Biologic heterogeneity of AML: Implications for prognosis and treatment

Clara D Bloomfield
The Ohio State University Comprehensive Cancer Center, USA

Adult acute myeloid leukemia (AML) was essentially incurable 50 years ago. Today 35-40% <60 years old and 5-15% ≥60 are cured. AML is a biologically heterogeneous disease significantly impacting prognosis and treatment. Most important for selecting therapy are cytogenetics and molecular genetics. Both are incorporated into the current AML World Health Organization (WHO) and European LeukemiaNet (ELN) classifications. Therapies are being developed that target the genetic aberrations.

In the 2016/2017 WHO AML classification AML with *NPM1* mutations and AML with biallelic CEBPA mutations are definite entities and AML with *BCR-ABL1* and AML with mutated *RUNX1* are provisional entities. The other major change is the addition of "myeloid neoplasms with germline predisposition".

The 2017 ELN divides AML into three risk categories. The Favorable category includes AML with t(8;21)(q22;q22), inv(16)(p13.1q22), mutated *NPM1* without *FLT3-ITD* or with *FLT3-ITD* with a low allelic ratio *(FLT3-ITD^{low})*, and biallelic mutated *CEBPA*. The Intermediate category includes mutated NPM1 and *FLT3-ITD^{high}*, wild-type *NPM1* without FLT3-ITD or with *FLT3-ITD^{low}*, t(9;11)(p21.3;q23.3) and cytogenetic abnormalities not favorable or adverse. The Adverse category includes AML with t(6;9)(p23;q34.1), t(v;11q23), t(9;22)(q34.1;q11.2), inv(3)(q21.3q26.2)/t(3;3)(q21.3;q26.2), -5/del(5q)/-7/-17/abn(17p), complex karyotype (≥3) or monosomal karyotype, wild-type *NPM1* and *FLT3-ITD^{high}*, mutated *RUNX1*, mutated *ASXL1* and mutated *TP53*.

Additional genes allow more precise classification of ELN genetic groups/subsets. Molecular understanding of AML is rapidly increasing. This is resulting in subgroups with apparent cure rates of >80% of younger and >40% of older patients without allogeneic transplantation in first complete remission, new predictors for treatment response and new targeted therapies.

e: Clara.Bloomfield@osumc.edu