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Prostate MOlecular Targeting to Enhance surgery using IR800 IAB2M

Submission date	Recruitment status	[ ] Prospectively registered
05/03/2018	Suspended	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
09/03/2018	Ongoing	[X] Results
Last Edited	**Condition category**	[ ] Individual participant data
16/07/2024	Cancer	

Plain English summary of protocol

Current plain English summary as of 23/11/2021:

Background and study aims
This study aims to test new imaging techniques in high-risk prostate cancer patients who are likely to have spreading disease that cannot be seen with the naked eye. Patients are injected with a special dye which carries a specific marker (IR800 IAB2M) that marks prostate cells only, and a special camera is used to make them shine in the dark. During keyhole surgery, the special dye and camera should allow the surgeon to see cancer cells, and the 'shining' areas will be sampled to check that they are cancerous. The aim of this study is to test whether the combination of the new dye and camera helps to see whether cancer has spread, and improves the precision of surgical removal of cancer, at the same time as avoiding unnecessarily removing healthy tissue.

Who can participate?
Men aged 18 or above with intermediate or high-risk prostate cancer eligible for robot-assisted laparoscopic radical prostatectomy (keyhole surgery to remove the prostate)

What does the study involve?
There are two stages in this study. Stage 1 is now complete, and aimed to find the best dose, timing of injection, and equipment settings in 24 men with high-risk prostate cancer. The researchers tested combinations of doses of the dye, and time intervals between the injection and surgery, to find out whether prostate cancer cells can be seen during surgery, and the general safety of the technique.
The aim of stage 2 is to test the technique in a further 60 patients, compared with a 'control' group of 60 similar patients who do not receive the imaging. The patients are randomly allocated to the two groups, which are compared to find out whether more cancer cells are removed using the new imaging and more normal tissue is preserved, improving both cancer outcomes and urinary and sexual function. The researchers also aim to find out whether the imaging technique has helped patients 5 years after surgery.

What are the possible benefits and risks of participating?
Participation in the study does not directly benefit patients. The main benefit of taking part is

that the information gathered as a result may help improve treatment options for men with intermediate and high-risk prostate cancer in the future. The IR800 IAB2M drug has been tested in 24 men in the stage 1 study and there were no safety concerns. Because it takes some time for the drug to work, patients who are randomised to receive the drug need to come to the hospital for an extra visit, 10 days before their operation, and need to stay for two hours after the injection to make sure that they are feeling well afterwards. There is potential for a hypersensitivity or allergic response following the injection, so patients are monitored for two hours to make sure that they don't have an adverse reaction. Apart from receiving an injection before surgery, treatment and follow up are the same as standard NHS care. The injection and the use of a cannula (thin tube used to administer medication) carry a small risk of infection and haematoma (a swelling containing blood). Patients are given a contact card with 24-hour contact details in case they feel unwell or notice any side effects after leaving clinic after having the injection.

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

When is the study starting and how long is it expected to run for?
January 2015 to October 2026

Who is funding the study?
Cancer Research UK

Who is the main contact?
Dr Claire Thomson

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Previous plain English summary:

Background and study aims
This study aims to test new imaging techniques in high-risk prostate cancer patients who are likely to have spreading disease that cannot be seen with the naked eye. Patients are injected with a special dye which carries a specific marker (IR800 IAB2M) that marks prostate cells only, and a special camera is used to make them shine in the dark. During keyhole surgery, the special dye and camera should allow the surgeon to see cancer cells, and the 'shining' areas will be sampled to check that they are cancerous. The aim of this study is to test whether the combination of the new dye and camera helps to see whether cancer has spread, and improves the precision of surgical removal of cancer, at the same time as avoiding unnecessarily removing healthy tissue.

Who can participate?
Men aged 18 or above with high-risk prostate cancer eligible for robot-assisted laparoscopic radical prostatectomy (keyhole surgery to remove the prostate)

What does the study involve?
There are two stages in this study. The aim of stage 1 is to find the best dose, timing of injection, and equipment settings in 20 men with high-risk prostate cancer. The researchers test combinations of two doses of the dye, two time intervals between the injection and surgery, whether prostate cancer cells can be seen during surgery, and the general safety of the technique. The aim of stage 2 is to test the technique in a further 50 patients, compared with a 'control' group of 50 similar patients who do not receive the imaging. The patients are randomly

allocated to the two groups, which are compared to find out whether more cancer cells are removed using the new imaging and more normal tissue is preserved, improving both cancer outcomes and urinary and sexual function. The researchers also aim to find out whether the imaging technique has helped patients 5 years after surgery.

