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A Multi-Institutional Phase II Open-Label Study of AMG 479 in Advanced Carcinoid and Pancreatic Neuroendocrine Tumors

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Background: The IGF pathway has been implicated in neuroendocrine tumor (NET) progression. We therefore investigated AMG 479, a human monocolonal antibody against IGF1-R, in patients with metastatic progressive carcinoid and pancreatic NETS.

Methods: This phase II study enrolled patients (≥18 yrs) with metastatic low and intermediate-grade carcinoid and pancreatic NETs. Inclusion criteria included evidence of progressive disease (by RECIST) within 12 months of enrollment, ECOG PS 0-2, and fasting blood sugar <160mg/dL. Prior treatments were allowed and concurrent somatostatin analog therapy was permitted as long as patients remained on a stable dose. The primary endpoint was objective response rate. Secondary endpoints included overall survival (OS), progression-free survival (PFS), and safety.

Results: 60 patients (30 carcinoid, 30 pancreatic NET) were treated with AMG 479 18mg/kg every 3 weeks and 54 patients were evaluable for response. There were no objective responders by RECIST. When best response to therapy was evaluated, 10/27 (37%) evaluable carcinoid patients and 8/26 (31%) evaluable pancreatic NET patients appeared to have experienced some degree of tumor shrinkage, while 17/27 (63%) of the carcinoid patients and 15/26 (58%) of the pancreatic NET patients appeared to experience continued tumor growth. Median PFS was 6.3 months (95% CI 4.2-12.6) for the entire cohort; 10.5 months for carcinoid patients and 4.2 months for pancreatic NET patients. The OS rate at 12 months was 70% (55%-81%) for the entire cohort. Median OS has not been reached. Treatment related grade 3/4 AEs were rare and consisted of hyperglycemia (4%), neutropenia (4%), thrombocytopenia (4%) and infusion reaction (1%).

Conclusions: While well-tolerated, treatment with AMG 479 was not associated with major tumor responses among patients with metastatic low-intermediate grade carcinoid or pancreatic NET. Subgroup analysis to identify characteristics of patients who may have benefited from therapy with AMG 479 is ongoing.