Clinical trial results:
Randomised phase II Trial of olaparib, chemotherapy or olaparib and cediranib in patients with platinum–resistant ovarian cancer

Summary

EudraCT number	2016-000559-28
Trial protocol	GB
Global end of trial date	26 October 2023

Results information

Result version number	v1 (current)
This version publication date	09 November 2024
First version publication date	09 November 2024
Summary attachment (see zip file)	OCTOVA results - BJC Manuscript publication (OCTOVA_BJCManuscript_Publication_20Jan2024.pdf)

Trial information

Trial identification

Sponsor protocol code	OCTO-062

Additional study identifiers

ISRCTN number	ISRCTN14784018
ClinicalTrials.gov id (NCT number)	NCT03117933
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	RGEA, University of Oxford
Sponsor organisation address	1st floor, Boundary Brook House, Churchill Drive, Headington , Oxford, United Kingdom, OX3 7GB
Public contact	Lisa Poulton, Oncology Clinical Trials Office (OCTO), +44 1865617075, octo-octova@oncology.ox.ac.uk
Scientific contact	Lisa Poulton, Oncology Clinical Trials Office (OCTO), +44 1865617075, octo-octova@oncology.ox.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	21 March 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 July 2021
Global end of trial reached?	Yes
Global end of trial date	26 October 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective is to assess the efficacy of olaparib compared to weekly paclitaxel or the combination of olaparib and cediranib in patients with ovarian, fallopian tube, primary peritoneal cancer who have relapsed within 12 months of previous platinum therapy

Protection of trial subjects:

The protocol was conducted in compliance with the UK Clinical Trials Regulations, the Principles of Good Clinical Practice (GCP) and the applicable policies of the sponsoring organisation. Together, these implement the ethical principles of the Declaration of Helsinki (1996) and the regulatory requirements for clinical trials of investigational medicinal products under the European Union Clinical Trials Directive.

Background therapy:

None.

Evidence for comparator:

Patients relapsing within 12 months of prior platinum therapy have a degree of platinum resistance, and therefore it is acceptable to consider the use of platinum sparing options, such as weekly taxol or Caelyx, in this group. Caelyx is often used earlier in the treatment pathway in combination with carboplatin, and therefore we chose weekly taxol as our comparator arm. A retrospective analysis demonstrated that weekly Taxol had similar efficacy in sporadic and BRCA-mutated relapsed ovarian cancer patients. The study, conducted in four cancer centres, analysed response and PFS following paclitaxel (3-weekly/weekly) monotherapy in BRCA-mutated relapsed ovarian cancer patients. There were 26 patients, 15 platinum-sensitive (58%) and 11 platinum-resistant (42%). The clinical benefit rate (complete or partial response, or stable disease) was 36%, with a median PFS of 21 weeks, which is consistent with the PFS of 4.7-5.3 months in the SaPPrOC study, in which patients with unknown BRCA status and platinum-resistant ovarian cancer received weekly Taxol.

Actual start date of recruitment	31 January 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 139
Worldwide total number of subjects	139
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)	63
From 65 to 84 years	75
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Start of recruitment: 30 May 2017
End of recruitment: 10 January 2020
139 participants were recruited in total (46 to Arm A, 46 to Arm B and 47 to Arm C)

Pre-assignment

Screening details:

258 patients were screened for the trial. 119 patients were excluded; 36 patients declined participation, 83 patients were not eligible and one patient consented but passed away prior to end of screening.

Period 1

Period 1 title	Part 1 (IMP administration) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	Arm A

Arm description:

IV weekly paclitaxel 80 mg/m2 on D1,8 & 15 every 28 days

Arm type	Active comparator
Investigational medicinal product name	Paclitaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection/infusion, Solution for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

80 mg/m2 administered weekly on on D1,8 & 15 every 28 days

Arm title	Arm B

Arm description:

Olaparib tablets will be supplied as 100 & 150mg (to allow for dose adjustments). Tablet formulation, 300 mg twice daily PO, continuous dosing.

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:

300 mg twice daily PO, continuous dosing. Olaparib will be dispensed to patients on Day 1 and every 4 weeks thereafter until the patient completes the study, withdraws from the study or closure of the study.