What are the possible benefits and risks of participating?
Participation in the study does not directly benefit patients. The main benefit of taking part is that the information gathered as a result may help improve treatment options for men with high-risk prostate cancer in the future. This is the first time that the IR800 IAB2M drug is being tested in patients, but a related product (89Zr-Df-IAB2M), which is made of the same active ingredient (IAB2M), has been used in studies. The active ingredient and the dye (IR800) attached to the drug were both shown to be safe when tested separately. Because it takes some time for the drug to work, patients need to come to the hospital for an extra visit, either 24 or 48 hours before their operation, and need to stay for two hours after the injection to make sure that they are feeling well afterwards. There is potential for a hypersensitivity or allergic response following the injection, so patients are monitored for two hours to make sure that they don't have an adverse reaction. Apart from receiving an injection before surgery, treatment and follow up are the same as standard NHS care. The injection and the use of a cannula (thin tube used to administer medication) carry a small risk of infection and haematoma (a swelling containing blood). Patients are given a contact card with 24-hour contact details in case they feel unwell or notice any side effects after leaving clinic after having the injection.

Where is the study run from?
Oxford University Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
January 2015 to October 2026

Who is funding the study?
Cancer Research UK

Who is the main contact?
Dr Claire Thomson

Contact information

Type(s)
Scientific

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Public

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Additional identifiers

EudraCT/CTIS number
2017-001332-19

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
37632

Study information

Scientific Title
Investigation of novel molecular imaging techniques for precision surgery and genomic characterisation of high-risk prostate cancer using IR800 IAB2M

Acronym
PROMOTE IR800 IAB2M

Study objectives
This study aims to test new imaging techniques in high-risk prostate cancer patients, likely to have spreading disease that we cannot see with the naked eye. Patients will be injected with a special ‘dye’ which carries a specific ‘marker’ (IR800 IAB2M) that will visualise prostate cells only, and use a special camera to make them shine in the dark. During keyhole surgery, the special dye and camera should allow the surgeon to see cancer cells, and the ‘shining’ areas will be sampled

to check that they are cancerous. The study will test whether the combination of the new dye and camera helps to see whether cancer has spread, and improves the precision of surgical removal of cancer at the same time as avoiding removing healthy tissue unnecessarily.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central - Oxford C Research Ethics Committee, 27/02/2018, ref: 18/SC/0103

Study design
Randomised; Interventional; Design type: Treatment, Drug, Imaging, Surgery

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See additional files

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

Interventions
Current interventions as of 23/11/2021:

This study will evaluate molecular imaging techniques in high-risk prostate cancer patients using deep red/near-infrared (NIR) fluorescence imaging with a fluorescent imaging molecule (IR800 IAB2M) during robot-assisted laparoscopic radical prostatectomy (RARP) to define extracapsular and nodal involvement and optimise the extent of surgical resection. This will happen in two stages:

Stage 1: Finding the best dose, timing of injection, and equipment settings in 20 men with high-risk prostate cancer. The study will test: combinations of two doses of the dye (20-50mg), two time-intervals between the injection and surgery (24-48 hours), whether prostate cancer cells can be seen during surgery, and general safety of the technique. Both the marker and the special dye have been used separately and safely in patients previously.

Stage 2: Testing the technique in a further 60 patients, compared with a ‘control’ group of 60 similar patients who will not receive the imaging. The patients will be assigned randomly to either group following consent using a computer programme. The groups will be compared to find out whether more cancer cells are removed using the new imaging, and more normal tissue is preserved to improve both cancer outcomes and urinary as well as sexual function. The study

will also find out whether the imaging technique has helped patients to improve their cure, and reduce treatment failure 5 years after surgery.

All patients in stage 1, and those randomised to molecular imaging in stage 2, will receive a single injection of IR800 IAB2M prior to RARP surgery. Patients in stage 1 will be followed up for 6 weeks post-surgery. Patients in stage 2 will be followed up for 5 years post-surgery via annual review of medical notes.

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Previous interventions:

This study will evaluate molecular imaging techniques in high-risk prostate cancer patients using deep red/near-infrared (NIR) fluorescence imaging with a fluorescent imaging molecule (IR800 IAB2M) during robot-assisted laparoscopic radical prostatectomy (RARP) to define extracapsular and nodal involvement and optimise the extent of surgical resection. This will happen in two stages:

Stage 1: Finding the best dose, timing of injection, and equipment settings in 20 men with high-risk prostate cancer. The study will test: combinations of two doses of the dye (20-50mg), two time-intervals between the injection and surgery (24-48 hours), whether prostate cancer cells can be seen during surgery, and general safety of the technique. Both the marker and the special dye have been used separately and safely in patients previously.

