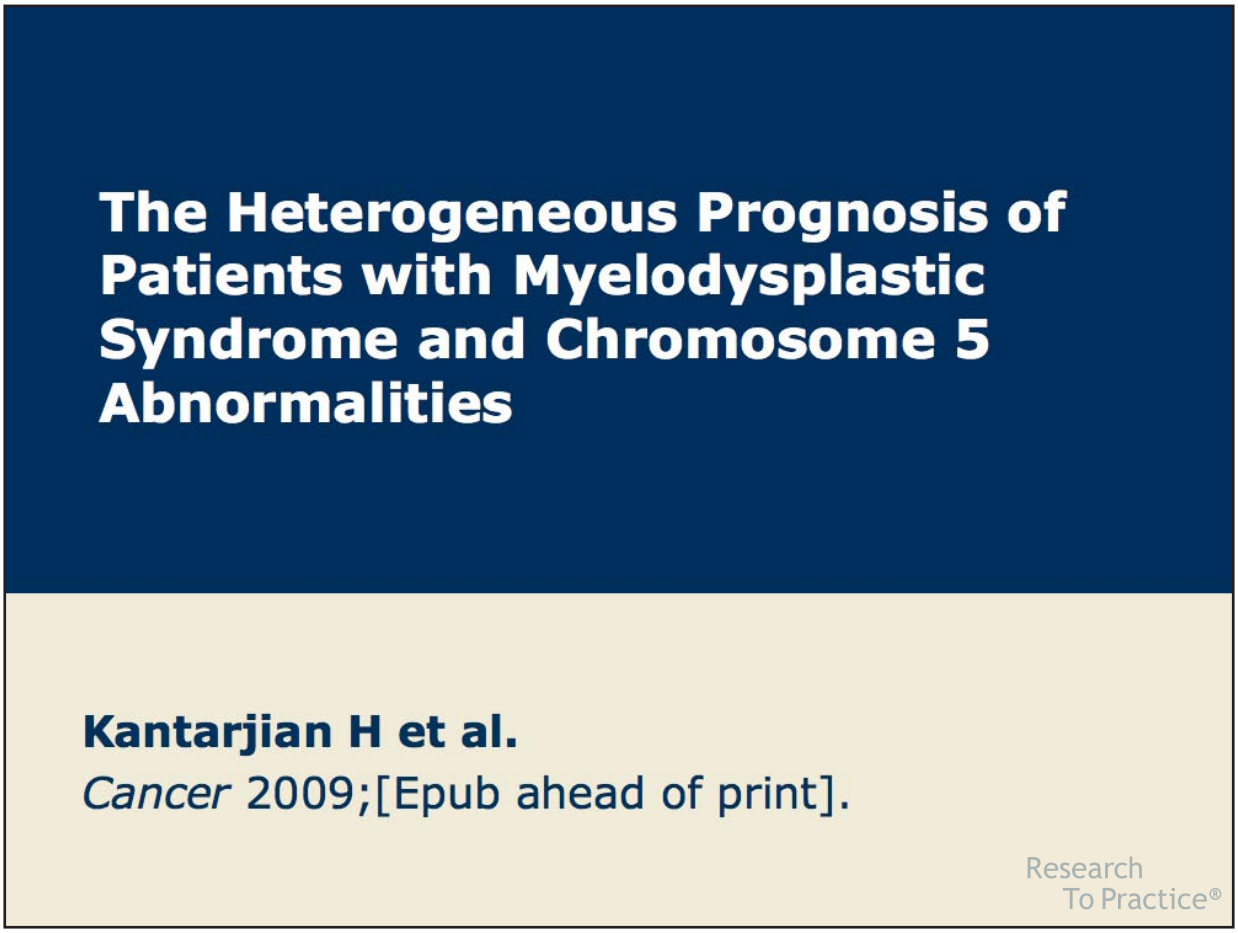
Outcome of Myelodysplastic Syndrome (MDS) with and without Chromosome 5 Abnormalities

Presentations discussed in this issue:

Kantarjian H et al. **The heterogeneous prognosis of patients with myelodysplastic syndrome and chromosome 5 abnormalities: How does it relate to the original lenalidomide experience in MDS?** *Cancer* 2009;[Epub ahead of print]. **Abstract**

Raza A et al. **Phase 2 study of lenalidomide in transfusion-dependent, low-risk, and intermediate-1 risk myelodysplastic syndromes with karyotypes other than deletion 5q.** *Blood* 2008;111(1):86-93. **Abstract**

Slides from the journal articles



Introduction

- Lenalidomide has demonstrated clinical benefit in patients with lower-risk MDS (IPSS low or intermediate-1), transfusion dependence and with deletion 5q (del 5q) (*NEJM* 2006;355:1456).
- Hematologic and cytogenetic response rates were similar in response to lenalidomide therapy in patients with del 5q with or without additional chromosomal abnormalities, and across IPSS risk groups and a range of percent marrow blasts (*NEJM* 2006;355:1456).
  - Perception has arisen that lenalidomide is equally active in all MDS subsets and in all MDS subsets with del 5q.

Source: Kantarjian et al. *Cancer* 2009;[Epub ahead of print].

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Introduction (continued)

- To establish the potential benefit of lenalidomide in patients with MDS and del 5q, randomized trials would be required or historical databases could be used to establish baseline expectations against which the benefit of lenalidomide could be compared.
- **Current study objectives:**
  - Using a historical database, define prognosis and establish baseline expectations of patients that have MDS and deletion 5q with or without other cytogenetic abnormalities.

Source: Kantarjian et al. *Cancer* 2009;[Epub ahead of print].

