ISRCTN02406823 https://doi.org/10.1186/ISRCTN02406823

Surgery alone In low rectal cancer

Submission date 14/04/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 06/06/2013	**Overall study status** Completed	
Last Edited 09/04/2019	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-surgery-alone-for-people-with-rectal-cancer-sailor

Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
CRT/LARC/ABM/v2.1

Study information

Scientific Title
Multicentre randomised phase II feasibility study evaluating neoadjuvant chemoradiotherapy plus surgery with Surgery Alone In LOw Rectal cancer

Acronym

SAILOR

Study objectives
Current hypothesis as of 24/02/2014:
To explore the feasibility of phase III through:
Primary objective to test willingness of eligible patients to be randomised to a surgery-alone arm
Secondary objectives to estimate the change in quality of life with omission of CRT in resectable low rectal cancer; to test whether omission of CRT for resectable locally advanced low rectal cancer changes oncological safety measured by rate of surgical margin involvement, local recurrence and systemic recurrence at 2 years.

Previous hypothesis:
The trial has a dual hypothesis. The first hypothesis is that the Health Related Quality of Life in patients having surgery-alone is significantly better than patients who receive chemoradiation before surgery.
The second hypothesis is that in there is no significant difference in the rates of surgical margin involvement when chemoradiation is omitted for selected patients with locally advanced rectal cancer, thus ensuring the safety of this selective approach.

On 24/02//2014 the following changes were made to the trial record:
1. The public title was changed from 'Pilot study comparing neoadjuvant chemoradiotherapy plus surgery and surgery alone in locally advanced rectal cancer' to 'Surgery Alone In LOw Rectal cancer'
2. The scientific title was changed from 'Multicentred randomised controlled trial comparing neoadjuvant chemoradiotherapy plus surgery and surgery alone in locally advanced rectal cancer: a pilot study' to 'Multicentre randomised phase II feasibility study evaluating neoadjuvant chemoradiotherapy plus surgery with Surgery Alone In LOw Rectal cancer'
3. The anticipated start date was changed from 01/01/2014 to 01/10/2014
4. The anticipated end date was changed from 01/01/2016 to 01/10/2018
5. The target number of participants was changed from 60 to 80
6. The sources of funding field was changed from 'Awaiting decision from National Institute for Social Care and Health Research (NISCHR), Research for Patient and Public Benefit Wales (RfPPB Wales) - UK' to 'Funding decision awaited from Cancer Research UK (July 2014)'.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Multicentred randomised controlled feasibility trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied

Rectal cancer

Interventions
Schedule of Treatment
Standardised radiotherapy: pre-operative radiotherapy with 45 Gy in 25 daily fractions over 5 weeks concurrent with either continuous-infusion 5-FU (225 mg/m2/day throughout the course of radiation therapy) 7 days a week for 5.5 weeks or capecitabine orally (PO) twice daily 5 days a week for 5.5 weeks.
Formation of defunctioning colostomy before neoadjuvant chemoradiotherapy is permissible in the situation of severe symptoms at the discretion of the recruiting clinician.
Assessment of response to CRT: Subsequent surgery is to be performed 8-12 weeks after completion of chemoradiotherapy. Patients should be restaged at 6 weeks after completion of CRT (minimum of CT thorax/abdomen/pelvis and MRI pelvis; endorectal ultrasound and examination under anaesthesia permitted depending on local policy). If complete clinical response (CCR) to CRT is suspected then patients are required by the protocol to undergo APER surgery as originally planned. See Criteria for Premature Withdrawal if this is not considered appropriate.
Surgery-The abdominal phase of the abdominoperineal excision can be performed by either laparoscopic or open approach at discretion of the surgeon. The patient positioning for the perineal phase can be either supine or prone according to surgeon preference. A cylindrical perineal excision of the tumour, taking the levator ani (pelvic floor) musculature widely at their origins, is an essential study requirement. The technique of perineal reconstruction is at the discretion of the surgeon. This may include primary closure, use of a biological implant or plastic surgical reconstruction (myocutaneous/fasciocutaneous flap).

Intervention Type
Other

Phase
Not Specified

Primary outcome(s)
Current primary outcome measures as of 24/02/2014:
This study will primarily test the feasibility of a phase III randomised study by measuring willingness of participants to be randomised; willingness of clinicians to recruit participants; and testing appropriateness of the proposed outcome measures, to include choice of QOL tools and measurement of response rates to questionnaires.
The paired principal outcomes are:
1. Disease-specific quality of life measures using the EORTC QLQ-C30 and QLQ-CR29 tools. Quality of life will be assessed at the same timepoints between the groups (enrolment, prior to surgery, 1 month after surgery, and at 3 months, 6 months, 12 months, 18 months and 24 months) with a supplementary timepoint in group 1 (at end of chemoradiotherapy)
2. Circumferential Resection Margin (CRM) distance (as early surrogate marker for local recurrence when less than 1 mm) and both local and systemic recurrence rates at 2 years based on CT imaging.

