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AdUP: AdNRGM; VDEPT + GMCSF in locally recurrent prostate cancer

Submission date 28/02/2013	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 28/02/2013	**Overall study status** Completed	
Last Edited 02/06/2023	**Condition category** Cancer	

Plain English summary of protocol
http://www.cancerresearchuk.org/cancer-help/trials/trials-search/a-trial-looking-biological-therapy-treat-prostate-cancer-come-back-after-radiotherapy-hormone-therapy-adup

Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2007-700341-13

Integrated Research Application System (IRAS)
45807

ClinicalTrials.gov (NCT)
NCT04374240

Protocol serial number
13599

Study information

Scientific Title
AdUP: A Phase I Clinical Trial of a replication defective type 5 adenovirus vector expressing nitroreductase and GMCSF (AdNRGM) given via trans-perineal, template-guided, intra-prostatic injection, followed by intravenous CB1954, in patients with locally relapsed hormone-refractory Prostate Cancer

Acronym
AdUP

Study objectives
The main purpose of this trial is to determine the safety and tolerability of a gene therapy strategy for the treatment of locally relapsed prostate cancer. The gene therapy is based on the intraprostatic injection of a viral vector (AdNRGM) carrying a gene called GMCSF which is able to induce a strong immune response against the prostate cancer, and a gene called NTR which is able to convert an inactive compound called CB1954 (prodrug) to a powerful anti-cancer drug. To ensure coverage of the whole prostate the vector will be administered by multiple stereotactically-guided intraprostatic injections. 48 hours after the injection of the viral vector, the prodrug CB1954 will be administered intravenously. It is expected that the combination of the immune response induced by the GMCSF and the activation of the prodrug C1954 operated by NTR within the tumour tissue will result in the death of a significant number of prostate cancer cells.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Oxford A, 07/12/2012, ref: 12_SC_0660

Study design
Non-randomised interventional; Design type: Treatment

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Current interventions as of 12/07/2016:
This is an open-label, non-randomised, phase I, sequential group trial which will explore the safety and tolerability of ascending doses of replication defective adenovirus type 5 vector

expressing nitroreductase and GMCSF (AdNRGM), in combination with CB1954. Five groups of three patients each will be treated with escalating doses of AdNRGM (1010, 3x1010, 1011, 3x1011, 1012 vp) followed 2 days later by intravenous CB1954 at a fixed dose (24mg/m2). The AdNRGM is given via trans-perineal, template-guided, intra-prostatic injection. Patients will be monitored on days 1, 2 and 5-7 following AdNRGM administration, with telephone contact on days 3 and 4; then seen at weeks 2, 3 and 4, then monthly for 12 months or until PSA progression.

Previous interventions:
AdNRGM Administration, Template-guided prostate brachytherapy
CB1954 Infusion, Infusion of 24 mg/m2

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Intraprostatic injection of a viral vector (AdNRGM)

Primary outcome(s)
Current primary outcome measures as of 26/07/2016:
1. Safety and tolerability of escalating doses of AdNRGM, followed by iv CB1954 determined by assessing local effects on tumour etc. and number of participants with treatment related adverse events by CTCAE v4.0 (Time Frame: 12 months)
1.1. Safety will be assessed in terms of local effects on the tumour, the prostate gland and the lower urinary tract as well as in terms of systemic effects. The data will be summarised descriptively
1.2. Adverse events and side effects will be determined as changes of the relevant clinical parameters as well as changes of haematological and clinical biochemistry data

Previous primary outcome measures:
Toxicity; timepoint(s): up to end of Month 11 visit

Key secondary outcome(s))
Current secondary outcome measures as of 26/07/2016:
1. PSA levels and PSA kinetics following treatment with AdNRGM and CB1954 (time frame: 12 months). Changes in the level and kinetics of the serum PSA will be measured to provide an indication of changes in tumour burden, growth rate and possible anti-tumour activity of the treatment.

