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ICR The Institute of Cancer Research

CANCER RESEARCH UK

The ROYAL MARSDEN NHS Foundation Trust

PIVOTALboost

A phase III trial of prostate alone vs. pelvic lymph node IMRT with or without prostate boost for intermediate and high risk localised prostate cancer

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Localised High Risk Prostate Cancer Trial Questions

- **Disease free survival**
  - 60-80% at 5 years
- **Local recurrence**
  - At the site of the dominant tumour
- **Is there any benefit from local treatment intensification**
  - HDR brachytherapy
  - Focal boost (HDR or IMRT)
- **Is there any benefit of lymph node radiotherapy**
  - Uncertain

Study Endpoints

Primary endpoint

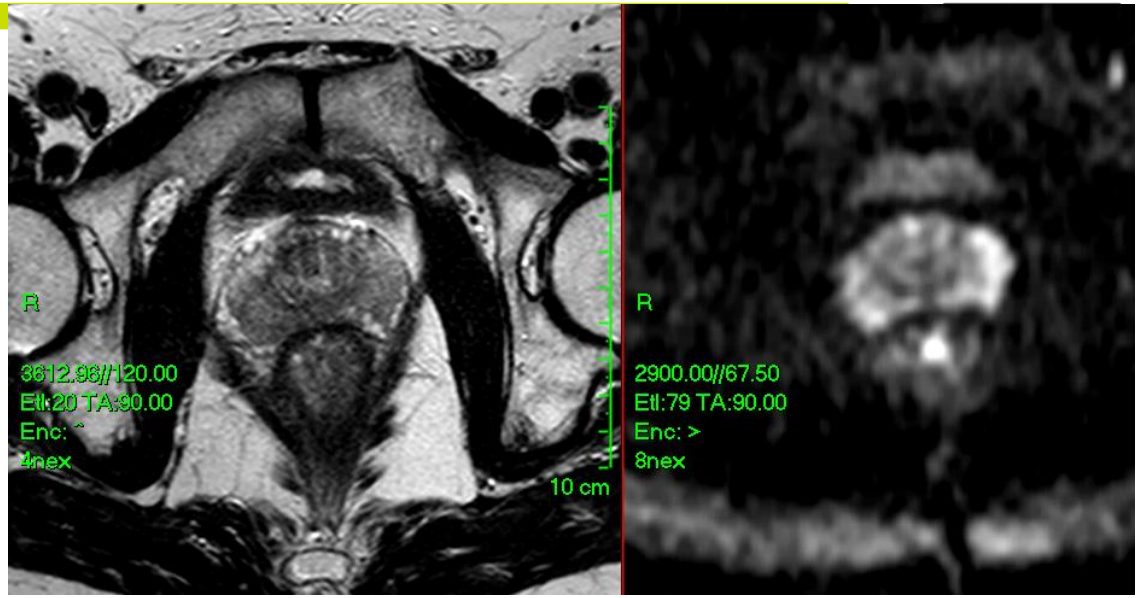
Failure-free survival (FFS)

- Biochemical failure.
- Recommencement of ADT.
- Local recurrence.
- Lymph node/pelvic recurrence.
- Distant metastases or death due to prostate cancer.

Secondary endpoints

- Adherence to dose constraints.
- Acute bladder and bowel toxicity at 3 months.
- Late toxicity.
- Quality of life.
- Health economic endpoints.

Trial Design
HDR



High-risk localised prostate cancer

No boost volume*

Arm A:
Prostate IMRT (control)

