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An Open-Label, Phase II Investigation of Trifluridine/Tipiracil in Patients With High-Grade, Extrapulmonary Neuroendocrine Carcinoma

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BACKGROUND: High-grade neuroendocrine carcinomas (NECs) of gastroenteropancreatic origin are rare but are associated with rapid disease progression, widespread metastatic disease, and poor overall survival. Treatment with platinum and etoposide is the generally accepted first-line therapy for advanced disease, but there is a paucity of data regarding management for relapsed or refractory disease. FTD/TPI, an oral combination of trifluridine and tipiracil, is currently approved for the treatment of metastatic colorectal cancer and metastatic gastric cancer in late-line settings. Based on remarkable activity of single agent FTD/TPI in a phase I study, an exploratory phase II trial was designed to further evaluate this therapy in a disease with historically dismal outcomes and minimal prospective data.

METHODS: This was an open-label study of high-grade, extrapulmonary neuroendocrine carcinoma patients who had failed first-line treatment with a platinum-containing regimen. A sample size of 14 patients was targeted with a primary endpoint of objective response rate (ORR). All patients received FTD/TPI in a 28-day treatment cycle at a dose of 35 mg/m2/dose twice daily on days 1-5 and days 8-12. Radiologic assessments were performed every 8 weeks. If no responses were noted within the first 7 patients, the study would be discontinued for inactivity.

RESULTS: A total of 7 patients were enrolled in the study. 1 patient withdrew and was considered not-evaluable. Of the remaining patients, no objective responses

were observed. Median TTP was 3.2 months, and median OS was 6.2 months. One patient experienced prolonged stable disease of 11.3 months, however, 3 of 6 patients experienced immediate disease progression at the first radiographic evaluation.

CONCLUSION: While one patient did experience prolonged stable disease, the study was halted due to pre-specified metrics of inactivity. FTD/TPI was not found to be effective in the second-line setting for high-grade, extrapulmonary neuroendocrine carcinoma.

ABSTRACT ID: 103