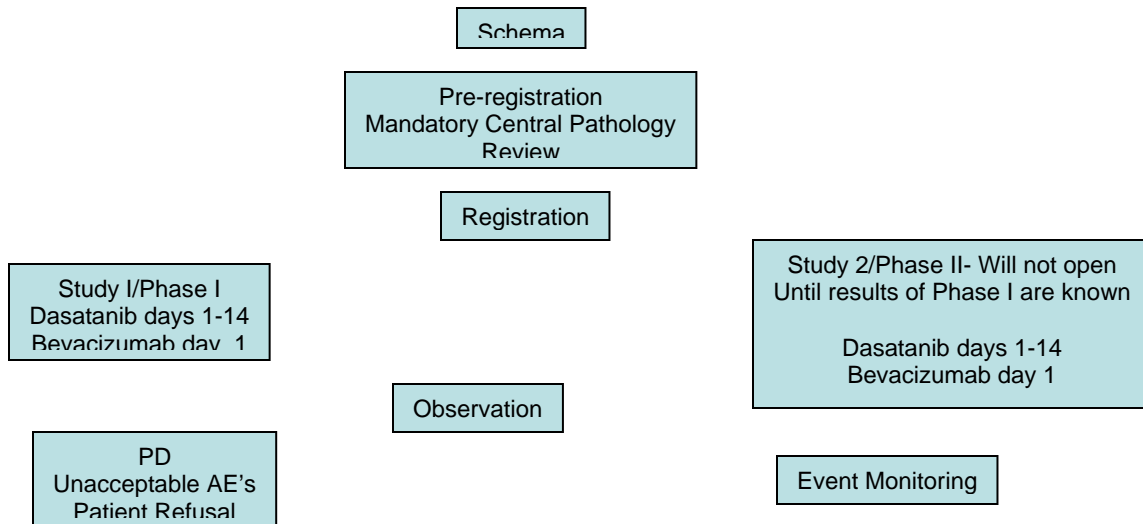


N0872-Phase I/II Study of Dasatinib/Bevacizumab in Recurrent Glioblastoma



This is a Phase I/II study looking at the combination of dasatinib and bevacizumab for the treatment of recurrent glioblastoma. The Phase I will look at the MTD for both drugs in combination and then will proceed to a Phase II with the MTD. Additionally the Phase II will look at the use of DCE-MRI for evaluation of treatment response (limited patients.)

Major Inclusion Criteria

- Study 1- Histologic confirmation of grade 3 or 4 glioma including astrocytoma, oligodendroglioma, and mixed gliomas by central review.
- Study II Histological confirmation of GBM (grade 4 astrocytoma) by central pathology review.
- Evidence of tumor progression by MRI or CT following RT or the most recent anti-tumor therapy ¹.
- Bidimensionally measurable of evaluable disease by MRI or CT scan.
- ECOG PS of 0, 1, or 2.
- Patient willing to discontinue use of aspirin or medications that inhibit platelet function ≥ 1 week prior to registration.
- Previous RT and ≥ 12 weeks since the completion of RT prior to registration.
- The following lab values obtained ≤ 21 days prior to registration (ANC ≥ 1500 ; PLT $\geq 100,000$; Hgb > 9.0 g/dL; T. bili ≤ 1.5 xULN; SGOT ≤ 3 xULN; Creatinine \leq ULN).
- UPC ratio < 1 ¹.
- Ability to complete questionnaire by themselves or with assistance.
- Willingness to return to NCCTG enrolling institution for follow up.
- Willing to provide mandatory tissue samples for research purposes.
- Study 1-Any number of prior chemotherapy regimens for recurrent disease.
- Study 2-Up to 2 prior chemotherapy regimens ≤ 1 regimen for recurrent disease.

Major Exclusion Criteria

- No pregnant or nursing women.
- Prior intratumoral therapy, SRS, or interstitial brachytherapy ¹.
- Prior treatment with bevacizumab.
- Inadequately controlled HTN ¹.
- Co-morbid systemic illness or other severe concurrent disease with would make the patient inappropriate for entry into this study.
- Immunocompromised patients (other than that r/t corticosteroid use) ¹.
- Any condition that impairs ability to swallow pills.
- Receiving therapeutic anticoagulation with Warfarin ¹.
- Evidence of bleeding diathesis or coagulopathy.
- Uncontrolled intercurrent illness or psychiatric illness that would limit compliance with study requirements.
- Receiving any other investigational agent as treatment for the primary neoplasm.
- Other active malignancy ≤ 3 years prior to registration ¹.
- History of MI or unstable angina ≤ 6 months prior to registration.
- NYHA Classification \geq class II.
- Major surgical procedure, open biopsy, or significant trauma ≤ 28 days prior to registration or anticipated need for surgical procedure during the course of the study.
- Core biopsy or other minor surgical procedure ≤ 7 days prior to registration.
- Significant vascular disease or recent peripheral arterial thrombosis ≤ 6 months prior to registration.
- History of hypertensive crisis or hypertensive encephalopathy.
- Known hypersensitivity to any of the components of dasatinib or bevacizumab.

- Serious, nonhealing wounds, ulcers, or bone fractures.
- History of abdominal fistula, GI perforation, or intra-abdominal abscess \leq 6 months prior to registration.
- Active or recent history of hemoptysis \leq 30 day prior to registration.
- History of stroke or TIA \leq 6 months prior to registration.
- Any evidence of CNS hemorrhage on baseline CT or MRI.
- Any Category I drugs that are generally accepted to have a risk of causing Torsades de Pointes \leq 7 days prior to registration ¹.
- Diagnosed congenital long QT syndrome or prolonged QTc interval on pre-entry ECG
- Any history of clinically significant ventricular arrhythmias.
- Patients with hypokalemia or hypomagnesemia not corrected prior to dasatanib start.
- Concomitant use of H2 blockers or PPI that cannot be discontinued.
- Use of EIAC's or other potent CYP3A4 inducer/inhibitors ¹.

¹ See protocol for more details