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The Antiproliferative Effect of Octreotide in Gastroenteropancreatic (GEP) Neuroendocrine Tumors (NETs)

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Background: Somatostatin analogs are the mainstay of medical therapy for the symptomatic relief of clinical syndromes associated with GEP-NETs (eg, carcinoid syndrome), which typically arise following liver metastasis. Although most patients with metastatic GEP-NETs will not achieve surgical cure and are resistant to traditional chemotherapy regimens, an analysis of the SEER database identified a lengthening in survival time among patients with metastatic NETs diagnosed 1988–2004 vs 1973–1987, coinciding with the introduction of octreotide in the US.

Methods: A review of the literature describing the outcomes of patients with GEP-NETs administered monotherapy with octreotide for symptomatic or antineoplastic treatment.

Results: Early uncontrolled studies found that 37–50% of patients with progressive metastatic GEP-NETs achieved stable disease with octreotide sc 200–1000 μg/tid, with tumor stabilization maintained >42 months in some patients (Saltz 1993; Arnold 1993 and 1996; diBartolomeo 1996). Uncontrolled studies of octreotide LAR 20–30 mg/month found tumor stabilization/response in 53% of patients with progressive metastatic gastrinomas for 5.5–54 months (Shojamanesh 2002), and 47% of patients with progressive metastatic GEP-NETs following failure with slow-release lanreotide (Ricci 2000). Recently, the first randomized, placebo-controlled, double-blind trial (PROMID) evaluated the antiproliferative effect of octreotide LAR in treatment-naïve patients with well-differentiated, metastatic midgut NETs. In this patient group, octreotide LAR 30mg significantly lengthened time to tumor progression versus placebo, regardless of functional status or hepatic tumor burden (14.3 vs 6.0 months; $P<0.000072$). At 6 months, partial response or stable disease was achieved in 29/42 patients with octreotide LAR and 17/43 patients with placebo ($P=0.0079$) (Arnold 2009).

Conclusions: Octreotide has been associated with tumor stabilization in heterogeneous populations of patients with GEP-NETs. The PROMID trial confirmed the antiproliferative effect of octreotide LAR in patients with well-differentiated, metastatic midgut NETs. Patients with functioning or non-functioning GEP-NETs should be considered for octreotide LAR 30mg.