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

Study Schema

Accrual goal = 80 patients.
Cycle = 28 days (arm A); 21 days (arm B).
Doses based on actual body weight.
All patients must submit imaging and radiology reports.
CBC will be monitored prior to drug administration.
Follow for survival up to 5 years. See Protocol Section 4.4.5 for submission instructions and Section 10 for outline.
*Treatment will continue until progression or unacceptable toxicity.
†Capecitabine dose in mg/m² is per dose; this dose should be taken every 12 hours.
‡Premedication required: ondansetron or approved 5-HT3 antagonist should be used as a premedication 30 to 60 minutes prior to temozolomide.
§Premedication with ondansetron (or other 5-HT3 antagonist) and dexamethasone prior to each chemotherapy administration (days 1–3) is required.
||Calvert formula is used for carboplatin dosing (refer to Protocol Section 5.1.2).
5-HT3 = 5-hydroxytryptamine type 3 (serotonin); GI = gastrointestinal; NETs = neuroendocrine tumors.
Overall EA2142 Study Objective

To examine whether the combination of temozolomide and capecitabine is more efficacious than the standard therapy (platinum and etoposide) in patients with advanced G3 gastroenteropancreatic neuroendocrine carcinomas of the non–small cell subtype

Study Objectives

Primary Objective

- Assess the progression-free survival (PFS) of platinum (cisplatin or carboplatin) and etoposide versus temozolomide and capecitabine in patients with advanced G3 non–small cell gastroenteropancreatic neuroendocrine carcinomas

Secondary Objectives

- Assess response rate (RR)
- Assess overall survival (OS)
- Evaluate toxicity

Laboratory Research Objectives

- Assess the impact of each treatment regimen on PFS, RR, and OS based on Ki-67 index
- Assess the prognostic significance of well- versus poorly differentiated non–small cell gastroenteropancreatic neuroendocrine tumors in relationship to survival and treatment response
- Assess the agreement in Ki-67 status reported by institutional pathologist and central pathology review

Eligibility Criteria*

Main Inclusion Criteria

- 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
- Life expectancy of ≥ 12 weeks
• Pathologically or histologically confirmed tumor of non–small cell histology
• Ki-67 proliferative index of 20% to 100% or at least 10 mitotic figures per 10 high-powered fields
• Measurable disease by RECIST 1.1; baseline measurements and evaluations of all disease sites must be obtained within 4 weeks prior to randomization and acquired by multiphasic CT or contrast MRI
• ≥ 18 years of age
• ECOG performance status 0-2
• Ability to swallow pills
• Ability to tolerate CT or MR imaging, including contrast agents
• Adequate hematologic, hepatic, and renal function within 14 days prior to randomization
• Use of effective contraception

*When evaluating patients for this study, please refer to the full protocol for the complete list of eligibility criteria.

Main Exclusion Criteria

• Prior systemic therapy for this malignancy (eg, chemotherapy, targeted therapy, PRRT). Prior palliative radiation is permitted, but irradiated lesions may not be used for measurement. Prior somatostatin therapy is permitted
• Received any of the protocol agents within 5 years prior to randomization
• Surgeries completed less than 4 weeks prior to randomization
• Receiving any other investigational agents or coumadin while on study treatment; other anticoagulants are allowed
• Brain metastases (remote or current) or presence of carcinomatous meningitis
• Known dihydropyrimidine dehydrogenase (DPD) deficiency, symptomatic peripheral vascular disease, active or uncontrolled infection, symptomatic heart failure, unstable angina pectoris, cardiac arrhythmia, or serious psychiatric illness/social situation that would limit compliance with study requirements
Main Exclusion Criteria (cont)

- History of allergic reactions attributed to compounds of similar chemical or biochemical composition to cisplatin, carboplatin, etoposide, temozolomide, or capecitabine
- Absorption issues that would limit the ability to absorb study agents
- History of arterial thromboembolic events, unstable angina, or myocardial infarction within ≤ 12 months of study entry
- Previous or concurrent malignancy. Exceptions: nonmelanoma skin cancer, in situ cervical cancer, superficial bladder cancer, or breast cancer in situ or prior malignancy completely excised or removed and patient continuously disease free for > 5 years or prior malignancy cured by nonsurgical modalities and patient continuously disease free for > 5 years
- HIV positivity or on combination antiretroviral therapy
- Pregnancy or breast-feeding