Cancer Research Consortium of West Michigan
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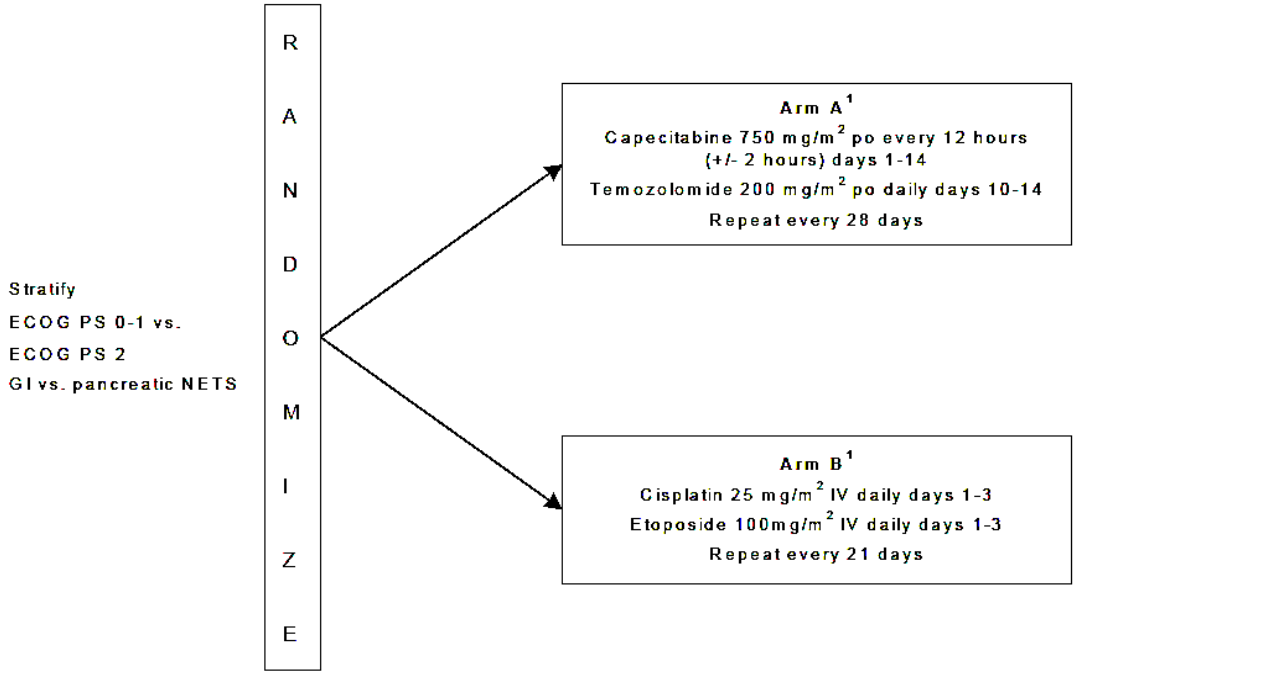
FAST FACTS

EA2142: Randomized Phase II Study of Platinum therapy and Etoposide versus Temozolomide and Capecitabine in Patients with Advanced G3 Non-Small Cell Gastroenteropancreatic Neuroendocrine Carcinomas

Schema



Accrual: 126
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/m^2 is PER DOSE and this dose should be taken every 12 hours.

Eligibility Criteria

1. Patients 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.
2. Patients must have pathologically/histologically confirmed tumor of non-small cell histology.
3. Patients must have a Ki-67 proliferative index of 20-100% OR at least 10 mitotic figures per 10 high powered fields.
4. Patients must have measurable disease by RECIST 1.1 criteria as defined in Section 6.1.2. Baseline measurements and evaluations of all sites of disease must be obtained within 4 weeks prior to randomization and must be acquired by multiphasic CT or contrast MRI. **NOTE:** PET-CT scans are allowed provided the CT portion of the exam is equivalent to a diagnostic CT scan and includes both oral and IV contrast.

5. Patients may not have had any prior systemic treatment for this malignancy (for example chemotherapy or somatostatin analogues). Prior palliative radiation is permitted but radiated lesions may not be used for measurement.
6. Patients may not have received any of the protocol agents within 5 years prior to randomization.
7. Any prior surgeries must have been completed at least 4 weeks prior to randomization.
8. Patients must be at least ≥ 18 years of age.
9. Patients must have an ECOG performance status of 0-2.
10. Patients may not be receiving any other investigational agents while on study treatment.
11. Patients may not be receiving Coumadin while on treatment. Other anticoagulants are allowed.
12. Patients must have normal organ and marrow function as definded below within less than or equal to 14 days prior to randomization:
    - Leukocytes ≥ 3,000/mm3
    - Absolute neutrophil count ≥ 1,500/mm3
    - Hemoglobin ≥ 9 g/dL
    - Platelets ≥ 100,000/mm3
    - Total bilirubin ≤ institutional upper limit of normal (ULN) or ≤ 1.5 X institutional ULN (if the patient has liver metastases).
    - AST (SGOT)/ALT (SGPT) ≤ 2.5 X institutional ULN or (≤ 5 X institutional ULN if the patient has liver metastases).
    - Serum creatinine ≤ 1.5 X institutional ULN and creatinine clearance ≥ 60 ml/min.
      NOTE: Creatinine Clearance must be calculated using the Cockcroft-Gault equation.
13. Patients must have a life expectancy of ≥ 12 weeks as determined clinically by the treating physician.
14. Patients with brain metastases (either remote or current) or presence of carcinomatous meningitis are not eligible
15. Patients with known DPD deficiency will be excluded as the use of capecitabine is contraindicated in these patients.
16. Patients must NOT have active or uncontrolled infection, symptomatic heart failure, unstable angina pectoris, cardiac arrhythmia or a serious psychiatric illness/social situation that would limit compliance with study requirements.
17. Patients with impaired decision making capacity may participate in the study if a legal authorized representative is available to consent.
18. Patients must NOT have a history of allergic reactions attributed to compounds of similar chemical or biochemical composition to cisplatin, carboplatin, etoposide, temozolomide or capecitabine.
19. Patients must NOT have absorption issues that would limit the ability to absorb study agents.
20. Patients with a history of the following within ≤ 12 months of study entry are not eligible:
    - Arterial thromboembolic events
    - Unstable angina
    - Myocardial Infarction
21. Patients with symptomatic peripheral vascular disease are not eligible.
22. Patients must NOT have previous or concurrent malignancy. Exceptions are made for patients who meet any of the following conditions:

- Non-melanoma skin cancer, in situ cervical cancer, superficial bladder cancer, or breast cancer in situ. OR
- Prior malignancy completely excised or removed and patient has been continuously disease free for > 5 years. OR
- Prior malignancy cured by non-surgical modalities and patient has been continuously disease free for > 5 years.

23. Women must not be pregnant or breast-feeding due to potential harm to the fetus from cisplatin, carboplatin, etoposide, temozolomide and/or capecitabine.
    All females of childbearing potential must have a blood test or urine study within 2 weeks prior to randomization to rule out pregnancy.
    A female of childbearing potential is any woman, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).
24. Women of childbearing potential and sexually active males must be strongly advised to use an accepted and effective method of contraception or to abstain from sexual intercourse for the duration of their participation in the study.
25. Patients must be able to swallow pills.
26. Patients must be able to tolerate CT or MR imaging including contrast agents as required for the treatment and the protocol.
27. Patients who are known to have HIV or are on combination antiretroviral therapy are ineligible because of the potential for pharmacokinetic interactions with cisplatin, carboplatin, etoposide, temozolomide, and/or capecitabine. In addition, these patients are at increased risk of lethal infections when treated with marrow-suppressive therapy. Appropriate studies will be undertaken in patients receiving combination antiretroviral therapy when indicated.

Pre-Study Parameters

- History/Physical exam, vitals, height, weight, PS
- Tumor measurements
- AE Assessments
- CBC/diff/platelets
- CMP, liver functions tests
- PT, INR, aPTT
- Pregnancy test
- Radiographic studies
- Image submissions, specimen submissions
- Mandatory pre-trial FFPE tumor
- Peripheral blood, ACD vacutainer