Units: Subjects			
Yes	48	24	22
No	2	25	27
Previous treatments for prostate cancer: Enzalutamide Units: Subjects			
Yes	14	27	29
No	36	22	20
Previous treatments for prostate cancer: Abiraterone or enzalutamide or both Units: Subjects			
Yes	49	43	45
No	1	6	4
Previous treatments for prostate cancer: Docetaxel Units: Subjects			
Yes	50	49	49
No	0	0	0
Previous treatments for prostate cancer: Cabazitaxel Units: Subjects			
Yes	29	15	22
No	21	34	27
Previous treatments for prostate cancer: Radium-223 Units: Subjects			
Yes	1	6	8
No	49	43	41
Previous treatments for prostate cancer: Denosumab Units: Subjects			
Yes	1	1	0
No	49	48	49
Previous treatments for prostate cancer: Zoledronic acid Units: Subjects			
Yes	14	1	2
No	36	48	47

Years since diagnosis of prostate cancer			
Units: Years			
median	5.0	3.5	5.2
inter-quartile range (Q1-Q3)	3.4 to 7.9	2.4 to 6.4	3.6 to 7.3
Years since confirmed castrate resistant disease			
Units: Years			
median	2.2	2.4	3.0
inter-quartile range (Q1-Q3)	1.7 to 3.9	1.2 to 3.7	1.8 to 4.0
PSA at diagnosis			
Units: ng/mL			
median	57.0	67.0	62.0
inter-quartile range (Q1-Q3)	17.5 to 637.0	19.0 to 170.5	20.1 to 244.5
CTC count at trial entry			
Units: cells/7.5ml blood			
median	37.0	6.0	6.5
inter-quartile range (Q1-Q3)	14.0 to 110	1.0 to 44.0	2.0 to 74.0
PSA at trial entry			
Units: ng/mL			
median	349.5	151.5	158.0
inter-quartile range (Q1-Q3)	153.0 to 806.0	49.0 to 444.9	45.5 to 472.0

Reporting group values	Total		
Number of subjects	148		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	50		
From 65-84 years	97		
85 years and over	1		
Age continuous			
Units: years			
median			
inter-quartile range (Q1-Q3)	-		
Gender categorical			
Units: Subjects			
Female	0		
Male	148		
Primary tumour stage at diagnosis			
Units: Subjects			
T0	8		
T1	7		
T2	61		
T3	36		
T4	28		

Unknown	8		
Lymphadenopathy at diagnosis Units: Subjects			
N0	58		
N1	48		
N2	2		
Unknown / NX	40		
Metastatic disease at diagnosis Units: Subjects			
Yes	72		
No	72		
Not available	4		
Lung metastases at diagnosis Units: Subjects			
Yes	2		
No	70		
No metastatic disease at diagnosis	76		
Lymph nodes metastases at diagnosis Units: Subjects			
Yes	33		
No	39		
No metastatic disease at diagnosis	76		
Liver metastases at diagnosis Units: Subjects			
Yes	4		
No	68		
No metastatic disease at diagnosis	76		
Bone metastases at diagnosis Units: Subjects			
Yes	63		
No	9		
No metastatic disease at diagnosis	76		
Gleason score at diagnosis Units: Subjects			
Score=5	2		
Score=6	3		
Score=7	27		
Score=8	28		
Score=9	65		
Score=10	8		
Unknown	15		
Neuroendocrine features present at diagnosis Units: Subjects			
Yes	3		
No	134		
Unknown	11		
Diagnosis of small cell prostate cancer Units: Subjects			
Yes	4		
No	134		

Unknown	10		
Method of progression at trial entry Units: Subjects			
PSA only	39		
Radiographic (with or without PSA progression)	109		
RECIST measurable disease at trial entry Units: Subjects			
Target lesions (TOPARP-A)	32		
Non-target lesions only (TOPARP-A)	10		
No target or non-target lesions (TOPARP-A)	8		
Bone lesions only (TOPARP-B)	10		
Non-measurable disease only +/ bone (TOPARP-B)	13		
Measurable disease +/ bone (TOPARP-B)	75		
ECOG performance status at trial entry Units: Subjects			
Status 0	36		
Status 1	92		
Status 2	20		
Received prior regimens for CRPC Units: Subjects			
2 regimens	3		
3 regimens	7		
>=4 regimens	40		
Not reported (TOPARP-B)	98		
DNA damage response aberration subgroup: BRCA1/2 Units: Subjects			
Yes	48		
No	99		
Unknown	1		
DNA damage response aberration subgroup: ATM Units: Subjects			
Yes	26		
No	121		
Unknown	1		
DNA damage response aberration subgroup: CDK12 Units: Subjects			
Yes	21		
No	126		
Unknown	1		
DNA damage response aberration subgroup: PALB2 Units: Subjects			
Yes	8		
No	139		
Unknown	1		
Previous treatments for prostate cancer:			

