MedicalXpress

Novel M.S. Drug Shows Promise In Two Lethal Leukemias

August 28 2007

A new study suggests that an experimental drug being tested for the treatment of multiple sclerosis and to prevent organ rejection might also help people with certain deadly forms of chronic and acute leukemia.

The laboratory and animal study focused on the drug, called fingolimod. Researchers said it might help patients with advanced chronic myelogenous leukemia (CML) or acute lymphocytic leukemia (ALL), and whose cancer cells show a particular genetic change called the Philadelphia chromosome.

The study found that the drug prevented the development of these cancers in mouse models, as well as killing laboratory-grown human CML and ALL cells.

Although the findings must be verified in humans through a future clinical trial, the new research also suggests that the drug might help patients with these leukemias who are resistant to imatinib (Gleevec) and dasatinib (Sprycel), two important current drugs for treating CML and those cases of ALL with the Philadelphia chromosome.

Presently, fingolimod is in advanced clinical-trials testing for the treatment of relapsing multiple sclerosis, and to prevent organ rejection following kidney transplantation.

The new study, led by researchers with the Ohio State University Comprehensive Cancer Center, is published online Aug. 23 in the

Journal of Clinical Investigation.

“This novel agent represents a promising new strategy for treating CML that is resistant to imatinib and related targeted agents,” says coauthor Guido Marcucci, associate professor of internal medicine and an oncologist who specializes in leukemia drug development at Ohio State's James Cancer Hospital and Solove Research Institute.

“These findings also suggest that it will be an important contribution to a new therapeutic approach to CML that considers combinations of molecular targeting compounds.”

In leukemic cells, the drug works by reactivating a protein called PP2A, which normally helps protect cells from becoming cancerous. The protein then causes the cells to self-destruct through a process called apoptosis.

“This was true even in leukemic cells from patients that were resistant to imatinib or to dasatinib,” says principal investigator Danilo Perrotti, assistant professor of molecular virology, immunology and medical genetics.

The drug had no effect on normal cells or control mice, suggesting that it is likely to have minimal or no side effects in humans.

“If this is verified in future studies, it means that this drug might help patients who do not respond to other therapies,” Perrotti says

Nearly all of the 4,570 cases of CML expected this year, and about 20 percent of the expected 5,200 cases of ALL, have the Philadelphia chromosome. This chromosome change results in the production of an abnormal protein that causes these two malignancies.

This study tested the drug on cell lines that modeled these leukemias, and on cells from patients with advanced CML or with ALL and the Philadelphia chromosome, including those who were resistant to imatinib and dasatinib.

The animal studies used mice with the two forms of leukemia. Whereas most of the 39 untreated animals had died by four weeks, 90 percent of the 39 animals treated with the drug were alive after six months.

The study's findings, Perrotti says, “support the use of this PP2A activator as a novel therapeutic approach in these particular leukemias and, perhaps, in other cancers that involve the functional loss of PP2A activity.”

Source: Ohio State University