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Phase 2 Dose Optimization Trial of Everolimus post Bland Hepatic Artery Embolization (Evero-Embo) in patients with Neuroendocrine Tumors.

Tsering Dolkar, Gaby E Gabriel, Donglin Yan, Jerod Stapleton, Joseph R McCorkle, Lowell B Anthony.

University of Kentucky Markey Cancer Center, Lexington, KY.

BACKGROUND

NETs are the second most common GI malignancy in the U.S., with an estimated prevalence of >170,000. Hepatic metastases are common with the 5-year overall survival < 25%. Treatment options include surgical resection and liver-directed therapies including hepatic artery embolization (HAE). Everolimus is approved for treating progressive NETs. The concurrent use of everolimus with HAE was previously reported NANETS 2021, C-41 [Gupta et al]. An analysis of 96 evero-embos was performed in 51 patients, 30/51 patients had 24 or more months of follow-up post-procedure. The median hPFS was 3.43 years with 95% confidence interval (2.85, 4.31 years). This compares to the literature median hPFS of 1.25 years for the HAE alone group in 155 patients reported [Chen et al].

METHODS

The primary objective is to determine whether the post-HAE optimal everolimus dose is 50% of the pre-HAE dose. This phase 2 open-label trial will include 9-12 well-differentiated, low-to intermediate grade liver dominant NET patients who can tolerate an everolimus dose of at least 5 mg daily for a minimum of 5 days (to ensure steady-state levels) prior to bland HAE. Pre-HAE everolimus blood levels will be obtained prior to the procedure. Everolimus will resume at 48 hours post-procedure at 50% of the pre-procedure dose and continue for 30 days. Everolimus blood levels will be repeated between D7-D14. Subjects who cannot tolerate 50% everolimus dose reduction will be replaced. A QOL hepatobiliary cancers (FACT-Hep) survey will be done during pre-procedure and each clinic visit.

RESULTS

Pre- and post-procedure everolimus blood concentrations will be compared using a pairwise t-test. The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 will be utilized for AE reporting.

CONCLUSIONS

The expected outcome is that patients will be able to tolerate half the pre-procedural everolimus dose for at least 30 days based on institutional experience. The optimal post-bland HAE everolimus dosing is expected to be at least 5 mg every other day. Once the post-HAE everolimus dosing has been identified, a Phase III clinical trial comparing the evero-embo optimized dosing regimen to the superior treatment arm (bland vs TACE) identified in the RETNET clinical trial [Soulen et al] is feasible.

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