A prospective, Phase 3, multi center, single-arm, imaging study investigating the safety and diagnostic performance of rhPSMA 7.3 (18F) PET ligand in men with suspected prostate cancer recurrence based on elevated PSA following prior therapy

Published: 27-05-2020
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To assess the patient level CDR and region level PPV of rhPSMA-7.3 (18F) PET for BCR of PCa using histopathology or imaging as a SoT. Secondary Objectives: 1. To assess the patient level CDR and region level PPV of rhPSMA-7.3 (18F) PET in the...

Ethical review	Approved WMO
Status	Completed
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON50086

Source
ToetsingOnline

Brief title
302 SPOTLIGHT

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Prostate cancer

Research involving
Human

Sponsors and support

Primary sponsor: Blue Earth Diagnostics
Source(s) of monetary or material Support: farmaceutische industrie

Intervention

Keyword: - PET scan, - prostate cancer, - rhPSMA

Outcome measures

Primary outcome

The purpose of this study is to assess co-primary endpoints of patient level Correct Detection Rate (CDR) and region level positive predictive value (PPV) of rhPSMA 7.3 (18F) PET for BCR of PCa using histopathology or imaging as a SoT. The CDR is defined as the percentage of all patients scanned who have at least one True Positive (TP) lesion (localized correspondence between rhPSMA-7.3 (18F) PET imaging and the reference standard) regardless of any coexisting FP findings. When determining the region level PPV, all rhPSMA-7.3 (18F) PET-positive regions will be categorized as TP or False Positive (FP) regions using histopathology or imaging. Regions will include the prostate bed, pelvic lymph nodes, and other (bone, extra-pelvic lymph nodes, viscera and other soft tissues); a region will be categorized as a TP region if at least one PET positive lesion in the region is confirmed as a TP. For the primary analysis, pelvic lymph nodes will include the right and left external iliac, obturator, hypogastric (internal iliac), perirectal and presacral lymph node groups.

The prostate-specific membrane antigen (PSMA) receptor is over expressed in the

majority of PCa. Although not approved in any country or region, PSMA PET tracers have been used in many centers around the world to image PCa patients. Initial results have demonstrated promising diagnostic performance. Most trials investigating diagnostic PSMA ligands have thus far focused on patients with prior negative conventional imaging. Going forward in routine clinical care, given the low sensitivities of these conventional imaging procedures, it is difficult to continue to support subjecting patients to two or three non-sensitive imaging procedures before the patient may receive a more sensitive one.

rhPSMA 7.3 (18F) injection is a PET ligand for the detection of PCa. rhPSMA 7.3 (18F) has already been administered to patients at the Technical University of Munich (TUM). Based on the retrospectively determined high sensitivity of PSMA ligands, this study is designed to establish the diagnostic performance of rhPSMA 7.3 (18F) PET irrespective of the findings of conventional imaging in order to support the use of rhPSMA-7.3 (18F) as an imaging option during the initial workup of these patients.

Secondary outcome

Secondary study parameters/outcome of the study

1. Patient level CDR and region level PPV in patients who have negative conventional imaging.

2. Patient level CDR and region level PPV of rhPSMA-7.3 (18F) PET for recurrence in those patients with and without reference standard histopathology available.

3. Patient level CDR and region level PPV of rhPSMA-7.3 (18F) PET stratified by

PSA level.

4. CDR of rhPSMA-7.3 (18F) PET in the following regions: local recurrence, pelvic lymph nodes, other.

5. Percentage of patients in whom rhPSMA-7.3 (18F) PET imaging results changed the intended patient management (major and other changes).

6. Reader kappa statistics of rhPSMA 7.3 (18F) scan interpretation by the blinded independent readers.

7. Safety (AEs and vital signs) of rhPSMA 7.3 (18F) injection in patients.

Exploratory objectives

1. Overall patient level detection rate (without SoT confirmation) (including subgroup analyses listed in Secondary Endpoints 1 to 4 above).

2. Patient level PPV in which a TP patient is defined as having at least one TP region, regardless of any coexisting FP regions.

3. Percentage of patients with incremental lesion findings (e.g. more sites of involvement) on rhPSMA 7.3 (18F) compared to conventional imaging.