Previous primary outcome measures:
The paired principal outcomes are:
1. Disease-specific quality of life measures, to include bowel, bladder and sexual function. The Quality of Life tools selected are FACT-C; EORTC QLQ-C30 and I-QOL (see supplementary files). Quality of life will be assessed at enrolment, at the end of chemoradiotherapy, prior to

surgery, 1 month after surgery, and at 3 months, 6 months, 12 months, 18 months and 24 months.
2. Circumferential Resection Margin (CRM) distance (as early surrogate marker for local recurrence when less than 1mm).

Key secondary outcome(s))

Current secondary outcome measures as of 24/02/2014:
1. Clinical endpoints:
1.1. Early disease-free survival at 2 years
1.2. Costs and consequences of neo-adjuvant CRT plus surgery compared with surgery alone through economic analysis and Patient Reported Outcome Measures (EQ-5D-5L);
2. Acute and late toxicity related to chemotherapy and/or radiotherapy:
2.1. EORTC Common Toxicity Criteria version 4 (2009),
2.2. RTOG/EORTC Late Morbidity Scoring Scheme
3. Rate of development of irresectable primary tumour after CRT;
4. Perioperative complication rates:
4.1. Organ specific (Cardiovascular, Respiratory, Renal/Urological, Gastrointestinal, Infectious /septic, abdominal wound related)
4.2. Rate of Perineal wound healing (at 3 months)
4.3. Transfusion requirement (within 30 days of surgery)
4.4. Return to theatre/reoperation
5. Length of stay (postoperative)
6. 30-day perioperative mortality
7. Time to commencement of adjuvant chemotherapy after surgery
8. Pathological outcomes to include:
8.1. T stage (TNM)
8.2. N stage (TNM)
8.3. Presence of extramural vascular invasion
8.4. Distance to circumferential resection margin
8.5. Distance to dentate line
8.6. Plane of mesorectal excision (mesorectal/ intramesorectal/ muscularis propria) and perineal excision (Levator/ sphincteric/ intrasphincteric) as proxy of surgical quality
8.7. Presence of specimen perforation
8.8. Tumour regression grade (in response to chemoradiotherapy)
8.9. Rate of pathological complete response

Previous secondary outcome measures:
1. Acute and late toxicity related to chemotherapy and/or radiotherapy (EORTC Common Toxicity Criteria version 4 (2009), RTOG/EORTC Late Morbidity Scoring Scheme)
2. Perioperative complication rates
Organ specific (Cardiovascular, Respiratory, Renal/Urological, Gastrointestinal, Infectious/septic, abdominal wound related)
3. Rate of Perineal wound healing (at 3 months)
4. Transfusion requirement (within 30 days of surgery)
5. Return to theatre/ reoperation
6. Length of stay (postoperative)
7. 30 day perioperative mortality
8. Pathological outcomes- Royal College of Pathologists Dataset for colorectal cancer (2nd edition), 2007, to include:
8.1. T stage (TNM)
8.2. Total node yield

8.3. Involved node number
8.4. N stage (TNM)
8.5. Presence of extramural vascular invasion
8.6. Distance to circumferential resection margin
8.7. Distance to dentate line
8.8. Plane of excision (mesorectal/intramesorectal/muscularis propria) as proxy of surgical quality
8.9. Tumour regression grade (in response to chemoradiotherapy)

Completion date
30/06/2019

Eligibility

Key inclusion criteria
Current inclusion criteria as of 24/02/2014:
1. Age 18 years and older
2. Histologically confirmed rectal adenocarcinoma
3. Radiologically measurable or clinically evaluable disease
4. Low rectal cancer, defined as within 6cm of anal verge on rigid sigmoidoscopy and considered to require abdominoperineal resection (APR) rather than restorative procedure (anterior resection)
5. Potentially resectable local disease by surgery alone with clear CRM (where visible on MRI) or predicted surgical resection margin (where CRM absent in distal tumours) as determined by MRI
6. Clinical disease stage (MRI+/- endorectal US):
6.1. cT3a/b (<10 mm) disease within 6 cm of anal verge; or for tumours at/below level of puborectalis
6.2. through full thickness of muscularis propria (cT2) disease at level of puborectalis
7. Involvement of internal anal sphincter or intersphincteric space without extension into adjacent levator plate,
8. TanyN1 (resectable)
9. WHO Performance status 0, 1, or 2
10. Neutrophil count ≥ 1,500/mm^3
11. Platelets ≥ 100,000/mm^3
12. Haemoglobin > 80 g/L
13. Total bilirubin ≤ 1.5x ULN
14. AST & ALT ≤ 3 x ULN
15. Creatinine ≤ 1.5 x ULN
16. Negative pregnancy test
17. Patient of child-bearing potential willing to employ adequate contraception
18. Willing to return to enrolling medical site for all study assessments
19. No other invasive malignancy ≤ 5 years prior to registration
20. No concurrent disease that, in the judgment of the clinician obtaining informed consent, would make the patient inappropriate for entry into this study
21. No chemotherapy within 5 years prior to registration (hormonal therapy is allowable if the disease-free interval is ≥ 5 years)
22. No prior pelvic radiation

Previous inclusion criteria:
1. Aged 18 years and older
2. Pathologically confirmed rectal adenocarcinoma

3. Radiologically measurable or clinically evaluable disease
4. Low rectal cancer, defined as within 6cm of anal verge on rigid sigmoidoscopy and considered to require abdominoperineal excision (APER)
5. Potentially resectable local disease by surgery alone with clear margins as determined by MRI
6. Clinical disease stage (MRI+/- endorectal US):
6.1. T3a/b/c disease
6.2. T4 disease with sole involvement of internal/external sphincter/ adjacent (<10mm) levator plate or posterior wall of vagina
6.3. TanyN1 (resectable)
7. WHO Performance status 0, 1, or 2
8. Neutrophil count ≥ 1,500/mm³
9. Platelets ≥ 100,000/mm³
10. Haemoglobin > 8.0 g/dL
11. Total bilirubin ≤ 1.5x ULN
12. AST & ALT ≤ 3 x ULN
13. Creatinine ≤ 1.5 x ULN
14. Negative pregnancy test
15. Patient of child-bearing potential willing to employ adequate contraception
16. Willing to return to enrolling medical site for all study assessments
17. No other invasive malignancy ≤ 5 years prior to registration
18. No concurrent disease that, in the judgment of the clinician obtaining informed consent, would make the patient inappropriate for entry into this study
19. No chemotherapy within 5 years prior to registration (hormonal therapy is allowable if the disease-free interval is ≥ 5 years)
20. No prior pelvic radiation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
3

Key exclusion criteria
Current exclusion criteria as of 24/02/2014:
1. Preoperative chemoradiotherapy absolutely indicated, for example MRI-predicted CRM/MRF involvement (<1 mm) by primary or nodal disease, or otherwise unresectable disease;
2. cT3c or d (>10 mm);
3. Adjacent organ involvement at entry (prostate, seminal vesicles, sacrum or coccyx; T4b) requiring multivisceral resection/ pelvic exenteration;

4. For low tumours at level of puborectalis sling: lateral extension of tumour into external anal sphincter or beyond puborectalis sling into levator plate;
5. Extramural vascular invasion on MRI;
6. Early stage rectal cancer (T1, T2 above level of levators) unless node positive;
7. Locally perforated disease (T4a);
8. Fistulating disease (vagina, perianal skin, adjacent hollow organ);
9. Disease extrusion through anus;
10. cN2 disease;
11. Lateral pelvic/ para-aortic lymphadenopathy (>10 mm by size criteria);
12. Unresectable metastatic disease (M1) (potentially resectable disease permitted);
13. Previous pelvic radiotherapy;
14. Unfit for major surgery;
15. Pregnancy;
16. Contraindication to MRI (metal implants etc);
17. Contraindication to 5-FU based chemotherapy (including drug interactions);
18. WHO Performance Status 3 or 4;
19. Unwilling to consent to trial participation

Previous exclusion criteria:
1. Preoperative chemoradiotherapy absolutely indicated, for example predicted CRM involvement (<2 mm) by primary or nodal disease, or otherwise unresectable disease;
2. Adjacent organ involvement (prostate, seminal vesicles, sacrum or coccyx; T4b) requiring multivisceral resection/pelvic exenteration; wide (>10mm) levator involvement
3. Early stage rectal cancer (T1, T2) unless node positive
4. Locally perforated disease (T4a)
5. Disease extrusion through anus
6. Lateral pelvic/ paraaortic lymphadenopathy
7. Metastatic disease (M1)
8. Previous pelvic radiotherapy
9. Pregnancy
10. Contraindication to 5-FU based chemotherapy
11. WHO Performance Status 3 or 4
12. Unwilling to consent to trial participation

Criteria for Premature Withdrawal
1. Withdrawal of consent
2. Failure to meet inclusion criteria (delayed)
3. Development of irresectable metastatic disease
4. Development of irresectable primary tumour after randomisation
5. Change in surgical procedure following chemoradiotherapy. In the event of significant tumour regression a sphincter-saving operation (low anterior resection) may be considered more appropriate by the responsible clinician than a sphincter-excising APR procedure.

Date of first enrolment
01/10/2014

Date of final enrolment
31/03/2019

Locations

Countries of recruitment
United Kingdom

Wales

Ireland

Study participating centre
Singleton Hospital
Swansea
United Kingdom
SA2 8QA

Sponsor information

Organisation
Morriston Hospital (UK)

ROR
https://ror.org/01p830915

Funder(s)

Funder type
Charity

Funder Name
Funding decision awaited from Cancer Research UK (July 2014)

Results and Publications

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?
Protocol article	protocol	21/11/2016		Yes	No