

Tozuleristide

Fluorescence-guided neurosurgery (FGS) can improve the **extent of resection** in **gliomas**. Tozuleristide (**BLZ-100**), a near-infrared imaging agent composed of the peptide **chlorotoxin** and a near-infrared fluorophore **indocyanine green**, is a candidate molecule for FGS of glioma and other tumor types.

Patil et al. performed a phase 1 dose-escalation study to characterize the safety, pharmacokinetics, and fluorescence imaging of tozuleristide in adults with suspected glioma.

Patients received a single intravenous dose of tozuleristide 3 to 29 h before surgery. Fluorescence images of tumor and cavity in Situ before and after resection and of excised tissue ex Vivo were acquired, along with safety and pharmacokinetic measures.

A total of 17 subjects received doses between 3 and 30 mg. No dose-limiting toxicity was observed, and no reported adverse events were considered related to tozuleristide. At doses of 9 mg and above, the terminal serum half-life for tozuleristide was approximately 30 min. Fluorescence signal was detected in both high- and low-grade glial tumors, with high-grade tumors generally showing greater fluorescence intensity compared to lower grade tumors. In high-grade tumors, signal intensity increased with increased dose levels of tozuleristide, regardless of the time of dosing relative to surgery.

These results support the safety of tozuleristide at doses up to 30 mg and suggest that tozuleristide imaging may be useful for FGS of gliomas ¹⁾.

Tumor Paint **BLZ-100**, a tumor ligand **chlorotoxin** (CTX) conjugated to **indocyanine Green** (ICG), has shown potential to be a targeted contrast agent. There are many infrared imaging systems (NIR) in use, but they are not optimized to the low concentration and amount of ICG

BLZ-100 has a very high affinity toward human gliomas. They also describe a small, cost-effective, and sensitive NIR system for visualizing brain tumors tagged using BLZ-100. Butte et al. hope that the use of BLZ-100 along with **near infrared optical imaging** imaging will be useful to delineate the brain tumors in real-time and assist surgeons in near-complete tumor removal to increase survival and reduce neurological deficits ²⁾.

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Patil CG, Walker DG, Miller DM, Butte P, Morrison B, Kittle DS, Hansen SJ, Nufer KL, Byrnes-Blake KA, Yamada M, Lin LL, Pham K, Perry J, Parrish-Novak J, Ishak L, Prow T, Black K, Mamelak AN. Phase 1 Safety, Pharmacokinetics, and Fluorescence Imaging Study of Tozuleristide (BLZ-100) in Adults With Newly Diagnosed or Recurrent Gliomas. *Neurosurgery*. 2019 Oct 1;85(4):E641-E649. doi: 10.1093/neuros/nyz125. PubMed PMID: 31069381.

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Butte PV, Mamelak A, Parrish-Novak J, Drazin D, Shweikeh F, Gangalum PR, et al: Near-infrared imaging of brain tumors using the Tumor Paint BLZ-100 to achieve near-complete resection of brain tumors. *Neurosurg Focus* 36(2):E1, 2014

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