New study may refine predicted survival outcomes and treatment in younger adults with acute leukemia

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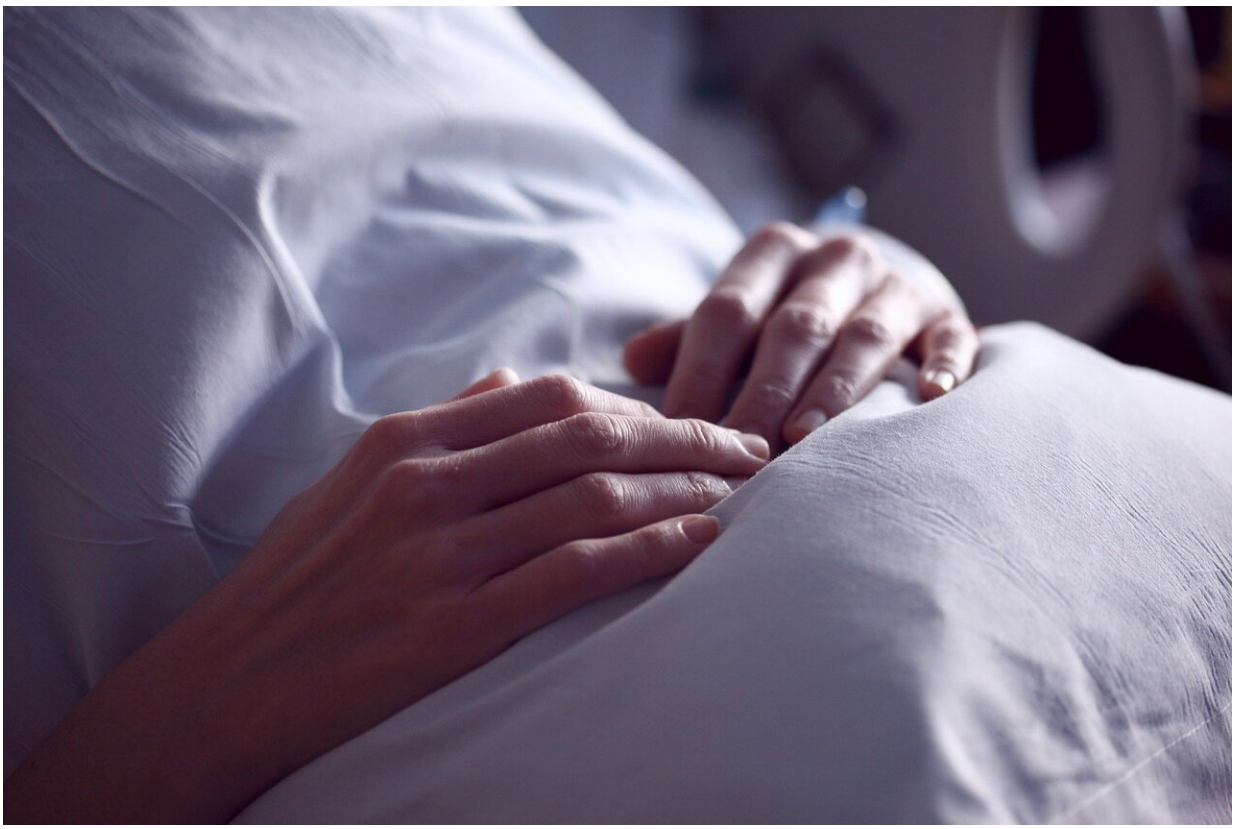

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The findings of a new study led by researchers at The Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer

Hospital and Richard J. Solove Research Institute (OSUCCC—James) could refine an important set of prognostic and treatment recommendations for younger adult patients with acute myeloid leukemia (AML).

The retrospective study evaluated the molecular characteristics and outcomes of 863 patients with AML who were treated according to 2017 European LeukemiaNet (ELN) recommendations. The patients were under age 60 with a median age 45 years.

ELN recommendations are internationally used for diagnosing and managing people with AML and other leukemias. AML is a neoplastic disease of the blood that affects about 19,900 Americans and kills nearly 11,200 of them yearly, according to the American Cancer Society. Only 35-40% of AML patients under age 60 achieve long-term survival, the researchers note.

The study, published in the journal *Leukemia*, found that:

- 9% of favorable-risk and 53% of intermediate-risk patients should be reclassified as adverse risk;
- 4% of favorable-risk and 9% of adverse-risk patients should be reclassified as intermediate risk.

"If verified, our findings may refine the ELN risk stratification of younger acute myeloid leukemia patients, which could improve patients' treatment choices and outcomes," says first author Ann-Kathrin Eisfeld, MD, an investigator in the OSUCCC—James Leukemia Research Program.

During this study, Eisfeld and her colleagues detected 2,354 mutations, an average of three per patient.

The researchers determined the frequency of mutations additional to those used to define current ELN risk-groups, and mutations in several "functional group" categories: RAS-pathway mutations, kinase and methylation-related mutations, and mutations in genes encoding for spliceosomes, transcription factors and tumor suppressors.

They compared the frequencies of the mutations within each ELN risk group—favorable, intermediate and high—to learn which were associated with better or worse outcomes and might therefore help refine the 2017 ELN classification.

Key findings include:

- BCOR- or SETBP1-mutated favorable-risk patients with non-core-binding-factor AML and IDH-mutated adverse-risk patients had intermediate-risk outcomes.
- Outcomes of NPM1/WT1 co-mutated patients and those of ZRSR2-mutated patients resembled outcome of adverse-risk patients.
- FLT3-ITDhigh allelic ratio conferred adverse risk, rather than intermediate risk, regardless of NPM1 mutation status.
- DNMT3A mutations signaled very poor survival.

More information: Alice S. Mims et al, Comparison of clinical and molecular characteristics of patients with acute myeloid leukemia and either TP73 or TP53 mutations, *Leukemia* (2020). DOI: 10.1038/s41375-020-1007-6

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