

# Promising new drug blocks mutation in bone marrow cancers

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Oregon Health & Science University Knight Cancer Institute researchers have found that an experimental drug successfully blocks an enzyme that causes some bone marrow cancers.

The oral drug, called CYT387, was tested in mice as well as in human cells. In both cases, it blocked the growth of certain bone marrow cancers called myeloproliferative disorders, also referred to as MPDs.

The research will be presented Tuesday, Dec. 9, during the 50th annual American Society of Hematology conference in San Francisco.

"The drug was found to be very effective against a specific type of cancer cells, cancer cells which are driven by an enzyme mutation called JAK2-V617F. In the mouse model, the drug blocked JAK2-V617F, normalized blood counts and reduced enlarged spleens back to a normal size. It is a very promising compound," said Thomas Bumm, M.D., Ph.D., a member of the research team.

The drug works by binding to the V617F mutation in the JAK2 enzyme. Without this drug, the mutated JAK2 enzyme leads to MPDs. The "big three" MPDs include polycythemia vera, essential thrombocythemia and primary myelofibrosis. Until now there have been no FDA-approved targeted treatments for these diseases.

"Based on the efficacy that we demonstrated in the mouse model, there is a good chance that CYT387 will enter clinical trials as early as 2009.

Those in greatest need include patients with myelofibrosis, a relentless disease for which there is currently no effective therapy. It is likely that JAK2 inhibitors will change the standard of care for these patients," said Michael Deininger, M.D., Ph.D., principal investigator and Head of the Hematological Malignancies Program Ph.D. He also is an associate professor of medicine (hematology/medical oncology), OHSU School of Medicine and a Scholar of the Leukemia & Lymphoma Society.

Researchers also discovered that CYT387 effectively blocks overproduction of inflammatory cytokines. Abnormal cells carrying the JAK2-V617F mutation produce a large amount of different inflammatory cytokines that help the cancer cells to grow and repress normal cells. In mice, the drug normalized 19 different inflammatory cytokine levels in the blood. The overproduction of cytokines can also be found in inflammatory conditions such as rheumatoid arthritis. This drug's effect on cytokines could benefit patients with inflammatory diseases, especially rheumatoid arthritis.

The next likely step will be to open clinical trials for people with MPD as soon as 2009 once formal preclinical toxicology studies are completed.

Source: Oregon Health & Science University

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