

# Does cediranib together with paclitaxel chemotherapy, or cediranib and olaparib, treat advanced endometrial cancer better than paclitaxel chemotherapy?

|  |   |   |
|--|---|---|
| <b>Submission date</b><br>16/06/2017   | <b>Recruitment status</b><br>No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol |
| <b>Registration date</b><br>18/08/2017 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>23/05/2025       | <b>Condition category</b><br>Cancer               | <input type="checkbox"/> Individual participant data  |

## Plain English summary of protocol

<http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-cediranib-and-olaparib-for-women-with-womb-cancer-copelia>

## Contact information

### Type(s)

Public

### Contact name

Dr Clare Freestone

### Contact details

Centre for Trials Research  
College of Biomedical & Life Sciences  
Cardiff University  
6th Floor, Neuadd Meirionnydd  
Heath Park  
Cardiff  
United Kingdom  
CF14 4YS  
+44(0)29 20687095  
COPELIA@cardiff.ac.uk

### Type(s)

Scientific

### Contact name

Dr Clare Freestone

### **Contact details**

Centre for Trials Research  
College of Biomedical & Life Sciences  
Cardiff University  
6th Floor, Neuadd Meirionnydd  
Heath Park  
Cardiff  
United Kingdom  
CF14 4YS  
+44(0)29 20687095  
COPELIA@cardiff.ac.uk

## **Additional identifiers**

### **ClinicalTrials.gov (NCT)**

NCT03570437

### **Clinical Trials Information System (CTIS)**

2016-004617-28

### **Integrated Research Application System (IRAS)**

216069

## **Study information**

### **Scientific Title**

A 3-Arm Randomised Phase II Evaluation of Cediranib in Combination with Weekly Paclitaxel or Olaparib Versus Weekly Paclitaxel Chemotherapy as Second-Line Therapy for Advanced/ Metastatic Endometrial Carcinoma or for disease relapse within 12 months of adjuvant carboplatin-paclitaxel chemotherapy

### **Acronym**

COPELIA

### **Study objectives**

The aim of this study is to evaluate the therapeutic benefit of two novel combination regimens: cediranib and weekly paclitaxel (Arm 2) and cediranib-olaparib (Arm 3) compared to a widely-accepted standard treatment of weekly paclitaxel (Arm 1) for measurable, recurrent endometrial cancer where disease recurrence or progression has occurred after first-line platinum-based chemotherapy.

### **Ethics approval required**

Old ethics approval format

### **Ethics approval(s)**

Approved 30/11/2017, South Central - Oxford B Research Ethics Committee (Whitefriars, Level 3, Block B, Lewin's Mead, Bristol, BS1 2NT, UK; Tel: +44 (0)207 104 8241; Email: nrescommittee.southcentral-oxfordb@nhs.net), REC ref: 17/SC/0536

## Study design

Randomized controlled three-arm open-label parallel group multi-arm multi-stage interventional trial

## Primary study design

Interventional

## Study type(s)

Treatment

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

Advanced/metastatic endometrial cancer

## Interventions

Participants are randomised into one of the three study arms to receive treatment.

Arm 1 (control): Paclitaxel will be administered at 80 mg/m<sup>2</sup> IV on days 1, 8 and 15 of a 28-day cycle for 6 cycles. This is standard treatment and is the control arm.

Arm 2: Paclitaxel at 80 mg/m<sup>2</sup> IV on days 1, 8 and 15 of a 28-day cycle for 6 cycles with cediranib 20 mg orally once daily continuously in 28 day cycles until disease progression.

Arm 3: Cediranib 20 mg orally once daily and Olaparib tablets 300 mg orally twice daily continuously in 28 day cycles until disease progression.

Participants in all study arms are followed up after three and six months.

## Intervention Type

Drug

## Phase

Phase II

## Drug/device/biological/vaccine name(s)

Paclitaxel, cediranib, olaparib

## Primary outcome(s)

Proportion of participants who are disease progression free at three months as determined by CT scan (RECIST v1.1 reporting) at three months.

## Key secondary outcome(s)

1. Radiological response rate during the trial assessed by CT scan (RECIST v1.1 reporting)
2. Median time until disease progression
3. Proportion of participants who are disease progression free at six months as determined by CT scan (RECIST v1.1 reporting) at six months
4. The median overall survival time, calculated as median time from participant enrolment to death with those still alive censored at date last seen
5. All toxicities associated with each treatment regimen as assessed by CTCAE version 4.03

monthly until disease progression, and at the end of treatment

6. Quality of life as measured by the EORTC QLQ-C30 and EN28 questionnaires at the start of the trial, monthly until disease progression, and at the end of treatment

