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ProMOTE EMI-137: Prostate Molecular Targeting to Enhance surgery using EMI-137

Submission date 08/12/2020	**Recruitment status** No longer recruiting	[_] Prospectively registered [X] Protocol
Registration date 11/01/2021	**Overall study status** Stopped	[_] Statistical analysis plan [_] Results
Last Edited 11/01/2021	**Condition category** Cancer	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims

This study aims to test whether a 'marker' called EMI-137 which is injected as a drug, makes it easier for surgeons to see prostate cancer cells during surgery.

EMI-137 binds to a type of prostate cancer cell that has a protein called 'c-Met' on its surface. EMI-137 is attached to a fluorescent dye that shines in the dark (and can bind to and highlight prostate cancer cells with 'c-Met' protein. This was shown to work in patients with colorectal cancer, but it is not known if it will work in patients with prostate cancer. The researchers think that being able to see cancer cells more clearly during surgery will help the surgeon to remove all of the cancer cells, which will help to stop the cancer from coming back. It will also help to avoid unnecessarily removing normal cells, which would improve outcomes after the prostate is removed, particularly related to urinary leakage and sexual activity.

The researchers want to test whether EMI-137 can bind to and highlight only prostate cancer cells during surgery, without highlighting any other tissue, which doesn't have cancer. They also want to find out the best dose and time to give the drug to patients before surgery. The lower dose will be tested first at 2 hours before surgery, if it highlights the prostate cancer cells well, without highlighting healthy tissue, there will be no need to change the timing or test the higher dose in patients. The dose given will depend on whether the drug has already been tested in patients and what the results showed.

The study also aims to look at whether there are any specific changes within the genetic makeup of each cell (the DNA) that can cause them to become cancerous or spread. To answer this question, the researchers will perform genetic tests on the tissue samples taken at the time of diagnosis, and those taken during surgery. The results will help the researchers to understand the differences between normal and cancerous cells. The researchers hope to find out which changes in DNA lead to prostate cancer development and progression.

Who can participate?

Men diagnosed with prostate cancer who have chosen to have surgery to remove their prostate.

What does the study involve?
Participants will be invited to attend an information appointment to discuss the study with a member of the research team. If they decide to take part in the study they will be asked to sign an informed consent form. Participants will also be asked to provide a blood sample, undergo a physical exam, vital signs assessment and have an electrocardiogram (ECG) (recording test to monitor heart activity).

Participants will be given EMI-137 drug via an injection. It takes some time for the drug to bind to prostate cancer cells, so they will be given the drug two to four hours before surgery. The surgery will be conducted as per routine NHS procedure using keyhole surgery and a special camera. The camera is used to identify the dye, as explained to participants by the treating consultant. The prostate will be removed and biopsies from any tissues highlighted by the dye will be taken. These biopsies will be looked at by a doctor who studies diseased tissue (histopathologist) to find out whether they contain cancerous cells. If any cancerous cells are found outside of the prostate, a doctor will discuss the results and the best course of action with participants at a routine follow up visit.

Participants will be asked to provide urine samples before and after drug injection, during their stay in hospital for the operation, between discharge from hospital and the routine follow-up visit 1, and at the routine follow-up visit 2. After surgery, participants will receive usual NHS care, including follow-up visits and regular Prostate Specific Antigen (PSA) tests. The research team will access and record routine PSA results.

What are the possible benefits and risks of participating?
The EMI-137 drug has already been tested in a Phase I study in 20 healthy volunteers and 15 patients with high suspicion of colorectal cancer. The study showed that a single injection of the drug at the highest dose (130 µg/kg) was well tolerated and safe.

Participants will not need to stay in hospital any longer than usual, their surgery and schedule of follow up visits will be the same as standard NHS care. If participants agree to take part in the trial, they will be asked to provide extra blood samples, have a physical exam, vital signs assessment and ECG after they sign the informed consent form and again at the 6-week follow-up visit. They will be asked to provide urine samples at different times.

Participants will also receive drug injection 2-4 hours before surgery. The injection and the use of a cannula (a thin tube used to administer medication) carries a small risk of infection and haematoma (a swelling containing blood). Providing blood samples carries a small risk of bruising, infection, and fainting.

The EMI-137 drug has a blue colour. Participants might experience a temporary change to the colour of their skin and/or urine during the 24 hours (or longer) after being given the drug.

Participation in the study will not directly benefit participants. The main benefit of taking part will be the information that can be gathered as a result. This may help to improve treatment options for men with high-risk prostate cancer in the future.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
From October 2019 to December 2020

Who is funding the study?
Cancer Research UK (UK)

Who is the main contact?
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Contact information

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Public

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Additional identifiers

EudraCT/CTIS number
2017-003026-32

IRAS number

233023

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 38875, IRAS 233023

Study information

Scientific Title
Investigation of novel molecular imaging techniques for precision surgery and genomic characterisation of high-risk prostate cancer using EMI-137

Acronym
ProMOTE EMI-137

Study objectives
1. EMI-137 can bind to and highlight only prostate cancer cells during surgery, without highlighting any healthy tissue
2. The optimal dose and timing of EMI-137 administration before surgery to remove the prostate can be identified and the safety of a single dose of EMI-137 can be confirmed

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 18/10/2018, South Central – Berkshire REC (Bristol REC Centre, Whitefriars, Level 3, Block B, Lewins Mead, Bristol, BS1 2NT; +44 (0)20 7104 8043; berkshire.rec@hra.nhs.uk), ref: 18/SC/0340

Study design
Single-centre open-label non-randomized trial

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional file ISRCTN97555789_PIS_v2.0_20Feb2019 (added 11/01/2021)

Health condition(s) or problem(s) studied

Prostate cancer

Interventions

In Stage 1, the study team will test the hypothesis that EMI-137 can bind to and highlight only prostate cancer cells during surgery, without highlighting any healthy tissue. Stage 1 is a non-randomised study and will recruit up to 20 patients with high-risk prostate cancer (PC). Results from Stage 1 will establish the best dose and timing of EMI-137 administration by injection, by comparing two doses (130 µg/kg or less) and time intervals (at 2 and 4 h before surgery) in four groups of up to five patients. Twenty patients will be sufficient to give a good assessment of the endpoints and enable the choice of the best dose and timing for the validation study (Stage 2). The investigator may replace patients who withdraw from the study in Stage 1.

