

Can we save the rectum by watchful waiting or transanal surgery following (chemo) radiotherapy versus total mesorectal excision for early rectal cancer?

Submission date 26/09/2016	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 20/10/2016	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 14/11/2022	Condition category Cancer	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

<https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-surgery-or-different-types-of-radiotherapy-for-rectal-cancer-star-trec>

Study website

<https://www.birmingham.ac.uk/research/crctu/trials/startrec/index.aspx>

Contact information

Type(s)

Scientific

Contact name

Mr Simon Bach

ORCID ID

<http://orcid.org/0000-0001-8412-7241>

Contact details

Cancer Research UK Clinical Trials Unit (CRCTU)
Institute of Cancer and Genomic Sciences
University of Birmingham
Edgbaston
Birmingham
United Kingdom
B15 2TT
+44 (0)121 414 7671
STAR-TREC@Trials.bham.ac.uk

Additional identifiers

EudraCT/CTIS number

2016-000862-49

IRAS number

ClinicalTrials.gov number

NCT02945566

Secondary identifying numbers

CPMS 31203

Study information

Scientific Title

STAR-TREC: Can we Save the rectum by watchful waiting or TransAnal surgery following (chemo) Radiotherapy versus Total mesorectal excision for early REctal Cancer?

Acronym

STAR-TReC

Study objectives

Current study hypothesis as of 28/06/2021:

The phase II component will assess the feasibility of a large, multi-centre randomised trial comparing radical surgery versus organ saving treatment using (chemo)radiotherapy followed by selective transanal microsurgery.

The phase III component will evaluate two contrasting organ preservation strategies (either long-course chemoradiotherapy or short-course radiotherapy) for the treatment of early stage rectal cancer in terms of organ preservation rates, toxicity (clinician and patient-reported) and Health-Related Quality of Life (HRQoL).

The phase III study will also include a standard TME radical surgery (non- randomised) comparator arm encompassing reconstructive (low anterior resection) and non-reconstructive (abdominoperineal excision, low Hartmann's procedure) approaches.

Previous study hypothesis:

The aim of this study is to assess the feasibility of successfully recruiting to a large, multi-centre randomised trial comparing radical surgery versus organ saving treatment using (chemo) radiotherapy followed by selective transanal microsurgery, to evaluate whether it is possible to accelerate patient recruitment from 2 per month, as attained in the previous TREC study, to 6 per month over a two-year period.

Ethics approval required

Old ethics approval format

Ethics approval(s)

East Midlands – Leicester Central Research Ethics Committee, 23/09/2016, 16/EM/0186

Study design

An international multi-centre randomized phase II feasibility trial and an international multi-centre open-label rolling phase II/III trial with a partially randomised patient preference design

Primary study design

Interventional

Secondary study design

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

Specialty: Cancer, Primary sub-specialty: Colorectal; UKCRC code/ Disease: Cancer/ Malignant neoplasms of digestive organs

Interventions

Current interventions as of 28/06/2021:

Patients will be recruited following informed consent, which will be conducted in accordance with Good Clinical Practice standards, after all baseline assessments are completed and all eligibility criteria have been confirmed. STAR-TREC is a rolling phase II/III study comprising the following components:

Phase II:

The STAR-TREC phase II feasibility component is an international, multi-centre, randomised trial, comprising a 1:1:1 randomisation for eligible subjects with a small, clinically localised rectal cancer between:

1. Conventional TME surgery
2. Organ saving utilising long course concurrent chemoradiation
3. Organ saving utilising short course preoperative radiotherapy.

The phase II component will be closed once approximately 120 patients are recruited and all necessary approvals for protocol version 4.0 implementing the phase III design are obtained. Target recruitment rates are ≥ 4 and ≥ 6 patients randomised per month at 12 and 24 months respectively for total accrual of 120 international cases. Each individual country will attempt to exceed the minimum recruitment required to sustain phase III (UK 75, the Netherlands 75, Denmark 30). If recruitment is on target in year two then consideration will be given to an early application for transition to phase III with a funding application and a formal protocol amendment.

