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First in-human intrathecal delivery of bevacizumab for leptomeningeal spread from recurrent glioblastoma: rationale for a dose escalation trial

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Abstract

Purpose: To outline the dose rationale for the first in-human intrathecal delivery of bevacizumab for LMS of GBM.

Methods: A 19-year-old female patient presented to Lenox Hill Hospital following thalamic GBM recurrence. She subsequently underwent two infusions of intra-arterial BEV (NCT01269853) and experienced a period of relative disease stability until progression in 2022. One month later, MRI disclosed diffuse enhancement representative of LMS of GBM. The patient subsequently underwent five cycles of IT BEV in mid-2022 (IND 162119). Doses of 25 mg, 37.5 mg, 50 mg, 50 mg, and 37.8 mg were delivered at two-week intervals between doses 1-4. The final 37.8 mg dose was given one day following her fourth dose, given that the patient was to be discharged, traveled several hours to our center, and was tolerating therapy well. Dosage was decreased due to the short interval between the final two treatments. Shortly after IT BEV completion, she received a third dose of IA BEV.

Results: Our patient did not show any signs of serious adverse effects or dose limiting toxicities following any of the treatments. It is difficult to determine PFS due to the rapid progression associated with LMS of GBM and rapid timeframe of treatment.

Conclusion: LMS continues to be a devastating progression in many types of cancer, including GBM, and novel ways to deliver therapeutics may offer patients symptomatic and therapeutic benefits.

Keywords: Bevacizumab; Glioblastoma; Intrathecal; Leptomeningeal metastasis.