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A Multicenter, Randomized, Blinded, Phase 3 Study of Pasireotide LAR vs Octreotide LAR in Patients with Metastatic Neuroendocrine Tumors (NET) with Disease-Related Symptoms Inadequately Controlled by Somatostatin Analogs

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Background: Pasireotide, a novel somatostatin analog (SSA) with a broader receptor binding profile than available SSAs (octreotide and lanreotide), was investigated in a phase 3 study (NCT00690430) for control of disease-related symptoms in patients with NET inadequately controlled by the maximum approved dose of available SSAs.

Methods: Patients (N=110) were randomized 1:1 to receive pasireotide LAR (P; 60 mg IM) or octreotide LAR (O; 40 mg IM) every 28 days and stratified by predominant symptom at baseline (diarrhea, flushing, or diarrhea+flushing). The primary outcome was symptom response at month 6. Other outcomes included tumor response, safety and progression-free survival (PFS).

Results: The study was terminated after an interim analysis suggesting futility for symptom response. Baseline characteristics of the patients enrolled in the P (n=53) and O (n=57) arms were well balanced. Primary tumor location was mainly the small intestine (P, 72%; O, 81%). Numbers of patients with symptom response at month 6 were 9/43 (21%) with P and 12/45 (27%) with O (OR=0.73; 95% CI, 0.27-1.97; *P*=0.53). Symptom response rates overall and by stratum for each drug are tabulated. Hyperglycemia (13% vs. 2%), diarrhea (11% vs. 7%), and abdominal pain (6% vs. 9%) were the most common grade 3/4 adverse events (AEs) in the P versus O arms, and 9 (17%) and 4 (7%) patients discontinued due to AEs. Median investigator-assessed PFS, an exploratory end point, was 11.8 months with P and 6.8 months with O (HR=0.46; *P*=0.045).

Conclusions: Except for the higher frequency of hyperglycemia seen with P, both drugs had similar safety profiles. P-treated patients had longer PFS (by 5 months) than O-treated patients, despite no differences in symptom response rates. These results warrant a phase 3 trial to evaluate the therapeutic potential of P in NET.

Stratum	Pasireotide LAR n^a/N^b (%) (95% exact CI)	Octreotide LAR n^a/N^b (%) (95% exact CI)	Between-Treatment OR (95%)
Diarrhea + flushing	5/37 (13.5) (4.5-28.8)	11/39 (28.2) (15.0-44.9)	0.40 (0.12-1.29)
Predominantly diarrhea	2/2 (100) (15.8-100)	1/5 (20.0) (0.5-71.6)	
Predominantly Flushing	2/4 (50.0) (6.8-93.2)	0/1 (0) (0.0-97.5)	
Overall	9/43 (20.9) (10.0-36.0)	12/45 (26.7) (14.6-41.9)	0.73 (0.27-1.97) *P*=0.53

CI, confidence interval; OR, odds ratio. [a]Number of responders; [b]Number of patients analyzed.

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