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Effect of Telotristat Ethyl on Growth of Small Bowel Neuroendocrine Hepatic Metastases

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BACKGROUND: The novel agent telotristat ethyl (telotristat), an inhibitor of tryptophan hydroxylase (the rate limiting enzyme of serotonin synthesis) is indicated for patients with metastatic small bowel neuroendocrine tumors (NETs) who have intractable carcinoid syndrome despite somatostatin analog (SSA) therapy. It is unknown whether telotristat affects tumor growth. This single-center study analyzed the difference in hepatic metastatic growth rates before and after telotristat therapy was initiated.

METHODS: This IRB-approved retrospective cohort review studied all consecutive patients prescribed telotristat (n=35) since 2015. Index hepatic metastases were measured on all cross-sectional imaging studies performed within 12 months of telotristat initiation. Largest orthogonal dimensions were measured to calculate axial cross-sectional areas. For available computed tomography CT studies, the arterial phase was utilized for measurements. Whereas, for MRI studies, the sequence with clearest margins was utilized. Pre- and post-telotristat slopes of the best-fit lines were calculated in all patients with at least 2 pre- and 2 post-telotristat studies. For each patient, the pre- and post-telotristat slopes were compared utilizing the Wilcoxon sign ranked test, with statistical significance set to 0.05.

RESULTS: Nine patients with metastatic small bowel NETs were included. All were also receiving SSA therapy (octreotide or lanreotide) prior to initiation of telotristat. On average, hepatic metastases were 130% of baseline index cross-sectional area at the time of telotristat initiation and 121% of index cross-sectional area by the latest available time point after telotristat initiation.

Comparing the pre- and post-telotristat area slopes (Table 1), a Wilcoxon W of 21 was calculated ($p>0.20$).

CONCLUSION: Preliminary results show that the distributions of slopes, pre- and post-telotristat initiation, are not statistically different. Notably, the study is not adequately powered for a small effect size. Whether tryptophan hydroxylase inhibition leads to downstream effects on regulatory mechanisms involved in tumor growth, is unknown.

Table 1:

Slopes of index metastatic growth rates before and after telotristat therapy initiation.

Patient	Pre-telotristat	Post-telotristat
1	0.004	-0.011
2	0.087	0.009
3	0.001	-0.001
4	0.092	0.082
5	-0.043	-0.014
6	-0.009	-0.027
7	0.224	-0.235
8	0.006	0.024
9	-0.004	-0.010