

Targeted radionuclide treatment achieves high response rate, minimal toxicities for advanced-stage neuroendocrine tumors

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Excellent sustained response in a 34-year-old male with pancreatic NET. The baseline 68Ga-DOTANOC PET maximum intensity projection image (MIP) reveals intense SSTR expression in the pancreas, multiple abdominopelvic lymph nodes, and extensive liver metastases. The patient underwent six cycles of 225Ac-DOTATATE (100-120 KBq/Kg body weight) and is under follow-up more than 48 months until now. Credit: Chandrasekhar Bal, Sanjana Ballal, and Madhav Yadav, All India Institute of Medical Sciences, New Delhi, Delhi, India.



A targeted radionuclide alpha therapy, ²²⁵Ac-DOTATATE, has been shown to have long-term anti-tumor effects in patients with advancedstage gastroenteropancreatic neuroendocrine tumors (GEP-NETs). Results from the Phase II study showed promising survival rates, high response rates and an acceptable toxicity profile, making ²²⁵Ac-DOTATATE a potential treatment option for patients who have exhausted other forms of therapy. This research was presented at the Society of Nuclear Medicine and Molecular Imaging 2022 Annual Meeting and was selected as the meeting's Abstract of the Year.

Each year, SNMMI chooses an abstract that best exemplifies the most promising advances in the field of nuclear medicine and molecular imaging. This year, the SNMMI Henry N. Wagner, Jr., Abstract of the Year was chosen from more than 1,000 abstracts submitted to the meeting and voted on by reviewers and the society leadership.

GEP-NETs are rare malignancies that arise from neuroendocrine cells and can be present all along the gastrointestinal tract. While patients with early-stage GEP-NETs can undergo surgery to cure the disease, the majority of patients are diagnosed with metastatic disease, making systemic treatment—such as targeted radionuclide therapy—their only option. ¹⁷⁷Lu-DOTATATE has been proven to be an effective targeted beta radionuclide therapy; little evidence, however, is available on targeted alpha radionuclide therapies for GEP-NETs.

In the study, researchers aimed to evaluate the long-term efficacy, <u>survival outcomes</u>, and safety of the targeted radionuclide alpha therapy ²²⁵Ac-DOTATATE in GEP-NET patients. Eighty-three GEP-NET patients (including 56 patients with prior ¹⁷⁷Lu-DOTATATE treatment and 27 ¹⁷⁷Lu-DOTATATE-naïve patients) received systemic treatment with ²²⁵Ac-DOTATATE intravenously at eight weekly intervals.

Hematologic, kidney and liver function tests were performed before and



after each cycle. Tumors were measured using RECIST 1.1 criteria at baseline and after two cycle intervals. Overall survival, radiographic progression-free survival, objective tumor response, and treatment-related adverse events were assessed.

After the treatment course, two patients (2.7 percent) had complete response, 32 (43.2 percent) had a partial response, 25 (34 percent) had stable disease, and 15 (20 percent) had progressive disease. Minimal toxicities were noted after treatment with ²²⁵Ac-DOTATATE.

"²²⁵Ac-DOTATATE is a promising therapy option that adds a new dimension to the treatment of end-stage GEP-NETs, especially for patients who have tried all other standard therapy options," said Chandrasekhar S. Bal, MD, DNB, DSc (HC), FAMS, FNASc, FASc, professor and head of the Department of Nuclear Medicine and PET at the All India Institute of Medical Science in New Delhi, India. "These results warrant a Phase III randomized control trial to assess the true efficacy of ²²⁵Ac-DOTATATE versus ¹⁷⁷Lu-DOTATATE."

"The results from this study not only emphasized the promise and success of targeted alpha therapies but also reflected growing global interest in these life-extending treatments," said Heather Jacene, MD, SNMMI Scientific Program Committee chair. "We look forward to further research on this topic in the future."

More information: Conference: <u>am.snmmi.org/iMIS/SNMMI-AM</u>

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