

# Trial of different drug and treatment combinations for patients who are considering further therapy to treat their ovarian cancer

<b>Submission date</b> 04/12/2017	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 19/01/2018	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 20/06/2025	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-different-treatments-for-women-who-have-ovarian-cancer-with-brca-gene-faults-octova>

## Study website

<https://www.oncology.ox.ac.uk/research/clinical-trials/oncology-clinical-trials-office-octo/completed-trials/octova-paclitaxel-olaparib-and-cediranib-in-platinum-resistant-ovarian-cancer>

## Contact information

### Type(s)

Public

### Contact name

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### Contact details

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## Additional identifiers

**EudraCT/CTIS number**

2016-000559-28

**IRAS number****ClinicalTrials.gov number**

NCT03117933

**Secondary identifying numbers**

CPMS 32967

## **Study information**

**Scientific Title**

Randomised phase II Trial of olaparib, chemotherapy or olaparib and cediranib in patients with platinum-resistant ovarian cancer

**Acronym**

OCTOVA

**Study objectives**

Study aim:

The aim of this study is to comparing efficacy and tolerability of single agent olaparib with:

1. Weekly paclitaxel
2. The combination of olaparib and cediranib

Hypothesis:

Olaparib will provide similar outcomes but less toxicity than paclitaxel and that olaparib /cediranib combination might provide better outcomes.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

London – Chelsea Research Ethics Committee, 25/01/2017, ref: 16/LO/2150

**Study design**

Randomized; Interventional; Design type: Treatment, Drug

**Primary study design**

Interventional

**Secondary study design**

Randomised controlled trial

**Study setting(s)**

Hospital

**Study type(s)**

Treatment

## **Participant information sheet**

See study outputs table

## **Health condition(s) or problem(s) studied**

Ovarian cancer

## **Interventions**

Current interventions as of 21/11/2019:

This study is a three-arm randomised trial. Participants are randomly allocated to one of the following groups:

Arm A: Participants receive weekly paclitaxel (repeating cycles days 1, 8 and 15 of 28)

Arm B: Participants receive twice-daily olaparib tablets

Arm C: Participants receive twice-daily olaparib and daily cediranib tablets

In all cases, treatment continues until disease progression (RECIST). In Arm A only, after progression patients can then switch to treatment with olaparib – this, like Arm B treatment, can continue until further progression.

Recruitment target is 138 patients, 46 per arm. Stratification factors are previous PARP, previous antiangiogenic therapy, and BRCA mutation.

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### **Previous interventions:**

This study is a three-arm randomised trial. Participants are randomly allocated to one of the following groups:

Arm A: Participants receive weekly paclitaxel (repeating cycles days 1, 8 and 15 of 28)

Arm B: Participants receive twice-daily olaparib tablets

Arm C: Participants receive twice-daily olaparib and daily cediranib tablets

In all cases, treatment continues until disease progression (RECIST). In Arm A only, after progression patients can then switch to treatment with olaparib – this, like Arm B treatment, can continue until further progression.

Recruitment target is 132 patients, 44 per arm. Stratification factors are previous PARP and previous antiangiogenic therapy.

## **Intervention Type**

Other

## **Phase**

Phase II

## **Primary outcome measure**

Progression free survival is measured using RECIST V1.1 criteria at 8-weekly.

## **Secondary outcome measures**

1. Overall survival is measured at 12 and 18 months
2. Objective response rate is measured using RECIST V1.1 and GCIG CA125 criteria at 8-weekly
3. Quality of life measured using EQ5D, EORTC-QLQ C30 and OV28 questionnaire at 4-weekly - baseline, Cycles 2+ day 1, End of Treatment visit
4. Safety and tolerability of the combination of olaparib and cediranib is measured using Adverse

Events using CTCAE v4.03 at weekly during Cycle 1, 2-weekly during Cycles 2 and 3, monthly from Cycle 4 onward

### **Overall study start date**

02/03/2015

### **Completion date**

02/11/2023

## **Eligibility**

### **Key inclusion criteria**

Current inclusion criteria as of 21/11/2019:

