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Fluoropyrimidine, oxaliplatin and targeted receptor pre-operative therapy: a controlled trial in high-risk operable colon cancer

Submission date
28/11/2006

Recruitment status
No longer recruiting

Registration date
30/03/2007

Overall study status
Completed

Last Edited
20/01/2025

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-chemotherapy-and-panitumumab-before-and-after-surgery-for-bowel-cancer

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2007-001987-55

ClinicalTrials.gov (NCT)
NCT00647530

Protocol serial number
N/A

Study information

Scientific Title
Fluoropyrimidine, Oxaliplatin and Targeted Receptor pre-Operative Therapy: a controlled trial in high-risk operable colon cancer

Acronym
FOxTROT

Study objectives
For patients with high risk, operable colon cancer:
1. Does giving potent Oxaliplatin/FluoroPyrimidine (OxFP) chemotherapy preoperatively facilitate surgical clearance and eradicate micrometastases more effectively than delayed post-operative chemotherapy?
2. Does the addition of the Epidermal Growth Factor Receptor (EGFR)-targeted therapy, panitumumab, enhance the efficacy of OxFP?

Ethics approval required
Old ethics approval format

Ethics approval(s)
West Glasgow Research Ethics Committee, 05/06/2007, ref: 07/S0703/57

Study design
Open multicentre randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
High risk, operable colon cancer

Interventions
Current interventions as of 05/01/2017:

An open, multicentre, randomised controlled trial.
First phase: randomised phase II assessing tolerability, feasibility and radiological/pathological downstaging.
Second phase: randomised phase III trial with primary endpoint relapse-free survival.

Arm A: Six weeks of pre-operative oxaliplatin/fluoropyrimidine chemotherapy followed by surgery then 18 weeks of post-operative oxaliplatin/fluoropyrimidine chemotherapy

Arm B: The same chemotherapy with concomitant panitumumab for the first six weeks
Arm C: Surgery then twenty four weeks of post-operative oxaliplatin/fluoropyrimidine chemotherapy

The two allowable oxaliplatin/fluoropyrimidine chemotherapy regimens are twelve two-week courses of Oxaliplatin and Modified deGramont (OxMdG), or eight three-week courses of Oxaliplatin and Capecitabine (OxCap). Patients randomised to receive panitumumab receive this by intravenous (IV) infusion over 60 minutes at 6 mg/kg on day one of each of the first three two-week OxMdG cycles, immediately prior to the start of the chemotherapy regimen.

Post-operative adjuvant therapy will be given, regardless of trial arm and operative histology.

Previous interventions:

An open, multicentre, randomised controlled trial.
First phase: randomised phase II assessing tolerability, feasibility and radiological/pathological downstaging.
Second phase: randomised phase III trial with primary endpoint relapse-free survival.

Arm A: Six weeks of pre-operative oxaliplatin/fluoropyrimidine chemotherapy followed by surgery then 18 weeks of post-operative oxaliplatin/fluoropyrimidine chemotherapy
Arm B: The same chemotherapy with concomitant panitumumab for the first six weeks
Arm C: Surgery then twenty four weeks of post-operative oxaliplatin/fluoropyrimidine chemotherapy
Arm D: Schedule C with concomitant panitumumab for the first six weeks of post operative therapy

The two allowable oxaliplatin/fluoropyrimidine chemotherapy regimens are twelve two-week courses of Oxaliplatin and Modified deGramont (OxMdG), or eight three-week courses of Oxaliplatin and Capecitabine (OxCap). Patients randomised to receive panitumumab receive this by intravenous (IV) infusion over 60 minutes at 6 mg/kg on day one of each of the first three two-week OxMdG cycles; or at 9 mg/kg on day one of each of the first two three-week OxCap cycles, immediately prior to the start of the chemotherapy regimen.

Post-operative adjuvant therapy will be given, regardless of trial arm and operative histology.

Intervention Type
Drug

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
Fluoropyrimidine, oxaliplatin, panitumumab

Primary outcome(s)
Current primary outcome measures as of 26/01/2018:
1. Freedom from recurrent of persistent disease (including failure of macroscopic disease clearance at primary surgery) within the first two years following randomisation
2. Pathological down-staging as measured by depth of extramural spread among patients allocated to preoperative chemotherapy with or without panitumumab

Previous primary outcome measures:
1. Pre- plus post-operative versus post-operative chemotherapy: freedom from recurrence (or residual disease) at two years after randomisation (arms A and B versus C and D)
2. Panitumumab versus not: pathological down-staging (arm B versus A)

Key secondary outcome(s))
Current secondary outcome measures as of 26/01/2018:
1. Death from colon cancer
2. Overall survival
3. Freedom from recurrence or persistent disease at 2 years (panitumumab comparison)
4. Pathological assessment of downstaging (involvement of lymph nodes, serosa, and resection margin) and quality of resection specimen
5. Quality of resection specimen and distance to high-tie
6. Radiological assessment of response to neoadjuvant treatment
7. Quality of life by EORTC QLQ C-30 and EuroQol EQ-5D
8. Length of hospital stay
9. Surgical morbidity/mortality
10. Chemotherapy toxicity
11. Adverse events

Previous secondary outcome measures:
1. Death from colon cancer
2. Overall survival
3. Health-related quality of life
4. Pathological assessment of down-staging (involvement of lymph nodes, serosa, resection margin), and quality of resection specimen
5. Radiological assessment of response in neoadjuvant treatment arms
6. CarcinoEmbryonic Antigen (CEA) level following neo-adjuvant therapy
7. Health Service resource usage
8. Adverse events
9. Surgical morbidity/mortality

Completion date
31/12/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 26/01/2018:
1. Histologically proven adenocarcinoma of the colon or high grade dysplasia on histology plus unequivocal radiological evidence of invasive cancer
2. A candidate for adjuvant oxaliplatin/ fluoropyrimidine chemotherapy based on:
2.1. Either radiological high risk (rT4 or rT3 tumour with extramural extension ≥ 5mm)
2.2. Or radiological intermediate risk (rT3 tumour with <5mm extramural extension) and younger age/good general health
3. Patients presenting with acute colonic obstruction may enter the trial only after obstruction is relieved by a successful defunctioning stoma, and when recovered to a fitness level consistent with the other eligibility criteria
4. Adequate full blood count: WBC >3.0 x109/l; Plts >100 x109/l. Anaemia (Hb < 10.0 g/dl) is not an exclusion, but should be corrected by transfusion prior to surgery and chemotherapy. If Hb remains low despite transfusions, surgery and chemotherapy can be given at the decision of the

surgical and oncology teams.
5. Adequate renal biochemistry: GFR >50 ml/min calculated by the Wright or Cockroft formula or EDTA clearance >70 ml/min
6. Adequate hepatobiliary function: bilirubin < 25 µmol/l (Patients with Gilbert's syndrome who have raised bilirubin but otherwise normal liver function tests are eligible for the study.)
7. Aged 18 or over
8. WHO performance status of 0, 1 or 2
9. If female and of childbearing potential, must:
9.1. Have a negative pregnancy test ≤72hours prior to initiating study treatment
9.2. Agree to avoid pregnancy during and for 6 months after study treatment
10. If male with a partner of childbearing potential, must:
- Agree to use adequate, medically approved, contraceptive precautions during and for 90 days after the last dose of study treatment
11. Patient able and willing to provide written informed consent for the study

Previous inclusion criteria:
1. Histologically proven colon cancer with a radiological staging of T3, NX, M0
2. Computed Tomography (CT) scan criteria of poor prognosis (T4 or T3 and more than 5 mm extramural depth and/or probable nodal involvement and/or probable vascular invasion)
3. Fit for the neoadjuvant treatments
4. Patients who have presented with acute colonic obstruction if a successful defunctioning or stent procedure has been performed
5. Patients able and willing to provide written informed consent for the study

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Current exclusion criteria as of 26/01/2018:
1. MorbidityAny patient for whom radiotherapy is advised by the MDT
2. Strong evidence of distant metastases or peritoneal nodules (M1)
3. Peritonitis (secondary to perforated tumour)
4. Colonic obstruction that has not been defunctioned
5. Serious medical comorbidity, eg uncontrolled inflammatory bowel disease, uncontrolled angina or recent (<6 months) MI
6. Another serious medical condition judged to compromise ability to tolerate neoadjuvant therapy and/or surgery
7. Any other malignant disease within the preceding 5 years with the exception of non-melanomatous skin cancer, carcinoma in situ and early stage disease with a recurrence risk <5%

Additional exclusion criteria for panitumumab randomisation
1. RAS-mutant or unknown RAS status tumours
2. Allocated post-operative chemotherapy
3. History of interstitial pneumonitis or pulmonary fibrosis
4. History of severe or life-threatening hypersensitivity reactions
5. Serum magnesium levels within the normal range at trial entry (which can include intravenous correction)

Previous exclusion criteria:
1. Tumour within 15 cm of the anal verge as judged by sigmoidoscopy, or below the level of the sacral promontory, as judged by sagittal CT
2. Indication for radiotherapy
3. Evidence of disseminated disease (M1)
4. Peritonitis (secondary to perforated tumour)
5. Under the age of 18 or pregnant
6. Serious medical co-morbidity

Date of first enrolment
01/04/2008

Date of final enrolment
23/12/2016

Locations

Countries of recruitment
United Kingdom

England

Denmark

Sweden

Study participating centre
University of Birmingham
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham (UK)

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) (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
Not provided at time of registration

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	Pilot/feasibility results	19/01/2023	20/01/2023	Yes	No
Interim results article		01/11/2012		Yes	No
Other publications		11/01/2025	20/01/2025	Yes	No
Plain English results	Study website			No	Yes
Study website		11/11/2025	11/11/2025	No	Yes