

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

<b>Submission date</b> 30/06/2010	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 30/06/2010	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 31/03/2022	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data

## 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

### Contact name

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### Contact details

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2009-013408-30

### ClinicalTrials.gov (NCT)

NCT00939848

### Protocol serial number

## 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

### Study design

Multicentre randomised interventional treatment trial

### Primary study design

Interventional

### 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<sup>2</sup> plus gemcitabine 1000 mg/m<sup>2</sup> 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  $3.0 \times 10^9/L$
  - 5.3. Absolute neutrophil count (ANC) greater than  $1.5 \times 10^9/L$
  - 5.4. Platelet count greater than  $100 \times 10^9/L$  (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  $1 \times 10^9/L$
- 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**

London

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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?
<a href="#">Results article</a>	results	01/08/2015		Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Participant information sheet</a>	Participant information sheet	11/11/2025	11/11/2025	No	Yes
<a href="#">Plain English results</a>			31/03/2022	No	Yes