ISRCTN79877428 https://doi.org/10.1186/ISRCTN79877428

A randomised trial assessing the role of two new agents in the management of advanced colorectal cancer

Submission date 06/04/2000	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/04/2000	**Overall study status** Completed	
Last Edited 15/10/2018	**Condition category** Cancer	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT00008060

Protocol serial number
E164/3; CR08

Study information

Scientific Title
A randomised trial assessing the role of two new agents in the management of advanced colorectal cancer

Acronym
MRC FOCUS (Fluorouracil, Oxaliplatin, CPT-11, Use and Sequencing)

Study objectives
1. The principal objective is to determine whether there is an advantage for patients for the use of combination chemotherapy for colorectal cancer compared with the standard approach of sequential single-agent therapies.
2. In addition the trial will determine whether combination therapy is best used in first-line management of advanced disease, or reserved for second-line treatment following standard first-line single-agent modified de Gramont (MdG).
3. Finally, the trial will compare the efficacy and toxicity of an irinotecan-containing combination versus the equivalent oxaliplatin-containing combination.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Added 17/07/2007: Northern and Yorkshire Medical Research Ethics Committee, approval given on 12/11/1999.

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Colorectal cancer

Interventions
This is a five-arm trial in which patients will be randomly allocated to one of five 'treatment plans'. These plans comprise first-line and, in some cases, a second-line chemotherapy treatment plan. The five plans are:

Plan A: First-line Modified de Gramont (MdG) regimen. In the event of radiological or clinical disease progression, MdG will be stopped, and, if appropriate, patients will receive second-line therapy with single-agent irinotecan.

Plan B: First-line MdG. In the event of radiological or clinical progression patients will, if appropriate, receive second-line therapy with MdG-plus-Irinotecan (IrMdG).

Plan C: First-line treatment with IrMdG.

Plan D: First-line MdG. In the event of radiological or clinical progression patients will, if appropriate, receive second-line therapy with MdG-plus-Oxaliplatin (OxMdG).

Plan E: First-line treatment with OxMdG.

The chemotherapy schedules employed in the plans are as follows:
MdG: l-folinic acid 175 mg iv infusion over two hours
5-fluorouracil 400 mg/m^2 intravenous bolus over five minutes
5-fluorouracil 2800 mg/m^2 intravenous infusion over 46 hours
Cycle repeat: 14 days

Irinotecan (single agent):
Irinotecan 300-350 mg/m^2 intravenous infusion over 30 minutes
Cycle repeat: 21 days

IrMdG: Irinotecan 180 mg/m^2 intravenous infusion over 30 minutes
l-folinic acid 175 mg/m^2 intravenous infusion over two hours
5-fluorouracil 400 mg/m^2 intravenous bolus over five minutes
5-fluorouracil 2400 mg/m^2 intravenous infusion over 46 hours
Cycle repeat: 14 days

OxMdG:Oxaliplatin 80 mg/m^2 intravenous infusion over two hours concurrent with
l-folinic acid 175 mg intravenous infusion over two hours
5-fluorouracil 400 mg/m^2 intravenous bolus over five minutes
5-fluorouracil 2400 mg/m^2 intravenous infusion over 46 hours
Cycle repeat: 14 days

In every case, chemotherapy schedules are continued for at least 24 weeks unless disease progression or unacceptable toxicity occurs. Dose reductions or delays for toxicity are defined in the full protocol.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Fluorouracil, Oxaliplatin, CPT-11

Primary outcome(s)
Survival from randomisation

Key secondary outcome(s))
1. Time to failure of first-line treatment
2. Time to failure of protocol treatment plan
3. Objective response rate
4. Patient assessment of quality of life and acceptability of treatment, health economics

Completion date
31/12/2003

Eligibility

Key inclusion criteria
1. Histologically confirmed adenocarcinoma of the colon or rectum
2. Inoperable disease (either locally advanced, recurrent or metastatic and not suitable for curative surgery or radiotherapy)
3. Measurable or evaluable disease
4. World Health Organization (WHO) performance status zero to two
5. Fit, able and willing to undergo any of the possible trial treatments and to comply with the quality of life questionnaires

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Not Specified

Sex
Not Specified

Key exclusion criteria
1. White Blood Cells (WBC) less than 4 x 10^9/l
2. Platelets less than 150 x 10^9/l
3. Bilirubin more than 1.25 x Upper Limit of Normal (ULN)
4. Alkaline phosphatase more than 3 x ULN
5. Aspartate aminotransferase (AST) or Alanine aminotransferase (ALT) more than 3 x ULN
6. Renal impairment (calculated Creatinine Clearance [CrCl] less than 60 ml/min, or measured Glomerular Filtration Rate [GFR] below normal range)
7. Serious uncontrolled medical co-morbidity

Date of first enrolment
12/05/2000

Date of final enrolment
31/12/2003

Locations

Countries of recruitment
United Kingdom

England

Study participating centre

MRC Clinical Trials Unit
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United Kingdom
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Sponsor information

Organisation
Medical Research Council (MRC) Clinical Trials Unit (UK)

ROR
https://ror.org/03x94j517

Funder(s)

Funder type
Research council

Funder Name
Medical Research Council (MRC) (UK)

Alternative Name(s)
Medical Research Council (United Kingdom), UK Medical Research Council, MRC

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

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	14/07/2007		Yes	No
Results article	results	01/06/2008		Yes	No
Results article	results on the association of molecular markers with toxicity outcomes	20/11/2009		Yes	No
Results article	results on the effect of KRAS and BRAF mutations on efficacy of treatment agents	10/12/2009		Yes	No
Plain English results				No	Yes