About Orbus Therapeutics

Orbus Therapeutics (orbustherapeutics.com) is dedicated to exploring new treatment options for patients with recurrent anaplastic astrocytoma, a rare form of brain cancer. Helping patients who are facing life-threatening or life-altering diseases is our passion and focus.

The team of experts at Orbus Therapeutics includes Victor A. Levin, MD, chairman of the Orbus clinical advisory board and senior medical advisor to Orbus. Dr. Levin has studied the use of eflornithine in brain cancers throughout his career. Dr. Levin is the former chair of the Department of Neuro-Oncology at M.D. Anderson Cancer Center and is the founder of the Society for Neuro-Oncology. He is the author of Cancer in the Nervous System, the first comprehensive medical textbook in neuro-oncology.

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References

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2. Levin VA et al.,J Natl Cancer Inst. 1992;84(18):1432-1437.
3. Levin VA et al. Clin Cancer Res. 2003;9(3):981-990.
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www.stellarstudy.com

Protocol Ammendment 5, dated January 14, 2019

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STELLAR

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The STELLAR Trial

A phase 3 clinical trial now recruiting patients with recurrent anaplastic astrocytoma at centers in North America and Europe

STELLAR

Patients with anaplastic astrocytoma (AA) that has recurred or progressed after radiation therapy and chemotherapy may be eligible to participate in the STELLAR trial.

The few available treatments for recurrent anaplastic astrocytoma (rAA) have limited efficacy. There are currently no targeted therapies for patients with this rare disease. That's why neuro-oncology experts at Orbus Therapeutics are conducting the STELLAR trial to evaluate eflornithine oral solution — a targeted therapy — for treating recurrent anaplastic astrocytoma.

About the STELLAR trial

The purpose of the STELLAR trial is to compare the efficacy and safety of oral eflornithine in combination with oral lomustine with oral lomustine alone in treating patients with AA that has recurred or progressed after radiation therapy and temozolomide (Temodar®) chemotherapy. STELLAR is a phase 3, randomized, open-label clinical trial. The primary outcome measure is overall survival.

The STELLAR trial is registered with the United States government clinical trials registry and with the European Union clinical trials registry. Orbus Therapeutics is the trial sponsor.

About eflornithine?

Eflornithine, also known as a-diflurormethylornithine, selectively targets and irreversibly inhibits ornithine decarboxylase (ODC), an enzyme essential for polyamine synthesis and DNA and RNA function.[1] Unlike multi-targeted tyrosine kinase inhibitors on the market or in development today, eflornithine targets only one enzyme, ODC.

Eflornithine injection was approved by the FDA in 1990 for the treatment of African trypanosomiasis (sleeping sickness), but it was never made commercially available in the United States. In 2000, the United States Food and Drug Administration (US FDA) approved a topical eflornithine cream for the reduction of unwanted facial hair in women.

Eflornithine oral solution is an investigational product that has not been proven to be safe and effective in treating patients with rAA. Eflornithine oral solution may only be administered to patients who participate in the STELLAR trial. Eflornithine oral solution is not licensed for the treatment of rAA in the United States or any other country.

In animal studies,[1] eflornithine has been shown to inhibit the growth of malignant tumors, including intracerebral high-grade gliomas. Eflornithine administration has also been shown to potentiate the antitumor activity of other chemotherapy agents.

In controlled, randomized, and single-arm clinical trials enrolling patients with newly diagnosed AA and rAA,[1,2,3] treatment with eflornithine oral solution increased survival. In these clinical trials, the primary and reversible side effects of eflornithine use in a small percentage of patients were diarrhea and hearing loss.

In 2014, eflornithine received breakthrough therapy designation from the US FDA for the treatment of patients with anaplastic glioma. A new drug may be designated as a breakthrough therapy by the US FDA if it is intended to treat a serious or life-threatening disease and preliminary evidence suggests it provides substantial improvement over existing therapies.

Is my patient eligible for the STELLAR clinical trial?

A patient may be eligible now if:

- They have WHO grade 3 AA
- They are 18 years of age or older
- This is the first recurrence or progression of disease
- First AA recurrence or progression has occurred within the past 6 months
- They have already been treated with temozolomide (Temodar®)
- They completed radiation therapy more than 6 months ago
- They have not been treated with any additional systemic therapy for recurrence of AA.

A patient may be eligible in the future if:

- They currently have WHO grade 2 astrocytoma or oligoastrocytoma that progresses to WHO grade 3 AA. Consider rapid referral to the STELLAR trial for patients who progress from grade 2 to grade 3 and meet the eligibility criteria above.

The World Health Organization published new guidelines in 2016 for the classification and grading of central nervous system tumors.[4]

How do I refer a patient to the STELLAR trial?

To contact a member of the STELLAR trial research team, visit **stellarstudy.com.** A representative from a clinical trial site or Orbus Therapeutics will be in touch with you as soon as possible.

STELLAR trial site locations

Currently, the STELLAR trial is being conducted at selected medical centers in North America and Europe. To see where these centers are located, visit **stellarstudy.com**.