UNIKLINIK KÖLN
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Patient information and declaration of consent for nuclear medicine therapy with Lutetium-177-labeled prostate-specific membrane antigen (PSMA) ligands in metastatic prostate cancer

Copy received

Patient: _____

Date of birth: _____

Address: _____

Therapy with Lutetium-177-labeled ligands against the prostate-specific membrane antigen (PSMA) is used to treat PSMA-expressing metastases of castration-resistant prostate cancer. For this purpose, a molecule is used that binds to an enzyme on the cell surface of prostate carcinoma cells, the so-called prostate-specific membrane antigen (PSMA). This molecule is coupled with a radioactive emitter (here: Lutetium-177 = Lu-177) for the therapy. This type of therapy has been offered at our clinic since November 2014.

The radioactive drug (Lutetium-177-labeled prostate-specific membrane antigen ligand) is administered as an infusion into a vein and quickly accumulates in the metastases previously detected by PET/CT (receptor imaging with Ga-68-PSMA or with F-18-PSMA-PET tracers). The tumors/metastases are thus irradiated locally, which is intended to achieve an inhibitory effect on the tumor tissue. The intensity of storage and tumor volume have an influence on the success of the therapy.

A therapeutic Lu-177-PSMA ligand has been approved in 2022 and is now also commercially available in Europe under the trade name PLUVICTO® following the favorable results of the VISION approval study. It is also possible to employ an analogous compound for therapy which is labeled with Lu-177 directly on site in the Radiopharmacy Department of the University Hospital of Cologne for the purpose of an individual treatment measure in accordance with the German Medicinal Products Act (§ 13 para. 2 AMG). Both treatment options (commercial procurement of PLUVICTO®, in-house production of a Lu-177-PSMA ligand) are currently used in patient care at the University Hospital of Cologne.

The effectiveness of the therapy concept has been documented by studies (TheraP study and VISION study) and numerous published observational studies. As a rule, it is not a curative therapy option, but one that slows down the progression of the disease or temporarily reduces the tumor burden. To date, this therapy has mostly been offered in an advanced, castration-resistant stage after established lines of therapy have been exhausted, often after pre-treatment with a modern androgen receptor signaling inhibitor and after chemotherapy (e.g. docetaxel). A response to Lu-177-PSMA ligand therapy cannot be guaranteed, but experience to date shows that around 50-60% of patients respond to Lu-177-PSMA ligand therapy.

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Lu-177-PSMA ligand therapy should primarily be considered in the third or higher line of therapy if the other established therapy methods have been exhausted, are contraindicated or unsuitable or are not tolerated. This means in concrete terms:

- Under androgen blockade, there is an increase in PSA and the extent of metastases is increasing. At this stage, a so-called castration-resistant, metastasized prostate carcinoma is present.
- After or during drug therapy with abiraterone (Zytiga®), enzalutamide (Xtandi®), apalutamide (Erleada®) or another modern androgen receptor signaling inhibitor, the PSA level has increased.
- First-line chemotherapy with docetaxel has already been given or is not an option (i.e. contraindicated, unsuitable or not tolerated) and second-line chemotherapy is also not an adequate alternative therapy.
- For symptomatic osseous metastases without visceral metastasis and without relevant lymphogenous metastasis, the treatment option of the alpha emitter radium-223 dichloride (Xofigo®) has been tested.

If the Lu-177-PSMA ligand therapy is well tolerated, 4 to 6 treatment cycles are generally planned at intervals of around 6 weeks. Each treatment cycle is associated with an in-patient stay of around 3 days (guidelines of the Radiation Protection in Medicine Directive). The accumulation of the Lu-177-PSMA ligand in the foci of the disease is recorded by whole-body scintigraphy during each cycle. The response to therapy can be assessed at the end of therapy and, if necessary, during therapy (e.g. if the PSA level rises or the patient's state of health unexplainedly deteriorates) by Ga-68-PSMA PET/CT or an F-18-PSMA PET/CT examination.

The prerequisites and safety instructions for Lu-177-PSMA ligand therapy are checked in advance:

- Proof of PSMA storage of the metastases by Ga-68-PSMA PET/CT or F-18-PSMA PET/CT (if PET/CT is not available by a Tc-labeled PSMA tracer).
- Sufficient bone marrow reserve, demonstrated by peripheral blood count including differential blood count. An interval of at least 6 weeks between the last chemotherapy or Xofigo® must be observed. The bone marrow reserve may be limited by the extent of the bone metastases, by the chemotherapy(ies) or by the previous treatment with Xofigo®.
- Sufficient renal function and exclusion of urinary outflow obstruction, verified by creatinine determination and, if necessary, MAG3 renal scintigraphy. Note: Lu-177-PSMA ligand therapy is possible with an internal ureteral stent or external urinary diversion.
- A sufficiently good general condition, adequate cognitive performance/temporal/spatial orientation ability and control of micturition must be ensured in order to comply with radiation hygiene.

The therapy can therefore not be performed in case of:

- Severe renal insufficiency
- Urodynamically significant urinary retention or urinary outflow restriction
- Bone marrow depression / serious blood count changes
- Uncontrollable urinary incontinence
- Markedly impaired general condition/cognitive impairment or disorientation or other factors that jeopardize compliance with radiation hygiene

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Side effects
Like all medicines, PLUVICTO® or the Lu-177-PSMA ligand can cause side effects, although they will not occur in each patient. Some side effects can be serious. These can be a combination of disease-related damage to individual organs, damage caused by previous therapies (chemotherapy, radiotherapy) and the drug. For example, the therapy can have side effects in the form of suppression of the blood-forming bone marrow (myelosuppression) as well as impairment of kidney function and it contributes to a therapy-related increase in long-term radiation exposure, which has been associated with an increased statistical risk of (secondary) cancer.

Serious side effects
If you notice any of the following serious side effects, inform your nuclear medicine specialist immediately:

Very common: may affect more than 1 in 10 people treated
- Tiredness; weakness, pale skin or shortness of breath (possible signs of a lack of red blood cells [anemia])
- Unusual tendency to bleed or bruise or bleed for longer than usual (possible signs of a lack of platelets [thrombocytopenia])
- Frequent infections with signs such as fever, sore throat or mouth ulcers (possible signs of a lack of white blood cells [leukopenia, lymphopenia])

Common: may affect up to 1 in 10 people treated
- Less frequent urination or significantly lower urine output than usual (possible signs of kidney problems [acute kidney injury]). In the case of pre-existing kidney disease or urinary retention in the kidney, this may result in permanent dialysis (blood washing).
- Tiredness, weakness, pale skin, shortness of breath, unusual tendency to bleed or bruise or bleed for longer than usual or more frequent infections with signs such as fever, chills, sore throat or mouth ulcers (possible signs of a lack of blood cells [pancytopenia])

Other possible side effects
The following side effects may also occur. If these side effects become severe, inform your nuclear medicine specialist.

Very common: may affect more than 1 in 10 people treated
- Tiredness (fatigue)
- Dry mouth
- Nausea
- Loss of appetite
- Altered bowel movements (constipation or diarrhea)
- Vomiting
- Frequent urination with pain or burning (urinary tract infection)
- Abdominal pain
- Weight loss

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Common: may affect up to 1 in 10 people treated
- Swollen hands, ankles or feet (peripheral edema)
- Dizziness
- Headache
- Fever (pyrexia)
- Dizziness with a spinning sensation (vertigo)
- Salivary/lacrimal gland dysfunction: salivary and lacrimal glands also express PSMA and are inevitably irradiated during therapy. This can cause the symptoms of pressure/pain in the salivary glands (salivary gland inflammation), dry mouth, taste disorders, susceptibility to tooth decay and dry eyes. These side effects can be permanent. According to previous experience, less than 5-10% of patients report such symptoms, which vary greatly from person to person. In severe cases, the long-term use of eye drops could become necessary to prevent the cornea from drying out.
- Functional impairment of the liver (if metastases in the liver), liver failure

Occasional: may affect up to 1 in 100 people treated
- Allergic reactions to the infusion of the prostate-specific membrane antigen ligand (peptide).
- Paravenous injections ("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 affected limb.
- The therapy contributes to a patient's overall long-term cumulative radiation exposure: Statistically, long-term cumulative radiation exposure is associated with an increased risk for cancer, a therapy-induced increased incidence of cancer/mutations cannot be excluded.
- Germ cell altering potential of radioactivity/risk of infertility: Male patients with female partners of reproductive potential are advised to use effective contraception during treatment and for 14 weeks after the last dose; if necessary, cryopreservation of sperm can be considered if family planning is not yet completed.
- Rare side effects cannot be ruled out, which may not yet be known due to the novelty of the therapy.

Measures to reduce the risks of treatment or to treat side effects

- If the number of red blood cells (erythrocytes), platelets (thrombocytes) or white blood cells (leukocytes) is low, a blood transfusion may be necessary. The risk of transmission of viruses (hepatitis, HIV) or bacteria through a blood cell transfusion is nowadays very low. After therapy, the blood count should be checked after 3 and 6 weeks; if necessary in shorter control intervals.
- The therapy can lead to a reduction in kidney function, which is therefore carefully monitored. In the case of pre-existing kidney disease, this may result in permanent dialysis (blood washing). To keep this risk as low as possible, kidney examinations are carried out during the preparatory phase (laboratory, MAG3 kidney scintigraphy) so that the doctor can assess the individual risk. Lu-177-PSMA ligand therapy cannot be carried out in the event of urinary retention. Before administering PLUVICTO® or the Lu-177-PSMA ligand, you should drink plenty of fluids and urinate as frequently as possible in the first few hours after administration. You should also drink plenty of fluids (approx. 2 liters of water or tea per day) for 2 days after the application of Pluvicto® or with the Lu-177-PSMA ligand in order to keep the burden on the kidneys as low as possible (accelerated excretion).
- Shortly before the infusion of PLUVICTO® or the Lu-177-PSMA ligand, you have the option of cooling your parotid glands with a cooling collar (with a protective intention).

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The following questions need to be answered in order to assess the individual risk:

1. Is there any pre-existing/known renal dysfunction? ☐ yes ☐ no

2. Is there any pre-existing/known impairment of the blood count? ☐ yes ☐ no

3. Is there involuntary urination (incontinence) or urinary retention? ☐ yes ☐ no

4. Has chemotherapy been administered in the past 6 weeks? ☐ yes ☐ no

5. Has radiotherapy been applied in the past 6 weeks? ☐ yes ☐ no

6. Have you received any previous chemotherapy or radiotherapy:
   - due to prostate cancer? ☐ yes ☐ no
   - due to any other cancer (not related to the prostate)? ☐ yes ☐ no

7. Is there a particular need for nursing care? ☐ yes ☐ no

Emergencies and unplanned hospitalization
If you require emergency medical treatment for any reason or are unexpectedly admitted to hospital within 7 days of your nuclear medicine treatment, you must inform the medical staff of the name, date and dose of your radioactive treatment.

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Informed consent

I was informed in detail about the Lu-177-PSMA ligand therapy in an informative discussion, also about the fact that the University Hospital Cologne uses Lu-177-PSMA ligands both from commercial production and from in-house production (individual treatment measure according to § 13 para. 2 of the German Medicines Act). I understand that no guarantee can be given for the desired success of the therapy. I was also informed that this is a therapy that has been approved since December 2022 and therefore rare side effects cannot be ruled out, about which there may not yet be comprehensive knowledge due to the newness of the therapy.

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

The necessity of follow-up examinations, also to document the success of the therapy, was explained to me.

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

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I have been informed that the therapy is only possible under in-patient conditions and that I am not allowed to leave the therapy ward or receive visitors to the therapy ward during my in-patient stay.

I have read and understood the information sheet and would like the treatment (nuclear medicine therapy with Lu-177-PSMA ligands) to be carried out on me.

The treatment of metastatic prostate cancer is subject to constant change. In the event of future participation in a therapy study, prior treatment with radioactive medication may be an exclusion criterion for participation in such a study.

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

Date and place:

Signature of the physician

Date and place:

Signature of the patient

Patient name in block letters

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Information about the therapy ward

The therapy ward is equipped 10 rooms (single to double occupancy) with shower, restroom, television, radio and telephone. For all patients, a shared fitness room, recreation room and a roof terrace are available.

The use of the television is free of charge, but there is a charge for using the telephone. Even if you only wish to be called, you will need a chip card, which you will receive on admission. This card must be topped up with credit (using Euro banknotes) at a machine located on our ward. To avoid frequent recharging, we recommend a minimum credit of €15. All units that you do not use during your in-patient stay and the chip card deposit will be refunded at the end of your stay.

You may use a cell phone / smartphone both in your room and on the roof garden.

You are welcome to bring radios, books etc. with you to keep you occupied during your in-patient stay. None of the objects or items of clothing you bring with you will be "contaminated" after your in-patient stay, so you can take them home again without any problems.

We provide you with disposable (paper) bed linen on the ward. If you wish, you can bring your own bed linen. These must be cleaned in the usual way at the end of your in-patient stay and can then be used again without any problems. The same applies to towels if you wish to bring your own.

If you have any further questions, please contact the responsible ward doctor or ward nurse.

Telephone number of the therapy ward (ward room): +49/221/478- 4059

Contact/Further Information:

University Hospital Cologne
Department for Nuclear Medicine
Director: Prof. Dr. med. A. Drzezga

Senior Physician and Head of the Radionuclide Therapy:
Prof. Dr. med. M. Schmidt, Specialist in Nuclear Medicine, FEBNM,

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