

# A randomised open-labelled multicentre trial of the efficacy of epirubicin, oxaliplatin and capecitabine (EOX) with or without panitumumab in previously untreated advanced oesophago-gastric cancer

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|--|---|---|
| <b>Submission date</b><br>05/03/2008   | <b>Recruitment status</b><br>No longer recruiting | <input checked="" type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol |
| <b>Registration date</b><br>21/04/2008 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>25/10/2022       | <b>Condition category</b><br>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-at-chemotherapy-with-or-without-panitumumab-for-advanced-cancer-of-the-food-pipe-or-stomach>

## Contact information

### Type(s)

Scientific

### Contact name

Prof David Cunningham

### Contact details

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## Additional identifiers

EudraCT/CTIS number

IRAS number

**ClinicalTrials.gov number**

NCT00824785

**Secondary identifying numbers**

CCR 3024

## **Study information**

**Scientific Title**

A randomised open-labelled multicentre trial of the efficacy of epirubicin, oxaliplatin and capecitabine (EOX) with or without panitumumab in previously untreated advanced oesophago-gastric cancer

**Acronym**

REAL3

**Study objectives**

Panitumumab is an antibody therapy which targets the epidermal growth factor receptor (EGFR). Drugs such as panitumumab may be useful treatments for certain types of cancer by blocking the effects of EGFR. Panitumumab has also been shown to be effective treatment for patients with advanced colorectal cancer who have previously been treated with standard chemotherapies.

**Study hypothesis:**

The addition of panitumumab to EOX chemotherapy will improve the overall survival of patients with locally advanced or metastatic adenocarcinoma or undifferentiated carcinoma of the oesophagus, gastro-oesophageal junction or stomach compared to EOX chemotherapy alone.

As of 22/02/2011 the overall trial end date was changed from 01/04/2011 to 30/06/2012.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

North West Research Ethics Committee, 17/03/2008, ref: 08/H1010/6

**Study design**

Multicentre phase II/III open-label randomised controlled trial

**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 contact Dr Jacqui Oates (Jacqui.Oates@rmh.nhs.uk) to request a patient information sheet.

## **Health condition(s) or problem(s) studied**

Advanced oesophago-gastric cancer

## **Interventions**

EOX (Epirubicin, oxaliplatin and capecitabine) chemotherapy, with or without panitumumab.

Epirubicin (50 mg/m<sup>2</sup>), oxaliplatin (130 mg/m<sup>2</sup>) and panitumumab (9 mg/kg) are all given intravenously on day 1 of a 21 day cycle, with capecitabine (1,250 mg/m<sup>2</sup>/day) given orally (divided into two doses) throughout treatment (8 cycles in the absence of disease progression or unacceptable toxicity).

## **Intervention Type**

Drug

## **Phase**

Phase II/III

## **Drug/device/biological/vaccine name(s)**

Panitumumab , epirubicin, oxaliplatin, capecitabine

## **Primary outcome measure**

Overall survival (OS): The time between randomisation and death from any cause). Follow-up will be every 3 months until disease progression or death from any cause.

## **Secondary outcome measures**

1. Response rate (RR), measured according to the RECIST criteria
2. Progression-free survival (PFS): The time between randomisation and disease progression (on CT or clinically)
3. Toxicity, measured according to CTCAE version 3.0
4. Quality of life, measured using the EORTC QLQ-C30 questionnaire, performed at baseline, prior to each cycle, then once during follow-up (3-months post treatment)
5. The effect of K-ras mutation status on OS, RR and PFS
6. Biomarkers (including K-ras mutation status and EGFR gene copy number) will be tested on the patients' diagnostic tumour sample

CT scans are planned at baseline, after 12 and 24 weeks, then to confirm clinically-apparent disease progression where appropriate.

