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Pasireotide LAR in Metastatic Carcinoid Tumors: A Randomized Phase I Study

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Background: Pasireotide is a novel multi-receptor ligand somatostatin analogue with high affinity for somatostatin receptor subtypes $sst_{1,2,3}$ and sst_5. Twice daily subcutaneous pasireotide has shown activity in controlling symptoms of metastatic carcinoid tumors in patients refractory or resistant to octreotide long-acting-release (LAR). An LAR formulation of pasireotide administered monthly has been developed, and PK and safety results from a randomized, open-label, multicenter, Phase I study of pasireotide LAR in patients with metastatic carcinoid tumors are presented.

Methods: Patients with histopathologically confirmed carcinoid, elevated 5- hydroxyindole acetic acid (HIAA) and/or chromogranin A (CgA), measurable tumor, and carcinoid syndrome inadequately controlled by other somatostatin analogues were enrolled. Patients received intramuscular depot injections of pasireotide LAR 20, 40 or 60 mg every 28 days for 3 doses. PK, safety, and tolerability were assessed regularly.

Results: A total of 42 patients received ≥1 dose of pasireotide LAR. Steady state was reached within three injections. Trough plasma concentrations of pasireotide on day 84 were 5.6 ± 2.0, 16.6 ± 10.2 and 25.0 ± 20.5 ng/mL for the 20, 40 and 60 mg dose levels respectively. Plasma concentrations with pasireotide LAR 40 and 60 mg were comparable to those achieved with pasireotide 600 and 900 µg sc bid, respectively; with comparable peak concentrations and ~2-fold higher trough concentrations. 60% of patients reported ≥1 treatment-related adverse event (AE), most of which were mild. AEs with a suspected pasireotide relationship occurring in ≥3 patients were related to glucose metabolism (diabetes mellitus [n=5]; hyperglycemia [n=5]; worsening of type 2 diabetes mellitus [n=3]).

Conclusion: Pasireotide LAR had dose-related PK and was generally well tolerated. Adverse events were similar to pasireotide sc. The availability of a long-acting release formulation of pasireotide will provide a convenient treatment option.