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A phase II clinical trial of MK-0646, an insulin-like growth factor-1 receptor inhibitor (IGF-1R) in patients with metastatic well differentiated neuroendocrine tumors (NETs)

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Background: Preclinical studies have implicated the IGF-1 receptor in the progression of neuroendocrine tumors. A therapy directed at IGFR mediated signaling pathways has potential for conferring enhanced anti-tumor activity. We evaluated the safety and efficacy of MK-0646, a monoclonal antibody (mab) that blocks the insulin-like growth factor receptor (IGF-1R), as monotherapy in metastatic well differentiated neuroendocrine patients.

Methods: A phase II study was performed in which patients received MK-0646 at a dose of 10 mg/kg iv over 1 hour weekly. Archived pretreatment tumor tissue was obtained for putative biomarkers.

Results: A total of 25 patients were treated (15 carcinoid, 10 PNETs) female, 40%; median age, 61 years, (range 36-82). No antitumor activity was seen in these 25 patients treated with MK-0646 monotherapy. Progression free survival was 4.2 months in the PNET cohort (range 0.7-6.7 months) and 2.7 months (range 2-3 months) in the carcinoid cohort. The most common serious adverse event (SAE) thought to be potentially related to MK-0646 was hyperglycemia (7 patients, 25%). Other SAEs included one grade 2 infusion-related reaction (4%), and 2 patients with grade 3 fatigue (8%).

Conclusions: MK-0646 alone was well tolerated with the exception of hyperglycemia that was manageable with antihyperglycemic medications, however, the degree of activity seen was insufficient to warrant further study as a monotherapy in well differentiated neuroendocrine tumors.