

# Is it safe to add cediranib to weekly paclitaxel chemotherapy in women with ovarian cancer who are at risk of developing malignant bowel obstruction?

<b>Submission date</b> 11/08/2017	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 06/10/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 08/07/2025	<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-cediranib-for-women-with-ovarian-cancer-at-risk-of-having-a-bowel-obstruction-ceboc>

## Contact information

### Type(s)

Public

### Contact name

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### Contact details

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## Additional identifiers

Clinical Trials Information System (CTIS)

2016-004618-93

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

216211

### **Protocol serial number**

CEBOC01

## **Study information**

### **Scientific Title**

Evaluation of the safety of CEdiranib in the prevention of Bowel perforation in platinum-resistant Ovarian Cancer

### **Acronym**

CEBOC

### **Study objectives**

Is it safe to add cediranib to weekly paclitaxel chemotherapy in women with ovarian cancer who are at risk of developing malignant bowel obstruction?

### **Ethics approval required**

Old ethics approval format

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

Not provided at time of registration

### **Study design**

Single-arm Phase II non-randomized trial

### **Primary study design**

Interventional

### **Study type(s)**

Treatment

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

Progressive, platinum-resistant or refractory, high-grade ovarian, fallopian tube or primary peritoneal cancer with high risk of bowel obstruction.

### **Interventions**

This is a single-arm trial where participants with recurrent platinum-resistant ovarian cancer and clinical and/or radiological features indicating an increased risk of developing subacute bowel obstruction. after registration participants receive oral cediranib 20 mg/day with weekly intravenous paclitaxel 70 mg/m<sup>2</sup>/week 1, 8 and 15 of a 21-day cycle. At the point of developing progressive disease, participants will have the option of ceasing paclitaxel and continuing cediranib 20 mg/day with oral olaparib 300 mg twice daily continuously until further progressive disease occurs. Participants are followed up 28 days after last dose of study drug.

The trial has a safety design where the number of patients developing bowel perforation or fistula will be monitored.

## Intervention Type

Drug

## Phase

Phase II

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

Paclitaxel, cediranib, olaparib

## Primary outcome(s)

Safety of combining cediranib with weekly paclitaxel is measured by the analysis of the number participants who are free of grade III-V gastrointestinal perforation and fistula, which is causally related to cediranib or the cediranib olaparib combination, during cediranib treatment for up to 4 weeks after stopping cediranib.

## Key secondary outcome(s)

1. The proportion of participants hospitalised for bowel obstruction
2. The number of grade III or more toxicities excluding gastrointestinal perforation/ fistula as assessed by CTCAE 4.03.
3. Treatment compliance, as assessed by the dose intensity of paclitaxel, cediranib and, expressed as the  $\{[\text{total delivered dose/actual time taken to complete therapy}]/[\text{standard dose /planned time to complete therapy}]\} \times (\text{actual number of cycle /planned number of cycles})$ , and the dose intensity of cediranib and olaparib treatment, expressed as  $[\text{number of days' drug was taken correctly} \times 100/ \text{number of days for which drug was prescribed}]$
4. Investigator-determined Objective Response Rate assessed by RECIST 1.1 within 18 weeks of starting paclitaxel
5. Progression Free Survival measured as the time from date of registration to date of investigator-assessed objective progression via RECIST v1.1 or death from any cause in the absence of progression
6. Overall survival defined as the time from date of registration to date of death

## Completion date

28/02/2023

## Eligibility

### Key inclusion criteria

1. Histologically confirmed, progressive, platinum-resistant or refractory, high-grade ovarian, fallopian tube or primary peritoneal cancer for which weekly paclitaxel would be a potential treatment option
2. Aged 16 years or over
3. Patients who are at risk of bowel obstruction are eligible for the trial. Features that are compatible with this diagnosis include increasing abdominal pain and swelling, borborygmi, change in bowel habit, extensive serosal disease or dilated or tethered bowel on radiological investigation. It is anticipated that one or more of these should be present in eligible patients. Previous bowel obstruction is permitted providing patients can take oral medication and there is no concern about absorption of oral medication. Recto sigmoid involvement is permitted.
4. Adequate haematological function: Hb  $\geq$  100 g/l, Neutrophils  $\geq$   $1.5 \times 10^9$ /l, Platelets  $\geq$   $100 \times 10^9$ /l; coagulation: INR  $<$ 1.4 (unless therapeutically anti-coagulated) and/or APPT ratio  $<$ 1.4
5. Adequate renal function defined as GFR  $\geq$ 50ml/min and Creatinine clearance  $\geq$ 50 mL/min

using modified Wright or Cockcroft-Gault formula

6. Adequate liver function: bilirubin  $\leq$  1.5 xULN, transaminases  $\leq$  3 xULN

7. Any number of previous anti-cancer treatments permitted including weekly paclitaxel in the first-line setting

8. Controlled hypertension permitted. Patients must have a blood pressure (BP) of  $\leq$  Systolic BP (SBP) :150/ Diastolic BP (DBP) 90 mmHg, with or without anti-hypertensive medication. BP measurements must be taken in the clinic setting by a medical professional within 2 weeks prior to starting study. A maximum of 3 anti-hypertensive medications are permitted and it is strongly recommended that patients who are on 3 anti-hypertensive medications be followed by a cardiologist or a primary care physician for management of BP while on study.

