Myelodyplastic Syndromes

Paul J. Shami, M.D.

Professor of Hematology, University of Utah
Member, Huntsman Cancer Institute
Objectives

• Define Myelodysplastic Syndromes (MDS)
• Explain how MDS are diagnosed and classified
• Discuss the different treatment options
• Identify patient education and support resources
• Better prepare patients to discuss their diagnosis, treatment, and care with their physicians, team, family, and friends
Terminology

- **Cancer**
  - Benign
  - Malignant
  - Metastatic

- **Blood (bone marrow)-related cancers**
  - Leukemia
  - Lymphoma
  - Myeloma
  - Myelodysplastic syndromes
  - Myeloproliferative disorders

- **Types of leukemia**
  - Acute vs. Chronic
  - Lymphoid vs. Myeloid
MDS: Bone Marrow-Related Cancers

Lymphoid Cells:
- Natural Killer Cell
- T Cell
- B Cell
- Red Blood Cell
- Platelets

Myeloid Cells:
- Monocyte
- Neutrophil
- Eosinophil
- Basophil
Myelodysplastic Syndromes

- Clinical diseases characterized by low blood counts (anemia, low WBC, low platelets)
- Bone marrow usually shows increased number of cells
- Can develop into AML
MDS Epidemiology

- Approximately 20,000 estimated new cases/year in US
- Predominantly a disease of the elderly
  - Median age > 60
  - Incidence greater in men than women
  - Incidence increases with age
- Median survival varies depending on risk category
MDS - Symptoms

- Many patients have no apparent symptoms, but are diagnosed after routine laboratory tests uncover abnormalities in the circulating blood cells.
- Fatigue is the most common symptom of MDS.
- Early symptoms of MDS may include:
  - Bruising
  - Bleeding
  - Shortness of breath
  - Rapid heart rate
  - Weight loss
  - Fever
  - Loss of appetite
MDS - Risk factors

• Cause of MDS unknown
• Damage to the DNA of bone marrow cells
• Environmental
  • Certain chemicals (Benzene)
  • Radiation exposure
  • Chemotherapy
MDS - Diagnosis

• History/Physical Exam
• Blood tests
  • Blood count
  • Chemistries
  • Iron studies
  • B12/Folate
  • Erythropoietin level
• Bone marrow biopsy
  • Morphology (examine slides under microscope)
  • Flow cytometry (check for abnormal cells)
  • Cytogenetics/FISH (chromosome test)
  • Molecular studies (DNA mutations)
MDS - Complications

- **Bleeding**
  - Low platelet count

- **Infections**
  - Low levels of normal white blood cells that fight infections

- **Acute Myeloid Leukemia**
MDS Classification

• French American British (FAB)
  • no longer used

• World Health Organization (WHO)
  • currently used and regularly updated

• International Prognostic Scoring System – Revised (IPSS-R)
  • used for prognostication and treatment planning
# MDS - WHO classification

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Blood</th>
<th>Bone marrow</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDS with single lineage dysplasia (MDS-SLD)</td>
<td>Single or bicytopenia</td>
<td>Dysplasia in ≥10% of one cell line, &lt;5% blasts</td>
</tr>
<tr>
<td>MDS with ring sideroblasts (MDS-RS)</td>
<td>Anemia, no blasts</td>
<td>≥15% of erythroid precursors w/ring sideroblasts, or ≥5% ring sideroblasts if $SF3B1$ mutation present</td>
</tr>
<tr>
<td>MDS with multilineage dysplasia (MDS-MLD)</td>
<td>Cytopenia(s), &lt;1 x 10^9/L monocytes</td>
<td>Dysplasia in ≥10% of cells in ≥2 hematopoietic lineages, ± 15% ring sideroblasts, &lt;5% blasts</td>
</tr>
<tr>
<td>MDS with excess blasts-1 (MDS-EB-1)</td>
<td>Cytopenia(s), ≤2%–4% blasts, &lt;1 x 10^9/L monocytes</td>
<td>Unilineage or multilineage dysplasia, 5%–9% blasts, no Auer rods</td>
</tr>
<tr>
<td>MDS with excess blasts-2 (MDS-EB-2)</td>
<td>Cytopenia(s), 5%–19% blasts, &lt;1 x 10^9/L monocytes</td>
<td>Unilineage or multilineage dysplasia, 10%–19% blasts, ± Auer rods</td>
</tr>
<tr>
<td>MDS, unclassifiable (MDS-U)</td>
<td>Cytopenias, ±1% blasts on at least 2 occasions</td>
<td>Unilineage dysplasia or no dysplasia but characteristic MDS cytogenetics, &lt;5% blasts</td>
</tr>
<tr>
<td>MDS with isolated del(5q)</td>
<td>Anemia, platelets normal or increased</td>
<td>Unilineage erythroid dysplasia, isolated del(5q), &lt;5% blasts</td>
</tr>
<tr>
<td>Refractory cytopenia of childhood</td>
<td>Cytopenias, &lt;2% blasts</td>
<td>Dysplasia in 1–3 lineages, &lt;5% blasts</td>
</tr>
<tr>
<td>MDS with excess blasts in transformation (MDS-EB-T)</td>
<td>Cytopenias, 5%–19% blasts</td>
<td>Multilineage dysplasia, 20%–29% blasts, ± Auer rods</td>
</tr>
</tbody>
</table>
MDS – IPSS-R

