Phase III study of [18F]PSMA-1007 positron emission tomography for the detection of prostate cancer lesions in patients with biochemical recurrence after previous definitive treatment for localized prostate cancer

Published: 16-12-2020
Last updated: 17-01-2025

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Ethical review	Approved WMO
Status	Completed
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52213

Source
ToetsingOnline

Brief title
ABX-CT-303

Condition

- Reproductive neoplasms male malignant and unspecified

Synonym
cancer, prostate cancer

Research involving

Human

Sponsors and support

Primary sponsor: ABX GmbH
Source(s) of monetary or material Support: Ministerie van OC&W,Industry (ABX GmbH)

Intervention

Keyword: Cancer, Imaging, PET, Prostate cancer

Outcome measures

Primary outcome

• Region-level positive predictive value (PPV) defined as the percentage of all PET-positive regions containing at least one true positive lesion (exactly localized correspondence between [18F]PSMA-1007 PET imaging and the reference standard), regardless of any co-existent false positive findings within the same region, out of all regions containing at least one [18F]PSMA-1007 PET-positive finding. Regions to be considered in the analysis are prostate bed, pelvic lymph nodes, skeleton, and other distant sites (extrapelvic lymph nodes and viscera).

• Patient-level *correct detection rate* defined as the percentage of patients who have at least one true PET-positive lesion (exactly localized correspondence between [18F]PSMA-1007 PET imaging and the reference standard), regardless of any co-existent false positive findings, out of all patients who are scanned.

Secondary outcome

• to assess the correct detection rate and PPV of the clinical investigator for [18F]PSMA-1007 for metastatic prostate cancer lesions (patient-based analysis)

• to assess detection rate and PPV of [18F]PSMA-1007 by body region for prostate cancer lesions (region-based analysis: prostate bed, pelvic lymph nodes, skeleton, and other distant sites [extrapelvic lymph nodes and viscera]). reads by investigator and 3 independent blinded readers)

• to assess the safety profile of [18F]PSMA-1007

Study description

Background summary

Other than skin cancer, prostate cancer is the most commonly diagnosed solid organ malignancy in men; in the United States, approximately 191,000 new diagnoses and over 33,000 deaths are expected in 2020, according to the American Cancer Society. The prevalence and mortality rates in western Europe are similar. Despite a five-year survival rate of approximately 98%, recurrence of prostate cancer is common, up to 40-50% in some populations.
The diagnosis of prostate cancer recurrence after prior definitive therapy is typically based on an increase in blood prostate-specific antigen (PSA) concentration, based on serial measurements. For localization of tumor lesions in patients with rising PSA, different diagnostic imaging methods are available (computed tomography [CT], magnetic resonance imaging [MRI], bone scintigraphy, positron-emission tomography [PET]). While the available diagnostic methods provide reasonable diagnostic accuracy at later stages with high PSA levels, none of these methods provides the required sensitivity and accuracy to detect recurrence at early stages (e.g., PSA below 1-2 ng/mL).
PET/CT imaging with the non-specific tumor marker C-11-choline or its analogue F-18-fluorocholine has been used for more than a decade for imaging prostate cancer. Choline PET/CT is recommended by the National Comprehensive Cancer Network (NCCN) [1] and the European Association of Urology (EAU) [2] for the detection of sites of recurrence of prostate cancer after initial radical treatment. According to the meta-analysis of 14 articles by Treglia et al [3], pooled detection rate of prostate cancer for radiolabeled choline PET/CT is 58%, increasing to 65% in patients with PSA doubling time of 6 months or less, and 71% in patients with PSA levels greater than 1 ng/mL.
Recently, PET with radiopharmaceuticals targeting prostate-specific membrane antigen (PSMA) have been reported to detect prostate cancer lesions with high sensitivity. PSMA is a type II membrane glycoprotein that is expressed in all types of prostate tissue, and a number of pharmacophores have been developed that bind to PSMA with high specificity. As such, PSMA is a promising target for PET imaging in prostate cancer. Von Eyben et al. [4] recently conducted a

