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An early clinical trial of 5-ALA sonodynamic therapy in recurrent high-grade glioma

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Abstract

Systemic administration of 5-aminolevulinic acid (5-ALA) results in accumulation of the sonosensitizing compound protoporphyrin IX in tumor cells because of their aberrant metabolism. Activation of protoporphyrin IX by noninvasive, magnetic resonance-guided focused ultrasound (MRgFUS) sonodynamic therapy (SDT) induces production of reactive oxygen species and tumor cytotoxicity. In this first-in-human, open-label, early clinical study ([NCT04559685](https://clinicaltrials.gov/ct2/show/study/NCT04559685)), safety and biological efficacy of ascending doses of MRgFUS combined with intravenous administration of 5-ALA (SONALA-001) were assessed in nine patients with recurrent high-grade glioma. The safety assessment revealed no drug-related or device-related toxicities. Pharmacokinetic analysis provided quantitative information on the concentration of 5-ALA and protoporphyrin IX in plasma, blood, and brain tissue. Comparison of pharmacodynamic markers between half of the tumor region treated with MRgFUS compared with the untreated tumor provided information on dose-related changes in markers of oxidative stress and cell death for each patient's tumor. This early phase clinical trial demonstrates proof of principle for 5-ALA SDT as a therapeutic modality for glioma. Further research is needed to optimize treatment parameters for clinical efficacy and to explore the potential of 5-ALA SDT in other types of cancer.

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