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Determination of the Intralesional Distribution of Theranostic ^{124}I-Omburtamab Convection-Enhanced Delivery in Treatment of Diffuse Intrinsic Pontine Glioma

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Abstract

This phase 1, dose-escalation study examined the use of the radiolabeled antibody ^{124}I-Omburtamab delivered directly to brain-stem tumors via convection-enhanced delivery (CED). CED bypasses the blood-brain barrier by injecting the agent under the pressure of a peristaltic pump to convectively drive the therapeutic agent through the brain tissue and tumor compartment, enabling high concentrations at the target site. We evaluated ^{124}I-Omburtamab's potential to deliver therapeutic radiation doses to diffuse intrinsic pontine glioma in children. PET and MRI were used to assess the alignment between the intended and actual distribution of the agent, with an analysis of tumor coverage and radiation absorbed doses. **Methods:** ^{124}I-Omburtamab doses ranging from 9.25 to 370 MBq were administered to 36 patients. Tumor distribution volumes were derived from PET images by placing volumes of interest over lesions and overlaying them onto T2-weighted fluid-attenuated inversion recovery MRI-delineated tumor volumes. Dosimetry metrics evaluated after CED included dose-volume histograms, tumor coverage percentage, and the Dice similarity coefficient between the antibody distribution and tumor volume. A 4-quadrant scatter plot of Dice similarity versus tumor coverage was used to classify treatment variations among patients. **Results:** Serial PET scans showed ^{124}I-Omburtamab localization in brain-stem lesions from 1 h to 7 d ± 1 d after dose administration. Coverage analysis revealed that 29 patients had tumor volume coverage greater than 50%, and 28 had a Dice similarity coefficient over 50%. The 4-quadrant statistical analysis-percentage of coverage versus Dice similarity coefficient-showed that 27 patients had acceptable coverage for treatment, and 4 patients experiencing suboptimal tumor coverage. **Conclusion:** CED of ^{124}I-Omburtamab is a novel approach for delivering radiolabeled therapies into brain-stem tumors. Imaging enabled quantification of radiation dose coverage within the MRI-defined tumor target, highlighting the importance of precise alignment between therapeutic agent distribution and tumor volume.

Keywords: PET Omburtamab; convection-enhanced delivery; dose-volume histogram; theranostic.

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