ISRCTN16448082 https://doi.org/10.1186/ISRCTN16448082

Using targeted radiotherapy to postpone the need to change treatment in men diagnosed with metastatic prostate cancer

Submission date 03/05/2024	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 04/10/2024	**Overall study status** Ongoing	
Last Edited 19/02/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
The aim of this study is to test whether a precise radiotherapy technique called stereotactic body radiotherapy (SBRT) can delay the progression of cancer in two groups of metastatic prostate cancer (cancer that has spread). SBRT has been shown to be safe and effective in other groups of cancer patients who have a small number of metastases. The treatment is now widely available within the UK and researchers want to test if it is effective in patients with more advanced prostate cancer. Radiotherapy to the prostate can prolong survival time for patients with a small number of metastases at diagnosis. In metastatic lung cancer, there is evidence that using radiotherapy in areas that have not responded well to drug therapy significantly prolongs the time before more treatment is needed compared to those who did not receive radiotherapy. Some patients with advanced prostate cancer may also get this clinical benefit. Delaying the progression of cancer or being able to delay the next treatment may mean that patients have a better quality of life for longer. The researchers also want to understand how best to manage patients who become resistant to initial drug treatment. They will use this knowledge to recommend SBRT to patients with a few (<5) metastases. They will also look for links between imaging findings and outcomes to see if these findings predict which patients benefit most from the addition of SBRT.

Who can participate?
This study will recruit participants in two different groups of metastatic prostate cancer. They will either:
1. Have on PSMA PET-CT scans an excellent response with 5 or fewer active sites (induced oligometastatic disease) after 6-12 months of systemic therapy
2. Be on first-line systemic therapy with evidence of an increase in PSA and on imaging have 5 or fewer active sites on scans (oligoprogression)

What does the study involve?
Patients in both abovementioned groups will be randomly allocated to either:
1. Continue first-line systemic therapy, which is to continue the treatment they are already having at the point of trial entry

2. Continue first-line systemic therapy and SBRT to metastases +/- prostate radiotherapy
The radiotherapy will be delivered to all metastases and/or prostate. The radiotherapy will be delivered in 3-5 appointments to the metastases and 5 appointments to the prostate over 2 weeks. The appointments to the metastases and prostate will be done simultaneously.
For induced oligometastatic disease participants are required to have a PSMA PET-CT scan to determine their eligibility. An MRI scan may also be performed with optional consent. All participants will be asked to complete questionnaires to examine any side effects of treatment and review the impact on quality of life. PSA tests and imaging will be conducted by sites to monitor how well the treatment has worked.

What are the possible benefits and risks of participating?
There is no guarantee that participants will benefit directly from taking part in this study. The aim is to find out whether SBRT can delay the progression of cancer in metastatic prostate cancer patients. We do not currently know whether this is the case. The information from this study may help in treating people with cancer in the future. Participants may experience side effects from the study treatment. The effects of the SBRT treatment are not completely known.

Where is the study run from?
This study is coordinated by the research centre at The Institute of Cancer Research Clinical Trials and Statistics Unit (ICR-CTSU) (UK). Participants will be recruited and treated at NHS hospitals.

When is the study starting and how long is it expected to run for?
January 2022 to September 2028

Who is funding the study?
Prostate Cancer UK

Who is the main contact?
Sandy Cheung, startrap-icrctus@icr.ac.uk

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-of-stereotactic-radiotherapy-for-prostate-that-has-spread-star-trap

Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
334445

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 59115, IRAS 334445

Study information

Scientific Title
Randomised phase II clinical trial of using stereotactic body radiotherapy (SBRT) on first line androgen receptor pathway inhibitor for metastatic prostate cancer

Acronym
STAR-TRAP

Study objectives
1. Using stereotactic body radiotherapy (SBRT) to treat patients with induced oligometastatic disease on androgen deprivation therapy and early additional systemic therapy will improve failure-free survival and maintain quality of life for longer.
2. Using SBRT to treat patients with oligoprogression on first-line systemic therapy will lead to durable ongoing disease control at responding sites, prolonged time to next treatment and maintained quality of life.
3. Biological response to initial treatment will identify patients who benefit from metastasis-directed radiotherapy.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Approved 11/07/2024, London - Chelsea Research Ethics Committee (London Centre, 2 Redman Place, HRA, E20 1JQ, UK; +44 (0)207 104 8150, +44 (0)207 104 8181, +44 (0)207 104 8156; chelsea.rec@hra.nhs.uk), ref: 24/LO/0335

Study design
Randomized; Interventional; Design type: Treatment, Radiotherapy

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
The method of randomisation is 1:1 allocation ratio using minimisation with a random element. The two cohorts will have separate minimisation algorithms.

Participants in the induced oligo-metastatic cohort will receive either:
1. Control arm: Continue on first-line systemic therapy
2. Experimental arm: Continue on first-line systemic therapy + SBRT (Up to 30 Gy/3-5 Fr to metastases and/or 33 Gy/5 Fr to prostate and seminal vesicles)

Participants in the oligo-progression cohort will receive either:
1. Control arm: Continue on first-line systemic therapy
2. Experimental arm: Continue on first-line systemic therapy + SBRT (Up to 30 Gy/3-5 Fr to metastases and/or 33 Gy/5 Fr to prostate and seminal vesicles)

The radiotherapy will be delivered to all metastases and/or prostate. The radiotherapy will be delivered in 3-5 appointments to the metastases and 5 appointments to the prostate over 2 weeks. The appointments to the metastases and prostate will be done simultaneously.

For induced oligometastatic disease participants are required to have a prostate-specific membrane antigen (PSMA) PET-CT to determine their eligibility. Whole-body magnetic resonance imaging (WBMRI) may also be performed provided optional consent. All participants will be asked to complete questionnaires so that we can examine any side effects of treatment and review the impact on quality of life. Prostate-specific antigen (PSA) and imaging will be conducted by sites to monitor how well the treatment has worked.

Intervention Type
Mixed

Primary outcome(s)
Induced oligometastatic cohort:
Failure-free survival, defined as the time from randomisation to first biochemical failure (PSA value); new, radiological progression; or prostate cancer death. PSA values and imaging will be

data collected throughout the trial. These assessments will be conducted as per sites' standard of care intervals.

Oligoprogressive cohort:
Time to discontinuation of first-line therapy, defined as the time from randomisation to time the patient discontinues their first-line therapy where the reason for stopping is related to progression and if a patient were to commence a new treatment for their prostate cancer it would need to be a second line therapy or related to palliative care. This will be collected throughout the trial.

Key secondary outcome(s))

1. Time to discontinuation of first-line therapy (induced oligometastatic cohort) - this is defined as the time from randomisation to time the patient discontinues their first-line therapy where the reason for stopping is related to progression and if a patient were to commence a new treatment for their prostate cancer it would need to be a second line therapy or related to palliative care. This will be collected throughout the trial.
2. Time to second-line systemic therapy – this is defined as the time from randomisation to the time the patient starts second-line systemic therapy. If a patient doesn't start a second-line therapy but stops first-line the date the patient stops their first-line therapy will be used instead. This will be collected throughout the trial.
3. Radiological progression-free survival – this is defined as the time from randomisation to radiographic progression or death from any cause. Imaging will be conducted as per sites' standard of care intervals. Imaging data will be collected throughout the trial.
4. Overall survival is defined as the time from randomisation to death from any cause. Survival status and cause of death will be collected throughout the trial.
5. Time to second progression-free survival – this is defined as the time from randomisation to first clinician-determined disease progression (PSA progression, radiographic progression, clinical progression or death from any cause) after patients stop their first-line therapy. PSA values and imaging will be data collected throughout the trial. These assessments will be conducted as per sites' standard of care intervals.
6. Patient-reported outcomes will be collected using the patient-reported outcomes version of the common terminology criteria for adverse events (PRO-CTCAE) and EQ5D-5L to report the frequency of each PRO-CTCAE. Patient-reported outcomes questionnaire will be collected at screening, end of SBRT (or equivalent timepoint for SOC arm), 12 weeks from the start of SBRT (or equivalent timepoint for SOC arm), 6,9, 12 months and every 4 months thereafter up to 36 months from randomisation.
7. Time to pain progression is defined as a 2-point increase from baseline (at randomisation) Brief Pain Index (BPI-SF) based on the 'worst pain' question. Patient-reported outcomes questionnaire will be collected at screening, end of SBRT (or equivalent timepoint for SOC arm), 12 weeks from the start of SBRT (or equivalent timepoint for SOC arm), 6, 9, 12 months and every 4 months thereafter up to 36 months from randomisation.
8. General pain measured using the Brief Pain Inventory - Short Form (BPI-SF). Patient-reported outcomes questionnaire will be collected at screening, end of SBRT (or equivalent timepoint for SOC arm), 12 weeks from the start of SBRT (or equivalent timepoint for SOC arm), 6,9, 12 months and every 4 months thereafter up to 36 months from randomisation.
9. Time to symptomatic skeletal event – this is defined as the time from randomisation to the first skeletal-related event (symptomatic pathologic fracture, spinal cord compression, radiation to bone or surgery to bone). In addition, the date of death from prostate cancer where the patient doesn't have a prior skeletal-related event will be included as an event. Where patients' death is not prostate-related, and they have no prior skeletal events the patients will be censored at the date of death. Skeletal event is collected throughout the trial as reported by

medical notes review by site every 3 months and patient reported on questionnaires. Patient-reported outcomes questionnaire will be collected at screening, end of SBRT (or equivalent timepoint for SOC arm), 12 weeks from the start of SBRT (or equivalent timepoint for SOC arm), 6,9, 12 months and every 4 months thereafter up to 36 months from randomisation.
10. SBRT delivered to all eligible metastases – this will be measured as the proportion of patients that received the target dose. Dose data will be collected.

Completion date
01/09/2028

Eligibility

Key inclusion criteria
1. Histologically confirmed adenocarcinoma of the prostate
2. Aged >=18 years
3. On ADT + ARPI (abiraterone, enzalutamide, apalutamide, darolutamide) +/- docetaxel
4. WHO performance status 0 to 2
5. Written informed consent

Additional cohort-specific eligibility:

Induced oligometastatic cohort
Registration part:
1. Metastatic hormone-sensitive prostate cancer, poly-metastatic at diagnosis (>5 metastases) confirmed on any imaging modality.
2. Receiving ADT + first-line systemic therapy (ARPI +/- docetaxel).
3. 5-12 months since initiating ADT (including LHRH agonists/antagonists and bicalutamide).
4. PSA <2 ng/ml (PSA <2 ng indicates patient 'eligible' to have PSMA PET-CT to determine oligometastatic status).

Randomisation part:
1. <=5 metastases on PSMA-PET-CT (performed after 6-12 months of first-line therapy). Patients should be randomised within 4 weeks of their PSMA-PET-CT.

Oligoprogression cohort
1. Metastatic hormone-sensitive prostate cancer. Patients may have any number of sites of metastases at diagnosis on any imaging modality.
2. Receiving ADT + first-line systemic therapy (ARTT and/either docetaxel).
3. <5 metastases and/or active disease within the prostate identified at the point of biochemical failure on any imaging modality (conventional/ /PET).
4. Has biochemical failure*

*Biochemical failure is defined either using the PCGW3 definition (a PSA increase that is >= 25% and >= 2 ng/ml above the nadir) OR a PSA increase of >= 25% above the nadir if PSA was <2 ng /ml at randomisation OR at clinician discretion. Progression needs to be confirmed by a second value >= 3 weeks later.

Participant type(s)
Patient

Healthy volunteers allowed

No

Age group
Adult

Lower age limit
18 years

Sex
Male

Key exclusion criteria
1. Prior radiotherapy at or near a metastatic site to be treated in STAR-TRAP that precludes the safe delivery of SBRT. Patients that have received prior SBRT to the prostate for localised prostate cancer treatment are permitted, but the patients will not be suitable to receive SBRT to the prostate in STAR-TRAP
2. Comorbidities precluding staging or follow-up imaging, or precluding procedures required to facilitate SBRT
3. Any single metastasis >6 cm (>5 cm for lung metastases)
4. Spinal cord compression, or impingement of the cord or any other situation whereby the clinician feels that urgent radiotherapy to the spine is required (within 24 hours). Patients are allowed to enter STAR-TRAP if they have a previous history of SCC, providing other eligibility criteria are met.
5. Any condition or significant clinical co-morbidities which would precludes the safe delivery of SBRT to any sites of metastatic disease and prostate (if applicable). A non-exhaustive list is provided below and research teams at site should consult this when assessing patient suitability for SBRT prior to randomisation:
5.1. A history of clinically significant diffuse interstitial lung disease or radiological evidence of idiopathic pulmonary fibrosis if SBRT to lung metastases or lesions adjacent to lungs are considered
5.2. Clinically significant colitis i.e. ulcerative colitis /Crohn’s disease if SBRT to the pelvis or abdomen is considered
6. Any active malignancies (i.e., progressing or requiring any treatment in the previous 36 months) other than prostate cancer (except non-muscle invasive bladder cancer; non-melanomatous skin cancer, small renal masses or a malignancy that is considered cured with minimal risk of recurrence)

Date of first enrolment
19/12/2024

Date of final enrolment
18/12/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
The Royal Marsden Hospital (surrey)
Downs Road
Sutton
United Kingdom
SM2 5PT

Study participating centre
The Royal Marsden Hospital (london)
Fulham Road
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SW3 6JJ

Sponsor information

Organisation
Institute of Cancer Research

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Charity

Funder Name
Prostate Cancer UK; Grant Codes: RIA21-ST2-015

Alternative Name(s)
Prostate Cancer, Prostate Action, ProstateUK, prostatecanceruk

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

Deidentified individual participant data, together with a data dictionary defining each field in the set, will be made available to other researchers on request. Trial documentation including the protocol is available online. The Institute of Cancer Research-Clinical Trials and Statistics Unit (ICR-CTSU) supports wider dissemination of information from the research it conducts and increased cooperation between investigators. Trial data are obtained, managed, stored, shared, and archived according to ICR-CTSU standard operating procedures to ensure the enduring quality, integrity, and utility of the data. Formal requests for data sharing are considered in line with ICR-CTSU procedures, with due regard given to funder and sponsor guidelines. Requests are via a standard proforma describing the nature of the proposed research and the extent of data requirements. Data recipients are required to enter a formal data-sharing agreement, which describes the conditions for release and requirements for data transfer, storage, archiving, publication, and intellectual property. Requests are reviewed by the trial management group in terms of scientific merit and ethical considerations, including patients' consent. Data sharing is undertaken if proposed projects have a sound scientific or patient benefit rationale, as agreed by the trial management group and approved by the independent data monitoring and steering committee, as required. Restrictions relating to patients' confidentiality and consent will be limited by aggregating and anonymising identifiable patients' data. Additionally, all indirect identifiers that could lead to deductive disclosures will be removed in line with ICR-CTSU data-sharing guidelines.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes