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Conservative approach in rectal cancer

Submission date 23/08/2013	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol
Registration date 30/10/2013	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 30/10/2013	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Locally advanced rectal cancer is usually treated with preoperative radiotherapy followed by surgery, regardless of the response to radiotherapy. There are issues with the surgical treatment of rectal cancer: surgical complications, illness and death. Patients with a major response at restaging workup (complete or near complete remission after radiochemotherapy) will be offered a local excision of the scar so that they avoid surgery.

Who can participate?
Patients with primary rectal cancer with clinical complete response or very good response after neo-adjuvant radiochemotherapy (a combined treatment using chemotherapy and radiotherapy).

What does the study involve?
Patients with complete or very good response after radiochemotherapy will undergo a local excision of the residual scar in a procedure called transanal endoscopic microsurgery (TEM). Patients who still have tumors after the radiochemotherapy will undergo a major surgical procedure called total mesorectal excision (TME).

What are the possible benefits and risks of participating?
Patients will not have to undergo surgery or will undergo less invasive surgery. As a result they will avoid the risks associated with surgery (such as wound and pelvic infection, chronic wound healing disturbances, abscess, colostomy, faecal or urinary incontinence, sexual dysfunction, death). A minority of patients (under 10%) is expected to develop a local failure, but most of those patients are expected to be cured by surgery.

Where is the study run from?
Patients will be recruited from the outpatient and inpatient clinic at the University Hospital of Ferrara, University Hospital of Modena and State Hospital of Forlì (Italy).

When is the study starting and how long is it expected to run for?
The study started recruiting in June 2013. Given the number of patients required, it is expected to last for at least 24 months.

Who is funding the study?
Emilia Romagna region, Italy.

Who is the main contact?
Dr Francesco Fiorica
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
P54B-GR2012

Study information

Scientific Title
An Improvement of tumor regression with a cancer-risk modulated Radiochemotherapy In local advanced rectal cancer (LARC) can avoid the need for major Surgery: a phase II study

Acronym
IRIS

Study objectives
Neo-adjuvant intensified radiochemotherapy in locally advanced rectal cancers can be used to obtain a high rate of complete or near complete remission. Patients with major response at restaging workup will be offered a local excision (TEM technique) of the scar. Patients with confirmed pathological complete response (PCR) or with a very good response (any ypT1 and ypT2-TRG2 score) will not undergo surgery. The TEM should be considered only as a staging procedure and the patients will be immediately submitted to TEM. The question is whether major surgery (with complications) can be avoided in patients with good response to radiochemotherapy.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Ethics Committee for Clinical Research of Ferrara University Hospital (03/2013)

Study design
Prospective single-stage phase II non-randomized clinical trial

Primary study design
Interventional

Secondary study design
Non randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Patients with primary local advanced rectal cancer

Interventions
Patients with major response (complete or very good response) after radiochemotherapy will undergo transanal endoscopic microsurgery (TEM) of the residual scar. After TEM, patients with confirmed PCR or with a minimal residual tumour (any ypT1 and ypT2-TRG2 score) will not be submitted to surgery. All patients will be closely followed by means of history taking, physical examination, endoscopy, MRI and CT or PET-CT.

Experimental treatment (radiochemotherapy intensified) is delivered to patients with locally advanced rectal cancer; patients with tumor disappearance, verified with local excision -TEM (transanal endoscopic microsurgery) are no more treated, instead patients wih tumors after radiochemotherapy are normally treated with major surgery (Total Mesorectal Excision).

Intervention Type
Other

Phase
Phase II

Primary outcome measure
Local recurrence at 2 and 5 years
All patients will be closely followed by means of history taking, physical examination, endoscopy, MRI and CT or PET-CT . During follow-up, quality of life and bowel function will be evaluated with EORTC QLQ-C30 and Bowel Function Questionnaire (BFQ) questionnaire respectively . Follow up will be every three months with a clear timetable.