## **Overall study start date**

01/04/2008

## **Completion date**

30/06/2012

## **Eligibility**

**Key inclusion criteria**

1. Male and female patients aged  $\geq 18$  years, with no upper age limit
2. Histologically verified inoperable locally advanced or metastatic adenocarcinoma or undifferentiated carcinoma of the oesophagus, oesophago-gastric junction, or stomach.
3. Slides of tumour tissue should be available for centralised EGFR staining
4. Uni-dimensionally measurable disease (computerised tomography [CT] or Magnetic resonance imaging [MRI] as per Response Evaluation Criteria In Solid Tumours [RECIST])
5. No prior chemotherapy including previous adjuvant chemotherapy
6. No prior radiotherapy including adjuvant radiotherapy
7. World Health Organisation Performance status 0, 1 or 2
8. Patients should have a projected life expectancy of at least 3 months
9. Completion of baseline quality of life questionnaire (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire for Cancer patients [EORTC QLQ-C30])
10. Adequate cardiac function; formal measurement of left ventricular ejection fraction is only required if clinically indicated
11. Adequate bone marrow function: absolute neutrophil count (ANC)  $\geq 1.5 \times 10^9/\text{l}$ ; white blood cell count  $\geq 3 \times 10^9/\text{l}$ ; platelets  $\geq 100 \times 10^9/\text{l}$ ; haemoglobin (Hb)  $\geq 9 \text{ g/dl}$  (can be post-transfusion)
12. Adequate renal function: calculated creatinine clearance  $\geq 50 \text{ ml/minute}$
13. Adequate liver function: serum bilirubin  $\leq 1.5 \times$  upper limit of normal (ULN); ALT/AST  $\leq 2.5 \times$  ULN; alkaline phosphatase (ALP)  $\leq 3 \times$  ULN (in the absence of liver metastases). If liver metastases are present, serum transaminases  $\leq 5 \times$  ULN are permitted.
14. Written informed consent must be obtained from the patient before any study-specific procedures are performed

**Participant type(s)**

Patient

**Age group**

Adult

**Lower age limit**

18 Years

**Sex**

Both

**Target number of participants**

730

**Total final enrolment**

553

**Key exclusion criteria**

1. Tumours of squamous histology
2. Patients with locally advanced oesophageal cancer suitable for definitive chemoradiotherapy.
3. Documented or symptomatic brain metastases and/or central nervous system metastases or leptomeningeal disease
4. Previous chemotherapy or radiotherapy
5. Any major surgery within 4 weeks prior to the start of study treatment
6. Any prior treatment with an epidermal growth factor receptor (EGFR) signal transduction

directed therapy

7. Treatment with non-permitted medication

8. Clinically significant (i.e. active) cardiac disease e.g. symptomatic coronary artery disease, uncontrolled cardiac dysrhythmia, or myocardial infarction within the last 12 months. Patients with any history of clinically significant cardiac failure are excluded from study entry

9. History of interstitial lung disease (e.g., pneumonitis or pulmonary fibrosis) or evidence of interstitial lung disease on baseline chest CT scan

10. Known peripheral neuropathy > Grade 1 (absence of deep tendon reflexes as the sole neurological abnormality does not render the patient ineligible)

11. Lack of physical integrity of the upper gastro-intestinal tract, malabsorption syndrome, or inability to take oral medication (administration of capecitabine by naso-gastric or jejunostomy feeding tube is permitted)

12. Known dihydropyrimidine dehydrogenase (DPD) deficiency

13. Known hypersensitivity to panitumumab, components of the EOX regimen, or any of the constituents of these agents

14. Known positive tests for human immunodeficiency virus (HIV) infection, hepatitis C virus, acute or chronic active hepatitis B infection

15. Other clinically significant disease or co-morbidity which may adversely affect the safe delivery of treatment within this trial

16. Female patients who may be pregnant or breastfeeding. Potential female patients of childbearing potential must have a negative pregnancy test within 7 days prior to randomisation, or have had amenorrhea for more than 2 years

17. Patients of child-bearing potential not consenting to use adequate contraceptive precautions or abstinence during the course of the study and for 6 months after the last study drug administration for females, and 1 month for males

18. Any other malignancies within the last 5 years (other than curatively treated basal cell carcinoma of the skin and/or in situ carcinoma of the cervix)

19. Treatment with another investigational agent within 30 days of commencing study treatment

**Date of first enrolment**

20/05/2008

**Date of final enrolment**

19/10/2011

## **Locations**

**Countries of recruitment**

England

United Kingdom

**Study participating centre**

**Royal Marsden Hospital**

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United Kingdom

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# Sponsor information

## Organisation

The Royal Marsden Hospital NHS Foundation Trust (UK)

## Sponsor details

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## Sponsor type

Hospital/treatment centre

## Website

<http://www.royalmarsden.nhs.uk/rmh>

## ROR

<https://ror.org/0008wzh48>

# Funder(s)

## Funder type

Government

## Funder Name

The Royal Marsden NHS Foundation Trust (UK)

## Funder Name

Panitumumab for the study to be provided by Amgen Ltd. without cost. In addition, Amgen Ltd is providing an educational grant to assist with the costs of study administration (UK)

# Results and Publications

## Publication and dissemination plan

Not provided at time of registration

## Intention to publish date

## Individual participant data (IPD) sharing plan

Not provided at time of registration

## IPD sharing plan summary

Not provided at time of registration

## Study outputs

| Output type                           | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---------------------------------------|---------|--------------|------------|----------------|-----------------|
| <a href="#">Results article</a>       | results | 01/05/2013   |            | Yes            | No              |
| <a href="#">Plain English results</a> |         |              | 25/10/2022 | No             | Yes             |