# Tolerability of concurrent EBRT + Lu-PSMA for node-positive prostate cancer (PROQURE-1)

Published: 24-06-2021
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This study has been transitioned to CTIS with ID 2024-514168-15-00 check the CTIS register for the current data. Primary: To determine the maximum tolerated dose (MTD) of 1 or 2 cycli Lu-PSMA when given concurrent with EBRT+ADT. Secondary: To...

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

## Summary

### ID

NL-OMON50800

**Source**
ToetsingOnline

**Brief title**
PROQURE-1

### Condition

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

**Synonym**
prostate cancer

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Antoni van Leeuwenhoek Ziekenhuis
**Source(s) of monetary or material Support:** farmaceutische bedrijf Advanced

Accelerator Applications;onderdeel van Novartis,Novartis

## Intervention

**Keyword:** Lu-PSMA, Prostate cancer, radiotherapy

## Outcome measures

### Primary outcome

Primary endpoint: The maximum tolerated dose (MTD) of the 4 selected doses of Lu-PSMA (3, 6, 9 or 2x7.4 GBq) when administered in combination with EBRT. Dose-limiting toxicity (DLT) will be acute toxicity CTCAE v 5.0 grade 3 of any type occurring from start of EBRT until 3 months after, determined to be related to study treatment.

### Secondary outcome

Secondary outcomes: late toxicity according to CTCAE v 5.0 at 6 months, PSA response at 6 months, quality of life according to EORTC QLQ-C30 and -PR25 questionnaires, combined dosimetry based on added dose distributions from EBRT+Lu-PSMA, and in vivo pharmacokinetics of Lu-PMSA during EBRT based on biodistribution imaging and blood samples.

# Study description

### Background summary

In the past, prostate cancer patients with nodal metastases (clinically N1M0) were not considered for curative treatment, based on the hypothesis that these patients are affected by systemic disease. Today, patients with primary diagnosed N1M0 prostate cancer increasingly receive curative intent high-dose external beam radiotherapy (EBRT) to the prostate and regional nodes combined with up to 3 years androgen deprivation therapy (ADT). This aggressive and lengthy multimodal treatment can achieve long-term disease-free and overall survival, but it also comes with significant toxicity and failure rates of up

to 47% within 5 years with locoregional recurrence within radiotherapy fields and/or distant progression. A new strategy is needed to (1) enhance EBRT to better control macroscopic tumor in the prostate and involved nodes, (2) better treat undetected microscopic disease inside and outside EBRT fields, and (3) potentially reduce or obviate the long use of ADT with its toxicity and associated poor quality of life. Radioligand therapy (RLT) with Lutetium-177 labeled PSMA-ligands (Lu-PSMA) can selectively deliver radiation dose to both macroscopic and microscopic tumor locations throughout the body, with limited systemic toxicity. Based on radiobiologic considerations, the hypothesis is that complementing EBRT with concurrent Lu-PSMA can provide synergistic anti-tumor effects, without prolonging overall treatment time and with limited toxicity. The feasibility of this innovative use of *RNT as the ultimate radiosensitizer for EBRT* now needs to be explored.

## Study objective

This study has been transitioned to CTIS with ID 2024-514168-15-00 check the CTIS register for the current data.

Primary: To determine the maximum tolerated dose (MTD) of 1 or 2 cycli Lu-PSMA when given concurrent with EBRT+ADT. Secondary: To demonstrate acceptable late toxicity at 6 months, superior dosimetric efficacy, anti-tumor efficacy at 6 months, feasibility of QoL evaluation, favorable pharmacokinetics.

## Study design

Multicenter prospective phase I dose-escalation study, using a BOIN design, with 4 dose levels for Lu-PSMA and a maximum of 24 patients.

## Intervention

Standard of care treatment (EBRT of prostate and pelvic nodes with concurrent ADT) is complemented with 1/2 concurrent cycle dose-escalated Lu-PSMA in week 2 (and 4).

## Study burden and risks

Participation in the study involves one day hospitalization per administration with IV catheter and administration of 3, 6, 9 or 2x7.4 GBq 177Lu-PSMA-617 in week 2 (and week 4) of EBRT, and during the week after each administration 3 SPECT/CT scans from pelvis to head for dosimetry and 11 blood samples for pharmacokinetics. Patient receive additional radiation exposure from Lu-PSMA, which comes with a low risk for acute toxicity (infusion reaction, nausea, vomiting), low risk for late toxicity (temporary salivary gland function loss), a maximum of one or two days hospitalization in isolation, and after discharge about 2 weeks radiation safety measures at home. These disadvantages are

considered acceptable for patients with node-positive prostate cancer, in the scope of potential improvements in tumor control with associated benefits in survival and QoL, for included patients as well as for future patients.

# Contacts

**Public**
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
AMSTERDAM 1066CX
NL
**Scientific**
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
AMSTERDAM 1066CX
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

- Histologically proven prostate cancer;
- cT2-4, partly determined by MRI;
- N1, determined by LND/SNP and/or PSMA PET/CT;
- iM0, determined by PSMA PET/CT;
- Accepted for curative intent treatment with EBRT of the prostate and regional nodes + 3y ADT;
- Visually PSMA-positive primary tumor and nodes, largest lesion higher or

equal to average liver uptake;
- WHO performance score 0-1;
- Age > 18 years;
- For patients who have partners of childbearing potential: Willingness to use a method of birth control with adequate barrier protection as described in section 4.4 during the study and for 6 months after the study drug administration; and
- Signed written informed consent.

### Exclusion criteria

- Inability to comply to study procedures;
- Inability to adhere to radiation safety measures in hospital or at home;
- Inability to undergo the required biodistribution scans;
- Prior or current malignant disease with potential impact on treatment outcome or survival;
- Prior treatment with EBRT;
- Prior treatment with ADT, already initiated >1 month before the start of EBRT;
- Prior treatment with radionuclide therapies, Lu-PSMA or other;
- Reduced bone marrow reserve (Hb<6 mmol/L, Leukocytes<2.5 10E9/L, or Platelets<100 10E9/L not older than 1 month before start of EBRT);
- Reduced renal function (GFR < 60 not older than 1 month before start of EBRT);
- Reduced salivary gland function (history of prior salivary gland disease); or
- Miction problems requiring pre-treatment with ADT.

## Study design

### Design

**Study type:** Interventional

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

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 20-12-2021 |
| Enrollment: | 24 |

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| Type: | Actual |

### Medical products/devices used

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|---|---|
| Product type: | Medicine |
| Brand name: | 177Lu-PSMA-617 |
| Generic name: | 177Lu-PSMA-617 |

## Ethics review

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| Approved WMO Date: | 24-06-2021 |
| Application type: | First submission |
| Review commission: | METC NedMec |
| Approved WMO Date: | 11-11-2021 |
| Application type: | First submission |
| Review commission: | METC NedMec |
| Approved WMO Date: | 07-03-2024 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |
| Approved WMO Date: | 16-05-2024 |
| Application type: | Amendment |
| Review commission: | METC Universitair Medisch Centrum Utrecht (Utrecht) |

## 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 |
|---|---|
| EU-CTR | CTIS2024-514168-15-00 |
| EudraCT | EUCTR2020-005577-27-NL |
| CCMO | NL75976.031.21 |