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

Submission date
17/05/2012

Recruitment status
No longer recruiting

Registration date
17/05/2012

Overall study status
Completed

Last Edited
24/01/2022

Condition category
Cancer

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
http://cancerhelp.cancerresearchuk.org/trials/trial-looking-chemotherapy-people-rectal-cancer-copernicus

Contact information

Type(s)
Scientific

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Additional identifiers

ClinicalTrials.gov (NCT)
NCT01263171

Clinical Trials Information System (CTIS)
2010-023083-40

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 pre-operative 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 x 109/L, neutrophil count =1.5 x109/L and platelet count =100 x109/L
10.2. Total bilirubin = 1.5 x ULRR, alkaline phosphatase = 5 x ULRR, and serum transaminase (either AST or ALT) =2.5 x 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
All

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 recruitment
United Kingdom

Wales

Study participating centre
Cardiff University
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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				No	No
HRA research summary			28/06/2023	No	No
Plain English results			24/01/2022	No	Yes