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Drug that modifies gene activity could help some older leukemia patients

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Older patients with acute myeloid leukemia (AML) might benefit from a drug that reactivates genes that cancer cells turn off, according to research at Washington University School of Medicine in St. Louis and collaborating institutions. The researchers say the findings support further investigation of the drug, decitabine, as a first-line treatment for these patients, who have limited treatment options.

Almost two-thirds of AML patients over age 65 do not receive treatment for the disease because standard therapy can be risky and often is ineffective. On average, such patients survive only 1.7 months after diagnosis.

"Older leukemia patients don't have good treatment options because the chemotherapy and stem cell transplants that we commonly use for younger patients are often too toxic for them," says lead author Amanda F. Cashen, M.D., assistant professor of medicine in the Division of Oncology and a bone marrow transplant specialist with the Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine.

"Furthermore, the biology of acute leukemia in the older patient population is different, making their response rate lower, their risk of relapse higher and their cure rates lower," she says. "So we definitely need new therapies in that patient population — treatments that are going to be both better tolerated and more effective."

The study, to be published in an upcoming issue of the Journal of Clinical Oncology and now available on-line, was conducted at three sites: Washington University School of Medicine; the University of California, Los Angeles; and the City of Hope National Medical Center in Duarte, Calif. The researchers tested decitabine in 55 AML patients with an average age of 74 years.

Decitabine can increase the activity of genes that have been silenced in cancer cells. It works by reducing the amount of DNA that is marked with a chemical tag called a methyl group. Scientists think that the excess methylation found in cancer cells inactivates genes that normally suppress tumor development.

All patients received the same decitabine dose for five consecutive days every four weeks until their disease stopped responding to the drug and began progressing or until an adverse event occurred to prevent further participation. By comparison to standard chemotherapy and stem cell transplantation, the treatment was considered a low-intensity treatment and was more tolerable for elderly patients, especially those with accompanying medical problems.

In 24 percent of the study participants, blood counts and bone marrow returned to normal, which is considered a complete response. It took 4.5 cycles of decitabine treatment on average to achieve a complete response. In those with a complete response, average survival time was 14 months. For all study participants, average survival time was 7.7 months.

Treatment-related adverse events included low blood counts (red cells, white cells and platelets), infection, fever and fatigue. Almost half of the study participants had at least one serious adverse event. Seven patients discontinued treatment, and three patients died as the result of adverse events.

"We have to wait for the results of further trials of decitabine to have a better estimate of the response rate and survival outcome compared to other low intensity options for older adults," Cashen says. "This study can't definitively establish decitabine's role for treating older adults with AML, but it certainly excites us to study it more."

More information: Cashen AF, Schiller GJ, O'Donnell MR, DiPersio JF. Multicenter, phase II study of decitabine for the first-line treatment of older patients with acute myeloid leukemia. *Journal of Clinical Oncology*. Dec. 21, 2009 (advance on-line publication). jco.ascopubs.org/cgi/content/a … t/JCO.2009.23.9178v1

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