ISRCTN91422391 https://doi.org/10.1186/ISRCTN91422391

To examine the clinical effectiveness of aspirin and/or Vitamin D3 to prevent disease progression in men on active surveillance for prostate cancer

Submission date 06/04/2014	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 16/04/2014	**Overall study status** Completed	
Last Edited 23/05/2023	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-of-active-surveillance-aspirin-and-vitamin-d-in-men-with-prostate-cancer-provent#undefined

Study website
www.provent.org.uk

Contact information

Type(s)
Public

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Additional identifiers

EudraCT/CTIS number
2014-001784-13

IRAS number

ClinicalTrials.gov number
NCT03103152

Secondary identifying numbers
PROVENT: Version 5.0

Study information

Scientific Title
PROVENT: A randomised, double blind, placebo-controlled feasibility study to examine the clinical effectiveness of aspirin and/or Vitamin D3 to prevent disease progression in men on active surveillance for prostate cancer

Acronym
PROVENT

Study objectives
That men enrolled onto an active surveillance programme for the management of prostate cancer will actively participate in a randomised chemoprevention study of standard (300mg) or low dose (100mg) aspirin vs placebo and/or Vitamin D vs placebo.

Ethics approval required
Old ethics approval format

Ethics approval(s)
London-Hampstead Committee London, 18/11/2014, ref: 14/LO/2033

Study design
Randomised double blind placebo-controlled feasibility study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Prevention

Participant information sheet
See additional files

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

Interventions
The principal method of randomisation will be by means of a purpose designed web-based application, developed by Barts CTU, which will be accessible to all relevant research staff. Staff will be trained in the use of this application. The applications' Case Report Forms will reaffirm the patient's eligibility and require confirmation that the consent form has been satisfactorily signed and countersigned.

Eligible participants will be randomised into one of 6 arms of the study to receive one of the following:

1. Aspirin 300mg + Vitamin D3
2. Aspirin 300mg + Vitamin D3 placebo
3. Aspirin 100mg + Vitamin D3
4. Aspirin 100mg + Vitamin D3 placebo
5. Aspirin placebo + Vitamin D3
6. Aspirin placebo + Vitamin D3 placebo

Randomised blocks will be used to maintain balance amongst these 6 arms. In addition, the aspirin placebo groups will be block randomised to either small or large aspirin placebo tablets. The allocated study number will correspond to pre-labelled pots of trial medication held in pharmacy.

In the event that the web application is unavailable, a paper backup system will be available, and randomisations may be made using a FAX backup system. Once a patient has been successfully randomised, the enrolment of the patient will be documented on the PROVENT Screening Log.

Dosage:
Vitamin D3: 4,000IU/0.1mg (6 drops) orally daily or matched placebo
Aspirin: 100mg daily orally or matched placebo
Aspirin: 300mg daily orally or matched placebo

Intervention Type
Supplement

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Aspirin, Vitamin D3

Primary outcome measure
Rate of patient recruitment to a randomised chemoprevention study in men enrolled on an Active Surveillance programme for prostate cancer. This will be determined by screening logs and screening/randomisation case report forms.

Secondary outcome measures
1. To report response to treatment as determined by serial multi-parametric magnetic resonance imaging (MRI) of the prostate - measured by performing repeat prostate MRI imaging
2. To report biochemical disease progression - measured by measuring serum PSA levels 3 monthly
3. To report histological disease progression - measured by measuring serum PSA levels 3 monthly
4. To report toxicity and/or allergy to both aspirin and Vitamin D. Toxicity will be evaluated 3 monthly using the Adverse Events Case Report Form and the patient diary cards on which patients will record side effects and adverse reactions
5. To evaluate an association between androgens and disease progression. Blood will be taken to measure serum androgen levels every 6 months - at baseline, 6 months, 12 months and 18 months
6. To evaluate markers of disease progression. Urinary markers of disease progression (PCA3 and TMPRSS2-ERG) will be evaluated at baseline and 12 months. Tissue will be collected from the baseline and 12 month prostate biopsies for Cell Cycle Progression scores.

