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Therapeutics + diagnostics = theranostics

EDITORIAL

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Theranostics is the combination of therapeutics and diagnostics. Based on principles of nuclear medicine, theranostics is enabling steadily more possibilities within personalised cancer treatment.

Theranostics is an emerging field of medicine that involves targeted therapy based on the identification and verification of a biological target. In nuclear medicine, theranostics entails diagnostic imaging using radioactively labelled tracers to identify a biological target structure, followed by internal radiation therapy using the same tracer. This ensures selective and targeted treatment of disease manifestations in the body.

The method is far from new and was developed more than 75 years ago using radioactive iodine (^{131}I) for diagnostic imaging and for the treatment of malignant and benign thyroid diseases (1, 2). In the 1980s, ^{131}I-

metaiodobenzylguanidine (^{131}I-MIBG), a noradrenaline analogue, was introduced in the diagnosis and treatment of neuroblastomas (3). However, it was not until radionuclide-labelled somatostatin analogues were used in the diagnosis and treatment of neuroendocrine neoplasia that the field of theranostics gained momentum. Radionuclide therapy with a peptide receptor for neuroendocrine neoplasia has become an established treatment option for inoperable and metastatic disease. The treatment has an excellent safety profile and a high disease control rate, and leads to an improved quality of life and survival (4, 5). Between 2002 and the autumn of 2019, before the treatment was introduced in Norway, patients in Norway were sent to Sweden and Denmark for treatment.

> *«Increased use of theranostic methods will challenge current infrastructures in the health service»*

The success of radionuclide therapy with a peptide receptor has stimulated further development in theranostics, an example of which is the prostate-specific membrane antigen (PSMA). PSMA-PET/CT imaging has already been established for investigating biochemical recurrence of prostate cancer. Systemic radiotherapy with ^{177}Lu-PSMA-617 was approved by the US Food and Drug Administration in March 2022 for patients with metastatic castration-resistant prostate cancer. The approval was based on the results of VISION, a randomised phase 3 trial, where survival and progression-free survival were significantly improved when participants were treated with ^{177}Lu-PSMA-617 as an addition to standard care (6). In Norway, a health technology assessment of PSMA radionuclide therapy is currently underway. Increased use of theranostic methods will challenge current infrastructures in the health service. In Germany, the Netherlands and the United States, this has led to the establishment of theranostic centres. In April 2022, a joint guide was published on how to set up a theranostic centre (7). The guide highlights the importance of a close interdisciplinary collaboration between clinical domains and nuclear medicine.

Extensive research is being conducted on new radionuclide treatments, and a number of theranostic tracer pairs are being tested both preclinically and clinically. Examples of this are fibroblast-activating protein expressed in cancer-associated fibroblasts (8, 9) and chemokine receptor 4 in conditions such as lymphoma and multiple myeloma (10).

Individual dose calculations (dosimetry) are essential for effective and safe radiotherapy. It is important to avoid both under- and over-treatment and to minimise toxicity (11). For some patients, this will require a reduction in the dose in order for the treatment to be safe, while for others it may require a higher dose due to individual variations in the expression of the biological process.

Theranostics represents major potential for future applications. In theory, it will be possible to treat all (oncological) diseases where there is a tracer that selectively recognises the pathological cells, but in practice there will be

numerous technical and biological challenges that need to be addressed first. Nevertheless, current developments indicate that such personalised treatment will be relevant for various patient populations in the future.

After the manuscript for this article was approved, the European Medicines Agency also approved systemic radiotherapy with ^{177}Lu-PSMA-617.

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