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Efficacy and Safety of Telotristat Ethyl in Patients With Carcinoid Syndrome Inadequately Controlled by Somatostatin Analogs: Analysis of the Completed TELESTAR Extension Period

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BACKGROUND: The phase III, placebo-controlled, randomized TELESTAR study evaluated efficacy and safety of telotristat ethyl (TE) in patients with diarrhea (≥4 bowel movements [BMs]/day) due to carcinoid syndrome (CS) inadequately controlled by somatostatin analogs (SSAs). TE, a tryptophan hydroxylase inhibitor, decreases peripheral serotonin. As add-on treatment to SSAs, TE 250 mg and TE 500 mg 3x/day (tid) significantly reduced BM frequency ($p<0.001$) compared with placebo over the 12-week Double-blind Treatment (DBT) period. After Week 12, patients crossed over to a 36-week Open-label Extension (OLE) with TE 500 mg tid; data from the full 48 weeks are presented.

METHODS: Changes from baseline in BM frequency (monitored weekly), urinary 5-hydroxyindoleacetic acid (u5-HIAA; Weeks 18, 24, and 48), European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30) score (Weeks 24 and 48), and safety during the OLE were evaluated.

RESULTS: Of 135 patients randomly assigned, 118 completed the DBT period; 115 patients subsequently entered (79 completed) the OLE. Of the 36 patients who discontinued the OLE, the most frequent reasons were adverse event (AE; 15 patients) and withdrawal of consent (9 patients). Treatment-emergent AEs led 18 patients to discontinue TE, most commonly due to gastrointestinal disorder (6 patients). Reductions from baseline in BM frequency (~2 BMs/day) and u5-HIAA (range –20.0 mg to –49.5 mg/24 hours) during the OLE were consistent with results of the DBT period and persisted through Week 48. Improvement in EORTC QLQ-C30 diarrhea subscale scores relative to baseline (range –18.8 to –30.6 points) was notable and persisted through Week 48. Crossover into the OLE was well tolerated. Treatment-emergent AEs were mainly mild to moderate and occurred at similar rates as in the DBT period.

CONCLUSION: Patients benefited from TE throughout the OLE, was well tolerated over 48 weeks, and showed efficacy consistent with previously reported data.