4. The number of positive rhPSMA-7.3 (18F) scans compared to conventional imaging in defined regions, leading to upstaging of the patient a) post RP and b) post RT.

5. Patient and regional level detection rates of rhPSMA 7.3 (18F) PET.

6. Patient and regional level detection rates of rhPSMA 7.3 (18F) PET as a function of PSA, prior Gleason score and PSAdt in a) post RP and b) post RT patients.

Study description

Background summary

Prostate cancer is one of the most common cancers in men. Recurrence (return) of prostate cancer is also common. One of the ways doctors detect recurrence is by measuring PSA levels in your blood. However, an increase in PSA levels alone does not tell the doctor where the cancer is or how much cancer there is. Imaging tests, like a bone scan, magnetic resonance imaging (MRI) and/or computed tomography (CT), are often performed to help the doctor determine where or how much cancer there is, and how best to treat the cancer.
This study looks at the ability of the study agent, used along with a PET scan, to guide your doctor in deciding the best treatment for you. The study agent binds to a protein called prostate specific membrane antigen (PSMA) that is found on the surface of cancer cells. The amount of this protein is known to be increased in prostate cancer. PET imaging helps to measure how the tracer attaches to this protein and the build up of the protein. Therefore, the study agent used together with a PET scan may help to detect sites where there is cancer and where it has spread.

Study objective

To assess the patient level CDR and region level PPV of rhPSMA-7.3 (18F) PET for BCR of PCa using histopathology or imaging as a SoT.
Secondary Objectives:
1. To assess the patient level CDR and region level PPV of rhPSMA-7.3 (18F) PET in the subgroup of patients who have negative baseline conventional imaging.
2. To assess the patient level CDR and region level PPV of rhPSMA-7.3 (18F) PET separated into subgroups of patients with reference standard histopathology available and unavailable.
3. To assess the patient level CDR and region level PPV of rhPSMA-7.3 (18F) PET stratified by PSA level.
4. To assess the CDR of rhPSMA-7.3 (18F) PET on a region level.
5. To assess the impact of rhPSMA 7.3 (18F) PET imaging results on the intended clinical management of study participants using a clinician survey.
6. To assess the inter- and intra reader agreement of rhPSMA-7.3 (18F) scan interpretation by the blinded independent readers.
7. To assess the safety of rhPSMA 7.3 (18F) injection in patients.
Exploratory objectives:
1. To assess the overall detection rate (without SoT confirmation) on a patient level and including all subgroup analyses listed in Secondary Endpoints 1-4 above.
2. To assess the patient level PPV in which a TP patient is defined as having at least one TP region, regardless of any coexisting FP regions.
3. To assess any incremental rhPSMA-7.3 (18F) PET findings (e.g. more sites of

involvement) compared to conventional imaging.
4. To assess the impact of rhPSMA 7.3 (18F) PET on upstaging patients with BCR of PCa a) post radical prostatectomy (RP) or b) post radiation therapy (RT) compared to conventional imaging.
5. To assess patient and regional level detection rates of rhPSMA 7.3 (18F) PET.
6. To assess patient and regional level detection rates of rhPSMA 7.3 (18F) PET as a function of PSA, prior Gleason score, and PSA doubling time (PSAdt) in a) post-RP or b) post RT patients.

