**MDS Prognostic Scoring System: IPSS-R**

<table>
<thead>
<tr>
<th>Prognostic Variables</th>
<th>Lille</th>
<th>IPSS</th>
<th>DIPSS</th>
<th>DIPSS Plus</th>
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<tbody>
<tr>
<td>Cytogenetic results (category)</td>
<td></td>
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<tr>
<td>Bone marrow blasts (%)</td>
<td>&lt;=2.0; &gt;2.0-&lt;5.0, 5.0-10.0, &gt;10.0</td>
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<tr>
<td>Degree of anemia (Hgb in g/dl)</td>
<td>&gt;= 10 vs. 8-10 vs. &lt; 8</td>
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<tr>
<td>Degree of neutropenia (x 10^9/L)</td>
<td>&gt;= 0.8 vs. &lt; 0.8</td>
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<tr>
<td>Degree of thrombocytopenia (x 10^9/L)</td>
<td>&gt;= 100 vs. 50-99 vs. &lt;50</td>
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*The Lille score identified a WBC > 30 x 10^9/L or a WBC of < 4 x 10^9/L as adverse indicators.

Other prognostic scoring systems such as WPSS include WHO risk classification, transfusion dependence, and cytogenetic class. The MDACC model incorporates age, performance status, leukocytosis, degree of anemia/thrombocytopenia, marrow blasts, and cytogenetic class.


In a large study conducted by the iWG-MDS, mutations involving TP53, CBL, EZH2, RUNX1, U2AF1, and ASXL1 had an independent, adverse impact on prognosis. Pts with mutated SF3B1, or without any such mutation had a more favorable prognosis.


*See www.aamds.org/mdsrisk for summary of MDS prognostic scoring systems.

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**Prognosis in Primary Myelofibrosis**

- Anemia (Hgb < 10g/dl)
- WBC > 25 x 10^9/L
- Circulating blasts ≥ 1%
- Constitutional symptoms
- Age > 65
- Abnormal karyotype
- Platelets <100 x 10^9/L
- RBC transfusion dependence

*The impact of the driver mutational profile on prognosis is becoming more clear. Pts with CALR mutations have a more favorable outcome, compared to those with JAK2 or MPL mutations, and especially those that lack JAK2/CALR/MPL (“triple-negative”).

Mutations in other genes also impact prognosis, and those with 1 or more mutations involving ASXL1, IDH, EZH2, and SRSF2 have a high risk profile. A particularly high risk profile may include pts that are CALR wild-type/ASXL1 mutated.

MDS/MPN Prognostic Variables

**Prognostic Variables in CMML**
- Advanced age (> 65)
- Decreased hemoglobin (< 10 g/dl)
- *Red cell transfusion dependency*
- Decreased platelets (< 100 x 10^9/L)
- Increased absolute monocyte count (> 10 x 10^9/L)
- Circulating immature myeloid cells
- CMML FAB subtype (*leukocyte < 13 x 10^9/L more favorable*)
- CMML WHO subtype (worse prognosis w/ increasing PB/BM blasts)
- *Cytogenetic risk category*
  - Low: Normal or –Y
  - High: +8, abn of 7, complex
  - Intermediate: All others
- *Presence of RUNX1, NRAS, SETBP1, ASXL1 mutations*

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**MDS: Refractory Cytopenias and Dysplasia**

**Clinical features**
- Constitutional symptoms less likely
- Refractory cytopenia(s)
- Organomegaly unusual

**Blood and marrow findings**
- Hyper > hypocellularity
- Peripheral/marrow blasts
- Single or multi-lineage dysplasia
- +/ring sideroblasts

**Cytogenetic and molecular features**
- CKA in 40-70%, even in absence of dysplasia (commonly 5q-, -7 or 7q-, +8, 20q-, and -Y)
- Mutations in SF3B1, TET2, SRSF2, ASXL1, DNMT3A, RUNX1, U2AF1, TP53, and EZH2 are commonly identified, but their presence alone is insufficient to diagnose a MDS

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**MDS/MPN Overlap Syndromes: Dysplastic Cytopenias with Proliferation**

**Clinical features**
- +/- Constitutional symptoms
- Cytopenia(s) with cytosis:
- Thrombocytosis (MDS/MPN with ring sideroblasts and thrombocytosis)
- Monocytosis (CMML)
- Organomegaly

**Blood and marrow findings**
- Hypercellularity
- Peripheral/marrow blasts
- Dysplasia
- Ring sideroblasts (RARS-T)

**Cytogenetic and molecular features**
- CKA in ~30% of CMML
- (+8, del(9q), +10, -11q, -12p, +17p, +19, and -Y)
- JAK2 V617F mutation (~50%) in MDS/MPN with ring sideroblasts and thrombocytosis often co-mutated with SF3B1 mutations
- CSF3R mutations are rarely identified in aCML, whereas SETBP1 and/or ETNK1 mutations can be seen in up to 30% of aCML cases
- SRSF2, TET2, and/or ASXL1 are frequently identified in CMML, whereas SETBP1, NRAS/KRAS, RUNX1, CBL, and EZH2 are less frequently identified

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**Myelofibrosis: Myeloproliferation**

**Clinical features**
- Constitutional symptoms likely
- Cytopenia or cytosis
- Increased LDH
- Organomegaly

**Blood and marrow findings**
- Leukerythroblastosis
- Peripheral/marrow blasts
- Variable cellularity
- Proliferating/typical megakaryocytes
- Reticulin/collagen fibrosis

**Cytogenetic and molecular features**
- CKA in ~50%
- (20q-, 13q-, abn chromosome 1 or 12, +8,+9,-5, and -7)
- JAK2 V617F (60%);
- CALR (20-25%);
- MPL (<10%)

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