Radical radiotherapy Units: Subjects			
Yes	61		
No	87		
Previous treatments for prostate cancer: Prostatectomy Units: Subjects			
Yes	20		
No	128		
Previous treatments for prostate cancer: Transurethral resection of the prostate Units: Subjects			
Yes	14		
No	134		
Previous treatments for prostate cancer: Abiraterone Units: Subjects			
Yes	94		
No	54		
Previous treatments for prostate cancer: Enzalutamide Units: Subjects			
Yes	70		
No	78		
Previous treatments for prostate cancer: Abiraterone or enzalutamide or both Units: Subjects			
Yes	137		
No	11		
Previous treatments for prostate cancer: Docetaxel Units: Subjects			
Yes	148		
No	0		
Previous treatments for prostate cancer: Cabazitaxel Units: Subjects			
Yes	66		
No	82		
Previous treatments for prostate cancer: Radium-223 Units: Subjects			
Yes	15		
No	133		
Previous treatments for prostate cancer: Denosumab Units: Subjects			
Yes	2		
No	146		
Previous treatments for prostate cancer: Zoledronic acid Units: Subjects			
Yes	17		
No	131		

Years since diagnosis of prostate cancer Units: Years median inter-quartile range (Q1-Q3)	-		
Years since confirmed castrate resistant disease Units: Years median inter-quartile range (Q1-Q3)	-		
PSA at diagnosis Units: ng/mL median inter-quartile range (Q1-Q3)	-		
CTC count at trial entry Units: cells/7.5ml blood median inter-quartile range (Q1-Q3)	-		
PSA at trial entry Units: ng/mL median inter-quartile range (Q1-Q3)	-		

End points

End points reporting groups

Reporting group title	TOPARP-A: Olaparib 400mg

Reporting group description:

Patients receive single agent olaparib at a dose of 400 mg twice daily, continuously on a 28-day cycle. Olaparib will be administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason.

Reporting group title	TOPARP-B: Olaparib 300mg

Reporting group description:

Patients randomised to receive 300mg twice daily, continuously on a 28-day cycle. Olaparib is administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason. Patients randomised to the 300mg group are offered the option of dose escalation to 400mg twice daily.

Reporting group title	TOPARP-B: Olaparib 400mg

Reporting group description:

Patients randomised to receive 400mg twice daily, continuously on a 28-day cycle. Olaparib is administered until objective disease progression or unacceptable toxicity or patient withdrawal for whatever reason.

Subject analysis set title	TOPARP-A biomarker positive
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patient was considered to be biomarker-positive if a homozygous deletion or deleterious mutation was identified in a gene reported to be involved either in DNA damage repair or sensitivity to PARP inhibition.

Subject analysis set title	TOPARP-A biomarker negative
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Patient was considered to be biomarker-negative if a homozygous deletion or deleterious mutation was NOT identified in a gene reported to be involved either in DNA damage repair or sensitivity to PARP inhibition.

Primary: Composite Response

End point title	Composite Response

End point description:

The primary endpoint is response, which is defined on the basis of the following outcomes; if any of these occur patients will be considered to have responded:

- Confirmed objective response by modified RECIST 1.1 (i.e. either complete response (CR) or partial response (PR))
- PSA decline of ≥50% from baseline, confirmed to be sustained by a second PSA value obtained four or more weeks later
- Conversion of circulating tumour cell count (CTC) from ≥5 cells/7.5 ml blood at baseline to <5 cells/7.5 ml confirmed by a second consecutive value obtained four or more weeks later.

Evaluable patients with no confirmed response as defined above will be classified as non-responders.

End point type	Primary

End point timeframe:

The first disease assessment is performed at 12 weeks post treatment start, then every 12 weeks onwards for RECIST and 4 weeks onwards for PSA and CTC.

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	TOPARP-A biomarker positive
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	49[1]	46[2]	46[3]	16[4]
Units: Response				
Composite response	16	18	25	14

Notes:

[1] - Evaluable population

[2] - Evaluable population

[3] - Evaluable population

[4] - Within evaluable population

End point values	TOPARP-A biomarker negative			
Subject group type	Subject analysis set			
Number of subjects analysed	33[5]			
Units: Response				
Composite response	2			

Notes:

[5] - Within evaluable population

Statistical analyses

Statistical analysis title	TOPARP-B Pick the winner

Statistical analysis description:

Under the TOPARP-B "pick-the-winner" design, each dose group is assessed independently for antitumour activity. If 19 or more of the planned 44 evaluable patients in one dose group respond (43%), then the dose group is considered successful. In the case where both dose groups are successful, the TOPARP-B SAP describes the strategy to select the successful dose based on response rates and secondary endpoints.

Comparison groups	TOPARP-B: Olaparib 300mg v TOPARP-B: Olaparib 400mg
Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	other[6]
P-value	= 0.144 [7]
Method	Chi-squared
Parameter estimate	Response rate
Confidence interval	
level	95 %
sides	2-sided

Notes:

[6] - As per the trial "pick-the-winner" design, each dose is assessed separately in the 92 evaluable patients:
- 300 mg BID dose group: 18/46 evaluable with confirmed response. RR 39.1% (95%CI 25.1-54.6).
- 400 mg BID dose group: 25/46 evaluable with confirmed response. RR 54.3% (95%CI 39.0-69.1).

[7] - Exploratory - design (pick the winner) not powered for direct comparison of doses.

Statistical analysis title	TOPARP-A response by BM status
Comparison groups	TOPARP-A biomarker positive v TOPARP-A biomarker negative

Number of subjects included in analysis	49
Analysis specification	Pre-specified
Analysis type	superiority[8]
P-value	< 0.001 [9]
Method	Fisher exact
Parameter estimate	Odds ratio (OR)
Point estimate	108.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.8
upper limit	850.5

Notes:

[8] - Association between biomarker status and response

[9] - Fisher's exact p-value

Secondary: PSA response

End point title	PSA response

End point description:

PSA partial response is defined as a ≥ 50% decline in PSA value from cycle1 day 1 (baseline). This PSA decline must be confirmed to be sustained by a second PSA value obtained 4 or more weeks later.

End point type	Secondary

End point timeframe:

PSA response is first evaluated at 12 weeks post treatment start and then evaluated at each cycle of treatment (every 4 weeks).

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49[10]	43[11]	46[12]	
Units: Subjects				
PSA responses	10	13	17	

Notes:

[10] - Evaluable population

[11] - PSA evaluable

[12] - PSA evaluable

Statistical analyses

No statistical analyses for this end point

Secondary: Time to PSA progression

End point title	Time to PSA progression

End point description:

PSA progression is defined as follows:

- If PSA while on treatment declines from baseline, PSA progression is defined when a ≥ 25% increase and an absolute increase of ≥ 2 ng/mL above the nadir is documented, which needs to be confirmed by a second consecutive value obtained 3 or more weeks later.
- If there is no decline from baseline, PSA progression is defined when a ≥ 25% increase and an absolute increase of ≥ 2 ng/mL above the baseline is documented after 12 weeks of treatment.

Time to PSA progression will be computed from date of start of olaparib to date of PSA progression. Patients who do not experience a PSA progression will be censored at the last PSA assessment date while on allocated treatment. In the TOPARP-B 300mg dose BID, PSA values after dose-escalation to 400mg BID are excluded from the analysis.

End point type	Secondary

End point timeframe:

The first PSA reading is obtained at 12 weeks post treatment start then evaluated at each cycle of treatment (every 4 weeks).

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	48[13]	46[14]	49[15]	
Units: Months				
median (inter-quartile range (Q1-Q3))	5.7 (2.8 to 11.1)	5.6 (2.8 to 14)	3.7 (2.8 to 10.9)	

Notes:

[13] - PSa-progression evaluable

[14] - PSA evaluable

[15] - PSA evaluable

Statistical analyses

No statistical analyses for this end point

Secondary: % Change in PSA to 12 weeks

End point title	% Change in PSA to 12 weeks

End point description:

Percentage of change in PSA from baseline to 12 weeks (or earlier for those who discontinue therapy).

End point type	Secondary

End point timeframe:

% Change in PSA from baseline to 12 weeks.
Maximum decline in PSA that occurs at any point in treatment.

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	46[16]	48[17]	
Units: %				
median (inter-quartile range (Q1-Q3))	38.7 (-29.3 to 136.8)	-4.6 (-38.1 to 55.3)	4.6 (-51.9 to 49.3)	

Notes:

[16] - PSA-change evaluable

[17] - PSA-change evaluable

Statistical analyses

No statistical analyses for this end point

Secondary: CTC response

End point title	CTC response

End point description:

The proportion of patients with a CTC conversion to <5/7.5 ml blood at nadir (confirmed by a second consecutive value four or more weeks later) will be presented along an exact two-sided 95% confidence interval. Waterfall plots of CTC falls will also be presented that show the percentage change in CTC counts from baseline to 12 weeks as well as maximal CTC count declines that occur at any point after treatment. In Part B, the dose group will be displayed using different colours. Longitudinal spaghetti plots of CTC values over time will also be presented to explore the different patterns of response in Part B this will be conducted for each dose group. CTC response's association with PFS and OS will be examined via landmark analyses (to compare OS or PFS between CTC responders and non-responders at a given time point).

End point type	Secondary

End point timeframe:

The first assessment of CTC response is at 12 weeks post treatment. CTC is then evaluated at every cycle (4 weeks).

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49[18]	27[19]	28[20]	
Units: Subjects	14	13	15	

Notes:

[18] - Evaluable population

[19] - CTC evaluable

[20] - CTC evaluable

Statistical analyses

No statistical analyses for this end point

Secondary: Radiographic progression free survival (rPFS)

End point title	Radiographic progression free survival (rPFS)

End point description:

Radiographic progression free survival (rPFS) will be defined by either RECIST progression and /or progression on bone scan. It will be measured from the date of trial entry to the first occurrence of radiographic progression or death from any cause. If no event exists, then rPFS will be censored at the last scheduled disease assessment on study.

End point type	Secondary

End point timeframe:

Trial entry to first occurrence of radiographic progression or death from any cause, or censoring time.

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	TOPARP-A biomarker positive
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	49[21]	49[22]	49[23]	16
Units: Months				
median (inter-quartile range (Q1-Q3))	2.9 (2.5 to 10.8)	5.6 (2.8 to 9.9)	5.5 (2.8 to 14.4)	10.8 (5.6 to 17.1)

Notes:

[21] - ITT population

[22] - ITT population

[23] - ITT population

End point values	TOPARP-A biomarker negative			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: Months				
median (inter-quartile range (Q1-Q3))	2.6 (2.4 to 2.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

Progression free survival will be measured from the date of trial entry until radiographic progression, unequivocal clinical progression or death. If no event exists, then PFS will be censored at the last scheduled disease assessment on study.

