

# **Internal irradiation of neuroendocrine tumours with <sup>177</sup>Lutetium-DOTATOC; a radiolabeled somatostatin analogue**

## **Patient information file**

Ladies and Gentlemen

You are diagnosed as having a neuroendocrine tumour and at the moment you are staying at our institute while undergoing treatment for your malignancy.

### **What is a neuroendocrine tumour?**

Every human has neuroendocrine cells. Neuroendocrine cells are widely spread over the whole body, but occur mainly in the bowel, in the pancreas and in the lungs. The job of neuroendocrine cells is the production of hormones (signal substances).

Probably years ago during the rebuilding process of a neuroendocrine cell (where a mother cell divides into daughter cells), an information translation failure happened. Now the new daughter cells do not know when to die, how many new cells to build and how to behave while coming in contact with normal cells. This leads to an overproduction of neuroendocrine cells which displace normal tissue. Luckily neuroendocrine cells normally grow slowly.

Neuroendocrine tumour cells often produce too many hormones which leads to several symptoms. These symptoms are called malignant carcinoid syndrome. Probably you know these symptoms as flushes, diarrhoea, alcoholic intolerance, wheezing or skin problems.

### **How does the Lutetium-177 (<sup>177</sup>Lu-DOTATOC) treatment work?**

Neuroendocrine cells carry somatostatin receptors. Receptors are like ears, nose and eyes of a cell. A hormone attached on the cell membrane will transmit information through a receptor. No other tissue than neuroendocrine express somatostatin receptors in such a high density.

DOTATOC has a high affinity for somatostatin receptors. It is linked to a therapeutic,  $\beta$ -emitting isotope, Lutetium-177 (<sup>177</sup>Lu). The radiation emitted from a radiolabeled hormone bound to a tumour cell kills the cell as well as the neighbouring cells (cross fire effect). Lutetium-177-DOTATOC (<sup>177</sup>Lu-DOTATOC) is injected intravenously and links to the tumour within a few minutes.

### **Is this therapy dangerous for me and shall I notice anything uncomfortable?**

The Lutetium-177-DOTATOC has been performed successfully in Basel since 2005. The comparable treatment with Yttrium-90-DOTATOC has been conducted since 1997, and is generally well tolerated.

The radioisotope Lutetium-177 (<sup>177</sup>Lu) has a penetration range of a few millimetres. Thus most of the irradiation you receive will be absorbed in the tumour and is especially suitable for the treatment of smaller tumors.

One of the few possible side effects is caused by kidney uptake of the radiopeptide. Lutetium-177-DOTATOC can damage the kidney. Therefore we block the kidney by infusing 1 liter of amino-acids. Amino acids are found as components in most animal and herbal products. Amino-acids are physiological and will not influence you. Despite the kidney blockade, you have a minimal risk of developing a renal insufficiency. In rare cases haemodialysis may be needed. Compared with Yttrium-90-DOTATOC, Lutetium-177-DOTATOC is less kidney damaging. While injecting DOTATOC, 20% of patients may suffer from up to 5 minutes of nausea. Usually, the latter time after injection is free of side effects. However, some patients may feel like they have a hangover for up to a week.

30 % of the patients experience a slight decrease of white and red blood cells as well as platelets count. Low blood cell counts are detected by regularly monitoring, a test called Complete Blood Count. Within 6 weeks, usually all parameters return to normal.

In case of widespread liver metastases, stenosis of the gall bladder duct while you are undergoing therapy is possible. This situation would be cleared up by implantation of a stent, if it occurs.

### **How is the course of the treatment?**

One therapy session lasts 3 - 4 days. The whole treatment consists in 2 to 3 repeated injections of <sup>177</sup>Lu-DOTATOC each separated by at least 10 weeks. On the day of admission your attending nuclear physician will explain to you the whole procedure and a routine blood work up will be performed. An intravenous line will be placed and before the <sup>177</sup>Lu-DOTATOC would be injected, a kidney protective solution will be administered. 200mL will be infused prior to the injection and will be continued over several hours to achieve 1L. <sup>177</sup>Lu-DOTATOC injection takes place in our radiation protected area and will be administered through the same venous catheter. While you will stay in our institution several scintigraphic controls will be performed.

### **What can I expect from this treatment and what can the current research tell me about it?**

It was shown in larger studies that more often a combination of Yttrium-90-DOTATOC and Lutetium-177-DOTATOC showed a better therapy response than a therapy with Yttrium-90-DOTATOC only. Treatment with only <sup>177</sup>Lu-DOTATOC has been shown to be gentle and effective in patients with low kidney or liver function.

For the similarly used <sup>90</sup>Y-DOTATOC, we found the following results: The response rates after treating patients with <sup>90</sup>Y-DOTATOC and according to the World Health Organization criteria are: complete remission 2%, partial remission (response with a decrease of more than 50%) 22%, minor response (decrease in size ranging from 25 to 49%) 12%, a stable disease in 49% of the cases and a progression in 15 % of the patients. Altogether 24% of the patients respond with a tumour decrease of more than 50%. For neuroendocrine tumours of the pancreas (a sub-type of neuroendocrine tumour) this rate rises to 36%.

In patients with Carcinoid syndrome (flush, diarrhoea, abdominal cramp) a significant subjective response can be assessed (83% for diarrhoea, 46% for flush)

Most of the patients treated with opiate before DOTATOC treatment could either step down to a milder pain killer or even stop this medication.

The analysis of the side effects showed a transient lymphopenia grade III-IV (decrease of one type of white blood cells) in 23% of the patients, anaemia grade III (low haemoglobin rate) in 3% and renal failure grade II and more in 3%.

## In summary

<sup>90</sup>Y-DOTATOC treatment is a successful and well tolerated therapy against neuroendocrine tumour and related symptoms.

With <sup>177</sup>Lu-DOTATOC one can expect comparable results and even better tolerance of the treatment. Due to the physical characteristics of the <sup>177</sup>Lu less kidney toxicity as well as a better tumour response for smaller or pre-treated tumours is expected.

## Literature:

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### **Legalities and costs**

The treatment conforms to Swiss laws as set forth by both the national and cantonal authorities. The protocol concerning the therapy was accepted by the ethic commission of the canton Basel-Stadt. The expenses of the Swiss patients are covered by their health insurance. The majority of foreign health insurance schemes also cover some of the costs. A guarantee for this however cannot be made by our institute. Please inform yourself before the therapy takes place as to who bears the costs.

You have the right at any time to withdraw from the therapy without giving any reason.

**Legal authority**

Please give us your permission to perform this treatment named above with your subscription. That means that this treatment was sufficiently explained to you and all your questions were sufficiently answered.

I agree that any of my medical notes and data collection during the PRRT, may be used for anonymised scientific evaluation.

Basel, date....., signature.....

Doctor's signature.....