

CCF IRB CC949

Full Title

A Phase 1 Ascending Dose Trial of the Safety and Tolerability of Toca 511 in Patients with Recurrent Glioblastoma Multiforme

Principal Investigator

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Objectives

- To identify the highest, safe and well tolerated dose of Toca 511 administered intratumorally via stereotactic, transcranial injection

Eligibility

Inclusion

1. Has the subject given written informed consent?
2. Is the subject at least 18 years old?
3. Does the subject have a single, supratentorial, histologically confirmed GBM (grade IV glioma) measuring between 1.0 cm and 3 cm inclusive in its longest dimension?
4. Has the subject undergone at least one prior surgical gross-total or subtotal tumor resection and a course of postoperative radiation therapy with concurrent temozolomide?
5. Has the subject received at least 2, cycles of maintenance temozolomide?
6. Has the subject elected not to undergo treatment with the Gliadel® wafer?
7. Does the subject have unequivocal evidence of tumor progression as defined by the following:
 - Subject must be at least 12 weeks post RT
 - Baseline post-radiation scan performed at least 2 weeks following RT
 - $\geq 25\%$ increase in bidirectional measurement of the lesion compared to baseline, post-RT scan
8. If the subject is being considered for part 2 of this protocol, does the subject have evaluable disease on Gd-MRI?
9. If receiving corticosteroids, has the subject been on a stable or decreasing dose of steroids for the past 7 days?

10. If age is 18-75, does the subject have a Karnofsky performance status \geq 60; if $>$ 75 year old, does the subject have a Karnofsky performance status \geq 70?
11. Does the subject have an absolute neutrophil count (ANC) \geq 1500/mm³?
12. Does the subject have an absolute lymphocyte count \geq 800/mm³ (normal or grade 1 lymphopenia)?
13. Does the subject have a platelet count \geq 100,000/mm³?
14. Does the subject have a Hgb \geq 10 g/dL?
15. Does the subject have a normal PT/PTT?
16. Does the subject have an estimated glomerular filtration rate of at least 70 mL/min (inclusive) by the Cockcroft-Gault formula?
17. Does the subject have an ALT/AST $<$ 3 times the upper limit of the laboratory reference range and total bilirubin $<$ 1.5 mg/dL?
18. Does the subject have a life expectancy of at least 3 months?
19. If the subject is a female of childbearing potential, has she had a negative serum pregnancy test within the past 21 days?
20. If the subject is a fertile female, is she willing to use effective contraception while participating in this study? If the subject is a male, is he willing to use condoms for contraception while participating in this study?

1. Is the subject willing and able to abide by the protocol?

Exclusions

1. Has the subject received cytotoxic chemotherapy within the past 4 weeks (6 weeks for nitrosoureas)?
2. Does the subject have PCR evidence of infection with XMRV?
3. Does the subject have a Gliadel® wafer or wafers implanted within the past 8 weeks?
4. Is the subject taking more than 8 mg of dexamethasone per day?
5. Does the subject's tumor communicate with the ventricular system?
6. Does the subject have evidence of increased intracranial pressure or clinical deterioration that would require acute intervention prior to the projected start of flucytosine at the beginning of Week 4?
7. Does the subject have, or has the subject had, within the past 4 weeks any infection requiring antibiotic, antifungal or antiviral therapy?
8. Does the subject have any bleeding diathesis, or must the subject take any anticoagulants, or antiplatelet agents, including NSAIDs that cannot be stopped for surgery?
9. Does the subject have poorly controlled seizures?
10. Does the subject have a history of allergy or intolerance to flucytosine?
11. Is the subject HIV positive?
12. Does the subject have any gastrointestinal disease that would prevent him or her from being able to ingest or absorb flucytosine?

13. Has the subject received any investigational treatment within the past 30 days?

14. Is the subject breast feeding?

Has the subject received Avastin® (bevacizumab) within 6 weeks of the projected Day 1 (injection)?