J Nucl Med. 2024 Aug 14:jnumed.123.266365. doi: 10.2967/jnumed.123.266365.

Theranostic Intratumoral Convection-Enhanced Delivery of ^{124}I-Omburtamab in Patients with Diffuse Intrinsic Pontine Glioma: Pharmacokinetics and Lesion Dosimetry

Neeta Pandit-Taskar [1 2], Pat B Zanzonico [3], Milan Grkovski [3], Maria Donzelli [4], Scott M Vietri [5 6], Christopher Horan [3], Brian Serencsits [3], Kavya Prasad [3], Serge Lyashchenko [6 7], Kim Kramer [4 8], Ira J Dunkel [4 8], Mark M Souweidane [9 10]

Affiliations

PMID: 39142829 DOI: 10.2967/jnumed.123.266365

Abstract

Diffuse intrinsic pontine glioma (DIPG) is a rare childhood malignancy with poor prognosis. There are no effective treatment options other than external beam therapy. We conducted a pilot, first-in-human study using ^{124}I-omburtamab imaging and theranostics as a therapeutic approach using a localized convection-enhanced delivery (CED) technique for administering radiolabeled antibody. We report the detailed pharmacokinetics and dosimetry results of intratumoral delivery of ^{124}I-omburtamab. **Methods:** Forty-five DIPG patients who received 9.0-370.7 MBq of ^{124}I-omburtamab intratumorally via CED underwent serial brain and whole-body PET/CT imaging at 3-5 time points after injection within 4, 24-48, 72-96, 120-144, and 168-240 h from the end of infusion. Serial blood samples were obtained for kinetic analysis. Whole-body, blood, lesion, and normal-tissue activities were measured, kinetic parameters (uptake and clearance half-life times) estimated, and radiation-absorbed doses calculated using the OLINDA software program. **Results:** All patients showed prominent activity within the lesion that was retained over several days and was detectable up to the last time point of imaging, with a mean ^{124}I residence time in the lesion of 24.9 h and dose equivalent of 353 ± 181 mSv/MBq. Whole-body doses were low, with a dose equivalent of 0.69 ± 0.28 mSv/MBq. Systemic distribution and activities in normal organs and blood were low. Radiation dose to blood was very low, with a mean value of 0.27 ± 0.21 mGy/MBq. Whole-body clearance was monoexponential with a mean biologic half-life of 62.7 h and an effective half-life of 37.9 h. Blood clearance was biexponential, with a mean biologic half-life of 22.2 h for the rapid α phase and 155 h for the slower β phase. **Conclusion:** Intratumoral CED of ^{124}I-omburtamab is a novel theranostics approach in DIPG. It allows for delivery of high radiation doses to the DIPG lesions, with high lesion activities and low systemic activities and high tumor-to-normal-tissue ratios and achieving a wide safety margin. Imaging of the actual therapeutic administration of ^{124}I-omburtamab allows for direct estimation of the therapeutic lesion and normal-tissue-absorbed doses.

Keywords: 124I-omburtamab; DIPG; convection-enhanced delivery; diffuse intrinsic pontine glioma; dosimetry; organ-absorbed doses.