

# Dismissed leukemia drug helps CLL patients, studies show

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Researchers at Ohio State devised a new dosing schedule for the drug to increase its anti-tumor activity.

A drug once dismissed as ineffective in patients with chronic lymphocytic leukemia (CLL) has shown promising results in two phase I and II clinical trials, according to researchers at The Ohio State University Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute.

Together, the trials involved 116 patients with advanced CLL who were treated with the drug flavopiridol (alvocidib). Responses were seen in approximately half of patients, many of whom had chromosomal abnormalities that made it unlikely they would be helped by standard therapies.

"Ohio State's success has reinvigorated interest in flavopiridol at the National Cancer Institute and other cancer centers," says Dr. Thomas Lin, a researcher and oncologist at Ohio State's Comprehensive Cancer Center – James Cancer Hospital and Solove Research Institute.

Lin, the study's first author and a member of the Experimental Therapeutics program at Ohio State's Comprehensive Cancer Center, will discuss the findings during the 50th Annual Meeting of the American Society of Hematology (ASH). Lin will explain the research during the ASH-ASCO Joint Symposium on Sunday morning (12/7), and later that day during an oral presentation on CLL therapy.

Earlier this year at the annual meeting of the American Society of Clinical Oncology, Ohio State investigators made an oral presentation on a phase II study of 64 patients treated with flavopiridol. The novel drug is effective in resistant CLL that does not respond to other therapies. Each year, ASH selects five ASCO abstracts to be featured during the Joint Symposium.

Chronic lymphocytic leukemia is the most common type of adult leukemia, with some 15,000 new cases this year. While therapy has improved, CLL remains incurable and patients often suffer significant infections as a consequence of the disease and treatment.

In the 1980s, animal tests showed flavopiridol to be a potent cancer-fighter. But when researchers gave it to humans in repeated trials using a continuous prolonged infusion, the drug proved ineffective and was essentially forgotten.

What wasn't known then – and what Ohio State researchers discovered later – is that flavopiridol binds to proteins in human blood, which ties up much of the available drug and leaves less free drug in the bloodstream to kill cancer cells. In essence, patients were not getting enough of the drug to be effective.

Researchers at Ohio State devised a new dosing schedule for the drug to increase its anti-tumor activity.

The new schedule increased the drug's blood level enough to kill cancer cells in humans, says Dr. Michael Grever, chairman of the department of internal medicine and co-leader of the Experimental Therapeutics program at Ohio State's Comprehensive Cancer Center.

"Flavopiridol has bridged the way for several CLL patients to receive a curative stem cell transplant," says Dr. John Byrd, associate director of

translational research and principal investigator of the phase II trial. Ohio State is now participating in a multi-center flavopiridol trial to see if other cancer centers have similar results with flavopiridol.

Source: Ohio State University Medical Center

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