End point type	Secondary

End point timeframe:

Trial entry to radiographic progression, unequivocal clinical progression or death, or censoring time.

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49[24]	49[25]	49[26]	
Units: Months				
median (inter-quartile range (Q1-Q3))	2.8 (2.8 to 8.2)	5.4 (2.7 to 8.5)	5.5 (2.8 to 11.5)	

Notes:

[24] - ITT population

[25] - ITT population

[26] - ITT population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of PSA response

End point title	Duration of PSA response

End point description:

Duration of PSA response is calculated from the time the PSA value first declines by at least 50% of the cycle 1 day 1 (baseline) value (must be confirmed by a second value) until the time there is an increase of 25% of PSA nadir, provided the absolute increase is at least 2 ng/mL. The increase must be confirmed by a second consecutive measurement that is at least 25% above the nadir. If the PSA never shows a 25% increase over the nadir value, then the patient will be censored at the last PSA measurement. Duration of PSA response will be summarised by the median and presented along its 95% confidence interval. Time to PSA response on the duration of response (e.g. by fitting left-truncated models of adjusting by time to response) may be explored.

End point type	Secondary

End point timeframe:

PSA response is first evaluated at 12 weeks post treatment start and then evaluated at each cycle of treatment (every 4 weeks).

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	TOPARP-A biomarker positive
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	16[27]	18[28]	25[29]	14[30]
Units: Months				
median (confidence interval 95%)	9.1 (6.8 to 13.8)	6.8 (4.4 to 12.9)	7.9 (4.4 to 13.7)	9.1 (7.1 to 14.8)

Notes:

[27] - Responders

[28] - Responders

[29] - Responders

[30] - Responders

End point values	TOPARP-A biomarker negative			
Subject group type	Subject analysis set			
Number of subjects analysed	2[31]			
Units: Months				
median (confidence interval 95%)	6.5 (2.2 to 10.8)			

Notes:

[31] - Responders

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival (OS)

End point title	Overall survival (OS)

End point description:

OS will be measured from the date of trial entry to the date of death (whatever the cause). Survival

time of living patients will be censored on the last date a patient is known to be alive or lost to follow-up.

End point type	Secondary

End point timeframe:

Trial entry to date of death or censoring.

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	TOPARP-A biomarker positive
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	49	49	49	16
Units: Months				
median (confidence interval 95%)	10.4 (7.5 to 14.5)	10.1 (9 to 14.7)	14.8 (10.1 to 18.3)	15.3 (10.4 to 17.4)

End point values	TOPARP-A biomarker negative			
Subject group type	Subject analysis set			
Number of subjects analysed	33			
Units: Months				
median (confidence interval 95%)	7.5 (4.6 to 11.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum % decline in PSA during treatment

End point title	Maximum % decline in PSA during treatment

End point description:

End point type	Secondary

End point timeframe:

Maximum decline in PSA that occurs at any point in treatment.

End point values	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 300mg	TOPARP-B: Olaparib 400mg	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	49	46[32]	49[33]	
Units: %				
median (inter-quartile range (Q1-Q3))	31.9 (-47.3 to 93.4)	-12.8 (-69.6 to 30.1)	-11.8 (-79.6 to 28.0)	

Notes:
[32] - PSA-change evaluable
[33] - PSA-change evaluable

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AE) were collected on a continuous basis using NCI-CTCAE v4.02 reporting criteria from screening until 30 days after the last dose of olaparib, or until a new anti-cancer therapy is started.

Adverse event reporting additional description:

TOPARP-A: MedDRA v14, CTCAE v4.02
TOPARP-B: MedDRA v22, CTCAE v4.02

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0, 22.0

Reporting groups

Reporting group title	TOPARP-A: Olaparib 400mg
Reporting group description: -	
Reporting group title	TOPARP-B: Olaparib 400mg
Reporting group description: -	
Reporting group title	TOPARP-B: Olaparib 300mg

Reporting group description: -

Serious adverse events	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 400mg	TOPARP-B: Olaparib 300mg
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 50 (40.00%)	24 / 49 (48.98%)	22 / 49 (44.90%)
number of deaths (all causes)	49	49	48
number of deaths resulting from adverse events	0	0	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia	Additional description: Acute myeloid leukaemia		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pancreatic carcinoma	Additional description: Pancreatic carcinoma		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Vascular disorders			
Circulatory collapse	Additional description: Circulatory collapse		

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolism	Additional description: Embolism		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Hypotension	Additional description: Hypotension		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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 disorders and administration site conditions			
Pyrexia	Additional description: Pyrexia		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pain	Additional description: Pain		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	2 / 50 (4.00%)	1 / 49 (2.04%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 5	0 / 1	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			

Pulmonary embolism	Additional description: Pulmonary embolism		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Bronchitis	Additional description: Bronchitis		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Cough	Additional description: Cough		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 50 (2.00%)	3 / 49 (6.12%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 1	1 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion	Additional description: Pleural effusion		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Psychiatric disorders			
Confusional state	Additional description: Confusional state		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
C-reactive protein increased	Additional description: C-reactive protein increased		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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

Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	2 / 50 (4.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall	Additional description: Fall		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Femoral neck fracture	Additional description: Femoral neck fracture		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture	Additional description: Femur fracture		
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fracture	Additional description: Fracture		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Hip fracture	Additional description: Hip fracture		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
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	Additional description: Humerus fracture		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Joint injury	Additional description: Joint injury		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm	Additional description: Vascular pseudoaneurysm		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
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 disorders			
Myocardial infarction	Additional description: Myocardial infarction		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Atrial fibrillation	Additional description: Atrial fibrillation		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Transient ischaemic attack	Additional description: Transient ischaemic attack		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Cauda equina syndrome	Additional description: Cauda equina syndrome		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Dizziness	Additional description: Dizziness		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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

Facial paresis	Additional description: Facial paresis		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Radiculopathy	Additional description: Radiculopathy		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Spinal cord compression	Additional description: Spinal cord compression		
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia	Additional description: Anaemia		
subjects affected / exposed	5 / 50 (10.00%)	4 / 49 (8.16%)	4 / 49 (8.16%)
occurrences causally related to treatment / all	6 / 6	4 / 5	6 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile neutropenia	Additional description: Febrile neutropenia		
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Nausea	Additional description: Nausea		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Large intestine perforation	Additional description: Large intestine perforation		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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

Intestinal obstruction	Additional description: Intestinal obstruction		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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

Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Constipation	Additional description: Constipation		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	1 / 50 (2.00%)	4 / 49 (8.16%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rectal haemorrhage	Additional description: Rectal haemorrhage		
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Vomiting	Additional description: Vomiting		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Small intestinal obstruction	Additional description: Small intestinal obstruction

subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Hepatobiliary disorders			
Jaundice	Additional description: Jaundice		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Renal and urinary disorders			
Acute kidney injury	Additional description: Acute kidney injury		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria	Additional description: Haematuria		
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydronephrosis	Additional description: Hydronephrosis		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Renal colic	Additional description: Renal colic		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
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 failure acute	Additional description: Renal failure acute		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Urinary retention	Additional description: Urinary retention		

subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Arthritis bacterial	Additional description: Arthritis bacterial		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain	Additional description: Bone pain		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Groin pain	Additional description: Groin pain		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Mobility decreased	Additional description: Mobility decreased		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (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
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia	Additional description: Myalgia		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (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
Back pain	Additional description: Back pain		

subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	4 / 49 (8.16%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis	Additional description: Pyelonephritis		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia	Additional description: Pneumonia		
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenic sepsis	Additional description: Neutropenic sepsis		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection	Additional description: Lung infection		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	2 / 49 (4.08%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection	Additional description: Infection		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis	Additional description: Cellulitis		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis	Additional description: Bronchitis		

subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal infection	Additional description: Abdominal infection		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection	Additional description: Respiratory tract infection		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
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	Additional description: Sepsis		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	1 / 50 (2.00%)	3 / 49 (6.12%)	3 / 49 (6.12%)
occurrences causally related to treatment / all	0 / 1	0 / 17	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis	Additional description: Urosepsis		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	1 / 50 (2.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperkalaemia	Additional description: Hyperkalaemia		
subjects affected / exposed	0 / 50 (0.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	TOPARP-A: Olaparib 400mg	TOPARP-B: Olaparib 400mg	TOPARP-B: Olaparib 300mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	50 / 50 (100.00%)	49 / 49 (100.00%)	47 / 49 (95.92%)
Vascular disorders			
Lymphoedema	Additional description: Lymphoedema		
subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	3 / 49 (6.12%)
occurrences (all)	4	3	4
Hypertension	Additional description: Hypertension		
subjects affected / exposed	3 / 50 (6.00%)	9 / 49 (18.37%)	11 / 49 (22.45%)
occurrences (all)	20	11	20
General disorders and administration site conditions			
Chest pain	Additional description: Chest pain		
subjects affected / exposed	9 / 50 (18.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	19	0	0
Fatigue	Additional description: Fatigue		
subjects affected / exposed	45 / 50 (90.00%)	33 / 49 (67.35%)	22 / 49 (44.90%)
occurrences (all)	246	58	46
Hot flush	Additional description: Hot flush		
subjects affected / exposed	5 / 50 (10.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	33	0	0
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	0 / 50 (0.00%)	3 / 49 (6.12%)	0 / 49 (0.00%)
occurrences (all)	0	4	0
Oedema	Additional description: Oedema		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	8	0	0
Oedema peripheral	Additional description: Oedema peripheral		
subjects affected / exposed	11 / 50 (22.00%)	9 / 49 (18.37%)	8 / 49 (16.33%)
occurrences (all)	42	15	10
Pain	Additional description: Pain		
subjects affected / exposed	5 / 50 (10.00%)	3 / 49 (6.12%)	1 / 49 (2.04%)
occurrences (all)	13	11	1
Pyrexia	Additional description: Pyrexia		

