ISRCTN65080435 https://doi.org/10.1186/ISRCTN65080435

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

Submission date 05/03/2008	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol
Registration date 21/04/2008	**Overall study status** Completed	[_] Statistical analysis plan [X] Results
Last Edited 25/10/2022	**Condition category** Cancer	[_] 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
Department of Medicine
Royal Marsden Hospital
Downs Road
Sutton
Surrey
United Kingdom
SM2 5PT

Additional identifiers

ClinicalTrials.gov (NCT)
NCT00824785

Protocol serial number
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

Study type(s)
Treatment

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^2), oxaliplatin (130 mg/m^2) and panitumumab (9 mg/kg) are all given intravenously on day 1 of a 21 day cycle, with capecitabine (1,250 mg/m^2/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(s)
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.

Key secondary outcome(s))
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.

Completion date
30/06/2012

Eligibility

Key inclusion criteria
1. Male and female patients aged >=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. Wrold 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) >=1.5 x 10^9/l; white

blood cell count >=3 x 10^9/l; platelets >=100 x 10^9/l; haemoglobin (Hb) >=9 g/dl (can be post-transfusion)
12. Adequate renal function: calculated creatinine clearance >=50 ml/minute
13. Adequate liver function: serum bilirubin <=1.5 x upper limit of normal (ULN); ALT/AST <=2.5x ULN; alkaline phosphatase (ALP) <=3 x ULN (in the absence of liver metastases). If liver metastases are present, serum transaminases <= 5 x ULN are permitted.
14. Written informed consent must be obtained from the patient before any study-specific procedures are performed

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

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
United Kingdom

England

Study participating centre
Royal Marsden Hospital
Surrey
United Kingdom
SM2 5PT

Sponsor information

Organisation
The Royal Marsden Hospital NHS Foundation Trust (UK)

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

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?
Results article	results	01/05/2013		Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Plain English results			25/10/2022	No	Yes