Arm title	Arm C

Arm description:

Olaparib 300mg bd with Cediranib 20mg bd. Cediranib will be supplied as 15mg and 20mg film coated tablets, to allow for dose adjustments. Patients will either receive 15mg or 20mg to avoid any dosing

errors.

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

Dosage and administration details:

Tablet formulation, 20 mg PO once daily, continuous. Cediranib will be dispensed to patients on Day 1 and every 4 weeks thereafter until the patient completes the study, withdraws from the study or closure of the study.
300 mg twice daily PO, continuous dosing. Olaparib will be dispensed to patients on Day 1 and every 4 weeks thereafter until the patient completes the study, withdraws from the study or closure of the study.

Number of subjects in period 1	Arm A	Arm B	Arm C
Started	46	46	47
Completed	46	46	47

Baseline characteristics

Reporting groups	
Reporting group title	Arm A
Reporting group description:	
IV weekly paclitaxel 80 mg/m2 on D1,8 & 15 every 28 days	

Reporting group title	Arm B
Reporting group description:	
Olaparib tablets will be supplied as 100 & 150mg (to allow for dose adjustments). Tablet formulation, 300 mg twice daily PO, continuous dosing.	

Reporting group title	Arm C
Reporting group description:	
Olaparib 300mg bd with Cediranib 20mg bd. Cediranib will be supplied as 15mg and 20mg film coated tablets, to allow for dose adjustments. Patients will either receive 15mg or 20mg to avoid any dosing errors.	

Reporting group values	Arm A	Arm B	Arm C
Number of subjects	46	46	47
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over			
Age continuous Units: years			
arithmetic mean	64	64	64
standard deviation	± 11	± 10	± 10
Gender categorical Units: Subjects			
Female	46	46	47
Male	0	0	0
PARP			
Poly ADP Ribose Polymerase			
Units: Subjects			
Yes	10	10	11
No	36	36	36
Angiogenic Units: Subjects			
Yes	15	15	17
No	31	31	30
BRCA			

Units: Subjects			
Yes	11	15	16
No	35	31	31

Reporting group values	Total		
Number of subjects	139		
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)	0		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	139		
Male	0		
PARP			
Poly ADP Ribose Polymerase			
Units: Subjects			
Yes	31		
No	108		
Angiogenic			
Units: Subjects			
Yes	47		
No	92		
BRCA			
Units: Subjects			
Yes	42		
No	97		

End points

End points reporting groups

Reporting group title	Arm A

Reporting group description:

IV weekly paclitaxel 80 mg/m2 on D1,8 & 15 every 28 days

Reporting group title	Arm B

Reporting group description:

Olaparib tablets will be supplied as 100 & 150mg (to allow for dose adjustments). Tablet formulation, 300 mg twice daily PO, continuous dosing.

Reporting group title	Arm C

Reporting group description:

Olaparib 300mg bd with Cediranib 20mg bd. Cediranib will be supplied as 15mg and 20mg film coated tablets, to allow for dose adjustments. Patients will either receive 15mg or 20mg to avoid any dosing errors.

Primary: Progression free survival (PFS)

End point title	Progression free survival (PFS)

End point description:

End point type	Primary

End point timeframe:

Time from date of randomisation to RECIST-defined progression or death from any cause (whichever is first)

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	46	47	
Units: month				
median (inter-quartile range (Q1-Q3))	3.9 (1.9 to 9.1)	3.7 (1.8 to 7.6)	5.4 (2.3 to 9.6)	

Attachments (see zip file)	KM plots/Figure_2.OCTOVA_KMplots.pdf

Statistical analyses

Statistical analysis title	Primary Outcome Analysis A vs B
Comparison groups	Arm A v Arm B

Number of subjects included in analysis	92
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.2 [1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	Other: 60 %
sides	2-sided
lower limit	0.72
upper limit	1.09

Notes:

[1] - A one-sided p-value of <0.2 was considered

Statistical analysis title	Primary Outcome Analysis B vs C
Comparison groups	Arm B v Arm C
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.2
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.73
Confidence interval	
level	Other: 60 %
sides	2-sided
lower limit	0.59
upper limit	0.89

Secondary: Overall survival	
End point title	Overall survival

End point description:

End point type	Secondary

End point timeframe:

From randomisation to death at 18 months

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	46	46	47	
Units: rate				
number (confidence interval 60%)	0.41 (0.34 to 0.49)	0.30 (0.24 to 0.38)	0.32 (0.26 to 0.39)	

Attachments (see zip file)	KM plots/Figure_2.OCTOVA_KMplots.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Object Response Rate

End point title	Object Response Rate
End point description: ORR as determined by RECIST	
End point type	Secondary
End point timeframe: 12 months	

End point values	Arm A	Arm B	Arm C	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	44	43	44	
Units: Response				
Response	15	7	6	
Non-response	29	36	38	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From day one of treatment until the 28 day follow-up visit	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	NCI-CTCAE
Dictionary version	4.03

Reporting groups	
Reporting group title	Arm A: Paclitaxel
Reporting group description: -	
Reporting group title	Arm B: Olaparib
Reporting group description: -	
Reporting group title	Arm C: Olaparib+Cediranib
Reporting group description: -	

Serious adverse events	Arm A: Paclitaxel	Arm B: Olaparib	Arm C: Olaparib+Cediranib
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 46 (43.48%)	16 / 46 (34.78%)	13 / 47 (27.66%)
number of deaths (all causes)	27	32	32
number of deaths resulting from adverse events	0	1	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
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 disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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
Pyrexia			

subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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
Pleural effusion			
subjects affected / exposed	3 / 46 (6.52%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (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
Pulmonary embolism			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	2 / 47 (4.26%)
occurrences causally related to treatment / all	0 / 1	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Troponin I increased			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Injury, poisoning and procedural complications			
Hip fracture			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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			
Pericardial effusion			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (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
Nervous system disorders			
Seizure			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	3 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (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
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 46 (4.35%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ascites			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			

subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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
Small intestinal perforation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vomiting			
subjects affected / exposed	5 / 46 (10.87%)	3 / 46 (6.52%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	2 / 6	2 / 3	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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
Hyperbilirubinaemia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			

subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
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			
Acute kidney injury			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	0 / 47 (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
Haematuria			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Clostridium difficile colitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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
Herpes zoster			

subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (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
Infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stoma site infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (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 tract infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Hypomagnesaemia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Arm A: Paclitaxel	Arm B: Olaparib	Arm C: Olaparib+Cediranib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	44 / 46 (95.65%)	44 / 46 (95.65%)	45 / 47 (95.74%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Embolism			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	1	2	1
Hot flush			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	1 / 47 (2.13%)
occurrences (all)	1	2	1
Hypertension			
subjects affected / exposed	4 / 46 (8.70%)	5 / 46 (10.87%)	14 / 47 (29.79%)
occurrences (all)	8	14	22
Hypotension			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Lymphoedema			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	0	0	2
Pelvic venous thrombosis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Thrombosis			

subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Surgical and medical procedures			
Ureteral stent insertion			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
asthenia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Axillary pain			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Catheter site pain			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Chest discomfort			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Chest pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	2 / 47 (4.26%)
occurrences (all)	0	1	2
Early satiety			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Facial pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	32 / 46 (69.57%)	26 / 46 (56.52%)	32 / 47 (68.09%)
occurrences (all)	73	46	61
Influenza like illness			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Localised oedema			

subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Oedema peripheral			
subjects affected / exposed	3 / 46 (6.52%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	3	1	1
Pain			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	3 / 47 (6.38%)
occurrences (all)	1	2	3
Peripheral swelling			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	1	2	0
Pyrexia			
subjects affected / exposed	7 / 46 (15.22%)	4 / 46 (8.70%)	0 / 47 (0.00%)
occurrences (all)	11	4	0
Vaccination site pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Pelvic haemorrhage			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Pelvic pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Vaginal discharge			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Vaginal haemorrhage			

subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	3	0	0
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Cough			
subjects affected / exposed	8 / 46 (17.39%)	13 / 46 (28.26%)	8 / 47 (17.02%)
occurrences (all)	10	16	10
Diaphragmalgia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Dysphonia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3
Dyspnoea			
subjects affected / exposed	11 / 46 (23.91%)	15 / 46 (32.61%)	10 / 47 (21.28%)
occurrences (all)	21	21	13
Dyspnoea exertional			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Epistaxis			
subjects affected / exposed	3 / 46 (6.52%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	4	0	0
Hiccups			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	3 / 46 (6.52%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	3	1	0
Oropharyngeal pain			
subjects affected / exposed	2 / 46 (4.35%)	2 / 46 (4.35%)	1 / 47 (2.13%)
occurrences (all)	2	2	1
Pleural effusion			

subjects affected / exposed	4 / 46 (8.70%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	6	0	0
Pneumonitis			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Productive cough			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	3	1	0
Pulmonary embolism			
subjects affected / exposed	5 / 46 (10.87%)	4 / 46 (8.70%)	6 / 47 (12.77%)
occurrences (all)	5	4	7
Rhinorrhoea			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Sinus congestion			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Sneezing			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	2	1	1
Confusional state			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Depressed mood			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	2	0	1
Insomnia			
subjects affected / exposed	3 / 46 (6.52%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	3	2	0

Irritability			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Panic attack			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Investigations			
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 46 (2.17%)	3 / 46 (6.52%)	4 / 47 (8.51%)
occurrences (all)	1	3	5
Blood creatine increased			
subjects affected / exposed	6 / 46 (13.04%)	7 / 46 (15.22%)	2 / 47 (4.26%)
occurrences (all)	7	8	3
Blood folate decreased			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Blood urea increased			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
C-reactive protein increased			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	2 / 47 (4.26%)
occurrences (all)	0	1	2
Gastrointestinal stoma output decreased			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal stoma output			

increased			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Glomerular filtration rate decreased			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Liver function test abnormal			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Lymphocyte count abnormal			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Mean cell volume increased			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Neutrophil count abnormal			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Paracentesis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	5 / 47 (10.64%)
occurrences (all)	0	2	5
Troponin I increased			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	0 / 46 (0.00%)	4 / 46 (8.70%)	3 / 47 (6.38%)
occurrences (all)	0	4	3
White blood cell count increased			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
White blood cell disorder			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	3	0	1
Fall			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Hip fracture			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Infusion related reaction			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Joint injury			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Rib fracture			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Spinal column injury			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Stoma site pain			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Wound haemorrhage			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Cardiac disorders			
Pericardial effusion			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Sinus tachycardia			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Tachycardia			

subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Tinnitus			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Nervous system disorders			
Akathisia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Ataxia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	3 / 46 (6.52%)	5 / 46 (10.87%)	2 / 47 (4.26%)
occurrences (all)	4	10	2
Dysgeusia			
subjects affected / exposed	6 / 46 (13.04%)	4 / 46 (8.70%)	4 / 47 (8.51%)
occurrences (all)	6	4	5
Headache			
subjects affected / exposed	7 / 46 (15.22%)	5 / 46 (10.87%)	6 / 47 (12.77%)
occurrences (all)	13	8	9
Lethargy			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	4 / 47 (8.51%)
occurrences (all)	3	2	4
Memory impairment			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Migraine			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Neuralgia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Neuropathy peripheral			
subjects affected / exposed	12 / 46 (26.09%)	1 / 46 (2.17%)	3 / 47 (6.38%)
occurrences (all)	18	1	3