Overall study start date
01/10/2014

Completion date
31/03/2020

Eligibility

Key inclusion criteria
Current inclusion criteria as of 10/12/2018:
1. Male subjects aged 16 years or over with an estimated life expectancy of more than three years
2. Willing and able to provide written informed consent
3. Corrected serum calcium <2.65 mmol/l
4. No previous treatment for prostate cancer (including surgery, hormone therapy, radiotherapy, cryotherapy)
5. All subjects must have had Magnetic Resonance Imaging (MRI) of the prostate with targeted biopsy of any lesions identified
6. Histologically confirmed prostate cancer* following prostate biopsy (including at least 10 cores of prostate tissue) in men opting for Active Surveillance as their primary cancer therapy

*PROVENT Prostate Cancer Criteria for Inclusion:
1. Gleason score 6 or 7 (Gleason 3+3 or 3+4)
2. Clinical and radiological stage <T3
3. Serum PSA of 15.0 ng/ml or below
Less than 10 mm of cancer in a single core

7. Patients must have undergone a multi-parametric MRI deemed assessable by the local radiologist, and any lesions seen must have undergone targeted biopsy (transrectal or transperineal) within 12 months of study enrolment.

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Participant type(s)
Patient

Age group
Adult

Lower age limit
16 Years

Sex
Male

Target number of participants
102

Total final enrolment
130

Key exclusion criteria

Current exclusion criteria as of 10/12/2018:
1. Previously treated prostate cancer (including radiotherapy, hormone therapy, brachytherapy or surgery)
2. Current enrolment in an investigational drug, device or other clinical research study or participation in such a study within 30 days of randomisation
3. Current daily use of aspirin or NSAIDs; or daily dietary supplements/medication containing more than 400 IU (10 micrograms per day)Vitamin D; or chronic use (defined as > 6 months continuous daily use) of either aspirin or Vitamin D within two years of study enrolment
4. Current or previous use of 5-alpha-reductase inhibitors such as finasteride or dutasteride
5. Not willing to comply with the procedural requirements of this protocol including repeat prostate biopsies
6. Known allergy/sensitivity to or intolerance of aspirin, other salicylates or NSAIDs e.g. ibuprofen/ naproxen
7. Prior history of gastro-intestinal bleeding or ulceration, severe dyspepsia or inflammatory bowel disease
8. Haemophilia or other bleeding diatheses
9. Prior history of renal stone disease
10. Chronic renal disease (≥ stage 4)
11. Known hypercalcaemia (corrected serum calcium >2.65 mmol/l) or untreated hyperparathyroidism
12. Any bowel condition that would make repeat transrectal biopsy hazardous or difficult to perform e.g. recto-urethral fistula, or prior bowel surgery such as abdomino-perineal resection.
13. Any malignancy (other than non-melanoma skin cancer) that has not been in complete remission for five years
14. Any serious co-existent medical condition that would make repeat prostate biopsy hazardous e.g. anti-coagulation requiring continuous administration
15. Severe Asthma
16. G6PD deficiency
17. Pre-existing macular degeneration
18. All contraindications to aspirin and Vitamin D (e.g. Sarcoidosis), including concomitant therapy with any medication that may interact with aspirin or Vitamin D
19. Tuberculosis
20. Regular consumption of alcohol units greater than the recommended daily limit of 3-4 units per day (men)

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18. All contraindications to aspirin and Vitamin D, including concomitant therapy with any medication that may interact with aspirin or Vitamin D (see section 4.10)
19. Regular consumption of alcohol units greater than the recommended daily limit of 3-4 units per day (men)

Date of first enrolment
16/12/2016

Date of final enrolment
16/12/2017

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Centre for Cancer Prevention
London
United Kingdom
EC1M 6BQ

Sponsor information

Organisation
Queen Mary University of London (UK)

Sponsor details
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Sponsor type
University/education

ROR
https://ror.org/026zzn846

Funder(s)

Funder type
Charity

Funder Name
Bart's and the London Charity (UK) - Clinical Trials Awards and Advisory Committee (CTAAC) endorsed

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer reviewed journal. Any information used for publication in peer reviewed journals will be anonymised and presented at aggregate, and not individual, level. Barts & the London Charity, and CR-UK will be informed of the results. In addition, they will be disseminated to the participants via the PROVENT website.

Intention to publish date
31/03/2021

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V3	05/05/2016	03/04/2017	No	Yes

Participant information sheet	version V4.0	16/02/2017	26/01/2018	No	Yes
Protocol file	version V4.0	16/02/2017	26/01/2018	No	No
Protocol file	version V5.0	18/08/2018	10/12/2018	No	No
Basic results		16/12/2020	20/05/2022	No	No
Results article		11/06/2022	08/07/2022	Yes	No
Plain English results			23/05/2023	No	Yes
HRA research summary			28/06/2023	No	No