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# Prostate Adenocarcinoma: TransCutaneous Hormones versus luteinising hormone-releasing hormone (LHRH) analogues

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| **Submission date**<br>14/07/2005 | **Recruitment status**<br>No longer recruiting | [_] Prospectively registered<br>[_] Protocol<br>[_] Statistical analysis plan<br>[_] Results<br>[_] Individual participant data<br>[_] Record updated in last year |
| **Registration date**<br>12/09/2005 | **Overall study status**<br>Completed | |
| **Last Edited**<br>13/05/2024 | **Condition category**<br>Cancer | |

**Plain English summary of protocol**
http://www.cancerhelp.org.uk/trials/a-trial-looking-at-hormone-patches-for-prostate-cancer

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**Clinical Trials Information System (CTIS)**
2005-001030-33

**ClinicalTrials.gov (NCT)**
NCT00303784

**Protocol serial number**

# Study information

### Scientific Title
A randomised controlled trial of transcutaneous oestrogen patches versus luteinising hormone-releasing hormone (LHRH) analogues in prostate cancer

### Acronym
PATCH

### Study objectives
Current hypothesis as of 17/04/2023:
The primary objective of the trial is to confirm that transdermal oestradiol is a safe and efficacious therapy for patients with locally advanced and metastatic prostate cancer. The final phase III evaluation of efficacy will test the hypothesis that transdermal oestradiol is non-inferior to standard ADT in terms of progression-free survival and overall survival. However, there is a possibility that transdermal oestradiol may improve overall survival compared to standard ADT. First, transdermal oestradiol may reduce treatment-associated morbidity and could potentially benefit overall survival. Second, up to 30% of people with castrate-resistant prostate cancer respond to oral oestrogen as post-relapse therapy, suggesting oestradiol therapy may potentially have additional direct anti-tumour effects. Hence, if transdermal oestradiol is shown to be non-inferior compared to LHRHa in terms of overall survival, it will also be assessed for superiority.

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Previous hypothesis as of 09/12/2014:
The primary objective of the trial is to confirm that transdermal oestrogen is a safe and efficacious therapy for patients with locally advanced and metastatic prostate cancer. The final phase III evaluation of efficacy will test the hypothesis that patches are non-inferior to LHRH in terms of overall survival and progression-free survival.

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Previous hypothesis:
The primary objective of this study is to confirm that oestrogen patches are a safe and efficacious therapy for patients with locally advanced and metastatic prostate cancer. Transcutaneous oestrogen avoids first-pass hepatic metabolism and therefore is not expected to be associated with the same level of cardiovascular system (CVS) toxicity as oral oestrogen. Patients with locally advanced or metastatic prostate cancer will be randomised between transcutaneous oestrogen patches and luteinising hormone-releasing hormone (LHRH) analogues in a 2:1 ratio in order to maximise experience with the patches. The primary endpoint of the study is CVS toxicity.

For a summary of a systematic review on the use of parenteral oestrogens in prostate cancer undertaken to inform the design of this study please see Appendix H or access the following link: http://www.york.ac.uk/inst/crd/pdf/parentoestrogen.pdf).

### Ethics approval required
Old ethics approval format

## Ethics approval(s)
Leeds (East) REC, 23/11/2005, ref: 05/Q1206/168

## Study design
Randomised controlled trial

## Primary study design
Interventional

## Study type(s)
Treatment

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

## Interventions
LHRH analogues versus transdermal oestrogen patches.

## Intervention Type
Drug

## Phase
Phase III

## Drug/device/biological/vaccine name(s)
Transdermal oestrogen

## Primary outcome(s)
Current primary outcome measures as of 09/12/2014:
The primary outcome measures for the final phase III evaluation of the patches are overall survival (OS) and progression-free survival (PFS). The outcome measure which will be used to assess efficacy of the patches during interim analyses is PFS.

Previous primary outcome measures:
CVS morbidity and mortality. Criteria for differing CVS events will be defined as follows:
1. Heart Failure: New clinical signs/symptoms and/or CXR changes of heart failure requiring the use or change of diuretics and/or angiotensin-converting enzyme inhibitors
2. Ischaemic Heart Disease:
Myocardial infarction diagnosed by at least two of the following:
2.1. Typical cardiac chest pain for 30 minutes or more
2.2. Cardiac enzymes greater than 2 times upper limit of normal
2.3. Typical ECG changes:
2.3.1. Unstable angina (typical cardiac chest pain at rest) for greater than 15 minutes
2.3.2. Stable angina-exercise induced pain with increasing frequency of attacks lasting greater than 15 minutes or a long-lasting attack (greater than 15 minutes) with newly developed ST-changes or T wave inversion
3. Cerebral ischaemic event: cerebral infarction seen on computerised tomography (CT) or magnetic resonance imaging (MRI). Transient ischaemic attacks with clear neurological symptoms from regions of the internal carotid or vertebral arteries.
4. Intermittent Claudication: severe intermittent claudication at a maximum walking distance of 200 metres

5. Venous thromboembolism: thromboses to be confirmed radiologically. Pulmonary embolism to be confirmed by means of ventilation/perfusion scans or angiography.
6. Death attributed to any of the above

All cardiovascular events will be reviewed by two blinded reviewers.