Neurotoxicity			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	2	0	3
Paraesthesia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Peripheral sensory neuropathy			
subjects affected / exposed	3 / 46 (6.52%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	3	2	0
Restless legs syndrome			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Seizure			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Tremor			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	18 / 46 (39.13%)	13 / 46 (28.26%)	11 / 47 (23.40%)
occurrences (all)	29	41	31
Leukocytosis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Leukopenia			
subjects affected / exposed	4 / 46 (8.70%)	0 / 46 (0.00%)	3 / 47 (6.38%)
occurrences (all)	8	0	22
Lymphopenia			
subjects affected / exposed	2 / 46 (4.35%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	8	1	0
Neutropenia			
subjects affected / exposed	4 / 46 (8.70%)	3 / 46 (6.52%)	4 / 47 (8.51%)
occurrences (all)	10	5	19
Neutrophilia			

subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Platelet disorder			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Thrombocytopenia			
subjects affected / exposed	1 / 46 (2.17%)	5 / 46 (10.87%)	3 / 47 (6.38%)
occurrences (all)	1	6	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Hypoacusis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	1	0	2
Vertigo			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Dry eye			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Eyelid oedema			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Lacrimation increased			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Vision blurred			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	0	0	2
Gastrointestinal disorders			

Abdominal distension			
subjects affected / exposed	7 / 46 (15.22%)	4 / 46 (8.70%)	2 / 47 (4.26%)
occurrences (all)	8	4	2
Abdominal pain			
subjects affected / exposed	16 / 46 (34.78%)	16 / 46 (34.78%)	21 / 47 (44.68%)
occurrences (all)	29	28	27
Anal incontinence			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Ascites			
subjects affected / exposed	6 / 46 (13.04%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	13	0	2
Clostridium difficile colitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	18 / 46 (39.13%)	14 / 46 (30.43%)	17 / 47 (36.17%)
occurrences (all)	30	20	24
Diarrhoea			
subjects affected / exposed	20 / 46 (43.48%)	11 / 46 (23.91%)	31 / 47 (65.96%)
occurrences (all)	41	14	75
Dry mouth			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Dry throat			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	11 / 46 (23.91%)	9 / 46 (19.57%)	4 / 47 (8.51%)
occurrences (all)	11	11	4
Enteritis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0

Flatulence			
subjects affected / exposed	2 / 46 (4.35%)	3 / 46 (6.52%)	1 / 47 (2.13%)
occurrences (all)	3	3	1
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	4 / 46 (8.70%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	5	0	2
Gingival pain			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Haemorrhoids			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Intestinal obstruction			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Large intestinal obstruction			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Lip ulceration			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Mucositis			
subjects affected / exposed	10 / 46 (21.74%)	6 / 46 (13.04%)	13 / 47 (27.66%)
occurrences (all)	10	6	13
Nausea			
subjects affected / exposed	28 / 46 (60.87%)	31 / 46 (67.39%)	34 / 47 (72.34%)
occurrences (all)	63	52	69

Oesophagitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Proctalgia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Rectal discharge			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	2	2	0
Rectal haemorrhage			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	2 / 47 (4.26%)
occurrences (all)	2	2	4
Retching			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Small intestinal obstruction			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Small intestinal perforation			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Vomiting			
subjects affected / exposed	23 / 46 (50.00%)	16 / 46 (34.78%)	25 / 47 (53.19%)
occurrences (all)	41	25	51
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Hyperbilirubinaemia			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	1	2
Jaundice			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	23 / 46 (50.00%)	1 / 46 (2.17%)	3 / 47 (6.38%)
occurrences (all)	35	1	4
Dry skin			
subjects affected / exposed	2 / 46 (4.35%)	2 / 46 (4.35%)	3 / 47 (6.38%)
occurrences (all)	2	2	3
Ephelides			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Itching			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Nail discolouration			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Nail disorder			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Nail ridging			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Night sweats			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	2	0	1
Onychoclasis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Onychomadesis			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Pain of skin			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	3 / 47 (6.38%)
occurrences (all)	1	0	3
Pruritus			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	4 / 47 (8.51%)
occurrences (all)	0	0	5
Rash			
subjects affected / exposed	6 / 46 (13.04%)	2 / 46 (4.35%)	5 / 47 (10.64%)
occurrences (all)	10	3	5
Skin induration			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Skin reaction			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Swollen tongue			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	3 / 46 (6.52%)	4 / 46 (8.70%)	0 / 47 (0.00%)
occurrences (all)	3	5	0
Dysuria			
subjects affected / exposed	1 / 46 (2.17%)	3 / 46 (6.52%)	3 / 47 (6.38%)
occurrences (all)	1	3	3
Haematuria			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	2 / 47 (4.26%)
occurrences (all)	0	2	2
Hydronephrosis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Lower urinary tract symptoms			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Micturition urgency			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0

