ISRCTN68510403 https://doi.org/10.1186/ISRCTN68510403

A trial looking at cediranib for ovarian cancer that has come back (ICON6)

Submission date
22/03/2007

Recruitment status
No longer recruiting

Registration date
13/08/2007

Overall study status
Completed

Last Edited
22/11/2023

Condition category
Cancer

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

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-standard-treatment-with-or-without-cediranib-for-ovarian-fallopian-tube-or-primary-peritoneal-cancer-that-has-come-back

Contact information

Type(s)
Scientific

Contact name
Prof Jonathan Ledermann

Contact details
University College London
Cancer Research UK and UCL Cancer Trials Centre
90 Tottenham Court Road
London
United Kingdom
W1T 4TJ

Type(s)
Public

Contact name
Ms Liz Clark

Contact details
ICON6 Trial Manager
University College London
Cancer Research UK and UCL Cancer Trials Centre
90 Tottenham Court Road

London
United Kingdom
W1T 4TJ
-
elizabeth.clark@ucl.ac.uk

Additional identifiers

ClinicalTrials.gov (NCT)
NCT00532194

Clinical Trials Information System (CTIS)
2007-001346-41

Protocol serial number
ACTRN1261000016003

Study information

Scientific Title
A double-blind, placebo-controlled, three-arm, randomised, multi-centre Gynaecologic Cancer InterGroup trial of cediranib (AZD2171), in combination with platinum-based chemotherapy and as a single agent maintenance therapy, in women with ovarian cancer relapsing more than 6 months following completion of first-line platinum-based treatment

Acronym
ICON6 (International Collaborative Ovarian Neoplasm 6)

Study objectives
Current hypothesis as of 13/03/2015:
That cediranib has an influence on progression-free survival when comparing patients receiving chemotherapy alone with patients receiving chemotherapy and cediranib (AZD2171).

Previous hypothesis:
Over three separate trial stages the study hypotheses are:

Stage 1:
That it is safe to add a once daily tablet of cediranib to standard platinum-based chemotherapy

Stage 2:
That cediranib has an influence on progression free survival when comparing patients receiving chemotherapy alone with patients receiving chemotherapy and cediranib (AZD2171)

Stage 3:
1. That cediranib has an effect on overall survival when taken at the same time as chemotherapy (placebo versus active), and when taken at the same time and then continued as a maintenance treatment (placebo versus active)
2. If the first Stage 3 assessments shows the product is effective, that cediranib has an effect on overall survival when taken at the same time as chemotherapy compared with at the same time and then continued as a maintenance treatment

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire Research Ethics Committee B, 16/07/2007, ref: 07/H0605/76

Primary study design
Interventional

Study design
Randomised three-arm double-blind placebo-controlled multicentre phase III trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Relapsed platinum-sensitive ovarian cancer

Interventions
Current interventions as of 13/03/2015:
Patients in Arm A (the reference arm) will receive standard platinum-based chemotherapy plus a daily oral placebo tablet for the duration of the chemotherapy and then until protocol defined disease progression occurs.

Patients in Arm B (concurrent cediranib arm) will also receive standard chemotherapy plus daily oral cediranib during chemotherapy only, and then an oral daily placebo tablet until protocol defined disease progression or toxicity limiting treatment occurs.

Patients in Arm C (concurrent and maintenance cediranib arm) will also receive standard chemotherapy plus oral cediranib daily during chemotherapy and until protocol defined disease progression or toxicity limiting treatment occurs.

Previous interventions:
Patients in Arm A (the reference arm) will receive standard platinum-based chemotherapy plus a daily oral placebo tablet for the duration of the chemotherapy and then for up to 18 months from the time of randomisation, or until protocol defined disease progression occurs.

Patients in Arm B (concurrent cediranib arm) will also receive standard chemotherapy plus daily oral cediranib during chemotherapy only, and then an oral daily placebo tablet for up to 18 months from the time of randomisation, or until protocol defined disease progression or toxicity limiting treatment occurs.

Patients in Arm C (concurrent and maintenance cediranib arm) will also receive standard chemotherapy plus oral cediranib daily during chemotherapy and then continued for up to 18 months from the time of randomisation, or until protocol defined disease progression or toxicity limiting treatment occurs.

The starting dose of cediranib is 30 mg taken orally once daily. This will be down titrated if required on medical assessment to 20 mg and then 15 mg.

Intervention Type

Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Cediranib (also known as AZD2171 and recentin)

Primary outcome(s)
Current primary outcome measures as of 13/03/2015:
Progression-free survival (PFS) in arms A vs C

Previous primary outcome measures:
Stage 1: Safety
Stage 2: Progression free survival
Stage 3: Overall survival

Data for the outcomes above will be collected approximately 3 weekly during chemotherapy, 6 weekly after chemotherapy up to 18 months, 3 monthly up to 3 years, 6 monthly during years 4 and 5, then annually until protocol defined disease progression or death.

Key secondary outcome(s)
Current secondary outcome measures as of 13/03/2015:
1. Progression-free survival (PFS) across arms A, B and C
2. Overall survival (OS)
3. Toxicity
4. Quality of Life (QoL)

Previous secondary outcome measures:
Stage 1: None
Stage 2: Overall survival and toxicity
Stage 3: Progression free survival, toxicity and quality of life

Quality of life assessment will be made using EORTC QLQ-C30 version 3 and EORTC QLQ-OV28. This information will be supplemented by health questionnaire EQ-5D. Other outcome measures will be assessed by clinical interview, blood tests and CT scans.

Data for the outcomes above will be collected approximately 3 weekly during chemotherapy, 6 weekly after chemotherapy up to 18 months, 3 monthly up to 3 years, 6 monthly during years 4 and 5, then annually until protocol defined disease progression or death.

