

**THE NEW RADIOLABELLED SOMATOSTATIN ANALOGUE
⁹⁰YTTRIUM-DOTA-OCTREOTATE FOR THE TREATMENT
OF METASTATIC NEUROENDOCRINE TUMORS:
Initial results and tolerability in a series of 47 patients.**

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Background: Neuroendocrine gastroenteropancreatic (GEP) tumors, which include pancreatic islet cell tumors, non-functioning neuroendocrine pancreatic tumors, and carcinoids, are generally slow growing. When these tumors have metastasized, treatment with "cold" somatostatin analogs results only in reduced hormonal overproduction and symptomatic relief in most cases.

New treatment modality for inoperable or metastasized GEP tumors is the use of radiolabeled somatostatin analogs. The majority of GEP tumors possess somatostatin receptors and therefore can be visualized in vivo with the radiolabeled somatostatin analog [¹¹¹In-diethylenetriaminepentaacetic acid (DTPA)⁰] octreotide (OctreoScan; Mallinckrodt Medical). A logical extension of this tumor visualization in patients therefore is to try to treat these patients with radiolabeled somatostatin analogs¹. This new therapeutical tool reflects a multidisciplinary synthesis of various disciplines from Basic Research and Clinical Subjects: Nuclear Medicine, Molecular Biology and Pathology, Pharmacology and Gastroenterology.

Previous studies have assessed radiolabelled octreotide, but recent evidence suggests that radiolabelled octreotate has even higher binding to type II SSSTR (Somatostatine Receptor).

Aim: Our study intended to estimate efficacy and tolerability of a new radiolabelled somatostatin analogue, ⁹⁰Yttrium-Tyr3-DOTA-octreotate (⁹⁰Y-DOTA-octreotate), in patients with metastatic neuroendocrine tumors which progressed, despite the administration of other treatments (chemotherapy, cold somatostatine analogue, α -Interferon).

Patients & Methods: Forty seven patients (mean age was 60.4 years, range: 34-85 years) with metastatic neuroendocrine tumors were studied. In most patients the tumours were either low or intermediate-grade, while eleven patients had high-grade tumours. The latter had

received chemotherapy in the past. All patients received 1-3 cycles of the ^{90}Y -DOTA-octreotate every 2-3 months, either intravenously (19/47,40.4%) or intra-arterially (28/47,59.6%). In 8 patients of the latter group the intrarterial administration was combined with particle embolization of hepatic metastases. Intravenous aminoacids were also administered for protection of renal function. Clinical and/or radiological response to treatment was defined as the improvement of symptoms and/or either stabilization or reduction of tumor growth, respectively. Mean follow-up period was 10.1 months (range:2-21 months).

Results: In all patients the post treatment scintigraphic scan demonstrated uptake and localization by the tumour. Clinical improvement was noted in 28/47 (59.5% patients) after 1-3 treatments. Stabilization of tumor growth was achieved in 11/17 (64.7%) patients, who had completed the 3 cycles of treatment, and in 7/13 (53.8%) in those who had 2 cycles so far. Radiological response, even lower (4/11,36.3%), was noted also, in the high-grade group of patients who had progressed despite chemotherapy. Bone marrow toxicity (criteria grade II according WHO) was noted in 6/47 (12.7%), persisting at 3 months in two patients with significant bone metastases. One of them who had chemotherapy in the past, developed also irreversible mild renal failure (WHO grade II), despite prophylactic aminoacids.

Conclusion: ^{90}Y -DOTA-octreotate seems to be a well-tolerated and safe treatment for patients with progressive neuroendocrine tumors, despite a risk for bone marrow toxicity in patients with large-volume bone metastases. Early results, regarding efficacy were promising. Longer follow-up and more patients are required for better evaluation of tumor response.

References

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