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A multicentre randomised phase II clinical trial comparing oxaliplatin (Eloxatin), capecitabine (Xeloda) and pre-operative radiotherapy with or without cetuximab followed by total mesorectal excision for the treatment of patients with magentic resonance imaging defined high risk rectal cancer

Submission date 09/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 03/10/2006	**Overall study status** Completed	
Last Edited 26/06/2014	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Prof David Cunningham

Contact details
Royal Marsden Hospital
Downs Road
Sutton
Surrey
United Kingdom
SM2 5PT

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MREC 05/Q1604/16

Study information

Scientific Title

Acronym
EXPERT-C

Study objectives
To evaluate the improvement in pathological complete response rate from the addition of cetuximab to neoadjuvant oxaliplatin and capecitabine followed by synchronous chemoradiation and Total Mesorectal Excision (TME) in patients with Magnetic Resonance Imaging (MRI) defined high risk rectal cancer.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxfordshire Research Ethics Committee A, approval was given on 05/04/2005

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

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
Rectal cancer

Interventions

Group one: receiving oxaliplatin (Eloxatin), capecitabine (Xeloda) and pre-operative radiotherapy with cetuximab followed by TME.
Group two: receiving oxaliplatin (Eloxatin), capecitabine (Xeloda) and pre-operative radiotherapy without cetuximab followed by TME.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Oxaliplatin, capecitabine, cetuximab.

Primary outcome measure
Pathological complete response at TME.

Secondary outcome measures
1. Radiological response rates after neoadjuvant chemotherapy and after completion of all neoadjuvant chemoradiotherapy
2. Complete resection rate (R0 resection) with microscopic clear resection margin (tumour observed more than 1 mm from the resection margin), especially circumferential resection margin
3. Perioperative measures including operation time, duration of in-patient stay, peri-operative transfusion requirement and mortality within 30 days of operation
4. Post-operative complications including wound infection, wound dehiscence fistula formation
5. Quality of TME as graded by audit of photographed surgical specimens
6. Rate of Abdomino-Peritoneal Excision (APE)
7. Rate of permanent defunctioning colostomies
8. Clinical and radiological anastomotic leak rate
9. Progression free survival and patterns of failure
10. Overall survival
11. Safety
13. Quality of life including long term bowel function
13. Evaluation of molecular and genetic predictors of response to anti-Epidermal Growth Factor Receptor (anti-EGFR) treatment
14. Evaluation of gene expression changes which occur in response to treatment with cetuximab, and to correlate these changes with response to treatment and prognosis.

Overall study start date
01/09/2005

Completion date
01/09/2012

Eligibility

Key inclusion criteria
1. Aged 18 years or over
2. Histological diagnosis of adeno- or undifferentiated non-small cell carcinoma of rectum

3. High risk operable rectal cancer as defined by the presence on MRI of at least one of the following:
a. tumours within 1 mm of mesorectal fascia i.e. circumferential resection margin threatened or involved
b. T3 tumours at/below levators
c. tumours extending into more than or equal to 5 mm into peri-rectal fat
d. T4 tumours (including the involvement of bladder or vagina if surgical resection is possible with clear margins)
e. presence of extra-mural venous invasion (primary tumour is therefore at least T3)
4. World Health Organisation (WHO) performance status of zero to two
5. No evidence of metastatic disease as determined by Computerised Tomography (CT) scan of chest and abdomen or other investigations such as Positron Emission Tomography (PET) scan or biopsy if required
6. Adequate bone marrow function with platelets more than 100 x 10^9/l, White Blood Cells (WBC) more than 3 x 10^9/l and neutrophils more than 1.5 x 10^9/l
7. Serum bilirubin less than 1.5 x Upper Limit of institutional Normal range (ULN) and transaminases less than 2.5 x ULN
8. Serum creatinine less than ULN or calculated creatinine clearance more than 50 ml/min
9. No concurrent uncontrolled medical condition
10. No active malignant disease other than non-melanotic skin cancer or carcinoma in situ of the uterine cervix in the last ten years
11. Life expectancy of more than three months
12. Adequate contraceptive precautions if relevant
13. Informed written consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
164

Key exclusion criteria
1. Any contraindications to MRI (e.g. patients with pacemakers)
2. Medical or psychiatric conditions that compromise the patients ability to give informed consent
3. Patients with rectal cancer which is deemed inoperable at diagnosis should not be entered into the study even if they are potentially operable if their primary is successfully downstaged by neoadjuvant treatment. This includes patients with locally advanced inoperable disease, such as tumour extending beyond the mesorectal fascia into pelvic side wall structures, or situations where surgical resection with clear margins is unlikely to be possible
4. T1-2 rectal cancer at any level
5. Presence of metastatic disease or recurrent rectal tumour

6. Concurrent uncontrolled medical conditions
7. Any previous chemotherapy or radiotherapy, and any investigational treatment for rectal cancer
8. Pregnancy or breast feeding
9. Patients with known malabsorption syndromes or a lack of physical integrity of the upper gastrointestinal tract
10. Clinically significant (i.e. active) cardiac disease (e.g. congestive heart failure, symptomatic coronary artery disease and cardiac dysrhythmia, e.g. atrial fibrillation, even if controlled with medication) or myocardial infarction within the last 12 months
11. Patients with any symptoms or history of peripheral neuropathy

Date of first enrolment
01/09/2005

Date of final enrolment
01/09/2012

Locations

Countries of recruitment
England

United Kingdom

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

Sponsor information

Organisation
Royal Marsden NHS Foundation Trust (UK)

Sponsor details
Downs Road
Sutton
Surrey
England
United Kingdom
SM2 5PT

Sponsor type
Hospital/treatment centre

Website
http://www.royalmarsden.nhs.uk/rmh

ROR
https://ror.org/0008wzh48

Funder(s)

Funder type
Industry

Funder Name
Professor Cunningham's Clinical Research Fund, Merck Pharmaceuticals (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

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	01/12/2013		Yes	No
Results article	results	23/06/2014		Yes	No