



NCI's partnership with Aadastra moves new brain cancer drug along the path to commercialization

A partnership between the National Cancer Institute and Aadastra Pharmaceuticals has led to an orphan drug designation for a new cancer treatment and a clinical trial to move the treatment closer to commercialization.

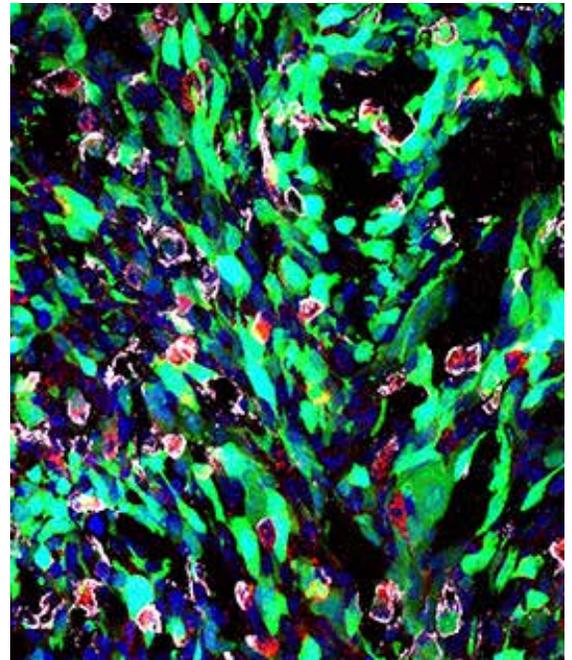
Zotiraciclib, developed by Princeton, New Jersey-based Aadastra, is an investigational cancer drug that is being evaluated for the treatment of patients with glioma, a type of brain tumor that is difficult to treat. Glioma represents 80% of all malignant primary brain tumors; types of gliomas include astrocytoma, ependymoma, and oligodendroglioma.

Despite recent advances in surgical techniques, radiation and chemotherapy, this disease remains incurable. Standard therapy consists of extensive surgery (if surgery is possible), followed by radiation therapy and chemotherapy. However, most patients experience relapse, and the median survival is less than 15 months. Thus, there is a large unmet need for the development of effective treatments of gliomas.

Zotiraciclib is a small molecule that inhibits multiple proteins known as kinases that regulate cellular processes such as DNA transcriptional regulation, cell cycle control, and DNA damage response, etc. Preclinical studies suggest zotiraciclib shuts down several specific pathways that glioma cells use to replicate and survive.

This novel anti-cancer agent is being studied and developed in a partnership between the National Cancer Institute and Aadastra Pharmaceuticals. NCI used several technology transfer mechanisms to initiate and advance the collaboration, starting with a Confidential Disclosure Agreement (CDA) so the parties could discuss collaborating, followed by a Material Transfer Agreement (MTA) for preclinical studies of zotiraciclib, then a Clinical Trial Agreement (CTA) for a Phase I/II clinical trial, and an MTA amendment for additional studies. Technology transfer advanced the collaboration by serving as a bridge between the development efforts and clinical priorities of Aadastra and the scientific concerns of the NCI investigators.

NCI played a key role in conducting several preclinical studies that provided the foundational data to justify a clinical trial of zotiraciclib. Based on positive data from these basic and translational preclinical studies, which were published in March 2018, NCI initiated the first clinical trial of zotiraciclib in brain tumor patients at the National Institutes of Health Clinical Center.



Above: Nanoparticles in the brain (courtesy of NCI Visuals Online).

In addition, zotiraciclib in December 2019 received orphan drug designation from the Food and Drug Administration (FDA) and the European Medicines Agency (EMA) for treatment of glioma.

One aspect of the excellence in the technology transfer effort was the speed with which the various agreements were negotiated and executed. These technology transfer efforts led zotiraciclib to be more rapidly translated from the bench (preclinical experiments done by NCI) to the bedside (first clinical trial in brain tumor patients). For example, the company's MTA template was negotiated and executed in eight days, and the CTA was negotiated and fully executed in two months. A rapid execution of the CTA allowed the NCI clinical trial to begin without delay. Data collection was completed in October 2020.

Since zotiraciclib targets multiple components of tumor cell survival and proliferation, it may enhance clinicians' ability to kill cancer cells and may reduce the potential for cancers to develop resistance to therapies – a particular challenge in treating glioblastoma. But in addition to glioblastoma, zotiraciclib has the potential to target multiple cancer indications, including hepatocellular tumors, as well as breast, ovarian, colorectal, pancreatic, and gastric cancers. ☞