

Drug shows promise for T315I-mutated chronic myeloid leukemia

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Results from a phase II clinical trial indicate a novel drug may provide a treatment option for chronic myeloid leukemia (CML) patients who do not respond to current therapies, researchers from The University of Texas M. D. Anderson Cancer Center report today at the 51st Annual Meeting of the American Society of Hematology.

The injectable drug omacetaxine achieved durable responses in some CML patients who harbor a mutation that renders otherwise effective treatments useless against their disease.

"Omacetaxine is a drug that has worked in CML in the past and we now find it to produce responses among CML patients who have the T315I mutation, a group that currently has no other pharmaceutical options," said principal investigator Jorge Cortes, M.D., professor in M. D. Anderson's Department of Leukemia.

Almost all cases of CML are caused by a chromosomal abnormality known as the Philadelphia chromosome that produces an aberrant protein which causes the overproduction of one type of white blood cell that drives the disease. CML has been successfully treated by imatinib, known commercially as Gleevec®, and other drugs that plug an active portion of the Bcr-Abl protein, blocking its activity. The Bcr-Abl T315I mutation prevents these tyrosine kinase inhibitors from working.

"Omacetaxine works by a completely different mechanism, inhibiting the synthesis of certain oncoproteins instead of directly attacking Bcr-

Abl," Cortes said. "This is a drug that we've known to work in CML and now has the potential for expanded use, probably in combination with other drugs."

Imatinib failed every patient and 79 percent have tried two or more tyrosine kinase inhibitors. Data were available on 81 patients in time to report results at ASH. Of these, 49 were in the chronic phase of the disease, 17 in the accelerated phase and 15 were in blast crisis, the most dangerous phase of CML.

Chronic Phase Results

Complete hematological response, a restoration of normal blood counts, was achieved in 42 patients for a total response of 85 percent. Another 27.5 percent achieved a cytogenetic response -the reduction or absence of cells with the Philadelphia chromosome in the bone marrow - with nine patients having a complete response.

A reduction in the baseline T315I clone was achieved in 57 percent of patients. Median survival time has not been reached in this group.

Accelerated and Blast Phases

A hematologic response was achieved in six patients (35 percent) in accelerated phase with five achieving a complete response and one returning to chronic phase. One achieved a complete cytogenetic response. Median survival for this group was 18.8 months.

In the blast phase, seven patients (47 percent) had a hematologic response, three were complete. Median survival was 2.1 months.

Side effects

Sixty-eight percent of all patients experienced grade 3/4 side effects, mostly hematological, with 58 percent experiencing low platelet levels, 36 percent having anemia and 33 percent experiencing reduced levels of the white blood cell neutrophils. Non-hematologic responses were mainly low grade and included diarrhea, fatigue and nausea. Half of all patients had their treatment delayed by a median of 12 days due to mainly hematological side effects.

"This treatment appears to be overall well-tolerated for the majority of patients, and the drug can be self-administered, which makes it convenient," Cortes said.

Source: University of Texas M. D. Anderson Cancer Center ([news](#) : [web](#))

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