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Evaluating Patient and Clinician-Reported Responses to Axatilimab in cGVHD

Announcer:
You're listening to *Project Oncology* on ReachMD. And now, here's your host, Dr. Brian McDonough.

Dr. McDonough:
Welcome to *Project Oncology* on ReachMD. I'm Dr. Brian McDonough, and today, we'll be examining an analysis of the AGAVE-201 study that was presented at the European Hematology Association 2025 Congress. In particular, the analysis looked at correlations of clinician-reported responses with other response measures in patients with chronic graft-versus-host disease, or cGVHD for short, who received treatment with axatilimab. And joining me to discuss this analysis and its potential impacts on cGVHD treatment is Dr. Christopher Graham. He's an Assistant Professor of Medicine in the Division of Hematology, Oncology, and Transplantation at the University of Minnesota. Dr. Graham, thanks for being here today.

Dr. Graham:
Thank you so much for having me, Dr. McDonough.

Dr. McDonough:
To set the stage for our discussion, Dr. Graham, could you briefly recap the AGAVE-201 trial and the main objectives behind this post hoc analysis?

Dr. Graham:
Yes. So the AGAVE-201 clinical trial was a phase two, multi-institution that compared axatilimab at three different doses: a 0.3-mg/kg, a one-mg/kg—both of those every two weeks—and a three-mg every-four-week dose of axatilimab to evaluate response in patients who have had at least two prior systemic therapies for chronic graft-versus-host disease.

They found that the 0.3-mg/kg dosing had a great response, with overall response rate over 70 percent and an improved failure-free survival compared to the other doses, and with pretty good tolerability, with low grade-three-to-four adverse events.

There was a post hoc analysis that was presented at EHA that was looking at clinician-reported outcomes as well as patient-reported responses in comparison to the NIH 2014 Assessment, or ORR.

Dr. McDonough:
With that background in mind, let's take a look at some of the findings. Among the 33 patients in the 0.3-mg/kg group who achieved a National Institutes of Health-Overall Response Rate, or NIH-ORR, 75.8 percent also had clinician-reported symptom improvement. Among the 14 with no NIH-ORR, 28.6 percent had clinician-reported symptom improvement. So what does this tell us about the utility and reliability of these two response measures?

Dr. Graham:
So the correlation between the two is quite fair. It seems that the NIH Overall Response Rate undercounts how many patients actually derive benefit based off of the clinician response rate. And that's mostly due to how the scoring is done, with pretty broad categories and response rates based off of the NIH score, compared to a global assessment on how the patient is doing based off the clinician assessment, which is usually a scale of zero to 10—with anything more than a two-point improvement being a modest to a very big improvement. And that's typically more associated with a favorable response based off of how the clinicians are evaluating the patients, whereas the NIH scoring sometimes can miss improvements.

For instance, with BSA as part of the NIH scoring, it can be anywhere from 18 to 50 percent whether a point changes. And patients can have improvement of their skin GVHD within that 18 to 50 percent, which is improvement and might impact their quality of life or how the physician sees their improvement for chronic graft-versus-host disease.

Dr. McDonough:
And if we zero in on the patient-reported data for a moment, 75.8 percent of patients in the 0.3-mg/kg group who achieved an overall response-reported improvement on the Modified Lee Symptom Scale, or mLSS. Out of the 15 with no overall response, 40 percent reported mLSS improvement. What do these findings suggest about how patients experience benefit, even in the absence of a formal overall response?

Dr. Graham:
Yeah, so typically, the NIH Response Scale seems to correlate poorly with a Modified B-Symptom Scale, or they seem to be incongruent, at least when it comes to what it classifies as non-responders.

Now, the Modified B-Symptom Scale looks at seven-day recall on patients based off of their chronic graft-versus-host disease symptoms and typically includes skin, mouth, eyes, joints, and lung symptoms. And what this shows is that patients tend to feel better, even though, based on objective data, it looks like they're not improving or not responding to the current NIH-ORR.

