A Phase II study of chemotherapy given before radiotherapy as treatment for patients with rectal cancer

Submission date	Recruitment status No longer recruiting	Prospectively registered			
17/05/2012		Protocol			
Registration date	Overall study status	Statistical analysis plan			
17/05/2012	Completed	[X] Results			
Last Edited	Condition category	[] Individual participant data			
24/01/2022	Cancer				

Plain English summary of protocol

http://cancerhelp.cancerresearchuk.org/trials/trial-looking-chemotherapy-people-rectal-cancercopernicus

Contact information

Type(s)

Scientific

Contact name

Dr Ruby AL-Mokhtar

Contact details

Cardiff University Neuadd Meirionnydd Heath Park Cardiff United Kingdom CF14 4YS

al-mokhtarr@cardiff.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)

2010-023083-40

ClinicalTrials.gov (NCT)

NCT01263171

Protocol serial number

11709

Study information

Scientific Title

A Phase II study of neoadjuvant chemotherapy given before short course of preoperative radiotherapy (SCPRT) as treatment for patients with MRI-staged operable rectal cancer at high risk of metastatic relapse

Acronym

COPERNICUS

Study objectives

Approximately 15,000 patients are diagnosed with rectal cancer in the UK per annum, 4800 of which would be considered operable. The current standard of care for these patients, is to deliver a short course of preoperative radiotherapy (SCPRT) followed by immediate surgery and postoperative chemotherapy to prevent relapse. However, several studies have highlighted poor compliance due to postoperative surgical morbidity and reduced performance status. There is thus a strong argument to evaluate pre-operative chemotherapy in patients with operable rectal cancer in order to increase patient tolerance, achievable dose intensity and minimize micrometastases by addressing this issue earlier on in treatment.

The overall aim of this study is to assess the feasibility of introducing eight weeks of oxaliplatin /5-Fluorouracil (OxMdG) chemotherapy prior to SCPRT and immediate surgery. Feasibility will be assessed as the percentage of patients undergoing surgery as well as assessing; the dose intensity achieved, treatment toxicities, postoperative morbidity/mortality and activity using histological measures of response in the resected specimen. If deemed to be feasible, the Phase II treatment regime will be taken forward to a Phase III trial where it will be compared against standard practice of SCPRT alone followed by immediate surgery.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Research Ethics Committee for Wales, ref: 12/WA/0051

Study design

Non-randomised interventional treatment

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Colorectal cancer

Interventions

Neoadjuvant chemotherapy, Patients who have enrolled into the COPERNICUS study will be treated with four, two weekly cycles of oxaliplatin and fluorouracil prior to short course preoperative radiotherapy followed by surgical removal of the tumour and adjuvant chemotherapy.

Intervention Type

Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)

Fluorouracil, oxaliplatin

Primary outcome(s)

The proportion of patients who commence neoadjuvant chemotherapy who then undergo surgical resection

Key secondary outcome(s))

- 1. Acute and late toxicity
- 2. Histological assessment of downstaging efficacy

Completion date

14/04/2015

Eligibility

Key inclusion criteria

- 1. Patient 18 years old or older
- 2. Tumour biopsy with histopathological confirmation of rectal adenocarcinoma
- 3. Inferior aspect of disease (primary tumour, mesorectal tumour deposits or extra-mural vascular invasion) is not less than 4 cm from anal verge on digital examination and pelvic MRI scan
- 4. Superior aspect of disease is not more superior than the anterior aspect of the S1/S2 interspace on pelvic sagittal MRI scan
- 5. Further MRI defined inclusion criteria include: Mesorectal fascia is not threatened or involved (i.e. tumour is > 1mm from mesorectal fascia) Primary tumour is: T3a-b (mesorectal primary tumour invasion seen = 5 mm beyond muscularis propria) in the presence of either:
- 5.1. Extra-mural vascular invasion or
- 5.2. Mesorectal lymph nodes(s)/tumour deposit(s) with irregular border or mixed signal intensity any T3c (primary tumour invasion seen >5mm beyond muscularis propria)-T4a (invasion of visceral peritoneum for tumours with a component above peritoneal reflection) Low tumours should not involve levator ani (i.e. there is >1 mm gap between tumour and levator ani) or anal sphincters
- 6. No evidence of established metastatic disease on CT of chest and abdomen. (Patients with equivocal lesions determined at MDT are eligible)
- 7. Patient with measurable disease at the baseline visit
- 8. The patient is a candidate for systemic therapy with OxMdG chemotherapy in the opinion of the primary oncologist treating the patient
- 9. ECOG Status: 0-1
- 10. Bloods: Adequate bone marrow, hepatic, renal and metabolic function (assessed within 14 days prior to consent):

