

Genetic profiling helps doctors more accurately predict prognosis, guide treatment decisions for leukemia patients

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Researchers have identified a set of genetic abnormalities in patients with acute myelogenous leukemia (AML) that doctors can use to more accurately predict patients' prognoses and select treatments that are most likely to benefit them. The study, led by investigators at Memorial Sloan-Kettering Cancer Center, will be published in the March 22 issue of the *New England Journal of Medicine*.

"Our study shows that [genetic profiling](#) makes it possible to more precisely categorize which [patients](#) are most likely to have their leukemia return after treatment," says the study's lead author Ross Levine, MD, a member of Memorial Sloan-Kettering's Human Oncology Pathogenesis Program. "We also want to use existing therapies more intelligently. It helps a great deal to know which subset of patients will actually benefit from intensive therapies, such as a higher dose of chemotherapy or a [bone marrow transplant](#)," adds Dr. Levine, who is also a medical oncologist on the Leukemia Service at Memorial Sloan-Kettering.

At present, clinicians rely on only a handful of known genetic biomarkers (early markers of disease) to predict outcome in leukemia patients, and these biomarkers provide useful information for only a subset of patients. For most people diagnosed with AML, it is difficult to predict the chance for a cure.

The method used in the study incorporates information from an array of genes and allows nearly two-thirds of patients to be categorized into clearly defined prognostic groups. "Our goal was not to ask whether a certain gene or two raised or lowered risk, but to determine whether a combination of characteristics from a set of genes made it possible to precisely stratify patients according to risk," Dr. Levine says.

The researchers analyzed blood or bone marrow samples from 502 patients with AML who were participating in a clinical trial. Such samples are routinely taken for research purposes during trials with patient consent. The trial, led by Martin S. Tallman, MD, Chief of Memorial Sloan-Kettering's Leukemia Service, explored whether increasing the standard dose of chemotherapy in AML patients under age 60 would improve survival.

The team that performed the genetic analysis, which included investigators from Memorial Sloan-Kettering, Weill Cornell Medical College, and other institutions, analyzed the samples for abnormalities, or mutations, within 18 genes known to have alterations in people with AML. The researchers noted the relationship between the mutations present in each patient and how that patient ultimately fared with the disease receiving either the standard or increased chemotherapy dose.

"Our findings have important clinical implications for patients with AML, demonstrating that genetic profiling can improve current prognostic models and help guide therapeutic decisions so patients have an optimal result," says Dr. Tallman, who is a co-author of the new study. "Moving forward, the challenge will be to provide this genetic information in a timely and affordable way to influence treatment decisions prospectively," he adds.

The analysis allowed the researchers to determine specific risk levels for a variety of gene-mutation combinations. They also were able to

establish that the higher chemotherapy dose used in the trial benefited only some of the patients. The investigators took into account variables such as patient age and gender and validated the results in a separate group of patients to ensure that the profiling approach will be generally applicable beyond the current trial.

Dr. Levine and his Memorial Sloan-Kettering colleagues are working to translate the results from the study into clinical use. "We've already developed genetic tests, which can be used to test for this set of mutations in patients, and we're in the process of making sure they work well in practice," he says. "We have preliminary evidence that they perform well, and we're hoping to have a pilot study soon as a step toward getting it into the clinic. We want to show this approach can be used not just at Memorial Sloan-Kettering but throughout the leukemia community."

The American Cancer Society estimates that 13,780 people in the United States will be diagnosed with AML in 2012 and that more than 10,000 people will die from the disease.

Provided by Memorial Sloan-Kettering Cancer Center

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