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Phase 1 Maximum-Tolerated Dose Study of Pasireotide LAR in Patients with Advanced Neuroendocrine Tumors

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Background: Pasireotide is a novel somatostatin analog (SSA) with a broader somatostatin receptor binding affinity than octreotide or lanreotide. A phase 1 dose-escalation study (NCT01364415) of pasireotide long-acting release (LAR) was designed to determine the maximum tolerated dose (MTD) or recommended phase 2 dose (RP2D) and to characterize the safety, tolerability, pharmacokinetics, and efficacy in patients with advanced neuroendocrine tumors (NET).

Methods: Patients with advanced, well-differentiated, or moderately differentiated NET received pasireotide LAR IM, beginning at a dose of 80 mg every 28 days.

Results: As of March 20, 2013, 21 patients have been treated in the dose-escalation phase of the study: 6 at 80 mg (median age, 57 years) and 15 at 120 mg (median age, 60 years). Primary tumor sites include small intestine (43%), lung (24%), and pancreas (14%). Most patients (86%) received previous SSA therapy; 95% had undergone previous resection. Median duration of exposure (based on 28-day cycles) was 7.6 cycles (80-mg group) and 4.9 cycles (120-mg group). Thirteen (62%) patients remain on treatment (80 mg, n=1; 120 mg, n=12); 8 (38%) patients discontinued. Mean plasma concentrations of pasireotide increased with dose escalation from 80 to 120 mg. No dose-limiting toxicities have been reported. The most frequent adverse events (AEs) were mild/moderate and similar between doses, including: hyperglycemia (76%), diarrhea (48%), abdominal pain (38%), fatigue (38%), nausea (33%), and anemia (29%). Three patients experienced grade 3/4 hyperglycemia (80 mg, n=2; 120 mg, n=1).

Conclusions: Pasireotide LAR appears to be well tolerated up to 120 mg in patients with advanced NET. This study is ongoing.

Supported by Novartis Pharmaceuticals Corporation.