TPS2092 **Poster Session**

Retifanlimab with bevacizumab and hypofractionated radiotherapy to treat recurrent glioblastoma.

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Background: Glioblastoma (GBM) is the most common primary brain malignancy in adults. GBM is universally recurrent and associated with dismal outcomes. Re-irradiation (reRT) is ideal for evaluating combination therapy for recurrent GBM (rGBM) due to its multifactorial mechanism of action, including downstream immunomodulatory activity. RT (especially multi-fraction) increases immunogenicity in preclinical models by promoting immune activation, immune migration, and antigen uptake. Additionally, a recent study demonstrated enhanced PD-L1 expression in the glioma tumor microenvironment (TME) following RT, and combining stereotactic RT with a PD-1 inhibitor improved survival in murine models. Retifanlimab is a humanized monoclonal anti-PD1 IgG4 antibody that received FDA approval for adults with metastatic or recurrent locally advanced Merkel cell carcinoma. Bevacizumab, an anti-VEGF antibody, is a treatment for radiation necrosis/cerebral edema with less immune suppression than corticosteroids. In a previous Phase 2 study, hypofractionated RT (HFRT), retifanlimab, and bevacizumab was associated with a 9-month overall survival (OS) rate of 71.4%. To demonstrate the efficacy of this regimen compared to HFRT and bevacizumab, we have designed a new randomized controlled Phase 2 trial. We hypothesize that combination reRT with retifanlimab will produce a more robust anti-tumor immune response and improve OS compared to reRT without retifanlimab. **Methods:** This is a multicenter, open-label, randomized, controlled Phase 2 study of retifanlimab, bevacizumab, and HFRT for adult patients with rGBM. Patients are randomized 1:1 to the experimental (bevacizumab + retifanlimab + HFRT) or control cohort (bevacizumab + HFRT). Key eligibility criteria include age ≥ 18 years, Karnofsky performance status ≥ 60, ≥ 4 months since administration of any prior bevacizumab, and dexamethasone dose ≤ 4 mg at the time of randomization. The primary endpoint is 9-month OS. Secondary endpoints include OS, progression-free survival, objective response rate, neurologic assessment by NANO criteria, and adverse events profile. Protocol treatment will continue up to two years, or until progression or intolerable toxicity. Survival follow up will continue every two months, up to four years. Seven of the planned 94 patients have been enrolled as of submission on 1/28/25. Clinical trial #: NCT06160206. Funding provided by Incyte. Clinical trial information: NCT06160206. Research Sponsor: Incyte Corporation.