Nocturia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	0	0	2
Pollakiuria			
subjects affected / exposed	3 / 46 (6.52%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	3	0	1
Polyuria			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	5
Renal impairment			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Urethral pain			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	8 / 46 (17.39%)	4 / 46 (8.70%)	4 / 47 (8.51%)
occurrences (all)	15	5	5
Arthritis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	4 / 46 (8.70%)	6 / 46 (13.04%)	5 / 47 (10.64%)
occurrences (all)	4	7	6
Bone pain			
subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Flank pain			

subjects affected / exposed	0 / 46 (0.00%)	2 / 46 (4.35%)	1 / 47 (2.13%)
occurrences (all)	0	2	1
Groin pain			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	2	1	1
Intervertebral disc protrusion			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Muscle spasms			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	5 / 47 (10.64%)
occurrences (all)	2	1	6
Muscular weakness			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Musculoskeletal chest pain			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal discomfort			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal pain			
subjects affected / exposed	5 / 46 (10.87%)	2 / 46 (4.35%)	0 / 47 (0.00%)
occurrences (all)	5	4	0
Musculoskeletal stiffness			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	1	0	2
Myalgia			
subjects affected / exposed	4 / 46 (8.70%)	0 / 46 (0.00%)	3 / 47 (6.38%)
occurrences (all)	5	0	3
Neck pain			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	2 / 47 (4.26%)
occurrences (all)	1	1	2
Pain in extremity			

subjects affected / exposed	5 / 46 (10.87%)	3 / 46 (6.52%)	7 / 47 (14.89%)
occurrences (all)	7	3	9
Tendon pain			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bacteraemia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Cellulitis			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	3	1	0
Clostridium difficile infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Cystitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3
Diverticulitis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Eye infection			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Fungal infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Herpes zoster			
subjects affected / exposed	1 / 46 (2.17%)	2 / 46 (4.35%)	1 / 47 (2.13%)
occurrences (all)	1	3	1

Hordeolum			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Influenza			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Liver function test increased			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Lower respiratory tract infection			
subjects affected / exposed	7 / 46 (15.22%)	4 / 46 (8.70%)	5 / 47 (10.64%)
occurrences (all)	9	4	5
Nasopharyngitis			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	5 / 47 (10.64%)
occurrences (all)	1	1	6
Omphalitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Onychomycosis			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Oral candidiasis			
subjects affected / exposed	3 / 46 (6.52%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	3	1	1
Oral herpes			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	1	1	1
Paronychia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	2	0	1
Pneumonia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	1	0	3

Respiratory tract infection			
subjects affected / exposed	0 / 46 (0.00%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Sepsis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Sinusitis			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Skin infection			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Stoma site infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Tooth infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	2
Upper respiratory tract infection			
subjects affected / exposed	4 / 46 (8.70%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	5	1	1
Urinary tract infection			
subjects affected / exposed	7 / 46 (15.22%)	6 / 46 (13.04%)	8 / 47 (17.02%)
occurrences (all)	9	8	11
Vaginal infection			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	16 / 46 (34.78%)	11 / 46 (23.91%)	16 / 47 (34.04%)
occurrences (all)	20	22	33
Dehydration			

subjects affected / exposed	0 / 46 (0.00%)	3 / 46 (6.52%)	2 / 47 (4.26%)
occurrences (all)	0	3	3
Hypercalcaemia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Hyperkalaemia			
subjects affected / exposed	1 / 46 (2.17%)	1 / 46 (2.17%)	0 / 47 (0.00%)
occurrences (all)	1	1	0
Hypernatraemia			
subjects affected / exposed	0 / 46 (0.00%)	0 / 46 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Hypoalbuminaemia			
subjects affected / exposed	2 / 46 (4.35%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Hypocalcaemia			
subjects affected / exposed	2 / 46 (4.35%)	1 / 46 (2.17%)	1 / 47 (2.13%)
occurrences (all)	2	1	1
Hypokalaemia			
subjects affected / exposed	3 / 46 (6.52%)	3 / 46 (6.52%)	2 / 47 (4.26%)
occurrences (all)	10	3	3
Hypomagnesaemia			
subjects affected / exposed	8 / 46 (17.39%)	5 / 46 (10.87%)	8 / 47 (17.02%)
occurrences (all)	12	6	16
Hyponatraemia			
subjects affected / exposed	4 / 46 (8.70%)	0 / 46 (0.00%)	2 / 47 (4.26%)
occurrences (all)	4	0	6
Hypophagia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Hypoproteinaemia			
subjects affected / exposed	1 / 46 (2.17%)	0 / 46 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Vitamin D deficiency			

