ISRCTN16951765 https://doi.org/10.1186/ISRCTN16951765

SPECTRE - Combined suppression of cholesterol bioavailability and androgen deprivation therapy to treat castration resistant prostate cancer

Submission date
16/02/2016

Recruitment status
No longer recruiting

Registration date
17/02/2016

Overall study status
Completed

Last Edited
16/05/2024

Condition category
Cancer

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol
http://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-using-a-drug-with-hormone-therapy-to-stop-prostate-cancer-from-spreading-spectre

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-003720-32

Protocol serial number

SPECTRE2015

Study information

Scientific Title
SPECTRE - Combined suppression of cholesterol bioavailability and androgen deprivation therapy to treat castration resistant prostate cancer: an interventional study

Acronym
SPECTRE

Study objectives
SPECTRE will establish whether inhibition of cholesterol biosynthesis in patients with ongoing ADT will suppress castration-resistant prostate cancer via a reduction in androgen mediated signalling.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Study design
Single-centre single-arm Phase II interventional study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Castration-resistant prostate cancer

Interventions
All eligible patients will receive a statin (Atorvastatin) to take orally for a 6 week period. Patients will be asked to attend the clinic once a week for 7 weeks, during the course of the trial. After completion of the trial medicine patients will attend for a further clinic visit, four weeks later. During each clinic visit, patients will be checked to ensure they are well, any side effects will be monitored and a blood test will be performed. Patients will also be asked to provide consent for additional blood samples at each study visit. These samples will be analysed in order to develop highly specific tests that will track the status of prostate cancer. Patients may also be requested to provide consent for two biopsy samples of their tumour; one before starting the trial medication, and another 5-7 weeks later. Biopsy samples will not be required from all patients taking part in the study.

Intervention Type
Drug

Phase

Phase II

Drug/device/biological/vaccine name(s)
Atorvastatin

Primary outcome(s)
Achievement of ≥50% drop from baseline in PSA levels at any time over the 6-week period of statins treatment (PSA response). The proportion of patients achieving PSA response rate will be presented together with an 80% confidence interval computed using the Clopper-Pearson approach.

Key secondary outcome(s)
1. Maximum percentage drop in PSA, determined for each patient and presented in a waterfall plot.
2. Change in levels of a number of biomarkers (circulating and tissue) following treatment with trial agent, including circulating cell-free tumour DNA (ctDNA), gene expression and other markers such as CTCs and exosomes

Completion date
20/12/2020

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 16/07/2018:
1. Proven adenocarcinoma of the prostate, defined as:
1.1. Histological or cytological evidence of prostate cancer,
1.2. PSA > 100 at time of diagnosis and presence of more than 4 bone metastases
2. Disease progression despite on-going castration therapy (either using LHRH analogue or prior surgical orchiectomy (with or without abiraterone or enzalutamide) as judged by rising serial PSA measurements. This will be based on a series of at least 3 readings each taken at least 7 days apart. The 3rd reading must be ≥ 2 ng/ml. In the event where an intermediate reading is lower than a previous reading, then the patient will still be eligible (i.e. the 3 readings do not need to be consecutive). In patients who have received prior bicalutamide, flutamide or nilutamide, PSA progression must be proven after withdrawal of this drug.
3. Castrate levels of serum testosterone
4. Ongoing castration therapy (either LHRH analogue or prior orchiectomy, with or without abiraterone or enzalutamide). Please note, although the continuation of abiraterone or enzalutamide may be permitted, this must firstly be discussed with the chief investigator for approval, prior to study entry.
5. No therapy with statins or other cholesterol-lowering drug during a 28 day period prior to initiation of trial medication.
6. Male aged 18 or over
7. Life expectancy greater than 6 months
8. Adequate hepatic, bone marrow, coagulation and renal function as defined by the following criteria:
8.1. Haemoglobin ≥ 9.0 g/dL
8.2. Platelets ≥ 100 x 109L
8.3. Creatinine
8.4. Hepatic function: total bilirubin ≤ 2 x ULN; ALT and AST ≤ 3 x ULN
8.5. Creatine kinase ≤ 5 x ULN

