ISRCTN80146950 https://doi.org/10.1186/ISRCTN80146950

A phase III randomised controlled trial of prostate and pelvis versus prostate alone radiotherapy with or without prostate boost

Submission date 08/01/2018	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 18/01/2018	**Overall study status** Ongoing	
Last Edited 12/09/2024	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-different-ways-of-giving-radiotherapy-for-cancer-of-the-prostate-pivotalboost#undefined

Study website
https://www.icr.ac.uk/our-research/centres-and-collaborations/centres-at-the-icr/clinical-trials-and-statistics-unit/our-research/clinical-trials/pivotalboost

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
219463

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 34511, IRAS 219463

Study information

Scientific Title
A phase III randomised controlled trial of prostate and pelvis versus prostate alone radiotherapy with or without prostate boost

Acronym
PIVOTALBoost

Study objectives
The primary objective of PIVOTALboost is to assess whether pelvic lymph node radiotherapy with or without dose escalation to the prostate with HDR, HDR incorporating a focal boost or focal boost IMRT when delivered at multiple centres can lead to improved failure free survival with similar levels of bladder (genitourinary) and bowel (gastrointestinal) side effects experienced by patients.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 19/05/2017, London-Chelsea Research Ethics Committee (Bristol Centre, Level 3, Block B, Whitefriars, Lewins Mead, Bristol, BS1 2NT, United Kingdom; +44 (0)207 1048055; chelsea.rec@hra.nhs.uk), ref: 17/LO/0731

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

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
Prostate cancer

Interventions
Participants are allocated to one of the following treatment arms:
A: Prostate alone Intensity-modulated radiation therapy (IMRT)
B: Prostate and pelvic IMRT
C: Prostate IMRT and prostate boost
D: Prostate and pelvic IMRT and prostate boost.
Randomisation into arms C and D depend on the boost volume identified by MRI (suitable for focal boost or not), availability of focal HDR or IMRT and patient suitability in case of HDR

Participants are eligible for entry into one of the following randomisation options according to:
1. Boost volume (whether the tumour volume identified on the staging MRI is suitable for focal boost or not),
2. Suitability and availability of HDR (e.g. patient not suitable for HDR brachytherapy or any other clinical reason) and,
3. Type of focal boost (IMRT or HDR brachytherapy).

In centres with no access to HDR or focal IMRT boost, all patients will enter randomisation option 1 (irrespective of having a suitable boost or not).

Randomisation Option 1 (Pelvic node randomisation): No suitable focal boost volume on the staging MRI* and not suitable for HDR brachytherapy.
Randomisation Option 2a (Pelvic node and whole gland boost): No suitable focal boost volume on the staging MRI* and suitable for HDR.
Randomisation Option 2b (Pelvic node and focal boost randomisation): Suitable focal boost volume.

The study doctor explains whether the patient is suitable for brachytherapy to the whole prostate and /or focal boost treatment. It depends on many factors: the patient's fitness, the position of the prostate in the pelvis, previous prostate surgery, the appearance of the cancer and the availability of the treatment techniques at the local cancer centre.

For patients without cancer nodules suitable for focal boost treatment: Patients without a prostate nodule on the MRI scan can be offered brachytherapy (short term internal radiation) to the whole prostate. This procedure is also called high dose rate (HDR) brachytherapy. This treatment delivers a high radiation dose to the prostate. It is combined with external beam radiotherapy to the prostate (15 fractions) or to the prostate and pelvic lymph nodes (20 fractions).

For patients with cancer nodules suitable for focal boost treatment: The radiotherapy dose can be increased to the area in the prostate containing the cancer; the rest of the prostate receives the standard dose. The focal boost treatment can be given either with HDR brachytherapy or external beam radiotherapy.

The post treatment follow up period is 10 years.

Intervention Type

Procedure/Surgery

Primary outcome measure
Failure-free survival is measured by the time to first biochemical failure, recommencement of androgen deprivation therapy, local recurrence, lymph node/pelvic recurrence, distant metastases or death due to prostate cancer for up to 10 years.

Secondary outcome measures
1. Time to loco-regional recurrence; time to biochemical failure or prostate recurrence; metastatic relapse free survival; overall and prostate cancer specific survival; time to recommencement of androgen deprivation therapy is measured using clinical assessment of disease status up to 10 years
2. Adherence to dose constraints is measured using collection of radiotherapy treatment doses /parameters at treatment
3. Acute bladder and bowel toxicity is measured using RTOG and CTC (v4.0) adverse event reporting at 3 months
4. Late toxicity is measured using RTOG and CTC (v4.0) adverse event reporting up to 10 years
5. Quality of life is measured using ALERT-B (Assessment of Late Effects of RadioTherapy - Bowel) screening tool, Gastrointestinal Symptom Rating Scale (GSRS), IIEF-5 Questionnaire (SHIM), International Prostate Symptom Score (IPSS), and Expanded Prostate Index Composite-26 (EPIC-26) Short Form questionnaire up to 10 years
6. Health economic endpoints are measured using EQ-5D up to 10 years

Overall study start date
08/08/2016

Completion date
31/12/2029

Eligibility

Key inclusion criteria
1. Histologically confirmed, previously untreated, non-metastatic adenocarcinoma of the prostate using the Gleason scoring or grade group system (histological confirmation can be based on tissue taken at any time, but a re-biopsy should be considered if the biopsy is more than 12 months old).
2. PSA <50ng/ml prior to starting ADT.
3. NCCN localised high risk or locally advanced disease: T3a, T3b or T4 N0M0 (clinical and/or MRI) and/or Dominant Gleason 4 or 5 (grade group 3, 4, or 5) and/or PSA >20; or
3.1. NCCN intermediate risk disease: T2b-c N0M0, and/or Gleason 3+4 (grade group 2) and /or PSA 10-20 ng/ml
and Adverse feature, for example: Maximum tumour length (MTL) >6mm and/or 50% biopsy cores positive and / or PI-RADS score 3, 4 or 5, DIL lesion >10mm axial dimension on staging MRI.
4. Age ≥18 years
5. Signed, written informed consent
6. WHO performance status 0-2 (Appendix 1)

Participant type(s)
Patient

Age group

Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
Planned Sample Size: 2229; UK Sample Size: 2229

Total final enrolment
2232

Key exclusion criteria
1. Prior radiotherapy to the prostate or pelvis
2. Prior radical prostatectomy
3. Prior ADT for > 6 months at consent (as patients will need to commence radiotherapy at months 3-5 (maximum 7) following start of ADT)
4. Adjuvant docetaxel chemotherapy
5. Radiologically suspicious or pathologically confirmed lymph node involvement
6. Evidence of metastatic disease
7. Life expectancy < 5 years
8. Bilateral hip prostheses or any other implants/hardware that would introduce substantial CT artifacts and would make pelvic node planning more difficult
9. For patients having fiducials inserted: Anticoagulation with warfarin/ bleeding tendency making fiducial placement or surgery unsafe in the opinion of the clinician.
10. For patients being considered for randomisation options C2 and D2 only and are undergoing a planning MRI scan: Contraindication to undergo a MRI scan.
11. For undergoing HDR brachytherapy: long-term anticoagulation therapy which cannot be temporarily stopped, prostate surgery (TURP) with a significant tissue cavity, a history of recent deep vein thrombosis or pulmonary embolus, significant cardiovascular comorbidity, unfit for prolonged general anaesthetic.
12. Medical conditions likely to make radiotherapy inadvisable e.g. inflammatory bowel disease, significant urinary symptoms
13. Previous malignancy within the last 2 years (except basal cell carcinoma or squamous cell carcinoma of the skin), or if previous malignancy is expected to significantly compromise 5 year survival
14. Any other contraindication to external beam radiotherapy to the pelvis

Date of first enrolment
02/01/2018

Date of final enrolment
30/08/2024

Locations

Countries of recruitment
England

Scotland

United Kingdom

Wales

Study participating centre
The Clatterbridge Cancer Centre
The Clatterbridge Cancer Centre Nhs Foundation Trust (Lead Site)
Clatterbridge Road
Bebington
Wirral
United Kingdom
CH63 4JY

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

Study participating centre
The Royal Marsden Hospita
The Royal Marsden Nhs Foundation Trust
Fulham Road
London
United Kingdom
SW3 6JJ

Study participating centre
Velindre Cancer Centre
Whitchurch Road
Cardiff
United Kingdom
CF14 2TL

Study participating centre
Lincoln County Hospital
United Lincolnshire Hospitals NHS Trust

Greetwell Road
Lincoln
United Kingdom
LN2 4AX

Study participating centre
Torbay Hospital
Torbay and South Devon NHS Foundation Trust
Hengrave House
Newton Road
Torquay
United Kingdom
TQ2 7AA

Study participating centre
Queen Elizabeth Medical Centre
University Hospitals Birmingham NHS Foundation Trust
Edgbaston
Birmingham
United Kingdom
B15 2TH

Study participating centre
Musgrove Park Hospital
Taunton and Somerset NHS Foundation Trust
Taunton
United Kingdom
TA1 5DA

Study participating centre
Norfolk and Norwich University Hospital
Norfolk and Norwich University Hospitals NHS Foundation Trust
Colney Lane
Colney
Norwich
United Kingdom
NR4 7UY

Study participating centre
Southampton General Hospital
University Hospital Southampton NHS Foundation Trust

Tremona Road
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SO16 6YD

Study participating centre
Freeman Hospital
The Newcastle Upon Tyne Hospitals NHS Foundation Trust
Freeman Road
High Heaton
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NE7 7DN

Study participating centre
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Hills Road
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Study participating centre
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Royal Free London NHS Foundation Trust
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London
United Kingdom
NW3 2QG

Study participating centre
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Brighton and Sussex University Hospitals NHS Trust
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Study participating centre
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S5 7AU

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IV2 3BW

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Barts Health NHS Trust
The Royal London Hospital
Whitechapel
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E1 1BB

Study participating centre
North Tees and Hartlepool NHS Foundation Trust
University Hospital of Hartlepool
Holdforth Road
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United Kingdom
TS24 9AH

Study participating centre
South Tees Hospitals NHS Foundation Trust
James Cook University Hospital
Marton Road

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United Kingdom
TS4 3BW

Study participating centre
Cuh at Colchester General Hospital
Colchester General Hospital
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CO4 5JL

Sponsor information

Organisation
Institute Of Cancer Research

Sponsor details
Royal Cancer Hospital
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London
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SW3 6JB

Sponsor type
Research organisation

ROR
https://ror.org/043jzw605

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Results and Publications

Publication and dissemination plan
The main trial results will be published in a peer-reviewed journal, on behalf of all collaborators. The manuscript will be prepared by a writing group, consisting of members of the TMG and selected participating clinicians. All participating clinicians will be acknowledged in the publication.

Intention to publish date
01/01/2030

Individual participant data (IPD) sharing plan
The 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?
HRA research summary			28/06/2023	No	No