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Phase 1 dose-escalation trial using convection-enhanced delivery (CED) of radio-immunotheranostic 124I-Omburtamab for diffuse intrinsic pontine glioma (DIPG)

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Abstract

Background: Median survival for patients with Diffuse Intrinsic Pontine Glioma (DIPG) is 8-12 months.

Methods: A phase 1, open label, 3 + 3 dose escalation trial delivered radiolabeled 124I-Omburtamab, targeting B7-H3, using MR-guided stereotactic convection enhanced delivery (CED) into the brainstem of pediatric DIPG patients. CED was performed after completion of standard-of-care external-beam radiation therapy (EBRT). Fifty children were treated and evaluable. 124I-Omburtamab activity was escalated from 0.25-10.0 mCi (9.25-370 MBq) and volume escalated from 0.25 ml-10.0 ml with serial PET/MRI post-administration. Safety was the primary outcome. National Cancer Institute Common Terminology Criteria for Adverse Events were assessed for 30 days following CED of 124I-Omburtamab. Secondary outcomes included overall survival and lesion-to-whole-body absorbed dose ratio.

Results: The maximum tolerated activity per study protocol was determined to be 6mCi (222 MBq). The overall mean (±SD) total absorbed dose in the lesion per unit injected activity was 35.2 ± 18 cGy/MBq with a high lesion-to-whole-body absorbed dose ratio averaging 816, across all activity levels. Eleven patients had treatment-related grade 3 CNS toxicities with no grade-4 or -5 CNS toxicities. Five dose-limiting toxicity events occurred. Median survival was 15.29 months from diagnosis (95% CI: 12.20 - 16.83 months). Survival rate estimates at 1, 2, and 3 years were 65.4% (CI 53.3-80.1%), 18.4% (CI: 10.2-33.2%), and 11.7% (CI: 5.3-25.7%), respectively.

Conclusions: Administration of 124I-Omburtamab via CED is a safe treatment option for DIPG, with a maximum tolerated activity level identified. This study represents the first in-human theranostic use of a 124I radiopharmaceutical, simultaneously, as an imaging and therapeutic agent.

Keywords: Convection-Enhanced Delivery; DIPG/DMG; Phase 1; Theranostic; radiopharmaceutical.