Could common diabetes drugs help fight leukemia?

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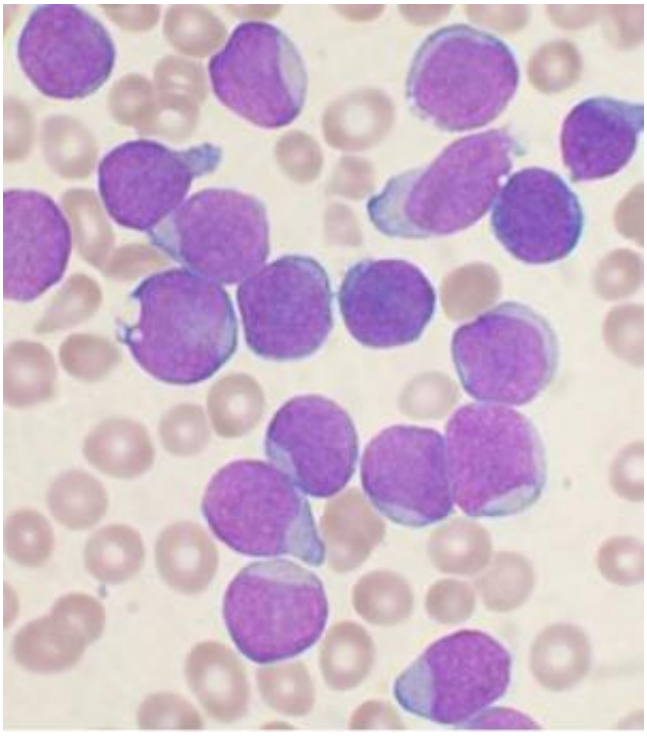

A Wright's stained bone marrow aspirate smear from a patient with precursor B-cell acute lymphoblastic leukemia. Credit: VashiDonsk/Wikipedia

Common diabetes drugs might help eradicate drug-resistant cancer cells in a certain form of leukemia when added to standard treatment, a small new study suggests.

Researchers found that patients with chronic myeloid leukemia (CML)

who received a glitazone—a class of drug for type 2 diabetes—along with the standard CML drug imatinib remained disease-free for up to nearly five years.

Imatinib, known commercially as Gleevec, boasts an impressive track record in controlling chronic myeloid leukemia and allowing patients to lead virtually normal lives. But despite its effectiveness, dormant, drug-resistant leukemic cells typically lay in wait in bone marrow. They can later transform into highly aggressive cells.

"Gleevec can control the disease but never get rid of the source of the disease," said Lee Greenberger, chief scientific officer for the Leukemia & Lymphoma Society, who wasn't involved in the new research.

"But adding in these glitazones, [the research] claims you can eliminate the disease entirely," said Greenberger. "These are still early days for this work, however."

Actos and Avandia are two well-known glitazones.

Chronic myeloid leukemia is a cancer that originates in the blood-forming cells of the bone marrow and invades the blood supply. More than 6,600 cases are expected to be diagnosed in the United States this year, and about 1,140 people will die from the condition, according to the American Cancer Society.

Seen mostly in adults, chronic myeloid leukemia tends to be slow-growing, but can transform into a rapidly growing form that can quickly kill.

Together with his team, study author Dr. Philippe Leboulch, a professor of medicine and cell biology at the University of Paris, temporarily administered pioglitazone in addition to imatinib to three patients with

chronic myeloid leukemia. Both drugs are available in pill form. Pioglitazone is marketed as Actos.

Although imatinib and other so-called tyrosine kinase inhibitors have significantly improved outcomes for this type of blood cancer, leukemia stem cells can develop a resistance to this standard treatment because of the dormant malignant cells in bone marrow.

In the study—published online Sept. 2 in the journal *Nature*—Leboulch described the molecular pathway leading to "quiescence," or cell dormancy, in chronic myeloid leukemia. The study suggested that glitazones can block this pathway, and, when used with imatinib, render patients disease-free for months to years after glitazones are discontinued.

It's unclear how the dormant, drug-resistant leukemia cells were killed using this combination therapy. But an editorial accompanying the study said the cells are "probably either killed directly or driven to exit quiescence, which may lead to their eradication by [imatinib]."

Dr. Jeffrey Schriber, a hematologist with Arizona Oncology in Scottsdale, said larger trials of this combination treatment are in progress and should yield results within the next three to five years.

But since drugs such as imatinib already enable 94 percent of chronic myeloid leukemia patients to remain alive five years after diagnosis—with only 2 percent dying of the disease in that time—adding in glitazones is "unlikely to make a significant difference" compared to current results, he said.

"From a scientific standpoint, however, the principles are critical and go beyond the therapy of CML," added Schriber, who specializes in the field of stem cell transplantation. "This principle could also be

potentially applied to other leukemias where the results are not nearly as promising," he said.

The major weakness in the new study is its small size, Schriber said, making it difficult to know if the results would hold up in a larger group. Greenberger said it would be ideal to run a randomized controlled trial directly comparing the effectiveness of combination therapy (imatinib and a glitazone) versus imatinib alone.

Patients can take glitazones for months without serious side effects, Greenberger said.

"It would be best to see over years if [the combination therapy] could molecularly remove this disease," he said.

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The U.S. National Cancer Institute offers more about chronic myeloid leukemia.