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A Phase 1 and Biodistribution study of Ifabotuzumab, a humanized agonistic EphA3-targeted antibody, in patients with recurrent glioblastoma

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Abstract

Purpose: To undertake a Phase 1 and Biodistribution study of the EphA3 antibody ifabotuzumab, and its zirconium labelled derivative 89Zr-ifabotuzumab, in glioblastoma patients.

Patients and methods: This multi-site study was conducted in adults with recurrent glioblastoma whose tumors were measurable by Response Assessment in Neuro Oncology (RANO) criteria and were ECOG 0-1. Patients underwent a biodistribution PET scans with zirconium 89 (89Zr) ifabotuzumab (89Zr-Ifabotuzumab), followed by three infusions of ifabotuzumab at either 3.5 mg/kg or 5.25 mg/kg before undergoing a second study with 89Zr-Ifabotuzumab PET scans. Resected patient diagnostic tumor samples were collected for multiplex immunofluorescence and spatial transcriptomics analysis.

Results: Twelve patients were recruited, six treated with 3.5 mg/kg and six with 5.25 mg/kg of ifabotuzumab. 89Zr-Ifabotuzumab and associated PET scanning were well tolerated, as was ifabotuzumab. There were no objective responses, but one patient had prolonged stable disease. In addition, two patients showed changes in peri-tumor edema that were suggestive of modulation of tumor vasculature. 89Zr-Ifabotuzumab scans showed highly specific tumor uptake in all patients concordant with disease sites on MRI and PET imaging, without evidence of non-specific binding. Spatial transcriptomics and immunofluorescence analysis of the patient's archival tissue specimens showed EphA3 was expressed in the tumor microenvironment (TME) in all patients and tumor cells with different transcriptional states.

Conclusions: Targeting EphA3 with ifabotuzumab in glioblastoma patients is safe and attractive, showing chronological stable expression across both tumour compartments (particularly in cells with mesenchymal phenotype) and non-tumour compartments (particularly the vascular compartment) with evidence of target modulation.