Study shows early success of a novel drug in treating a rare and chronic blood cancer

February 21 2024

Credit: Pixabay/CC0 Public Domain

A novel treatment for polycythemia vera, a potentially fatal blood cancer, demonstrated the ability to control overproduction of red blood cells, the hallmark of this malignancy and many of its debilitating

symptoms in a multi-center clinical trial led by the Icahn School of Medicine at Mount Sinai.

In the phase 2 study, the drug rusfertide limited excess production of red blood cells, the main manifestation of polycythemia vera, over the 28-week course of treatment. The results suggest it could replace therapeutic phlebotomy, a common form of treatment which has proven to be a burden for many patients. The results of the study were published today (Feb. 21) in *The New England Journal of Medicine.*

"Rusfertide appears to represent a significant step forward in treating polycythemia vera through its unique approach of limiting the amount of iron available for blood cell production," says Marina Kremyanskaya, MD, Ph.D., Associate Professor of Medicine (Hematology and Medical Oncology) at Icahn Mount Sinai and lead author of the study.

Dr. Kremyanskaya, who serves as Medical Director for inpatient oncology at The Mount Sinai Hospital, has conducted leading-edge research into myeloid blood cancers. "Pending further clinical studies, this injectable agent could become a valuable therapeutic tool for a disease which many patients and their physicians struggle to bring under control," she says.

"This groundbreaking work would not have been possible without my Mount Sinai co-investigators, Ronald Hoffman, MD, and Yelena Ginzburg, MD. With their close collaboration, we were able to take laboratory findings from the bench to bedside," says Dr. Kremyanskaya.

Dr. Hoffman is Professor of Medicine (Hematology and Medical Oncology) at Icahn Mount Sinai, a senior author on the publication, and a prominent researcher and clinician in the field of myeloproliferative neoplasms. Dr. Ginzburg, Professor of Medicine (Hematology and Medical Oncology) at Icahn Mount Sinai, is an expert in iron metabolism

; her basic science work provided a significant preclinical rationale for the investigation.

Polycythemia vera is a rare type of chronic myeloproliferative neoplasm, with 1–3 new cases per 100,000 people diagnosed each year in the United States. It occurs when the bone marrow overproduces blood cells, a condition also known as erythrocytosis, which can thicken the blood and increase the risk of heart attack, stroke, and other blood clots.

Current therapies include aspirin; medications that can reduce red blood cells in the bloodstream, such as hydroxyurea, interferon, and ruxolitinib; and phlebotomy, which involves withdrawing blood using a needle in a vein to reduce blood volume.

Frequent phlebotomies have proven onerous for patients due to the need for prolonged physician visits. They can also worsen iron deficiency symptoms that already afflict many polycythemia vera patients. In addition, patients are often intolerant or fearful of this treatment option.

Moreover, studies have shown that with currently available treatment options, many patients will often have hematocrits, the percentage of red cells in your blood, above the clinically safe level of 45%, leaving these patients at higher risk for complications.

The Mount Sinai-led REVIVE trial was conducted at 16 centers in the United States and India. Rusfertide was evaluated for safety and efficacy in 70 phlebotomy-dependent polycythemia vera patients.

The researchers found that the agent was associated with improved and sustained control of hematocrit levels below 45% during the 28-week dose-discovery period, and was superior to placebo during the ensuing 12-week withdrawal period. Patients with a high burden of symptoms such as pruritis (itchy skin), night sweats, difficulty concentrating, and

fatigue also reported improvements following treatment with rusfertide, which was well tolerated.

Rusfertide is an injectable medication that patients can self-administer at home. It works in the body by mimicking hepcidin, a hormone produced by the liver that serves as a master regulator of iron trafficking. It blocks the export of iron to the blood in a dose-dependent manner, which results in functional iron deficiency and decreased red blood cell production.

"Rusfertide shows great promise for achieving sustained hematocrit control in polycythemia vera patients. Just as importantly, it decreased the need for repeat phlebotomies, with some patients remaining virtually free of the procedure for more than two and a half years," notes Dr. Kremyanskaya.

A phase 3 clinical trial is now underway at global sites, with Mount Sinai again playing a leadership role.

More information: Marina Kremyanskaya et al, Rusfertide, a Hepcidin Mimetic, for Control of Erythrocytosis in Polycythemia Vera, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2308809

Provided by The Mount Sinai Hospital