

# Safety study of AZD8931 for oesophago-gastric cancer

<b>Submission date</b> 27/04/2012	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 27/04/2012	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 26/10/2022	<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-of-azd8931-with-chemotherapy-for-cancer-of-oesophagus-or-junction-of-stomach-and-oesophagus-debioc>

## Contact information

### Type(s)

Scientific

### Contact name

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## Additional identifiers

### Clinical Trials Information System (CTIS)

2011-003169-13

### Protocol serial number

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

## Study type(s)

Treatment

## 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/m<sup>2</sup> IV in 250-500 ml of 5% glucose over 2 hours. Capecitabine 1250mg/m<sup>2</sup>/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(s)**

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

## **Key secondary outcome(s)**

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

## **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/ $\mu$ l
  - 5.3. Platelet count = 100.000/ $\mu$ l
  - 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

**Healthy volunteers allowed**

No

**Age group**

Adult

**Lower age limit**

18 years

**Sex**

All

**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**

United Kingdom

England

Northern Ireland

**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)

**ROR**  
<https://ror.org/052gg0110>

## **Funder(s)**

**Funder type**  
Industry

**Funder Name**  
AstraZeneca (UK)

**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

Cancer Research UK

### 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

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?
<a href="#">Results article</a>	results	01/01/2020	26/11/2019	Yes	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Plain English results</a>			26/10/2022	No	Yes
<a href="#">Study website</a>	Study website	11/11/2025	11/11/2025	No	Yes