Phase III:

International, multi-centre, open-label, rolling phase II/III trial with a partially randomised patient preference design. Patients will choose organ preservation or standard surgery. Those who prefer organ preservation will be randomised 1:1 between:

1. Organ preservation with mesorectal CRT. Capecitabine: 825 mg/m² orally, b.d., on radiotherapy days. Radiotherapy: A dose of 50 Gy applied to the primary tumour and surrounding mesorectum in 25 fractions of 2 Gy, 5 days a week.
 2. Organ preservation with mesorectal SCRT. A dose of 25 Gy applied to the primary tumour and surrounding mesorectum in 5 fractions of 5 Gy, 5 days a week.
- Those who prefer standard surgery or have no preference will undergo standard TME surgery without neoadjuvant radiotherapy treatment.

Phase II and III:

For organ-preserving strategies, clinical response to radiotherapy determines the next treatment step. Radiotherapy response is evaluated using clinical exam, endoscopy and MRI. The first assessment at 11-13 weeks (from radiotherapy start) using composite clinical, endoscopic and MRI based assessment will identify a minority of non-responders who should convert to TME surgery. Patients demonstrating a satisfactory radiotherapy response at 11-13 weeks will be reassessed by endoscopy at 16-20 weeks. Re-evaluation at 16-20 weeks determines if the STAR-TREC criteria for complete response (CR) are met. Patients who achieve CR may progress directly to active surveillance. Those who do not fulfil the criteria for CR will progress to excision biopsy with TEM.

Previous interventions:

After all eligibility criteria have been confirmed and following informed consent, which will be conducted in accordance with Good Clinical Practice standards, and completion of the baseline assessments, patients will be randomised to one of three groups in a 1:1:1 basis using a computer-generated program at the Birmingham Clinical Trials Units (BCTU).

Group 1: Participants undergo conventional TME surgery. This will encompass both reconstructive and non-reconstructive approaches to rectal resection using the principles of TME surgery. The former includes low anterior resection, the latter abdominoperineal excision or low Hartman's procedure. Surgeons may use either a laparoscopic, robotic or open approach to surgery. Hybrid approaches (combined laparoscopic and open) are also permitted. The quality of surgery will be measured using a standardised histopathological assessment that grades whether surgery was performed according to the principles of TME.

Group 2: Participants undergo organ using long course concurrent chemoradiation (CRT). This involves concurrent chemoradiotherapy consisting of treatment with capecitabine, administered at a dose of 825 mg/m² bid on days of radiotherapy treatment (excluding weekend days when patients do not undergo radiotherapy treatment). Capecitabine is taken orally twice a day in equal doses for 5 days per week (normally Monday – Friday), on the days of radiotherapy administration only, throughout the 5 week course of radiotherapy. If radiotherapy is not given (e.g. due to machine maintenance or bank holiday), then capecitabine should not be given that day either. Capecitabine treatment can begin on any day of the week; however, there is normally no capecitabine treatment on Saturday or Sunday, unless radiotherapy is given on one of these days. Patients are asked to take capecitabine with a glass of water each day within 30 minutes after the ingestion of food (ideally after breakfast and evening meals), commencing the morning of the first dose of radiotherapy treatment. If patients have difficulty swallowing tablets, it is possible to dissolve the tablets in approximately 200 ml of lukewarm water. There is no stability data for any form of capecitabine suspension, so this should be done immediately prior to use and the solution swallowed immediately, rinsing to ensure all of the suspension has been ingested. As the solution has a bitter taste, flavouring with a fruit juice or squash (except grapefruit juice) is allowed.

Group 3: Participants undergo organ using short course radiotherapy (SCPRT). This involves a dose of 25Gy, applied, to the primary tumour and surrounding mesorectum in 5 fractions of 5 Gy, 5 days a week. A total dose of 25 Gy in 5 daily fractions over a total time of 1 week should be delivered, treating 5 days per week, 1 fraction per day, using 5 Gy per fraction.

For participants in group 1, surgical morbidity will be recorded post-operatively until 30 days after surgery. Follow-up after standard TME surgery will differ significantly compared to the organ preserving strategies. Both will include regular clinical follow-up as per usual national practice. Each centre can perform additional visits, endoscopies or imaging as per national protocol or patient/doctors preference. The minimal required follow-up after TME surgery will be at 30-days post-operatively and then 3, 6 12, 24 and 36 months after TME surgery and is detailed in the protocol. CT of chest-abdomen is required in order to have a reliable disease free survival of all patients in this study after 24 months. CT or MRI pelvis is also required in order to have a reliable pelvic recurrence rate of all patients in this study after 24 months. The information routinely recorded in normal clinical notes should be sufficient for completion of the annual follow-up case report forms.

For participants in groups 2 and 3, radiotherapy will be administered as per protocol and radiotherapy delivery and toxicities up to 3 weeks after the completion of radiotherapy will be recorded. Follow-up after (chemo)radiotherapy will include regular follow-up as per usual practice. To monitor the need for local excision, radical surgery or watchful waiting, mucosal or lymph node recurrence should be carefully monitored and additional examinations are mandatory as listed below. If patients are treated with radical surgery (TME) the follow-up schedule as described in above for patients in group 1, 'Clinical assessments and follow-up after TME surgery' will be used. In the first year, all organ preserved patients will undergo a MRI and endoscopy every 3 months. CT of chest-abdomen is required in order to have a reliable disease free survival of all patients in this study after 24 months. The information routinely recorded in normal clinical notes should be sufficient for completion of the annual follow-up case report forms. If patients will undergo TME surgery because of incomplete response after (chemo) radiation therapy or in case of recurrence, follow up will be performed at 3, 4.5, 6, 9, 12, 18, 24 and 36 months after (Chemo) Radiation Therapy and specifics are detailed in the protocol.

Intervention Type

Mixed

Primary outcome measure

Current primary outcome measure as of 28/06/2021:

Phase II:

Recruitment rate measured by recording the number of eligible participants who consent to participate in the trial at 12 and 24 months.

Phase III:

Proportion of patients who prefer organ preservation with successful organ preservation measured by recording the number of participants with an in-situ rectum (includes patients subject to transanal local resection), no defunctioning stoma, and an absence of active loco-regional cancer failure at 30 months from the first day of (chemo)radiotherapy treatment

Previous primary outcome measure:

Recruitment rate is measured by recording the number of eligible participants who consent to participate in the trial at 12 and 24 months.

Secondary outcome measures

Current secondary outcome measures as of 28/06/2021:

Phase II:

1. Procurement of STAR-TREC funding by one international partner
2. Opening of STAR-TREC by one international partner
3. Efficacy of organ preserving treatment arm on completion of phase II study measured by the organ saving rate at 12 months (following randomisation) in the experimental arms, where efficacy is defined as an organ saving rate of >50%.
4. Additional outcome measures pertinent to a future phase III study examining the safety and efficacy of organ saving versus standard surgery will also be collected:
 - 4.1. Safety will be assessed using:
 - 4.1.1. Accuracy of MRI in predicting STAR-TREC eligibility
 - 4.1.2. 30-day mortality
 - 4.1.3. 6 month mortality
 - 4.1.4. Surgical morbidity
 - 4.1.5. Rate of tumour recurrence or regrowth within the bowel wall (experimental arm)
 - 4.1.6. Rate of tumour recurrence within the mesorectum (experimental arm)
 - 4.1.7. Rate of distant metastases
 - 4.1.8. Pelvic failure rate: expressed as a sum of the following unresectable pelvic tumour, cases requiring beyond TME surgery, or tumour recurrence or regrowth ≤ 1 mm from the circumferential surgical margin after TME surgery.
 - 4.1.9. Bowel, bladder and sexual dysfunction (measured by EORTC QLQ CR29 & C30, LARS score, and ICIQ-MLUTS/ICIQ-FLUTS) at 12 and 24 months compared to baseline.
 - 4.2. Efficacy will be assessed using:
 - 4.2.1. Proportion of patients with/ without a stoma at 30 days and one year
 - 4.2.2. Histopathological assessment of tumour down-staging following radiotherapy according to depth of tumour invasion and the incidence of other high-risk features in comparison to non-irradiated (control) group
 - 4.2.3. Proportion of patients identified by clinical and MRI assessment as suitable for active monitoring
 - 4.2.4. Conversion rates from organ saving to radical surgery
 - 4.2.5. Disease free survival
 - 4.2.6. Quality of life (measured by EORTC QLQ CR29 & C30, EuroQol EQ-5D, LARS score and ICIQ-MLUTS/ICIQ-FLUTS) at 12 and 24 months compared to baseline.
 - 4.2.7. Overall survival

Phase III:

Secondary outcomes for the randomised comparison between organ-preserving strategies:

1. Clinician-reported acute treatment related toxicity up to 30 days following completion of (chemo)radiotherapy
2. Proportion of patients with CR to (chemo)radiation therapy
3. Proportion of patients undergoing transanal local excision
4. Time to event of organ loss assessed for patients who prefer organ preservation; defined as the length of time from the start date of trial treatment until TME surgery
5. Non-regrowth pelvic tumour control to 36 months; defined as the length of time from the start date of trial treatment until death (any cause) or development of unequivocal pelvic recurrence but not including patients who developed local regrowth which was resected with clear margins using standard TME surgery
6. Metastasis free survival to 36 months; defined as the length of time from the start date of trial treatment until death (any cause) or detection of distant metastasis
7. Non-regrowth -disease free survival to 36 months; defined as the length of time from the start of trial treatment until death (any cause), detection of local pelvic recurrence or distant

metastasis but not including patients who developed local regrowth which was resected with clear margins using standard TME surgery

8. Overall survival to 60 months defined as the length of time from the start date of trial treatment until death (any cause)

Secondary endpoints for analyses incorporating the standard surgery comparator (phase II: randomised comparison; phase III: non-randomised comparison):

1. Clinician-reported acute treatment related toxicity up to 30 days following completion of (chemo)radiotherapy or date of initial surgery
2. Non-regrowth pelvic tumour control to 36 months; defined as the length of time from the start date of (chemo)radiotherapy or date of initial surgery until death (any cause) or development of unequivocal pelvic recurrence but not including patients who preferred organ preservation and developed local regrowth which was resected with clear margins using standard TME surgery
3. Metastasis-free survival to 36 months; defined as the length of time from the start date of trial treatment or date of initial surgery until death (any cause) or detection of distant metastasis
4. Disease-free survival to 36 months; defined as the length of time from the start date of trial treatment or date of initial surgery until death (any cause), detection of local pelvic recurrence or distant metastasis but not including patients who developed local regrowth which was resected with clear margins using standard TME surgery
5. Overall survival to 60 months defined as the length of time from the start date of trial treatment or date of initial surgery until death (any cause)
6. Decision regret measured using the validated Decision regret scale questionnaire/Treatment decision questionnaire at 24 months. The Decision Regret Scale is a 5-item Likert-type measure written to assess regret or remorse following a medical decision that takes less than 5 minutes to complete. High scores suggest high regret over a health care decision. Scores may be transformed to a scale of 0 (no regret) to 100 (high regret).

Secondary endpoint for analyses of patient-reported outcomes including symptomatic toxicity and health-related quality of life (HRQoL).

1. Patient-reported symptomatic toxicity, health economics and HRQoL, measured using the following questionnaires at baseline (after informed consent is obtained but before trial entry), 3, 12, 24, and 36 months after the start of trial-specific treatment:

1.1. European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30, a 30-item questionnaire developed by the European Organization for Research and Treatment to assess generic aspects of QoL of cancer patients; such as physical, psychological, and social functions. It is composed of 5 multi-item scales (physical, role, social, emotional and cognitive functioning) and 9 toxicity related single items.

1.2. The Colorectal Cancer Module developed by the European Organization for Research and Treatment (EORTC QLQ-CR29) is used in conjunction with the EORTC QLQ-C30 to assess quality of life in patients with colorectal cancer.

1.3. The EuroQol 5-dimension 3-level questionnaire (EuroQoL EQ-5D-3L) collects information about five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression and is the standard questionnaire used in health economic evaluation. The results can be combined into a 5-digit number that describes the patient's health state which in turn can be assigned a utility score. The questionnaire also includes a visual analogue scale to record the patient's self-rated health on a vertical visual scale.

1.4. The International Consultation on Incontinence Modular Questionnaire on Male Lower Urinary Tract Symptoms (ICIQ-MLUTS) is a questionnaire for evaluating male lower urinary tract symptoms and impact on quality of life composed of 13 items which was derived from the fully validated ICSmaleSF questionnaire.

