177Lu-PSMA Radioligand therapy in patients with lymph node metastatic hormone-sensitive prostate cancer undergoing robot-assisted laparoscopic radical prostatectomy and extended pelvic lymph node dissection

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON29417

Source
Nationaal Trial Register

Brief title
SHEPHERD trial

Health condition

Prostate Cancer

Sponsors and support

Primary sponsor: To be determined
Source(s) of monetary or material Support: To be determined

Intervention

Outcome measures

Primary outcome

Histopathological response to 177Lu-PSMA RLT in the resected prostate specimen and in the resected lymph nodes

Secondary outcome

- To study the tolerability of study medication and assessment of quality of life (QoL) by patient reported outcome measures and specific QoL questionnaires using the EORTC Quality of Life Questionnaire for cancer patients (EORTC-QLQC30 and EORTC-QLQ-BM22) [19] at baseline and four weeks after each cycle of 177Lu-PSMA RLT.

- To assess the prostate-specific antigen (PSA) free survival at 12 months after two cycles of 177Lu-PSMA RLT and concurrent RARP and ePLND.

Study description

Background summary

Rationale:
Prostate-specific membrane antigen (PSMA) is a receptor on the surface of prostate cancer cells that is revolutionizing the way we image and treat men with prostate cancer (PCa). New small molecule peptides with high-binding affinity for the PSMA receptor have allowed high quality, highly specific positron emission tomography (PET) imaging, in addition to the development of targeted radionuclide therapy for men with PCa. This targeted therapy for PCa has, to date, predominately used 177Lutetium (Lu)-labeled PSMA peptides. Early clinical studies evaluating the safety and efficacy of 177Lu-PSMA radioligand therapy (RLT) have demonstrated promising results with a significant proportion of men with metastatic castration resistant prostate cancer (mCRPC), who have already failed other therapies, responding clinically to 177Lu-PSMA RLT.

Although 177Lu-PSMA RLT is showing exciting treatment responses in men with mCRPC and suggests a low toxicity profile, it has not been investigated in patients with hormone-sensitive prostate cancer (HSPCa). Before a systemic treatment can be implemented into clinical practice, treatment verification by the histologically evaluation of obtained tissue is mandatory. The current study protocol gives a unique opportunity to assess the effect of 177Lu-PSMA RLT on histological parameters, both within the prostate tumor and in resected lymph-nodes, thus offering the gold standard verification of treatment to the surgically resected specimens.

Besides, the study will focus on the quality of life (QoL) and well-being of men undergoing 177Lu-PSMA RLT and will investigate the 12-month prostate-specific antigen (PSA) free

survival in those who undergo 177Lu-PSMA RLT and subsequently undergo robot-assisted laparoscopic radical prostatectomy (RARP) and extended pelvic lymph node dissection (ePLND).

This is the first study to be performed in patients with suspicion of lymph node-positive PCa metastases on PSMA PET/CT imaging (miN1 disease) undergoing RARP and ePLND, (pre)treated with 177Lu-PSMA RLT.

Hypothesis:
As for now, 177Lu-PSMA has not been widely studied in patients within earlier phases of disease such as lymph node metastatic HSPCa. In theory, RLT could be more effective in low volume disease because of the very high tumor uptake of radioligands in small lesions.

Objective:
To investigate the therapeutic effect of two cycles of 177Lutetium (Lu)-labeled prostate-specific membrane antigen (PSMA) radioligand therapy (RLT) on histopathological variables in the resected prostate gland and lymph-nodes, in patients with newly diagnosed lymph node metastatic HSPCa (1-3 metastases; miN1). Secondly, to study the quality of life (QoL) and well-being of patients receiving 177Lu-PSMA RLT. And thirdly, to study the PSA progression-free survival at 12 months after 177Lu-PSMA RLT and surgery.

Study design:
This is a prospective, non-randomized, phase I-II cohort trial on the tolerability and efficacy of systemic 177Lu-PSMA RLT.

Study population:
Ten patients with locally advanced, i.e. lymph node metastatic HSPCa (1-3 metastases), who are planned to undergo RARP and ePLND, and who are deemed clinically fit for 177Lu-PSMA RLT, will be recruited.

Methods:
After screening and baseline imaging with either [68Ga] or [18F] PSMA PET/CT and mpMRI, patients with locally advanced HSPCa will be planned for two cycles of pre-operative 177Lu-PSMA RLT.