Other pre-specified outcome measures:
2. Evidence for local tumour destruction, and immune infiltration, in tumour biopsies taken after the treatment (time frame: 12 months). Treatment-induced immune responses will be assessed by measurement of T cell responses to prostate cancer antigens in blood samples collected at baseline and at intervals (2, 3, 4, and 8 weeks) following treatment.
3. Changes in cellular immune response to prostate cancer antigens following treatment with AdNRGM and CB1954 (time frame: 12 months). Evidence of tumour destruction and immune infiltration will be assessed by looking at patterns of tissue damage, residual tumour tissue and immune cell infiltrates detected by immunohistochemistry in post-treatment prostate biopsies

Previous secondary outcome measures:
PSA level and kinetics; timepoint(s): Up to end of Month 11

Completion date
31/07/2021

Eligibility

Key inclusion criteria
1. Patients who present with biopsy proven local recurrence of prostate cancer following radical radiotherapy and a rising PSA while on androgen suppression with LHRH agonist therapy or after bilateral orchidectomy. A rising PSA is defined as 3 consecutive increases (measured by the same laboratory) over a minimum period of 6 weeks, with timepoints separated by at least 15 days. If the patient is on LHRH agonist therapy, this therapy should be continued.
2. Life expectancy greater than 3 months
3. Aged at least 18 years
4. Written informed consent
5. WHO performance status of 0-1 (Appendix 2)
6. PSA value = 4 and = 25 ng/ml at study entry
7. Adequate hepatic function (i.e. bilirubin, AST, ALT all < 1.5 x upper limit of normal for Institution)
8. Normal renal function (<1.25 x upper normal limit for the Institution)
9. Adequate haematological function (i.e. haemoglobin > 10g/dl, WCC > 3x109/l, platelets > 150x109/l) and normal clotting (INR and APTT <1.2)
10. Patients must agree not to father a child within 12 months following AdNRGM administration, and must practice a barrier method of contraception starting from the time of AdNRGM administration for at least 12 months
11. No known immunoincompetence

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Total final enrolment
18

Key exclusion criteria
1. Patients with a prostate or tumour which is deemed clinically unsuitable for transperineal templateguided injection

2. Patients who have previously been treated with prostate brachytherapy
3. Patients who have received chemotherapy, radiotherapy or immunotherapy within 28 days of study entry
4. Acute active infection (viral, bacterial, or fungal) which requires specific therapy
5. Chronic hepatitis B or C infection, HIV positive patients (patients will be tested for HBV/HCV, but not HIV)
6. Concurrent severe medical illnesses incompatible with the treatment including psychiatric pathology likely to affect protocol compliance
7. Tumours of other organs or tissues still active or treated radically less that 3 years before (except that successfully treated, nonmetastatic skin cancers are not an exclusion criterion)
8. Concurrent corticosteroids, or any medication known to have significant immunosuppressive action
9. Patients unable to travel for regular hospital assessments
10. Evidence of adenovirus infection and/or shedding at prescreening

Date of first enrolment
15/03/2013

Date of final enrolment
05/08/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston
Birmingham
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Sponsor information

Organisation
University of Birmingham (UK)

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK (UK); Grant Codes: C198/A9699

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
The datasets generated during and/or analysed during the current study will be available upon request. Scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. Requests should be made by returning a completed Data Sharing Request Form and curriculum vitae of the lead applicant and statistician to newbusiness@trials.bham.ac.uk. The Data Sharing Request Form captures information on the specific requirements

of the research, the statistical analysis plan, and the intended publication schedule. The request will be reviewed independently by the Cancer Research UK Clinical Trials Unit (CRCTU) Directors at University of Birmingham in discussion with the Chief Investigator and Trial Management Group. In making their decision the Director's Committee will consider the scientific validity of the request, the qualifications of the Research Group, the views of the Chief Investigator and Trial Management Group, consent arrangements, the practicality of anonymizing the requested data and contractual obligations. Where the CRCTU Directors and appropriate Trial Committees are supportive of the request, and where not already obtained, consent for data transfer will be sought from the Sponsor of the trial before notifying the applicant of the outcome of their request. It is anticipated that applicants will be notified of a decision within 3 months of receipt of the original request.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results	version 1.0	01/06/2023	02/06/2023	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes