ISRCTN68093791 https://doi.org/10.1186/ISRCTN68093791

Safety study of AZD8931 for oesophago-gastric cancer

Submission date 27/04/2012	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 27/04/2012	**Overall study status** Completed	
Last Edited 26/10/2022	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-azd8931-with-chemotherapy-for-cancer-of-oesophagus-or-junction-of-stomach-and-oesophagus-debioc

Study website
https://www.oncology.ox.ac.uk/trial/debioc

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2011-003169-13

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
11855

Study information

Scientific Title
A phase I dose-escalating and safety study of AZD8931 in combination with oxaliplatin and capecitabine chemotherapy in patients with oesophago-gastric adenocarcinoma

Study objectives
AZD8931 blocks a growth pathway that is important in some cancers. In the escalation phase this trial will define the dose of AZD8931 that can safely be given with standard chemotherapy for oesophageal (gullet) cancer. We will then (in the expansion phase) compare the side effects of chemotherapy alone with those of AZD8931 with chemotherapy in 30 people with operable gullet cancer. This will to decide how to run future studies of AZD8931 with chemotherapy. This trial is supported by the Experimental Cancer Medicine Centres - Astrazeneca Combinations Alliance, and by the New Agents committee of Cancer Research UK. It is being run at hospitals in Oxford, Leicester and Belfast. Patients who go on the trial will need to undergo extra tests to check it is safe for them to take part, and to monitor them whilst on treatment.

Ethics approval required
Old ethics approval format

Ethics approval(s)
ref: 12/SC/0090

Study design
Both; Interventional; Design type: Treatment

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Upper gastro-intestinal cancer

Interventions

Dose Escalation In the dose escalation phase of the study patients with metastatic or inoperable disease will be recruited and no surgery is planned. Patients who successfully complete the screening will receive AZD8931 monotherapy for three days (days -3 to -1) [20mg bd in cohort 1, 40 mg bd in cohort 2 and 60 mg bd in cohort 3]. Xelox chemotherapy will be added in on day 4 of AZD8931 treatment AZD8931 tablets will be taken orally, continuously, twice daily. Patients will receive oxaliplatin and capecitabine on day one of every cycle every 21 days. Oxaliplatin will be given at 130 mg/m2 IV in 250-500 ml of 5% glucose over 2 hours. Capecitabine 1250mg/m2/day will be given orally in two divided doses continuously from days 1-21 of each 3 week cycle. In this phase patients will receive a maximum of 8 cycles of daily AZD8931 in combination with Xelox. AZD8931 may be continued following cessation of the Xelox, providing the patient has no evidence of tumour progression and continues to tolerate treatment.

Dose Expansion - In the dose expansion phase of the trial, we propose a randomised component. Patients will receive two cycles of Xelox chemotherapy ± AZD8931 prior to undergoing an oesophago-gastrectomy. Twenty patients will receive Xelox and AZD8931 and 10 patients Xelox alone. The expectation is that this randomisation will allow us to assess any additive toxicity due to the combination of AZD8931 and Xelox over the toxicities associated with the Xelox backbone of chemotherapy alone. AZD8931 monotherapy will be used as maintenance therapy, in patients who were randomised to the combination and who have successful surgery, for a maximum of 12 months starting 6 to 12 weeks after surgery. Patients may therefore receive treatment for 58 weeks over a maximum 18 months period.

Maintenance Phase - To investigate the safety and feasibility of maintaining patients on AZD8931, to reduce the risk of recurrence, patients who have successful surgery will be allowed to continue AZD8931 if they were randomised to the combination, for a maximum of 12 months starting 6 to 12 weeks after surgery.

Intervention Type

Drug

Phase

Phase I

Drug/device/biological/vaccine name(s)

AZD8931, capecitabine, oxaliplatin

Primary outcome measure

1. Assessment of efficacy for the combination of AZD8931 + Xelox in patients with operable OG carcinoma
2. 6-month progression-free survival rate
3. R0 resection rate
4. Progression free and overall survival

Secondary outcome measures

1. Pharmacokinetics (PK) of AZD8931 when co-administered with Xelox
2. Serum AZD8931 concentration
3. Tolerability of post-operative maintenance therapy with AZD8931
4. Adverse events using CTCAE v4.03
5. Number of patients starting maintenance therapy

