Myelodysplastic Syndrome & Acute Myeloid Leukemia

**The European Leukemia Net (ELN)**

2017 Genetic Risk Stratification of AML

<table>
<thead>
<tr>
<th>Risk Category*</th>
<th>Genetic Abnormality</th>
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<tr>
<td><strong>Favorable</strong></td>
<td>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&lt;sup&gt;low†&lt;/sup&gt; Biallelic mutated CEBPA</td>
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<td><strong>Intermediate</strong></td>
<td>Mutated NPM1 and FLT3-ITD&lt;sup&gt;high†&lt;/sup&gt; Wild-type NPM1 without FLT3-ITD or with FLT3-ITD&lt;sup&gt;low†&lt;/sup&gt; (without adverse-risk genetic lesions) T(9;11)(p21.3;q23.3); MLLT3-KMT2A&lt;sup&gt;‡&lt;/sup&gt; Cytogenetic abnormalities not classified as favorable or adverse</td>
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<td><strong>Adverse</strong></td>
<td>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 ll Wild-type NPM1 and FLT3-ITD&lt;sup&gt;high†&lt;/sup&gt; Mutated RUNX1¶ Mutated ASXL1¶ Mutated TP53#</td>
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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.

‡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)(q23.3), t(6;9), inv(3) or t(3;3); AML with BCR-ABL1.

II Defined by 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).

¶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.