Secondary outcome measures
1. Overall survival
2. Disease-free survival
3. Distant metastasis-free survival at 2 and 5 years
4. Pathologic response rate
5. Accuracy of restaging work-up
6. Quality of life
7. Toxicity

Overall study start date
01/06/2013

Completion date
31/07/2016

Eligibility

Key inclusion criteria
1. Patients (aged above 18) with histological proven adenocarcinoma of the distal part of the rectum (between 3 and 10 cm from anal verge)
2. T2-3 tumour without lymph nodes > 1.5 cm and/or lateral pelvic lymph nodes > 1 cm at MRI and/or endoanal ultrasound
3. Tumour size less than or equal to 5 cm
4. No evidence of metastatic disease as determined by CT scan of chest, abdomen, pelvis or other investigations such as PET scan or biopsy if required
5. Absolute Neutrophil Count (ANC) more than 1.5 x 109/l
6. Thrombocytes > 100 x 109/l
7. Creatinin clearance >50ml/min (according to the Cockcroft-Gault formula)
8. Total serum bilirubin < 24 mol/l or below <1.5 times the upper limit of the normal
9. Aspartate Aminotransferase (ASAT), Alanine Aminotransferase (ALAT): up to 5 times the upper limit
10. Colonoscopy or virtual colonoscopy should exclude synchronous colorectal lesions in other parts of the colon
11. Eastern Cooperative Oncology Group (ECOG) performance score 0-2
12. Fertile women should have adequate birth control during treatment
13. Mental/physical/geographical ability to undergo treatment and follow-up
14. Written informed consent (Italian language)

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
A maximum of 44 patients is required for this study. To obtain those 44 patients, it is necessary to treat 110 patients considering a complete and major tumor response of 40%.

Key exclusion criteria
1. Preoperative staging by pelvic MRI and/or EUS of any cT1, any cT4, or cT2, N0.
2. Patients with circumferential rectal tumor or tumors who are by other means unacceptable for TEM surgery (e.g. intra anal tumors, tumors within 3mm of mesorectal fascia).
3. Tumours which are mucinous (>50% mucin seen on MRI), as these are more likely to be PET negative.
4. Patients with faecal incontinence prior to the diagnosis of rectal cancer (complaints of soiling due to the tumor will not be an exclusion criterium).
5. Any contra-indication to MRI scanning
6. Severe uncontrollable medical or neurological disease.
7. Patients with secondary prognosis determining malignancies.
8. Patients who have been treated with radiotherapy on the pelvis.
9. Fenytoine and Allopurinol use.
10. Known DPD deficiency
11. Uncontrolled active infection,immune status, psychosis, or CNS disease.
12. Pregnant or lactating women.
13. Clinically significant (i.e. active) cardiovascular disease for example cerebrovascular accidents (≤ 6 months prior to treatment), myocardial infarction (≤ 6 months prior to treatment),
14. Unstable angina, New York Heart Association (NYHA) grade II or greater congestive heart failure, serious cardiac arrhythmia requiring medication.
15. Evidence of other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding giving reasonable suspicion of a disease or condition that contraindicates use of Capecitabine or patients at high risk for treatment complications.
16. History or evidence upon physical examination of CNS disease unless adequately treated (e. g., seizure not controlled with standard medical therapy).

Date of first enrolment
01/06/2013

Date of final enrolment
31/07/2016

Locations

Countries of recruitment
Italy

Study participating centre
Corso Giovecca 203
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44100

Sponsor information

Organisation
Regional Health and Social Agency (Agenzia Sanitaria e sociale Regionale- Regione Emilia Romagna) (Italy)

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40127

Sponsor type
Government

Website
http://www.saluter.it/

ROR
https://ror.org/01w36fb33

Funder(s)

Funder type
Research organisation

Funder Name
This protocol has been supported by the Emilia Romagna Region-University Research Program, called Young Researchers Alessandro Liberati 2012 (Programma di ricerca Regione-Università, Regione Emilia-Romagna, bando Giovani Ricercatori Alessandro Liberati 2012), Ref: PRUAO1GR-2012-009, Italy

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