C-5

Time to Sustained Improvement in Bowel Movement Frequency With Telotristat Ethyl: Analysis of the Phase 3 TELESTAR Study

Joseph S. Dillon[1]; *Matthew H. Kulke[2]; Marianne Pavel[3,4]; Dieter Hörsch[5]; Lowell B. Anthony[6]; Richard R. P. Warner[7]; Emily Bergsland[8]; Staffan Welin[9]; Thomas M. O'Dorisio[1]; Nilay Patel[10]; Pablo Lapuerta[10]*

[1]University of Iowa; [2]Dana-Farber Cancer Institute; [3]Charité–Universitätsmedizin; [4]Friedrich-Alexander-Universität; [5]Zentralklinik Bad Berka; [6]University of Kentucky; [7]Icahn School of Medicine at Mount Sinai; [8]UCSF Helen Diller Family Comprehensive Cancer Center; [9]Uppsala University Hospital; [10]Lexicon Pharmaceuticals, Inc.

BACKGROUND: Telotristat ethyl is approved to treat carcinoid syndrome diarrhea in combination with somatostatin analog (SSA) therapy. In the Phase 3, randomized, placebo-controlled, double-blind TELESTAR study, patients with carcinoid syndrome experiencing ≥4 bowel movements (BMs) per day while on SSA therapy were treated with telotristat ethyl 250 mg 3 times per day (tid), telotristat ethyl 500 mg tid, or placebo tid. Time to sustained improvement in BM frequency during the Double-blind Treatment (DBT) period is presented.

METHODS: The time to the first occurrence of sustained response was defined as the time from the first dose to the first day of a continuous 14 days of ≥30% reduction from Baseline in BM frequency during the DBT period. The time to the first sustained response in the TELESTAR study was examined among treatment groups and analyzed using Cox regression to analyze hazard ratios and the log-rank test for treatment comparisons.

RESULTS: Each treatment arm had 45 patients. Sustained improvement in BM frequency over the 12-week DBT period was achieved in 34, 31, and 19 patients

in the telotristat ethyl 250 mg, telotristat ethyl 500 mg, and placebo groups. Median time to sustained ≥30% improvement was 3–4 weeks with telotristat ethyl at both dosing levels, and no median was reached on placebo (Table 1). Hazard ratio estimates suggest treatment with telotristat ethyl increases the likelihood of a sustained improvement in BM frequency more than 2-fold as compared with placebo. The first day of sustained improvements in BM frequency occurred within 5 days (25th percentile) and 73 days (75th percentile) of treatment initiation.

CONCLUSION: Time to sustained clinical benefit with telotristat ethyl may vary across patients. Some patients experienced initiation of sustained improvement in BM frequency within days of beginning telotristat ethyl treatment, whereas the median time on therapy for this effect was 3–4 weeks.

Table 1:
Analysis of Time to First Occurrence of Sustained ≥ 30% Improvement in BM Frequency

	Placebo tid	Telotristat ethyl 250 mg tid	Telotristat ethyl 500 mg tid
Number of patients	45	45	45
Number of patients with a sustained response	19	34	31
25th percentile, days (95% CL)	18.0 (4.0, 50.0)	5.0 (1.0, 12.0)	10.0 (1.0, 15.0)
Median percentile, days (95% CL)	NR	19.0 (9.0, 44.0)	27.0 (13.0, 40.0)
75th percentile, days (95% CL)	NR	73.0 (NC)	NR (NC)
HR (telotristat ethyl/ placebo) (95% CL)		2.29 (1.32, 4.10)	2.15 (1.22, 3.89)
p-value		0.004	0.009

BM, bowel movement; CL, confidence level; HR, hazard ratio; NC, not calculated; NR, not reached; tid, 3 times per day