ISRCTN16320634 https://doi.org/10.1186/ISRCTN16320634

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

Submission date
16/06/2017

Recruitment status
No longer recruiting

Registration date
18/08/2017

Overall study status
Completed

Last Edited
23/05/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] 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)
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Additional identifiers

Clinical Trials Information System (CTIS)
2016-004617-28

Integrated Research Application System (IRAS)
216069

ClinicalTrials.gov (NCT)
NCT03570437

Protocol serial number
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/m2 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/m2 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 ≥ 10 mm in the longest diameter (lymph nodes must have short axis ≥ 15 mm) as determined by CT
9. Adequate haematological function: Hb ≥ 100.0 g/l with no requirement for blood transfusion in the last 28 days, neutrophils ≥ 1.5 x 109/l, platelets ≥ 100 x 109/l; coagulation: INR <1.4 (unless therapeutically anti-coagulated) and APPT ratio <1.4
10. Adequate liver function: bilirubin ≤1.5 x ULN, transaminases (ALT and AST ≤2.5x ULN. AST or ALT <5x 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 ≥ 51 ml/min or measured radioisotopic GFR ≥ 51ml/min
12. Urine protein:creatinine ratio (UPC) ≤1 OR ≤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 ≥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 ≥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
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M20 4BX

Study participating centre

University College London Hospital
235 Euston Road
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Study participating centre
Mount Vernon Cancer Centre
Mount Vernon Hospital
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Study participating centre
Velindre Cancer Centre
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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?
Results article			23/05/2025	Yes	No
HRA research summary			28/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes