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A Prospective, Multi-Institutional Phase II Study of Pazopanib and Depot Octreotide in Advanced, Well-Differentiated Neuroendocrine Tumors

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Background: Treatment options for advanced well-differentiated neuroendocrine tumors (NET) remain limited. The mTOR inhibitor everolimus and the tyrosine kinase inhibitor sunitinib are active and approved for use in advanced pancreatic neuroendocrine tumors (pNET); no treatment has yet been approved for tumor control in patients with advanced carcinoid. Pazopanib is an orally bioavailable small molecule multitargeted kinase inhibitor inhibiting VEGF receptors 1, 2, and 3. We performed a prospective study of pazopanib with octreotide in patients with advanced NET.

Methods: We performed a two-cohort study in patients with advanced carcinoid or advanced pNET, using a 2-stage design. The primary endpoint was objective response rate (ORR), with secondary endpoints of progression-free survival (PFS), overall survival (OS), and toxicity.

Results: 52 patients (32 pNET and 20 carcinoid) were enrolled between 4/07 and 7/09. By intention to treat analysis, the pNET ORR was 21.9% (95% CI 11-38.8). There were no responses in the first stage of the carcinoid cohort, and accrual was terminated at 20 patients. Median PFS was 14.4 months in the pNET cohort and 12.2 months in the carcinoid cohort.

Conclusions: Treatment with pazopanib is associated with tumor regression and an encouraging PFS duration in patients with pNET. Further studies evaluating pazopanib in advanced pancreatic NET are warranted.

Trial Registration: www.clinicaltrials.gov Idenitifier: NCT00454363