A Phase II Study of Checkpoint Blockade Immunotherapy in Patients with Somatically Hypermutated Recurrent WHO Grade 4 Glioma

Pre-Registration Eligibility Criteria (see Section 3.0)

- Histologically confirmed glioblastoma (WHO grade IV) presenting at first or second recurrence including secondary glioblastoma.
  - Glioblastoma IDH-wildtype CNS WHO grade 4.
  - Astrocytoma, IDH-mutant CNS WHO grade 4.
- Presence of measurable disease, as defined by a bidimensionally measurable lesion on MRI with a minimum diameter of 10 mm in both dimensions, prior to resection or biopsy of recurrent tumor.
- Tissue available from surgical resection or biopsy of recurrent tumor ≤28 days prior to pre-registration or planned surgery or biopsy of recurrent tumor ≤28 days after pre-registration.

Required Laboratory Values

- Absolute Neutrophil Count ≥ 1500/mm3
- Platelet count ≥ 100,000/mm3
- Total bilirubin ≤ 1.5 x ULN
- Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 2.0 x ULN
- Creatinine ≤ 1.5x ULN or creatinine clearance (CrCl) ≥ 50 mL/min

- Does not require > 4 mg dexamethasone daily beyond the perioperative period defined as the time ≤ 2 weeks after surgical procedure.
- No active autoimmune disease or history of autoimmune disease.
- No prior treatment with checkpoint blockade therapies (anti-CTLA4, anti-PD1/PD-L1) or bevacizumab.
- No prior treatment with laser ablation at the time of recurrent tumor tissue sampling. Patients who have previously undergone laser ablation ≥ 4 months prior to recurrent tumor tissue sampling can be included.
- At least 18 years of age
- ECOG Performance Status ≤ 2
- Adequate marrow and organ function
- Able to undergo brain MRI with contrast

Registration Eligibility Criteria (see Section 3.0)

- Tissue obtained from biopsy or resection at first or second recurrence exhibits TMB ≥ 10 on FoundationOne CDx testing
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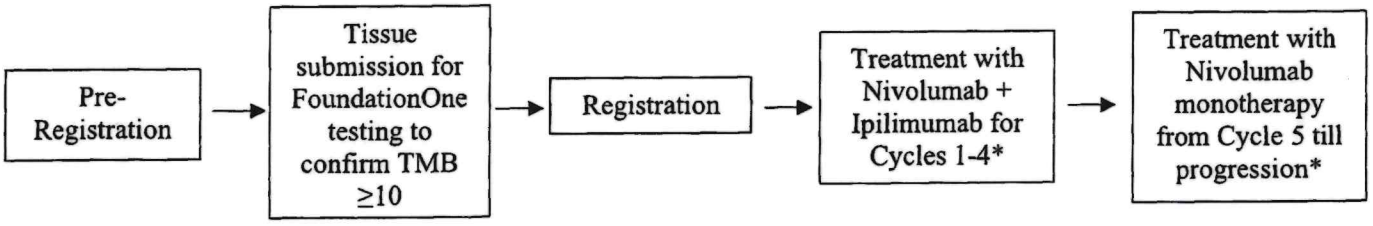
Schema



* During Cycles 1-4, one cycle is defined as 3 weeks. Beginning at Cycle 5, one cycle is defined as 4 weeks.

Treatment is to continue until disease progression, unacceptable toxicity, or withdrawal of consent. Patients will be followed for survival and progression every 3 weeks during Cycle 1-4 and every 4 weeks after Cycle 5 until progression, and then for survival every 3 months until 3 years after registration or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.