

Cisplatin and Etoposide or Temozolomide and Capecitabine in Treating Patients With Neuroendocrine Carcinoma of the Gastrointestinal Tract or Pancreas That Is Metastatic or Cannot Be Removed by Surgery

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Background: Poorly differentiated (G3) GEPNECs are rare tumors for which little prospective data are available. Historically these tumors have been treated akin to small cell lung cancer with platinum and etoposide based on histologic similarities. Emerging pathologic and clinical data suggest heterogeneity amongst G3 GEPNECs based on histology (small cell vs. non-small cell), Ki-67, response to therapy (platinum based vs. temozolomide based) and survival. Temozolomide based therapy appears the most promising alternative option. The proposed study will provide the first prospective data regarding the role of cisplatin and etoposide vs. temozolomide and capecitabine for G3 GEPNECs and their correlation with clinical parameters.

Methods: This is a multi-center, randomized phase II trial. Pts with locally advanced/unresectable or metastatic G3 GEPNEC are randomized to receive capecitabine 750 mg/m² PO every 12 hours days 1-14 and temozolomide 200 mg/m² PO daily days 10-14 (Arm A) or cisplatin 25 mg/m² IV daily days 1-3 and etoposide 100 mg/m² IV daily days 1-3 (Arm B). Cycle length: 28 days (Arm A), 21 days (Arm B). Eligibility criteria include G3 non-small cell histology, Ki-67 proliferative index 20-100%, ≥ 10 mitotic figures per 10 high powered fields, measurable disease, no prior chemotherapy. Primary endpoint is progression free survival (PFS); secondary endpoints include response rate (RR), overall survival (OS) and toxicity. Tissue specimens will be collected for central pathology review with assessment of Ki-67 and its correlation with PFS, OS and response. CT, PET and octreoscan images will be banked. A total of 126 pts will be needed to accrue 120 eligible cases to detect an improvement in PFS from 6 months in the control arm (Arm B) to 10 months in the experimental arm (Arm A) with 90% power and a one-sided significance level of 0.10 using a log-rank test. Planned accrual is 4 pts per month over 30 months with an additional 12 months of follow-up. The trial was activated in November 2015. Clinical trial information: NCT02595424.