

## Management of Elderly and Frail Patients with Comorbidities and Myelodysplastic Syndromes (MDS): A Case Study

### Figures, Tables and References

**Figure 1.** International Prognostic Scoring System (IPSS) for MDS

# IPSS Tool for Risk Stratification of MDS

Score Value					
Prognostic variable	0	0.5	1.0	1.5	2.0
Bone marrow blasts	< 5%	5% to 10%	--	11% to 20%	21% to 30%
Karyotype*	Good	Intermediate	Poor	--	--
Cytopenias†	0/1	2/3	--	--	--

Total Score						
	0	0.5	1.0	1.5	2.0	≥ 2.5
Risk	Low	Intermediate I		Intermediate II		High
Median survival, yr	5.7	3.5		1.2		0.4

\*Good = normal, -Y, del(5q), del(20q); intermediate = other karyotypic abnormalities; poor = complex (≥ 3 abnormalities) or chromosome 7 abnormalities.  
†Hb < 10 g/dL; ANC < 1800/μL; platelets < 100,000/μL.

Greenberg P, et al. *Blood*. 1997;89:2079-2088.

**Figure 2A. Revised International Prognostic Scoring System (IPSS-R) for MDS – Cytogenetic Groups**

## Cytogenetic Groups in the IPSS-R

Risk group	Included karyotypes (19 categories)	Median survival, months	Proportion of patients in this group
Very good	del(11q), -Y	60.8	2.9%
Good	Normal, del(20q), del(5q) alone or with 1 other anomaly, del(12p)	48.6	65.7%
Intermediate	+8, del(7q), i(17q), +19, +21, any single or double abnormality not listed, two or more independent clones	26.1	19.2%
Poor	der(3q), -7, double with del(7q), complex with 3 abnormalities	15.8	5.4%
Very poor	Complex with > 3 abnormalities	5.9	6.8%

Adapted with permission from Schanz J, et al. *J Clin Oncol*. 2012;30(11):820-829. Greenberg PL, et al. *Blood* 2012;120:2454-65.

**Figure 2B. Revised International Prognostic Scoring System (IPSS-R) for MDS – Scoring**

## Scoring for the IPSS-R

His Score = 2 by IPSS-R

Parameter	Categories and Associated Scores				
Cytogenetic risk group	Very good	Good	Intermediate	Poor	Very Poor
	0	1	2	3	4
Marrow blast proportion	≤ 2%	> 2% - < 5%	5% - 10%	> 10%	
	0	1	2	3	
Hemoglobin (g/dL)	≥ 10	8 - < 10	< 8		
	0	1	1.5		
Platelet count (x 10 <sup>9</sup> /L)	≥ 100	50 - < 100	< 50		
	0	0.5	1		
Abs. neutrophil count (x 10 <sup>9</sup> /L)	≥ 0.8	< 0.8			
	0	0.5			

Possible range of summed scores: 0-10

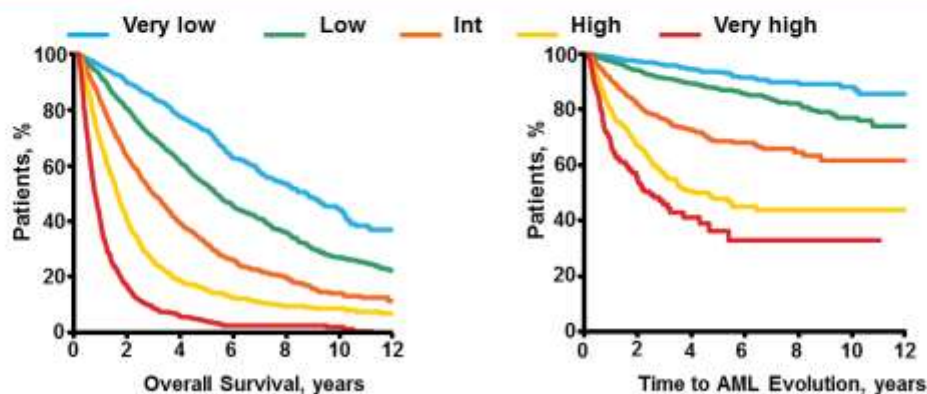
Adapted with permission from Schanz J, et al. *J Clin Oncol.* 2012;30(11):820-829. Greenberg PL, et al. *Blood* 2012;120:2454-65.

**Figure 2C. Revised International Prognostic Scoring System (IPSS-R) for MDS – Prognosis for Different Risk Groups**

## Risk Groups for the IPSS-R

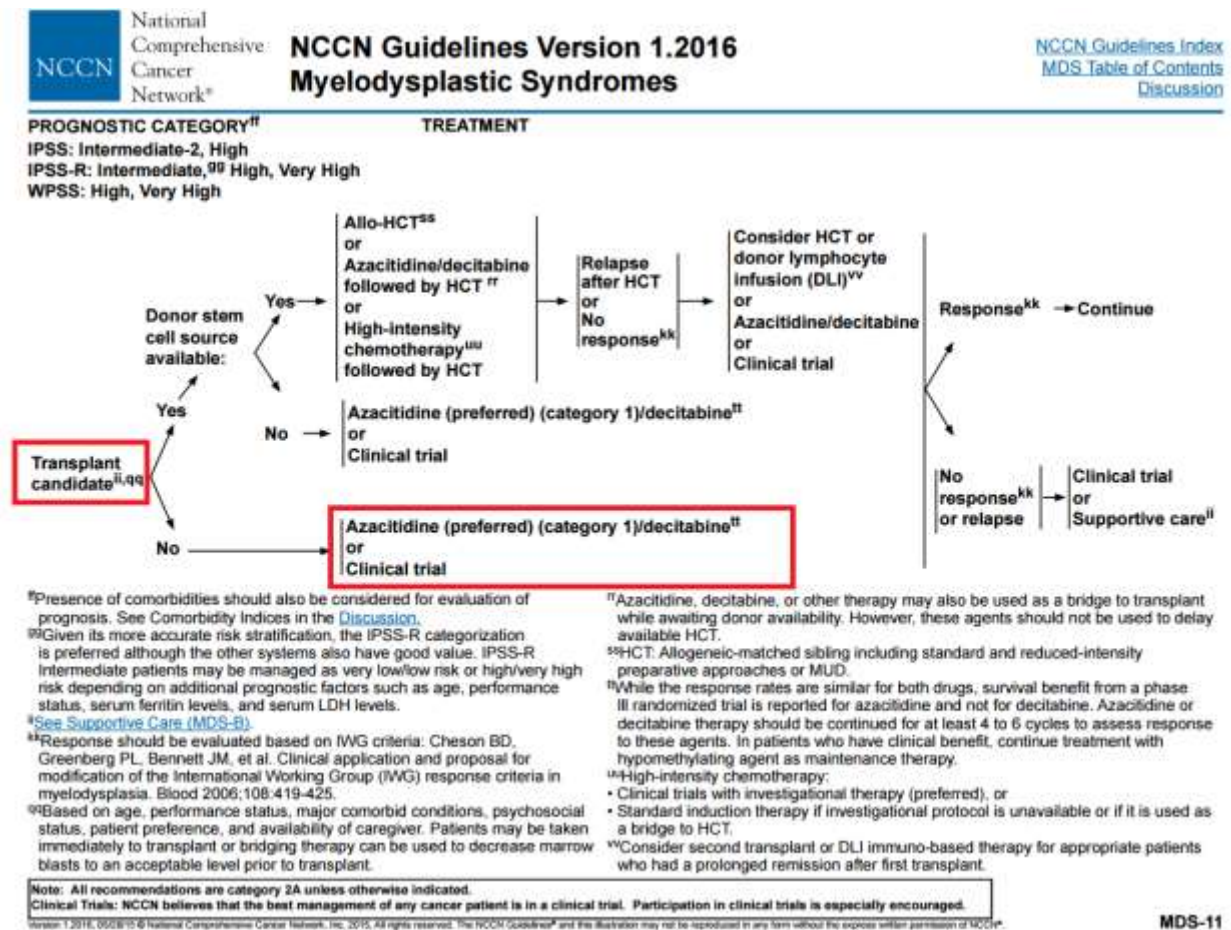
His Score = 2 by IPSS-R

Risk group	Points	% of Patients	Median survival, years	Time until 25% of patients develop AML, years
Very low	≤ 1.5	19 %	8.8	Not reached
Low	> 1.5 – 3	38 %	5.3	10.8
Intermediate	> 3 – 4.5	20 %	3.0	3.2
High	> 4.5 – 6	13 %	1.6	1.4
Very High	> 6	10 %	0.8	0.73



Adapted with permission from Schanz J, et al. *J Clin Oncol.* 2012;30(11):820-829. Greenberg PL, et al. *Blood* 2012;120:2454-65.

**Figure 3. NCCN Guidelines Version 1.2016 MDS; Treatment Recommendations for IPSS-R: Intermediate, High, Very High**



**Table 1. Peripheral blood and bone marrow findings in myelodysplastic syndrome (MDS) - The 2008 revision of the World Health Organization (WHO) classification of myeloid neoplasms and acute leukemia**

Disease	Blood findings	Bone marrow (BM) findings
Refractory cytopenia with unilineage dysplasia (RCUD): [refractory anemia (RA); refractory neutropenia (RN); refractory thrombocytopenia (RT)]	Unicytopenia or bicytopenia  No or rare blasts (<1%)	Unilineage dysplasia: ≥10% of the cells in one myeloid lineage <5% blasts <15% of erythroid precursors are ring sideroblasts
Refractory anemia with ring sideroblasts (RARS)	Anemia No blasts	≥15% of erythroid precursors are ring sideroblasts Erythroid dysplasia only <5% blasts
Refractory cytopenia with multilineage dysplasia (RCMD)	Cytopenia(s) No or rare blasts (<1%) No Auer rods <1 × 10 <sup>9</sup> /L monocytes	Dysplasia in ≥10% of the cells in ≥2 myeloid lineages (neutrophil and/or erythroid precursors and/or megakaryocytes) <5% blasts in marrow No Auer rods ± 15% ring sideroblasts
Refractory anemia with excess blasts-1 (RAEB-1)	Cytopenia(s) < 5% blasts No Auer rods <1 × 10 <sup>9</sup> /L monocytes	Unilineage or multilineage dysplasia 5%-9% blasts <sup>1</sup> No Auer rods
Refractory anemia with excess blasts-2 (RAEB-2)	Cytopenia(s) 5%-19% blasts. Auer rods ± <1 × 10 <sup>9</sup> /L monocytes	Unilineage or multilineage dysplasia 10%-19% blasts <sup>1</sup> Auer rods ± <sup>1</sup>
Myelodysplastic syndrome—unclassified (MDS-U)	Cytopenias <1% blasts	Unequivocal dysplasia in <10% of cells in one or more myeloid lineages when accompanied by a cytogenetic abnormality considered as presumptive evidence for a diagnosis of MDS <5% blasts

Disease	Blood findings	Bone marrow (BM) findings
MDS associated with isolated del(5q)	Anemia Usually normal or increased platelet count No or rare blasts (<1%)	Normal to increased megakaryocytes with hypolobated nuclei <5% blasts Isolated del(5q) cytogenetic abnormality No Auer rods

Vardiman, et al. *Blood* 2009;114:937-951.

**Table 2A. Revised International Prognostic Scoring System (IPSS-R)**

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	—	—	—	—	—



**Table 2B. Revised International Prognostic Scoring System (IPSS-R)-Cytogenetic Prognostic Subgroups and Corresponding Risk Score**

Cytogenetic prognostic subgroups	Risk score
Very good	-Y; del(11)q
Good	Normal; del(5)q; del(12)p; del(20)q; double including del(5)q
Intermediate	Del(7)q; +8; +19; i(17)q; any other single or double independent clones
Poor	-7; inv(3)/t(3)q/del(3)q; double including -7/del(7)q, Complex: 3 abnormalities
Very poor	Complex >3 abnormalities

**Table 2C. Revised International Prognostic Scoring System (IPSS-R)-Risk Category, Risk Score and Corresponding Median Survival (years)**

Risk category	Risk score	Median years of survival
Very low	≤1.5	8.8
Low	>1.5-3	5.3
Intermediate	>3-4.5	3.0
High	>4.5-6	1.6
Very high	>6	0.8

