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

Submission date
11/08/2017

Recruitment status
No longer recruiting

Registration date
06/10/2017

Overall study status
Completed

Last Edited
29/01/2025

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English Summary
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

Study website
http://www.cardiff.ac.uk/centre-for-trials-research/research/studies-and-trials/view/ceboc

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2016-004618-93

IRAS number
216211

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
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 hypothesis
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

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet’

Condition
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/m2/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 measure
Safety of combining cediranib with weekly paclitaxel is measured by the analysis of the number participants who are free of grade III-V gastrointestinal of 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.

Secondary outcome measures
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 {[total delivered dose/actual time taken to complete therapy]/ [standard dose /planned time to complete therapy]} x (actual number of cycle /planned number of cycles), and the dose intensity of cediranib and olaparib treatment, expressed as [number of days' drug was taken correctly x 100/ number of days for which drug was prescribed]
4. Investigator-determined Objective Response Rate assessed by RECIST 1.1 within 18 weeks of starting paclitaxe
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

Overall study start date
01/10/2016

Overall study end date

28/02/2023

Eligibility

Participant 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 ≥ 100 g/l, Neutrophils ≥ 1.5 x 109/l, Platelets ≥ 100 x 109/l; coagulation: INR <1.4 (unless therapeutically anti-coagulated) and/or APPT ratio <1.4
5. Adequate renal function defined as GFR ≥50ml/min and Creatinine clearance ≥50 mL/min using modified Wright or Cockcroft-Gault formula
6. Adequate liver function: bilirubin ≤ 1.5 xULN, transaminases ≤ 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 ≤ 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

Age group
Adult

Lower age limit
16 Years

Sex
Female

Target number of participants
30

Total final enrolment
30

Participant 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 ≥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

Recruitment start date
31/10/2017

Recruitment end date
31/10/2019

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Christie NHS Foundation Trust
Winslow Road
Manchester
United Kingdom
M20 4BX

Sponsor information

Organisation
University of Manchester

Sponsor details
Christie Building
Manchester
England
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M13 9PL

Sponsor type
University/education

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The main trial results will be published in the name of the trial in a peer-reviewed journal, on behalf of all collaborators. The manuscript will be prepared by a writing group, appointed from

amongst the TMG, and high accruing clinicians. All participating centres and clinicians will be acknowledged in this publication together with staff from the CTR. All presentations and publications relating to the trial must be authorised by the TMG and sponsor, on whose behalf publications should usually be made. Authorship of any secondary publications e.g. relating to the various biological studies will reflect the intellectual and time input into these studies, and will not be the same as on the primary publication. No investigator may present or attempt to publish data relating to the CEBOC trial without prior permission from the TMG and sponsor.

Intention to publish date
30/09/2023

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?
Protocol file	version 4.0	23/08/2021	22/08/2022	No	No
Plain English results			28/01/2025	No	Yes
Results article		01/07/2024	28/01/2025	Yes	No