TPS2101 Poster Session

Dual targeting of VEGF and PD-1: A phase I/II trial of ivonescimab, a novel bispecific antibody, in recurrent glioblastoma.

Anuj Dilip Patel, Ashley Aaroe, Carlos Kamiya-Matsuoka, Ruitao Lin, Nazanin Majd, Barbara Jane O'Brien, Chirag B. Patel, Shiao-Pei S. Weathers, Vinay K. Puduvalli; University of Texas MD Anderson Cancer Center, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX

Background: Patients with recurrent glioblastoma have limited effective treatment options due to the highly immunosuppressive microenvironment and rapid proliferation fueled by neo-angiogenesis. Anti-angiogenic therapy, including targeting vascular endothelial growth factor (VEGF) with bevacizumab, and immune checkpoint inhibition with programmed cell death protein 1 (PD-1) inhibitors, have independently had limited efficacy in these tumors. Ivonescimab is a humanized tetravalent bispecific antibody against PD-1 and VEGF, which has demonstrated cooperative binding *in vitro* leading to increased binding of PD-1 in the presence of VEGF and vice-versa[1]. Ivonescimab has shown activity in multiple phase 3 trials conducted in China in non-small cell lung cancer, including one trial which demonstrated activity in patients with brain metastases, but has not yet been evaluated in patients with primary brain tumors. This trial evaluates ivonescimab in patients with recurrent glioblastoma. **Methods:** This investigator-initiated study consists of a phase I and II component; the primary objectives are safety and tolerability for phase I and determining progression-free survival for phase II. The phase I component evaluates 3 dose levels of ivonescimab (7.5, 10, and 20 mg/kg every 3 weeks), employing a Bayesian optimal interval (BOIN) design for assessing toxicity. Once the recommended phase II dose is determined, the phase II portion will follow a Bayesian optimal phase II (BOP2) design, with interim analyses at pre-specified enrollment points allowing for monitoring of efficacy as well as ongoing evaluation of toxicity. The maximum accumulative sample size at the target dose will be 30 patients. Radiographic assessment will utilize the Response Assessment in Neuro-Oncology 2.0 criteria. Key eligibility criteria include adults with recurrent glioblastoma, IDH-wildtype (by WHO CNS 2021 classification) at first or second recurrence with Karnofsky Performance Scale ≥60 and normal blood counts and organ function. Prior therapy with anti-angiogenic agents (including bevacizumab) or check-point inhibitors is excluded, as well as concurrent corticosteroids ≥ 2 mg/day dexamethasone or equivalent. Samples of archival tumor, blood and stool microbiome will be collected for correlative studies as an exploratory evaluation of predictive biomarkers of response or resistance to ivonescimab. The study has been approved by the institutional review board and accrual to phase I will commence in the first quarter of 2025. 1. Zhong T, Huang Z, Pang X, et al. 1194 Mechanism of action of ivonescimab (AK112/SMT112): a first-in-class tetravalent Fc-silent bispecific antibody with dual blockade of PD-1 and VEGF that promotes cooperative biological effects. Journal for ImmunoTherapy of Cancer 2023;11:doi: 10.1136/jitc-2023-SITC2023.1194. Clinical trial information: NCT06672575. Research Sponsor: Summit Therapeutics.