For Patients with Advanced Gastroenteropancreatic Neuroendocrine Tumors

EA2142 Available Through ECOG-ACRIN Cancer Research Group
Randomized Phase II Study of Platinum and Etoposide versus Temozolomide and Capecitabine in Patients with Advanced G3 Non-Small Cell Gastroenteropancreatic Neuroendocrine Tumors including Poorly Differentiated Neuroendocrine Carcinomas and Well-Differentiated Neuroendocrine Neoplasms

Patient Population
See Section 3.0 for Complete Eligibility Details

- Age ≥ 18 years, ECOG PS 0-2 and adequate lab values
- Must have a locally advanced and unresectable or metastatic gastroenteropancreatic neuroendocrine carcinoma that is either known or suspected to be of GI origin; primary tumors arising from the lung, gynecologic organs, or prostate are not permitted
- Must have pathologically/histologically confirmed tumor of non-small cell histology
- Must have a Ki-67 proliferative index of 20-100% OR at least 10 mitotic figures per 10 high powered fields
- Must have measurable disease (RECIST 1.1) defined per protocol; obtained by multiphasic CT/contrast MRI
- May not have had any prior systemic therapy (chemo, targeted, PRRT) for this malignancy; may not have received any of the protocol agents within 5 years of randomization
- May not be receiving Coumadin while on treatment
- Must have a life expectancy of ≥ 12 weeks
- No brain metastases (either remote or current) or presence of carcinomatous meningitis
- No known DPD deficiency
- No active/uncontrolled infection, symptomatic heart failure, unstable angina pectoris, cardiac arrhythmia, or serious psychiatric illness/social situation that would limit compliance with study requirements
- No history of allergic reactions attributed to compounds of similar chemical/biochemical composition to cisplatin, carboplatin, etoposide, temozolomide, or capecitabine
- No absorption issues that would limit the ability to absorb study agents; must be able to swallow pills
- No arterial thromboembolic event, unstable angina, or myocardial infarction within 12 months of study entry
- No symptomatic peripheral vascular disease

Treatment Plan
See Section 5.0 for Complete Treatment Details

Arm A– Capecitabine and Temozolomide:
- Cycle = 28 days (+/- 2 days)
- Capecitabine 750 mg/m² by mouth every 12 hours (+/- 2 hours) on days 1-14
- Temozolomide 200 mg/m² by mouth once daily on days 10-14
- Premedication is required (see protocol)
- Patients are required to return their completed Patient Pill Calendar at each clinic visit

Arm B– Cisplatin (or Carboplatin) and Etoposide:
- Cycle = 21 days (+/- 2 days)
- Cisplatin 25 mg/m² daily days 1-3 to be administered per institutional guidelines OR
- Carboplatin target AUC of 5 once on day 1 to be administered per institutional guidelines AND
- Etoposide 100 mg/m² daily days 1-3 to be administered per institutional guidelines

Continue treatment until patient develops disease progression or unacceptable toxicity

Notes:
- Doses are based on actual body weight; the Calvert formula will be used for carboplatin dosing (cap at 150mg/AUC)
- CBC and platelet count will be monitored per protocol
- Premedication is required per protocol (see details re: aprepitant)
- Choice of platinum is per treating physician (no changes once picked)

Patient Enrollment
All Sites: Oncology Patient Enrollment Network (OPEN), https://open.ctsu.org

Protocol Information

Please Enroll Your Eligible Patients!
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Schema

**Arm A**
- Capecitabine 750 mg/m² po every 12 hours (+/- 2 hours) days 1-14
- Temozolomide 200 mg/m² po daily days 10-14

**Arm B**
- Cisplatin 25 mg/m² IV daily days 1-3
- Etoposide 100 mg/m² IV daily days 1-3
  OR
- Carboplatin target AUC of 5 on day 1³
- Etoposide 100 mg/m² IV daily days 1-3

Stratify
- ECOG PS 0-1 vs. ECOG PS 2
- GI vs. pancreatic NETS

Annual: 80
Cycle: Arm A: 28 days
Arm B: 21 days

All doses are based on actual body weight.
Images and radiology report submissions are required. See Section 4.4.5 for submission instructions and Section 10 for outline.

1. Treatment will continue until progression or unacceptable toxicity.
2. Capecitabine dose in mg/m² is PER DOSE and this dose should be taken every 12 hours.
3. Please refer to Section 5.1.2 for specific dose for Carboplatin.