CCF IRB CC603 Case 1308

Full Title
Phase II Trial of Sunitinib As Maintenance Therapy After Stereotactic Radiosurgery In Patients with 1-3 Newly Diagnosed Brain Metastases

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Objectives
Primary Objective:
To determine the CNS progression-free survival rate in patients with 1 to 3 brain metastases who receive with stereotactic radiosurgery followed by sunitinib.
Secondary Objectives:
1. To determine the rate of local (site of SRS treatment) failure at 12 months
2. To determine the median time to central nervous system (CNS) disease progression
3. To determine the overall survival
4. To determine the time to progression of systemic disease
5. To evaluate the safety of sunitinib in patients with 1 to 3 brain metastases after SRS
6. To assess the neurocognitive effects of SRS followed by sunitinib.

Eligibility
Inclusion

1. Histologically or cytologically-confirmed carcinoma with 1-3 newly diagnosed CNS metastases that are amenable to stereotactic radiosurgery.
2. Patients may enroll up to 14 days after the completion of stereotactic radiosurgery provided they can undergo the required neuropsychiatric battery before beginning treatment.
3. Patients must begin treatment within 14 days of stereotactic radiosurgery.
4. Age $\geq$ 18 years
5. Life expectancy greater than six weeks
6. Karnofsky performance status $\geq$ 70 (RTOG RPA class I or II) – See Appendix 4
7. End organ function as determined by the following:

    - Serum aspartate transaminase (AST; serum glutamic oxaloacetic transaminase [SGOT]) and serum alanine transaminase (ALT; serum glutamic pyruvic transaminase [SGPT]) $\leq$ 2.5 x laboratory upper limit of normal (ULN)
    - Total serum bilirubin $\leq$ 1.5 x ULN
    - Absolute neutrophil count (ANC) $\geq$ 1500/μL
    - Platelets $\geq$ 100,000/μL
    - Hemoglobin $\geq$ 9.0 g/dL (transfusion permitted)
    - Serum calcium $\leq$ 12.0 mg/dL
    - Serum creatinine $\leq$ 2.5 mg/dL

8. Patients with stable systemic disease on systemic therapy are permitted to continue this therapy upon study entry. The systemic regimen must be one for which a safety record has been established. A list of these regimens is in Appendix 1. Systemic therapy will be managed by the patient's treating medical oncologist.
9. No prior cranial external beam radiation therapy
10. Stable dose of steroids for $\geq$ 1 week
11. Patients requiring antiepileptic agents must be converted to an agent(s) with minimal or no induction of hepatic enzymes (see list in Appendix 1)
12. No prior sunitinib
13. Sexually active women of child-bearing potential and sexually active men must agree to use adequate contraception (hormonal or barrier method of birth control; abstinence) prior to study treatment and for the duration of study treatment.
14. Patients must have no medical problems unrelated to the malignancy that would pose an undue risk or that would limit full compliance with the study.
15. Signed and dated informed consent document indicating that the patient has been informed of all pertinent aspects of the trial prior to enrollment.
16. Willingness and ability to comply with scheduled visits, treatment plans, laboratory tests, and other study procedures.

Exclusions

1. CNS metastases from lymphoma or small cell lung cancer
2. Leptomeningeal metastases
3. CNS complications requiring urgent neurosurgical intervention (e.g., resection, shunt placement)
4. Unresolved bowel obstruction
5. Concomitant administration of Coumadin® or other agents containing warfarin, with the exception of low dose Coumadin® (1 mg or less daily) administered prophylactically for maintenance of in-dwelling lines or ports
6. Concomitant use of hepatic enzyme-inducing anticonvulsants
7. Uncontrolled infectious process
8. Pregnant or nursing women
9. Evidence of bleeding diathesis or coagulopathy. Patients with hematuria from the primary renal tumor are eligible provided all other eligibility criteria are met.
10. Any of the following within the 6 months prior to study drug administration: myocardial infarction, severe/unstable angina, severe peripheral vascular disease (claudication) or procedure on peripheral vasculature, coronary/peripheral artery bypass graft, New York Heart Association grade II or greater congestive heart failure, cerebrovascular accident or transient ischemic attack, clinically significant bleeding, deep venous thrombosis or pulmonary embolism.
11. Hypertension that cannot be controlled by medications to < 160/90.
12. Other severe acute or chronic medical or psychiatric conditions or laboratory abnormality that may increase the risk associated with study participation or study drug administration, or may interfere with the interpretation of study results, and in the judgment of the investigator would make the patient inappropriate for entry into this study.