1.5. The International Consultation on Incontinence Modular Questionnaire on Female Lower

Urinary Tract Symptoms (ICIQ-FLUTS) is a validated questionnaire for evaluating female lower urinary tract symptoms and impact on quality of life composed of 12 items which was derived from the fully validated BFLUTS-SF questionnaire.

1.6. Low Anterior Resection Syndrome (LARS) Score is a validated, concise and easy-to-use questionnaire for assessment of bowel dysfunction following a sphincter-preserving low anterior resection with or without radiotherapy for rectal cancer. The results distinguish 3 clinically meaningful severity categories ("no LARS," "minor LARS," and "major LARS").

2. Analysis of patient-reported symptomatic toxicity and HRQoL health-related quality of life at 3, 12, 24, and 36 months compared to baseline will be conducted incorporating the following comparisons:

2.1. Randomised comparison between organ-preserving strategies

2.2. Randomised (phase II data) and non-randomised (phase III data) comparisons between organ preserving strategies and the standard surgery comparator

Previous secondary outcome measures:

1. Ability of a single international partner to procure independent funding in year 1 is assessed through seeing whether the study being carried out internationally

2. Ability of a single international partner to open the study to recruitment in year 1 is assessed through seeing whether the study being carried out internationally

3. Organ saving rate in the experimental arms at 12 months (from randomisation) is assessed through review of data collected on the annual follow-up form

4. Proportion of patients undergoing TME surgery accurately staged and satisfying inclusion/exclusion criteria is assessed through the MRI data collected at baseline

5. Proportion of patients identified by MRI suitable for active monitoring based on mrTRG assessment is assessed through the MRI data collected at baseline

6. Three-year pelvic failure rate defined as the proportion of patients in each arm with:

6.1. Unresectable pelvic tumor

6.2. Uelvic tumour requiring beyond TME surgery

6.3. ≤ 1 mm circumferential resection margin after TME surgery

and is assessed through the data collected on the 36-month annual follow-up form and also the 36 Month MRI scan

7. Overall survival is assessed through the annual follow-up at 12, 24, and 36 months

8. Stoma free survival is assessed through the annual follow-up form at 30 days and 12 months post-surgery

9. Health Related Quality of Life (HR QoL) measured by EORTC QLQ CR29 & C30, EuroQoL EQ-5D will be assessed baseline and 12, 24 months post randomisation

10. Bowel, bladder, and sexual dysfunction measured by LARS score and ICIQ-MLUTS/ICIQ-FLUTES will be assessed baseline and 12, 24 months post randomisation

Overall study start date

01/07/2016

Completion date

31/12/2027

Eligibility

Key inclusion criteria

Current participant inclusion criteria as of 28/06/2021:

1. Biopsy proven adenocarcinoma of the rectum

2. MRI-defined $\leq T3b$ (with ≤ 5 mm of mesorectal invasion) rectal tumour or endorectal ultrasound-

defined \leq uT3b rectal cancer (optional: in centres where high quality endorectal ultrasound (ERUS) is available or patient unable to tolerate MRI)

3. MDT determines that all of the treatment options TME surgery, CRT, SCPRT, and TEM are feasible

4. Eastern Cooperative Oncology Group (ECOG) performance status 0-1

5. Able and willing to provide written informed consent for the study

For patients choosing organ preservation only:

1. If female and of childbearing potential must fulfil both of the following:

1.1. Have a negative pregnancy test within 7 days prior to study entry

1.2. Agree to use adequate, medically approved, contraceptive precautions from trial entry until 6 months after the end of study treatment

2. If a non-sterilised male with a partner of childbearing potential, must agree to use adequate, medically approved, contraceptive precautions from trial entry until 6 months after the end of study treatment

Previous participant inclusion criteria:

1. Biopsy proven adenocarcinoma of the rectum

2. mriT1-3bN0 (with \leq 5mm of mesorectal invasion) rectal tumour or endorectal ultrasound defined rectal cancer uT1- uT3b (optional: in centres where high quality ERUS is available and patient unable to tolerate MRI)

3. MDT determines that all of the following treatment options are feasible: (a) TME surgery, (b) CRT (c) SCPRT d) TEM Patients with equivocal radiological lesions e.g. mesorectal, retroperitoneal, liver, lung are eligible if agreed by MDT

4. Aged 16 or over in UK (18 or over in the Netherlands and Denmark).

5. Estimated creatinine clearance >50 mls/min

6. Absolute neutrophil count $>1.5 \times 10^9/l$; platelets $>100 \times 10^9/L$

7. Serum transaminase

Participant type(s)

Patient

Age group

Adult

Lower age limit

16 Years

Sex

Both

Target number of participants

Phase II: Aggregate total of 120 international cases (80 patients recruited to the organ preservation arms, CRT and SCRT, and 40 patients recruited to the standard surgery arm). Phase III: Aggregate total of 300 patients randomised to the organ preservation arms (CRT and SCRT). Estimated 80 patients recruited internationally to the standard surgery comparator arm.

Key exclusion criteria

Current participant exclusion criteria as of 28/06/2021:

1. Concomitant or previous malignancies within 3 years prior to trial entry, except those that in the opinion of the MDT are unlikely to relapse within 3 years or lead to death within 5 years

2. Unequivocal evidence of metastatic disease (includes resectable metastases). Patients with equivocal radiological lesions (e.g. retroperitoneal, liver, lung) that are not classified as M1 are eligible if agreed by MDT.
3. MRI node positive ($\geq N1$, defined by protocol guidelines)
4. MRI extramural vascular invasion (mriEMVI) positive (defined by protocol guidelines)
5. MRI defined mucinous tumour
6. Mesorectal fascia threatened (≤ 1 mm on MRI or ERUS)
7. Maximum tumour diameter >40 mm (either measured from everted edges on sagittal MRI or on ERUS)
8. Tumour position anterior, above the peritoneal reflection on MRI or EUS
9. No residual luminal tumour following endoscopic resection
10. Contraindications to radiotherapy including previous pelvic radiotherapy
11. Uncontrolled cardiorespiratory comorbidity (includes patients with inadequately controlled angina or myocardial infarction or arrhythmia within 6 months prior to randomisation)
12. Known dihydropyrimidine dehydrogenase (DPYD) deficiency
13. Known Gilberts disease (hyperbilirubinaemia)
14. Taking coumarin-derivative anticoagulants (e.g. warfarin) that cannot be discontinued at least 7 days prior to starting treatment or substituted by low molecular weight heparin
15. Taking phenytoin or sorivudine or its chemically related analogues, such as brivudine, within 4 weeks of trial entry (see Section 8.3.5 for further details)
16. Taking metronidazole at study entry
17. Pregnant or lactating
18. History of severe and unexpected reactions to fluoropyrimidine therapy
19. Aged <16 years (UK) or <18 years (other countries)

Previous participant exclusion criteria:

1. Unequivocal evidence of metastatic disease (includes resectable metastases)
2. MRI node positive (defined by protocol guidelines)
3. MRI extramural vascular invasion (mriEMVI) positive (defined by protocol guidelines)
4. MRI defined mucinous tumour
5. Mesorectal fascia threatened (< 1 mm on MRI)
6. Maximum tumour diameter > 40 mm as measured from everted edges on sagittal MRI
7. Tumour position anterior, above the peritoneal reflection on MRI or EUS
8. No residual luminal tumour following endoscopic resection
9. Contraindications to radiotherapy including previous pelvic radiotherapy
10. Uncontrolled cardiorespiratory comorbidity (includes patients with inadequately controlled angina or myocardial infarction within 6 months prior to randomisation)
11. Known dihydropyrimidine dehydrogenase (DPYD) deficiency
12. Known Gilberts disease (hyperbilirubinaemia)
13. Taking warfarin that cannot be discontinued at least 7 days prior to starting treatment or substituted by low molecular weight heparin
14. Taking phenytoin or sorivudine or its chemically related analogues, such as brivudine (see Section 8.4.5 for further details)
15. Pregnant, lactating or pre-menopausal women not using adequate contraception
16. Unable or unwilling to provide written informed consent

