

# Conservative approach in rectal cancer

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<b>Registration date</b> 30/10/2013	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 30/10/2013	<b>Condition category</b> Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> 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 Forli (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

f.fiorica@ospfe.it and francesco.fiorica@unife.it

## Contact information

### Type(s)

Scientific

### Contact name

Dr Francesco Fiorica

### Contact details

Corso Giovecca 203

Ferrara

Italy

44100

f.fiorica@ospfe.it

## Additional identifiers

### Protocol serial number

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)

## Primary study design

Interventional

## Study design

Prospective single-stage phase II non-randomized clinical trial

## Study type(s)

Treatment

## 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 with tumors after radiochemotherapy are normally treated with major surgery (Total Mesorectal Excision).

## Intervention Type

Other

## Phase

Phase II

## Primary outcome(s)

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.

## Key secondary outcome(s)

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

## 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  $1.5 \times 10^9/l$
6. Thrombocytes >  $100 \times 10^9/l$
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

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

All

### **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 ( $\leq 6$  months prior to treatment), myocardial infarction ( $\leq 6$  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

Ferrara

Italy

44100

## Sponsor information

**Organisation**

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

**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**

**Individual participant data (IPD) sharing plan**

**IPD sharing plan summary**

Not provided at time of registration