New drug shows potential for treatment-resistant leukemia

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A study from Tufts Medical Center researchers published today finds that a novel drug shows promise for treating leukemia patients who have few other options because their disease has developed resistance to standard treatment.

Appearing in the journal *Cancer Cell,* the study is the first published report showing that the drug, DCC-2036, fights chronic myeloid leukemia (CML) in a mouse model of the disease and is effective against human leukemia cells.

"These findings demonstrate that DCC-2036 is an excellent candidate for clinical development as a treatment for resistant CML. Not all drugs that work in a test tube will actually be effective in a living organism such as our mouse model," said Richard Van Etten, MD, PhD, Director of Tuft's Medical Center's Cancer Center and senior author of the study.

Other authors of the study are scientists with Deciphera Pharmaceuticals LLC of Lawrence, Kansas, and Emerald Biostructures of Bainbridge Island, WA.

DCC-2036 is a tyrosine kinase inhibitor (TKI), a class of drugs that block the action of an abnormal enzyme, BCR-ABL1, that sends chemical messenges that tell CML cells to grow. The development of TKI drugs such as imatinib (Gleevec®) dramatically improved the prognosis for patients with CML, which strikes about 5,000 new patients each year in the United States. But about a third of patients will

eventually relapse, principally because of mutations that render BCR-ABL1 resistant to the TKI. Such patients are left with few treatment options other than bone marrow transplantation.

The study showed that in human cells taken from treatment-resistant patients who had received the new drug, DCC-2036 tamped down the mutant enzyme that led to their relapse. The study also found that the drug killed malignant cells and prolonged survival in a mouse model of CML developed by Van Etten's team.

Deciphera Pharmaceuticals, LLC used crystal structures of BCR-ABL1 to custom-design the novel drug to inhibit the mutant enzyme that leads to treatment resistance in CML patients. "The study illustrates the power of designing drugs based upon structures of the target and initial testing of these drugs in mouse models before proceeding to the clinic. This type of targeted design is a paradigm for how cancer treatments will be developed in the 21st century," Van Etten said.

Provided by Tufts Medical Center