UNIVERSITY of MARYLAND MEDICAL CENTER

MDS: Classification and Risk Scores

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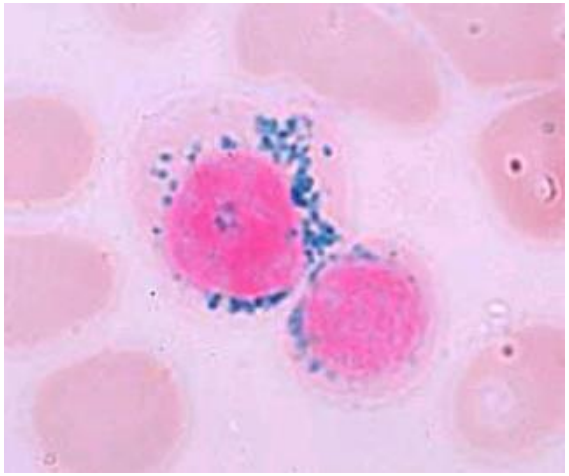
World Health Organization (WHO) Classification

- Latest revision in 2016
- Based on morphology, blast percentage, and karyotype
- 6 different sub-types:
  - MDS with Ring Sideroblasts
  - MDS with Single Lineage Dysplasia
  - MDS with Multilineage Dysplasia
  - MDS with Isolated del(5q)
  - MDS with Excess Blasts
  - MDS Unclassifiable

MDS with Ring Sideroblasts (MDS-RS)

- ≥15% ring sideroblasts
- Associated with *SF3B1* mutation
- Sub-classified into:
  - MDS-RS with single lineage dysplasia (MDS-RS-SLD)
  - MDS-RS with multilineage dysplasia (MDS-RS-MLD)
- No increased myeloid blasts
- Generally has a better prognosis



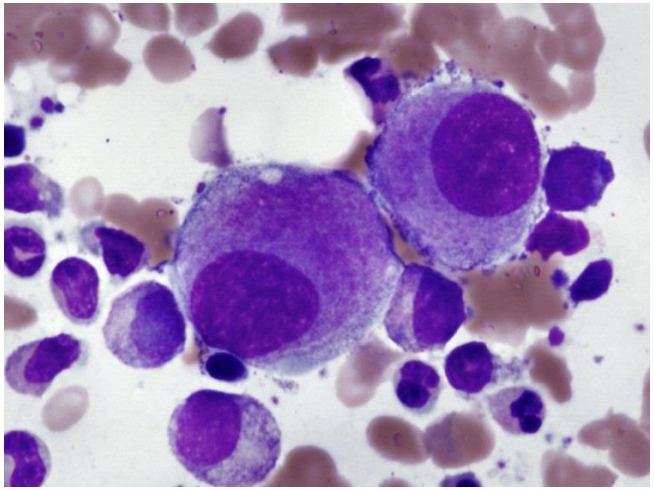
MDS with single or multilineage dysplasia

Classification	Ring Sideroblasts	Myeloid Blasts	Dysplasia	Cytopenias
MDS with single lineage dysplasia (MDS-SLD)	Not increased	Not increased	1 cell line	1 or 2
MDS with multilineage dysplasia (MDS-MLD)			2 or 3 cell lines	1-3

- Lower risk of disease progression
- MDS-SLD has a better prognosis than MDS-MLD

MDS with isolated del(5q)

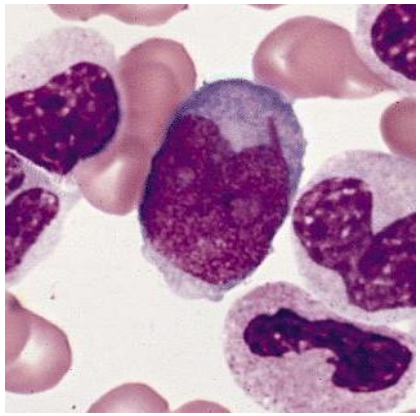
- Most common cytogenetic abnormality in MDS (~10-15%)
- Presentation
  - No increased myeloid blasts
  - Usually isolated anemia
  - Female predominance



