

## Poster Presentations - Novel Delivery Technologies

### Abstract 5606: Gallium maltolate inhibits brain tumor volume and blood volume in xenograft model.

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Purpose: There are limited treatment options for glioblastomas (GBM). Tumor cells have a high requirement for iron; the latter is taken up by cells through transferrin receptor-mediated endocytosis of transferrin-iron. These receptors are highly expressed on GBM cells, which makes them an attractive target for transferrin receptor-directed therapies. Gallium is a group IIIa metal that can function as an iron mimetic by avidly binding to transferrin and incorporating into cells through the transferrin receptor. No studies have been performed to determine the efficacy of gallium-based therapies in brain tumors. Consequently, the goal of this study was to evaluate gallium maltolate in the treatment of a U87 xenograft brain tumor model. Methods: Athymic rats bearing U87 human grade IV astrocytoma cells were studied. Gallium maltolate (50 mg/kg/day, n=5) or saline (n=3) was given intravenously via an alzet mini pump in the jugular vein. Magnetic resonance imaging (MRI) was performed on days 8 and 18 on a Bruker 9.4 T scanner. Enhancing tumor volumes were determined from the post-contrast T1w images, in all slices showing enhancing tumor. The spin and gradient echo relaxation rate changes were then determined giving estimates of microvascular and total blood volume. ( $CBV_{micro} \approx R2 = R2_{MION} - R2_{pre-MION}$ ;  $CBV_{Total} \approx R2^* = R2^*_{MION} - R2^*_{pre-MION}$ ). Results: Gallium maltolate inhibited tumor growth (377132%), as measured by enhancing tumor volume, compared to saline controls (863481%). Treatment shows decrease of  $CBV_{micro}$  and  $CBV_{Total}$  compared to the controls. The ratio of  $R2^* / R2$ , which is a measure of mean vessel diameter, increased in saline treated controls but remained unchanged for the gallium maltolate treated rats. To our knowledge this is the first study performed that uses physiologic MRI measurements to investigate the effects of gallium maltolate on brain tumor xenografts. The differences shown are not statistically significant a result likely due to the small sample sizes, which is being remedied by ongoing additional studies. For the imaging studies included here tissue markers of proliferation (Ki67), hypoxia (HIF1) transferrin receptors, and vascular density (vWF) are being analyzed to provide additional information regarding mechanism of action. In general these results demonstrate, for the first time, that the novel gallium maltolate treatment holds promise for the treatment of malignant brain tumors.

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