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Axatilimab for Chronic Graft-Versus-Host Disease: A Look at a Phase 3 Trial

Dr. Blevins:
You're listening to *Project Oncology* on ReachMD, and this is an *AudioAbstract*. I'm Dr. Hallie Blevins, and today, I'll be discussing the rationale, design, and endpoints of an ongoing Phase 3 study evaluating axatilimab compared with the best available therapy in patients with chronic graft-versus-host disease, or cGVHD, who've received at least two prior lines of systemic therapy. These results were presented as a trial-in-progress poster at the 2025 European Hematology Association Congress.

Now, first, it's important to note that cGVHD is one of the most significant late complications after allogeneic hematopoietic stem cell transplantation, and it remains a major cause of long-term morbidity and nonrelapse mortality. The disease can affect multiple organ systems, with symptoms that can be highly debilitating, often requiring prolonged systemic therapy. So, what does this mean in terms of treatment? Let's take a look at where there's still an unmet need.

The current standard approach begins with corticosteroids, frequently in combination with other immunosuppressive drugs such as ruxolitinib. While these therapies can be effective initially, many patients will either not respond adequately or will relapse once the treatment is tapered.

And for those with refractory disease, treatment options are limited. In addition, chronic reliance on broad immunosuppression carries its own risks, such as infection, metabolic complications, and organ toxicity. This means the search for targeted, disease-modifying approaches is critical.

Now, here's where axatilimab comes in—and why it's different. Axatilimab is a high-affinity monoclonal antibody targeting the colony-stimulating factor 1 receptor, or CSF-1R. This receptor is expressed on monocytes and macrophages, immune cells that are known to play a central role in driving inflammation and fibrosis in cGVHD. And by preferentially depleting CSF-1R–dependent monocytes and reducing pro-fibrotic macrophage populations within affected tissues, axatilimab offers a novel mechanism of action that is distinct from broad immunosuppressive agents.

So, let's go over the study design for this Phase 3 trial. It's an open-label randomized study with plans to enroll about 300 patients aged 12 years or older across 130 sites in 16 European countries. All study participants must have active, moderate-to-severe cGVHD, and must have received at least two prior systemic regimens, including corticosteroids and ruxolitinib.

Patients will be randomized one-to-one to receive either axatilimab 0.3 milligrams per kilogram every two weeks, or investigator-selected best available therapy from a predefined list. It includes commonly used agents such as calcineurin inhibitors, mTOR inhibitors, extracorporeal photopheresis, mycophenolate mofetil, rituximab, and others. Treatment is planned for up to 24 months, delivered in 28-day cycles, with the option to extend to 60 months for those continuing to derive benefit.

An important feature of this trial is the crossover option. Patients on best available therapy may switch to axatilimab if they don't achieve at least a partial response, they experience worsening disease, or they develop unacceptable toxicity after the six-month primary endpoint assessment.

So now let's talk through the study endpoints. The primary endpoint is objective response at six months, defined as complete or partial response per the 2014 NIH Consensus Criteria without the need for new systemic therapy.

And beyond that main outcome, the study's also looking closely at several important secondary measures. These include failure-free survival, symptom improvement as measured by a minimum seven-point gain in the modified Lee Symptom Scale, objective response

at 12 months, best overall response, duration of response, organ-specific responses, corticosteroid dose reduction or discontinuation, overall survival, and nonrelapse mortality. Safety and tolerability are also major components, with adverse events monitored closely and performance status assessed throughout treatment.

So, why does all this matter for patients and clinicians? Well, by directly comparing axatilimab to best available therapy in a randomized setting, this trial is designed to generate definitive evidence for a differentiated third-line option, one that addresses the cellular drivers of cGVHD pathology rather than broadly suppressing the immune system. If successful, the results could support a shift toward more targeted, mechanism-based treatment strategies for patients who've exhausted conventional options.

Looking ahead, this study has the potential to shape the cGVHD treatment landscape. Beyond the primary readout, the breadth of secondary and exploratory endpoints will provide valuable insights into symptom control, quality of life, organ-specific improvement, and the potential for reducing steroid dependence: all areas that matter greatly to patients and treating clinicians alike.

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Reference

Kwon M, Bonifazi F, Broers AEC, et al. PF1090: Trial in progress: a randomized, open-label, phase 3 study of axatilimab vs best available therapy in patients with chronic graft-versus-host disease after ≥2 prior lines of systemic therapy. Poster presented at EHA 2025 Congress; June 12-15, 2025; Milan, Italy.