Stage 2: Testing the technique in a further 50 patients, compared with a ‘control’ group of 50 similar patients who will not receive the imaging. The patients will be assigned randomly to either group following consent using a computer programme. The groups will be compared to find out whether more cancer cells are removed using the new imaging, and more normal tissue is preserved to improve both cancer outcomes and urinary as well as sexual function. The study will also find out whether the imaging technique has helped patients to improve their cure, and reduce treatment failure 5 years after surgery.

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Intervention Type
Other

Phase
Phase I

Primary outcome measure
Visibility of lesions including autofluorescence; Timepoint(s): At surgery

Secondary outcome measures
Stage 1:
Adverse events assessment from consent up to 6 weeks post-surgery

Stage 2:
1. Biochemical relapse measured using a Prostate Specific Antigen blood test at 6 weeks post-surgery
2. Time to administration of salvage therapy such as external beam irradiation and/or androgen suppression measured by recording the time between intervention and the administration of salvage therapy during follow up routine NHS care in the clinic up to 5 years post-surgery
3. Disease specific and overall mortality assessed annually by reviewing medical notes up to five years post-surgery
4. Safety measured using adverse events assessment from consent up to 6 weeks post-surgery

Overall study start date
01/01/2015

Completion date
31/10/2026

Eligibility

Key inclusion criteria
Current inclusion criteria as of 23/11/2021:

1. Histologically proven intermediate/high-risk untreated PC undergoing radical prostatectomy, where the indication for sparing the neurovascular bundle on either or both sides is equivocal.
2. Suitable for surgery by 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. Participant is willing and able to give informed consent for participation in the study.
5. Aged 18 years or above

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Previous inclusion criteria:

1. Men with histologically proven high-risk non-metastatic localized or locally advanced (cT3) PC with any of the following risk criteria:
Risk 1: Serum PSA 10-20ng/ml and Gleason 4+3 or greater
Risk 2: Serum PSA ≥20 ng/ml
Risk 3: Grade group 4 or 5
Risk 4: Clinical T3
2. Eligible for robot-assisted laparoscopic radical prostatectomy by 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. Participant is willing and able to give informed consent for participation in the study
5. Aged 18 years or above

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
23

Key exclusion criteria
Current exclusion criteria as of 23/11/2021:

1. Unfit for radical surgery
2. History of any cancer, except non-melanoma skin cancer
3. Presence of metal implants/stents in the urethra
4. Men with renal impairment with a Glomerular Filtration Rate (GFR) of <35ml/min (unable to tolerate Gadolinium dynamic contrast enhanced Magnetic Resonance Imaging (MRI))
5. Serious nonmalignant disease (e.g., hydronephrosis, liver failure, or other conditions) that could compromise protocol objectives in the opinion of the investigator and/or the sponsor.
6. Unable to provide informed consent to participate in the trial as judged by the attending clinician

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Previous exclusion criteria:

1. Unfit for radical surgery as assessed by Consultant Anaesthetist
2. History of any cancer, except non-melanoma skin cancer
3. Men who have had androgen suppression/hormone treatment within the previous 12 months for their PC
4. Men who have had previous High Intensity Focussed Ultrasound (HIFU), cryosurgery, thermal or microwave therapy to the prostate
5. Men who have undergone a Transurethral Resection of the Prostate (TURP) for symptomatic lower urinary tract symptoms within six months. These patients may be included within the trial if deferred from consenting and screening until at least six months following the TURP
6. Presence of metal implants/stents in the urethra
7. Men with renal impairment with a Glomerular Filtration Rate (GFR) of < 35ml/min (unable to tolerate Gadolinium dynamic contrast enhanced Magnetic Resonance Imaging (MRI))
8. Serious nonmalignant disease (eg, hydronephrosis, liver failure, or other conditions) that could compromise protocol objectives in the opinion of the investigator and/or the sponsor
9. Unable to provide informed consent to participate in the trial as judged by the attending clinician

Date of first enrolment
01/04/2017

Date of final enrolment

01/10/2021

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Churchill Hospital
Oxford University Hospitals NHS Foundation Trust
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Sponsor information

Organisation
University of Oxford

Sponsor details
Clinical Trial and Research Governance
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Sponsor type
University/education

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK; Grant Codes: C1380/A18444

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

Results and Publications

Publication and dissemination plan
Results will be disseminated in the form of presentations at national and international learned societies and published in abstracts and full manuscripts in peer-reviewed journals around one year after the overall trial end date.

Intention to publish date
31/10/2027

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version V2.0	01/03/2018	09/03/2018	No	Yes
HRA research summary			28/06/2023	No	No
Results article		10/06/2024	16/07/2024	Yes	No