Myelodysplastic Syndromes (MDS)
A challenge, especially in elderly patients
(SIOG, Berlin, 2009)

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### The risk score IPSS (International prognostic scoring system)

<table>
<thead>
<tr>
<th>Prognostic variable</th>
<th>Score value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Bone marrow blasts (%)</td>
<td>&lt;5</td>
</tr>
<tr>
<td>Karyotype ¹</td>
<td>Good</td>
</tr>
<tr>
<td>Cytopenia ²</td>
<td>0/1</td>
</tr>
</tbody>
</table>

¹ Karyotype: Good: Normal, Y-, 5q-, 20q-; Intermediate: All other; Poor: Chr. 7 aberration and/or ≥3 aberrations.
2 Cytopenia: Hb<100 G/l; neutrophil count <1,8 G/l; platelet count < 100 G/l

<table>
<thead>
<tr>
<th>IPSS Group</th>
<th>IPSS Total Score</th>
<th>Survival (median; yrs)</th>
<th>25% AML evolution (yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Age at diagnosis</td>
<td>Age at diagnosis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>≤70yrs</td>
<td>&gt;70yrs</td>
</tr>
<tr>
<td>Low</td>
<td>0</td>
<td>9</td>
<td>3,9</td>
</tr>
<tr>
<td>Intermediate-1</td>
<td>0,5-1,0</td>
<td>4,4</td>
<td>2,4</td>
</tr>
<tr>
<td>Intermediate-2</td>
<td>1,5-2</td>
<td>1,3</td>
<td>1,2</td>
</tr>
<tr>
<td>High</td>
<td>≥2,5</td>
<td>0,4</td>
<td>0,4</td>
</tr>
</tbody>
</table>

Greenberg et al., 1997
### The prognostic score WPSS (WHO based Prognostic Scoring System)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td><strong>WHO Category(^1)</strong></td>
<td>RA, RARS, 5q-</td>
</tr>
<tr>
<td><strong>Karyotype(^2)</strong></td>
<td>Good</td>
</tr>
<tr>
<td><strong>Transfusion requirement(^3)</strong></td>
<td>No</td>
</tr>
</tbody>
</table>

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1 Based on WHO classification (Table 1)

2 Karyotype (definition identical to IPSS; Table 2)

3 **Transfusion requirement**
   At least one RBC transfusion every 8 weeks over a period of 4 months

*Malcovati et al., 2007, JCO*
**Nordic Score to predict response to Erythropoiesis-stimulating factors (ESFs) in MDS**

<table>
<thead>
<tr>
<th>Score</th>
<th>Transfusion requirement (RBC)</th>
<th>Serum Epo$^1$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt; 2U/month</td>
<td>&lt; 500 U/L</td>
</tr>
<tr>
<td>Score</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>≥ 2U/month</td>
<td>≥ 500 U/L</td>
</tr>
<tr>
<td>Score</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Probability of response:**
- Total Score 0: 74% ; 1: 23% ; 2: 7%

**Legend:**
- $^1$ Serum Erythropoietin level before treatment

*Hellstrom-Lindberg et al., 2003*
Symptomatic anemia, granulopenia, thrombopenia

Supportive therapy including transfusions & iron-chelation

- Del(5q)
- ESA (Lenalidomid\(^1\))
- EPO < 500 U/l and/or low transfusion need \(^2\)
- ESA ± G-CSF
- EPO ≥ 500 U/l and/or high transfusion need \(^2\)
- Valproic-acid
- (5-Azacytidine\(^4\))
- Hypoplastic MDS HLA-DR15 \(^3\)
- CyA (ATG)

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\(^1\) In MDS approval so far only by FDA; EMEA approval is pending.
\(^2\) Based on predictive model (Nordic score) for ESA treatment in anemic MDS patients. G-CSF augments the erythroid response to ESAs particularly in MDS with an increase of ring sideroblasts (RARS).
\(^3\) Response more frequent in younger patients, in hypoplastic MDS and in HLADR-15.
\(^4\) 5-Azacytidine might be effective in low risk MDS even in granulopenia and thrombopenia. EMEA approval so far for high-risk MDS and CMML. Role in low-risk MDS is analysed in clinical studies.
Treatment options in Elderly High-Risk MDS (IPSS Intermediate II und High grade)

Intensive therapy \(^1\)

- Yes
  - Donor
    - RIC-HSCT \(^2\)
  - No Donor
    - AML-like induction/consolidation or 5-Azacytidine
- No
  - 5-Azacytidine \(^3\) or Clinical study or BSC \(^4\)

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\(^1\) Depending on age, performance status, comorbidities, feasibility, karyotype and patient preference.

\(^2\) Upper age limits applied are 50-55yrs for myeloablative HSCT (haematopoietic stem-cell transplantation) and 65-70yrs for RIC-HSCT (reduced intensity conditioning HSCT).

\(^3\) 5-Azacytidine represents the treatment of choice in elderly patients who are not eligible for intensive therapies like AML-induction or HSCT. AZA is effective even in unfavourable karyotype like monosomy 7 or complex aberrations.

\(^4\) BSC (best supportive care).
MDS – Individualised therapy

TREATMENT DECISION

• **Risk factor**
• **Predictive factor**
  (for response, tolerance)
• **Response parameter**

SOIL
PATIENT
Age, Sex
Function
Comorbidities
Cognition
Social support
Nutritional situation
QoL

SEED
DISEASE
BM-blasts
Cytogenetics
Cytopenia
Serum LDH etc.

Transfusion need
Serum ferritin