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

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To investigate if surgery is feasible and safe in patients with newly diagnosed lymph node metastatic HSPCa who have received two cycles of (neo-adjuvant) systemic 177Lutetium (Lu)-labeled prostate-specific membrane antigen (PSMA) radioligand…

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

Summary

ID

NL-OMON52075

Source
ToetsingOnline

Brief title
SHEPHERD-trial

Condition

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

Synonym

prostate cancer, prostate malignancy

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Astellas Pharma,Astellas Pharma B.V.

Intervention

Keyword: Lu-PSMA, N1-disease, prostate cancer

Outcome measures

Primary outcome

It is hypothesized that neo-adjuvant systematic treatment with 177Lu-PSMA RLT does not impede the timing of the surgical procedure nor the surgical procedure itself.

Secondary outcome

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

Study description

Background summary

Rationale: Prostate*specific membrane antigen (PSMA) is a receptor on the

surface of prostate cancer (PCa) cells that is revolutionizing the way we image and treat men with prostate cancer [1,2]. New small molecule peptides with high* binding affinity for the PSMA receptor allows high quality, highly specific positron emission tomography (PET) imaging [3,4], 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 [5,6]. 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 [7-9].

Although 177Lu-PSMA RLT is showing promising treatment responses in men with mCRPC and suggests a low toxicity profile, it has not been widely investigated in patients with metastatic hormone-sensitive prostate cancer (HSPCa). As of today, neo-adjuvant treatment with systemic drugs prior to curative treatment is proof of concept in advanced or metastatic HSPCa as well as in other cancer types and leads to improved oncological outcome, potentially by eradicating micro-metastatic disease [10-12]. It is well worth investigating whether systemic 177Lu-PSMA RLT could be used as neo-adjuvant treatment prior to robot-assisted laparoscopic radical prostatectomy (RARP) and extended pelvic lymph node dissection (ePLND) in patients with oligometastatic HSPCa. Before a systemic treatment can be implemented into clinical practice, and as a neo-adjuvant treatment before curative surgery, it first needs to be assessed whether the surgery itself is not impeded by the neo-adjuvant therapy such as by drug-induced toxicity. Drug-induced toxicity might result in a delay in the timing of surgery and/or may lead to drug-related surgical difficulties. Secondly, the current study protocol gives a unique opportunity to assess the effect of systemic 177Lu-PSMA RLT on histological parameters, both within the prostate tumor and in the 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 patients who undergo 177Lu-PSMA RLT and subsequently undergo RALP and 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.

Study objective

To investigate if surgery is feasible and safe in patients with newly diagnosed lymph node metastatic HSPCa who have received two cycles of (neo-adjuvant) systemic 177Lutetium (Lu)-labeled prostate-specific membrane antigen (PSMA) radioligand therapy (RLT). Secondly, to study the therapeutic effect of

177Lu-PSMA RLT on histopathological variables in the resected prostate gland and the resected pelvic lymph nodes. Thirdly, to assess the toxicity of 177Lu-PSMA RLT, fourthly, to study the quality of life (QoL) and well-being of patients receiving 177Lu-PSMA RLT. Fifthly, to study the PSA progression-free survival at 12 months after 177Lu-PSMA RLT and radical surgery.

Study design

This is a single center, single arm, prospective, non-randomized, phase I-II pilot study on the feasibility, safety, tolerability and efficacy of systemic 177Lu-PSMA RLT.

Intervention

After screening and baseline imaging with either [68Ga] or [18F] PSMA PET/CT and mpMRI, patients with lymph node metastatic HSPCa will be planned for two cycles of neo-adjuvant systemic 177Lu-PSMA RLT.

Study burden and risks

The study will require time and effort from participating patients. All patients will undergo a PSMA PET/CT and a mpMRI prior to inclusion. Also, for monitoring, they will receive several blood draws for safety evaluation and patients will be required 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 [7,8].

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

- Men over 18 years of age
- ECOG performance score (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 with a maximum of 6 weeks before study entry
- An mpMRI of the abdomen with a maximum of 12 weeks before study entry
- 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

- 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)
- >3 lymph node metastases on preoperative PSMA PET
- Complete urinary incontinence, not willing to have an indwelling urinary catheter.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	02-06-2023
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lutetium-PSMA
Generic name:	Lutetium-PSMA

Ethics review

Approved WMO Date:	23-06-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	28-09-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	EUCTR2020-004991-16-NL
CCMO	NL78133.029.21