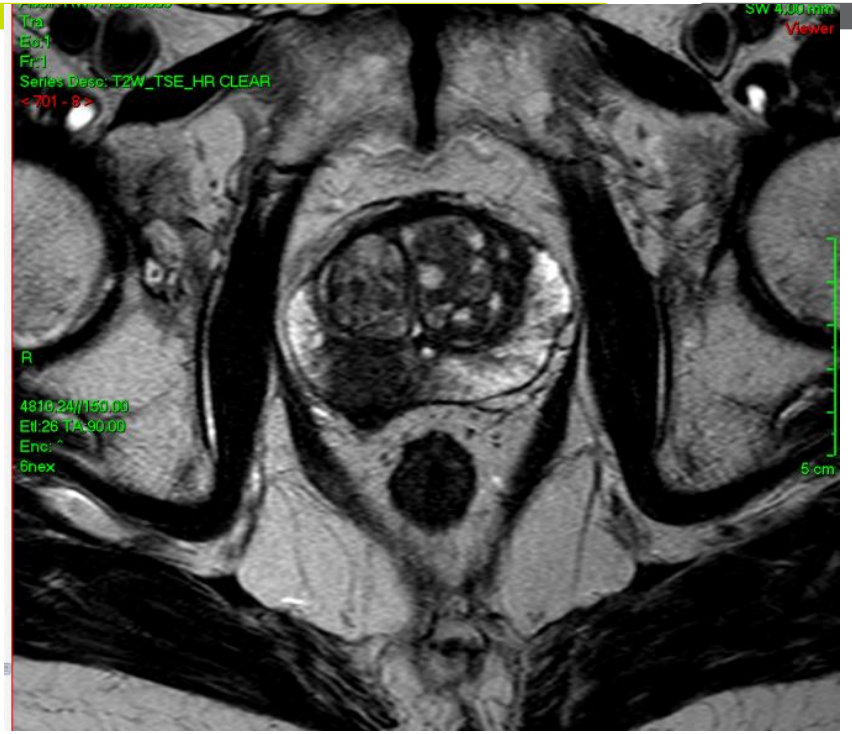
Arm B:
Prostate IMRT + pelvic IMRT

Arm C1:
Prostate IMRT
+
Whole prostate HDR

Arm D1:
Prostate IMRT + pelvic IMRT
+
Whole prostate HDR

*Either diffuse abnormalities or boost volume too large

Trial Design
HDR focal boost



High-risk localised prostate cancer with a

Boost volume

Arm A:
Prostate IMRT (control)

Arm B:
Prostate IMRT + pelvic IMRT

Arm C:
Prostate IMRT + prostate boost

*HDR with focal boost

Arm D:
Prostate IMRT + pelvic IMRT + prostate boost

*HDR with focal boost

*there is also an IMRT option

Main Inclusion Criteria

- Histologically confirmed, adenocarcinoma of the prostate

- PSA <50ng/ml

- **NCCN high risk disease** (clinical and/or MRI)

  T3a, T3b or T4 N0M0 and/or dominant Gleason 4 or 5 and/or PSA >20

or

- **NCCN intermediate risk disease** (clinical and/or MRI)

  T2b-c N0M0, and/or Gleason 3+4 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 lesion >10mm on staging MRI.

Exclusion criteria

Prior Treatment

- ADT for >6months, adjuvant docetaxel

Planning issues

- Bilateral hip prostheses or any other implants/hardware
- Contraindication to undergo MRI scan
- Anticoagulation which cannot be temporarily stopped.

HDR brachytherapy:

- Long-term anticoagulation, TURP, recent DVT or PE, significant cardiovascular comorbidity, unfit for prolonged general anaesthetic.

Other

- Life expectancy <5 years.
- Inflammatory bowel disease, significant urinary symptoms.
- Previous malignancy within the last 2 years.

Randomisation options

1. **Check eligibility**
2. **Look at the staging MRI (suitable boost yes or no)**
3. **Choose the randomisation option (investigator choice)**

- **No boost volume**

  Randomisation option 1: Pelvic node

  Or

  Randomisation Option 2a: Pelvic node and whole gland HDR

2-arm, A vs B

4-arm, A vs B vs C1 vs D1

- **A Boost volume**

  Randomisation Option 2b: Pelvic node and focal boost

4-arm, A vs B vs C2 vs D2

Definition of a suitable focal boost volume

On the **pre-biopsy** staging multi-parametric MRI scan, a dominant intra-prostatic lesion (DIL) has:

- **PI-RADS (v.2) 4 or 5 score lesion**

  Both T2 and DWI are important and this depends on tumour location in the gland.

- **DIL >5mm**

  Smaller dimension

- **Total DIL volume <50% total prostate volume**.
  If there are 2 or 3 DILs, add the individual volumes. Volumes can be estimated with measurement of dimension in 3 directions.

Patients with **a post-biopsy** MRI will not be eligible for a focal boost, but can be randomised to A vs B or A vs B vs C1 vs D1.

RTQA process HDR centres

You have to do

- Outline boost volume (GTVpb) patient 1
- Outline CTVp, CTVpsv, GTVpb and CTVn patient 2
- One IMRT planning case
- One HDR planning case

Help on the website

- RTQA protocol
- Pelvic node atlas
- Boost outlining atlas
- Outlining example

Trial status

19th May 2017	Initial Ethics approval
12th June 2017	Boost outlining workshop
27th July 2017	HRA approval
12th September 2017	Boost outlining webinar
19th September 2017	Trial launch
2nd January 2018	1st site opened to recruitment

Sample size: 1952

Number of centres needed: 40 (12 in 1st year)

17 patients randomised from 3 centres in the first 2 months

Thank you

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