

Identifying acute myeloid leukemia gene mutations may indicate risk, best treatment

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An international group of researchers, including those from Moffitt Cancer Center in Tampa, Fla., have published a paper in the March 14 issue of the *New England Journal of Medicine* reviewing the results of a study that analyzed mutations in 18 genes of 398 patients who had acute myeloid leukemia (AML). They found that several mutated genes predicted improved outcomes when patients with certain gene mutations were given high-dose induction chemotherapy. Their findings suggest that mutational profiling could potentially be used for both risk stratification and also in helping health care providers make therapeutic decisions for some AML patients.

"Previous studies have found that AML is a highly heterogenic disorder," said study co-author Hugo F. Fernandez, a senior member at Moffitt and associate chief of Moffitt's Blood and Marrow Transplantation Division. "Moreover, recent studies have revealed that a number of genetic mutations in AML patients might have prognostic value. The question of the presence of these gene mutations altering outcomes based on current therapy had not been answered to date."

Their paper cites a clinical trial carried out by the Eastern Cooperative Oncology Group (ECOG) in which dose-intensified chemotherapy improved outcomes in two age sets of AML patients. Based on these findings, the research team hypothesized that carrying out mutational analysis of all known molecular alterations occurring in more than 5 percent of patients with AML might allow for the identification of distinct, molecularly defined subgroups of patients who might benefit

from dose-intensified chemotherapy.

The laboratory research team subsequently performed a mutational analysis on diagnostic samples from 398 patients enrolled in the ECOG clinical trial they cited and used patients' frozen sample cells for extraction and profiling. The researchers validated the results of this latter group of 104 patients.

"We found that intensification of the dose of anthracycline significantly improved outcomes and overall survival in patients with mutations in DNMT3A, NPM1 or MLL translocations," said Fernandez. "This finding suggests that mutational profiling could be used to determine which AML patients will benefit from dose-intensive induction therapy."

"Most importantly," said Fernandez, "this study demonstrates how integrated mutational profiling of samples from a clinical trial cohort can advance understanding of the biologic characteristics of AML."

Provided by H. Lee Moffitt Cancer Center & Research Institute

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