subjects affected / exposed	2 / 50 (4.00%)	3 / 49 (6.12%)	3 / 49 (6.12%)
occurrences (all)	3	3	5
Reproductive system and breast disorders			
Pelvic pain	Additional description: Pelvic pain		
subjects affected / exposed	3 / 50 (6.00%)	3 / 49 (6.12%)	1 / 49 (2.04%)
occurrences (all)	5	4	1
Respiratory, thoracic and mediastinal disorders			
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	4	0	0
Cough	Additional description: Cough		
subjects affected / exposed	9 / 50 (18.00%)	8 / 49 (16.33%)	3 / 49 (6.12%)
occurrences (all)	22	8	3
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	5 / 50 (10.00%)	9 / 49 (18.37%)	3 / 49 (6.12%)
occurrences (all)	14	11	6
Productive cough	Additional description: Productive cough		
subjects affected / exposed	1 / 50 (2.00%)	4 / 49 (8.16%)	0 / 49 (0.00%)
occurrences (all)	2	5	0
Psychiatric disorders			
Depression	Additional description: Depression		
subjects affected / exposed	3 / 50 (6.00%)	2 / 49 (4.08%)	0 / 49 (0.00%)
occurrences (all)	20	3	0
Insomnia	Additional description: Insomnia		
subjects affected / exposed	5 / 50 (10.00%)	2 / 49 (4.08%)	4 / 49 (8.16%)
occurrences (all)	15	2	4
Investigations			
Aspartate aminotransferase increased	Additional description: Aspartate aminotransferase increased		
subjects affected / exposed	8 / 50 (16.00%)	5 / 49 (10.20%)	4 / 49 (8.16%)
occurrences (all)	10	9	4
Blood alkaline phosphatase increased	Additional description: Blood alkaline phosphatase increased		
subjects affected / exposed	3 / 50 (6.00%)	6 / 49 (12.24%)	3 / 49 (6.12%)
occurrences (all)	3	10	3
Blood bilirubin increased	Additional description: Blood bilirubin increased		

subjects affected / exposed	1 / 50 (2.00%)	4 / 49 (8.16%)	1 / 49 (2.04%)
occurrences (all)	1	10	2
Blood creatinine increased	Additional description: Blood creatinine increased		
subjects affected / exposed	9 / 50 (18.00%)	6 / 49 (12.24%)	9 / 49 (18.37%)
occurrences (all)	29	17	20
Gamma-glutamyltransferase increased	Additional description: Gamma-glutamyltransferase increased		
subjects affected / exposed	3 / 50 (6.00%)	5 / 49 (10.20%)	3 / 49 (6.12%)
occurrences (all)	3	12	5
Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 50 (0.00%)	1 / 49 (2.04%)	3 / 49 (6.12%)
occurrences (all)	0	1	3
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	0 / 50 (0.00%)	5 / 49 (10.20%)	3 / 49 (6.12%)
occurrences (all)	0	5	3
Weight decreased	Additional description: Weight decreased		
subjects affected / exposed	12 / 50 (24.00%)	16 / 49 (32.65%)	10 / 49 (20.41%)
occurrences (all)	28	22	12
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	0 / 50 (0.00%)	4 / 49 (8.16%)	2 / 49 (4.08%)
occurrences (all)	0	13	2
Alanine aminotransferase increased	Additional description: Alanine aminotransferase increased		
subjects affected / exposed	4 / 50 (8.00%)	5 / 49 (10.20%)	2 / 49 (4.08%)
occurrences (all)	6	8	3
Cardiac disorders			
Dyspnoea	Additional description: Dyspnoea		
subjects affected / exposed	10 / 50 (20.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	23	0	0
Nervous system disorders			
Dizziness	Additional description: Dizziness		
subjects affected / exposed	5 / 50 (10.00%)	3 / 49 (6.12%)	3 / 49 (6.12%)
occurrences (all)	10	3	5
Dysgeusia	Additional description: Dysgeusia		
subjects affected / exposed	4 / 50 (8.00%)	4 / 49 (8.16%)	6 / 49 (12.24%)
occurrences (all)	19	6	6
Headache	Additional description: Headache		

subjects affected / exposed	7 / 50 (14.00%)	3 / 49 (6.12%)	2 / 49 (4.08%)
occurrences (all)	26	4	2
Neuropathy peripheral	Additional description: Neuropathy peripheral		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences (all)	13	0	1
Paraesthesia	Additional description: Paraesthesia		
subjects affected / exposed	3 / 50 (6.00%)	1 / 49 (2.04%)	1 / 49 (2.04%)
occurrences (all)	7	1	1
Peripheral sensory neuropathy	Additional description: Peripheral sensory neuropathy		
subjects affected / exposed	10 / 50 (20.00%)	1 / 49 (2.04%)	0 / 49 (0.00%)
occurrences (all)	38	1	0
Spinal cord compression	Additional description: Spinal cord compression		
subjects affected / exposed	0 / 50 (0.00%)	4 / 49 (8.16%)	0 / 49 (0.00%)
occurrences (all)	0	6	0
Blood and lymphatic system disorders			
Platelet count decreased	Additional description: Platelet count decreased		
subjects affected / exposed	0 / 50 (0.00%)	12 / 49 (24.49%)	13 / 49 (26.53%)
occurrences (all)	0	38	29
Thrombocytopenia	Additional description: Thrombocytopenia		
subjects affected / exposed	7 / 50 (14.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	13	0	0
White blood cell count decreased	Additional description: White blood cell count decreased		
subjects affected / exposed	0 / 50 (0.00%)	3 / 49 (6.12%)	2 / 49 (4.08%)
occurrences (all)	0	3	2
Anaemia	Additional description: Anaemia		
subjects affected / exposed	45 / 50 (90.00%)	37 / 49 (75.51%)	32 / 49 (65.31%)
occurrences (all)	198	160	130
Leukopenia	Additional description: Leukopenia		
subjects affected / exposed	7 / 50 (14.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	30	0	0
Lymphocyte count decreased	Additional description: Lymphocyte count decreased		
subjects affected / exposed	0 / 50 (0.00%)	4 / 49 (8.16%)	2 / 49 (4.08%)
occurrences (all)	0	9	2
Neutropenia	Additional description: Neutropenia		
subjects affected / exposed	9 / 50 (18.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	17	0	0

