

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	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 06/04/2000	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 15/10/2018	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Not provided at time of registration

Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

NCT00008060

Secondary identifying numbers

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

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

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/m² intravenous bolus over five minutes
5-fluorouracil 2800 mg/m² intravenous infusion over 46 hours
Cycle repeat: 14 days

Irinotecan (single agent):
Irinotecan 300-350 mg/m² intravenous infusion over 30 minutes
Cycle repeat: 21 days

IrMdG: Irinotecan 180 mg/m² intravenous infusion over 30 minutes
l-folinic acid 175 mg/m² intravenous infusion over two hours
5-fluorouracil 400 mg/m² intravenous bolus over five minutes
5-fluorouracil 2400 mg/m² intravenous infusion over 46 hours
Cycle repeat: 14 days

OxMdG: Oxaliplatin 80 mg/m² intravenous infusion over two hours concurrent with
l-folinic acid 175 mg intravenous infusion over two hours
5-fluorouracil 400 mg/m² intravenous bolus over five minutes
5-fluorouracil 2400 mg/m² 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 measure

Survival from randomisation

Secondary outcome measures

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

Overall study start date

12/05/2000

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

Age group

Not Specified

Sex

Not Specified

Target number of participants

700 in arm one and 350 each in other arms

Key exclusion criteria

1. White Blood Cells (WBC) less than $4 \times 10^9/l$
2. Platelets less than $150 \times 10^9/l$
3. Bilirubin more than $1.25 \times$ Upper Limit of Normal (ULN)
4. Alkaline phosphatase more than $3 \times$ ULN
5. Aspartate aminotransferase (AST) or Alanine aminotransferase (ALT) more than $3 \times$ 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

England

United Kingdom

Study participating centre

MRC Clinical Trials Unit

London

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Sponsor information

Organisation

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

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Sponsor type

Research council

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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

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	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