And what that shows is that, as we know, chronic graft-versus-host disease is a very comorbid condition with a lot of morbidity, and directly affects patients' quality of life, how they feel about their treatment, and how they're doing. Adding patient-reported outcomes shows to have some benefit in addition to just the standard objective scoring system. And what it can tell us, and what can help predict with us is that patients might tolerate treatment a lot longer if they're feeling better on it, if they feel like they're doing well on it, and their symptoms are improving. And that, at the end of the day, is what we're here for when we're treating graft-versus-host disease: to improve the morbidity and improve survival in patients with this debilitating condition.

Dr. McDonough:
Now, the final data point I'd like to explore is durability. Analysis of the failure-free survival, or FFS, shows significantly longer FFS in patients from the 0.3-mg/kg group who had clinician-reported improvement compared to those who did not. How could these findings help inform treatment decisions, such as whether to continue or taper therapy?

Dr. Graham:
So usually when physicians see the patients before they can have a total NIH score, you can see some degree of improvement. It doesn't meet the full criteria—the NIH-ORR—so being able to see these patients and how they're doing based off of how the physician sees them, whether their GVHD is improving or not, can help guide whether or not to stop therapy or to proceed to another therapy. And if the patients are doing extremely well, for those that actually did have a great response, you actually can de-escalate therapy based off of how the patient is doing, less based on the NIH score.

For patients that are not doing well, or those that are progressing, then that would be an early indicator that maybe the therapy isn't working. Even though, traditionally, as you might be aware, the axatilimab median duration of response can be anywhere from four to eight weeks. So assessing the patients between that time, after several doses of axatilimab, you'll be able to tell if the patient is responding or not and change therapies if they're not improving.

Dr. McDonough:
For those just tuning in, you're listening to *Project Oncology* on ReachMD. I'm Dr. Brian McDonough, and I'm speaking with Dr. Christopher Graham about response measures in patients with chronic graft-versus-host disease receiving axatilimab.

Now that we've examined the data, let's talk about the practical application. How should we balance objective response data with symptom-based data assessments when deciding whether to adjust treatment?

Dr. Graham:
So I think it all comes down to what the patient desires or what the patient needs. For instance, if a patient states that they're feeling a lot better from a chronic graft-versus-host disease standpoint but their objective data does not support that, that goes to continuing treatment because the patient is doing well and it's improving their quality of life and their ability to tolerate day-to-day acts of living. When it comes to clinician response, if you see that a patient is doing well and they are looking better to you, that would also guide continuing treatment.

So I think it's important to incorporate both the patient response as well as the clinician response, in addition to the NIH score, which is great and is a great ballpark for monitoring GVHD, but is not the end-all be-all with how the patient is doing in our clinical practice at this time. And I think incorporating both clinician assessments in addition to the NIH score and PROs, patient-reported outcomes, in the form

of the Modified B-Symptom Scale or the PROMIS-29, helps benefit patients.

Dr. McDonough:
As we come to the end of our program, Dr. Graham, how do you believe these findings could shape the way we define response criteria or treatment goals?

Dr. Graham:
So there has been an increased shift in how we evaluate clinical trials, even in the past five years, when it comes to chronic graft-versus-host disease. Before, we were mostly focused on the NIH score, but now we've been further and further increasing our use of patient-reported outcomes because we know how key and pivotal it is for the lives of our patients, how they're feeling, and how they're doing on treatment.

I think it's beneficial both with AGAVE-201, as well as some other previous studies that looked at other drugs, such as belumosudil, that started to incorporate patient-reported outcomes when it comes to response rates. And both of those drugs have shown that even if they're not having improvement by NIH score, if they're having some degree of symptomatic control, that—based off the patient, what they're experiencing—it's beneficial to the patient.

So I think what we'll see is we'll have more focus on patient-reported outcomes when it comes to clinical trials and patients with chronic graft-versus-host disease. Because again, at the end of the day, it all depends on how the patient feels, how they're doing, and how they see success for their disease.

Dr. McDonough:
With those final insights in mind, I want to thank my guest, Dr. Christopher Graham, for joining me to discuss how response data from the AGAVE-201 study can inform decision-making for patients with chronic graft-versus-host disease. Dr. Graham, it was great having you on the program.

Dr. Graham:
Thank you so much for having me.

Announcer:
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