Locally advanced disease is defined as a pre-operative [68Ga] or [18F] PSMA PET/CT scan showing increased PSMA expression in the lymph nodes within the surgical template suspicious for lymph node metastatic disease (1-3 metastases; miN1).

Patients will receive two intravenous applications of 7.4GBq 177Lu-PSMA RLT 12 and 6 weeks respectively before surgery. Four weeks after each treatment injection, patients will be monitored for toxicity and adverse events. Furthermore, QoL will be assessed using standardized questionnaires (EORTC-QLQC30 and EORTC-QLQ-BM22) prior and four weeks after each treatment injection. After surgery, the follow-up regime will be standard of care.

Main study parameters/endpoints:
It is hypothesized that systematic treatment with 177Lu-PSMA RLT and concurrent local radical treatment leads to a histological response in the resected prostate specimen and in

the resected lymph nodes. Furthermore, it is hypothesized that 177Lu-PSMA RLT leads to a sustained disease-free survival in a substantial subset of patients in newly diagnosed, locally advanced, HSPCa with an acceptable toxicity and a minimal effect on QoL after 12 months.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
The study will require time and effort from participating patients. All patients will undergo a PSMA PET/CT and an mpMRI prior to inclusion. Also, for monitoring, they will receive several blood draws for safety evaluation and need to complete questionnaires that deal with quality-of-life. The extensive monitoring is also beneficial for the patients (see study protocol below). A potential risk is the therapeutic injection with 177Lu-PSMA RLT itself, as it is not completely clear yet what the long-term toxicity of this new treatment is. However, it is important to note that the administered radiation doses are in the lower range of the previously published data in mCRPC patients.

Study objective

As for now, 177Lu-PSMA has not been widely studied in patients within earlier phases of disease such as lymph node metastatic HSPCa. In theory, RLT could be more effective in low volume disease because of the very high tumor uptake of radioligands in small lesions.

Study design

6 timepoints:
t = -6 / 0 Screening
t = 0 Injection first Cycle 177Lu-PSMA RLT
t = 2 Adverse event evaluation
t = 6 QoL questionnaires, Injection second Cycle 177Lu-PSMA RLT
t = 8 Adverse event evaluation
t = 12 QoL questionnaires, RARP + ePLND

Regular follow-up

Intervention

Two cycles of 177Lu-PSMA RLT in patients, prior to RARP + ePLND

Contacts

Public
Amsterdam UMC, VU University Medical Center
Dennie Meijer

0204443289

Scientific
Amsterdam UMC, VU University Medical Center
Dennie Meijer

0204443289

Eligibility criteria

Inclusion criteria

In order to be eligible to participate in this study, a subject must meet all of the following criteria:

- Men over 18 years of age
- ECOG PS 0-1
- Histologically proven adenocarcinoma of the prostate cancer of any grade and/or stage
- Any prostate-specific antigen (PSA)-level
- Planned to undergo radical prostatectomy (RARP) and extended pelvic lymph node dissection (ePLND)
- A pre-operative [68Ga] or [18F] PSMA PET/CT positive for lymphogenic metastatic disease (1-3 metastases; miN1) in the surgical template
- Deemed clinically fit for 177Lu-PSMA RLT
- eGFR ≥ 30 mL/min/1.73 m2
- Hemoglobin (Hb) ≥ 5.6 mmol/L
- Leucocytes ≥ 3.0 x 109/L
- Thrombocytes ≥ 100 x 109/l
- Provided informed consent

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- Previous treatment with any of the following within 6 months of inclusion: Strontium-89, Samarium-153, Rhenium-186, Rhenium-188, Radium-223, hemi-body irradiation
- Previous PSMA-targeted radioligand therapy
- Any systemic anti-cancer therapy (e.g. chemotherapy, immunotherapy or biological therapy [including monoclonal antibodies]) within 28 days prior to day of inclusion
- Known hypersensitivity to the components of the study therapy or its analogs
- Other concurrent cytotoxic chemotherapy, immunotherapy, radioligand therapy, or investigational therapy
- Patients with signs of M1a-b-c disease on pre-operative PSMA PET/CT

- Prior systemic hormonal therapy (ADT)

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2021
Enrollment:	10
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL8968
Other	METc VUmc : To be determined

Study results