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COMICE: A Randomised Double Blind Placebo Controlled Phase II Clinical Trial of Cediranib and Olaparib Maintenance in Advanced /Recurrent Cervical Cancer

Submission date
27/11/2017

Recruitment status
No longer recruiting

Registration date
19/01/2018

Overall study status
Completed

Last Edited
29/01/2024

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-olaparib-and-cediranib-for-advanced-cervical-cancer-comice

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2016-004215-13

Integrated Research Application System (IRAS)

209375

Central Portfolio Management System (CPMS)
33260

Study information

Scientific Title
Randomised phase II trial of Cediranib and Olaparib Maintenance in advanced/recurrent Cervical Cancer (COMICE)

Acronym
COMICE

Study objectives
The primary purpose of this study is to compare median survival of patients with metastatic or recurrent cervical cancer when treated with Cediranib (antiangiogenic agent) and Olaparib (PARP inhibitor) compared with a placebo after having platinum based chemoradiotherapy. Secondary to this is to examine drug toxicity and tolerability to the combination of drugs.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 29/12/2017, North West Greater Manchester South Research Ethics Committee;), ref: (3rd Floor, Barlow House 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 (0)207 1048014; gmsouth.rec@hra.nhs.uk), ref: 17/NW/0634

Primary study design
Interventional

Study design
Randomised; Interventional; Design type: Treatment, Drug

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Cervical cancer

Interventions
Participants are randomly allocated to one of two study arms:

ARM 1: Cediranib 20mg OD + Olaparib 300mg BD
ARM 2: Placebo Cediranib + Placebo Olaparib

Participants are treated until progression of disease, unacceptable toxicity or withdrawal of consent. Participation in the study continues until there is a withdrawal of consent or death.

Participants who stop treatment before having developed progressive disease (PD) are assessed every 8 weeks for response until PD occurs.

The study ends when the last participant recruited has completed a minimum of seven month follow up. The anticipated recruitment period is 14 months therefore the maximum duration of a patient on this study will be 21 months.

After study end participants still deemed to be benefitting from study medication are allowed to continue off study with discretionary use of the drugs until disease progression.

Intervention Type
Other

Phase
Phase II

Primary outcome(s)
Progression Free Survival is measured from date of randomisation until the earlier of date of progression or death, progression measured using RECIST 1.1 from results of CT/MRI scans scheduled every 8 weeks (additional scans may be performed between scheduled visits if it is believed that the patient has progressive disease), and compared to results obtained prior to starting study treatment.

Key secondary outcome(s)
1. Overall Survival Overall survival is measured from date of randomisation to date of death
2. Best Objective Response Is measured as the highest value of response observed using RECIST 1.1 comparing results from 8-weekly scheduled MRI/CT scans to results obtained prior to starting study treatment
3. Quality of Life Is measured using results from FACT-Cx questionnaire completed at 4-weekly intervals until the earlier of disease progression or 28 weeks treatment
4. Toxicity Is measured using AE data (described using CTCAE v4.03) collected at 4-weekly visits whilst on study treatment and from SAE data (described using CTCAE v4.03) collected whilst patient is on study

Completion date
30/06/2023

Eligibility

Key inclusion criteria
1. Patients over 18 years of age
2. Histologically proven carcinoma of the cervix (squamous, adenocarcinoma or mixed adeno /squamous)
3. Completion of first line platinum-based chemotherapy for advanced /recurrent disease, leading to either a complete response, partial response or stable disease
4. ECOG performance status 0 or 1
5. Randomisation within 6 weeks of completion of chemotherapy
6. Patients may have received previous chemoradiotherapy and neoadjuvant chemotherapy given with a curative intent.
7. Creatinine Clearance ≥ 51mls/min
8. Adequate haematological and biochemical function, as follows:

8.1. Haemoglobin > 10g/dl (with no blood transfusion in the 28 days prior to randomisation) Neutrophils > 1.5 x 109/l
8.2. Platelets > 100 x 109/l
8.3. Bilirubin < 1.5 x ULN
8.4. ALT or AST/ SGOT < 3 x ULN (or ≤5 x ULN if hepatic metastases present)
8.5. Alkaline Phosphatase < 3 x ULN (or ≤5 x ULN if hepatic metastases present)
8.6. Adequate coagulation, as follows:
8.7. Prothrombin ratio (PTR) / INR ≤ 1.5 or
8.8. PTR / INR between 2.0 and 3.0 for patients on stable doses of anticoagulants
8.9. Partial thromboplastin time <1.2 x control
9. Life expectancy >12 weeks
10. Informed written consent
11. Contrast enhanced computerised tomography (CT) scan or magnetic resonance imaging (MRI) of the abdomen and pelvis and a CT scan of the chest within 28 days prior to commencing randomisation (with RECIST 1.1)
12. Adequately controlled thyroid function, with no symptoms of thyroid dysfunction
13. 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
18 Years

