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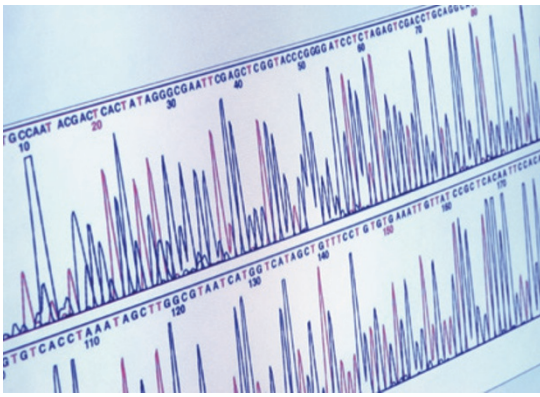
HAEMATOLOGICAL CANCER

European LeukemiaNet AML genetic classification works



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A diagnosis of acute myeloid leukaemia (AML) encompasses a wide range of prognoses, and it is important to attempt to classify each patient as accurately as possible within the disease continuum. There have been different classifications of prognostic groups of AML for some time, but in 2010 the European LeukemiaNet put together a classification system that combines previously used cytogenetic prognostic factors with newer molecular markers. This system was based on rigorously proven science, and now it has been tested in 1,550 patients with primary AML, and been shown to work.

The validation of the classification system was undertaken by a large team led by Krzysztof Mrózek, Guido Marcucci and Clara D. Bloomfield. Mrózek explains, "we decided to apply the European LeukemiaNet classification to a relatively large cohort of 1,550 adult patients with AML to assess its usefulness for the prognostic classification of both younger (aged <60 years) and older (≥60 years) patients." The researchers had the optimal pool of patients for this study, those who have been treated in Cancer and Leukemia Group B (now the Alliance for Clinical Trials in Oncology) first-line trials. The included patients had pretreatment cytogenetics available, and, for cytogenetically normal patients, the mutational statuses of *NPM1*, *CEBPA* and *FLT3* were known.

The patients were chosen carefully to limit possible confounding factors, as Mrózek describes: "to avoid the confounding effects of AML type (primary versus secondary) and different postremission therapies (chemotherapy versus allogeneic stem-cell transplantation), we included only patients with primary AML who had not undergone allogeneic stem-cell transplantation in first complete remission per protocol." The 1,550 patients were divided according to the European LeukemiaNet classification system into favourable, intermediate-I, intermediate-II and adverse groups, with those in the favourable group anticipated to have better prognoses than those in the intermediate-I group, and so on.

"The major finding of our large study with prolonged follow-up," outlines Mrózek, "has been a demonstration that application of the European LeukemiaNet reporting system allows clear separation of the genetic groups by outcome, both in the younger and older patients with primary AML. This has been achieved for all outcome end points analysed and was shown to be independent from other prognostic factors by multivariable analyses." Therefore, it seems that at least for patients in this category, there is now a system that can be used consistently in clinical trials for categorizing patients.

In this cohort of patients, 31% were classed in the favourable group, 18% in the intermediate-I, 24% in the intermediate-II, and 26% in the adverse group. However, there was a significant difference between the younger patients and the older patients in terms of the percentage of patients in each group. In the favourable group, the proportion of younger patients classified was twice that of older patients. In addition to the differences in the proportion of patients in each European LeukemiaNet classification group, older patients had a different genetic profile to the younger patients. For example, although more than half of the younger patients in the favourable group had core binding factor-AML, only a quarter of older patients did, and this difference was significant.

Another important difference between the younger and older patients was that older patients in the same prognostic group had significantly worse outcomes than the younger patients. This observation is likely associated with the fact that older patients are frequently treated with less-intensive regimens, in part because they have more comorbidities than younger patients. As Mrózek points out, "these results strongly support the notion that the European LeukemiaNet classification should be applied to younger and older patients separately."

The new European LeukemiaNet classification system has been rigorously tested and shown to have value in this study, which supports smaller studies that have previously been carried out. As Mrózek describes, "we already are using the European LeukemiaNet classification to analyse outcome data in ongoing projects aimed at identifying molecular markers that have prognostic significance." He continues, "future studies will test additional prognostic markers that could improve outcome prediction within the European LeukemiaNet Genetic Groups. This could lead to potential modification of the European LeukemiaNet classification once new convincing data are acquired."

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Original article Mrózek, K. *et al*. Prognostic significance of the European LeukemiaNet standardized system for reporting cytogenetic and molecular alterations in adults with acute myeloid leukemia. *J. Clin. Oncol*. doi:10.1200/JCO.2012.43.4738

Further reading Cornelissen, J. J. *et al*. The European LeukemiaNet AML Working Party consensus statement on allogeneic HSCT for patients with AML in remission: an integrated-risk adapted approach. *Nat. Rev. Clin. Oncol*. doi:10.1038/nrclinonc.2012.150