- 10.1. Haemoglobin = 9 g/dL, leucocyte count = $3 \times 109/L$, neutrophil count = $1.5 \times 109/L$ and platelet count = $100 \times 109/L$
- 10.2. Total bilirubin = $1.5 \times \text{ULRR}$, alkaline phosphatase = $5 \times \text{ULRR}$, and serum transaminase (either AST or ALT) = $2.5 \times \text{ULRR}$
- 10.3. Estimated creatinine clearance = 50 ml/min (calculated according to Cockroft and Gault). (Confirmed with 24 hour urine creatinine clearance or EDTA if estimated creatinine clearance < 50 ml/min)
- 10.4. Calcium =LLRR
- 11. No known significant impairment of intestinal absorption (e.g. chronic diarrhoea, inflammatory bowel disease)
- 12. Baseline ECG showing no evidence of established or acute ischaemic heart disease (e.g. left bundle branch block, pathological q waves, ST elevation or ST-segment depression) and normal clinical cardiovascular assessment
- 13. Note, a defunctioning colostomy or ileostomy is permitted to relieve impending rectal obstruction or severe local bowel symptoms
- 14. Lower age limit 18 years

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

Αll

Key exclusion criteria

- 1. Disease threatening the mesorectal fascia (i.e. disease = 1 mm from mesorectal fascia whether this is primary tumour, extra-mural vascular invasion or tumour deposit with irregular border or mixed signal intensity)
- 2. Stage T4b cancer with invasion into adjacent organs or structures
- 3. Enlarged pelvic sidewall (internal iliac) lymph nodes considered to be involved
- 4. Unequivocal evidence of metastatic disease (includes resectable metastases)
- 5. Severe local bowel symptoms of tenesmus, frequency (at least baseline grade 3 diarrhoea) or incontinence that have not been relieved by a defunctioning colostomy/ileostomy.
- 6. Pelvic sepsis
- 7. Metallic colonic/rectal stent in situ
- 8. Patient who has received previous pelvic radiotherapy
- 9. Patient with an uncontrolled infection
- 10. Pregnant, breast feeding or trying to conceive
- 11. Previous treatment with another investigational antitumoral therapy in the 30 days prior to beginning treatment (including chemotherapy, hormonal treatment, antibody therapy, immunotherapy, gene therapy, vaccine therapy, angiogenesis inhibitors, matrix metalloproteinase inhibitors, thalidomide, anti-VEGF/Flk-1 monoclonal antibodies, or other experimental drugs)

- 12. Patients with another previous or current malignant disease which in the judgement of the treating investigator is likely to interfere with treatment or the assessment of response.
- 13. Clinically significant cardiovascular disease (including myocardial infarction, unstable angina, symptomatic congestive heart failure, serious uncontrolled cardiac arrhythmia) = 1 year before enrollment
- 14. History of interstitial lung disease e.g. pneumonitis or pulmonary fibrosis or evidence of interstitial lung disease on baseline chest CT scan
- 15. Subject (male or female) is not willing to use highly effective methods of contraception (per institutional standard) during treatment and for 6 months (male or female) after the end of treatment
- 16. Previous malignancies in the preceding five years except for:
- -In situ cancer of the uterine cervix
- -Adequately treated basal cell skin carcinoma
- -Any early stage malignancy

Date of first enrolment 01/05/2012

Date of final enrolment 01/04/2013

Locations

Countries of recruitmentUnited Kingdom

Wales

Study participating centre
Cardiff University
Cardiff
United Kingdom
CF14 4YS

Sponsor information

Organisation

Cardiff University (UK)

ROR

https://ror.org/03kk7td41

Funder(s)

Funder type

Charity

Funder Name

Cancer Research 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	results	01/09/2018	11/04/2019	Yes	No
Basic results	Participant information sheet			No	No
HRA research summary		11/11/2025	28/06/2023		No
Participant information sheet			11/11/2025	No	Yes
Plain English results			24/01/2022	No	Yes