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Experimental drug is first targeted therapy to improve survival in high-risk AML patients

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Midostaurin added to standard chemotherapy is the first targeted treatment to improve survival of a high-risk, genetically defined subgroup of patients with acute myeloid leukemia (AML), reported Dr. Richard Stone, of Dana-Farber Cancer Institute, on behalf of the Alliance for Clinical Trials in Oncology group, in a plenary session at the 57th American Society of Hematology (ASH) Annual Meeting and Exposition in Orlando.

The AML subgroup included patients ages 18 to 60 - considered "young adults" - whose cancer cells carried mutations in the FLT-3 gene. The mutated gene drives aggressive growth, so that such patients have a poor prognosis and a high chance of relapse. Treatment with chemotherapy is directed at achieving a remission so that patients can undergo stem cell transplant.

The clinical trial randomized 717 patients to receive standard chemotherapy plus midostaurin, a multi-kinase inhibitor, or chemotherapy plus a placebo, including one year of maintenance therapy. With a median follow-up of 57 months, those in the midostaurin arm had a 23 percent lower risk of dying than those in the placebo group, and experienced a five-year survival rate of 50.9 percent versus 43.9 percent in the placebo arm.

"We were pleased to learn that patients who had midostaurin added to

their therapy survived more commonly and longer than those who received placebo," said Richard M. Stone, MD, director of the Adult Acute Leukemia Program at Dana-Farber, presenting results from the CALGB 10603/RATIFY trial.

About 20,830 new cases of AML are expected to be diagnosed in 2015, with 10,460 deaths. Children with AML can be treated with a high success rate. Most cases, however, are in adults and they are more difficult to treat, particularly the 30 percent of patients who carry the FLT-3 mutation.

"This trial is the first step in applying the theories of personalized medicine to patients with AML, specifically those patients with AML who have a FLT-3 mutation who we have shown are likely to benefit from the addition of this targeted agent, midostaurin, to standard chemotherapy," said Stone.

Previous research suggested that individuals whose cancers lacked the FLT-3 gene mutation were not good candidates for treatment with FLT-3 inhibitors like midostaurin, but Stone said it would be worth trying the drug in those patients, as well as in older AML patients. Individuals older than 60 weren't included in the trial because this chemotherapy regimen is too aggressive for them.

The study revealed no additional toxicity in the cohort that received midostaurin in addition to chemotherapy. "There was no increase in side-effects in patients assigned to midostaurin compared to those who were assigned placebo," explained Stone. "This may have been because the side-effects of chemotherapy dwarfed any that might have been attributed to the midostaurin."

Provided by Dana-Farber Cancer Institute