Study design

This is a prospective, Phase 3, multi center, single-arm, single dose study designed to evaluate the safety and diagnostic performance of radiohybrid prostate specific membrane antigen (rhPSMA) 7.3 (fluorine-18 [18F]) positron emission tomography (PET) ligand for imaging in men with suspected biochemical recurrence (BCR) of prostate cancer (PCa) based on elevated prostate specific antigen (PSA) following prior therapy.
A number of measures have now been put in place to streamline the study for patients* safety due to the continued impact of the Corona Virus Disease 19 (COVID-19) pandemic on daily life.
Patients with a diagnosis of BCR of PCa being worked up for re staging and eligible for potential salvage treatment will be consented and enrolled. After enrollment (either before or after conventional imaging if not already completed), patients will receive 8 mCi (296 MBq) ± 20% rhPSMA 7.3 (18F), delivered as an intravenous (IV) bolus injection, followed by PET imaging.
If feasible, the patient will undergo image-guided biopsy of a PET-positive lesion(s) suspicious for recurrence of PCa within 45 days following rhPSMA 7.3 (18F) PET imaging. Note: due to the COVID-19 pandemic, this may be extended up to 60 days.
If necessary, confirmatory imaging (for Standard of Truth [SoT]) will be performed within 45 days following rhPSMA-7.3 (18F) PET imaging or attempted biopsy and, if necessary, additional follow up confirmatory imaging may be performed up to 90 days after rhPSMA-7.3 (18F) PET. Patients may receive salvage treatment following further consultation with their physician (outside of the scope of this study). The salvage treatment prescribed will be recorded.
If treatment consists of a surgical resection, the histology obtained will be correlated with rhPSMA 7.3 (18F) PET imaging. (and will serve as the SoT for PET-positive lesions resected). Follow-up confirmatory imaging, as part of the SoT algorithm, should not delay the patient*s treatment.
Notes: due to the COVID-19 pandemic, biopsy and surgical procedures performed to obtain SoT histology and initial confirmatory imaging assessments (in patients not undergoing biopsy/resection) may be delayed up to Day 60 to ensure the safety (i.e., decreased potential exposure to severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]) of enrolled patients. In patients with multiple PET-positive regions, confirmation of at least one PET positive lesion in each region is required either by biopsy/surgical resection or confirmatory imaging.

Safety (adverse events [AEs] and vital signs) will be monitored during the study.

Intervention

What participation involves
If you are eligible for the study and give your consent, some standard imaging procedures like a bone scan, MRI and/or CT will be done.
The exact duration of your participation could vary depending on the procedures that will be performed to confirm the spread of cancer, but it will not exceed 90 days from the date of the study scan.

Screening
First we determine whether you can participate. Then you will be asked to sign this consent form if you agree to take part in this study.
The following assessment and procedures will take place during screening:
• All details of your participation in the study will be recorded into a study database as well as your patient records.
• Details such as your date of birth and gender will be noted in the study database. Your height and weight will be measured.
• You will be asked about your medical history including a history of when prostate cancer was first diagnosed and any previous prostate cancer treatments. Other laboratory reports or scan reports performed by your doctor to investigate your prostate cancer will be reviewed.
• You will be asked about any medicines that you are currently taking.
• Your vital signs (blood pressure, pulse, respiration rate, and temperature) will be measured.
• Standard imaging like bone scan, CT scan or MRI of the pelvic and stomach area and a chest CT may be performed at this screening visit if the previous scans were taken at least 90 days before Screening. If the standard imaging is not done at or before Screening, it may be done within 2 weeks of Visit 2.
Sometimes we find something not associated with Prostate Cancer during the scan that requires further medical investigation. We will always tell you. Further investigation is carried out by the primary care physician or specialist. The cost of this will be borne by your own insurance.
If the study doctor decides that you are not eligible to take part in this study, he/she will tell you and discuss with you further treatment options for your condition outside of this study.
Treatment
Study Agent Administration
On the day of the study PET scan, the study staff will place an intravenous (IV) catheter (a long, thin tube) into a vein in your arm. The study agent will be administered through this tubing. The PET imaging will be done between 50 to 90 minutes after the study agent is injected.
PET Scan
PET imaging produces detailed 3-dimensional images of the inside of the body. In this study, it works by detecting the radiation given off by the study agent

injected into your arm.
During the scan, you will lie on your back on the scanning bed, preferably with your arms rested above your head. The bed will move slowly through the PET scanner. The PET scan is used in combination with a CT scan. The CT portion of the scan usually takes about 1 minute. The PET portion of the scan usually takes about 20 minutes.
Visits and Tests
For the study, after the screening visit, you have to visit the hospital 2 times (visit 2 and 3) in 45 days. A visit will take 1-4 hours.
During these visits, most of the procedures from the screening will be repeated. In addition, the following will take place:

Visit 2
• Any change in the medications from the Screening Visit will be noted.
• Before the PET scan, your weight, and vital signs (blood pressure, pulse, respiration rate, and temperature) will be measured.
• You will be asked about any side effects or changes in your health since your last visit.
• You will be administered the study agent in a safe and correct manner as described earlier in this document.
• Your vital signs will be measured again after the PET scan.
• You will undergo a PET scan as described earlier in this document.
• Your Visit 3 will be booked within 7 days.
Visit 3
• You will be asked about any side effects or changes in your health that you have had since your last visit and any changes to or new medicines you are taking.
• Your imaging results will be discussed with you and if required further procedures will be scheduled. If the results of the PET scan do not show suspicions of the cancer coming back, then you will finish the study at this visit. If there are findings on the PET scan you will remain in the study until reports from tissue biopsies and/or other imaging tests are obtained to confirm the location and extent of cancer.
Follow-up Procedures
• If there appears to be a cancerous lesion on the PET scan, a sample of tissue (biopsy) from the area may be taken for testing to confirm the spread of cancer.
• If you have a planned surgery, then the study doctor will note the date of the surgery. The doctor may also request results of the tests which were performed on the tissue that is removed during the surgery.
• Other scanning tests such as an ultrasound, a CT scan or an MRI may also be ordered by your doctor.
• You will be asked about any side effects or changes in your health since your last visit and any changes to or new medicines you are taking.
*
Secondary Follow-up Procedures
• If needed, further standard imaging tests will be done to confirm the results

of the PET scan. However, this will not delay or affect your cancer treatment.
• If you have had a surgery after your last appointment, then your study doctor will compare the results of the tests done which was performed on the tissue removed during the surgery with the results of your PET scan.
• The study doctor will also note if you are undergoing any other cancer treatment after the PET scan visit.
• You will be asked about any side effects or changes in your health since your last visit and any changes to or new medicines you are taking

Possible side effects and discomforts
The new diagnostic study agent may have side effects and may involve unknown risks. Any medication or procedure can have temporary and permanent side effects and can cause unforeseen adverse reactions.

Possible risks related to the study agent
The study agent has already been given to both men with prostate cancer and healthy volunteers and there have been very few side effects. There have been no reported side effects considered to be directly related to the study agent. There may be side effects that are not known at this time.

Possible risks related to study procedures.
• Radiation: This study involves exposure to a small amount of radiation from the study agent. Radiation is part of our natural environment. We are exposed to background radiation from materials in the earth itself, from naturally occurring radon in the air, from outer space, and from inside our own bodies (as a result of the food and water we consume). You will be exposed to radiation from the study agent. The total radiation burden in this study is approximately 8 mSv (Milli-Sievert is the unit of measurement for the radiation dose) from the main study examination (study agent and PET/CT scan). In comparison, the background radiation in the Netherlands is ~2.5 mSv, per year. If you often participate in scientific research with a radiation burden, you should discuss with the investigator whether participation at this time is sensible. The radiation used during the study may cause damage to your health. The main risk associated with all radiation exposure is the possibility of developing a radiation-induced cancer later in life. At these exposure levels, the risk is small. We advise you not to participate in another scientific study with a radiation burden in the near future. There is no objection to research or treatment with radiation for medical reasons.
• PET Scan: You may feel uncomfortable during the tests, since you are not allowed to move during the imaging procedure, and you may feel frightened by the cramped space in

Study burden and risks

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• PET Scan: You may feel uncomfortable during the tests, since you are not allowed to move during the imaging procedure, and you may feel frightened by the cramped space inside the machine.
• Blood draw/IV insertion: You will be asked to give blood samples during this study. When blood samples are taken from a vein, there is a risk of bruising, discomfort and pain at the site. Sometimes a person may become dizzy or faint when blood is drawn and there is a rare possibility of infection.
• Delay in treatment: Depending on the results of the images, your study doctor may need to take a biopsy or schedule additional imaging as part of this study and your treatment may be delayed until these are completed. Treatment will not be delayed any longer than 45 days after the PET Scan.
• Biopsy: A biopsy involves taking a small sample of body tissue, so it can be examined under a microscope. Most biopsies will only require local anesthetic, which means you will not need to stay in hospital overnight. But an overnight stay is may be required when the procedure is carried out under general anesthetic. Most types of biopsy are painless once the anesthetic starts to work, although this depends on where the sample is taken from. You may experience a dull ache, which can be treated with pain medication on the advice of your doctor. You may need to have stitches, or a dressing applied before you leave.
• Additional imaging: If a biopsy cannot be taken or if the biopsy failed to produce a reliable result, additional imaging may be required. Additional imaging may consist of