- Patients are stratified into five risk groups according to survival and risk of AML transformation.

- Scoring system based on % of bone marrow blasts, chromosomes and severity of blood count abnormalities.
**Table 3. IPSS-R prognostic score values**

<table>
<thead>
<tr>
<th>Prognostic variable</th>
<th>0</th>
<th>0.5</th>
<th>1</th>
<th>1.5</th>
<th>Intermediate</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytogenetics</td>
<td>Very good</td>
<td>—</td>
<td>Good</td>
<td>—</td>
<td>Intermediate</td>
<td>Poor</td>
<td>Very poor</td>
<td></td>
</tr>
<tr>
<td>BM blast, %</td>
<td>≤ 2</td>
<td>—</td>
<td>&gt; 2% - &lt; 5%</td>
<td>—</td>
<td>5% - 10%</td>
<td>&gt; 10%</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>≥ 10</td>
<td>—</td>
<td>8 - &lt; 10</td>
<td>&lt; 8</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>Platelets</td>
<td>≥ 100</td>
<td>50 - &lt; 100</td>
<td>&lt; 50</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
<tr>
<td>ANC</td>
<td>≥ 0.8</td>
<td>&lt; 0.8</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td></td>
</tr>
</tbody>
</table>

— indicates not applicable.

**Table 4. IPSS-R prognostic risk categories/scores**

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Risk score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very low</td>
<td>≤ 1.5</td>
</tr>
<tr>
<td>Low</td>
<td>&gt; 1.5-3</td>
</tr>
<tr>
<td>Intermediate</td>
<td>&gt; 3.45</td>
</tr>
<tr>
<td>High</td>
<td>&gt; 4.5-6</td>
</tr>
<tr>
<td>Very high</td>
<td>&gt; 6</td>
</tr>
</tbody>
</table>

*Blood* 120: 2454-2465, 2012
IPSS-R Survival (n=7012)
IPSS-R Freedom from AML Transformation

Months

very good

good

int

poor

very poor
MDS - Management

1- Determine disease risk based on IPSS-R score.
2- Consider observation to determine pace of disease progression.
3- Stratify patients according to risk.
4- Individualize approach based on patient’s age, performance status, health, etc...
MDS - Management
Low risk disease

1- Treat if clinically significant low blood counts.
2- Transfusion support as needed.
3- Iron chelation therapy if indicated.
4- If 5q- present - treat with Lenalidomide (Revlimid).
5- If 5q- absent - consider treatment with growth factors (erythropoietin +/- G-CSF).
6- If no response to growth factors, consider hypomethylating agents (decitabine, azacitidine).
7- Determine if patient is eligible for immunosuppressive therapy (cyclosporine, ATG) and treat accordingly.
MDS - Management
High risk disease

1- Azacitidine or decitabine.

2- Transplant if patient is candidate.
Talking With Your Team: 
What Position Do You Play?

- Ask questions about your disease and treatment
- Keep your doctors’ appointments
- Keep your doctor & nurse informed of side effects
- Inform your doctor & nurse before taking other medications
- Avoid supplements
- Avoid alcohol
- Look at your attitude and explore support options
Patient Education and Support Services

- Myelodysplastic Syndromes Foundation
  - www.mds-foundation.org

- The Leukemia & Lymphoma Society
  - www.lls.org

- National Cancer Institute
  - www.cancer.gov