UNIKLINIK KÖLN
Klinik und Poliklinik für Nuklearmedizin
Direktor: Univ.-Prof. Dr. A. Drzezga
Kerpener Straße 62 • 50937 Köln
Tel.: 0221 / 4784059
https://nuklearmedizin.uk-koeln.de

Patient information and consent form for nuclear medical therapy with lutetium-177-labelled ligand of the prostate-specific membrane antigen (PSMA) in metastatic prostate cancer

Patient: _____

Born: _____

Address: _____

Radionuclide therapy is used for the nuclear medical treatment of PSMA-expressing metastases of prostate cancer. A molecule is used which binds to a surface antigen (a structure on the cell surface), the so-called prostate-specific membrane antigen. This molecule is coupled with a radioactive emitter (here: Lutetium-177) for therapy.

The radioactively labeled molecule is applied as an infusion into a vein and quickly accumulates in the metastases previously detected by PET/CT (functional imaging with Ga-68 PSMA or F-18 PSMA-PET). The tumors/metastases are thus irradiated locally, which is expected to have an inhibitory effect on the tumor tissue. It can be assumed that the therapeutic effect depends on the intensity of storage and the volume of the tumors.

The therapeutic substance is not generally approved, i.e. it is not a commercial preparation of the pharmaceutical industry. Rather, the therapeutic substance is produced individually for each patient in the radiopharmacy of the University Hospital Cologne. It is therefore an individual treatment measure in accordance with the German Drug Law (§ 13 para. 2 AMG). Such an application is not subject to the approval requirement according to the Radiation Protection Ordinance (§ 23 StrlSchV). It is not a study or clinical research.

The efficacy of the therapy has not yet been proven by clinical trials with an untreated control arm (which would be necessary for approval). However, already published observational studies indicate a possible therapeutic benefit of the therapy. According to current knowledge, it is usually not a curative therapy, but a therapy option that slows down the course of the disease or temporarily suppresses the tumor.

Lutetium-177 PSMA therapy should only be considered as an individual curative measure when the established therapeutic procedures have been exhausted, are contraindicated, unsuitable or are not tolerated. This means in concrete terms:

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- Under androgen blockade, PSA levels rise and the extent of metastasis is increasing. This stage is known as castration-resistant metastatic prostate cancer.
- PSA levels have increased after or during drug therapy with abiraterone (Zytiga®) or enzalutamide (Xtandi®).
- First-line chemotherapy with docetaxel and second-line chemotherapy with cabazitaxel have already been performed or are no longer considered (i.e. are contraindicated, unsuitable or are not tolerated).
- In symptomatic osseous metastases without visceral metastasis and without relevant lymphogenic metastasis, therapy with the alpha emitter radium-223 dichloride (Xofigo®) has been performed.

If lutetium-177 PSMA therapy is well tolerated, 4 treatment cycles are generally scheduled at intervals of (6 to) 8 weeks. After 2 cycles of Lutetium-177 PSMA, the response to therapy is evaluated before the 3rd and 4th cycles are administered. In individual cases, more than 4 cycles may be given if the treatment response is good and in consideration of other treatment options. Each treatment cycle is associated with an inpatient stay of about 3 days (guideline for radiation protection in medicine).

As prerequisites and safety instructions for the Lutetium-177 PSMA therapy will be checked with you in advance:

- Proof of PSMA storage of metastases by Ga-68 PSMA PET/CT or F-18 PSMA PET/CT
- Sufficient bone marrow reserve, proven by the peripheral blood count including differential blood count. An interval of at least 6 weeks must be observed between the last chemotherapy or Xofigo® therapy. The bone marrow reserve may be limited by the extent of bone metastases, by first-line and second-line chemotherapy or by pretreatment with Xofigo®.
- Sufficient renal function and exclusion of urinary flow obstruction, as demonstrated by creatinine measurement and renal scintigraphy. Note: Lutetium-177 PSMA therapy is possible with an internal ureteral splint or external urinary diversion.
- Radiation hygiene must be maintained, i.e. cognitive function incuding temporal/spatial orientation must be preserved as well as the ability to control micturition.

The therapy can therefore not be performed in case of:

- pregnancy
- Severe renal insufficiency
- Urinary retention
- Bone marrow depression / serious blood count changes
- Uncontrollable urinary incontinence or cognitive impairment with lack of temporal / spatial orientation

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The following side effects can be caused by the therapy:

- The number of red blood cells (erythrocytes), blood platelets (thrombocytes) and white blood cells (leukocytes) may decrease. The consequences of this are anemia with fatigue, a tendency to bleed and susceptibility to inflammatory diseases, possibly the need for a blood cell transfusion. The risk of transmission of viruses (hepatitis, HIV) or bacteria through a blood cell transfusion is very low nowadays. After therapy, the blood count must be checked every week for an initial period of about 2 months; if necessary, shorter control intervals may be necessary.
- The therapy may lead to a reduction in kidney function, which is therefore carefully monitored. In case of a previous kidney disease, permanent dialysis (blood washing) may be necessary. In order to keep this risk as low as possible, kidney examinations are carried out in the preparatory phase (laboratory, sonography, scintigraphy) so that the doctor can assess the individual risk. Lutetium-177 PSMA therapy cannot be performed in the event of urinary retention.
- Functional impairment of the liver (excretion-related)
- Acute nausea and vomiting can occur immediately after therapy.
- Allergic reactions to the infusion of the prostate-specific membrane antigen ligand (peptide) can rarely occur.
- Paravenous injections/infusions ("injection next to the vein") can lead to local inflammation and tissue damage with the consequence of a poorly healing wound and restricted use of the arm.
- Long-term effects or harmful long-term effects such as blood cancer or other secondary tumors are rare and occur after one year or even decades. Destruction of the haematopoietic bone marrow (myelodysplastic syndrome) is rarely the result of nuclear medical treatment. Rather, the bone marrow reserve is determined by the extent of the disease in the bone marrow and the intensity of previous chemotherapy as well as the number and field size of previous radiation therapy.
- Germ cell changing potential of radioactivity: contraception for 6 months, if necessary, the cryopreservation of spermatozoa should be considered in case of existing desire for children.
- Since the salivary and lacrimal glands also express PSMA, these organs will inevitably be irradiated as well. This can cause the symptoms of pressure pain in the salivary glands (inflammation of the salivary glands), dry mouth, impaired taste, susceptibility to dental caries and dry eye. Theoretically, the permanent application of eye drops may be necessary to prevent the cornea from drying out.
- Rare side effects cannot be excluded, which may not be known yet due to the novelty of the therapy.

In order to be able to estimate the individual risk, the following questions must be answered:

1. Is there a kidney dysfunction ?	□ yes	□ no
2. Is there an impairment of the blood count?	□ yes	□ no
3. Does urine leakage or retention occur involuntarily ?	□ yes	□ no
4. Has chemotherapy been performed in the past 6 weeks ?	□ yes	□ no
5. Has radiotherapy been performed in the past 6 weeks?	□ yes	□ no

On the day of therapy, several liters of fluid must be drunk in order to keep the strain on the kidneys as low as possible (accelerated excretion).

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Declaration of consent

In an informative conversation, I was informed in detail about the radionuclide therapy with the 177-lutetium-labeled prostate-specific membrane-antigen ligand, also that it is an individual treatment measure according to § 13 para. 2 of the German Drug Law, that no guarantee for the desired success of the therapy can be given and that there is no comprehensive knowledge about possible side effects.

My consent also refers to any follow-up measures that may become necessary during the treatment as well as to the recording of my data in a database.

The necessity of control examinations also for the documentation of the success of the therapy was explained to me.

I had the opportunity and sufficient time to ask all questions that were important to me about the nature and necessity of the treatment and the risks and side effects associated with the therapy. I was comprehensively informed about any follow-up measures and treatment alternatives that might be necessary.
The following questions were discussed in detail:

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I was informed that the therapy is only possible under inpatient conditions and that I am not allowed to visit the therapy ward during my inpatient stay.

I have read and understood the information sheet and would like the treatment (nuclear medicine therapy with 177-lutetium-labeled prostate-specific membrane-antigen ligand) to be performed at my place of treatment.

I agree that my data may be passed on in anonymized form for uni- or multi-center evaluations.

I am aware that I can withdraw my consent at any time without giving reasons. This will have no influence on other future therapies.

place and date:

Signature physician

place and date:

Signature of the patient

Printed patient name:

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Information about the ward

Finally some information about the ward itself. We have 10 rooms on the station with shower, WC, TV, radio and telephone.
The use of the television is free of charge and the use of the telephone is subject to a charge. Even if you only want to be called, you will need a chip card, which you will receive at admission. This must be topped up with credit at a machine set up at our station (with Euro banknotes). In order to avoid frequent reloading, we recommend a minimum credit of 15 €. All units that you do not consume during your inpatient stay and the chip card deposit will be refunded at the end of your stay.
You may use a cell phone both in your room and on the roof garden. For internet access, please bring your own surf stick to the ward.

You are welcome to bring your own radios, books, etc. for use during your stay. None of the objects or clothing you bring with you will be "contaminated" after your stay in the ward and can therefore be taken home again without any problems.
We are obliged to provide you with synthetic (paper) bed linen on the ward. If you wish, you can bring your own bed linen. These can be cleaned in the usual way after your stay on the ward and can then be used again without any problems. The same applies to towels if you wish to bring your own towels.
If you have any further questions, please contact the responsible ward physician or the ward nurse.

Phone number of the therapy ward (ward room): 0221 478 4059

Informations:

Universitätsklinikum Köln
Klinik und Poliklinik für Nuklearmedizin
Direktor: Univ.-Prof. Dr. med. A. Drzezga
Oberarzt: Prof. Dr. med. M. Schmidt, Facharzt für Nuklearmedizin, FEBNM,
Head of radionuclide therapy
Kerpener Str. 62 (Gebäude 60)
50937 Köln
Tel.: 0221 / 478 – 5024
Fax: 0221 / 478 – 89085