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New data shed light on potential advantages of pacritinib for patients with myelofibrosis

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Compared with standard therapy, pacritinib significantly reduces spleen size among people with myelofibrosis who have very low levels of platelets, according to a late-breaking study being presented today during the 58th American Society of Hematology (ASH) Annual Meeting and Exposition in San Diego. The study investigators also reported that patients taking a twice-daily dose of this investigational oral multikinase inhibitor experienced significant improvements in symptoms.

Myelofibrosis is a chronic, potentially life-threatening blood cancer that affects approximately 20,000 Americans. The condition is associated with inflammation and scarring in the bone marrow, which disrupts the production of blood cells and can cause severe anemia, weakness, and fatigue. As the liver and spleen begin to take over blood cell production, these organs can become enlarged. People with an enlarged spleen are more prone to infection, anemia, potentially fatal bleeding or rupture, and abdominal discomfort and weight loss, so finding effective treatments to reduce spleen size is important for this group of patients.

PERSIST-2, an open label, Phase III study, was designed to compare the safety and efficacy of pacritinib with currently available therapies, including ruxolitinib, a JAK2 inhibitor approved by the U.S. Food and Drug Administration (FDA) in 2011 to treat intermediate- or high-risk myelofibrosis. The challenge, researchers explain, is that ruxolitinib is not indicated for people with platelet counts under 50,000 per microliter (μl), who represent approximately one-third of myelofibrosis patients. These patients are at much greater risk for complications and have

limited to no treatment options.

"Despite the fact that these patients have very low platelet counts and in approximately 45 percent of the cases had previously been treated with ruxolitinib, we were able to administer this drug effectively, thereby significantly reducing spleen volume and also significantly improving symptoms in a subset of patients who received pacritinib twice daily," said lead study author John Mascarenhas, MD of Tisch Cancer Institute, Icahn School of Medicine at Mount Sinai in New York. "This is a very vulnerable patient population. My hope is that pacritinib might become an option for them because even though ruxolitinib is well tolerated, one of the downsides is often myelosuppression, and many patients with myelofibrosis start with low baseline platelet counts."

Researchers say this study builds on the results seen in the earlier PERSIST-1 trial, and specifically provides more insight into the optimal dosing of pacritinib, as well as its safety in patients with very low platelets. The FDA imposed a clinical hold on studies of pacritinib earlier this year due to safety concerns about increases in risk of bleeding and cardiac events. But according to Dr. Mascarenhas, the full data analyses do not show a significant difference in deaths across groups; during the course of the study, 10, 15, and 14 patients died in the pacritinib twice daily, once daily and best available treatment groups, respectively. Similarly, cardiac and bleeding events were rare and comparable. "The safety profile remains reasonable given the fact that we are treating patients with low platelet counts who are already at risk for both bleeding and cardiac events," he said.

A total of 221 out of the originally intended 311 patients with platelet counts ?100,000/ µl were randomly assigned to receive pacritinib at either 200 mg twice daily or 400 mg once daily or best available therapy. About half of the PERSIST-2 study population had platelet counts