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A Phase III trial comparing either COntinuous chemotherapy plus cetuximab or INtermittent chemotherapy with standard continuous palliative combination chemotherapy with oxaliplatin and a fluoropyrimidine in first line treatment of metastatic colorectal cancer

Submission date 09/08/2004	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 22/10/2004	**Overall study status** Completed	
Last Edited 19/10/2018	**Condition category** Cancer	

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/a-trial-looking-at-treatment-for-advanced-bowel-cancer

Study website
http://www.ctu.mrc.ac.uk/studies/CR10.asp

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
2004-002951-16

IRAS number

ClinicalTrials.gov number
NCT00182715

Secondary identifying numbers
CR10

Study information

Scientific Title
A Phase III trial comparing either COntinuous chemotherapy plus cetuximab or INtermittent chemotherapy with standard continuous palliative combination chemotherapy with oxaliplatin and a fluoropyrimidine in first line treatment of metastatic colorectal cancer

Acronym
COIN

Study objectives
This randomized phase III trial is studying combination chemotherapy and cetuximab to see how well they work compared to combination chemotherapy alone as first-line therapy in treating patients with metastatic colorectal cancer.

More details can be found at: http://www.ctu.mrc.ac.uk/research_areas/study_details.aspx?s=10

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration.

Study design
Randomised controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Metastatic colorectal cancer

Interventions
Chemotherapy
The Oxaliplatin regimens used in the trial can be selected on a per patient basis, but prior to knowledge of the treatment randomisation. This conforms with the NICE guidance regarding allowing patient choice with respect to oral or intravenous (IV) therapy. Some centres may be subject to practical constraints such that only one of the regimens will be feasible. In this case the centre may make a policy that all patients treated in that centre will receive one or other regimen. There is no data yet to indicate that one regimen is superior to the other. The regimen will be either:
OxMdG: a combination of folinic acid (200 mg/m^2 IV over 2 h), concurrent administration of Oxaliplatin (85 mg/m^2 IV over 2 h) plus bolus 5FU (400 mg/m^2) followed by a 46 hour IV infusion of 5FU 2400 mg/m^2 repeated every 2 weeks.
or:
XELOX: a combination of Capecitabine plus Oxaliplatin: Oxaliplatin 130 mg/m^2 IV over 2 hours day 1, plus Capecitabine 1000 mg/m^2 twice a day (bd), orally (po) days 1-14 repeated 3 weekly.

Treatment duration and breaks
Arm A:
Continuous chemotherapy (Control Arm): These patients will continue the chemotherapy regimen (with dose reductions as required) until progressive disease is identified on radiological grounds (RECIST), or the development of cumulative toxicity or because of patient choice to stop chemotherapy. Patients in this arm should continue on treatment with no more than a three week interval off treatment for any reason. The cumulative toxicity that is most likely to occur is the neuropathy associated with Oxaliplatin, which increases in incidence from about 7 months duration of therapy. If this occurs, patients may continue on the fluoropyrimidine component of the regimen with dose increment until evidence of disease progression. If the neuropathy resolves to < grade 1 the Oxaliplatin may be reintroduced cautiously at the investigator's discretion. These patients will be evaluated with 12 weekly computed tomography (CT) scans to assess radiological evidence of progression.

Arm B:
Continuous chemotherapy plus Cetuximab: These patients will continue chemotherapy plus Cetuximab as Arm A above. Cetuximab will be continued if chemotherapy is stopped because of toxicity or patient choice, but should be discontinued on evidence of disease progression or unacceptable Cetuximab toxicity. These patients will be evaluated with 12 weekly CT scans to assess radiological evidence of progression.

Arm C:
Intermittent chemotherapy: These patients will be treated for 12 weeks. Chemotherapy will then stop and they will be monitored clinically, at least 6 weekly, and with CT scans at 12 weekly intervals. On evidence of progression of disease using RECIST criteria or on clinical evidence of deterioration, the same chemotherapy will be restarted, for a further 12 weeks course. At that point treatment will again be interrupted. Patients with chemo-sensitive disease may have an unlimited number of 12-week treatments alternating with treatment breaks. When the patient demonstrates resistance to this treatment as evidenced by progressive disease during a period on chemotherapy or clinical choice, they will move on to second-line therapy or supportive care.

