CC845 CASE 4309

Full Title
A Phase I/II Trial of SRS Plus Bevacizumab in patients with recurrent/progressive GBM

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Purpose
This is a multicenter, open-label, ascending-dose trial of the safety and tolerability of increasing doses of Toca 511administered to subjects with recurrent GBM who have undergone surgery followed by adjuvant radiation and chemotherapy.

Eligibility
Inclusion:

1. Histologically proven diagnosis of glioblastoma or gliosarcoma (WHO grade IV) at primary or subsequent resection.
2. Completed standard concurrent conventional fractionated radiotherapy plus daily temozolomide (75 mg/m2/day)
3. Radiographic evidence of tumor recurrence/progression
4. Unifocal enhancing disease. The enhancing focus must be <= 3 cm in maximum diameter.
5. The patient must have recovered from the effects of prior therapy before study entry. The patient must not have received chemotherapy within the following time frames:
   - Non-cytotoxic agents: 2 weeks
   - Cytotoxic agents: 3 weeks
   - Nitrosoureas: 6 weeks
7. Documentation of steroid doses within 14 days prior to registration.
8. Karnofsky performance status > 60; Age ≥ 18
9. Laboratory values as defined per the protocol.
10. Electrocardiogram without evidence of acute cardiac ischemia within 14 days prior study entry
11. Prothrombin time/international normalized ratio (PT INR) < 1.4 for patients not on warfarin confirmed by testing within 14 days prior to study entry.
12. Patients on full-dose anticoagulants (e.g., warfarin or LMW heparin) must meet both of the following criteria:
    - No active bleeding or pathological condition that carries a high risk of bleeding (e.g., tumor involving major vessels or known varices)
    - In-range INR (between 2 and 3) on a stable dose of oral anticoagulant or on a stable dose of low molecular weight heparin

Exclusion:

1. Prior invasive malignancy (except for non-melanomatous skin cancer) unless disease free for ≥ 3 years. (For example, carcinoma in situ of the breast, oral cavity, and cervix are all permissible).
2. More than one focus of enhancement
3. Involvement of the brainstem (defined as the midbrain or lower), or proximity to the optic chiasm/optic nerves requiring radiosurgery dose reduction.
4. Prior use of chemotherapy wafers or any other intratumoral or intracavitary treatment are not permitted. Prior radiosurgery is not permitted.
5. Prior treatment with intravenous bevacizumab
6. Severe, active co-morbidity, defined as in detail in the protocol.