subjects affected / exposed occurrences (all)	0 / 46 (0.00%) 0	0 / 46 (0.00%) 0	1 / 47 (2.13%) 1

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 August 2017	The amendment concerned a number of changes to the protocol and patient materials. 'Patients with increased risk of thrombotic events or who have a history of thrombotic events' was removed from the trial exclusion criteria. The exclusion criterion relating to cardiac function (ECHO) was also clarified to reflect the cardiac function requirements detailed in the drug management section of the protocol for patients on Arm C (olaparib and cediranib). The requirement to fast when taking olaparib was removed from the protocol based on updated information in the olaparib IB. The amendment also concerned removal of PK sampling and changes to drug modification in response to toxicity. The olaparib investigator brochure Edition 14 was also submitted to act as the updated RSI.
21 September 2017	Updated olaparib label (removing fasting language)
13 March 2018	The amendment concerned a number of changes to the protocol and patient materials. The requirement to wait 6 months after administration of bevacizumab was reduced to 6 weeks (1 half-life). The screening Hb requirement was reduced to 9g/dL from 10g/dL. The exclusion criterion relating to cardiac risk of 'Prior treatment with anthracyclines' has been refined to exclude liposomal doxorubicin. The requirement for a patient receiving paclitaxel to be assessed by a doctor has been reduced to once a cycle, as per standard of care. Similarly research nurses may review AEs at other treatment visits as per local site policy.The cediranib investigator brochure Edition 20 was submitted to the MHRA to act as the reference safety information for the trial.
21 June 2018	Addition of new site.
05 October 2018	The amendment concerned a number of changes to the protocol and patient materials. The inclusion criteria was updated to include BRCA wildtype patients.The guidance for management of rotator cuff injury was removed from the protocol as this adverse event has been removed from the list of possible cediranib/olaparib combination toxicities in the current cediranib investigator brochure approved for the study (Edition 20). Two sites included in the original IRAS were removed prior to activation, Guy's and St Thomas and Birmingham due to feasibility issues.
20 August 2019	The amendment concerned a number of changes to the protocol and patient materials. Scans were reduced to 12 weekly once participants had been on treatment for 12 months. A third dose reduction was also proposed for olaparib of 150mg BD. A requirement for patients to start treatment within 8 days of randomisation was also added to the protocol. Guidance on concomitant use of a new class of anti-coagulant, novel oral anticoagulants (NOACs) was added, as use of these NOACs was becoming more frequent amongst this patient population. Clarification was also made to the trial inclusion criterion 12, adverse event reporting and the trial schedule of events. The latest version of the olaparib investigator brochure, Edition 17, was submitted to the MHRA as the reference safety information for the study.
16 April 2020	A change of PI at UCLH.

18 June 2021	The amendment concerned clarification of the end of trial definition. The protocol was also updated to include a section on management of patients remaining on treatment past 18 months and the safety assessments that are required. The olaparib investigator brochure Edition 20 was submitted to the MHRA as the updated reference safety information for the trial.
13 October 2021	The amendment concerned a change of PI at a participating site. The protocol was also updated to clarify the requirements for CT scans for participants that continue on trial beyond 18 months of treatment.
22 June 2022	The olaparib investigator brochure Edition 21 was submitted to the MHRA as the updated reference safety information for the trial. The Patient Information sheet was updated to reflect the adverse drug reactions.

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.

None reported

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/38245661