Novel combination therapy found to significantly reduce spleen volume in patients with myelofibrosis

December 11 2023

Credit: Pixabay/CC0 Public Domain

Combining the JAK inhibitor ruxolitinib with the BCL-xL inhibitor navitoclax was twice as effective in reducing enlarged spleens—a major

indicator of clinical improvement—compared with standard-of-care ruxolitinib monotherapy for adult patients with intermediate or high-risk myelofibrosis, a rare bone marrow cancer, according to results of the Phase III TRANSFORM-1 trial reported by researchers from The University of Texas MD Anderson Cancer Center.

Data from the global, randomized, placebo-controlled clinical trial were presented at the 2023 American Society of Hematology (ASH) Annual Meeting by Naveen Pemmaraju, M.D., professor of Leukemia.

At the time of data cut-off, 63.2% of patients who received ruxolitinib and navitoclax achieved a spleen volume reduction of at least 35% within 24 weeks, compared to 31.5% of patients receiving ruxolitinib plus placebo, meeting the study's primary endpoint.

"By adding a second drug to an approved therapy, we were able to improve spleen volume reduction compared to the current standard of care. This is an important measurement of the clinical benefits of this novel drug combination because treatments can be less effective when the spleen remains enlarged," Pemmaraju said. "If we can treat myelofibrosis earlier on in the disease course, we may have an opportunity to impact overall disease modification, improve patient outcomes and reduce symptom burden."

Currently, there are few Food and Drug Administration-approved drugs for the treatment of myelofibrosis. Available options provide patients with spleen and symptom improvement, but a substantial unmet need remains for therapies that provide durable spleen size reduction and other longer-term clinical. Allogenic stem cell transplants are an effective treatment option, but not all patients qualify.

This international trial enrolled 252 patients with intermediate or high-risk myelofibrosis and measurable spleen enlargement who had not

received prior JAK inhibitor treatment. The trial randomized 125 patients to receive the navitoclax and ruxolitinib combination and 127 patients to receive ruxolitinib plus placebo. Most patients were male (57%) and the median age was 69.

The trial met its primary endpoint of spleen volume reduction at 24 weeks. Spleen volume reduction at any time was achieved by 77% of patients on the combination arm and 42% of patients on the control arm. The median time to first spleen volume reduction response was 12.3 weeks with the combination and 12.4 weeks with monotherapy. At 24 weeks, there were no significant differences between the groups in a myeloproliferative neoplasm symptom assessment, a secondary endpoint of the study.

Patients treated with the combination therapy, patients experienced side effects that were manageable and consistent with previous trials. The most common treatment-related side effects were thrombocytopenia, anemia, diarrhea and neutropenia. Serious adverse events were experienced by 26% of patients on the combination arm and 32% on the control arm.

"This study marks a notable achievement in the field of myelofibrosis, as one of the first reported global Phase III frontline randomized combination clinical trials in our field," Pemmaraju said.

"This dataset now opens the door for additional research and investigation into combination therapies to treat myelofibrosis and, importantly, highlights a potential new era of investigating disease modification for patients. Additional data from the TRANSFORM-1 study is being evaluated."

Provided by University of Texas M. D. Anderson Cancer Center