



Patient information and consent form concerning:

**Radiotherapy with lutetium-octreotate as treatment for patients with neuroendocrine tumors**

**Direct dial** +31-10-4635963

**Fax number** +31-10-4635997

**Room number** L-242

**E-mail**

**Our reference** PIF Lutate

**Date** March 13, 2007

Dear Madam / Sir,

Your physician has suggested that you participate in the medical trial that is mentioned above and has informed you what it is about. In order that you may well decide whether or not to partake in this trial, we also hand out to you this information in print, so as to give you the opportunity to (re)read this information and discuss it with others. At any time you can ask for extra information from the doctors who are listed at the end of this form.

**Your current medical situation**

From all the discussions that you have had, it will be clear that you suffer from a malignant disease that cannot be cured anymore by surgery and/or that does not respond anymore to the treatment that was given before. Because there is no accepted other treatment for your disease, you are asked to participate, on a voluntary basis, in this trial on a new form of radiotherapy with a radiolabeled peptide called lutetium-octreotate. Recently you had a scan in the department of Nuclear Medicine called somatostatin-receptor scan or OctreoScan. This scan pointed out that the malignant cells in your body are capable of binding the carrier-peptide which is linked to a radioactive substance. Because of this the disease can be irradiated from inside. The intention of this treatment is to reach all malignant cells in the body.

**Aims of the trial**

The aims of this trial in patients with neuroendocrine tumors are:

- To assess the efficacy of the treatment with lutetium-octreotate.
- To evaluate the safety of treatment with lutetium-octreotate and to register the side-effects.

**Background of the study**

Because of binding of lutetium-octreotate to the malignant cells, the disease is irradiated from within. Much experience has been acquired with this type of treatment in patients with neuroendocrine tumors over the past years. Since January 2000 more than 1700 treatments with lutetium-octreotate were performed in over 500 patients. The preliminary results in patients with neuroendocrine tumors are promising. Tumorshrinkage was found in 47% of patients and stable disease in 35%.

**Treatment Plan**

Lutetium-octreotate is administered by intravenous infusion. On the treatment day a drip is placed and you are admitted to the Nuclear Medicine ward. First, an anti-emetic is administered. After that, two driplines are attached, one with saline and one with a solution of aminoacids. This is not the infusion with radioactivity. The aminoacid solution is to reduce the radiation dose to the kidneys. The infusion of the aminoacid solution takes 4 hours. The administration of the radioactive peptide starts

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P.O. box 2040  
3000 CA Rotterdam, NL

**Street address**

Dr. Molewaterplein 40  
3015 GD Rotterdam, NL

Accessible by taking tram 8,  
bus 44 or the Caland line  
metro (Dijkzigt stop).

**Head of Department**

Prof. dr. E.P. Krenning

**Medical staff**

drs. B.L.R. Kam  
dr. D.J. Kwekkeboom  
drs. P. van Noorden  
dr. H.Y. Oei  
dr. R. Valkema  
drs. M.J.A. Verhaegen  
drs. A.C. Vos-Fröberg

**Scientific staff**

dr. W.H. Bakker  
dr. W.A.P. Breeman  
dr. ir. M. de Jong  
ir. P.P.M. Kooij  
ir. A.E.M. Reijs

half an hour after the start of the infusion of the aminoacid solution and takes half an hour. The next day the level of radioactivity in your body is measured in order to see whether it has decreased sufficiently to be discharged from the ward. Until now this was the case in all patients.

Basically, each patient will have 4 treatments with an interval of 6-9 weeks.

After the treatment and in between treatments you need to be checked by your referring physician. Especially blood tests need to be done for changes in white blood cell counts, platelet counts and kidney function. Therefore, blood tests should be performed 4 weeks after the treatment and 2 to 4 weeks before the next treatment. The test at 4 weeks after the treatment does not qualify for retreatment and needs to be repeated.

### **Potential risks and discomforts**

You may experience side-effects. Not all side-effects will occur in all patients. If you have unexplained signs or symptoms we ask you to contact your referring physician.

Based on our experience of more than 6 years we know that most patients with neuroendocrine tumors tolerate the treatment with lutetium-octreotate well. The most frequent side-effects are a decrease in the number of white blood cells and blood platelets. This decrease is usually mild and temporary. After less than 5% of treatments especially the platelets dropped more profoundly, which was reason to temporarily postpone the next treatment. Blood platelets assist in the clotting of blood. A decrease in platelet count may increase the risk of bruises and bleedings, and a decrease in white blood cell count may result in infections. We did not observe an increased frequency of infections or bleedings.

Other, more frequent side-effects were fatigue, nausea (30%) and vomiting (15%) on the day of the infusion, and hairloss (no boldness) (65%). Hair starts regrowing after the therapy is concluded.

On the longer run more serious side-effects occurred in 9 out of more than 500 patients.

Myelodysplastic Syndrome (MDS), usually a pre-stage of leukemia, occurred in 4 patients. Although in one patient previous chemotherapy was the more likely cause of MDS, we have to assume that in the other 3 patients MDS was a side-effect of our treatment.

In 2 patients, a serious deterioration of kidney function occurred. In one patient, renal insufficiency developed one year after the last treatment. This patient already had periods of unexplained decreased kidney function in the year preceding the therapy. It is therefore not certain whether the therapy was the cause of the further deterioration of the kidney function. In the other patient, a serious deterioration of kidney function occurred 3½ years after the last therapy. This was most likely attributable to heart valve insufficiency and not treatment related.

Lastly, in 3 patients with very extensive, diffuse liver metastases, a deterioration of liver functions occurred in the weeks following the therapy. In 2 patients this was temporary, whereas the other patient died shortly after.

### **Pregnancy and breast-feeding**

Pregnant and breast-feeding women are excluded from this trial. Premenopausal women should take precautions so as not to get pregnant during the trial or within 6 months after the last treatment. If applicable, your attending physician can discuss the most suited method of contraception. If, despite all precautions, you do get pregnant during the trial period, please contact your attending physician immediately. The potential hazard of this treatment to your unborn child is not exactly known.

### **Extra burden because of the trial**

For this trial, extra investigations and tests are necessary. The results of the treatment are evaluated by means of blood tests, urine tests, radiological procedures (usually CT or MRI scans), and if necessary, additional tests. Your attending physician will continue to monitor the

course of your disease closely. In this respect, it is very important to register potential side-effects and their severity. You will be asked frequently whether you experienced any side-effects.

### **Privacy**

Trial data that can be traced to your person can only be consulted after your permission has been obtained, by authorized persons. These are members of the team conducting the trial, authorized government employees, and members of the Medical Ethical Committee of the Erasmus Medical Center, Rotterdam. Consultation may be necessary to verify the reliability and quality of the trial data. The trial data will be handled in accordance with the law on the protection of personal data and the privacy regulations of Erasmus MC.

Personal data that are collected during this trial, will be substituted by a codenumber. Only this codenumber will be used for trial documentation, in reports or publications on this trial. Only the person who has the key to the code (the principal investigator) knows which person is represented by the codenumber. The trial data are kept during the trial, and, with your permission, during 15 years afterwards.

We also want to keep your data in order to possibly perform other research at a later timepoint. If you do not want this, we will of course respect this; you can confirm your refusal in print on the consent form. If you have no objections, you can also confirm that on the consent form; we will inform you if any other research will take place. You can then still decide whether or not your data may be used for that research. We will only inform you about this other research if the Medical Ethical Committee that approved this trial also approved the additional research.

## **Insurance**

For patients participating in this trial an insurance was closed. This insurance covers damage from death or injury caused by participating in this trial, which occurs during the participation in the trial or within 4 years thereafter. The damage is considered to have occurred at the time the insurer was notified. If you think that you have suffered damage from the trial, we advise you to contact the insurer listed below as soon as possible. In that case you need to provide the insurer with all necessary information. If you do not meet these requirements, you may not be compensated.

Akkermans Van Elten Assurantiën BV  
Postbus 181  
6660 AD Elst  
Phone: +31-481-367000  
Contactperson: Mr O. Zondervan

The insurance has a maximum coverage of € 450.000 per participant in the trial, with a maximum amount of € 3.500.000 for the whole trial. The coverage of specific damage and costs is limited to specific amounts. This is part of the "Act compulsory insurance for medical scientific research in man". Information on this topic can be found on the website of the "Centrale Commissie Mensgebonden Onderzoek": [www.ccmo.nl](http://www.ccmo.nl) (in dutch and english). You can also ask your questions to the investigator.

For this insurance there are a number of exclusions. The insurance does not cover:

- damage that because of the nature of the trial was certain or very likely to occur;
- health damage that would also have occurred if you had not participated in the trial;
- damage caused by not or not fully complying with directions and instructions;
- damage to your offspring, as a consequence of side-effects of the treatment to you or your offspring;
- in trials investigating accepted treatments: damage caused by one of these treatments;
- in trials investigating the treatment of specific health problems: damage caused because these health problems did not improve or deteriorated.

## **Refusal before and during the trial**

You are free to participate in this trial or refuse your participation. Also, you can stop your participation in the trial at any moment, without any further explanation from your side. Even if you consent to participate in the trial now, you can withdraw your consent later on without explanation. Whatever you decide, this will not have any consequences for your further treatment and the support to you and your family. The treatment will follow the preconceived design as closely as possible. Of course, your physical response to the treatment or newly discovered facts may force us to change the treatment. If this happens, we will discuss these items with you directly, in order that you can decide whether or not you want to continue with the treatment. We do ask you to comply with the instructions of the physician who is attending you. Also, we ask you not to seek treatment elsewhere without your attending physician's knowledge.

## **Consent**

You were asked to participate in a medical scientific trial. This trial is being conducted after approval by the hospital's Board of Directors, after approval by the Medical Ethics Committee Erasmus MC. The international guidelines for this trial will be complied with closely.

It is also possible that at the end of this trial you are being asked to participate in a sequel to this trial. If you do not want this, you can indicate this on the consent form.

### **Further information**

If you have any questions about the trial, whether before or during the trial, you can contact your attending physician or one of the doctors in the department of Nuclear Medicine listed below:

Erasmus MC Centrumlocatie

Phone: 010-4635963

Drs. M. van Essen

Drs. B.L.R. Kam

Dr. D.J. Kwekkeboom

Prof. Dr. E.P. Krenning

If you are in doubt about your participation, you can consult an independent physician, who is not involved in the trial but who has expert knowledge in the field of this trial and on neuroendocrine tumors. You can also contact the independent physician if you have questions that you do not wish to pose to the investigators. The independent physician is Dr. W.W. de Herder, department of Endocrinology, Erasmus MC, phone: 010-4635950, or via the operator: 010-4639222.

If you are not satisfied with the trial or the treatment, you can contact the hospital's independent complaint committee, which can be reached via phonenumber: 010-4633198.

If you decide to participate in the trial, we ask you to fill out and sign the attached consent form and hand it over to your attending physician from the Nuclear Medicine department.

**CONSENT FORM**

for participation in the scientific trial:

**Radiotherapy with lutetium-octreotate as treatment for patients with neuroendocrine tumors**

I confirm that I have read the information form for patients. I understand the information. I had the opportunity to ask additional questions. These questions have been answered satisfactorily. I had sufficient time to think about my participation.

I know that my participation is voluntary and that I can withdraw my consent at any time without any need to explain why I do so.

I give permission to inform my general practitioner about my participation in this trial.

I give permission to inform my attending physicians about my participation in this trial.

I give permission to grant inspection of my medical data and trial data to members of the team conducting the trial, authorized government employees, and members of the Medical Ethical Committee of the Erasmus Medical Center, Rotterdam.

I give permission to use the data for the aims that were described on the information form.

I do/do not\* give permission to keep my data for a maximum of 15 years after termination of the trial.

I give permission for participation in the trial mentioned above.

Patient Name :

Signature : Date : \_\_ / \_\_ / \_\_

Physician's Name :

Signature : Date : \_\_ / \_\_ / \_\_

\* delete whichever is not applicable.

**CONSENT FORM**

**Return to Erasmus MC**

for participation in the scientific trial:

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Signature :

Date : \_\_ / \_\_ / \_\_

Physician's Name :

Signature :

Date : \_\_ / \_\_ / \_\_

\* delete whichever is not applicable.