TPS2085: Efficacy and Safety Study of Neoadjuvant Efineptakin alfa (NT-I7) and Pembrolizumab in Recurrent Glioblastoma

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ABSTRACT

- Glioblastoma (GBM) is the most common and aggressive form of brain tumor in adults and has a dismal prognosis.
- Poor outcomes for GBM may be due in part to an immune-suppressive microenvironment with a low number of tumor-infiltrating lymphocytes (TIL).
- Lymphopenic GBM patients have shorter survival.
- Interleukin 7 (IL-7) plays a key role in T cell homeostasis and survival. The physiological level of IL-7 increases to stimulate T cell expansion in lymphopenic condition.
- Efineptakin alfa (NT-I7), a long-acting IL-7, has been shown to increase central and effector memory cells and reduce suppressor T-regulatory cells in murine GBM models, with subsequently improved OS.
- Combination therapy with NT-I7 and pembrolizumab, an anti-PD-1 antibody, improves survival in murine glioma models.
- We recently completed a Phase I dose escalation study which showed that NT-I7 monotherapy up to 720 mcg/kg is safe, well-tolerated, and increased absolute lymphocyte counts (ALC) in newly diagnosed GBM patients.
- We hypothesize that by giving combination therapy with NT-I7 and pembrolizumab, we can break tumor-mediated lymphodepletion by increasing TILs and thereby enhancing the effect of checkpoint inhibitor blockade in recurrent GBM patients.

HYPOTHESIS

- The combination of NT-I7 and pembrolizumab for patients with recurrent glioblastoma is more efficacious than approved therapies.

STUDY OBJECTIVES

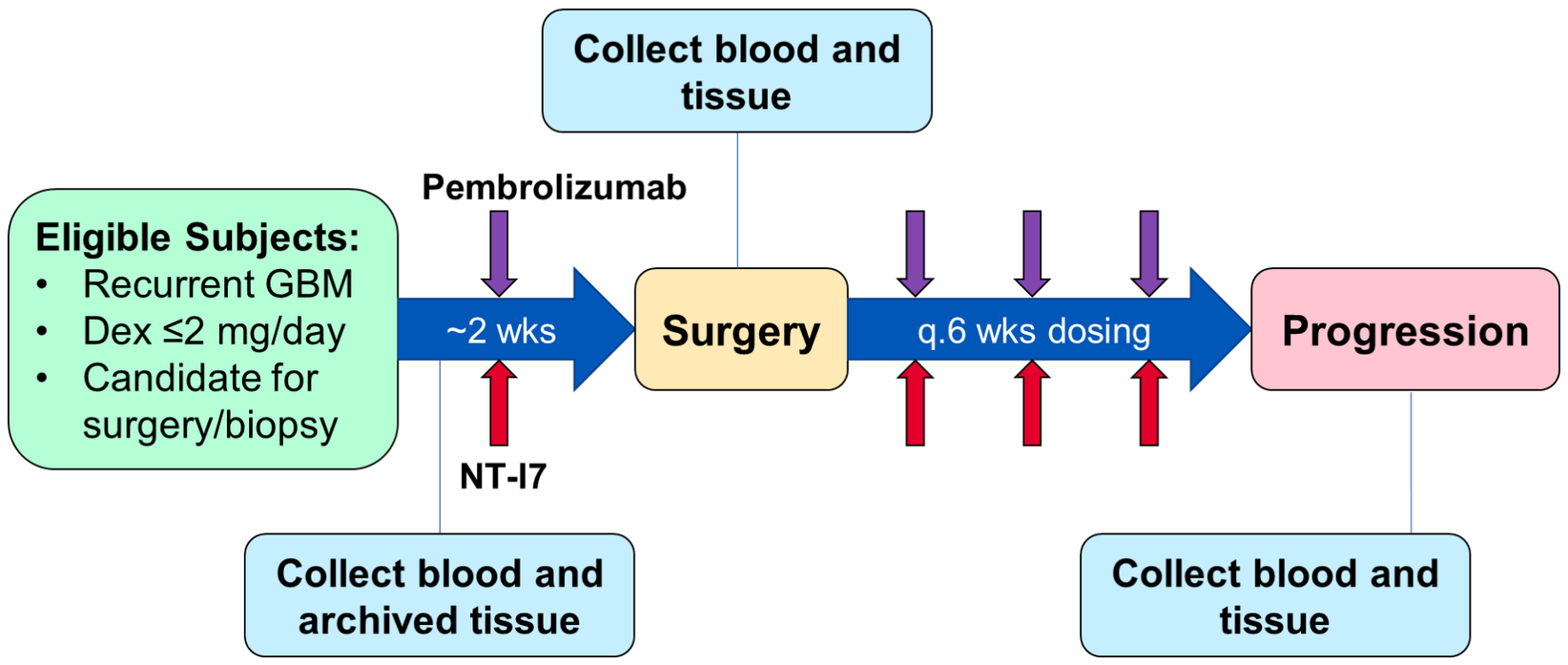
Primary Objective

- Overall survival at 9 months time

Secondary Objectives

- Progression free survival
- Objective response rate
- Change in ALC

Schema



Agent	Dose Level	Route	Day	Repeat Dosing
Pembrolizumab	400 mg	IV	Day 1 of each cycle	q.6 weeks
NT-I7	720 mcg/kg	IM	Day 1 of each cycle	q.6 weeks

ELIGIBILITY

Inclusion:

- Age ≥ 18 years
- ECOG Performance Status of 0 or 1 and KPS ≥ 70
- Progressive or recurrent WHO Grade IV IDH wildtype glioblastoma (including molecular glioblastoma and gliosarcoma)
- Previously treated with maximum feasible resection or biopsy, radiation, and temozolomide
- Have an enhancing mass on MRI amenable to resection or biopsy
- Adequate organ and marrow function

Exclusion:

- Prior treatment with bevacizumab ≤ 28 days prior to registration
- Any prior anti-PD-1, PD-L1, or PD-L2 agent.
- Dexamethasone dose of > 2mg/day ≤ 2 days prior to registration.
- Failure to recover from any adverse events prior to registration.
- Active autoimmune disease requiring systemic treatment ≤ 2 years prior to registration.
- Pregnancy and/or breastfeeding

STATISTICAL DESIGN

- This is an open-label single arm one-stage Phase II study with a safety run-in cohort, evaluated by the 9-month overall survival rate.
- A safety run-in will be performed for the initial 6 patients.
- Primary endpoint is OS-9, with historical control (Taal, et Al., 2014) OS-9 of 40.0% for unmethylated GBM patients who received lomustine after a first recurrence post RT/TMZ.
- OS-9 will be estimated with 87.4% power at 1-sided alpha of 0.048 to detect a 25% improvement in the OS-9 (65% vs. 40%).
- Sample size: 30 evaluable patients

CORRELATIVE STUDIES

- Immunophenotyping of peripheral T cells and cytokine analysis
- Immunohistochemical analysis of GBM tissue
- Cerebrospinal fluid analysis (if available)

ACCRUAL

- Activation January 20th, 2023.
- Anticipated accrual: 2 patients/month
- Available at Mayo Clinic in Rochester, MN.

CONTACT INFORMATION

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- ClinicalTrials.gov: NCT05465954

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