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Telotristat Etiprate Shows Benefit in Treating Patients with Carcinoid Syndrome that is Inadequately Controlled by Somatostatin Analog Therapy in the Phase 3 TELESTAR Clinical Trial

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Background: Overproduction of serotonin from within neuroendocrine tumors (NET) causes carcinoid syndrome (CS), which includes diarrhea, flushing, and heart valve damage. Telotristat etiprate (TE) inhibits tryptophan hydroxylase (TPH),

an enzyme that converts tryptophan to serotonin in the NET cell. TELESTAR is a pivotal phase 3 global clinical trial.

Methods: Patients with metastatic NET and inadequately controlled CS (≥4 daily BMs despite SSA therapy) were randomized (1:1:1) to receive TE (250 or 500 mg) or placebo (PBO) given tid, while continuing SSA. The primary endpoint was the reduction in the mean number of daily BMs averaged over the 12-week double-blind period of the trial.

Results: 135 patients (baseline mean BMs/day 5.7, baseline urinary 5-HIAA 88 mg/24hr) were randomized. The primary objective was met; BM frequency in both treatment groups was less than PBO (Hodges Lehman Estimator TE minus placebo of -0.813 (TE 250) and -0.689 (TE 500) BM/day, ($p<0.001$ for both comparisons). Decrease in mean daily BMs at Week 12 was 17% (PBO), 29% (TE 250), and 35% (TE 500). The proportion of patients with durable response (≥30% reduction in BM frequency for ≥50% of study) was 20% (PBO), 44% (TE 250) and 42% (TE 500), ($p\leq0.040$ for both comparisons). Week 12 reductions in 24-hr u5-HIAA were 30.1 mg (TE 250), and 33.8 mg (TE 500) compared to PBO ($p<0.001$ for both dosages). Overall AE frequency was similar in all 3 groups. Mild/moderate depression was reported in 3 (PBO), 2 (TE 250), and 6 patients (TE 500), all events resolved while continuing therapy; 87% of randomized patients continued onto open-label treatment with TE 500 mg tid.

Conclusions: Telotristat etiprate provided statistically significant and clinically meaningful reductions in BM frequency and represents a promising potential new class of treatment for patients with CS inadequately controlled by standard of care SSA therapy.