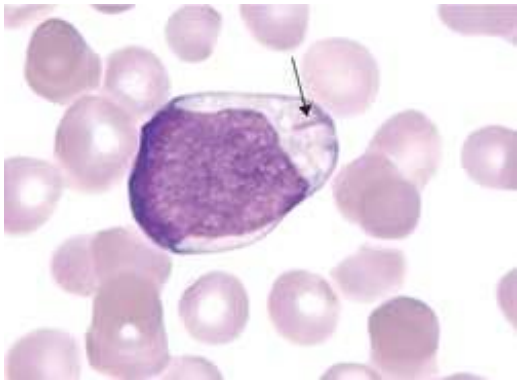
- Lower risk of disease progression
- Often responds to lenalidomide

MDS with Excess Blasts (MDS-EB)

- Increased bone marrow blasts
  - MDS-EB1: 5-9%
  - MDS-EB2: 10-19%



- Associated with higher risk of progression to AML, poorer prognosis

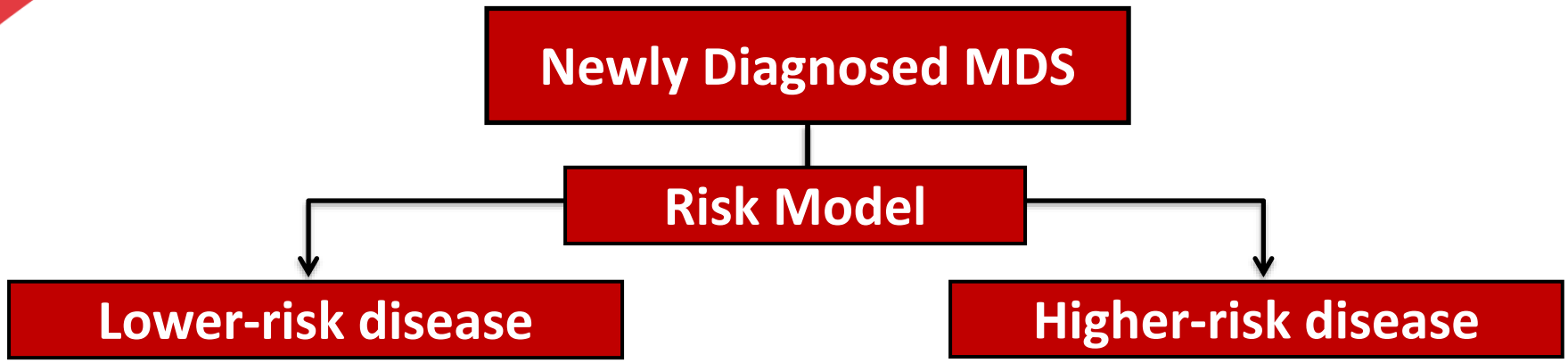


MDS Unclassifiable

- Includes MDS with a defining cytogenetic abnormality
  - Any cytopenia(s)
  - <5% bone marrow blasts
  - No dysplasia
  - Any of the following cytogenetic abnormalities:

-7 or del(7q)	**-5 or del(5q)**	**i(17q) or t(17p)**	**inv(3)**	**del(11q)**
t(11;16)	**idic(X)(q13)**	**del(12p) or t(12p)**	**t(3;21)**	**t(1;3)**
-13 or del(13q)	**t(6;9)**	**del(9q)**	**t(2;11)**	

Risk Assessment



- Decrease transfusion burden
- Decrease symptoms
- Improve quality of life

- Alter natural history of disease
- Prevent progression to acute myeloid leukemia
- Improve overall survival

International Prognostic Scoring System

	0	0.5	1.0	1.5	2
BM blasts (%)	**<5**	**5-10**	**--**	**11-20**	**21-30**
Chromosomes*	**Good**	**Intermediate**	**Poor**		
Low blood counts	**0/1**	**2/3**			

*Good: nl, -y, del(5q), del(20q) Poor: complex or chromosome 7 abn
Int: all others

Low: 0	**Lower Risk**
Intermediate-1: 0.5-1	
Intermediate-2: 1.5-2	**Higher Risk**
High: ≥ 2.5	