1. Female patients, age 16 years and older with epithelial ovarian, primary peritoneal or fallopian tube cancer who have relapsed within 12 months of previous platinum-based therapy. Their most recent chemotherapy does not have to have been platinum-based.
2. Patients can have received prior PARP inhibitor but there must be a > 6 month interval since treatment
3. Patients can have received prior anti-angiogenic therapy, but there must be a > 6 month interval since treatment; except for bevacizumab where a 6 week interval is required
4. Measurable disease by RECIST Version 1.1 performed in past 4 weeks. At least one lesion, not previously irradiated, that can be accurately measured at baseline as  $\geq 10$  mm in the longest diameter (except lymph nodes which must have short axis  $\geq 15$  mm) with computed tomography (CT) or magnetic resonance imaging (MRI) and which is suitable for accurate repeated measurements.
5. Sufficient archival tissue confirming histological diagnosis available
6. ECOG PS 0-2
7. Able to swallow and retain oral medications
8. Life expectancy > 12 weeks in terms of disease related mortality
8. Patient is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up
10. Written (signed and dated) informed consent prior to any study specific procedures and be capable of co-operating with protocol
11. Patients must have haemoglobin  $\geq 9.0$  g/dL and no blood transfusions in the 28 days prior to randomisation
12. Patients must have normal organ and bone marrow function measured within 14 days prior to administration of study treatment as defined below:
  - 12.1. Absolute neutrophil count (ANC)  $\geq 1.5 \times 10^9/L$
  - 12.2. Platelet count  $> 100 \times 10^9/L$
  - 12.3. Total bilirubin  $\leq 1.5 \times$  institutional upper limit of normal (ULN)
  - 12.4. AST (SGOT)/ALT (SGPT)  $\leq 2.5 \times$  institutional upper limit of normal unless liver metastases are present in which case it must be  $\leq 5 \times$  ULN
  - 12.5. Serum creatinine  $\leq 1.5 \times$  institutional upper limit of normal (ULN) or calculated creatinine clearance  $> 50$  ml/min calculated using Cockcroft-Gault, Jelliffe or Wright (see Appendix 4)
  - 12.6. Urine dipstick for proteinuria  $< 2+$ . If urine dipstick is  $\geq 2+$  on two occasions more than one week apart then a 24-hour urine must demonstrate  $\leq 1$  g of protein in 24 hours or protein/creatinine ratio  $< 1.5$

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### **Previous inclusion criteria:**

1. Female patients, age 16 years and older with relapsed BRCA (germline or somatic) mutated

epithelial ovarian, primary peritoneal or fallopian tube cancer who have relapsed in a platinum resistant time frame, i.e. have progressed within 6 months of previous platinum-based therapy. Their most recent chemotherapy does not have to have been platinum-based.

2. Patients can have received prior PARP inhibitor and antiangiogenic therapy, but there must be a > 6 month interval since treatment
3. Measurable disease by RECIST Version 1.1 performed in past 4 weeks. At least one lesion, not previously irradiated, that can be accurately measured at baseline as  $\geq 10$  mm in the longest diameter (except lymph nodes which must have short axis  $\geq 15$  mm) with computed tomography (CT) or magnetic resonance imaging (MRI) and which is suitable for accurate repeated measurements.
4. Sufficient archival tissue confirming histological diagnosis available
5. ECOG PS 0-2
6. Able to swallow and retain oral medications
7. Life expectancy > 12 weeks in terms of disease related mortality
8. Patient is willing and able to comply with the protocol for the duration of the study including undergoing treatment and scheduled visits and examinations including follow up
9. Written (signed and dated) informed consent prior to any study specific procedures and be capable of co-operating with protocol
10. Patients must have:
  - 10.1. Haemoglobin  $\geq 10.0$  g/dL and no blood transfusions in the 28 days prior to randomisation
11. Patients must have normal organ and bone marrow function measured within 14 days prior to administration of study treatment as defined below:
  - 11.1. Absolute neutrophil count (ANC)  $\geq 1.5 \times 10^9/L$ 
    - 11.1.1. No features suggestive of MDS/AML on peripheral blood smear
  - 11.2. White blood cells (WBC)  $> 3 \times 10^9/L$
  - 11.3. Platelet count  $> 100 \times 10^9/L$
  - 11.4. Total bilirubin  $\leq 1.5 \times$  institutional upper limit of normal (ULN)
  - 11.5. AST (SGOT)/ALT (SGPT)  $\leq 2.5 \times$  institutional upper limit of normal unless liver metastases are present in which case it must be  $\leq 5 \times$  ULN
  - 11.6. Serum creatinine  $\leq 1.5 \times$  institutional upper limit of normal (ULN) or calculated creatinine clearance  $> 50$  ml/min calculated using Cockcroft-Gault, Jelliffe or Wright (see Appendix 4)
  - 11.7. Urine dipstick for proteinuria  $< 2+$ . If urine dipstick is  $\geq 2+$  on two occasions more than one week apart then a 24-hour urine must demonstrate  $\leq 1$  g of protein in 24 hours or protein/creatinine ratio  $< 1.5$

