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/project-oncology/advances-in-chronic-gvhd-care-insights-from-the-agave-201-trial/32950/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Advances in Chronic GVHD Care: Insights from the AGAVE-201 Trial

Announcer:
You're listening to *Project Oncology* on ReachMD. And now, here's Dr. Robert Walker.

Dr. Walker:
Welcome to ReachMD. Today, we're diving into recent research from the *New England Journal of Medicine* on managing chronic graft-versus-host disease, or GVHD, with axatilimab.

As we know, chronic GVHD is a serious complication of allogeneic hematopoietic stem-cell transplantation, affecting nearly half of transplant recipients. It significantly impacts patient quality of life, often leading to severe inflammatory and fibrotic complications across multiple organ systems. And despite available therapies, many patients continue to experience inadequate responses.

Researchers in the Phase II AGAVE-201 trial aimed to address this gap by evaluating the efficacy and safety of axatilimab, a monoclonal antibody that blocks the colony-stimulating factor 1 receptor, or CSF1R. This receptor plays a key role in activating the monocytes and macrophages that drive chronic GVHD pathology.

The multinational study enrolled 241 patients with recurrent or refractory disease after at least two prior systemic therapies. Patients were randomized into three dosing groups of intravenous axatilimab, from lowest to highest:

- 0.3 milligrams per kilogram of body weight every two weeks,
- one milligram per kilogram every two weeks, and
- three milligrams per kilogram every four weeks.

The primary endpoint was overall response rate, defined as a complete or partial response within the first six treatment cycles. And a key secondary endpoint measured clinically meaningful symptom reduction, defined as a greater than five-point improvement on the modified Lee Symptom Scale.

So, how did axatilimab perform? Let's break it down.

The primary endpoint was met across all dose levels, meaning axatilimab demonstrated clinical activity regardless of the dosing regimen. The overall response rates were

- 74 percent of patients in the lowest-dose group,
- 67 percent in the mid-dose group, and
- 50 percent in the highest-dose group.

As we can see, higher doses didn't necessarily lead to better response rates. And when looking at symptom improvement, there's a similar trend:

- 60 percent of patients in the lowest-dose group reported a meaningful improvement in symptoms compared to
- 69 percent in the mid-dose group, and
- 41 percent in the highest-dose group.

Most patients responded quickly to axatilimab, seeing improvement within two months. It's also worth noting that many patients on glucocorticoids at the start of the study were able to reduce or even stop their steroid use.

Beyond the numbers, researchers noted that clinical response wasn't tied to baseline disease characteristics. Patients saw benefit regardless of chronic GVHD severity, the number of organs involved, the duration of disease, or prior treatments. That's a critical insight, reinforcing axatilimab's potential across a broad patient population.

Now, let's talk about safety. As expected for a CSF1R inhibitor, on-target effects—including laboratory abnormalities and periorbital edema—were dose-dependent, but they were generally transient and asymptomatic.

Grade three or higher adverse events with axatilimab occurred in

- 49 percent in the lowest-dose group,
- 60 percent in the mid-dose group, and
- 71 percent in the highest-dose group.

And serious adverse events led to treatment discontinuation in six percent, 22 percent, and 18 percent, respectively.

So, what does this mean for patients with chronic GVHD? Axatilimab appears to offer a targeted and effective option for those with recurrent or refractory chronic GVHD, even in cases where standard-of-care therapies have failed. The lowest dose of 0.3 milligrams per kilogram every two weeks may strike a better balance between efficacy and tolerability, making it an option worth further exploration.

And here's something worth emphasizing: about half of patients not only responded to the therapy, but also experienced a rapid, clinically meaningful reduction in symptoms. For patients with chronic GVHD—who often face severe complications from both the disease and its treatments—this could translate into significant quality-of-life improvements.

That said, important questions remain, including "How durable are these responses long-term?" and "How does axatilimab compare to other emerging treatments?" Further research can help clarify where axatilimab fits in the chronic GVHD treatment landscape.

Announcer:
You've been listening to *Project Oncology*. To access this and other episodes inour series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening!

Reference:
Wolff D, Cutler C, Lee SJ, et al. Axatilimab in Recurrent or Refractory Chronic Graft-versus-Host Disease. *N Engl J Med*. 2024;391(11):1002-1014. doi:10.1056/NEJMoa2401537