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PNOC015: Repeated convection enhanced delivery (CED) of MTX110 (aqueous panobinostat) in children with newly diagnosed diffuse intrinsic pontine glioma (DIPG)

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Abstract

Objective: To determine the safety, tolerability and distribution of MTX110 (aqueous panobinostat) delivered by convection enhanced delivery (CED) in patients with newly diagnosed diffuse intrinsic pontine glioma (DIPG) who completed focal radiation therapy (RT).

Methods: Patients with DIPG (2-21 years) were enrolled after RT. CED of MTX110 combined with gadoteridol was completed across seven dose levels (DL) (30-90 μM; volumes ranging from 3 mL to two consecutive doses of 6 mL). An accelerated dose escalation design was used. Distribution of infusate was monitored with real-time MR imaging. Repeat CED was performed every 4-8 weeks. Quality of life (QOL) assessments were obtained at baseline, every 3 months on therapy, and end of therapy.

Results: Between May 2018-March 2020 seven patients, who received a total of 48 CED infusions, were enrolled (median age 8 years, range 5-21). Three patients experienced dose-limited toxicities. Four grade 3 treatment related adverse events were observed. Most toxicities were transient new or worsening neurologic function. Median overall survival (OS) was 26.1 months (95% CI: 14.8-not reached). Progression free survival was 4-14 months (median, 7). Cumulative percentage of tumor coverage for combined CED infusions per patient ranged from 35.6-81.0%. Increased CED infusions was negatively associated with self-reported QOL assessments.

Conclusion: Repeat CED of MTX110 with real time imaging with gadoteridol is tolerable for patients with DIPG. Median OS of 26.1 months compares favorably with historical data for children with DIPG. The results support further investigation of this strategy in a larger cohort.

Keywords: DIPG; MTX110; convection enhanced delivery; real time imaging monitoring.