### Myelodysplastic Syndrome & Acute Myeloid Leukemia

**MATTER:**

Multidisciplinary Approach To Testing and Diagnosis, Evaluation of Risk, and Personalized Treatment Selection

**AML Risk Stratification: Indications for Transplant**
(Reduced Intensity Conditioning for Older Patients)

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<th>Risk Category*</th>
<th>Genetic Abnormality</th>
<th>Post-remission Therapy</th>
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| **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<sup>low</sup>†  
Biallelic mutated CEBPA | Consolidation |
| **Intermediate** | Mutated NPM1 and FLT3-ITD<sup>high</sup>†  
Wild-type NPM1 without FLT3-ITD or with FLT3-ITD<sup>low</sup>†  
(without adverse-risk genetic lesions)  
T(9;11)(p21.3;q23.3); MLLT3-KMT2A‡  
Cytogenetic abnormalities not classified as favorable or adverse | Allogeneic Transplantation |
| **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 ll  
Wild-type NPM1 and FLT3-ITD<sup>high</sup>†  
Mutated RUNX1¶  
Mutated ASXL1¶  
Mutated TP53# | Allogeneic Transplantation |

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)(v;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 monosom al karyotype.