Clinical trial with Sarabesin 3, a GRP receptor antagonist, labelled with gallium-68, in patients with prostate cancer confined to the primary organ

Published: 09-12-2013
Last updated: 24-04-2024

In this proposed study, we aim to test not only the safety and biodistribution of [68Ga]Sarabesin 3, but also its potential to visualise prostate cancer. If the peptide proves to be successful, a next study will be initiated to test the potential to...

Ethical review	Approved WMO
Status	Pending
Health condition type	Reproductive neoplasms male malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON39894

Source
ToetsingOnline

Brief title
Imaging of prostate cancer using GRP

Condition

- Reproductive neoplasms male malignant and unspecified
- Prostatic disorders (excl infections and inflammations)

Synonym
prostate cancer, prostate carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: bombesin, gastrin releasing peptide, nuclear imaging, prostatic neoplasms

Outcome measures

Primary outcome

Primary objectives

- to assess the safety of 275 MBq [68Ga]Sarabesin 3 (40 µg peptide) in patients

with PC;

= endpoints: adverse events (AE), with severity grading according to NCI

CTCAE version 4.0; the causality of each AE to [68Ga]Sarabesin 3;

= outcome measures: blood pressure, heart rate, haemoglobin, leucocytes,

thrombocytes, CRP, sodium, potassium, calcium, phosphate, urea, creatinine,

total protein, albumin, bilirubin, alkaline phosphatase, ALT, AST, gamma-GT,

uric acid, glucose, and gastrin;

- to determine the biodistribution of [68Ga]Sarabesin 3 in patients with PC;

= endpoint: biodistribution of [68Ga]Sarabesin 3 will be assessed by PET;

= outcome measures: qualitative and quantitative data per region of interest

per patient within the available time points;

Secondary outcome

Secondary objectives

- to evaluate the pharmacokinetics of [68Ga]Sarabesin 3 in patients with PC;

= endpoint: pharmacokinetic assessment of [68Ga]Sarabesin 3 in blood and if

achievable in urine;

= outcome measures: determination of degradation products, in plasma 5, 10, 30 and 60 minutes p.i. and urine samples 30 and 60 minutes p.i., time activity curve in blood from 5 min to 180 min p.i.; activity measurement in urine in 4 time frames: 0-30, 30-60, 60-90, 90-180 min p.i.;

- to assess the potential of [68Ga]Sarabesin 3 to visualise tumour lesions in patients with biopsy-proven PC that is assumed to be confined to the primary organ;

= endpoint: visualisation of primary carcinoma.

= outcome measures: imaging judged by two experienced nuclear physicians.

- to compare imaging results with receptor expression estimated on tissue samples in vitro;

= endpoint: correlation of visibility of prostate cancer lesions by imaging (visual grading and if achievable quantitative) with GRPr density by autoradiography;

= outcome measures: in consensus scored scans; SUVmax of tumour lesions; GRPr density in DLU/mm2 on tumour tissue;

- to compare histological results with receptor expression estimated on tissue samples in vitro;

= endpoint: correlation of results of histological evaluation performed by the pathologist with GRPr density by autoradiography;

= outcome measures: Gleason score, size of lesion, GRPr density in DLU/mm2 on tumour tissue.

Study description

Background summary

Crucial for the design of the optimal treatment schedules of prostate cancer patients is accurate staging of the disease. If the tumour is still confined to the prostate, curative treatment - surgical removal or local radiotherapy - is the best choice. However, these therapies can lead to severe adverse effects like erectile or urinary tract dysfunction and should only be offered to patients who are treated with a curative intent. Besides the need for accurate staging at presentation of the disease, a sensitive diagnostic technique is needed to detect local relapse or metastatic disease of prostate cancer in patients with rising PSA after local therapy. In almost 95 % of cases the rising PSA is the only indication for relapse: physical examination, CT, bone scan, and other routinely used imaging procedures are usually negative. A sensitive imaging method might visualize tumour tissue more accurately and thereby improve patient management.

Study objective

In this proposed study, we aim to test not only the safety and biodistribution of [68Ga]Sarabesin 3, but also its potential to visualise prostate cancer. If the peptide proves to be successful, a next study will be initiated to test the potential to visualise lymphe node and distant metastases in patients with more advanced disease.

Study design

The study is a single-centre, non-randomized, non-therapeutic, phase I study of radiolabelled Sarabesin 3 given in a single intravenous bolus for the imaging of PC. In this phase I study the focus lies on safety, biodistribution, and pharmacokinetics of the radiopeptide and its potential to visualise proven primary prostate cancer lesions.

Study burden and risks

The patient will have to come extra to the hospital for one day for study purposes. The whole study procedure will take about 5 hours, during which the patient will be scanned several times. Whenever possible regular pauses are included in the protocol. The follow-up for the study will be performed in combination with routine clinical follow-up visits(after prostatectomy).

There are some very low risks associated with placement, presence, and removal of venflons and the urine catheter. The risks of administrating the investigational product are prevented by working according to Good

Manufacturing Practice. The product will only be administered if it passes all quality controls listed in the IMPD. Biological effects caused by the compound are not expected as this is a receptor antagonist and the amount of peptide is very small. In a pilot study in Bad Berka, Germany (see below) a similar dose was used without any side effects.

No data concerning dosimetry of [68Ga]Sarabesin 3 are published yet. The estimated mean dose of the proposed imaging protocol is 11.8 mSv.

Direct benefits for the patients included in this study are not expected since only patients without suspicion of metastases are selected. In the unexpected case of suspicion of metastases on the images, the urologist will decide how to use this information.

One of the aims of this study is to explore the potential of [68Ga]Sarabesin 3 imaging in prostate cancer patients. If the peptide proves promising, it might help to more accurately stage PC by detecting metastases in (other) PC patients. Improved staging of individual patients suffering from PC will result in optimized care.

Patients scheduled for prostatectomy are required, because a comparison will be made between imaging results, histopathology, and in vitro autoradiography of GRPr density.

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

- male patients of 18 years and older;
- histologically confirmed prostate cancer, no clinical suspicion of metastasis;
- patient is scheduled for radical prostatectomy;
- capable of cooperating with imaging procedure and follow-up;
- World Health Organisation (WHO) performance status 0-2;
- signed and dated informed consent.

Exclusion criteria

- current severe and/or uncontrolled and/or unstable other medical disease (e.g. poorly controlled diabetes, unstable and uncontrolled hypertension, chronic renal or hepatic disease, severe pulmonary disease);
- other known malignancies (except local skin cancer);
- chemotherapy, radiotherapy, or anti-hormonal therapy prior to study;
- 5-alpha-reductase inhibitors prior to study;
- significant cardiac arrhythmia current or in patient history;
- prior NYHA (New York Heart Association) class III-IV cardiac disease or concurrent congestive heart failure;
- prior major thoracic and/or abdominal surgery from which the patient has not yet recovered;
- known sensitivity to the study drug or components of the preparation;
- other concurrent investigational drugs within the past four weeks;
- other condition that, in the opinion of the investigators, would make the patient unsuitable for this clinical trial.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2014
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.
Generic name:	Sarabesin 3

Ethics review

Approved WMO Date:	09-12-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-02-2014
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	EUCTR2011-005859-13-NL
CCMO	NL38643.078.13