Neutrophil count decreased	Additional description: Neutrophil count decreased		
subjects affected / exposed	0 / 50 (0.00%)	7 / 49 (14.29%)	7 / 49 (14.29%)
occurrences (all)	0	26	13
Gastrointestinal disorders			
Abdominal distension	Additional description: Abdominal distension		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	5	0	0
Abdominal pain	Additional description: Abdominal pain		
subjects affected / exposed	2 / 50 (4.00%)	10 / 49 (20.41%)	5 / 49 (10.20%)
occurrences (all)	2	16	5
Constipation	Additional description: Constipation		
subjects affected / exposed	13 / 50 (26.00%)	8 / 49 (16.33%)	7 / 49 (14.29%)
occurrences (all)	34	11	7
Dry mouth	Additional description: Dry mouth		
subjects affected / exposed	2 / 50 (4.00%)	0 / 49 (0.00%)	5 / 49 (10.20%)
occurrences (all)	2	0	5
Nausea	Additional description: Nausea		
subjects affected / exposed	28 / 50 (56.00%)	15 / 49 (30.61%)	18 / 49 (36.73%)
occurrences (all)	69	23	29
Vomiting	Additional description: Vomiting		
subjects affected / exposed	12 / 50 (24.00%)	15 / 49 (30.61%)	9 / 49 (18.37%)
occurrences (all)	22	19	11
Diarrhoea	Additional description: Diarrhoea		
subjects affected / exposed	11 / 50 (22.00%)	11 / 49 (22.45%)	9 / 49 (18.37%)
occurrences (all)	27	15	10
Skin and subcutaneous tissue disorders			
Alopecia	Additional description: Alopecia		
subjects affected / exposed	4 / 50 (8.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	23	0	0
Nail disorder	Additional description: Nail disorder		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	13	0	0
Renal and urinary disorders			
Haematuria	Additional description: Haematuria		
subjects affected / exposed	2 / 50 (4.00%)	4 / 49 (8.16%)	4 / 49 (8.16%)
occurrences (all)	15	5	4
Hydronephrosis	Additional description: Hydronephrosis		

subjects affected / exposed	1 / 50 (2.00%)	1 / 49 (2.04%)	3 / 49 (6.12%)
occurrences (all)	2	1	3
Nocturia	Additional description: Nocturia		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences (all)	3	0	1
Pollakiuria	Additional description: Pollakiuria		
subjects affected / exposed	9 / 50 (18.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	49	0	0
Urinary incontinence	Additional description: Urinary incontinence		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	20	0	0
Musculoskeletal and connective tissue disorders			
Musculoskeletal chest pain	Additional description: Musculoskeletal chest pain		
subjects affected / exposed	5 / 50 (10.00%)	8 / 49 (16.33%)	3 / 49 (6.12%)
occurrences (all)	8	12	4
Arthralgia	Additional description: Arthralgia		
subjects affected / exposed	20 / 50 (40.00%)	15 / 49 (30.61%)	12 / 49 (24.49%)
occurrences (all)	84	24	17
Back pain	Additional description: Back pain		
subjects affected / exposed	26 / 50 (52.00%)	14 / 49 (28.57%)	18 / 49 (36.73%)
occurrences (all)	103	21	26
Bone pain	Additional description: Bone pain		
subjects affected / exposed	17 / 50 (34.00%)	4 / 49 (8.16%)	1 / 49 (2.04%)
occurrences (all)	42	6	1
Groin pain	Additional description: Groin pain		
subjects affected / exposed	7 / 50 (14.00%)	3 / 49 (6.12%)	3 / 49 (6.12%)
occurrences (all)	28	3	3
Muscle spasms	Additional description: Muscle spasms		
subjects affected / exposed	1 / 50 (2.00%)	6 / 49 (12.24%)	3 / 49 (6.12%)
occurrences (all)	6	7	4
Muscular weakness	Additional description: Muscular weakness		
subjects affected / exposed	7 / 50 (14.00%)	6 / 49 (12.24%)	4 / 49 (8.16%)
occurrences (all)	17	6	4
Musculoskeletal pain	Additional description: Musculoskeletal pain		