Completion date
31/12/2016

Eligibility

Key inclusion criteria
1. Females aged 18 years or older with previous histologically proven diagnosis of:
1.1. Epithelial ovarian carcinoma
1.2. Fallopian tube carcinoma
1.3. Primary serous peritoneal carcinoma

Relapsing more than 6 months after completion of first-line platinum-based chemotherapy
2. Signed informed consent and ability to comply with the protocol
3. Ability to commence treatment within 2 weeks of randomisation
4. Computerised Tomography (CT) or Magnetic Resonance Imaging (MRI) proven relapsed disease, more than six months since completion of first-line platinum-based chemotherapy
5. Eastern Cooperative Oncology Group (ECOG) performance status 0-1
6. Life expectancy more than 12 weeks
7. If there is a past history of a solid tumour, this must have been treated curatively more than five years ago with no evidence of recurrence
8. Adequate bone marrow function
8.1. Absolute Neutrophil Count (ANC) greater than or equal to 1.5 x 109/l
8.2. Platelets (Plt) greater than or equal to 100 x 109/l
8.3. Haemoglobin (Hb) greater than or equal to 9g/dl (can be post transfusion)
9. Adequate liver function (within 14 days before randomisation)
9.1. Serum bilirubin (BR) = 1.5 x Upper Limit of Normal (ULN)
9.2. Serum transaminases = 2.5 x ULN
10. Adequate renal function
10.1. Serum creatinine = 1.5 ULN
10.2. Urine dipstick for proteinuria less than 2+. If urine dipstick is greater than or equal to 2+ on two occasions more than one week apart then a 24 hour urine must demonstrate less than or equal to 1 g of protein in 24 hours

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
Female

Key exclusion criteria
1. Non-epithelial ovarian cancer, including malignant mixed Mullerian tumours and mucinous carcinoma of the peritoneum
2. Poorly controlled hypertension (persistently elevated >150/100 mmHg despite anti-hypertensive medication)
3. History of inflammatory bowel disease (Crohn's disease or ulcerative colitis)
4. Malignancies other than ovarian cancer within 5 years prior to randomisation, except for adequately treated carcinoma in situ of the cervix and/or basal cell skin cancer. Patients who have a past history of a solid tumour, treated curatively, more than five years prior to randomisation, with no evidence of recurrence, are still eligible to enter ICON6
5. Previous radiotherapy within 21 days prior to randomisation
6. Treatment with any other investigational agent within 30 days prior to entering this trial. Patients are still eligible for entry into ICON6 if they have received previous treatment for ovarian cancer with either bevacizumab, erlotinib, or a Cox-2 inhibitor as long as more than 30

days have elapsed since the last treatment
7. Arterial thrombotic event (including Transient Ischaemic Attack [TIA], cerebrovascular accident [CVA) and peripheral arterial embolus) within the previous 12 months
8. Gastrointestinal (GI) impairment that could affect ability to take, or adsorption of, oral medicines including sub acute or complete bowel obstruction
9. Known hypersensitivity to AZD2171 or other Vascular Endothelial Growth Factor (VEGF) inhibitors
10. Major surgery within 2 weeks before entry into the trial
11. Significant haemorrhage of >30 ml in a single episode within 3 months or any haemoptysis
12. Evidence of severe or uncontrolled cardiac disease
12.1. Myocardial Infarct (MI) or unstable angina within 12 months
12.2. New York Health Association (NYHA) = grade 2 Congestive Heart Failure (CHF)
12.3. Cardiac ventricular arrhythmias requiring medication
12.4. History of 2nd or 3rd degree atrioventricular conduction defects
13. Prolonged QTc (corrected) interval of >470 msec on electrocardiogram (ECG), or a family history of long QT syndrome
14. Persisting = Grade 2 CTC (Common Toxicity Criteria) toxicity (except alopecia and neuropathy) from previous anti-cancer treatment. If peripheral sensory or motor neuropathy = grade 2 then paclitaxel can be omitted from the chemotherapy at the discretion of the treating physician
15. History or clinical suspicion of brain metastases or spinal cord compression. CT/MRI of the brain is mandatory in the case of suspected brain metastases. Spinal MRI is mandatory in the case of suspected spinal cord compression. Patients with unstable untreated brain or meningeal metastases are not eligible
16. Inability to attend or comply with treatment or follow-up scheduling
17. Evidence of any other disease, metabolic dysfunction, physical examination finding or laboratory finding giving reasonable suspicion of a disease or condition that contra-indicates the use of an investigational drug or puts the patient at high risk for treatment-related complications
18. Fertile women of childbearing potential not willing to use adequate contraception for the duration of trial treatment and at least 6 months after
19. Any other severe uncontrolled medical condition or disease

Date of first enrolment
29/11/2007

Date of final enrolment
23/12/2011

Locations

Countries of recruitment
United Kingdom

England

Australia

Canada

New Zealand

Spain

Study participating centre
University College Hospital
London
United Kingdom
NW1 2BU

Sponsor information

Organisation
Medical Research Council (UK)

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Industry

Funder Name
Cancer Research UK (ref: C444/A6862)

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
AstraZeneca (ref: D8480C00037) (International)

Alternative Name(s)

AstraZeneca PLC, Pearl Therapeutics, AZ

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
Medical Research Council

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
National Health and Medical Research Council

Alternative Name(s)
National Health and Medical Research Council, Australian Government, NHMRC National Health and Medical Research Council, NHMRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
Australia

Results and Publications

Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	27/09/2011		Yes	No
Results article	results	12/03/2016		Yes	No
Results article	quality of life results	15/07/2017		Yes	No
Results article	results	01/10/2019	02/09/2020	Yes	No
Results article		01/04/2021	01/11/2021	Yes	No
Plain English results				No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes