TPS8126 **Poster Session**

A phase 1/2 clinical trial of quaratusugene ozeplasmid gene therapy and atezolizumab maintenance therapy in patients with extensive stage small cell lung cancer (ES-SCLC).

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Background: The addition of atezolizumab (atezo) to both induction therapy and maintenance therapy for patients with ES-SCLC has improved median progression free survival (PFS) and overall survival (New Eng J Med. 2018;379:2220-9). However, the median PFS from starting atezo maintenance was only 2.6 months (J Thoracic Onc. 2022;17:1122-9). Expression of TUSC2, a tumor suppressor gene, is absent in 41% of SCLC patients and is decreased in 100% of SCLC patients (Clin Cancer Res 2008;14(1):41–47). Quaratusugene ozeplasmid (QuarOze) gene therapy consists of a DNA plasmid expressing the *TUSC2* gene encapsulated in a positively charged lipoplex which delivers the *TUSC2* gene to cancer cells, restoring TUSC2 expression. Xenograft studies using a SCLC cell line in a humanized mouse model treated with a combination of QuarOze and atezo demonstrated significantly increased tumor cell killing compared to that of atezo alone. In addition, infiltration of immune cells was increased in the tumor tissue, whereas myeloid derived suppressor cells were decreased (Meraz IM et al, AACR/NCI/EORTC 2023). Thus, in this study QuarOze is added to atezo maintenance therapy with the aim of improving PFS after the start of maintenance therapy. **Methods:** Eligible patients have ES-SCLC and have completed 3-4 cycles of induction therapy with etoposide, a platinum agent, and atezo without disease progression, and are thus eligible for maintenance therapy. QuarOze is administered IV every 21 days in escalating dose cohorts in Phase 1 and atezo 1200 mg is also administered IV every 21 days. Dexamethasone, acetaminophen, and diphenhydramine are given prior to each treatment to prevent delayed infusion-related reactions. Efficacy is evaluated after every even cycle of treatment using RECIST 1.1 criteria. Safety is evaluated using CTCAE v5, with dose limiting toxicities generally defined as ≥Gr 3 adverse events (AEs). TUSC2 protein expression is measured by a validated immunohistochemistry assay in paraffin sections to determine if PFS is related to pretreatment TUSC2 levels. A validated assay measures pharmacokinetics in all patients. In Phase 1, two planned dose levels (0.09, and 0.12 mg/kg) of QuarOze were administered, and a standard dose escalation with 3-6 patients/dose level was used. The Phase 2 portion of the trial will enroll 50 patients which provides 80% power at a one-sided alpha level of 0.05 to detect an 18-week PFS rate of 52% compared to a historical 18-week PFS rate of 34% with atezo alone. This corresponds to a median PFS of approximately 4.3 months compared to a historical median PFS of 2.6 months with atezo alone. A Safety Review Committee (SRC) reviewed safety data at the end of each dose level of Phase 1 to make recommendations about dose escalation. The Phase 2 portion of the trial opened for enrollment in December, 2024. Clinical trial information: NCT05703971. Research Sponsor: Genprex, Inc.