Overall study start date
30/04/2012

Completion date
15/11/2018

Eligibility

Key inclusion criteria
1. Age = 18 years
2. WHO performance status 01
3. Adequate respiratory and cardiac function
4. Able to give informed consent and be capable of cooperating with protocol
5. Haematological and biochemical indices within the ranges shown below:
5.1. Haemoglobin (Hb) =10g/dl
5.2. Neutrophils = 1500/µl
5.3. Platelet count = 100.000/µl
5.4. AST or ALT = 3 ULN, alkaline phosphatase = 2x ULN
5.5. Serum Bilirubin = 1.5 ULN
5.6. Creatinine Clearance = 50ml/min
6. Able to swallow oral medication
7. Women of child bearing potential must use an acceptable method of contraception during the study, and have a negative pregnancy test
8. Male patients must use a barrier method of contraception - male condom (female condom or diaphragm are not acceptable) during the study.
9. For the dose escalation phase patients with locally advanced or metastatic oesophageal or gastro-oesophageal junction adenocarcinoma (including Siewert type I and II). In the dose expansion phase
10. Histologically confirmed carcinoma of the oesophagus and gastrooesophageal junction [GOJ]
11. Siewert Type I and II Operable disease: any combination T13 / N01 [BUT EXCLUDES T1N0]
12. T4 involvement of mediastinal pleura and diaphragmatic crus where the MDT consider this resectable.
13. Deemed suitable for neoadjuvant chemotherapy by regional upper gastrointestinal Multi-Disciplinary Team;
14. Target Gender: Male & Female
15. Lower Age Limit 18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants

Planned Sample Size: 54; UK Sample Size: 54

Total final enrolment
24

Key exclusion criteria
1. Previous chemotherapy for oesophagogastric adenocarcinoma
2. Siewert Type III GOJ tumours and gastric cancer
3. Squamous cell pathology
4. Uncontrolled angina, myocardial infarction within 6 months, heart failure or impaired LV function on echocardiogram/MUGA, uncontrolled arrhythmias.
5. History of interstitial lung disease
6. Known peripheral neuropathy >Grade 1
7. Other experimental treatment = 4 weeks prior to this study (including chemotherapy and immunotherapy)
8. Known or expected dihydropyridime dehydrogenase deficiency
9. Resting ECG with QTc >480msec at 2 or more time points within a 24h period
10. Requirement for medication known to inhibit or induce CYP3A4 or 2D6, or medication known to prolong QT interval
11. History of other malignancy less than 5 years before the diagnosis of oesophageal cancer, EXCLUDING the following: Non-melanoma skin cancer, in situ carcinoma of the cervix treated surgically with curative intent, other malignant tumours that have been treated curatively and patient is deemed disease-free
12. Active infections (including chronic hepatitis type B or C and HIV infection if status known), severe immunologic defect, compromised bone marrow function
13. Prior diagnosis of dry eye syndrome or eyelid/eyelash abnormalities. History of eye injury, corneal surgery, orbital irradiation, collagen vascular, chronic inflammatory or denegerative disease with eye involvement, clinically significant ocular surface disease 14. Known hypersensitivity to any component of chemotherapy
15. Pregnancy, inadequate or unreliable contraceptive measures during participation in the trial; breast feeding.
16. Other psychological, social or medical condition, physical examination finding or a laboratory abnormality that the Investigator considers would make the patient a poor trial candidate or could interfere with protocol compliance or the interpretation of trial results.

Date of first enrolment
30/04/2012

Date of final enrolment
11/05/2016

Locations

Countries of recruitment
England

Northern Ireland

United Kingdom

Study participating centre
Belfast City Hospital
Lisburn Road
Belfast
United Kingdom
BT9 7AB

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre
Bristol Haematology & Oncology Centre
Horfield Road
Bristol
United Kingdom
BS2 8ED

Study participating centre
St. James University Hospital
Bexley Wing
Beckett Street
Leeds
United Kingdom
LS9 7TF

Sponsor information

Organisation
University of Oxford (UK)

Sponsor details
Clinical Trials and Research Governance
Joint Research Office
Block 60
Churchill Hospital
Headington
England
United Kingdom
OX3 7LJ

Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Industry

Funder Name
AstraZeneca (UK)

Alternative Name(s)
AstraZeneca PLC, Pearl Therapeutics

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Funder Name
Cancer Research UK

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan
To be confirmed at a later date

Intention to publish date
30/04/2018

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/01/2020	26/11/2019	Yes	No
Plain English results			26/10/2022	No	Yes
HRA research summary			28/06/2023	No	No