Medical Xpress

B cell receptor inhibitor causes chronic lymphocytic leukemia remission

December 11 2011

A new, targeted approach to treating chronic lymphocytic leukemia has produced durable remissions in a Phase I/II clinical trial for patients with relapsed or resistant disease, investigators report at the 53rd Annual Meeting of the American Society of Hematology.

"PCI-32765, one of a new class of experimental drugs called B cell receptor inhibitors, has shown impressive potential in this clinical trial for its effectiveness and particularly for its relatively minimal toxicity," said lead investigator Susan O'Brien, M.D., professor in the Department of Leukemia at The University of Texas MD Anderson Cancer Center.

According to the National Cancer Institute's Surveillance Epidemiology and End Results database, an estimated 14,570 people will receive a diagnosis of CLL in 2011 and about 4,380 patients will die of the disease.

Six-month progression free survival of 90-92 percent

Of 27 CLL patients treated at a dose of 420 milligrams daily, 70 percent had complete or partial remission at 10.2 months of median follow-up. Six-month progression-free survival was 92 percent. Patients received a median three prior treatments before entering the clinical trial.

At a higher dose of 840 mg, 44 percent of 34 patients achieved complete or partial remission at 6.5 months median follow-up, similar to the

response rate of the lower-dose cohort at 6.2 months. Progression free survival at 6 months was 90 percent. Study participants had received a median of five prior treatments.

Overall, five patients (8 percent) of the 61 from both arms had progressive disease and 50 (82 percent) remained on the therapy.

Drug does not suppress blood cell production

CLL presently is treated with combination chemotherapies that can cause myelosuppression - inhibited bone marrow function leading to decreased production of blood cells. The resulting susceptibility to infection can be a problem for patients, O'Brien said.

"PCI-32765 is not myelosuppressive. The main side effect is mild diarrhea that is usually self-limiting," O'Brien said.

Chronic lymphocytic leukemia is caused by overproduction of defective B cell lymphocytes, white blood cells that fight infection by producing antibodies.

PCI-32765 is orally administered and inhibits the Burton's tyrosine kinas (BT) enzyme, which is central to B cell receptor signaling. The drug causes programmed cell death and hinders cell migration and adhesion in malignant B cells.

A Phase III clinical trial is planned. The clinical trial was funded by Pharmacyclics, Inc., the drug's developer.

Provided by University of Texas M. D. Anderson Cancer Center