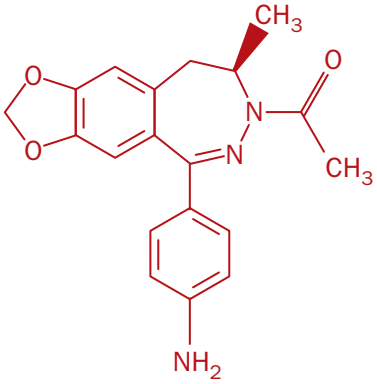
NEURO-ONCOLOGY

Talampanel enhances survival in glioblastoma

Talampanel, a glutamate receptor blocker, can safely be added to the current standard therapy for glioblastoma multiforme, concludes a new study involving 72 patients. Those treated with talampanel showed no signs of toxicity, and their median survival and percentage survival at 24 months was encouraging compared with that observed in patients given standard treatment only. "We saw a significant improvement in survival from this non-toxic, oral agent when administered in conjunction with radiation and temozolomide," notes lead author Stuart Grossman.

Talampanel blocks the AMPA receptor, a glutamate receptor that is present on both neurons and glial cells. Gliomas tend to produce excess glutamate, which is toxic to nearby glia and neurons, and evidence is accumulating that the glutamatergic system stimulates the growth and migration of gliomas, thereby enhancing disease progression. Blocking glutamate receptors *in vitro* and in animal models can halt glioma division and slow down invasion of surrounding tissues. "Preclinical data strongly suggest that the glutamate pathway could be of importance in the treatment of glioblastoma," notes Grossman.



The 72 patients who were given talampanel as part of their treatment within the New Approaches to Brain Tumor Therapy (NABTT) trial had a median overall survival of 18 months. The results from 60 patients aged between 18 and 70 years were compared with those obtained from patients in that age range from the European Organisation for Research and Treatment of Cancer clinical trial, which compared radiotherapy alone with radiotherapy plus temozolomide for the treatment of glioblastoms. Talampanel had marked effects both on median survival (20.3 months versus 14.6 months) and on the percentage of patients surviving for 2 years (41.7% versus 26.5%). This result was obtained despite the fact that fewer patients in the NABTT study had methylation of the *MGMT* gene promoter—a factor that was recently shown to significantly influence survival in glioblastoma multiforme.

"The NABTT patients were at higher risk to do poorly so the results are even more compelling—but the effectiveness of this agent and the therapeutic potential of the glutamate pathway must still be confirmed in a phase III, randomized, placebo-controlled trial. If this larger study is positive, this would provide confirmation that the glutamate pathway is an important therapeutic target in patients with glioblastoma," comments Grossman. Other agents that interfere with the glutamatergic pathway exist, and future research is likely to focus on the toxicity and efficacy of these compounds, as well as of combinations of agents that target this pathway.

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Original article Grossman, S. A. *et al.* Talampanel with standard radiation and temozolomide in patients with newly diagnosed glioblastoma: a multicenter phase II trial. *J. Clin. Oncol.* **27**, 4155–4166 (2009).