## **Participant type(s)**

Patient

## **Age group**

Adult

## **Lower age limit**

16 Years

## **Sex**

Female

## **Target number of participants**

Planned Sample Size: 138; UK Sample Size: 138

## **Total final enrolment**

## Key exclusion criteria

1. Received previous single agent weekly paclitaxel for relapsed disease
2. Pregnant or breast-feeding women or women of childbearing potential unless effective methods of contraception are used during the trial and for 6 months after stopping treatment. Negative urine or serum pregnancy test within 28 days of study treatment, confirmed prior to treatment on day 1. Pregnancy test will be performed monthly in women of child bearing potential.  
Postmenopausal is defined as: Amenorrheic for 1 year or more following cessation of exogenous hormonal treatments, LH and FSH levels in the post-menopausal range for women under 50, radiation-induced oophorectomy with last menses >1 year ago, chemotherapy-induced menopause with >1 year interval since last menses, or surgical sterilisation (bilateral oophorectomy or hysterectomy).
3. Treatment with any other investigational agent, systemic chemotherapy, or participation in another interventional clinical trial within 28 days prior to enrolment
4. Radiotherapy within 2 weeks from the last dose prior to study treatment
5. Started a stable dose of bisphosphonates for bone metastases less than 4 weeks prior to treatment with study drug e.g. patient is eligible and can continue to take bisphosphonates if these were started at least 4 weeks prior to treatment with study drug
6. Concomitant use of known CYP3A4 inhibitors such as ketokonazole, itraconazole, ritonavir, indinavir, saquinavir, telithromycin, clarithromycin and nelfinavir
7. Concomitant use of potent inducers of CYP3A4 such as rifampicin, carbamazepine, phenobarbital, phenytoin and St. John Wort
8. Persistent toxicities ( $\geq$ CTCAE grade 2), with the exception of alopecia, caused by previous cancer therapy
9. Resting ECG with QTc > 470msec on 2 or more time points within a 24 hour period or family history of long QT syndrome.
10. Blood transfusions within 1 month prior to study start
11. Patients with myelodysplastic syndrome/acute myeloid leukaemia.
12. Patients with symptomatic, untreated, uncontrolled brain or meningeal metastases or tumour
  - 12.1. A scan to confirm the absence of brain metastases is not require
  - 12.2. Patients with radiological evidence of stable brain metastases are eligible, providing that they are asymptomatic and:
    - 12.2.1. Do not require corticosteroids, or
    - 12.2.2. Have previously been treated with corticosteroids, with clinical and radiological evidence of stabilisation at least 10 days after discontinuation of steroids
    - 12.2.3. The patient can receive a stable dose of corticosteroids before and during the study as long as these were started at least 28 days prior to treatment.
13. Major surgery within 14 days of starting study treatment
14. Patients who have not recovered from any effects of any major surgery.
15. Patients considered a poor medical risk due to a serious, uncontrolled medical disorder, non-malignant systemic disease or active, uncontrolled infection. Examples include, but are not limited to, uncontrolled ventricular arrhythmia, recent (within 3 months) myocardial infarction, unstable spinal cord compression (untreated and unstable for at least 28 days prior to study entry), superior vena cava syndrome, extensive bilateral lung disease on HRCT scan
16. Any psychiatric disorder that prohibits obtaining informed consent.
17. Left Ventricular Ejection Fraction (LVEF) < institutional lower limit of normal, when:
  - 17.1. Prior treatment with anthracyclines
  - 17.2. Prior treatment with trastuzumab