### **Completion date**

07/03/2025

## **Eligibility**

### **Key inclusion criteria**

1. Histologically confirmed advanced or recurrent endometrial carcinoma or carcinosarcoma
2. Aged >16 years
3. One prior line of platinum-containing chemotherapy for advanced/ recurrent disease or relapse within 12 months of adjuvant platinum-based chemotherapy
4. Ability to provide written informed consent that includes genetic research on tissue derived from biopsies and biomarker research. (If a participant declines to participate in optional exploratory genetic research or the optional biomarker research, there will be no penalty or loss of benefit to the participant. The participant will not be excluded from other aspects of the study).
5. Willing and able to comply with the trial visits and undergo treatment as scheduled
6. ECOG Performance Status 0-2
7. Life expectancy greater than 16 weeks
8. Measurable disease by RECIST v1.1 including at least one not previously irradiated lesion that is  $\geq 10$  mm in the longest diameter (lymph nodes must have short axis  $\geq 15$  mm) as determined by CT
9. Adequate haematological function: Hb  $\geq 100.0$  g/l with no requirement for blood transfusion in the last 28 days, neutrophils  $\geq 1.5 \times 10^9/l$ , platelets  $\geq 100 \times 10^9/l$ ; coagulation: INR  $<1.4$  (unless therapeutically anti-coagulated) and APPT ratio  $<1.4$
10. Adequate liver function: bilirubin  $\leq 1.5 \times$  ULN, transaminases (ALT and AST  $\leq 2.5 \times$  ULN. AST or ALT  $<5 \times$  ULN allowed in the presence of parenchymal liver metastases
11. Adequate renal function defined as calculated creatinine clearance using modified Wright or Cockcroft-Gault formula  $\geq 51$  ml/min or measured radioisotopic GFR  $\geq 51$  ml/min
12. Urine protein:creatinine ratio (UPC)  $\leq 1$  OR  $\leq 2+$  proteinuria on two consecutive dipsticks taken no less than 1 week apart. Patients with 2+ proteinuria on dipstick must also have UPC  $<0.5$  on 2 consecutive samples
13. Adequately controlled thyroid function, with no symptoms of thyroid dysfunction
14. Ability to swallow oral medication (tablets)
15. Willing to stop taking herbal supplements, and (if allocated to Arm 3) willing to not consume grapefruit or grapefruit juice, during the treatment period and for 30 days after end of trial treatment

### **Participant type(s)**

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

16 years

## Sex

Female

## Total final enrolment

124

## Key exclusion criteria

1. Uncontrolled brain metastases or seizures. A scan to confirm the absence of brain metastases is not required
2. Known positivity for hepatitis B, hepatitis C or HIV due to the risk of transmitting the infection through blood or other body fluids.
3. Resting ECG with QTc > 470 ms on 2 or more time points within a 24 hour period or family history of long QT syndrome
4. Concomitant use of known strong CYP3A inhibitors (eg. itraconazole, telithromycin, clarithromycin, protease inhibitors boosted with ritonavir or cobicistat, indinavir, saquinavir, nelfinavir, boceprevir, telaprevir) or moderate CYP3A inhibitors (eg. ciprofloxacin, erythromycin, diltiazem, fluconazole, verapamil). The required washout period prior to starting olaparib is two weeks
5. Concomitant use of known strong (eg. phenobarbital, enzalutamide, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine and St John's Wort) or moderate CYP3A inducers (eg. bosentan, efavirenz, modafinil). The required washout period prior to starting olaparib is 5 weeks for enzalutamide or phenobarbital and 3 weeks for other agents.
6. Pregnant or lactating. Pregnancy status in women of child bearing potential will be confirmed via a serum or urine pregnancy test no more than one week prior to randomisation, monthly during the treatment period, and at the end of treatment assessment.
7. Of child bearing potential AND not willing to ensure they use effective contraception throughout the treatment period and for six months following the end of treatment. Acceptable methods of contraception are:
  - 7.1. True sexual abstinence (when this is in line with the preferred and usual lifestyle of the participant)
  - 7.2. A combination of male condom plus one of the following:
    - 7.2.1. Vasectomised sexual partner, with participant assurance that partner received post-vasectomy confirmation of azoospermia
    - 7.2.2. Tubal occlusion
    - 7.2.3. Intrauterine device provided coils are copper-banded
    - 7.2.4. Etonogestrel implants (eg, Implanon®, Norplant®)
    - 7.2.5. Normal and low dose combined oral pills
    - 7.2.6. Hormonal shot or injection (eg, Depo-Provera)
    - 7.2.7. Intrauterine system device (eg, levonorgestrel-releasing intrauterine system -Mirena®)
    - 7.2.8. Norelgestromin/ethinyl estradiol transdermal system
    - 7.2.9. Intravaginal device (eg, ethinyl estradiol and etonogestrel)
    - 7.2.10. Cerazette (desogestrel). Cerazette is currently the only highly efficacious progesterone based pill.
8. Side effects of previous treatments have not resolved to grade 1 or less, with the exception of alopecia that is considered related to cytotoxic chemotherapy
9. Radiotherapy, chemotherapy, surgery or tumour embolisation within 28 days before the first dose of IMP
10. Additional concurrent anti-cancer therapy
11. Causes of malabsorption, e.g. uncontrolled diarrhoea or poorly controlled stoma

12. Bowel obstruction, fistulae, or extensive rectosigmoid involvement by cancer
13. Inadequately controlled hypertension, defined as  $\geq 150/90$  mmHg
14. Prior or concurrent therapy with a PARP or VEGF inhibitor
15. Known hypersensitivity to olaparib, cediranib or paclitaxel or any of the excipients of the products
16. Exposure to an investigational agent within 30 days or 5 half-lives (whichever is the longer) prior to enrolment
17. 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, uncontrolled major seizure disorder, unstable spinal cord compression, superior vena cava syndrome, extensive interstitial bilateral lung disease on High Resolution Computed Tomography (HRCT) scan or any psychiatric disorder that prohibits obtaining informed consent
18. Myelodysplastic syndrome (MDS), acute myeloid leukaemia (AML) or other clonal blood disorder, or features suggestive of MDS/AML
19. Other malignancy within the last 5 years except: adequately treated non-melanoma skin cancer, curatively treated in situ cancer of the cervix, ductal carcinoma in situ (DCIS), or other solid tumours including lymphomas (without bone marrow involvement) curatively treated with no evidence of disease for  $\geq 5$  years
20. Prior allogeneic bone marrow transplant or double umbilical cord blood transplantation

**Date of first enrolment**

12/02/2018

**Date of final enrolment**

31/12/2021

## **Locations**

**Countries of recruitment**

United Kingdom

England

Scotland

Wales

**Study participating centre**

**The Christie NHS Foundation Trust**

Wilmslow Road

Manchester

United Kingdom

M20 4BX

**Study participating centre**

**University College London Hospital**

235 Euston Road  
Fitzrovia  
London  
United Kingdom  
NW1 2BU

**Study participating centre**

**Mount Vernon Cancer Centre**

Mount Vernon Hospital  
Rickmansworth Road  
Northwood  
United Kingdom  
HA6 2RN

**Study participating centre**

**Velindre Cancer Centre**

Velindre University NHS Trust  
Velindre Road  
Whitchurch  
Cardiff  
United Kingdom  
CF14 2TL

**Study participating centre**

**Bristol Haematology & Oncology Centre**

Clinical Trials Unit  
Bristol Haematology & Oncology Centre  
University Hospitals Bristol NHS Foundation Trust  
Horfield Road  
Bristol  
United Kingdom  
BS2 8ED

**Study participating centre**

**Churchill Hospital**

c/o Dr Rene Roux  
Old Road  
Headington  
Oxford  
United Kingdom  
OX3 7LE

**Study participating centre**  
**The Royal Marsden Hospital (Surrey)**  
c/o Dr Susana Banerjee  
Downs Road  
Sutton  
United Kingdom  
SM2 5PT

**Study participating centre**  
**The Royal Marsden Hospital**  
c/o Dr Susana Banerjee  
Fulham Road  
Chelsea  
London  
United Kingdom  
SW3 6JJ

**Study participating centre**  
**Beatson West of Scotland Oncology Centre**  
c/o Dr Azmat Sadoyze  
Gartnavel General Hospital  
1089 Great Western Road  
Glasgow  
United Kingdom  
G12 0YN

**Study participating centre**  
**Northern Centre for Cancer Care**  
c/o Dr Yvette Drew  
Freeman Hospital  
Freeman Road  
High Heaton  
Newcastle upon Tyne  
United Kingdom  
NE7 7DN

**Study participating centre**  
**Royal Surrey County Hospital**  
Egerton Road

Guildford  
United Kingdom  
GU2 7XX

**Study participating centre**  
**Leicester Royal Infirmary**  
c/o Dr Joey Wood  
Hope Clinical Trials Facility  
Level 2 Osborne Building  
Leicester  
United Kingdom  
LE1 5WW

**Study participating centre**  
**Clatterbridge Cancer Centre**  
Clatterbridge Road  
Bebington  
Wirral  
United Kingdom  
CH63 4JY

**Study participating centre**  
**Guys and St Thomas NHS Trust**  
c/o Dr Rebecca Kristeleit  
OHCT  
1st floor Chapel Wing  
Guy's Hospital  
London  
United Kingdom  
SE1 9RY

**Study participating centre**  
**Airedale NHS Foundation Trust**  
c/o Dr Clara Sentamans  
Skipton Road  
Steeton  
Bradford  
United Kingdom  
BD20 6TD

**Sponsor information**

**Organisation**

University of Manchester

**ROR**

<https://ror.org/027m9bs27>

## Funder(s)

**Funder type**

Industry

**Funder Name**

AstraZeneca

**Alternative Name(s)**

AstraZeneca PLC, Pearl Therapeutics, AZ

**Funding Body Type**

Government organisation

**Funding Body Subtype**

For-profit companies (industry)

**Location**

United Kingdom

## Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are/will be available upon request upon consideration by the TMG.

**IPD sharing plan summary**

Available on request

**Study outputs**

| Output type                          | Details       | Date created | Date added | Peer reviewed? | Patient-facing? |
|--------------------------------------|---------------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a>      |               |              | 23/05/2025 | Yes            | No              |
| <a href="#">HRA research summary</a> |               |              | 28/06/2023 | No             | No              |
| <a href="#">Study website</a>        | Study website | 11/11/2025   | 11/11/2025 | No             | Yes             |