Intervention Type
Drug

Phase
Phase III

Drug/device/biological/vaccine name(s)
Various

Primary outcome measure
Not provided at time of registration.

Secondary outcome measures
Not provided at time of registration.

Overall study start date
01/08/2003

Completion date
01/08/2005

Eligibility

Key inclusion criteria
1. Confirmed colorectal adenocarcinoma:
- either previous or current histologically confirmed primary adenocarcinoma of colon or rectum, together with clinical or radiological evidence of advanced and/or metastatic disease
- or histologically/cytologically confirmed metastatic adenocarcinoma, together with clinical and /or radiological evidence of colorectal primary tumour
2. Inoperable metastatic or locoregional disease. Patients who are currently eligible for combination first-line chemotherapy prior to liver resection under National Institute for Clinical Excellence (NICE) guidance are ineligible for this study.
3. Unidimensionally measurable disease (Response Evaluation Criteria in Solid Tumors [RECIST])
4. No previous systemic palliative chemotherapy for metastatic disease
5. Adjuvant chemotherapy with 5-Fluorouracil (5FU) +/- folinic acid (FA), Capecitabine or irinotecan may have been given, if completed >6 months prior to trial entry
6. Rectal chemoradiotherapy with 5FU +/- FA may have been given, if completed >1 month prior to trial entry
7. World Health Organistion (WHO) performance status (PS) 0, 1 or 2 and considered by responsible consultant to be fit to undergo combination chemotherapy
8. Baseline laboratory tests (within 1 week prior to randomisation):
White blood cell count (WBC) ≥4 x 10^9/l, neutrophils ≥1.5 x 10^9/l and platelet count >150 x 10^9/l.
Serum bilirubin ≤1.25 x upper limit of normal (ULN), alkaline phosphatase ≤5 x ULN, and serum transaminase (either aspartate transaminase [AST] or alanine transaminase [ALT]) ≤3 x ULN.
Estimated creatinine clearance >50 ml/min or measured glomerular filtration rate (GFR) (ethylene diamine tetraacetic acid [EDTA] clearance) >50 ml/min.
9. For women of childbearing potential, negative pregnancy test and adequate contraceptive

precautions
10. Consent to allow surplus pathological material to be analysed for epidermal growth factor receptor (EGFR) testing

Participant type(s)
Patient

Age group
Not Specified

Sex
Both

Target number of participants
Added 10/03/2011: 2421 (2015 achieved)

Key exclusion criteria
1. Patients who are unfit for the chemotherapy regimens in this protocol e.g.
Severe uncontrolled concurrent medical illness (including poorly-controlled angina or very recent myocardial infarction [MI], i.e. in previous 3 months) likely to interfere with protocol treatments
Any psychiatric or neurological condition which is felt likely to compromise the patient's ability to give informed consent or to comply with oral medication
Partial or complete bowel obstruction
Pre-existing neuropathy (>grade 1)
2. Patients requiring ongoing treatment with a contraindicated concomitant medication
3. Patients with another previous or current malignant disease which, in the judgement of the treating investigator, is likely to interfere with COIN treatment or assessment of response

Date of first enrolment
01/08/2003

Date of final enrolment
01/08/2005

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Wales Cancer Network Co-ordinating Office
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Sponsor information

Organisation
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Sponsor type
Research council

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Charity

Funder Name
The trial is funded by Cancer Research UK and Medical Research Council (MRC), via the Clinical Trials Advisory and Awards Committee (CTAAC). The CRUK grant award reference number is C1210-A4528

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?
Plain English results				No	Yes
Other publications	review	01/08/2008		Yes	No
Results article	toxicity results	27/01/2009		Yes	No
Results article	phase 3 results	18/06/2011		Yes	No
Results article	results	25/09/2012		Yes	No