

Myelodysplastic Syndromes

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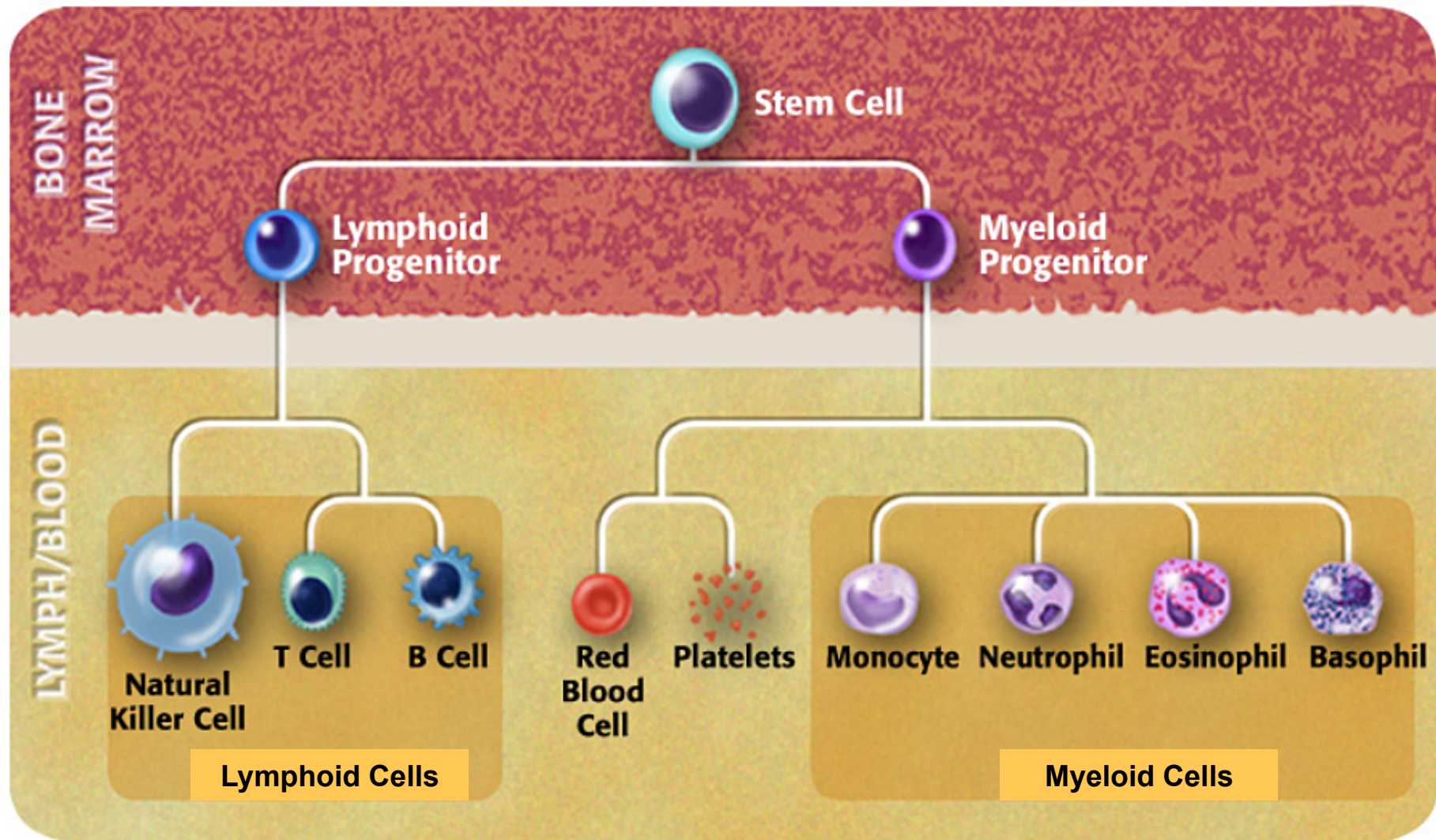
Objectives

- **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*



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

- **~ 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

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

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**

MDS – IPSS-R

Table 3. IPSS-R prognostic score values

Prognostic variable	0	0.5	1	1.5	2	3	4
Cytogenetics	Very good	—	Good	—	Intermediate	Poor	Very poor
BM blast, %	≤ 2	—	> 2%- < 5%	—	5%-10%	> 10%	—
Hemoglobin	≥ 10	—	8- < 10	< 8	—	—	—
Platelets	≥ 100	50-< 100	< 50	—	—	—	—
ANC	≥ 0.8	< 0.8	—	—	—	—	—

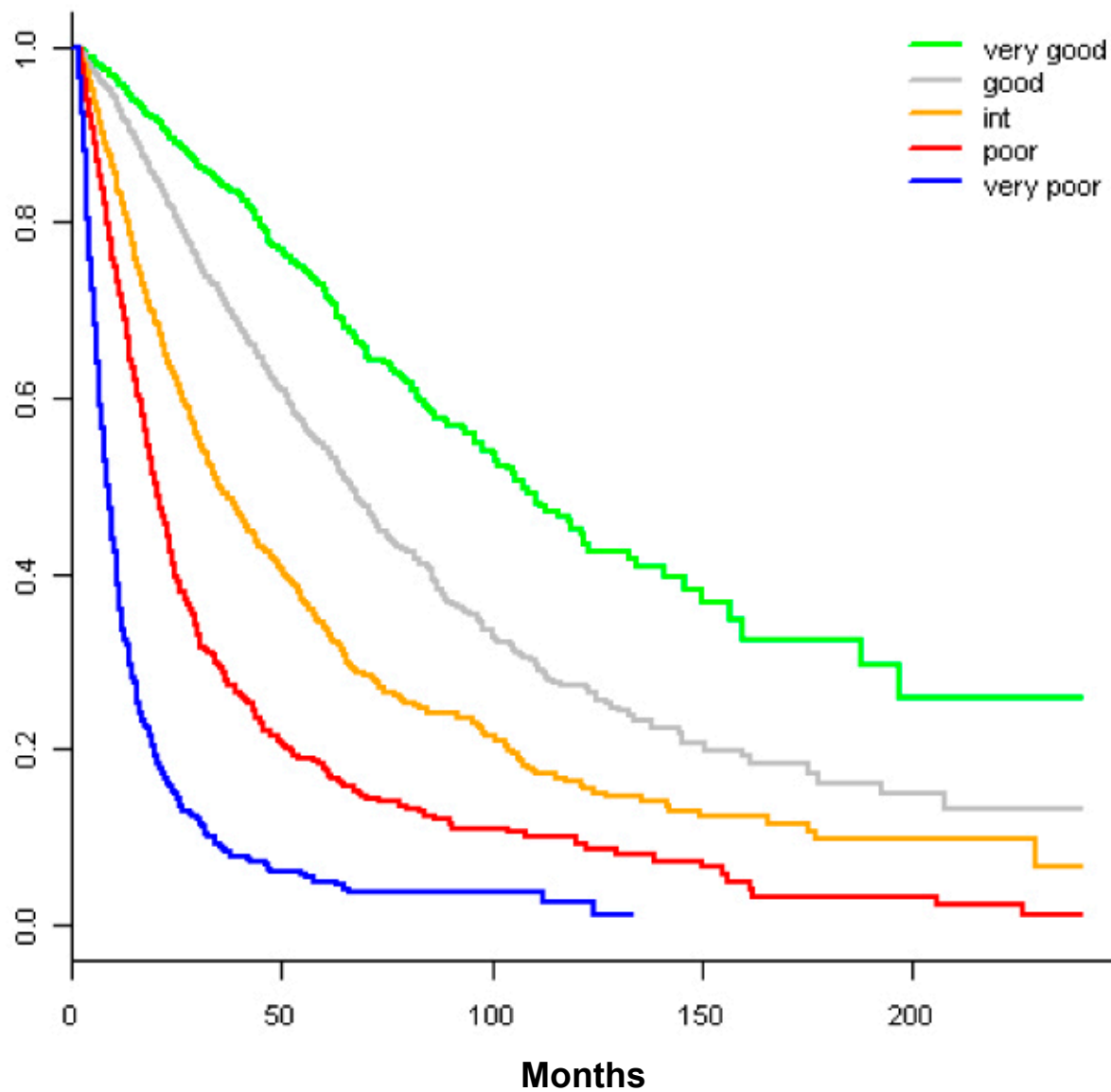
— indicates not applicable.

Table 4. IPSS-R prognostic risk categories/scores

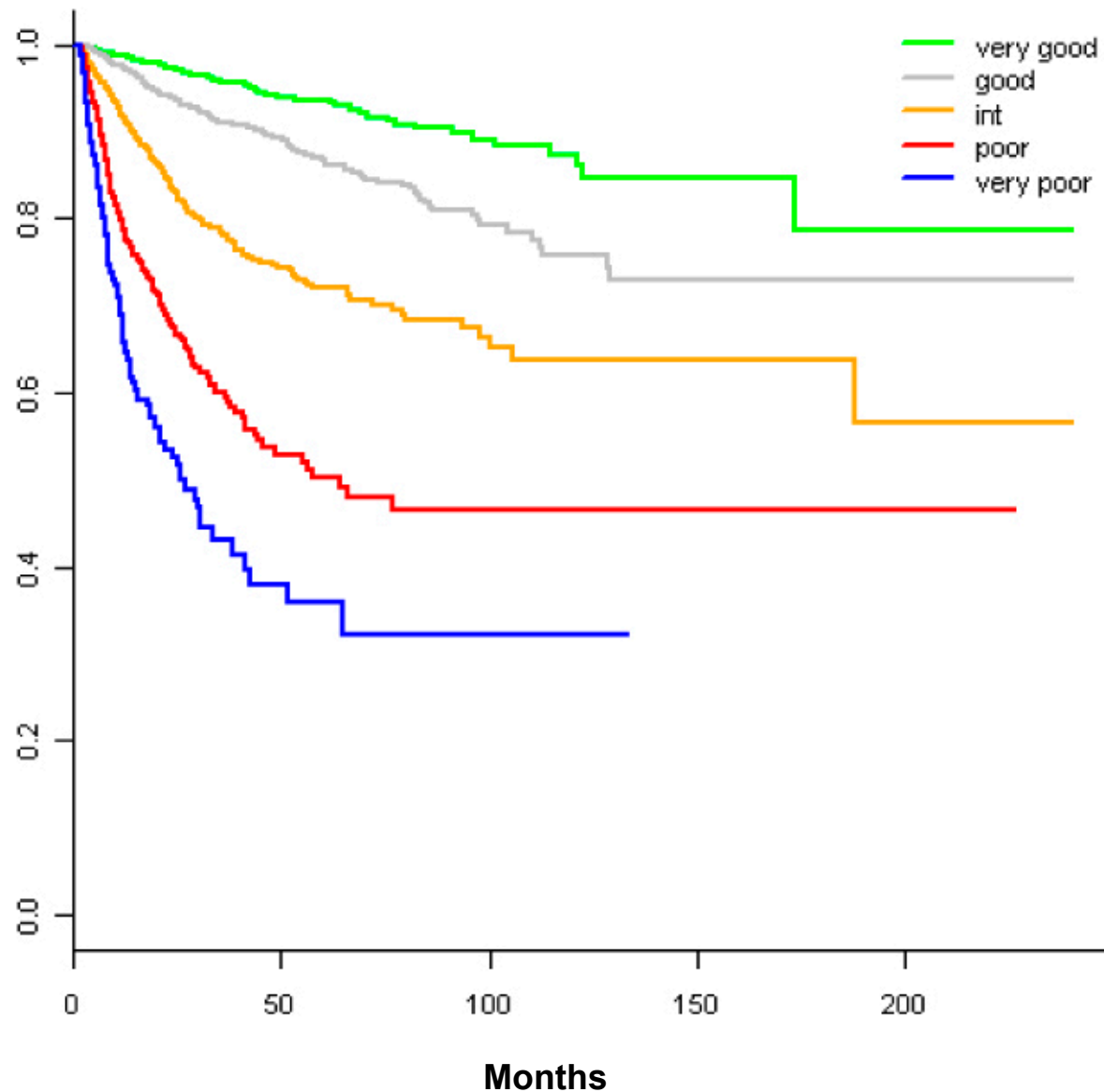
Risk category	Risk score
Very low	≤ 1.5
Low	> 1.5-3
Intermediate	> 3-4.5
High	> 4.5-6
Very high	> 6

Blood 120: 2454-2465, 2012

IPSS-R Survival (n=7012)



IPSS-R Freedom from AML Transformation



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