### Key secondary outcome(s))
Current secondary outcome measures as of 09/12/2014:
The secondary outcome measures include prostate cancer specific survival, hormone levels, CVS and other toxicity, and quality of life (QL). In the first stage of the trial (completed in 2010), the primary outcome measure was CVS toxicity.

Previous secondary outcome measures:
1. Activity (castrate levels of hormones): luteinishing hormone (LH) and follicle-stimulating hormone (FSH) will be measured pre-randomisation and then at 12 weeks, 6 months and then at 1 and 2 years post randomisation. Testosterone will be measured pre-randomisation and then at 4 and 12 weeks, 6 months and then at 1 and 2 years post randomisation to confirm that castrate levels are achieved and maintained. Adjustments to the dose of the patches will be made if necessary. Sex hormone binding globulin (SHBG) will be measured at pre-randomisation and then at 4 and 12 weeks, 6 months and then at 1 year post randomisation. Oestrone and oestradiol levels will be measured at baseline and at 4, 8 and 12 weeks, 6 months and then at 2 years. Fasting glucose, insulin and lipids will be measured at baseline, 6 months and 1 and 2 years. Urinary metabolites (hydroxyproline) will also be measured at baseline, 1 and 2 years. Clotting studies will include measurement of INR, APTT, Von Willebrand Factor, fibrinogen, and platelets at baseline, 6 months and 1 year.
2. Failure-free survival (FFS) (including biochemical failure)
3. Other toxicity (osteoporosis, hot flushes, gynaecomastia, anaemia): bone scans, CXR and CT /MRI scans of abdomen, pelvis and chest will be performed as clinically appropriate. Toxicity resulting in the patient stopping treatment will be measured, as will grade 3 or 4 toxicity at pre-specified time points using the NCI Common Toxicity Criteria (CTCv3).
4. Quality of life (QoL): QoL will be measured using patient-completed questionnaires (EORTC QLQ-C30 and PR25 which is prostate specific).

### Completion date
01/02/2026

## Eligibility

### Key inclusion criteria
Current inclusion criteria as of 09/12/2014:
Newly diagnosed patients with one of the following:
1. Stage T3/4 NO or NX M0 histologically confirmed prostate adenocarcinoma with PSA ≥20 ng /ml or Gleason sum score ≥6
2. Stage Tany N+ M0 or Tany Nany M+ histologically confirmed prostate adenocarcinoma
3. Multiple sclerotic bone metastases with a PSA ≥50 ng/ml without histological confirmation of prostate cancer
OR
Patients with histologically confirmed prostate adenocarcinoma previously treated with radical surgery and/or radiotherapy who are now relapsing, with at least one of the following:

1. PSA ≥4 ng/ml and rising with doubling time less than 6 months
2. PSA ≥20 ng/ml
3. Documented evidence of metastatic disease with PSA >4 ng/ml

Note: Prior hormone therapy for localised disease must have been completed at least 12 months previously and have been no longer than 12 months in duration. It can have been given as adjuvant or neoadjuvant therapy. Patients who have started bicalutamide or flutamide (up to 4 weeks prior to date of randomisation) are eligible. Patients who have started cyproterone acetate prior to randomisation are not eligible.

AND
For all patients
1. Intention to treat with continuous long-term ADT (> 3 years)
2. Fit for all protocol treatment and follow-up, WHO performance status 0-2
3. Should have completed the appropriate investigations prior to randomisation
4. Normal testosterone level prior to hormone treatment (>6 nmol/L)
5. Written informed consent
6. Willing and expected to comply with follow-up schedule
7. For newly diagnosed N0M0 patients only - Intention to treat with radical radiotherapy

Previous inclusion criteria:
Newly diagnosed patients with one of the following:
1. Stage T3/4 NX M0 histologically confirmed prostate adenocarcinoma with prostate specific antigen (PSA) greater than or equal to 20 ng/ml or Gleason sum score greater than or equal to 6
2. Stage Tany N+ M0 or Tany Nany M+ histologically confirmed prostate adenocarcinoma
3. Multiple sclerotic bone metastases with a PSA greater than or equal to 50 ng/ml without histological confirmation

OR

Patients with histologically confirmed prostate adenocarcinoma previously treated with radical surgery or radiotherapy who are now relapsing with one of:
1. PSA greater than or equal to 4 ng/ml and rising with doubling time less than 6 months
2. PSA greater than or equal to 20 ng/ml

Note: Prior hormone therapy for localised disease must have been completed at least 12 months previously and have been no longer than 12 months in duration. It can have been given as adjuvant or neoadjuvant therapy.

