

## Telotristat Etiprate (TE) in a Subset of Patients with Carcinoid Heart Disease Included in Two Phase 2 Trials for Carcinoid Syndrome

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**Background:** Serotonin is a key mediator of carcinoid syndrome (CS). High levels of urinary 5-hydroxyindoleacetic acid (u5-HIAA, a serotonin metabolite) have also been linked with carcinoid heart disease (CaHD). Telotristat etiprate, a novel, oral inhibitor of serotonin synthesis, is in Phase 3 development for the treatment of CS. There is limited information on the potential benefits of serotonin reduction in patients with CaHD.

**Methods:** We retrospectively reviewed data on all patients who received telotristat etiprate in Phase 2 trials for CS. In patients with prior history of CaHD, we assessed baseline characteristics, reductions in u5-HIAA, adverse events, and procedures while on telotristat etiprate.

**Results:** Of the 38 enrolled patients, 5 patients (13%) had a history of CaHD and were evaluable. All had elevated baseline u5-HIAA levels (mean 144 mg/24 hours, range: 10-282), despite use of somatostatin analogs (SSAs) (5/5 patients) and prior tumor-directed therapies (4/5 patients). In all patients, levels of u5-HIAA decreased over time (mean maximum reduction 82%, range: 78–86%). As of Oct 2013, mean duration of telotristat etiprate exposure was 71 weeks (range: 12-164 weeks); 2 patients remain in the study, with >128 weeks exposure at the highest dose of telotristat etiprate (500 mg tid), including 1 patient who received a pulmonary valve replacement ~2 years ago. There were 4 serious adverse events (including 2 heart valve surgeries), none of which were considered drug-related.

**Conclusions:** In 5 patients with CaHD, u5-HIAA levels decreased substantially while on telotristat etiprate. Additional studies are warranted.