Results from Phase 0/1 trial of ribociclib plus everolimus in patients with high-grade glioma announced

Reviewed by Emily Henderson, B.Sc. Sep 13 2021

The Ivy Brain Tumor Center at Barrow Neurological Institute, the largest early-phase drug development program for brain cancer in the world, announced results from their Phase 0/1 clinical trial of ribociclib plus everolimus in patients with high-grade glioma (HGG). The study found that ribociclib achieved pharmacologically-relevant concentrations in gadolinium (Gd)-non-enhancing tumor, consistent with the observed tumor pharmacodynamics (PD) effects; while everolimus demonstrated minimal penetration in the (Gd)-non-enhancing compartment of the tumor.

The purpose of the study was to determine the combined effect of RB-CDK4/6 and mTOR inhibitors on recurrent HGGs by evaluating the tumor pharmacokinetics (PK) and tumor pharmacodynamics (PD). The results were published in the journal of *Neuro-Oncology* and will also be presented at the EANO Meeting on September 26, 2021 by Nader Sanai, MD, director of the Ivy Brain Tumor Center and director of neurosurgical oncology at Barrow Neurological Institute.

The Ivy Brain Tumor Center has been investigating ribociclib in a monotherapy clinical trial for glioblastoma and while ribociclib exhibited good brain penetration, the single drug therapy had limited clinical efficacy. Longitudinal analysis of samples from the monotherapy trial provided the rationale for this first combination trial with ribociclib and everolimus to undermine resistance mechanisms.

> *Our primary focus is to discover new therapeutic drug combinations that can penetrate the blood-brain barrier, modulate their targets and ultimately prevent regrowth of cancer cells. This study demonstrated that everolimus does not sufficiently penetrate the brain tumor and its further development for this patient population is not recommended. Whereas, we continue to see positive results from ribociclib and believe there is promise in*

> *CDK4/6 inhibitors combined with other targeted therapies for the treatment of brain cancer."*
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> *Shwetal Mehta, PhD, chief operating officer and deputy director of the Ivy Brain Tumor Center*

In the last 30 years, there has only been one drug approved by the FDA with a survival benefit for glioblastoma, the most common brain cancer. The standard-of-care is not curative and most patients experience tumor progression after treatment. Unlike conventional Phase 1, 2 or 3 trials, the Ivy Center's Phase 0 trials bridge the gap between initial drug testing and definitive efficacy studies. The goal is to quickly identify how a drug works in patients and whether it should be fast-tracked for further development.

"An integral component of our Phase 0 clinical trials is genetic testing. We match new targeted drug combinations to our patients and can measure their effect in about 10 days," said Nader Sanai, MD. "The speed in which our clinical trials operate are paramount to our patients who desperately need effective treatment options for their case without losing valuable time."

Source:

Ivy Brain Tumor Center

Journal reference:

Sanai, N., *et al.* (2021) A Phase 0/1 'Trigger' Trial of Ribociclib Plus Everolimus in Recurrent High-Grade Glioma. *Neuro-Oncology.* doi.org/10.1093/neuonc/noab180.024.
