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Bevacizumab-IRDye800CW for tumor detection in fluorescence-guided meningioma surgery (LUMINA trial): a single-center phase I study

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Abstract

Objective: Meningiomas are one of the most frequently occurring brain tumors and can be curatively treated with gross-total resection. A subtotal resection increases the chances of recurrence. The intraoperative identification of invisible tumor remnants by using a fluorescent tracer targeting an upregulated biomarker could help to optimize meningioma resection. This is called molecular fluorescence-guided surgery (MFGS). Vascular endothelial growth factor α (VEGFα) has been identified as a suitable meningioma biomarker and can be targeted with bevacizumab-IRDye800CW.

Methods: The aim of this prospective phase I trial was to determine the safety and feasibility of bevacizumab-IRDye800CW for MFGS for intracranial meningiomas by administering 4.5, 10, or 25 mg of the tracer 2-4 days prior to surgery. Fluorescence was verified during the operation with the standard neurosurgical microscope, and tissue specimens were postoperatively analyzed with fluorescence imaging systems (Pearl and Odyssey CLx) and spectroscopy to determine the optimal dose. Uptake was compared in several tissue types and correlated with VEGFα expression.

Results: No adverse events related to the use of bevacizumab-IRDye800CW occurred. After two interim analyses, 10 mg was the optimal dose based on ex vivo tumor-to-background ratio. Although the standard intraoperative imaging revealed no fluorescence, postoperative analyses with tailored imaging systems showed high fluorescence uptake in tumor compared with unaffected dura mater and brain. Additionally, tumor invasion of the dura mater (dural tail) and invasion of bone could be distinguished using fluorescence imaging. Fluorescence intensity showed a good correlation with VEGFα expression.

Conclusions: Bevacizumab-IRDye800CW can be safely used in patients with meningioma; 10 mg bevacizumab-IRDye800CW provided an adequate tumor-to-background ratio. Adjustments of the currently available neurosurgical microscopes are needed to achieve visualization of targeted IRDye800CW intraoperatively. A phase II/III trial is needed to methodically investigate the benefit of MFGS with bevacizumab-IRDye800CW for meningioma surgery in a larger cohort of patients.

Keywords: bevacizumab; fluorescence-guided surgery; meningioma; neurosurgery; tumor; vascular endothelial growth factor.