

Supplemental Figure 1

Class-defining cytogenetic abnormalities		Prognostic genetic alterations (according to 2022 ELN recommendations)
<p><u>Recurrent chromosomal translocations</u> t(15;17)(q24.1;q21.2); <i>PML::RARA</i>* ^ t(8;21)(q22;q22.1); <i>RUNX1::RUNX1T1</i>* inv(16)(p13.1q22) or t(16;16)(p13.1;q22); <i>CBFB::MYH11</i>* t(9;11)(p21.3;q23.3); <i>MLLT3::KMT2A</i>* ^ t(6;9)(p22.3;q34.1); <i>DEK::NUP214</i>* inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); <i>GATA2::MECOM(EVI1)</i>* ^ t(1;3)(p36.3;q21.3); <i>PRDM16::RPN1</i>* t(1;22)(p13.3;q13.1); <i>RBM15::MRTF1</i>* t(3;5)(q25.3;q35.1); <i>NPM1::MLF1</i>* t(8;16)(p11.2;p13.3); <i>KAT6A::CREBBP</i>* t(16;21)(p11.2;q22.2); <i>FUS::ERG</i>* t(16;21)(q24.3;q22.1); <i>RUNX1::CBFA2T3</i>* t(9;22)(q34.1;q11.2); <i>BCR::ABL1</i>** <u>Myelodysplasia-related cytogenetic abnormalities **</u> Complex karyotype^d Unbalanced abnormalities: del(5q)/t(5q)/add(5q); -7/del(7q); +8; del(12p)/t(12p)(add(12p)); i(17q); -17/add(17p) or del(17p); del(20q); idic(X)(q13)</p>		<p><u>Favorable risk</u> t(8;21)(q22;q22.1); <i>RUNX1::RUNX1T1</i> inv(16)(p13.1q22) or t(16;16)(p13.1;q22); <i>CBFB::MYH11</i> Mutated <i>NPM1</i>^a without <i>FLT3</i>-ITD bZIP in-frame <i>CEBPA</i> mutations ^b</p>
<p>Class-defining mutations</p>		<p><u>Intermediate risk</u> Mutated <i>NPM1</i>^a and <i>FLT3</i>-ITD^c Wild-type <i>NPM1</i> with <i>FLT3</i>-ITD^c t(9;11)(p21.3;q23.3); <i>MLLT3::KMT2A</i> Cytogenetic and/or molecular abnormalities not classified as favorable or adverse</p>
<p><i>TP53</i>** (VAF≥10%) <i>NPM1</i>* bZIP in-frame <i>CEBPA</i>*</p>	<p><u>Myelodysplasia-related mutations**</u> <i>ASXL1</i> <i>BCOR</i> <i>EZH2</i> <i>RUNX1</i> <i>SF3B1</i> <i>SRSF2</i> <i>STAG2</i> <i>U2AF1</i> <i>ZRSR2</i></p>	<p><u>Adverse risk</u> t(6;9)(p23;q34.1); <i>DEK::NUP214</i> t(v;11q23.3); <i>KMT2A</i>-r t(9;22)(q34.1;q11.2); <i>BCR::ABL1</i> t(8;16)(p11;p13); <i>KAT6A::CREBBP</i> inv(3)(q21.3q26.2) or (3;3)(q21.3;q26.2); <i>GATA2,MECOM(EVI1)</i> t(3q26.2;v), <i>MECOM(EVI1-r)</i> -5 or del(5q); -7; -17/del(17p) Complex karyotype^d, monosomal karyotype^e ^fMutated <i>ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1, or ZRSR2</i> Mutated <i>TP53</i> (VAF≥10%)</p>
<p>Additional clinically actionable mutations</p>		
<p><i>FLT3</i> <i>IDH1</i> <i>IDH2</i></p>		

*Bone marrow or peripheral blood blast must be $\geq 10\%$ to classify as AML

**Bone marrow or peripheral blood blast must be $\geq 20\%$ to classify as AML; cases with 10%-19% blast counts are designated as MDS/AML

***Complex karyotype, or unbalanced abnormalities: del(5q)/t(5q)/add(5q); -7/del(7q); +8; del(12p)/t(12p)(add(12p); i(17q) as the sole aberration; -17/add(17p) or del(17p); del(20q); idic(X)(q13), or balanced abnormalities: t(2;11)(p21;q23.3); t(5;7)(q32;q11.2); *HIP1::PDGFRB*; t(5;10)(q32;q21.2); *CCDC6::PDGFRB*; t(5;11)(q35.2;p15.4); *NUP98::NSD1*; t(5;12)(q32;p13.3); *ERC1::PDGFRB*; t(5;17)(q32;p13.2); *RABEP1::PDGFRB*; t(11;16)(q23.3;p13.3); *KMT2A::CREBBP*

^ Other recurring translocations involving *RARA*, *MECOM*, and *KMT2A* should be reported specifically when the partner gene is appropriately identified. (according to ICC 2022 recommendations).

a If co-occurring with other adverse risk chromosomal alterations then classify as adverse-risk, regardless of *FLT3* status.

b Biallelic or monoallelic

c Regardless of allelic ratio

d ≥ 3 unrelated chromosome abnormalities in the absence of other class-defining translocations and inversions; excludes hyperdiploid karyotypes based on multiple trisomies

e A single chromosomal monosomy (excluding -X or -Y) in addition to at least one other monosomy or structural abnormality (excluding core-binding factor AML)

f These mutations do not signify adverse risk if co-occurring in the context of other favorable-risk AML subtypes