Transcript Details
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mIDH Gliomas Explained: Characteristics and Management Strategies

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 characteristics of mutated isocitrate dehydrogenase, or mIDH, gliomas, and key considerations for treating them, which she spoke about at the 2025 American Academy of Neurology Annual Meeting. Let's hear from Dr. Taylor now.

Dr. Taylor:
To talk a little bit about what makes these isocitrate dehydrogenase, or IDH-mutant, gliomas unique from other types of tumors that arise in the brain, of which there are over 100, is this specific mutation within the isocitrate dehydrogenase pathway. So this is a functional enzyme that is present both in the mitochondria as well as in the cytoplasm of cells and is involved in the Krebs cycle, and during its normal function, isocitrate dehydrogenase ends up producing alpha-ketoglutarate, which goes on to power cells. And when this is mutated, for reasons that are not known, within brain tumors, the alpha-ketoglutarate gets translated into 2-hydroxyglutarate. And what we've learned about 2-hydroxyglutarate is that actually is an oncometabolite, so it promotes inappropriate cell division, DNA methylation, DNA demethylation, and tumor formation.

This is a slow process. These tumors happen more commonly in younger individuals, and we think—though, of course, we don't know—that it may take decades for these tumors to form. And this is in contradiction to glioblastoma, which is the most common primary brain tumor, which does not harbor this IDH mutation. That tumor is more common and much more aggressive with the shorter survival, and it's seen in older patients.

The treatment approach for these mutant IDH gliomas has historically been pretty controversial. I think because these are younger patients, this is a very rare tumor type, but it has a longer prognosis, so people are living longer with these types of tumors. So if you add up all of the patients who are living with a primary brain tumor, a lot of them end up having mutant IDH gliomas versus those with glioblastoma, who have a shortened survival. And because of that, deciding the best course of treatment has historically been a bit controversial, and that's because of the balance of quality of life that we're trying to help these patients preserve over potentially the course of decades. So long-term effects of things like radiation therapy and certain chemotherapies can, while helping to extend life, really significantly affect cognition, workability, seizures, and other key quality of life factors for patients, so it's really a very personalized approach.

I think one of the key components is how much of this tumor can be resected, and how can that be done safely. These IDH-mutant gliomas are within a category that does include glioblastoma of diffuse gliomas, so I describe this often to patients as weeds in a garden where the surgeon's trying to pull out a chunk of weeds, but we know there to be diffuse or microscopic disease always left behind. And so how much is able to be removed, and therefore, how much has to be left behind for maximal safe resection, often is one of the key factors that dictates the decisions of treatment. For a slow-growing, grade 2, IDH mutant tumor, we may just watch that patient over time.

Other patients that have more aggressive features histologically or patients for whom there is significant residual burden of disease based on the location of their tumor may require a more aggressive upfront treatment, such as radiotherapy or chemotherapy. And even the type of chemotherapy has been very controversial for how to manage these patients—either combination of procarbazine, CCNU and vincristine, or temozolomide, which is something that we use in a lot of other glioma types. And again, thinking about the long-term effects of those different treatments.

Announcer:
That was Dr. Jennie Taylor discussing characteristics of mIDH gliomas and how to treat them. To access this and other episodes in our series, visit *NeuroFrontiers* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!