Targeted therapy momelotinib provides significant symptom and anemia improvements in patients with myelofibrosis

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Patients with myelofibrosis had clinically significant improvement in disease-related symptoms, including anemia and spleen enlargement,

when treated with the targeted therapy momelotinib, according to results from the international Phase III MOMENTUM trial led by researchers at The University of Texas MD Anderson Cancer Center.

The findings, published today in *The Lancet*, support the use of momelotinib—a potent ACVR1/ALK2 and JAK1/2 inhibitor—over the standard therapy danazol in treating myelofibrosis patients that were resistant, refractory or intolerant to firstline therapy, especially symptomatic patients and those with anemia.

"Current options for managing anemia in our myelofibrosis patients provide only modest and temporary benefits, so we are excited about these findings," said study lead Srdan Verstovsek, M.D., Ph.D., professor of Leukemia. "The trial results suggest that momelotinib is safe, well-tolerated and can improve one of the most common and debilitating clinical problems for this patient population."

Myelofibrosis is an uncommon bone marrow cancer that is part of a group of diseases known as myeloproliferative neoplasms. A hallmark of the disease is dysregulated JAK signaling, which disrupts the body's normal production of blood cells and leads to common symptoms, including an enlarged spleen and anemia. Chronic anemia in these patients is associated with poor prognoses.

Currently approved JAK inhibitors can improve spleen responses and other disease-related symptoms, but they also can worsen anemia. In this trial, momelotinib improved anemia and reduced transfusion dependency in myelofibrosis patients previously treated with a JAK inhibitor. Momelotinib can be administered and maintained at full dose because it does not suppress bone marrow activity like other JAK inhibitors.

The MOMENTUM trial is the first randomized Phase III study to

evaluate a JAK1/2 and ACVR1/ALK2 inhibitor in patients with myelofibrosis and anemia. The trial was designed to compare the clinical benefits of momelotinib to danazol, a synthetic androgen currently used to treat anemia in symptomatic myelofibrosis patients.

The study enrolled 195 adult patients from 107 research sites across 21 countries. Trial participants were randomly assigned (2:1) to receive momelotinib plus placebo or danazol plus placebo. Sixty-three percent of participants were male and 37% were female. The median age of participants for the momelotinib group was 71 years and for the danazol group 72 years.

The trial's primary endpoint was symptom reduction after 24 weeks of treatment, defined as a 50% or more reduction in Myelofibrosis Symptom Assessment Form Total Symptom Score. A significantly greater proportion of patients who received momelotinib saw benefits in their disease symptoms (25%) compared to those receiving danazol (9%).

Patients treated with momelotinib also experienced a significant reduction in their spleen size, with 25% responding after 24 weeks of therapy. Additionally, these patients required fewer blood transfusions compared to those receiving danazol.

The safety profile of momelotinib was comparable to previous clinical trials. The most common non-hematological side effects experienced by trial participants in the momelotinib group included diarrhea, nausea, weakness and itching or irritated skin.

"If approved, momelotinib could offer an effective option for patients with myelofibrosis to improve anemia, splenomegaly and other disease-related symptoms over other approved medications so far," Verstovsek said. "Momelotinib may also be an ideal partner for combinations with

other investigational agents in development to further control myelofibrosis symptoms."

Patient follow-up is ongoing and long-term survival continues to be monitored.

More information: Srdan Verstovsek et al, Momelotinib versus danazol in symptomatic patients with anaemia and myelofibrosis (MOMENTUM): results from an international, double-blind, randomised, controlled, phase 3 study, *The Lancet* (2023). DOI: 10.1016/S0140-6736(22)02036-0

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