

# CLINICAL TRIAL TO EVALUATE A NOVEL DRUG COMBINATION TO INCREASE GLIOBLASTOMA SURVIVAL RATES

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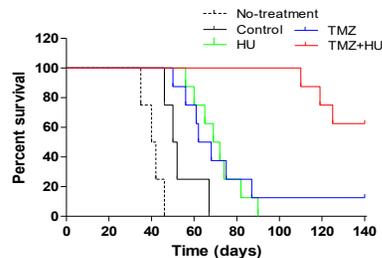
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## PROPOSED TREATMENT

We propose the use of a novel and relatively inexpensive use of two drugs, hydroxyurea and TMZ, to fight GBM in Phase I/II human trials.

Through a repurposing drug screen in patient-derived GBM cells in culture and in animal models, we have determined that a novel combination of hydroxyurea and TMZ has produced very promising increased survival rates. Although hydroxyurea has been evaluated for the treatment of malignant gliomas in combination with radiation or cytotoxic chemotherapy—and shown to have limited efficacy—it was never evaluated in conjunction with an agent with proven efficacy for GBM such as TMZ.

Our preclinical analysis revealed an increase in the overall [survival rate of all mice treated with the combined therapy, some of which became tumor free.](#)



Analysis showing the increase in survival rate of mice with GBM tumors treated with the combined therapy (TMZ+HU) as opposed to TMZ alone.

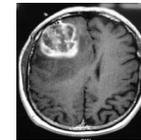
## SUMMARY STATEMENT

Clinical trial evaluating the efficacy of hydroxyurea and temozolomide as a combination therapy to extend typical survival-past-diagnosis for glioblastoma patients.

## DISEASE/CONDITION

Glioblastomas (GBM) is the most common and lethal form of brain cancer in adults. Because there is no clear way to prevent the disease, developing effective treatments is absolutely essential.

- Even when following standard-of-care, the cancer usually recurs.
- The most common length of survival following diagnosis is only 12–15 months and less than 10% of patients survive >5 years.



## CURRENT TREATMENT

Standard treatment involves radiation, chemotherapy, and maximal surgical resection of the tumor. The DNA alkylating agent, temozolomide (TMZ), is the standard chemotherapy, but only works in half the patients. The [five-year survival rate of patients with GBM is less than 10%](#), in large part due to acquired and/or intrinsic resistance to TMZ.

## PROJECT

Determine the optimal dose and safety profile of daily hydroxyurea in combination with TMZ in patients with recurrent GBM and estimate the overall survival.

The trial will enroll a cohort of 30 recurrent GBM patients. Oral hydroxyurea and oral TMZ will be given to patients every day in 28-day cycles for a year or until unacceptable toxicity, intolerance, progressive disease or withdrawal of consent.

We will estimate the progression-free survival at 6 months of treatment, a standard metric in this patient population. We will employ revised radiographic response criteria as well as conventional criteria to assess response and define tumor progression.

In a follow-up study, we will use the hydroxyurea/TMZ dosage data obtained from our Phase I trial to conduct a Phase II trial on both newly diagnosed and recurrent GBM patients, who are following the standard of care (i.e., surgery, radiation, chemotherapy), to determine optimal dosing to increase survival rates for two years, five years and longer.

