Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/neurofrontiers/from-diagnosis-to-treatment-challenges-in-glioblastoma-care/32784/

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From Diagnosis to Treatment: Challenges in Glioblastoma Care

Announcer:
You're listening to *NeuroFrontiers* on ReachMD. On this episode, Dr. Lauren Schaff will discuss updates in glioblastoma management. She's a neuro-oncologist at Memorial Sloan Kettering Cancer Center, and she spoke on this topic at the 2025 American Academy of Neurology Annual Meeting. Let's hear from Dr. Schaff now.

Dr. Schaff:
Glioblastomas are the most common primary brain tumor, but they are very unique in terms of how they behave and are quite different from other brain tumors, like lower-grade gliomas, circumscribed gliomas, or, of course, meningiomas. From a molecular standpoint, we've come to understand that glioblastomas are different from other gliomas. By definition, they lack a mutation in a gene called isocitrate dehydrogenase, or IDH, and because of that, they seem to behave differently. They seem to be more aggressive. They seem to be less responsive to certain treatments, including chemotherapy. They are either grade 4 by histology, meaning they look fast-growing under the microscope or they have recruitment of new blood vessels—what we call neovascular proliferation or necrosis or increased mitoses—or they have a particular molecular marker that indicates they're capable of grade 4 behavior. So the three markers that we look for in a glioma to determine that are eGFR amplification, a TERT promoter mutation, or the simultaneous gain of chromosome 7 with loss of chromosome 10. And any single one of those things in the setting of an IDH wild-type glioma will constitute diagnosis of a GBM.

And then practically, they tend to occur in older patients than the other types of gliomas typically do. The median age of onset is about 60, and symptoms come on very quickly. These are very fast-growing tumors, so typically, symptoms develop over the course of weeks or months. They behave very aggressively, and quite honestly, they're hard to treat, and survival is shorter with these tumors than other brain tumor types.

You know, unfortunately, there have not been a lot in the way of recent advancements in terms of early detection or early diagnosis, and some of the reason for that is they come up so quickly. Patients can have had a clean MRI six months prior and then will be sitting in my office with a very symptomatic glioblastoma, so it's hard to really find them much earlier than they present. Where diagnostics have changed, though, is really how we think about these tumors and how we define what a glioblastoma is. We can better counsel patients who have a glioma that might not have fit the classic GBM criteria based on histology, but have a molecular signature that we now recognize to be very worrisome or aggressive, like the TERT promoter mutation, the EGFR amplification, or those chromosomal abnormalities. And we know how to counsel them and how to guide them. We have a better sense of what the natural history of their tumor is going to be, and we could be aggressive from the outset. That's really where things have changed in recent years.

In terms of promising therapeutics, there's a number of them. I think the two most exciting areas right now are, of course, immunotherapy, which everyone's very excited about, and then some of these more targeted or personalized approaches based on a tumor's genetic signature. We now have a number of studies that are looking at increasing neoantigen exposure, increasing response to immunotherapy. There's been some studies recently looking at vaccine therapy. CAR-T therapy is obviously an area of excitement for us, as it is for many in oncology. There's been a number of trials published with some mixed results, but recently, there have been some that look a bit more promising, including one that came out of Boston, which was a CAR-T agent combined with what's called a TEAM, or a T-cell engaging antibody molecule.

A lot of us in the field are optimistic that immunotherapy is a promising strategy that we just haven't quite figured out yet, but there's certainly a lot of work being poured into figuring out that space. And then in terms of targeted therapies, there are a few exciting studies looking at things like PARP inhibition or PMRT5 inhibition, and there are probably some glioblastomas that are going to be more

sensitive to these strategies than others based on the molecular profile or the next-generation sequencing, and so I think that's another exciting area of interest. That may not end up being applicable for everybody, but certainly, for certain tumors, I think we're going to make some progress.

There's a number of challenges when it comes to finding a cure for glioblastoma. This is a fairly rare tumor, which makes it hard to run large studies that we need to answer questions. Obviously, it's very eloquent brain tissue, so it's not always easy to obtain tissue at diagnosis and certainly not easy to follow along with what's happening in a tumor as patients are being exposed to different therapies, and that information could be very helpful in having us see what might be making what impact before we're having to follow all the way out to survival. They're very heterogeneous, so one part of the tumor might not look like the other part of the tumor. They could have different molecular signatures. It could have different driver mutations. That is definitely a challenge with some of our chemotherapeutics and targeted agents. And then, of course, it confers substantial morbidity and mortality.

I do think we're getting closer every day to overcoming some of these challenges. We're making a lot of progress, and I do believe that there are going to be substantial advancements, certainly in my lifetime, probably in my career. I'm hoping within the next decade even. I don't know that these advances will really lead to a cure, which would be wonderful, but maybe pie in the sky at this point. But I do think the goal of being able to control these tumors that patients can live with them and then minimizing toxicity for these survivors would be a huge win.

Announcer:
That was Dr. Lauren Schaff discussing updates in glioblastoma care. 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!