

Transcript Details

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Momelotinib vs. Ruxolitinib: Comparing Efficacy in Myelofibrosis and Anemia Patients

Announcer:

You're listening to *Project Oncology* on ReachMD, and this episode is brought to you by GlaxoSmithKline. Here's Dr. Matt Birnholz.

Dr. Birnholz:

JAK inhibitors like ruxolitinib are a mainstay of treatment for myelofibrosis, but they may exacerbate anemia in some patients, affecting as many as one-third at diagnosis and nearly all over the course of treatment. Which begs the question: are there any other effective approaches we can use to manage myelofibrosis and anemia?

This is *Project Oncology* on ReachMD, and I'm Dr. Matt Birnholz. On today's episode, we'll dive into a post-hoc, subgroup analysis of the SIMPLIFY-2 trial, which compared the efficacy of momelotinib to best available therapy, which was primarily continued ruxolitinib, in patients with myelofibrosis and anemia who were previously treated with a JAK inhibitor.

Now for some background on the study, SIMPLIFY-2 was a randomized, open-label, phase 3 trial. Its goal was to examine if patients with baseline hemoglobin levels below 100 grams per liter and those who were transfusion dependent at baseline could achieve transfusion independence by week 24 with momelotinib. The study also examined momelotinib's effects on spleen volume reduction and symptom response from baseline to 24 weeks. Now to achieve these objectives, patients were randomized 2:1 to receive momelotinib daily or continue best available therapy, with 104 patients enrolled with moderate-to-severe anemias and 105 who were transfusion dependent. Across the subgroups, the mean duration of prior ruxolitinib treatment was greater than 59 weeks.

So with that background in mind, let's zero in on the results. Better mean hemoglobin levels and control along with higher median transfusion independence rates were observed over time in both subgroups.

Additionally, momelotinib was able to better manage splenomegaly, as evidenced by higher response rates of at least 35 percent. Similarly, a higher rate of symptom response, as defined by a total symptom score reduction of 50 percent or greater, was also observed in patients who were treated with momelotinib, regardless of the subgroup.

And collectively, these results suggest that momelotinib potentially offers a more comprehensive management strategy by addressing the underlying molecular mechanism of anemia, which may be due to its mechanistic difference from available therapies like ruxolitinib. Specifically, while both ruxolitinib and momelotinib inhibit JAK1/JAK2, momelotinib mechanistically differs by also inhibiting activin A receptor type 1. And this is supported by comparable safety results of these subgroups in previous reports.

So while additional research is warranted to evaluate the long-term benefits and its wide applicability, momelotinib appears to offer better outcomes for myelofibrosis patients with moderate-to-severe anemia and/or transfusion dependence who were previously treated with JAK inhibitors.

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Reference

Harrison, C.N., Vannucchi, A.M., Recher, C. *et al.* Momelotinib versus Continued Ruxolitinib or Best Available Therapy in JAK Inhibitor-Experienced Patients with Myelofibrosis and Anemia: Subgroup Analysis of SIMPLIFY-2. *Adv Ther* 41, 3722–3735 (2024). <https://doi.org/10.1007/s12325-024-02928-4>

