Journal of Nuclear Medicine, published on June 30, 2016 as doi:10.2967/jnumed.116.178145

REPLY:

The future of radiopeptide therapy in patients with progressive meningioma

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Short Title: PRRT in meningioma

Text: 432 words, 10 references

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REPLY: We appreciate the thoughtful comments regarding our paper "Somatostatin receptor-targeted radiopeptide therapy with ^{90}Y-DOTATOC and ^{177}Lu-DOTATOC in progressive meningioma: long-term results of a phase II clinical trial" (1), and we are grateful for the opportunity to be part of the ongoing discussion concerning the management of progressive meningiomas.

Meningiomas are the most common primary brain tumors, with an incidence twenty-times higher than that of neuroendocrine tumors. About 80% of meningiomas are benign and curable with gross total resection, while about 20% of meningiomas are atypical or anaplastic and demonstrate malignant potential, significantly higher recurrence rates, and shorter survival. There is currently no standard of care for patients with progressive meningiomas, and the *National Comprehensive Cancer Network* recommends hydroxyurea, alpha-interferon, and somatostatin analogues (2).

Our study as well as other recent work (3, 4) suggests that somatostatin receptor-targeted radiopeptides represent a promising therapeutic option for patients with progressive meningiomas. Herein lies an opportunity for the field of Nuclear Medicine, in collaboration with Neuro-Oncology, Radiation Oncology, and Neurosurgery, to translate this tool from a promising option into a validated therapy.

There may be some clinical utility in determining the ideal radiopeptide and radioisotope combination, such as DOTATOC vs. DOTATATE or yttrium-90 vs. lutetium-177. However, establishing the value of radiopeptide therapy in progressive meningioma, as single treatment or in combination with other drugs, will ultimately yield true clinical benefit. With this in mind, we look forward to an interdisciplinary preclinical and clinical approach.

Prospective clinical trials will be essential to compare the benefits and harms of somatostatin receptor-targeted radiopeptides with those of the currently recommended therapeutics hydroxyurea, alpha-interferon, and somatostatin analogues in patients with progressive meningiomas. These studies are particularly promising given the high expression of somatostatin receptors in meningiomas (5). In addition, meta-analyses evaluating existing data regarding these treatments may prove helpful.

Preclinical studies, on the other hand, will be valuable to assess potential synergies between somatostatin receptor-targeted radiopeptides and other drugs. These drugs should include established as well as some of the newly developed therapeutics from the families of cytotoxic compounds, hormonal agents, receptor antagonists, and small molecule inhibitors (6). These studies are equally promising given that radio-sensitizing effects were found for drugs already tested for progressive meningioma in phase II trials, including sunitinib (7), imatinib (8), and vatalanib (9). Finally, high-throughput screens may prove a valuable approach to identify targets for radiotracers in meningiomas other than the somatostatin receptor (10).

A multifaceted approach combining expertise from various clinical fields with preclinical and clinical research methods will provide a chance to establish targeted radiopeptide therapy as a viable treatment option for progressive meningioma.

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