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Weight Change Associated With Telotristat Ethyl in the Treatment of Carcinoid Syndrome

Martin O. Weickert[1]; *Gregory Kaltsas[1]; Dieter Hörsch[2]; Pablo Lapuerta[3]; Marianne Pavel[4,5]; Juan W. Valle[6]; Martyn E. Caplin[7]; Emily Bergsland[8]; Pamela L. Kunz[9]; Lowell B. Anthony[10]; Enrique Grande[11]; Kjell Öberg[12]; Staffan Welin[12]; Richard R. P. Warner[13]; Catherine Lombard-Bohas[14]; Rosanna Fleming[3]; Ashwin Kittur[3]; Karie Arnold[3]; Qi M. Yang[3]; Matthew H. Kulke[15]*

[1]University Hospitals Coventry and Warwickshire NHS Trust; [2]Zentralklinik Bad Berka; [3]Lexicon Pharmaceuticals, Inc.; [4]Charité–Universitätsmedizin; [5]Friedrich-Alexander-Universität; [6]University of Manchester/The Christie NHS Foundation Trust; [7]Royal Free Hospital; [8]UCSF Helen Diller Family Comprehensive Cancer Center; [9]Stanford University; [10]University of Kentucky; [11]Hospital Universitario Ramón y Cajal; [12]Uppsala University; [13]Icahn School of Medicine at Mount Sinai; [14]Hôpital Edouard Herriot, Hospices Civils de Lyon; [15]Dana-Farber Cancer Institute

BACKGROUND: In the Phase 3 TELESTAR study, the oral tryptophan hydroxylase inhibitor telotristat ethyl (TE) significantly reduced bowel movement (BM) frequency compared with placebo over a 12-week Double-blind Treatment (DBT) period in patients with carcinoid syndrome (CS). Weight loss (WL) has previously been associated with uncontrolled CS and may result in reduced survival, so it is important to examine weight changes in patients with neuroendocrine tumors (NETs).

METHODS: We conducted a prespecified analysis of the incidence of weight change of ≥3% at Week 12 in TELESTAR. Patients with metastatic NETs, CS, and ≥4 BMs/day were randomly assigned to receive placebo, TE 250 mg, or TE 500 mg 3x/day (tid) for 12 weeks, in addition to somatostatin analog therapy.

RESULTS: Each group had 45 patients. Mean baseline age was 63.5 years, with 5.8 BMs/day and mean body mass index 24.87 kg/m2. Weight gain (WG) ≥3% at Week 12 was observed in 2/39 (5.1%), 7/41 (17.1%), and 13/40 (32.5%) patients on placebo, TE 250 tid, and TE 500 mg tid, respectively. The Cochran–Armitage test for trend in WG incidence across groups yielded p = 0.0017. Among 20 patients with a ≥3% WG on TE, 10 experienced a reduction of at least 30% in BM frequency at Week 12 (maximum reduction 75%). WL ≥3% at Week 12 occurred in 5 (12.8%), 4 (9.8%), and 6 (15.0%) patients on placebo, TE 250 tid, and TE 500 mg tid. Adverse events of vomiting, decreased appetite, cachexia, and performance status decreased were reported during the DBT period among those with WL but not those with WG.

CONCLUSION: The incidence of WG on TE was dose related and greater than that on placebo. It was possibly related to reduced diarrhea severity and may be a relevant aspect of TE efficacy among patients with functioning metastatic NETs.