TPS2095 **Poster Session**

Liposomal curcumin and standard radiation and temozolomide for newly diagnosed high-grade gliomas: A phase 1/2 study.

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Background: Curcumin, derived from turmeric (Curcuma spp.), exhibits anti-inflammatory and antitumoral activity in preclinical studies, including inducing cell cycle arrest, apoptosis, autophagy and disrupting key cancer signaling pathways (e.g., STAT-3, AKT, VEGF, NF-κB, and IDO). Despite its promise, oral curcumin has limited bioavailability. Liposomal curcumin (LC), a novel intravenous formulation, achieves plasma curcumin levels over 1000 times higher than oral administration and preferentially accumulates in tumor cells. In preclinical glioma models, LC has antitumoral efficacy, particularly when combined with cytotoxic therapies. Previous trials in healthy volunteers and cancer patients demonstrated LC's safety, pharmacokinetics, and manageable adverse effects, with doses up to 300 mg/m^2 being well-tolerated. However, a case of hemolytic anemia was observed in a prior study at this dose in a patient who was also taking several known hemolytic drugs, suggesting the need for further safety evaluation at this and potentially higher doses. **Methods:** This Phase I/II open-label, study evaluates LC combined with standard radiation (RT) and concomitant and adjuvant temozolomide (TMZ) in newly diagnosed HGG patients (NCT05768919). The primary endpoints are MTD, RP2D and safety. Secondary endpoints include treatment feasibility (≥80% adherence to LC, RT, and ≥60% to TMZ), and exploratory efficacy measures (PFS, OS by RANO criteria). The study has two phases: (1) dose-escalation using the TITE-BOIN method to determine MTD, and (2) dose-extension to evaluate RP2D safety and feasibility. Up to 50 patients will be screened to enroll 30. LC is given weekly at 4 dose levels (240, 300, 350, and 400 mg/m^2) alongside standard adjuvant TMZ (150–200 mg/m^2 x 5 days every 28 days) and RT. Treatment continues for up to 6 TMZ cycles, with LC monotherapy possible afterward until progression or toxicity. MRI is done before and 4 weeks post-chemoradiation, then every 2 cycles of TMZ, as per standard of care. DLTs are evaluated over 10 weeks to determine the MTD which will be determined by TITE-BOIN dose escalation rule and Safety Review Committee's guidance. A separate exploratory protocol is offered to patients interested in additional imaging, which uses chemical exchange saturation transfer (CEST) MRI to visualize liposome accumulation in tumor tissue non-invasively. As of 1/24/2025, 14 patients have been enrolled in the dose-escalation part of this study. Clinical trial information: NCT05768919. Research Sponsor: SignPath Pharma.