

Telotristat Etiprate Produces Clinical and Biochemical Responses in Patients with Carcinoid Syndrome: Update of a Phase 2, Multicenter, Open-label, Serial-ascending, European Study

Marianne Pavel¹; Bertram Wiedenmann¹; Martyn Caplin², Dieter Hoersch³; Joel Freiman⁴; Linda Law⁴; Phillip Banks⁴; Kenny Frazier⁴; Jessica Jackson⁴; Brian Zambrowicz⁴

¹Charité - Universitätsmedizin, Berlin Germany

²Royal Free London NHS Foundation Trust, London, United Kingdom,

³Zentralink Bad Berka GmbH, Bad Berka, Germany

⁴Lexicon Pharmaceuticals, Inc., The Woodlands, TX USA

Background: Excess serotonin (5-HT) may cause gastrointestinal (GI) symptoms (eg, diarrhea) in carcinoid syndrome (CS) patients. Telotristat etiprate is an oral serotonin synthesis inhibitor (tryptophan hydroxylase inhibitor) designed to reduce peripheral 5-HT levels and alleviate GI distress.

Methods: This study evaluated the safety and tolerability of inpatient dose escalation (150, 250, 350, and 500 mg tid) of telotristat etiprate in CS patients, averaging ≥ 4 bowel movements (BMs)/day, with or without background somatostatin analog therapy. Dose strength was increased following every 2 weeks of therapy with no dose-limiting toxicity (DLT). The maximum dose for each patient was extended for an additional 4 weeks. Objectives included evaluation of symptomatic response (including number of BM/day, and flushing episodes), global assessment of symptoms, and biochemical response (urinary 5-hydroxyindole acetic acid [5-HIAA]).

Results: 15 patients enrolled with a mean baseline BMs/day of 5.9, flushing 2.8/day, and urinary 5-HIAA of 127.8 mg/24 hrs. 12/15 patients escalated to 500 mg tid. Data collected during the final 4 wks of therapy demonstrated that 11 (73%) had mean reductions of $\geq 30\%$ and 5 (33%) had $\geq 50\%$ reduction in BMs/day; 11 of 15 patients had baseline flushing and 5 (45%) had mean reductions of $\geq 30\%$ in flushing/day. 5-HIAA levels decreased an average of 54% from baseline. There were no drug-related SAEs and no dose-limiting toxicities.

Conclusion: Telotristat etiprate (≤ 500 mg tid) produced clinically relevant biochemical and clinical responses in patients with carcinoid syndrome. Telotristat etiprate was safe and well tolerated through 12 weeks of therapy. The program will be advanced into further clinical studies.