Once an eligible patient has consented to join the study they will be asked to attend the clinic either 2 or 4 h before their scheduled surgical procedure in order to have the EMI-137 administered by injection. During the surgical procedure, the surgeon may take biopsies of any tissue outside of the prostate that is highlighted by the drug and new optical system. This is the only difference from standard NHS care.

Stage 2 cannot start until the Stage 1 data has been analysed and it has been confirmed that it is possible to see prostate cancer cells in at least 50% of patients. In Stage 2 the study team will test the benefit of fluorescence image-guided RARP using EMI-137 by comparing two matched groups of patients. In Stage 2, the hypothesis that fluorescence image-guided RARP using EMI-137 makes it easier for surgeons to see prostate cancer cells, leading to complete removal of cancer cells and less healthy tissue, which may stop the cancer coming back, will be tested. 100 patients will be recruited and randomised equally using OCTRU's RRAMP system to either standard RARP, or to fluorescence image-guided RARP using EMI-137. Randomisation will be stratified by age, PSA level, and Gleason scoring. This sample size will provide 80% power and 5% (2-sided) significance to detect a large reduction in positive surgical margin rates (a reduction from 45% to 20%) in patients with high-risk PC. Patients who withdraw from the study may not be replaced in this stage.

The same recruitment criteria will be used for high-risk PC as used in Stage 1. 100 men will be randomly allocated to receive either ‘molecular imaging’ with fluorescence image-guided RARP, or standard RARP, following informed consent. The procedure for image-guided RARP will be finalised based on the results obtained during Stage 1.

Patients in the fluorescence image-guided RARP group will attend the clinic at the optimal time identified in Stage 1 before their scheduled surgical procedure to have EMI-137 administered by injection using the optimal dose identified in Stage 1. During the surgical procedure, the surgeon may take biopsies of any tissues outside of the prostate that are highlighted by the drug. This is the only difference to standard NHS care. No biopsies of tissue outside of the prostate will be taken in patients undergoing standard RARP. Patients in the standard RARP (control) group will be treated as per standard NHS care throughout.

There are no planned interim analyses/reports.

Intervention Type

Procedure/Surgery

Primary outcome measure

1. Optimal dose and timing of administration of EMI-137 before radical prostatectomy surgery measured using fluorescence image-guided RARP at 2 or 4 h after EMI-137 injection

Secondary outcome measures
There are no secondary outcome measures

Overall study start date
01/01/2014

Completion date
17/12/2020

Reason abandoned (if study stopped)
Participant recruitment suspended during the coronavirus (SARS-CoV-2) pandemic and the study was closed as an alternative IMP (ISRCTN10046036) was identified for further investigation

Eligibility

Key inclusion criteria
1. Men with histologically proven high-risk non-metastatic localized or locally advanced prostate cancer (PC):
1.1. Risk 1: serum PSA 10-20ng/ml and Gleason ≥4+3
1.2. Risk 2: serum PSA ≥20 ng/ml
1.3. Risk 3: grade group 4 or 5
1.4. Risk 4: clinical T3
2. Eligible for robot-assisted laparoscopic radical prostatectomy by the local standard of care
3. An understanding of the English language sufficient to understand written and verbal information about the trial and its consent process
4. Willing and able to give informed consent for participation in the study
5. Aged ≥18 years

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
Planned Sample Size: 120; UK Sample Size: 120

Total final enrolment
2

Key exclusion criteria
1. Unfit for radical surgery as assessed by Consultant Anaesthetist
2. History of any cancer, except non-melanoma skin cancer
3. Androgen suppression/hormone treatment within the previous 12 months for PC
4. Previous High-Intensity Focussed Ultrasound (HIFU), cryosurgery, thermal or microwave therapy to the prostate.
5. Transurethral Resection of the Prostate (TURP) for symptomatic lower urinary tract symptoms within 6 months. These patients may be included within the trial if deferred from consenting and screening until ≥6 months following the TURP.
6. Presence of metal implants/stents in the urethra
7. Renal impairment with a Glomerular Filtration Rate (GFR) of < 35ml/min (unable to tolerate Gadolinium dynamic contrast enhanced Magnetic Resonance Imaging)
8. Unable to provide informed consent to participate in the trial as judged by the attending clinician

Date of first enrolment
22/10/2019

Date of final enrolment
25/03/2020

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Oxford University Hospitals NHS Foundation Trust
John Radcliffe Hospital
Headley Way
Headington
Oxford
United Kingdom
OX3 9DU

Sponsor information

Organisation
University of Oxford

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Sponsor type
Hospital/treatment centre

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
Cancer Research UK

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

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Funder Name
National Institute for Health Research (NIHR) (UK)

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
This study is part of a wider programme grant with planned publication in a high-impact peer reviewed journal.

Intention to publish date

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available as the study was terminated early (after recruiting and completing follow up on 2 patients) based on the more promising performance of another tracer which was being evaluated simultaneously.

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version v2.0	20/02/2019	11/01/2021	No	Yes
Protocol file	version v3.0	20/02/2019	11/01/2021	No	No
HRA research summary			28/06/2023	No	No