Greenberg P et al, Blood 1997; 89:2079-88

Revised IPSS

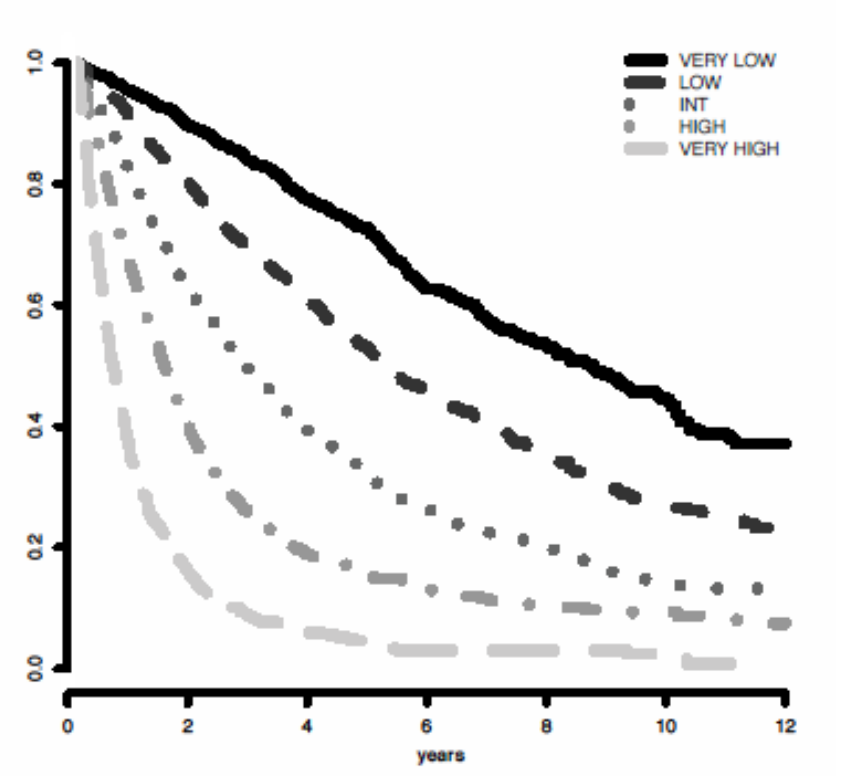
Prognostic Subgroup	Cytogenetic Abnormality
Very Good	-Y, del(11q)
Good	Normal, del(5q), del(12p), del(20q), double including del(5q)
Intermediate	del(7q), +8, +19, i(17q), any other single or double independent clones
Poor	-7, inv(3)/t(3q)/del(3q), double including-7/ del(7q), complex: 3 abnormalities
Very Poor	Complex: > 3 abnormalities

Prognostic variable	0	0.5	1	1.5	2	3	4
Chromosomes	Very good	--	Good	--	Int	Poor	Very Poor
BM blast, %	≤ 2	--	>2 - <5	--	5 - 10	>10	--
Hemoglobin, g/dL	≥ 10	--	8 - <10	< 8	--	--	--
Platelets, K/μL	≥ 100	50 - <100	< 50	--	--	--	--
ANC, K/μL	≥ 0.8	< 0.8	--	--	--	--	--

Greenberg P. Blood 2012;120: 2454-2465

Revised IPSS

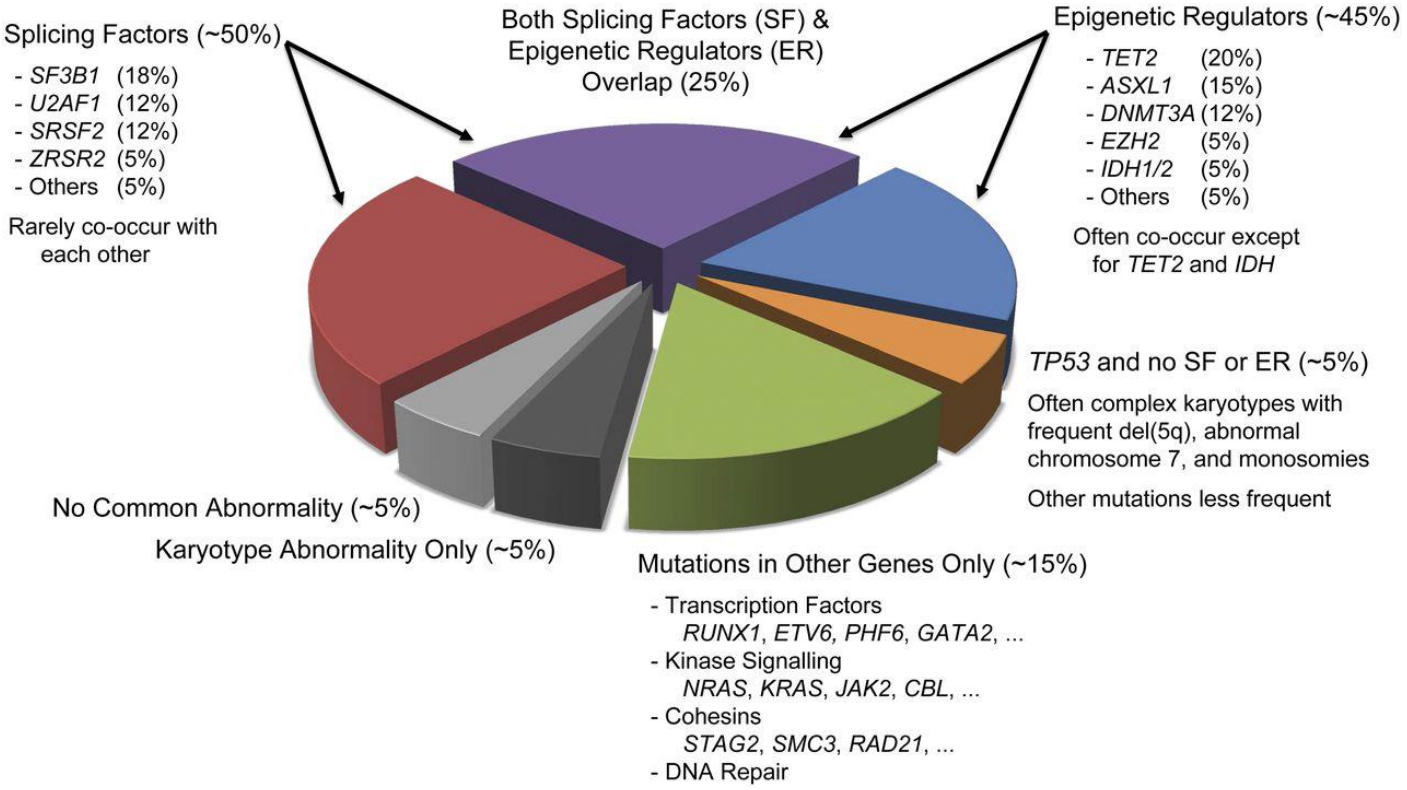
Category	Score	
Very Low	≤ 1.5	Lower
Low	> 1.5 – 3	
Intermediate	> 3 – 4.5	
High	> 4.5 – 6	Higher
Very High	> 6	



Greenberg P. Blood 2012;120: 2454-2465

Molecular Mutations in MDS

- >90% of patients with MDS have at least 1 mutation



Bejar R and Steensma D, Blood 2014

Molecular Mutations in MDS

Mutated gene	Frequency (%)	Blasts <5%	Blasts 5%-30%
TET2	~20	Neutral	Neutral
SF3B1	~20	Favorable	Neutral
ASXL1	15-20	Adverse	Neutral
SRSF2	10-20	Adverse	Neutral
DNMT3A	10-15	Neutral	Neutral
RUNX1	~10	Adverse	Adverse
U2AF1	10-15	Adverse	Neutral
EZH2	~5	Adverse	Adverse
TP53	5-10	Adverse	Adverse
IDH1/IDH2	~5	Neutral	Neutral

Other Prognostic Factors

- Therapy-related: prior chemotherapy or radiation therapy
- Albumin
- Ferritin (iron stores)
- Presence of peripheral blasts
- Age, general health, performance status
- Bone marrow fibrosis
- Many others