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Chronic GVHD Care: Examining the Efficacy and Safety of Axatilimab

Dr. Caudle:
Welcome to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and joining me to discuss his plenary session talk at the 2023 American Society of Hematology Annual Meeting and Exposition is Dr. Daniel Wolff. He's a Professor in the Department of Internal Medicine at the University Hospital Regensburg in Germany, and his research focused on the safety and efficacy of axatilimab at three different doses in patients with chronic graft-versus-host disease, or GVHD, for short.

Dr. Wolff, thank you so much for being here today.

Dr. Wolff:
You're very welcome.

Dr. Caudle:
So if we start off with some background, Dr. Wolff, how does axatilimab work to treat patients with chronic graft-versus-host disease?

Dr. Wolff:
I need to start with chronic graft-versus-host disease, which is a long-term complication and the most prominent long-term complication after allogenic stem cell transplantation, which leads to inflammation, destruction, and subsequent fibrosis of tissues of the patient, which leads those patients to be cured by their malignancy but experiencing disability to this fibrosing process. And one of those pathways active in this fibrosing process is the axatilimab target, which is the CSF-1 receptor.

This was first identified in mice, and then subsequently, an antibody, axatilimab, targeting the CSF-1 receptor was explored in a phase 1/2A trial in humans with chronic graft-versus-host disease, which led to significant success. And the trial I shared at the last ASH meeting was a pivotal trial exploring axatilimab in a much larger patient population and trying to identify the optimal dose for further treatment of patients with chronic graft-versus-host disease.

Dr. Caudle:
Excellent. Thank you so much for that. And with that in mind, let's zero in on your research. How was the study designed? And what methods were used?

Dr. Wolff:
This was a randomized trial—not randomized against something else—but a randomized trial comparing different doses of axatilimab with two schedules and three different doses aiming to identify that optimal dose with regard to efficacy and safety.

And acknowledging that the number of patients in a phase 1/2A trial was feared too low to identify that optimal dose, this was a global trial run across the globe in very different regions. In fact, the region didn't make a difference in response, and I've already said this at the beginning, but this trial is aiming to kind of settle the dose of axatilimab to be used in the future.

Dr. Caudle:
Excellent. Thank you. And for those of you who are just tuning in, you're listening to *Project Oncology* on ReachMD. I'm your host, Dr. Jennifer Caudle, and I'm speaking with Dr. Daniel Wolff about his research focusing on the safety and efficacy of axatilimab in patients with chronic graft-versus-host disease.

So, Dr. Wolff, if we turn our attention to the findings, what were the results regarding the primary endpoint?

Dr. Wolff:

So the primary endpoint was assessed at 6 months, and that was overall response in patients treated. The lower threshold was to find a successful response rate of 30 percent. In fact, all three doses had reached that margin, leaving a response rate ranging between 74 percent and 50 percent. So basically, at least half the patient responded to the treatment, and the most interesting finding was that the lowest dose performed best with the 74 percent response rate. Although it's not fair to say that this was because of the lowest dose because the trial was never powered to compare efficacy with dose.

Dr. Caudle:
Excellent. And how about the secondary and exploratory endpoints? What were the findings there?

Dr. Wolff:
One of those findings were that the speed of the response was fairly high as seen in the overall response but also in the reduction of symptom burden and a median responded within the first 1.5 months, which was pretty quick given that those patients had mostly fibrotic disease, which was hard to resolve on other treatments. This was a surprising finding.

The second issue was that patients showed significant reduction in symptom burden. Axatilimab worked across all organs, including those with fibrotic manifestations like lung disease, esophageal involvement, and also skin involvement, showing a significant reduction in the body surface involved and also in the sclerosing changes.

One remarkable thing to be mentioned was that patients were also included in the presence of severe lung disease, which is usually a form of the disease excluded from other trials. And one other remarkable finding that was neither the number of organs, the severity of organs, nor the prior treatment affected response to axatilimab.

So regardless of how long the patients were treated, how sick they were, and which agents were used, all patients showed the same benefit from being treated with axatilimab.

Dr. Caudle:
Thank you for that. And now if we focus on the safety profile of axatilimab, can you tell us about the adverse events you saw in the study?

Dr. Wolff:
The adverse events were pretty low and manageable. And the adverse effect rate increased with dosing. So while there was only a minority of patients stopping treatment off axatilimab due to adverse effects in the low-dose open 3 mg/kg arm, there was a significant larger proportion in the high-dose arm. And there was one specific side effect associated with the CSF1 receptor pathway, which is periorbital edema, which increased with dosing and was pretty minor in low doses.

There is another side effect, which is not a classic side effect but a diagnostic dilemma; axatilimab depletes Kupffer cells in the liver, leading to prolonged circulation of liver enzymes and pancreatic enzymes, which is not marker of organ damage but makes it difficult to assess organ damage. And also, this was dose-dependent with those patients receiving the low dose and had pretty minor problems with that.

There were no signs of increased infectious rates, which is a very important safety aspect in patients being immunocompromised by disease and immunocompromised by prior immunosuppression, and the rate of severe infectious complications, especially in the low-dose arm, was pretty low given those heavily pretreated patients.

Dr. Caudle:
Thank you so much for breaking all that data down for us, Dr. Wolff. And just to bring this all together before we close, what conclusions can we draw from this study? And how might these findings impact the way we manage patients with chronic graft-versus-host disease?

Dr. Wolff:
So to conclude, axatilimab with a dose of 0.3 mg/kg given every second week is a safe agent with remarkably high efficacy in advanced chronic graft-versus-host disease; it comes with a manageable safety profile. In fact, compared to other agents, a favorable safety profile. The AGAVE-201 trial exploring axatilimab also demonstrated that different phases of chronic graft-versus-host disease may require different approaches, given that we treated patients with fibrotic manifestations who failed multiple prior lines and had a response rate of up to 74 percent, which leads to the question whether axatilimab could be also used in earlier phases of the disease to prevent this damage to happen, which are trials that are just now starting.

Dr. Caudle:
That's a great way to round out our discussion today, and I'd like to thank my guest, Dr. Daniel Wolff, for joining me to discuss his talk at the plenary session of the 2023 American Society of Hematology Annual Meeting and Exposition.

Dr. Wolff, it was great having you on the program today.

Dr. Wolff:
You're highly welcome.

Dr. Caudle:
For ReachMD, I'm your host, Dr. Jennifer Caudle, and to access this and other episodes in our series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening.