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Radioligand Therapy (RLT) with 177Lutetium-PSMA is the Treatment of Choice for the Progressive Prostate Cancer

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ABSTRACT

There are a number of types of cancer with low survival rates. Although most prostate cancer can be treated well, there is a subgroup of patients who are resistant to treatment and often die from metastases. Two studies have been carried out for these very suffering patients, in which radioligand therapy (RLT) proved to be successful and superior to the usual treatments. The treatment is non-invasive and specifically targets cancer cells, similar to radioiodine therapy for thyroid cancer. It is therefore indicated in such cases and for these progressions.

Keywords

Prostate cancer, Therapy-resistant cancer, Radioligand therapy, RLT, Nuclear medicine therapy.

Introduction

Prostate cancer is one of the most common cancers of all. There are a number of treatment methods available. Surgery is still the treatment of choice in many places [1-3]. However, physical methods are also used, such as cold or heat applications. These treatment methods have not achieved a convincing breakthrough, especially not for metastases. Patients who prove resistant to castration therapy (inhibition of the androgen receptor signaling pathway, ARPI) often produce metastases and can hardly be treated successfully [4]. Finally, the semi-synthetic taxane *Docetaxel* (from the European yew, Taxus baccata) is frequently used [5-7].

Mechanism

The discipline of nuclear medicine has been proving for decades that it can be successful when it comes to cancer that absorbs and stores certain radioisotopes. After storage, these destroy the cancer cells with their beta rays. We are talking here, for example, about radioiodine therapy with 131iodine [8]. Differentiated follicular and papillary thyroid carcinomas can be treated almost 100% successfully (also autonomous adenomas and Graves disease). The author himself has carried out this therapy on an outpatient fractionated basis for many years, with excellent success. Up to doses varying from country to country, 131iodine can be drunk on an outpatient basis (e.g. 37 MBq/week). When a previously calculated optimum dose is reached, a break is taken to monitor the effect. The advantage of this therapy is the absolute specificity of the tumor tissue for the radionuclide, so that the rest of the body is not exposed. If any metastases are also differentiated, which is usually the case, they are also successfully treated.

About Prostate Cancer

With regard to prostate cancer, there is no simple radionuclide that is absorbed, but so-called radioligand therapy (RLT) [9]. The radionuclide 177Lutetium (177Lu-PNT2002 or 177Lu-PSMA-617) is bound to the prostate cancer molecule PSMA [10-12]. About PSMA: Prostate-specific membrane antigen (synonyms: Glutamate carboxypeptidase II, NAALADase I = N-acetyl-L-aspartyl-L-glutamate peptidase I) is a membrane-bound glycoprotein. PSMA has the function of an enzyme. It is a carboxypeptidase that cleaves glutamic acid from the C-terminus. In humans, the gene coding for PSMA is located on chromosome 11 gene locus p11.12. [2] Figure 1.

PSMA is found on normal prostate cells and prostate cancer cells. The expression of PSMA increases with the degree of progression and metastasis [13] and its high specificity as a tumor marker

makes it an ideal target antigen for new therapeutic approaches against prostate cancer [14,15]. For diagnostic purposes, PSMA-specific monoclonal antibodies can be used in PET (positron emission tomography) [16].

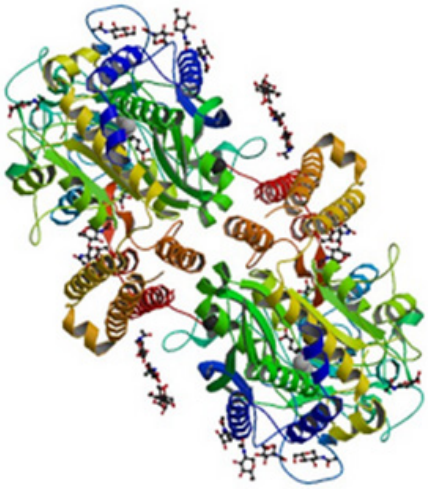

Figure 1: The PMSA enzyme molecule.

Studies

Oliver Sartor from the Mayo Clinic Rochester conducted a randomized double-blind study with 412 patients (Phase III study SPLASH, 17). The patients had metastatic castration-resistant carcinomas and were treated with 177Lu-PNT2002 (6.8 GBq intravenously every eight weeks, four cycles). The endpoint was radiographic progression-free survival. The control group received standard ARPI. As Sartor announced at the ESMO Congress (European Society for Medical Oncology) 2024 in Barcelona, the radionuclide therapy proved to be significantly superior in all respects and according to all criteria. Similar results were reported by Arun Azad from the Peter MacCallum Cancer Center in Melbourne [18]. He used 177Lu-PSMA-617 and the endpoint was a PSA value of close to zero after 48 weeks. Here too, radionuclide therapy proved to be clearly superior. Subsequently, castration therapy could be continued without any problems.

Discussion

Prostate cancer is one of the most common types of cancer. The therapy usually impairs the patient's quality of life until the end of their life. It is therefore necessary to give preference to non-invasive therapies, provided they are available in centers with nuclear medicine. Unfortunately, this is not always the case. The usual cancer therapies suffer from the fact that they have a generalized effect and are not specifically tailored to the cancer cells. The entire organism, or at least an entire system, is regularly treated and thus burdened [19]. In contrast, radionuclide therapy offers the great advantage that only the cancer cells are irradiated, as the beta rays of the radionuclides have a range of a few millimeters in the tissue [20]. RLT cannot be compared with conventional radiotherapy, as this is not specifically aimed at cancer cells, but at an area containing cancer.

Conclusion

In the two studies cited, it was demonstrated that radioligand therapy RLT has proven to be superior in progressive prostate cancer, with a low rate of side effects or sequelae. This is an indication especially for the problem group of metastatic and therapy-resistant patients, who have so far consistently suffered. RLT should be used here as the therapy of choice. Insofar as there is not a sufficient frequency of nuclear medicine departments, these should be established.

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