Sex
Female

Total final enrolment
74

Key exclusion criteria
1. Disease that is potentially treatable with exenterative surgery
2. Relapse confined to the pelvis after radical surgery in circumstance where radiotherapy or chemoradiotherapy would be appropriate
3. More than one line of prior chemotherapy for advanced/recurrent disease. Neoadjuvant chemotherapy is not counted
4. Prior treatment with anti-angiogenic agents (with the exception of bevacizumab given as part of first line chemotherapy)
5. Persisting > = Grade 2 CTCAE from previous anti-cancer previous systemic anti-cancer therapy except haematological toxicity (see inclusion criteria “Adequate haematological function”) and alopecia
6. History of other malignancy within the previous 5 years except for:
6.1. Curatively treated basal cell or squamous cell carcinoma of skin; in situ cancer of the cervix, ductal carcinoma in situ of the breast or stage 1, grade 1 endometrial carcinoma

6.2. Curatively treated other solid tumors including lymphomas (without bone marrow involvement) with no evidence of disease for > = 5 years prior to start of IPs
7. Pregnant or lactating women
8. Fertile woman of childbearing potential not willing to use adequate contraception (oral contraceptives, intrauterine device or barrier method of contraception in conjunction with spermicidal jelly or surgically sterile) for the study duration and at least six months afterwards
9. Evidence of uncontrolled infection. (Defined as infection that cannot be resolved readily with antibiotics prior to patient entry into the trial for example a pelvic collection)
10. History of pelvic fistulae
11. History of abdominal fistula that has been surgically corrected within 6 months of starting treatment. Patient should be deemed low risk of recurrent fistula
12. Sub-acute or acute intestinal obstruction
13. Major surgery within 28 days or anticipated while on study
14. Non-healing wound, ulcer or bone fracture
15. Active bleeding
16. History or evidence of thrombotic or haemorrhagic disorders
17. History of stroke or transient ischemic attack within 6 months
18. Proteinuria > 1+ on dipstick on two consecutive dipsticks taken no less than 1 week apart, unless urinary protein is < 1.5g in a 24 hour period.
19. Significant cardiovascular disease (arterial thrombotic event within 12 months, uncontrolled hypertension, myocardial infarction or angina within 6 months, NYHA grade 2 or worse congestive cardiac failure, grade > = 3 peripheral vascular disease or cardiac arrhythmia requiring medication). Patients with rate-controlled atrial fibrillation are eligible
20. Prolonged QTc (corrected) interval of > 470ms on ECG or a family history of long QT syndrome
21. Patients with symptomatic uncontrolled brain or meningeal metastases CNS disease
(A scan to confirm the absence of brain metastases is not required)
22. A history of poorly controlled hypertension or resting BP> 140/90 mmHG in the presence or absence of a stable regimen of anti-hypertensive therapy (measurements will be made after the patient has been resting supine for a minimum of 5 minutes. Two or more readings should be taken at 2 minute intervals and averaged. If the first two diastolic readings differ by more than 5mmHG, then an additional reading should be obtained and averaged)
23. History of significant gastrointestinal impairment. Defined as active inflammatory bowel disease, bowel obstruction or any condition judged by the investigator to adversely impact on drug absorption or within 3 months prior to starting treatment
24. Patients with myelodysplastic syndrome/acute myeloid leukaemia
25. 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
26. Patients who have been treated with potent inhibitors of CYP3A4 and 2C8 such as amiodaraone, clarithromycin, erythromycin, simvastatin, atorvastatin, lovastatin, montelukast sodium, verapamil, ketoconazole, miconazole, indinovir (and other antivirals) and diltiazem within 2 weeks of the first planned dose of cediranib will be excluded [NB These drugs are also prohibited during trial period]
27. Patients treated with CYP3A inhibitorsWithin 2 weeks of the first planned dose for strong inhibitors, and at least 1 week for moderate inhibitors
28. Concomitant use of known strong CYP3A inducers
29. (LVEF) < lower limit of normal (LLN) per institutional guidelines, or < 55%, if threshold for normal not otherwise specified by institutional guidelines
30. Patients who are known to be serologically positive for Hepatitis B, Hepatitis C or HIV, or who are receiving immunosuppressive treatment
31. History of intra-abdominal abscess within 3 months prior to starting treatment

32. Uncontrolled intercurrent illness
33. No prior allogeneic bone marrow transplant or double umbilical cord b

Date of first enrolment
01/03/2018

Date of final enrolment
30/11/2022

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
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Sponsor information

Organisation
The Clatterbridge Cancer Centre NHS Foundation Trust

ROR
https://ror.org/05gcq4j10

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca UK Limited

Results and Publications

Individual participant data (IPD) sharing plan

The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No