

Transcript Details

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Vorasidenib and mIDH Gliomas: Reviewing the Efficacy Data

Announcer:

You're listening to *NeuroFrontiers* on ReachMD. On this episode, we'll hear from Dr. Jennie Taylor, who's an Associate Professor of Neurology and Neurological Surgery at the University of California, San Francisco. She'll be discussing advancements and challenges in managing mutated isocitrate dehydrogenase, or mIDH, gliomas, which she spoke about at the 2025 American Academy of Neurology Annual Meeting. Let's hear from Dr. Taylor now.

Dr. Taylor:

I think that the current and future landscape of how to manage these mutant IDH gliomas is incredibly exciting. So the IDH mutation was originally discovered in about 2009, and here we are in 2025 with the first targeted treatment for mutant IDH cancers specifically for glioma patients. Vorasidenib was approved by the FDA in August of 2024, and it specifically was tested in patients who have histologically grade 2 IDH-mutant gliomas. This large phase III clinical trial—called the INDIGO study—was conducted in patients who had only received surgery at least a year ago and no more than five years ago with one of many different IDH mutations. The most common IDH mutation is IDH1 R132H. There are some noncanonical mutations, and there's no known prognostic relationship with which type of IDH mutation that you actually have.

So in the INDIGO study, these were all patients with known grade 2 tumors. These were patients who were essentially treatment naïve, aside from surgery, and had either residual or progressive nonenhancing or slow-growing changes on the MRI scans, and they were randomized to vorasidenib, which is an oral daily pan-IDH inhibitor and or placebo.

And so the updated data actually demonstrated that patients who were receiving vorasidenib at study entry versus those who were receiving placebo had essentially twice as long a time of progression-free survival. The primary outcome for this study was a radiologic endpoint, and this was a very well-designed clinical trial in that they also looked at some key secondary analyses, one being time to next intervention, and so this is really a very much a real-world experience. This was not a radiologist who was volumetrically looking at the MRI scans. This is the clinician who is seeing the patient on a day-by-day basis. And similarly, there was a significant improvement in patients who were receiving vorasidenib versus patients who were randomized to placebo at study entry.

This is really exciting data. There were about 300 patients enrolled in the study—very well balanced between the two groups. And however you slice and dice the data—based on the age, how large the tumor is, the number of prior surgeries, or the histology subtype of astrocytoma versus oligodendroglioma—all of these patients seem to equally benefit from receiving vorasidenib versus placebo.

Very excitingly, there does seem to be a demonstration of reduction in tumor growth by volume. It does seem to take a while for this treatment to work. I think these are slow-growing tumors and that, therefore, maybe they are slow to respond to this, but there does seem to be a trend that we'll learn more about over time where there actually is visual shrinkage of this tumor on the MRI scan and similarly a significant reduction in the number of seizures that patients are having.

I think the durability of this response is very much to be determined. So how long do these patients need to stay on this medication? These are young people who are early on in their careers, trying to decide how to have families. How do you navigate that component of needing to get bloodwork once a month and figuring out about your fertility plans and doing all that in the context of this drug that you may be on forever?

The INDIGO trial looked at vorasidenib in a very narrow window of patients, and I think that was actually very well designed, but it's also left a lot of questions to be answered. Does this work in patients who have grade 3 tumors? Does this work in people who've received radiation or chemotherapy in the past? One of the challenges of getting clinical trials done in low-grade gliomas for patients who live

decades is it takes a really, really, really long time to know if a drug actually improves survival, and I think there's a lot of questions that exist.

Announcer:

That was Dr. Jennie Taylor discussing the future of mIDH glioma management. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD dot com, where you can Be Part of the Knowledge. Thanks for listening!