For all patients:
1. Intention to treat with long-term androgen deprivation therapy (ADT)
2. Fit for all protocol treatment and follow-up, World Health Organization (WHO) performance status 0 - 2
3. Have completed the appropriate investigations prior to randomisation
4. Normal testosterone level prior to hormone treatment
5. Written informed consent
6. Willing and expected to comply with follow-up schedule

## Participant type(s)
Patient

## Healthy volunteers allowed

No

## Age group
Mixed

## Sex
Male

## Total final enrolment
1854

## Key exclusion criteria
Current exclusion criteria as of 09/12/2014:
1. Prior systemic therapy for locally advanced or metastatic prostate cancer except as listed in participant inclusion criteria
2. Any other previous or current malignant disease or CVS disease which is thought likely to compromise the patient's ability to tolerate therapy or affect assessment
3. Cardiovascular exclusions:
3.1. Any history of cerebral ischaemia (e.g. stroke or TIA) within 2 years of randomisation
3.2. Any history of DVT or PE confirmed radiologically or a known thrombophilic disorder (e.g. Protein C, protein S, or antithrombin deficiency)
3.3. History of myocardial infarction/acute coronary syndrome:
3.3.1. Within the last 6 months
3.3.2. Greater than 6 months with evidence of q-wave anterior infarct on ECG
3.4. Unstable angina (typical cardiac chest pain at rest lasting more than 15 minutes) within the last year
3.5. Angina that occurs on walking 100 metres on the level or after climbing one flight of stairs at a normal pace and in normal condition, or angina that causes marked limitation of ordinary physical activity or occurs at rest
3.6. Heart failure: if patients have symptoms such as shortness of breath or oedema that are attributable to heart failure and this causes marked limitation of activity and/or they are comfortable only at rest then they should be excluded from the study
3.7. BP ≥160/100 (if either systolic or diastolic BP is greater than or equal to these values then the patient is not eligible)
3.8. Pulmonary oedema on CXR
4. Known porphyria

Previous exclusion criteria:
1. Prior systemic therapy for locally advanced or metastatic prostate cancer
2. Any other previous or current malignant disease or CVS disease which, in the judgement of the responsible physician, is likely to interfere with PATCH treatment or assessment.
3. Cardiovascular exclusions:
3.1. Any history of cerebral ischaemia (e.g. stroke or transient ischaemic attack [TIA])
3.2. Any history of deep vein thrombosis (DVT) or pulmonary embolism (PE) confirmed radiologically
3.3. History of myocardial infarction
3.3.1. Within the last 6 months
3.3.2. Greater than 6 months with evidence of q-wave anterior infarct on electrocardiogram (ECG) (right lead [RL])
3.4. Unstable angina (typical cardiac chest pain at rest lasting more than 15 minutes) within the last year

3.5. Angina that occurs on walking 100 metres on the level or after climbing one flight of stairs at a normal pace and in normal condition, or angina that causes marked limitation of ordinary physical activity or occurs at rest
3.6. Heart failure: If patients have symptoms such as shortness of breath or oedema that are attributed to heart failure and this causes marked limitation of activity and/or they are comfortable only at rest then they should be excluded from the study
3.7. Blood pressure (BP) greater than or equal to 160/100 (if either systolic or diastolic BP greater than these values then the patient is not eligible)
3.8. Pulmonary oedema on chest x-ray (CXR)

Patients that have a history of ischaemic heart disease or heart failure are required to have an Echocardiogram (ECHO) or multiple-gated acquisition scan (MUGA). Patients with left ventricular ejection fraction less than 40% will be excluded.

### Date of first enrolment
01/09/2005

### Date of final enrolment
01/04/2020

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
**Hammersmith Hospital**
London
United Kingdom
W12 0NN

## Sponsor information

### Organisation
Imperial College London (UK)

### ROR
https://ror.org/041kmwe10

## Funder(s)

### Funder type

Charity

**Funder Name**
Cancer Research UK

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

**Funding Body Type**
Private sector organisation

**Funding Body Subtype**
Other non-profit organizations

**Location**
United Kingdom

**Funder Name**
Medical Research Council (MRC) (UK)

**Alternative Name(s)**
Medical Research Council (United Kingdom), UK Medical Research Council, Medical Research Committee and Advisory Council, MRC

**Funding Body Type**
Government organisation

**Funding Body Subtype**
National government

**Location**
United Kingdom

# Results and Publications

**Individual participant data (IPD) sharing plan**
Not provided at time of registration

**IPD sharing plan summary**

**Study outputs**

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Other publications | Early hormonal data | 01/08/2008 | | Yes | No |

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| Other publications | Cardiovascular outcomes | 01/04/2013 | | Yes | No |
| Other publications | 1-yr change in lumbar spine bone mineral density in a subset of participants | 01/06/2016 | | Yes | No |
| Other publications | Long-term cardiovascular mortality and morbidity | 13/02/2021 | 15/02/2021 | Yes | No |
| Study website | Study website | 11/11/2025 | 11/11/2025 | No | Yes |