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Cediranib versus placebo plus cisplatin /gemcitabine chemotherapy for patients with advanced biliary tract cancers

Submission date 30/06/2010	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 30/06/2010	**Overall study status** Completed	
Last Edited 31/03/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-cediranib-people-advanced-biliary-tract-cancers-abc03

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00939848

Clinical Trials Information System (CTIS)
2009-013408-30

Protocol serial number

8446

Study information

Scientific Title
Randomised phase II trial of cediranib (AZD2171) versus placebo in addition to cisplatin /gemcitabine chemotherapy for patients with advanced biliary tract cancers

Acronym
ABC-03

Study objectives
This trial aims to evaluate the efficacy and safety of cediranib (AZD2171) in combination with cisplatin/gemcitabine (CisGem) chemotherapy compared to CisGem and placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West REC 5 - Haydock Park, 23/08/2010, ref: 10/H1010/42

Primary study design
Interventional

Study design
Multicentre randomised interventional treatment trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: National Cancer Research Network; Subtopic: Upper Gastro-Intestinal Cancer; Disease: Biliary Tract

Interventions
Translational studies:
Blood samples will be collected from patients at several points during the trial for biological research including KRAS testing.

Treatment:
All patients will receive combined chemotherapy consisting of cisplatin 25 mg/m^2 plus gemcitabine 1000 mg/m^2 on days 1 and 8 of a 21-day cycle. In addition, patients will take either cediranib (AZD2171) 20 mg orally once daily (continuous dosing) (experimental arm) or a matching placebo once daily (continuous dosing) (standard arm). All patients will receive four cycles of treatment in the first instance.

Study entry: single randomisation only

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Cediranib (AZD2171), cisplatin (Cis), gemcitabine (Gem)

Primary outcome(s)
Progression-free survival (PFS), calculated as the time from randomisation until evidence of progression is observed. For patients in whom no progression is seen, the PFS will be calculated as the time from randomisation until their most recent clinic visit.

Key secondary outcome(s)
Objective tumour response in patients at 3 monthly intervals for 2 years post-treatment, using the Response Evaluation Criteria in Solid Tumours (RECIST) guidelines.

Completion date
30/09/2012

Eligibility

Key inclusion criteria
Current inclusion criteria as of 03/05/2011:
There will be no exception to the eligibility requirements at the time of randomisation. Queries in relation to the eligibility criteria should be addressed prior to calling for randomisation.
1. A histopathological/cytological diagnosis of non-resectable or recurrent/metastatic biliary tract carcinoma (intra- or extra-hepatic), gall bladder or ampullary carcinoma
2. Eastern Cooperative Oncology Group (ECOG) performance status 0, 1, or 2
3. Aged greater than or equal to 18 years, either sex
4. Estimated life expectancy greater than 3 months
5. Adequate haematological function:
5.1. Haemoglobin greater than 10 g/dl (prior transfusions for patients with low haemoglobin are allowed)
5.2. White blood cell count (WBC) greater than 3.0 x 10^9/L
5.3. Absolute neutrophil count (ANC) greater than 1.5 x 10^9/L
5.4. Platelet count greater than 100 x 10^9/L (updated on 03/05/2011)
6. Adequate liver function:
6.1. Total bilirubin less than or equal to 1.5 x upper limit of normal (ULN) (except for patients with known documented cases of Gilbert's syndrome)
6.2. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) less than or equal to 2.5 x ULN (if liver metastases are present, ALT or AST less than 5 x ULN) (updated on 03/05/2011)
6.3. Alkaline phosphatase less than or equal to 5 x ULN
7. Adequate renal function:
7.1. Serum urea less than 1.5 x ULN
7.2. Serum creatinine less than 1.5 x ULN
7.3. Calculated glomerular filtration rate (GFR) greater than or equal to 45 mL/min. If the calculated GFR is below 45mL/min, isotope ethylenediaminetetraacetic acid (EDTA) confirmation of adequate renal function is required.
8. No evidence of active uncontrolled infection (patients on long-term antibiotics are eligible provided signs of active infection have resolved)

9. Women of child-bearing potential must have a negative pregnancy test prior to study entry and be using an adequate contraception method, which must be continued for 3 months after completion of chemotherapy
10. Patient must have given written informed consent