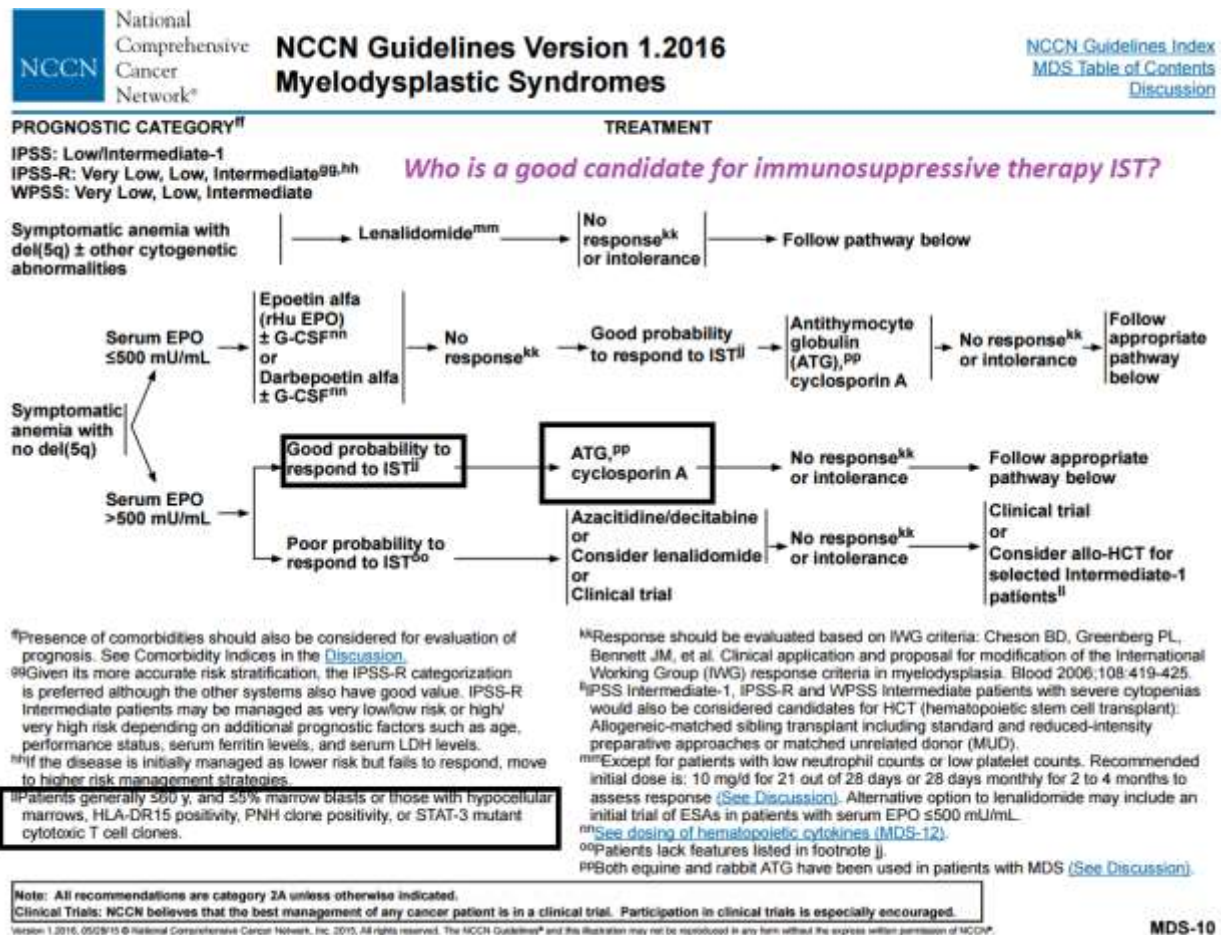
Greenberg, et al. *Blood*. 2012;120:2454-2465.

**Table 3. Hematological adverse events at a glance (lenalidomide-001-trial, total number of patients, n = 43)<sup>11</sup>**

	Grade 1 or 2 (NCI)	Grade 3 or 4 (NCI)	All patients, all grades
Neutropenia	0	28 (65%)	28 (65%)
Thrombocytopenia	9 (21%)	23 (53%)	32 (74%)



**Table 4. NCCN Guidelines Version 1.2016 Myelodysplastic Syndromes – Who is a good candidate for immunosuppressive therapy (IST)?**



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