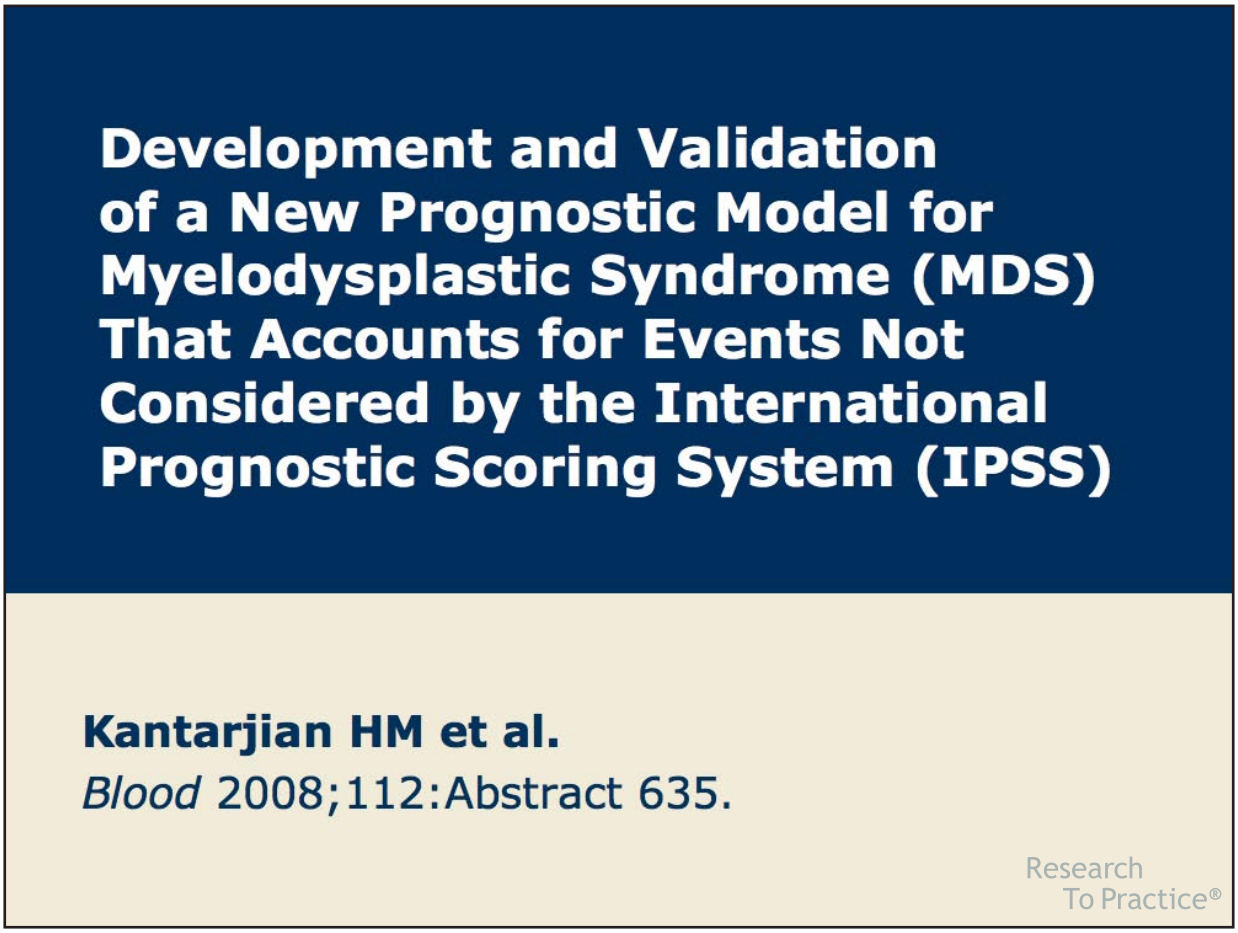
A Prognostic Model for MDS that Accounts for Events Not Considered by the International Prognostic Scoring System (IPSS)

Presentation discussed in this issue:

Kantarjian H et al. **Development and validation of a new prognostic model for myelodysplastic syndrome (MDS) that accounts for events not considered by the International Prognostic Scoring System (IPSS).** *Blood* 2008;112:635. **Abstract**

Slides from journal article



Introduction

- The IPSS risk model provides survival projections for patients with de novo MDS who are managed with supportive measures alone.
- Patients with MDS who have received investigational treatments require a prognostic stratification model that can be applied at intervals after diagnosis and adjusts for the following factors:
  - Impact of prior therapy
  - Secondary forms of disease
  - Proliferative chronic myelomonocytic leukemia (CMML)
  - Adverse cytogenetic subsets (chromosome 7 abnormalities [abn], having three cytogenetic abn)
- **Current study objectives:**
  - To develop a new MDS risk model that accounts for subsets not included in IPSS, that refines prognostic subsets, and that applies at any point during the course of MDS.

Source: Kantarjian HM et al. *Blood* 2008;112:Abstract 635.

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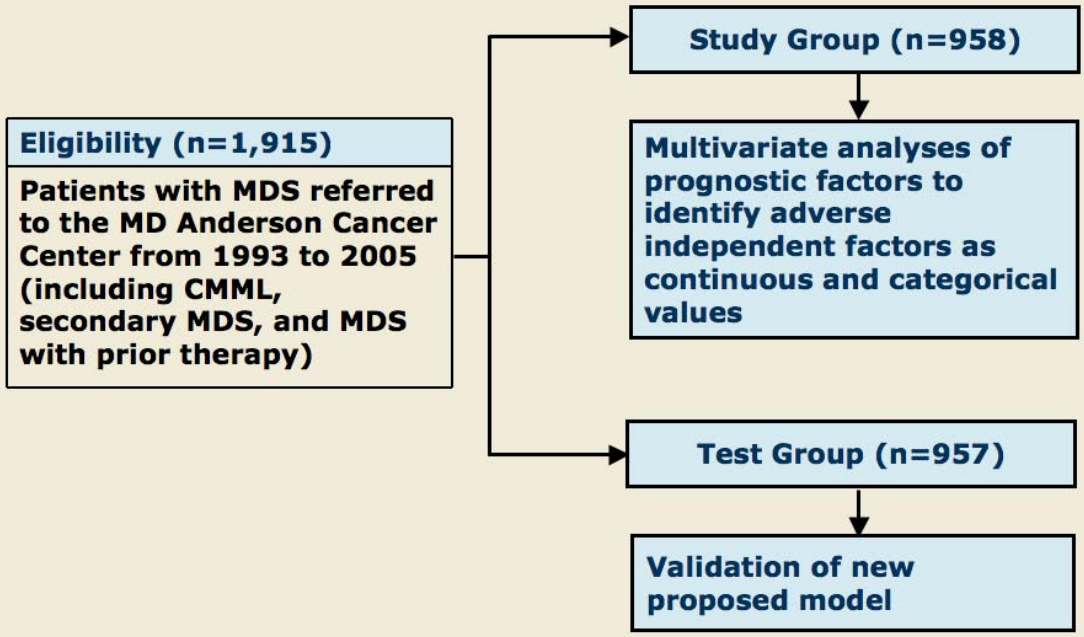
New MDS Prognostic Model Retrospective Study Design



Source: Kantarjian HM et al. *Blood* 2008;112:Abstract 635.

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Weighted Points of Prognostic Factors

Prognostic Factor	Coefficient	Score Points
Hemoglobin (g/dL) <12.0	0.274	2
Age (yrs) 60 - 64 ≥65	 0.179 0.336	 1 2
Platelets (x 10^9/L) <30 30 - 49 50 - 199	 0.418 0.270 0.184	 3 2 1
Marrow blast % 5 - 10 11 - 29	 0.222 0.260	 1 2

Source: Kantarjian HM et al. *Blood* 2008;112:Abstract 635.

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Weighted Points of Prognostic Factors (continued)

Prognostic Factor	Coefficient	Score Points
White blood cells (x 10^9/L) >20	0.258	2
Karyotype (chromosome 7 or ≥3 abn)	0.479	3
Prior transfusion Yes	0.107	1
Performance status ≥2	0.267	2

Source: Kantarjian HM et al. *Blood* 2008;112:Abstract 635.

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Segregation of Patients (Pts.) into Prognostic Groups in New MDS Prognostic Model

		Study Group (n=958)		Test Group (n=957)	
Risk	Score	No. Pts.	Median Survival	No. Pts.	Median Survival
Low	0 - 4	157	54 mos	159	45 mos
Intermediate 1	5 - 6	229	25 mos	228	23 mos
Intermediate 2	7 - 8	233	14 mos	244	13 mos
High	≥9	341	6 mos	326	6 mos

Application of new model's prognostic scores within the four IPSS risk groups was highly prognostic in each. Application of IPSS scores within the four risk groups of the new model was not prognostic.

Source: Kantarjian HM et al. *Blood* 2008;112:Abstract 635.

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Prognosis for Patients in Multiple MDS Subsets According to the New Prognostic Model

	Median Survival (mos)/1 yr Survival (%)			
Disease	Low	Int. 1	Int. 2	High
CMML (n=176)	33 mos	19 mos	12 mos	8 mos
MDS - prior therapy (n=702)	38 mos	19 mos	12 mos	8 mos
MDS - no prior therapy (n=507)	56 mos	36 mos	14 mos	9 mos
Secondary MDS (n=571)	43 mos	19 mos	16 mos	6 mos
Decitabine trial 2007[1] three-arm (n=124)	Not reached[2]	42 mos	19 mos	13 mos
Postdecitabine failure (n=59) (% 1 yr survival)	100%	54%	41%	18%

[1] Kantarjian et al. *Blood* 2007;110:42 [Abstract 115].
[2] 100% at 3 years

Source: Kantarjian HM et al. *Blood* 2008;112:Abstract 635.

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Summary and Conclusions

- A new prognostic model was developed and validated for MDS that accounts for all MDS or CMML cases regardless of prior therapy.
- The model was demonstrated to be superior to IPSS.
- The model was highly prognostic in a group of patients (n=507) with newly diagnosed MDS (as per the original IPSS groups).
- The new prognostic model was used to demonstrate an improved survival with decitabine compared to the expected (historical) survival calculated with the new risk model.
  - Median survival vs historical control: Overall (20 mos vs 13 mos), Low-intermediate-1 risk (44 mos vs 30 mos) and Intermediate-2-high risk (15 mos vs 10 mos).
- Additional validations are necessary in independent MDS populations.

Source: Kantarjian HM et al. *Blood* 2008;112:Abstract 635.

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