The following prior therapy is allowed (provided there has been a full recovery):
11. Surgery - patients may have undergone a non-curative operation (i.e. R2 resection [with macroscopic residual disease] or palliative bypass surgery only). Patients who have previously undergone curative surgery, must have evidence of non-resectable disease relapse requiring systemic chemotherapy prior to study entry.
12. Radiotherapy - patients may have received prior radiotherapy (with or without radio-sensitising low-dose chemotherapy) for localised disease. However, there must be clear evidence of disease progression prior to inclusion in this study.
13. Prior systemic chemotherapy for locally advanced or metastatic disease is not allowed, unless it has been given in low-dose as a radio-sensitiser in conjunction with radiotherapy. Prior adjuvant chemotherapy is allowed provided neither gemcitabine nor cisplatin were used and the treatment was completed at least 6 months before trial entry.
14. Photodynamic therapy for localised disease only with no evidence of metastatic disease - patients may have received prior photodynamic therapy (PDT), provided the patient has fully recovered and at least 28 days have elapsed since the PDT and there is clear evidence of disease progression at the local site or disease or at a new metastatic site.
15. PDT for localised disease to relieve biliary obstruction in the presence of metastatic disease - patients may have received prior PDT provided the patient has fully recovered and at least 28 days have elapsed since the PDT. Patients may enter ABC-03 provided the non-PDT treated lesion(s) only are followed for response assessment.

Previous inclusion criteria:
5.4. Platelet count greater than 1 x 10^9/L
6.2. Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) less than or equal to 5.0 x ULN (if liver metastases are present, ALT or AST less than 5 x ULN)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
124

Key exclusion criteria

1. Significant haemorrhage (greater than 30 mL bleeding/episode in previous 3 months) or haemoptysis (greater than 5 mL fresh blood) within 4 weeks of randomisation.
2. Patients with history of poorly controlled hypertension with resting blood pressure greater than 150/100 mmHg in the presence or absence of a stable regimen of anti-hypertensive therapy, or patients who are requiring maximal doses of calcium channel blockers to stabilise blood pressure
3. Incomplete recovery (Common Toxicity Criteria of Adverse Events [CTCAE] grade greater than 1) from previous anti-cancer therapy (except haematological toxicity - see inclusion criteria for adequate haematological function), or alopecia
4. Unresolved biliary tree obstruction
5. Any evidence of severe or uncontrolled systemic diseases which, in the view of the investigator, makes it undesirable for the patient to participate in the trial (e.g. unstable or uncompensated respiratory, cardiac, hepatic or renal disease)
6. Untreated unstable brain or meningeal metastases. Patients with radiological evidence of stable brain metastases are eligible providing that they are asymptomatic and either do not require corticosteroids or have been treated with corticosteroids, with clinical and radiological evidence of stabilisation at least 10 days after discontinuation of steroids.
7. Greater than +1 proteinuria on two consecutive dipsticks taken no less than 1 week apart unless urinary protein less than 1.5 g in a 24-hour period or protein/creatinine ratio less than 1.5
8. History of significant gastrointestinal impairment, as judged by the Principal Investigator that would significantly affect the absorption of cediranib
9. Mean QTc with Bazetts correction greater than 480 msec in screening electrocardiogram (ECG) or history of familial long QT syndrome
10. Recent (less than 14 days) major thoracic or abdominal surgery prior to randomisation, or a surgical incision that is not fully healed
11. Pregnant or breast-feeding women
12. Known hypersensitivity to cediranib or any of its excipients
13. Known risk of the patient transmitting human immunodeficiency virus (HIV), hepatitis B or C via infected blood
14. Treatment with an investigational drug within 30 days prior to randomisation
15. Other concomitant anti-cancer therapy (except steroids)
16. Patients undergoing current treatment with curative intent
17. History of prior malignancy that will interfere with the response evaluation (exceptions include in-situ carcinoma of the cervix treated by cone-biopsy/resection, non-metastatic basal and/or squamous cell carcinomas of the skin, any early stage (stage I) malignancy adequately resected for cure greater than 5 years previously)
18. Any psychiatric or other disorder (e.g. symptomatic brain metastases) likely to impact on informed consent

N.B. Whilst not excluded, patients with significant impaired hearing must be made aware of potential ototoxicity and may choose not to be included. If included, it is recommended that audiograms be carried out at baseline and prior to cycle 2.

Date of first enrolment
20/04/2011

Date of final enrolment
30/09/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cancer Research UK & UCL Cancer Trials Centre
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Sponsor information

Organisation
University College London (UCL) (UK)

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (UK) - Clinical Trials Advisory and Awards Committee (CTAAC) grant (ref: C2930/A11428)

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

Results and Publications

Individual participant data (IPD) sharing plan
Not provided at time of registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/08/2015		Yes	No
HRA research summary			28/06/2023	No	No
Plain English results			31/03/2022	No	Yes