8.6. Prothrombin time ≤ 1.5 x ULN; APTT ≤ 1.5 x ULN
9. Willingness to comply with scheduled visits, medication plans and laboratory tests and other trial procedures
10. Ability to swallow oral medications
11. Willing to undergo two biopsies for research purposes with a lesion (either primary or secondary) amenable to biopsy

Previous participant inclusion criteria:
1. Histologically proven adenocarcinoma of the prostate (patients may or may not have evidence of metastatic disease)
2. Disease progression despite on-going castration therapy (either using LHRH analogue or prior surgical orchiectomy) as judged by rising serial PSA measurements: This will be based on a series of at least 3 readings each taken at least 7 days apart. The 3rd reading must be ≥2 ng/ml. In the event where an intermediate reading is lower than a previous reading, then the patient will still be eligible (i.e. the 3 readings do not need to be consecutive). In patients who have received prior bicalutamide, flutamide or nilutamide, PSA progression must be proven after withdrawal of this drug
3. Castrate levels of serum testosterone (<1.7 nmol/l)
4. Ongoing castration therapy (either LHRH analogue or prior orchiectomy)
5. No therapy with statins or other cholesterol-lowering drug during a 2-month period prior to initiation of trial medication
6. Male aged 18 or over
7. Life expectancy greater than 6 months
8. Adequate hepatic, bone marrow coagulation and renal function as defined by the following criteria:
8.1. Haemoglobin > 9.0 g/dL
8.2. Platelets > 100 x 109L
8.3. Creatinine <2 x ULN
8.4. Hepatic function: total bilirubin ≤ 2 x ULN; ALT and AST ≤ 3 x ULN
8.5. Creatine kinase ,≤ 5 x ULN
8.6. Fasting glucose ≤ 5.6 mmol/L
8.7. Prothrombin time ≤ 1.5 x ULN; APTT ≤ 1.5 x ULN
8.8. Platelets ≥ 100
9. Willingness to comply with scheduled visits, treatment plans and laboratory tests and other trial procedures
10. Ability to swallow oral medications
11. Willing to undergo two biopsies

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex

Male

Total final enrolment
14

Key exclusion criteria
Current participant exclusion criteria as of 16/07/2018:
1. Uncontrolled hypertension (defined as systolic ≥ 170 mmHg and/or diastolic ≥ 100 mmHg, despite optimal therapy)
2. The requirement for strong opiates to control cancer related pain (codeine and tramadol are permitted)
3. NYHA class III or IV heart failure or Childs-Pugh liver failure class B or worse
4. Patients with symptomatic or radiographic disease progression (Note: Imaging studies will not be conducted specifically to meet this criterion but only if clinically indicated in accordance with standard of care)
5. Other severe or uncontrolled systemic disease or evidence of any other significant disorder or lab finding that makes it undesirable for the patient to participate in the trial
6. History of physical or psychiatric disorder that would prevent informed consent and compliance with protocol, or any psychological, familial, sociological or geographical consideration potentially hampering compliance with the trial protocol and follow up schedule.
7. Administration of any investigational drug within 28 days of receiving the first dose of trial medication
8. Major surgery within 28 days prior to trial registration
9. Active condition which affects drug absorption (e.g. prior gastrectomy or active peptic ulcer disease)
10. Planned change in systemic therapy for 6 weeks after study medication initiation
11. Planned requirement for radiotherapy or surgery for 6 weeks after study initiation
12. Prior hypersensitivity to atorvastatin or its constituents
13. Requirement for on-going anti-coagulant therapy (including heparins and warfarin)

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Date of first enrolment
20/12/2016

Date of final enrolment
20/12/2019

Locations

Countries of recruitment
United Kingdom

Scotland

Study participating centre
Beatson West of Scotland Cancer Centre
1053 Great Western Road
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G12 0YN

Sponsor information

Organisation
NHS Greater Glasgow and Clyde

ROR
https://ror.org/05kdz4d87

Organisation
University of Glasgow

Funder(s)

Funder type
Charity

Funder Name

Prostate Cancer UK

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
Not provided at time of registration

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results		16/08/2020	16/06/2022	No	No
Plain English results			16/05/2024	No	Yes