subjects affected / exposed	8 / 50 (16.00%)	8 / 49 (16.33%)	7 / 49 (14.29%)
occurrences (all)	34	10	12
Myopathy	Additional description: Myopathy		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	12	0	0
Neck pain	Additional description: Neck pain		
subjects affected / exposed	3 / 50 (6.00%)	1 / 49 (2.04%)	3 / 49 (6.12%)
occurrences (all)	19	1	3
Pain in extremity	Additional description: Pain in extremity		
subjects affected / exposed	14 / 50 (28.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	39	0	0
Myalgia	Additional description: Myalgia		
subjects affected / exposed	2 / 50 (4.00%)	3 / 49 (6.12%)	1 / 49 (2.04%)
occurrences (all)	7	3	1
Infections and infestations			
Lower respiratory tract infection	Additional description: Lower respiratory tract infection		
subjects affected / exposed	0 / 50 (0.00%)	2 / 49 (4.08%)	4 / 49 (8.16%)
occurrences (all)	0	2	6
Influenza like illness	Additional description: Influenza like illness		
subjects affected / exposed	0 / 50 (0.00%)	5 / 49 (10.20%)	3 / 49 (6.12%)
occurrences (all)	0	6	4
Urinary tract infection	Additional description: Urinary tract infection		
subjects affected / exposed	5 / 50 (10.00%)	8 / 49 (16.33%)	6 / 49 (12.24%)
occurrences (all)	5	13	6
Metabolism and nutrition disorders			
Decreased appetite	Additional description: Decreased appetite		
subjects affected / exposed	23 / 50 (46.00%)	13 / 49 (26.53%)	15 / 49 (30.61%)
occurrences (all)	75	14	24
Hyperglycaemia	Additional description: Hyperglycaemia		
subjects affected / exposed	4 / 50 (8.00%)	0 / 49 (0.00%)	1 / 49 (2.04%)
occurrences (all)	4	0	1
Hypoalbuminaemia	Additional description: Hypoalbuminaemia		
subjects affected / exposed	3 / 50 (6.00%)	0 / 49 (0.00%)	0 / 49 (0.00%)
occurrences (all)	3	0	0
Hypokalaemia	Additional description: Hypokalaemia		

subjects affected / exposed	6 / 50 (12.00%)	8 / 49 (16.33%)	3 / 49 (6.12%)
occurrences (all)	17	9	4
Hyponatraemia	Additional description: Hyponatraemia		
subjects affected / exposed	7 / 50 (14.00%)	3 / 49 (6.12%)	2 / 49 (4.08%)
occurrences (all)	8	3	3

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 March 2012	Provide clarification to end of treatment and end of study definition, follow up time frames, assessment time frames and removal of data collection not necessary for study analysis.
12 November 2012	Updates of adverse events in line with Olaparib Investigator Brochure Edition 8. Clarification of the requirement for archival tumour tissue and fresh biopsy. Clarification that CTC count at screening must be confirmed by central laboratory. Additional guidance of fasting requirements prior to some blood sample collection. Addition of sample collection at specified time points
15 April 2014	Clarification of measurement of CTC conversion. Updated inclusion criteria on how long patients should be independent of transfusions for and albumin value. Clarification of the therapies not permitted after termination of olaparib use and recommended time before commencing a new anticancer treatment. Extension of CTC sample collection window prior to start of olaparib. Update to allow biopsy and blood samples taken prior to consent, within a specified window, to be used at screening. Addition of Coagulation studies at specified time points. Addition of whole genome sequencing.
26 June 2015	Specification of requirements and procedures for TOPARP A and TOPARP B. Addition of TOPARP B: patients will be randomised to receive 300mg or 400 mg twice daily. Amendment from 44 patients to 88 patients (44 in each group) in TOPARP B. Addition of the dose of 300mg ID to study the tolerability and antitumour activity of both dose level in TOPARP B. Patients receiving 300mg will be allowed to escalate to 400mg upon disease progression in clinically indicated. Amendment to modified RECIST 1.1 from modified RECIST. Removal of objective response (PSA-ORR) as secondary endpoint. Addition of secondary endpoint as percentage change of PSA from baseline to 12 weeks (or earlier if discontinued therapy) and maximise PSA decline while on treatment; TOPARP B only - Cmax and AUC after first dose and at steady state for the 400mg and 300mg BID dose levels. Addition of exploratory endpoint - TOPARP B only - to evaluate the response rate following dose-escalation from 300mg to 400mg BID. Addition of post confirmation of the presence of the putative predictive biomarkers in TOPARP B. Addition of pre-screening stage to confirm presence of biomarker. Addition of 250mg for dose reduction and removal of 100mg dose reduction. Clarification that fresh biopsy is optional in TOPARP B. Clarification that patients can be discontinued on clinical progression as well as radiological progression. Addition of pharmacokinetic analysis for TOPARP B.
15 March 2018	Updates of adverse events in line with olaparib Investigator Brochure Edition 14. Extension of follow up scans beyond 2 years whilst on study treatment. Clarification and updates of inclusion criteria. Updates to permitted windows and time pointes for study assessments. Updates on pharmacokinetic samples in line with PK sub-study closure. Update to SAE reporting period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported