Classifications pronostiques cytogénomiques

LAM adulte (ELN 2017)

vs LAM enfant (Myechild 2019)

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Diagnosis and management of AML in adults: 2017 ELN recommendations from an international expert panel

Hartmut Döhner,[1] Elihu Estey,[2] David Grimwade,[3] Sergio Amadori,[4] Frederick R. Appelbaum,[2] et al.

Table 5. 2017 ELN risk stratification by genetics

Risk category*	Genetic abnormality
Favorable	t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*
	inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MYH11*
	Mutated *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low}†
	Biallelic mutated *CEBPA*
Intermediate	Mutated *NPM1* and *FLT3*-ITD^{high}†
	Wild-type *NPM1* without *FLT3*-ITD or with *FLT3*-ITD^{low}† (without adverse-risk genetic lesions)
	t(9;11)(p21.3;q23.3); *MLLT3-KMT2A*‡
	Cytogenetic abnormalities not classified as favorable or adverse
Adverse	t(6;9)(p23;q34.1); *DEK-NUP214*
	t(v;11q23.3); *KMT2A* rearranged
	t(9;22)(q34.1;q11.2); *BCR-ABL1*
	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GATA2,MECOM(EVI1)*
	−5 or del(5q); −7; −17/abn(17p)
	Complex karyotype,§ monosomal karyotype‖
	Wild-type *NPM1* and *FLT3*-ITD^{high}†
	Mutated *RUNX1*¶
	Mutated *ASXL1*¶
	Mutated *TP53*#

Frequencies, response rates, and outcome measures should be reported by risk category, and, if sufficient numbers are available, by specific genetic lesions indicated.

*Prognostic impact of a marker is treatment-dependent and may change with new therapies.

†Low, low allelic ratio (<0.5); high, high allelic ratio (≥0.5); semiquantitative assessment of *FLT3*-ITD allelic ratio (using DNA fragment analysis) is determined as ratio of the area under the curve "*FLT3*-ITD" divided by area under the curve "*FLT3*-wild type"; recent studies indicate that AML with *NPM1* mutation and *FLT3*-ITD low allelic ratio may also have a more favorable prognosis and patients should not routinely be assigned to allogeneic HCT.[57-59,77]

‡The presence of t(9;11)(p21.3;q23.3) takes precedence over rare, concurrent adverse-risk gene mutations.

§Three or more unrelated chromosome abnormalities in the absence of 1 of the WHO-designated recurring translocations or inversions, that is, t(8;21), inv(16) or t(16;16), t(9;11), t(v;11)(v;q23.3), t(6;9), inv(3) or t(3;3); AML with *BCR-ABL1*.

‖Defined by the presence of 1 single monosomy (excluding loss of X or Y) in association with at least 1 additional monosomy or structural chromosome abnormality (excluding core-binding factor AML).[116]

¶These markers should not be used as an adverse prognostic marker if they co-occur with favorable-risk AML subtypes.

#*TP53* mutations are significantly associated with AML with complex and monosomal karyotype.[37,66-69]

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	Wild-type *NPM1* and *FLT3*-ITD^{high}†
	Mutated *RUNX1*¶
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	Mutated *TP53*#

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APPENDIX 1 – RISK GROUP STRATIFICATION

Cytogenetic and molecular abnormalities

Good Risk cytogenetic and molecular abnormalities

- t(8;21)(q22;q22)/*RUNX1-RUNX1T1*
- inv(16)(p13q22)/t(16;16)(p13;q22)/*CBFB-MYH11*
- Mutation of *NPM1* without *FLT3*-ITD
- Double mutation of *CEPBA* without *FLT3*-ITD

Intermediate Risk Cytogenetic abnormalities

- t(9;11)(p21;q23)/*MLL-MLLT3*
- t(11;19)(q23;p13.3)/*MLL-MLLT1*
- All other *MLL* rearrangements not classified as high risk
- All other abnormalities which are neither good or poor risk

Poor risk cytogenetic and molecular abnormalities

- inv(3)(q21q26)/t(3;3)(q21;q26) abn(3q26) ***MECOM/EVI1*** **+(FISH)**
- -5/del(5q)
- -7
- t(6,9)(p23;q34)/*DEK-NUP214*
- t(9;22)(q34;q11)/*BCR-ABL1*
- 12p abnormalities
- t(6,11)(q27;q23)/*MLL-MLLT4*
- t(4;11)(q21;q23)/*MLL-AFF1*
- t(10;11)(p11~14;q23)/*MLL-MLLT10* ➡ **all 10p/*MLL*r**
- t(5;11)(q35;p15.5)/*NUP98-NSD1* ➡ **all *NUP98r***
- t(7;12)(q36;p13)/*MNX1-ETV6*
- inv(16)(p13.3q24.3)/*CBFA2T3-GLIS2*
- *FLT3*-ITD without NPM1 or CBF

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- t(10;11)(p11~14;q23)/*MLL-MLLT10* → **all 10p/*MLL*r**
- t(5;11)(q35;p15.5)/*NUP98-NSD1* → **all *NUP98r***
- t(7;12)(q36;p13)/*MNX1-ETV6*
- inv(16)(p13.3q24.3)/*CBFA2T3-GLIS2*
- *FLT3*-ITD without NPM1 or CBF

Other poor risk categories

- Secondary leukaemia without good risk cytogenetics
- Induction failure after course 1: morphological failure confirmed by flow MRD in Good Risk /Standard Risk patients

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