Date of first enrolment

01/11/2016

Date of final enrolment

31/12/2023

Locations

Countries of recruitment

Denmark

England

Netherlands

Scotland

United Kingdom

Wales

Study participating centre

Cardiff & Vale Health Board

University Hospital of Wales

Heath Park Way

Cardiff

United Kingdom

CF14 4XW

Study participating centre

Velindre NHS Trust

Velindre Cancer Centre

Velindre Rd

Cardiff

United Kingdom

CF14 2TL

Study participating centre

Manchester University NHS Foundation Trust

Manchester Royal Infirmary

Oxford Road

Manchester

United Kingdom

M13 9WL

Study participating centre

The Christie NHS Foundation Trust

Christie Hospital

27 Palatine Rd

Manchester
United Kingdom
M20 3JJ

Study participating centre
East Suffolk and North Essex NHS Foundation Trust
Colchester Hospital
Turner Rd
Colchester
United Kingdom
CO4 5JL

Study participating centre
University Hospitals Birmingham NHS Trust
Queen Elizabeth Hospital Birmingham
Mindelsohn Way
Birmingham
United Kingdom
B15 2TH

Study participating centre
University Hospitals Birmingham NHS Trust
Good Hope Hospital
Rectory Rd
Sutton
Coldfield
United Kingdom
B75 7RR

Study participating centre
The Leeds Teaching Hospitals NHS Trust
St James's University Hospital
Beckett St
Harehills
Leeds
United Kingdom
LS9 7TF

Study participating centre
Tayside Health Board
Ninewells Hospital

James Arrott Dr
Dundee
United Kingdom
DD2 1SG

Study participating centre

Norfolk and Norwich University Hospitals NHS Foundation Trust
Norfolk and Norwich University Hospital
Colney Ln
Norwich
United Kingdom
NR4 7UY

Study participating centre

North Bristol NHS Trust
Southmead Hospital
Southmead Rd
Bristol
United Kingdom
BS10 5NB

Study participating centre

Oxford University Hospitals NHS Foundation Trust
Churchill Hospital
Old Rd
Headington
Oxford
United Kingdom
OX3 7LE

Study participating centre

Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Study participating centre

York and Scarborough Teaching Hospitals NHS Foundation Trust

York Hospital
Wigginton Rd
Clifton
York
United Kingdom
YO31 8HE

Study participating centre

Bradford Teaching Hospitals NHS Foundation Trust

Bradford Royal Infirmary
Duckworth Ln
Bradford
United Kingdom
BD9 6RJ

Study participating centre

Cambridge University Hospitals NHS Foundation Trust

Addenbrooke's Hospital
Hills Rd
Cambridge
United Kingdom
CB2 0QQ

Study participating centre

Radboud University Medical Center

Geert Grooteplein Zuid 10
Nijmegen
Netherlands
6525 GA

Study participating centre

Antoni van Leeuwenhoek Ziekenhuis / The Netherlands Cancer Institute

Plesmanlaan 121
Amsterdam
Netherlands
1066 CX

Study participating centre

Leiden University Medical Center

Albinusdreef 2

Leiden
Netherlands
2333 ZA

Study participating centre
Laurentius Ziekenhuis
Monseigneur Driessenstraat 6
Roermond
Netherlands
6043 CV

Study participating centre
Isala Ziekenhuis
Dokter Stolteweg 92
Zwolle
Netherlands
8025 AV

Study participating centre
Amphia Ziekenhuis
Molengracht 21
Breda
Netherlands
4818 CK

Study participating centre
Elisabeth Tweesteden Ziekenhuis
Doctor Deelenlaan 5
Tilburg
Netherlands
5042 AD

Study participating centre
Diakonessenhuis Utrecht
Bosboomstraat 1
Utrecht
Netherlands
3582 KE

Study participating centre

Catharina Ziekenhuis

Michelangelolaan 2
Eindhoven
Netherlands
5623 EJ

Study participating centre

Amsterdam UMC (locatie VUmc)

De Boelelaan 1117 1118
Amsterdam
Netherlands
1081 HV

Study participating centre

Medisch Centrum Leeuwarden

Henri Dunantweg 2
Leeuwarden
Netherlands
8934 AD

Study participating centre

IJsselland Ziekenhuis

Prins Constantijnweg 2
Capelle aan den IJssel
Netherlands
2906 ZC

Study participating centre

OLVG

Oosterpark
Amsterdam
Netherlands
91091 AC

Study participating centre

OLVG

Jan Tooropstraat 164
Amsterdam
Netherlands
1061 AE

Study participating centre**OLVG**

Spuistraat 239a

Amsterdam

Netherlands

1012 VP

Study participating centre**Deventer Ziekenhuis**

Nico Bolkesteinlaan 75

Deventer

Netherlands

7416 SE

Study participating centre**Odense University Hospital**

Søndre Blvd. 29

Odense C

Denmark

5000

Study participating centre**Aarhus University Hospital**

Palle Juul-Jensens Blvd. 161

Aarhus

Denmark

8200

Sponsor information**Organisation**

University of Birmingham

Sponsor details

Research Support Group

Birmingham

England

United Kingdom

B15 2TT

+44 121 414 7618
researchgovernance@contacts.bham.ac.uk

Sponsor type
University/education

Website
<https://www.birmingham.ac.uk/>

ROR
<https://ror.org/03angcq70>

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Publication and dissemination plan

Current publication and dissemination plan as of 28/06/2021:

Results of this trial will be submitted for publication in peer-reviewed journals.

Meetings will be held after the end of each phase of the trial to allow discussion of the main results among the collaborators prior to publication. The success of STAR-TREC depends on the collaboration of a large number of clinicians across several countries. For this reason, all publications arising from this work will be attributed to the 'STAR-TREC Collaborative Group'. Publications will conform to the International Committee of Medical Journal Editors (ICMJE) guidelines (December 2015). When manuscripts are submitted, the corresponding author will specify the name of the STAR-TREC group, and clearly identify the group members who can take credit and responsibility for the work as authors. The byline will include the STAR-TREC name

and allow MEDLINE to list the names of individual group members who are authors or who are collaborators. There will be a note associated with the byline clearly stating that the individual names are elsewhere in the paper and whether those names are authors or collaborators. In this way, all contributors to the STAR-TREC study will be recognised.

The results obtained from patients recruited during the phase II part of the trial, including general results such as organ preservation and cancer recurrence rates and Quality of Life analyses, will be submitted for publication while the phase III part of the trial is ongoing. These publications will report blinded results of both organ preservation arms combined versus results of the radical surgery arm, in order to avoid disclosing results of the phase III primary outcome (direct comparison between organ preservation arms).

The TMG must review any secondary publications and presentations prepared by Investigators. Authors must acknowledge that the trial was performed with the support of the funders and the University of Birmingham as the Coordinating Sponsor. Intellectual property rights will be addressed in the agreements between Coordinating Sponsor, NCCs and sites.

The results of the trial will also be published on a clinical trials registry and a lay summary made available on the Cancer Research UK website.

Intention to publish date

31/12/2028

Individual participant data (IPD) sharing plan

The current data sharing plans for the current study are unknown and will be made available at a later date.

Previous publication and dissemination plan:

A meeting will be held after the end of the study to allow discussion of the main results among the collaborators prior to publication. The success of STAR-TREC depends on the collaboration of a large number of clinicians across several countries. For this reason, all publications arising from this work will be attributed to the ‘STAR-TREC Collaborative Group’.

Publications will conform with the ICMJE guidelines (December 2015). When manuscripts are submitted, the corresponding author will specify the name of the STAR-TREC group, and clearly identify the group members who can take credit and responsibility for the work as authors. The byline will include the STAR-TREC name and allow MEDLINE to list the names of individual group members who are authors or who are collaborators. There will be a note associated with the byline clearly stating that the individual names are elsewhere in the paper and whether those names are authors or collaborators.

In this way, all contributors to the STAR-TREC study will be recognised.

The Trial Management Group must review any secondary publications and presentations prepared by Investigators. Authors must acknowledge that the trial was performed with the support of the funders and The University of Birmingham as study Sponsor.

Further publication details to be confirmed and will be provide in due course at a later date.

IPD sharing statement:

The current data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
-------------	---------	--------------	------------	----------------	-----------------

Protocol article	protocol	28/12/2017	Yes	No
Other publications	radiotherapy quality assurance	18/02/2020 28/06/2021	Yes	No
Other publications	rationale behind radiotherapy treatment target volume	04/02/2020 28/06/2021	Yes	No
Protocol article		24/03/2022 14/11/2022	Yes	No