TPS2098 **Poster Session**

Trial in progress: Feasibility of CSF and plasma ctDNA in BRAF-altered glioma during treatment with plixorafenib.

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Background: Gliomas with BRAF alterations are often difficult to treat in the recurrent setting due to emergent resistance to FDA-approved targeted therapies. Additionally, it can be difficult to assess response to treatment given the limitations of radiographic techniques and the infeasibility of serial tissue sampling. This protocol serves as a prototype for determining the feasibility of using CSF and plasma circulating tumor DNA (ctDNA) as biomarkers for response to a novel-BRAF inhibitor, plixorafenib. Plixorafenib is a small-molecule selective inhibitor of BRAF-V600E and BRAF-fusion alterations that does not induce paradoxical reactivation of MAPK signaling. **Methods:** This study is a single institution trial of plixorafenib in patients (18+ years of age) with BRAF-V600E mutant glioma following progression on prior BRAF-targeted therapy who are recommended for a clinically-indicated diagnostic or debulking surgery. Eligible patients have recurrent BRAF-V600E mutant glioma (any grade) with measurable disease (by RANO 2.0), have a Karnofsky performance status $>$ 70, and are able to undergo surgery. Leptomeningeal disease is allowed. A total of 12 evaluable patients will be enrolled. Enrolled patients undergo clinically-indicated resection or biopsy for confirmation of disease progression and characterization of putative resistance alterations. All patients have a ventricular reservoir placed at time of surgery with CSF and plasma sampling. Patients will initiate oral plixorafenib 900mg daily with cobicistat, a CYP3A inhibitor and PK enhancer, when clinically recovered from surgery. Patients will take the drug continuously under fasting conditions. MRI, CSF, and plasma assessments will occur approximately every two months to evaluate disease status. The primary endpoint is proportion of samples with detectable tumor ctDNA baseline and after one month of treatment with plixorafenib. Secondary endpoints include the correlation of ctDNA with disease status over time and response rate to plixorafenib. The trial is IRB approved and currently open to enrollment. Clinical trial identifier NCT06610682. Clinical trial information: NCT06610682. Research Sponsor: Ivy Brain Tumor Foundation; Fore Biotherapeutics.