

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

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

Contact information

Type(s)

Public

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Additional identifiers

Clinical Trials Information System (CTIS)

2016-000559-28

ClinicalTrials.gov (NCT)

NCT03117933

Protocol serial number

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

Study type(s)

Treatment

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.

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(s)

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

Key secondary outcome(s)

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

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 ≥ 10 mm in the longest diameter (except lymph nodes which must have short axis ≥ 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 ≥ 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 ≤ 1 g of protein in 24 hours or protein/creatinine ratio < 1.5

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 ≥ 10 mm in the longest diameter (except lymph nodes which must have short axis ≥ 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 ≥ 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 ≤ 1 g of protein in 24 hours or protein/creatinine ratio < 1.5

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

16 years

Sex

Female

Total final enrolment

139

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: Amenorrhic 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

United Kingdom

England

Northern Ireland

Scotland

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

ROR

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

Funder(s)

Funder type

Industry

Funder Name

AstraZeneca UK Limited

Results and Publications

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? |
|-------------|---------|--------------|------------|----------------|-----------------|
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|---|---------------|------------|------------|-----|-----|
| Results article | | 20/01/2024 | 22/01/2024 | Yes | No |
| Protocol article | protocol | 15/01/2021 | 18/01/2021 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Participant information sheet | version 10.0 | 27/05/2022 | 20/06/2025 | No | Yes |
| Participant information sheet | version 4.0 | 04/07/2017 | 20/06/2025 | No | Yes |
| Plain English results | | | 20/12/2024 | No | Yes |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |