High-impact radiopeptide therapy halts neuroendocrine cancer

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Research introduced at SNM's 58th Annual Meeting could be a sign of hope for patients with neuroendocrine cancer not responding well to standard therapies. Most radiotherapies use medical isotopes that emit beta radiation. The therapy in this study employs alpha particles, which have potential for higher potency. In fact, one single atom could be enough to kill an entire cancer cell.

"Until now, the usage of alpha radionuclides was limited to direct injection into the tumor or the use of only very small doses," says Clemens Kratochwil, MD, lead author of the study from the University of Heidelberg, Heidelberg, Germany, and the Institute for Transuranium Elements, European Commission, Joint Research Centre, Karlsruhe, Germany. "This is the first patient study of dose escalation involving the injection of a specific tumor-targeted peptide tagged with an alpha-emitter. This provides additional options for patients with therapy-resistant cancers; further studies could expand the development and safe use of alpha-emitter therapies for patients with other forms of cancer."

Neuroendocrine cancer affects cells that translate neuronal information into hormonal information. Hormones and neuroendocrine nerve cells control a range of physiological processes, including efficiency of digestion, cellular metabolism, blood flow and the reproductive cycle. This type of cancer can therefore affect organs including the pancreas, the bowel, the thyroid gland and the lungs, among many others. Neuroendocrine cancer can go undetected for years and spread (metastasize) to other organs, especially the liver, bones and lymph

nodes.

Standard therapy for neuroendocrine cancer is surgery and chemotherapy, as well as radiotherapy. Radiotherapy uses ionizing radiation to kill cancer cells by damaging their DNA. More targeted therapies come in the form of radioimmunotherapy and radiopeptide therapy, comprising a radionuclide bound or used in conjunction with an antibody or peptide that specifically targets the cancer tissue. A range of radionuclides, also known as medical isotopes, are used depending on the type of cancer, the kind of tumor and stage of disease. Most radiotherapies use beta-emitting particles, but more recently researchers have been conducting studies regarding the use of alpha-emitting particles, which have a very near-range and high-energy effect where administered. The benefit of alpha-therapy is its high cytotoxicity, or ability to kill cells—both cancerous and healthy cells. For this reason, scientists must test the safety of alpha-therapy and identify the most appropriate dose to avoid toxicity in normal tissues.

This study is focused on a cancer therapy called 213Bi-DOTATOC peptide receptor alpha-therapy. DOTATOC, as a tumor-targeting probe labeled with different radionuclides, has been under investigation in the University Hospital of Heidelberg for more than a decade. This peptide analog mimics the endocrine-system regulating hormone somatostatin. The latest advance for the treatment is the use of alpha-emitter 213 Bismuth, a radionuclide that is bound to DOTATOC and injected. Researchers administered the therapy to 14 patients with neuroendocrine liver metastases resistant to previous treatment with beta-particle peptide therapy. The therapy was found to be highly effective for targeting neuroendocrine tumors and inducing remission of metastases without dangerous toxicity to healthy tissues. Further studies are scheduled to escalate dosage further for even greater cancer-killing power for metastatic neuro-endocrine cancer patients. Additional alpha-emitter therapy studies are also continuing to determine their efficacy for

treating other therapy-resistant cancers.

More information: Scientific Paper 29: C. Kratochwil, F. Giesel, A. Morgenstern, F. Bruchertseifer, W. Mier, C. Zechmann, C. Apostolidis, U. Haberkorn, University Hospital, Heidelberg, Germany; Institute for Transuranium Elements, European Commission JRC, Karlsruhe, Germany; "Regional 213Bi-DOTATOC peptide receptor alpha-therapy in patients with neuroendocrine liver metastases refractory to beta-radiation," SNM's 58th Annual Meeting, June 4-8, 2011, San Antonio, TX.

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