

Post Hoc Analysis Highlights Impact of Cytopenias on Response Rates in Acute GVHD



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A recent *Between the Lines* program hosted by CancerNetwork reviewed a post hoc analysis of the phase 3 REACH2 study (NCT02913261), which investigated the occurrence of patients who experienced cytopenias when treated with ruxolitinib (Jakafi) or best available therapy for steroid-refractory acute graft-vs-host disease (GVHD).¹ Nelson J. Chao, MD, MBA, and Michael Grunwald, MD, discussed the impact of the treatment and its adverse effects (AEs) on this patient population.

During the program, Chao and Grunwald discussed GVHD as a whole and evaluated current guidelines for treatment and the results of the REACH2 study. They also considered how these new data might affect the standard of care in treating patients with GVHD.

Acute vs Chronic GVHD

Grunwald began the conversation by reviewing the onset of GVHD occurring within the first 100 days of treatment. He noted that it can occur farther out, specifically if a patient is undergoing immunosuppression. When GVHD occurs, the

digestive system or the liver is most affected, Grunwald said. “[GVHD] happens quickly when it manifests in the skin. We usually see this as a sunburnlike rash, and it can be severe in some circumstances,” he said.

Diarrhea, nausea, or vomiting can signal to clinicians that the condition has affected the digestive system. In particular, when the GVHD is attacking the liver, patients will have increased bilirubin levels and can become jaundiced.

Chao mentioned the differences between chronic and acute GVHD; they present in different ways. “Chronic GVHD is much more of an auto-immunelike disease rather than acute hyperinflammation,” Chao said.

Grunwald noted that when chronic GVHD occurs, patients will often experience sclerosis of the skin and sickle cell syndrome. If patients previously had acute GVHD, they may be susceptible to chronic GVHD as well.

Grunwald said he considers chronic GVHD to be a rheumatologic type of condition that includes features from many different autoimmune conditions. Regarding acute GVHD,

when immunosuppression such as tacrolimus is tapered, symptoms can occur after more than 100 days, he said.

The current National Comprehensive Cancer Network guidelines for the treatment of patients with acute GVHD include the only FDA-approved agent, ruxolitinib.² However, there are multiple treatment options recommended for both acute and chronic GVHD. “It’s a little bit of a free-for-all when we think about the other therapies that we can use in that context for steroid-refractory GVHD. There are some data with these therapies that patients can respond to, but not on the level of a randomized-controlled trial,” Grunwald said.

REACH2 Trial

The REACH2 trial enrolled 309 patients, with 302 assigned in the efficacy population to either the ruxolitinib arm (n = 152) or the best available therapy arm (n = 150). Patients were given 10 mg twice daily of ruxolitinib or the best available therapy.

Overall response rates (ORRs) for patients who experienced cytopenias were evaluated on day 28, and durable

response rates were evaluated on day 56. Patients were stratified into subgroups by white blood cell (WBC) count of less than 5×10^9 cells/L, absolute neutrophil count of less than 1×10^9 cells/L, platelet count of less than 30×10^9 cells/L, and hemoglobin of less than 8 g/dL.

The ORR was higher with ruxolitinib compared with best available therapy, as indicated by odds ratios (ORs), for those in the WBC (low OR, 2.7; 95% CI, 1.6-4.6; not-low OR, 1.9; 95% CI, 0.6-6.3), absolute neutrophil count (low OR, 5.2; 95% CI, 2.0-6.3; not-low OR, 2.0; 95% CI, 1.2-3.5), platelet count (OR, 2.6; 95% CI, 1.3-5.0; not-low OR, 2.5; 95% CI, 1.3-4.9), and hemoglobin (low OR, 4.8; 95% CI, 2.1-10.8; not-low OR, 1.8; 95% CI, 1.0-3.2) subgroups.

Similarly durable response rates were higher with ruxolitinib vs best available therapy for those in the WBC (low OR, 1.6; 95% CI, 0.8-3.2; not-low OR, not eligible), absolute neutrophil count (low OR, 0.7; 95% CI, 0.2-2.9; not-low OR, 1.8; 95% CI, 0.8-3.9), platelet count (low OR, 1.2; 95% CI, 0.5-3.1; not-low OR, 1.4; 95% CI, 0.6-3.8), and hemoglobin (low OR, 3.9; 95% CI, 1.0-15.1; not-low OR, 1.1; 95% CI, 0.5-2.3) categories.

Through week 24, the mean platelet counts and hemoglobin concentrations were decreasing over the first 4 to 8 weeks and then recovering. Additionally, the WBC counts decreased through week 8 and then were lower in the ruxolitinib arm at week 24. Within the first 4 weeks of treatment, the median ruxolitinib dose was at or near 20 mg/dL in nearly all the subgroups regardless of cytopenia status.

“The authors concluded that, regardless of the presence or absence of cytopenias, most patients treated with ruxolitinib showed treatment responses,” Chao said.

As cytopenias are typically a sign of GVHD, in this situation, Grunwald said he feels confident when he sees them

emerge on this treatment because they are AEs. “Looking at these data inspires me to want to press on with ruxolitinib when I see a little bit of a dip in the counts. However, if a patient is experiencing significant toxicity, we will hold ruxolitinib.”

Chao agreed, noting that the response rates in the trial aren't bad for ruxolitinib use in the patient population. Because there are limited treatment options in the acute GVHD setting, clinicians will often push thrombocytopenia by the transfusion of platelets, hoping to get a response during the first few weeks, he added.

Key Takeaways

Grunwald stressed that it's important to be confident in continuing ruxolitinib treatment even when cytopenias are occurring, because a response may happen. Additionally, a dose adjustment, a transfusion, or holding of treatment is acceptable for patients in order for them to experience a response, he said.

Chao reviewed an unmet need in the space, which is a continued response. Although the ORR was “quite good,” there still needs to be longer-term follow-up data to confirm the results, he concluded. ■

References

1. Mahmoudjafari Z, Socié G, Bhatt V, Galvin J, Xue Z, Mohty M. Impact of cytopenias in patients treated with ruxolitinib versus best available therapy for steroid-refractory acute graft-versus-host disease: a REACH2 post hoc analysis. Presented at: 2023 Transplantation & Cellular Therapy Meetings of ASTCT and CIBMTR; Orlando, FL; February 15-19, 2023.
2. NCCN. Clinical Practice Guidelines in Oncology. Hematopoietic cell transplantation, version 1.2023. Accessed May 23, 2023. <https://bit.ly/42azCXu>