9. ECOG performance status 0-2 and life expectancy of over 12 weeks

10. Adequately controlled thyroid function, with no symptoms of thyroid dysfunction

11. Measurable disease by RECIST 1.1

12. Previous bevacizumab is permitted but patients cannot have been treated with VEGF RTKi previously

13. Written informed consent

14. Able to swallow and retain oral medications and without gastrointestinal (GI) illnesses that would preclude absorption of cediranib or olaparib

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

Patient

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

16 years

### **Sex**

Female

### **Total final enrolment**

30

### **Key exclusion criteria**

1. Patients with a known hypersensitivity to olaparib, cediranib or paclitaxel or any of the excipients of the products

2. Concurrent medical illness that would impact on compliance with the protocol including myelodysplastic syndrome (MDS)/ acute myeloid leukaemia (AML) or with features which suggestive of MDS/AML

3. Uncontrolled brain metastases or seizures. A scan to confirm the absence of brain metastases is not required. Central nervous system metastases:

3.1. Symptomatic uncontrolled brain metastases requiring corticosteroid treatment

3.2. History of spinal cord compression unless after definitive treatment the patient has clinically stable disease (SD) for at least 28 days prior to starting IMPs. In the absence of these features and in an asymptomatic patient a scan to confirm the absence of brain metastases is not required.

4. Known positivity for Hep B, Hep C or HIV

5. Resting ECG with QTc > 470msec on 2 or more time points within a 24- hour period or family history of long QT syndrome
6. Concomitant use of known strong CYP3A4/5 inhibitors such as such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, telithromycin, clarithromycin and nelfinavir. Concomitant use of inducers or inhibitors (e.g., phenobarbital, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine and St John's Wort) is also excluded. The required washout period prior to starting olaparib is 2 weeks.
7. Concomitant use of known strong (e.g. phenobarbital, enzalutamide, phenytoin, rifampicin, rifabutin, rifapentine, carbamazepine, nevirapine and St John's Wort) or moderate CYP3A inducers (e.g. bosentan, efavirenz, modafinil). The required washout period prior to starting olaparib is 5 weeks for enzalutamide or phenobarbital and 3 weeks for other agents.
8. Another cancer, which has been active within the previous 5 years, except for adequately treated cone-biopsied in situ carcinoma of the cervix uteri and basal or squamous cell carcinoma of the skin and no evidence of recurrence of other malignancy
9. Female patients who are able to become pregnant (or are already pregnant or lactating) unless the following apply: Those who have a negative serum or urine pregnancy test before enrolment and agree to use two highly effective forms of contraception (oral, injected or implanted hormonal contraception and condom, have an intra-uterine device and condom, diaphragm with spermicidal gel and condom) for four weeks before entering the trial, during the trial and for six months afterwards are considered eligible. Alternatively if the patient can abstain from sexual intercourse for the same interval, then they are eligible to participate.
10. Patients who are planning to receive maintenance bevacizumab
11. Radiotherapy, surgery or tumour embolization within 28 days before the first dose of cediranib
12. No additional concurrent anti-cancer therapy is permitted
13. No cause of malabsorption e.g. uncontrolled diarrhoea or poorly controlled stoma, is permitted
14. Patients who have or have had prior leukoencephalopathy, recent (within the past 6 months) arterial thromboembolic event (MI/CVA within previous 6 months), previous or concurrent fistula, previous or concurrent GI perforation, concurrent intra-abdominal abscess, previous VEGF RTKi or clinically relevant proteinuria, are excluded
15. Inability to comply with the protocol
16. Major surgery within two weeks of starting study treatment and patients must have recovered from any effects of any major surgery.
17. 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, unstable angina, recent (within 6 months) myocardial infarction, uncontrolled major seizure disorder, unstable spinal cord compression, superior vena cava syndrome, resting ECG with clinically significant abnormal findings, NYHA grade III/IV cardiac failure, extensive interstitial bilateral lung disease on High Resolution Computed Tomography (HRCT) scan or any psychiatric disorder that prohibits obtaining informed consent. Left ventricular ejection fraction (LVEF) < lower limit of normal (LLN) per institutional guidelines, or <55%, if threshold for normal not otherwise specified by institutional guidelines, for patients with the following risk factors:
  - 17.1. Prior treatment with anthracyclines– except liposomal doxorubicin, which is permitted
  - 17.2. Prior treatment with trastuzumab
  - 17.3. Prior central thoracic RT, including exposure of heart to therapeutic doses of ionizing RT
  - 17.4. History of myocardial infarction within 6-12 months prior to start of IMPs
  - 17.5. Prior history of other significant impaired cardiac function
18. Patients unable to swallow orally administered medication and patients with gastrointestinal disorders likely to interfere with absorption of the study medication
19. Breast feeding women

- 20. Patients with known active hepatitis (i.e. Hepatitis B or C) due to risk of transmitting the infection through blood or other body fluids
- 21. Patients receiving any systemic chemotherapy or radiotherapy (except for palliative reasons) within 3 weeks prior to study treatment
- 22. Persisting  $\geq$ Grade 2 CTCAE toxicity (except alopecia and Grade 2 peripheral neuropathy) from previous anti-cancer treatment(s)
- 23. No prior allogeneic bone marrow transplant or double umbilical cord blood transplantation

**Date of first enrolment**

31/10/2017

**Date of final enrolment**

31/10/2019

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**The Christie NHS Foundation Trust**

Winslow Road

Manchester

United Kingdom

M20 4BX

## **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 on 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>		01/07/2024	28/01/2025	Yes	No
<a href="#">Plain English results</a>			28/01/2025	No	Yes
<a href="#">Plain English results</a>			08/07/2025	No	Yes
<a href="#">Protocol file</a>	version 4.0	23/08/2021	22/08/2022	No	No
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes