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Safety Analysis of Patients with Neuroendocrine Tumors (NETs) Receiving Concomitant Treatment with Telotristat Ethyl (TE) and Everolimus (EVE) in Phase 3 TELEPATH Study

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BACKGROUND: TE is a tryptophan-hydroxylase 1 (TPH1) inhibitor approved for treatment of carcinoid syndrome diarrhea (CSD) in combination with somatostatin analogues (SSAs) in adults inadequately controlled with SSAs alone.

METHODS: Subjects who participated in 1 of 2 phase 2 (NCT00853047, NCT01104415) or two phase 3 trials (NCT01677910, NCT02063659) investigating safety and efficacy of TE for treatment of CSD were eligible to enroll, after completion of the trial, into the "Expanded Treatment for Patients with Carcinoid Syndrome Symptoms (TELEPATH)" study (NCT02026063). The primary objective of TELEPATH was to evaluate long-term safety and tolerability of orally administered TE. Patients received treatment with SSAs and TE 500 mg tid, and concomitant antitumor therapies were allowed. We report data on serious adverse events (SAEs) observed in 12 patients participating in the TELEPATH study who received concomitant treatment with SSA, TE and EVE.

RESULTS: A total of 12 patients (8 women and 4 men, median age 68 years, range 47-82 years) enrolled in TELEPATH (data cut-off date 23Dec2016) and received treatment with EV at multiple dose levels (2.5, 5, 7.5, and 10 mg.) SAEs were reported for 9/12 patients and led to treatment discontinuation in 2 patients.

Almost all reported SAEs (24/25) were considered not-related to treatment, and 1 SAE was considered to be unlikely related to treatment. SAEs occurring in >1 patient were abdominal pain and diarrhea. Most common SAE term reported was “gastrointestinal disorders” with 7 SAEs (28%). The reported SAEs were severe in 52% (13/25) of cases, moderate in 40% (10/25 cases) and mild in 8% (2/25) cases.

CONCLUSION: Post hoc review of safety in 12 patients treated concomitantly with SSAs, TE and EVE in the TELEPATH study suggests that the safety profile of the combination is consistent with the known safety profiles of each of the approved therapies.