o CT scan: A CT scan is a type of X-ray. In some cases, a contrast medium may be needed. There is a risk of allergies to the contrast medium.
o MRI: Magnetic resonance imaging is a type of scan that uses magnetic fields and radio waves to take a picture of the body part being scanned. MRI machines produce loud banging noises, which cause some people to become stressed or upset. You may also feel uncomfortable inside the magnet if you do not like to be inside small places.
o PET Scan with a different radiotracer. You are not allowed to move during the imaging procedure, and you may feel uncomfortable by the cramped space inside the machine.
• New findings: In a small percentage of men scanned for prostate cancer the PET scan has detected other (non-prostate cancers) which were not suspected at the time of scanning. This could provide useful information but may also result in additional stress or anxiety.

Contacts

Public
Blue Earth Diagnostics

The Oxford Science Park, Magdalen Centre, Robert Robinson Avenue OX4 4GA
Oxford -
GB
Scientific
Blue Earth Diagnostics

The Oxford Science Park, Magdalen Centre, Robert Robinson Avenue OX4 4GA
Oxford -
GB

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Elderly (65 years and older)

Inclusion criteria

1. Patient willing to provide signed informed consent and willing to comply with all required study schedule events, where safe and feasible.
2. Patient is male and aged >18 years old.
3. Patient with a history of localized adenocarcinoma of the prostate with prior curative intent treatment, experiencing BCR of PCa potentially eligible for salvage therapy with curative intent, following prior treatment with one or more of the following: a) RP, b) RP plus adjuvant RT, c) RP plus adjuvant androgen deprivation therapy (ADT), d) external beam radiation therapy or e) focal gland therapies (e.g. brachytherapy, high-intensity focused ultrasound [HIFU]).
- At least 6 weeks must have elapsed after RP.
- If previously taking ADT, it should have been discontinued at least 16 weeks prior to screening.
- In the case of focal gland therapies (e.g. HIFU) and RT, the treatment will have occurred at least 1 year prior to screening.
4. An elevated PSA, clinically suspicious for biochemically recurrent disease:
- Following RP: initial PSA >=0.2 ng/mL followed by a subsequent confirmatory PSA value >=0.2 ng/mL.
- Following RT (e.g. radical radiotherapy or brachytherapy): nadir +2 ng/mL.
- Following focal gland therapies (e.g. HIFU): nadir +2 ng/mL
5. Patient willing to undergo biopsy for histological confirmation of rhPSMA-7.3 (18F) PET findings, where safe and feasible.

Exclusion criteria

1. Patients with any medical condition or circumstance (including receiving an IP) that the investigator believes may compromise the data collected or lead to a failure to fulfil the study requirements.
2. Patients who are planned to have an x-ray contrast agent or other PET radiotracer <24 hours prior to the PET scan.
3. Patients currently receiving ADT (defined as surgical orchidectomy; luteinizing hormone releasing hormone [LHRH] agonist alone [continuous or intermittent]; LHRH antagonist alone [continuous or intermittent]; administration or use of a first generation or second generation anti androgen alone or in combination with an LHRH agonist/antagonist).
4. Patients participating in an interventional clinical trial within 30 days and having received an IP within five biological half-lives prior to administration of rhPSMA-7.3 (18F).

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	01-10-2020
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	rhPSMA-7.3 (18F)
Generic name:	rhPSMA-7.3 (18F)

Ethics review

Approved WMO Date:	27-05-2020
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	28-08-2020
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	17-09-2020
Application type:	Amendment

Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	22-09-2020
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	24-11-2020
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	03-12-2020
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	06-07-2021
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	08-07-2021
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2019-003382-18-NL
ClinicalTrials.gov	NCT04186845
CCMO	NL72637.075.20

Study results

Date completed: 13-01-2021

Results posted: 09-11-2022

First publication
15-12-2021