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FOCUS 2: Drug treatment for bowel cancer - making the best choices when a milder treatment is needed

Submission date 08/09/2005	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 02/11/2005	**Overall study status** Completed	
Last Edited 18/10/2018	**Condition category** Cancer	

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

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

NCT00070213

Secondary identifying numbers
CR09

Study information

Scientific Title
FOCUS 2: Drug treatment for bowel cancer - making the best choices when a milder treatment is needed

Acronym
FOCUS 2/CR09

Study objectives
Oncologists usually base decisions on whether to offer full-dose, reduced-dose or no chemotherapy on factors including performance status, co-morbidity and age. In FOCUS2, we will assess treatment success in relation to objective criteria of general health and fitness at baseline. Therefore, a comprehensive health assessment (CHA) tool is applied before starting therapy. The success of treatment will then be measured using standard criteria. However, a major determinant of the success of palliative chemotherapy is its impact upon general health and quality of life, which are not necessarily reflected by response, progression-free survival and overall survival. In FOCUS2, both physical and mental aspects of general health will be assessed at intervals during treatment, as outcome measures both for treatment comparison. The FOCUS2 schedules are reduced-dose versions of regimens used in recent randomised clinical trials and pilot studies. These studies recruited predominantly young, fit patients, but data for the selected minority of elderly patients taking part in them is encouraging. For example, a recent report from Sanofi combined evidence from 3 trials including 1408 patients receiving FOLFOX4 (dG + oxaliplatin), 213 of whom were aged 70-75. Response rates were maintained and treatment was felt to be tolerable, although higher rates of grade 3-4 toxicities were seen in patients over 70, supporting the concept of dose modification for pharmacokinetic/dynamic reasons in older patients. This is also supported by meta-analysis data showing age to be a strong independent predictor of grade 3-4 toxicity with 5FU/FA treatment. In the MRC trial CR06, 10% of patients were over the age of 75, and 22% were of borderline performance status (World Health Organisation [WHO] PS2). Good safety and quality of life (QoL) data for the two infusional 5FU arms in that trial confirm that it can be safely applied across a wide range of patients. The CR08 FOCUS trial includes a lower proportion of elderly and PS2 patients, but interim analysis has shown no evidence of safety problems with the MdG or OxMdG schedules (data on file, MRC CTU).
Phase III studies have included 603 patients treated with capecitabine, with median age 64, and median Karnofsky PS 90% (=PS1). Some elderly (age up to 86) and low PS (Karnofsky 70%) patients were included, but the numbers treated, and toxicity in these patients, is not reported. Since its licensing, many oncologists have used a reduced starting dose of capecitabine when treating elderly or frail patients, although this practice is currently not evidence-based.

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)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Advanced Colorectal Cancer

Interventions
Plan D: MdG (80% Standard Treatment) for 12 weeks, usually 6 cycles. 14 day cycle where drug is only given on days 1 and 2. At 6-week review (cycle 4), a dose increase to full dose may be considered at the clinician's discretion. At approximately 14 weeks a clinical/radiological review should be done to determine if the outcome of treatment has been 'Treatment benefit' or 'No treatment benefit'. Patients with 'No treatment benefit' may be considered for second-line therapy. If they are considered suitable for second-line therapy they should then be given OxMdG 2nd-line.

Plan E: OxMdG (80% Standard Treatment) for 12 weeks, usually 6 cycles. 14 day cycle. At 6-week review (cycle 4), a dose increase to full dose may be considered at the clinician's discretion.

Plan F: Cap (80% Standard Treatment) for 12 weeks, usually 4 cycles. 21 day cycle. At 6-week review (cycle 3), a dose increase to full dose may be considered at the clinician's discretion. At approximately 14 weeks a clinical/radiological review should be done to determine if the outcome of treatment has been 'Treatment benefit' or 'No treatment benefit'. Patients with 'No treatment benefit' may be considered for second-line therapy. If they are considered suitable for second-line therapy they should then be given OxCap 2nd-line.

Plan G: OxCap (80% Standard Treatment) for 12 weeks, usually 4 cycles. 21 day cycle. At 6-week review (cycle 4), a dose increase to full dose may be considered at the clinician's discretion.

Intervention Type
Drug

Phase
Not Applicable

Primary outcome measure
The principal outcome measures are progression-free survival (for the oxaliplatin comparison) and QoL (for the FU/capecitabine comparison).

Secondary outcome measures
Secondary outcome measures (both randomisations) also include Limited Health Assessments (LHA), chemotherapy toxicity/adverse events, overall failure-free survival and overall survival. Baseline CHA will be correlated with outcome in each treatment arm to identify thresholds for treatment benefit. Cross-trial comparisons will be made with FOCUS, which shares two treatment arms.

Overall study start date
29/01/2004

Completion date
31/01/2007

Eligibility

Key inclusion criteria
1. Confirmed colorectal adenocarcinoma: Either previous or current histologically confirmed primary adenocarcinoma of colon or rectum & clinical/radiological evidence of advanced /metastatic disease or histologically/cytologically confirmed metastatic adenocarcinoma, with clinical/radiological evidence of colorectal primary tumour
2. Unidimensionally measurable disease (Response Evaluation Criteria in Solid Tumors [RECIST] criteria)
3. No previous systemic palliative chemotherapy for metastatic disease. (Adjuvant chemotherapy with 5-fluorouracil (5FU) +/- folinic acid (FA) allowed if completed >4 months prior to trial entry. Rectal chemoradiotherapy with 5FU +/- FA allowed if completed >1 month prior to trial entry.)
4. WHO performance status 0, 1 or 2
5. Baseline laboratory tests (within 1 week prior to randomisation): white blood cell count (WBC) >3 x 10^9/l and platelet count >100 x 10^9/l, serum bilirubin ≤3 x upper limit of normal (ULN), and serum transaminase (either aspartate aminotransferase [AST] or alanine aminotransferase [ALT]) ≤2.5 x ULN either estimated creatinine clearance >50 ml/min or measured glomerular filtration rate (GFR) (ethylene diamine tetraacetic acid [EDTA] clearance) >30 ml/min. Patients with GFR of 30-49 ml/min, if allocated oxaliplatin and/or capecitabine receive 25% reduced dose.
6. For women: negative pregnancy test and adequate contraceptive precautions
7. Informed Consent

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
460

Key exclusion criteria

1. Patients who are fit and suitable for full-dose combination chemotherapy e.g. suitable and willing to be entered into the main FOCUS trial or equivalent; eligible and suitable for 1st-line combination as per NICE guidance
2. Patients who are unfit for the reduced-dose treatments in this protocol e.g. severe uncontrolled concurrent medical illness (including poorly-controlled angina or very recent myocardial infarction [MI]) 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 edication; partial or complete bowel obstruction; pre-existing neuropathy (>grade 1)
3. Patients requiring ongoing treatment with a contraindicated concomitant medication
4. Patients with another previous or current malignant disease which, in the judgement of the treating consultant, is likely to interfere with FOCUS2 treatment or assessment of response

Date of first enrolment
29/01/2004

Date of final enrolment
07/07/2006

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cookridge Hospital
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Sponsor information

Organisation
Medical Research Council (UK)

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Sponsor type
Research council

Website
http://www.ctu.mrc.ac.uk/

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (CRUK) Ref: C6003/A3830

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

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
Results article	results	21/05/2011	Yes	No