- 17.3. A NYHA classification of II controlled with treatment (see Appendix 2)
- 17.4. Prior central thoracic RT, including RT to the heart
- 17.5. History of myocardial infarction within the prior 12 months
- 18. Poorly controlled hypertension (persistently elevated > 150/100mmHg, either systolic or diastolic or both, despite anti-hypertensive medication)
- 19. History of inflammatory bowel disease
- 20. History of cerebrovascular accident (including transient ischaemic attacks) within last 12 months.
- 21. Gastro intestinal impairment that could affect ability to take, or absorption of, oral medicines including sub- acute or complete bowel obstruction
- 22. Evidence of severe or uncontrolled cardiac disease
- 23. Evidence of active bleeding or bleeding diathesis. Defined as significant haemorrhage (>30mL bleeding/episode in previous 3 months) or haemoptysis (>5mL fresh blood in previous 4 weeks).
- 24. Known treatment limiting hypersensitivity to cediranib, olaparib, paclitaxel or any of its excipients
- 25. Other psychological, social or medical condition, physical examination finding or a laboratory abnormality that the Investigator considers would make the patient a poor trial candidate or could interfere with protocol compliance or the interpretation of trial results
- 26. Any other active malignancy, with the exception of adequately treated cone-biopsied in situ carcinoma of the cervix uteri and non-melanoma skin lesions, requiring treatment/or whose prognosis will prevent readout from trial endpoints
- 27. Patients who are known to be serologically positive for Hepatitis B, Hepatitis C or HIV
- 28. Immunocompromised patients e.g., patients who are taking immunosuppressive drugs

**Date of first enrolment**

09/03/2017

**Date of final enrolment**

10/01/2020

## **Locations**

**Countries of recruitment**

England

Northern Ireland

Scotland

United Kingdom

Wales

**Study participating centre**

**Beatson West of Scotland Cancer Centre**

1053 Great Western Road

Glasgow  
United Kingdom  
G12 0YN

**Study participating centre**

**Christie Hospital**

Wilmslow Road  
Manchester  
United Kingdom  
M20 4BX

**Study participating centre**

**Churchill Hospital**

Old Road  
Headington  
Oxford  
United Kingdom  
OX3 7LE

**Study participating centre**

**Clatterbridge Cancer Centre**

Clatterbridge Road  
Birkenhead  
Wirral  
United Kingdom  
CH63 4JY

**Study participating centre**

**Mount Vernon Cancer Centre**

Rickmansworth Road  
Northwood  
United Kingdom  
HA6 2RN

**Study participating centre**

**Royal Marsden Hospital Chelsea**

203 Fulham Road  
Chelsea  
London  
United Kingdom  
SW3 6JJ



**Study participating centre**  
**Royal Marsden Hospital Sutton**  
Downs Road  
Sutton  
United Kingdom  
SM2 5PT

**Study participating centre**  
**Royal United Hospital**  
Combe Park  
Avon  
Bath  
United Kingdom  
BA1 3NG

**Study participating centre**  
**University College London Hospital**  
Cancer Institute  
Huntley Street  
London  
United Kingdom  
WC1E 6AG

**Study participating centre**  
**Velindre Cancer Centre**  
Velindre Road  
Cardiff  
United Kingdom  
CF14 2TL

**Study participating centre**  
**Hammersmith Hospital**  
72 Du Cane Rd  
Shepherd's Bush  
London  
United Kingdom  
W12 0HS

**Study participating centre**  
**St Bartholomew's Hospital**  
West Smithfield  
London  
United Kingdom  
EC1A 7BE

**Study participating centre**  
**Nottingham City Hospital**  
Hucknall Road  
Nottingham  
United Kingdom  
NG5 1PB

**Study participating centre**  
**Belfast City Hospital**  
51 Lisburn Road  
Belfast  
United Kingdom  
BT9 7AB

**Study participating centre**  
**Royal Surrey County Hospital**  
Egerton Road  
Guildford  
United Kingdom  
GU2 7XX

## **Sponsor information**

**Organisation**  
University of Oxford

**Sponsor details**  
Clinical Trials and Research Governance  
Oxford  
England  
United Kingdom  
OX1 2JD

**Sponsor type**

Hospital/treatment centre

ROR  
<https://ror.org/052gg0110>

## Funder(s)

Funder type  
Industry

Funder Name  
AstraZeneca UK Limited

## Results and Publications

Publication and dissemination plan  
Planned publication in a high-impact peer reviewed journal.

Intention to publish date  
31/12/2023

Individual participant data (IPD) sharing plan  
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary  
Data sharing statement to be made available at a later date

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>	protocol	15/01/2021	18/01/2021	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Results article</a>		20/01/2024	22/01/2024	Yes	No
<a href="#">Plain English results</a>			20/12/2024	No	Yes
<a href="#">Participant information sheet</a>	version 10.0	27/05/2022	20/06/2025	No	Yes
<a href="#">Participant information sheet</a>	version 4.0	04/07/2017	20/06/2025	No	Yes