meta-analysis to evaluate the detection rate, diagnostic test accuracy, and adverse effects of Ga-68-HBED-CC-PSMA (Ga-68-PSMA-11) PET/CT or PET/MRI for staging of patients with prostate cancer and for restaging of patients with rising PSA after initial treatment. Fifteen studies with 1,256 patients met the inclusion criteria. Seven studies of staging PET/CT or PET/MRI detected a regional site of cancer for 203 of 273 patients (74%). Nine studies of restaging PET/CT detected sites of recurrence in 799 of 983 patients (81%) with a 50% detection rate (74 of 147 patients) for restaging patients with PSA of 0.2-0.49 ng/mL, and a 53% detection rate (56 of 195 patients) for restaging PSA of 0.50-0.99 ng/mL. None of the studies reported complications from PET/CT imaging.
Ga-68 has several shortcomings as a radiolabel, including short half-life and non-ideal energies for PET imaging, and PSMA-11 has high renal clearance, which is not optimal for pelvic imaging. Recently, the F-18 labeled PSMA ligand PSMA-1007 was described as a tracer for PET imaging [5]. [18F]PSMA-1007 demonstrates high labelling yields, outstanding tumor uptake and fast, non-urinary background clearance [5]. Radiation dosimetry in three healthy volunteers resulted in an effective dose of 4.4-5.5 mSv per 200-250 MBq. In comparison to other PSMA-targeting PET-tracers, [18F]PSMA-1007 has reduced urinary clearance enabling excellent assessment of the prostate. Similar to F-18-DCFPyL and with slightly slower clearance kinetics than PSMA-11, favorable tumor-to-background ratios are observed 2-3 h after injection. Giesel et al. [5] were able to successfully validate diagnostic [18F]PSMA-1007 findings by histopathology. In their study, [18F]PSMA-1007 PET/CT detected 18 of 19 lymph node metastases in the pelvis, including nodes as small as 1 mm in diameter. In an ongoing comparative trial (ABX-CT-301, NCT04102553), 200 patients with suspicion of recurrent prostate cancer were included, of whom 191 underwent [18F]PSMA-1007 PET/CT. The imaging results are compared to 18F-fluorocholine PET/CT for the detection of prostate cancer lesions. Patient enrollment and imaging is complete, but clinical follow-up in that study is still ongoing, and no efficacy results are available. A preliminary safety assessment found a total of six adverse events (AEs) contemporaneous with the PSMA-PET imaging; none of those AEs were reported by the investigator to be related to the study drug. There were no serious AEs.
Further details about [18F]PSMA-1007 can be found in the investigator*s brochure which contains comprehensive information on the study drug.

Study objective

There are two co-primary study objectives:
• Region-level positive predictive value (PPV) defined as the percentage of all PET-positive regions containing at least one true positive lesion (exactly localized correspondence between [18F]PSMA-1007 PET imaging and the reference standard), regardless of any co-existent false positive findings within the same region, out of all regions containing at least one [18F]PSMA-1007 PET-positive finding. Regions to be considered in the analysis are prostate bed, pelvic lymph nodes, skeleton, and other distant sites (extrapelvic lymph nodes

and viscera).
• Patient-level *correct detection rate* (DR) defined as the percentage of patients who have at least one true PET-positive lesion (exactly localized correspondence between [18F]PSMA-1007 PET imaging and the reference standard), regardless of any co-existent false positive findings, out of all patients who are scanned.

The primary objectives will be assessed in a blinded manner using 3 independent readers for imaging and an independent clinical panel for *truth*.

Secondary objectives
• to assess the correct detection rate and PPV of the clinical investigator for[18F]PSMA-1007 for metastatic prostate cancer lesions (patient-based analysis)
• to assess detection rate and PPV of [18F]PSMA-1007 by body region for prostate cancer lesions (region-based analysis: prostate bed, pelvic lymph nodes, skeleton, and other distant sites [extrapelvic lymph nodes and viscera]). Reads by investigator and 3 independent blinded readers.
• to assess the safety profile of [18F]PSMA-1007

Study design

This is a multi-center, open-label, nonrandomized study in patients with biochemical recurrence of prostate cancer, incorporating independent evaluation of PET imaging and an independent truth panel to determine clinical truth. The analysis population includes three cohorts of patients: approximately 60 evaluable patients to be recruited into this protocol (ABX-CT-303EUR), approximately 60 evaluable patients to be recruited into a companion study (ABX-CT-303US) to be conducted in the United States, and all evaluable patients who completed study ABX-CT-301. Newly recruited patients will undergo the following procedures:
1. Screening
2. PET/CT imaging with [18F]PSMA-1007
3. A follow-up visit one day after PET imaging for safety assessments
4. In selected patients, a follow-up visit for MRI or biopsy
5. 6 months of clinical follow-up (collection of all additional diagnostic information including imaging, as required for clinical purposes); investigators will be encouraged to seek biopsy confirmation of positive findings in [18F]PSMA-1007 PET

The true disease state at the time point of imaging will be determined by an expert panel on the basis of all relevant information from pre-inclusion to the end of the follow-up period, excluding data from [18F]PSMA-1007 PET.

Intervention

Recruited patients will undergo the following procedures:
PET examination with [18F]PSMA-1007
6 months follow-up (collection of all additional diagnostic information including imaging, as required for clinical purposes). During follow-up, selected patients will undergo multiparametric magnetic resonance imaging. Other selected patients may undergo biopsy.

Safety assessments will include:
adverse events
clinical laboratory (blood chemistry, hematology, urinalysis)
12-lead electrocardiogram
Vital signs
Safety assessments will end the day following the PET examination.

Study burden and risks

In this study, participating patients with suspicion of prostate cancer recurrence or persistence will undergo one PET/CT examination with [18F]PSMA-1007.
The use of [18F]PSMA-1007 in prostate cancer patients has been reported in several hundred patients without relevant safety signal. The radiation exposure with [18F]PSMA-1007 is comparable (0.019 mSv/MBq) to that of fluorocholine (0.017 mSv/MBq) and fluorodeoxyglucose (0.020 mSv/MBq). In addition to the radiation exposure from fluorine-18, there is the additional exposure from computed tomography, which varies from approximately 2 mSv for a low-dose CT to approximately 10 mSv for a diagnostic CT. The total radiation exposure is well below the limit of 30 Gy often considered to be an acceptable upper limit for subjects in a clinical trial. Overall, the risk for adverse events is considered to be low for patients participating in this trial.
Patients participating in this trial may have a personal benefit from undergoing [18F]PSMA-1007 PET/CT. The imaging results will be made available to treating physicians and may lead to a more accurate diagnosis and treatment. Considering the potential personal benefit, the severity of the underlying disease, and the low probability for severe and serious adverse events, the benefit-risk ratio of this study is regarded as acceptable and positive.
This study will commence during the COVID-19 pandemic and the intended study population (males typically older than 60 years of age) constitutes a risk group for COVID-19. In general, patients with recurrence or persistence of prostate cancer have a higher morbidity and mortality than the general older male population and could benefit from a better understanding of the location and extent of their disease. We consider the short-term risk of COVID-19 to patients and study staff to be reasonable, as the study visits all require only minimal interaction between patient and staff. However, because the pandemic situation is very fluid and varies by study site, study investigators are encouraged to incorporate appropriate mitigation strategies where appropriate for the local condition. Such mitigation strategies might include combination of visits 1 and 2 or a temporary hold on study recruitment while a local

outbreak is brought under control.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Male with original diagnosis of adenocarcinoma of the prostate with prior definitive therapy
2. Suspicion of recurrence or persistence
-- after radiotherapy or cryotherapy: 3 consecutive PSA rises and/or PSA rise by 2.0 ng/mL or more above nadir (ASTRO-Phoenix)
-- after prostatectomy, PSA > 0.2 ng/mL on 2 or more determinations (recurrence), or failure of PSA to fall to undetectable levels post-prostatectomy (persistence) (American Urological Association)
3. For patients who previously had radical prostatectomy, salvage radiotherapy

is one likely treatment plan; for patients who initially underwent radiotherapy (including brachytherapy), confirmation of low volume disease is needed to define (local) treatment.
4. Life expectancy of 6 months or more as judged by the investigator
5. Willing and able to undergo all study procedures
6. Informed consent in writing (dated and signed)

Exclusion criteria

1. Age: less than18 years
2. Contraindications to any of the ingredients of [18F]PSMA-1007
3. Close affiliation with the investigational site; e.g. first-degree relative of the investigator
4. At the time of enrolment into this study, participating in another therapeutic clinical trial or has completed study participation in another therapeutic clinical trial within 5 days of enrolment into this trial
5. Having been previously enrolled in this clinical trial
6. Mental conditions rendering the subject incapable to understand the nature, scope, and consequences of the trial
7. Being clinically unstable or requiring emergency treatment
8. Patients who are unwilling to consider a biopsy if clinically recommended
9. Patients who are unable to undergo a PET/CT scan (e.g,, patients who are extremely obese, unable to lie flat or remain still, or have uncontrollable claustrophobia)
10. Patients for whom systemic therapy is the most likely course regardless of PET findings.

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):	13-09-2021
Enrollment:	45
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]PSMA-1007
Generic name:	[18F]PSMA-1007

Ethics review

Approved WMO Date:	16-12-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	09-06-2021
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2020-004235-24-NL
ClinicalTrials.gov	NCT04742361
CCMO	NL75225.091.20