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LETTER TO THE EDITOR (BY INVITATION)

# Response to the commentary on our work: a new uPAR-targeting fluorescent probe for optical guided intracranial surgery in resection of a meningioma—a case report

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Dear Editor.

We appreciate the interest in our published case with uPAR targeting of an intracranial meningioma by our colleague Dr. Suero-Molina and co-authors. We hereby omit our response.

The patient in the case report was included in a first-in-human study of FG001 in patients with contrast-enhancing suspected malignant glioma. This patient was excluded from all other trial evaluations for safety, as the patient was not diagnosed with malignant glioma. The full study result is being prepared for publication and will provide more details.

The authors ask whether the optical signal is passive extravasation or specific binding to uPAR. We believe FG001 leaves the blood vessels and thereafter are specifically bound to cells expressing uPAR. The specificity of FG001 to uPAR has elegantly been shown in Juhl et al. [1] where co-administration of uPA—the natural ligand to uPAR—demonstrated significant reduced binding of FG001.

In our discussion, we stated that the optimal dose has not yet been established; the patient reported in the case report thus received 8 mg FG001 only, being part of the third dose cohort. In our dose-escalating study, we have later established the optimal dose and time of administration. These results are pending for publication.

Regarding the ability of FG001 to pass the BBB, the patient included in the case report had a contrast-enhancing tumor and therefore would light up regardless of BBB-penetrating abilities of FG001. However, FG001 has indeed been shown in a predictive in vitro model of the BBB to penetrate the BBB. However, whether FG001 penetrates the BBB in patients and its clinical relevance remain to be studied.

We agree that clinical trials for obtaining approval as a new drug by the FDA and EMA need to be well thought through and properly designed.

Sincerely
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