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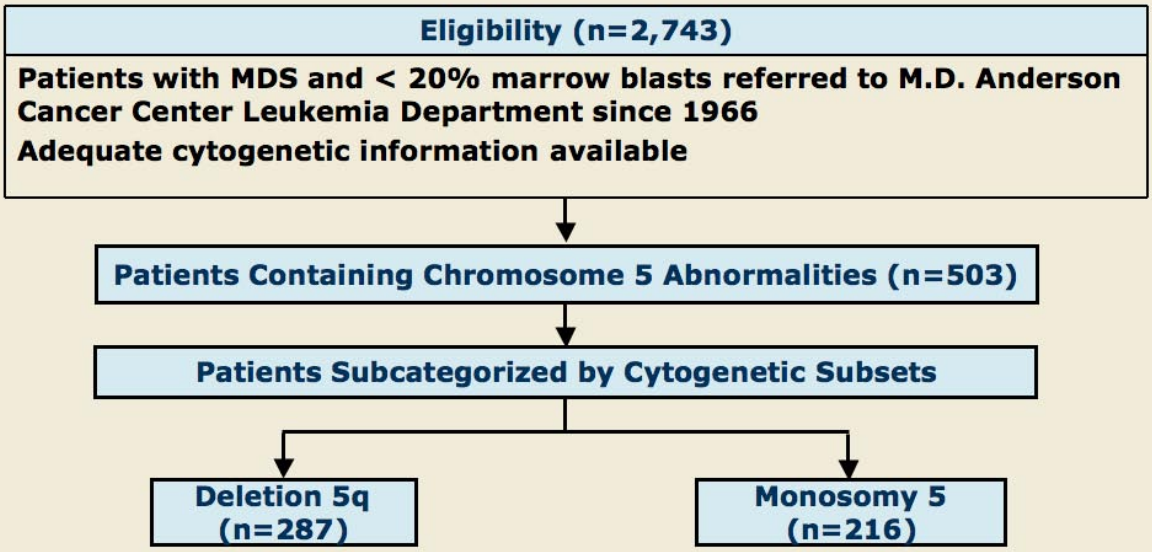
Retrospective Analysis of the Prognosis of Patients with MDS and Chromosome 5 Abnormalities



Survival measured from the date of referral to M.D. Anderson Cancer Center.

Source: Kantarjian et al. *Cancer* 2009;[Epub ahead of print].

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Survival of Patients with or without Chromosome 5 Abnormalities

Patient Group	Median Survival	2-year Survival Rate
No chromosome 5 abn. (n=2,240)	**17 mos**	**38%**
Del 5q: All patients (n=287)	**9 mos**	**23%**
Monosomy 5 (n=216)	**6 mos**	**3%**
Del 5q alone	33 mos	64%
+1 abn.	17 mos	40%
+2 abn.	12 mos	34%
+ ≥3 abn.	6 mos	0%
+ Chromosome 7 abn.	7 mos	2%

Compared to monosomy 5, deletion 5q was more frequently associated with lower IPSS risks (IPSS low and intermediate 1 risk rates of 32% vs 7%, p < 0.001) and with lower incidence of additional chromosomal abnormalities (60% vs 97%, p < 0.0001).

Abn = abnormalities

Source: Kantarjian et al. *Cancer* 2009;[Epub ahead of print].

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Survival of Patients with Lower-Risk* MDS According to Chromosome 5 Abnormalities

Patient Group	Median Survival	2-year Survival Rate
Del 5q: All patients (n=93)	**29 mos**	**60%**
Del 5q alone (n=55)	41 mos	67%
Del 5q + 1 abn. (n=19)	24 mos	48%
Del 5q + 2 abn. (n=7)	27 mos	67%
Del 5q + ≥ 3 abn. (n=6)	NR	NR
Del 5q + Chromosome 7 (n=6)	13 mos	0%

**Lower-risk MDS encompasses IPSS low and intermediate-1 risk groups.*

Source: Kantarjian et al. *Cancer* 2009;[Epub ahead of print].

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Median Survival of Patients with MDS According to % of Marrow Blasts

Patient Group	< 5% Blasts	< 10% Blasts
Del 5q: All patients (n=115, 198)	**15 mos**	**12 mos**
Del 5q alone (n=41, 53)	44 mos	41 mos
Del 5q + 1 abn. (n=15, 24)	29 mos	24 mos
Del 5q + 2 abn. (n=11, 14)	14 mos	12 mos
Del 5q + ≥ 3 abn. (n=21, 43)	5 mos	6 mos
Del 5q + Chromosome 7 (n=27, 64)	6 mos	7 mos

Source: Kantarjian et al. *Cancer* 2009;[Epub ahead of print].

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Summary and Conclusions

- It may not be appropriate for oncologists to consider patients with MDS and deletion 5q as one group.
  - Prognosis of patients with MDS and low-risk MDS containing chromosome 5 abnormalities is heterogeneous and is worsened by the presence of other abnormalities in addition to deletion 5q.
  - Monosomy 5 was associated less often with low-risk MDS (IPSS low and intermediate 1 risk) and more often with the presence of other adverse cytogenetic findings.
- Based on analysis of this study and on the entry criteria of the original lenalidomide study, the percentage of patients who are candidates for lenalidomide would be 2% to 3%.
  - Oncologists may be offering lenalidomide to subsets of patients with MDS in which the drug is untested in controlled trials and where it may not be effective.
- Prognosis and baseline expectation data established by this study may be used for comparative purposes with the lenalidomide experience.

Source: Kantarjian et al. *Cancer* 2009;[Epub ahead of print].

Phase 2 Study of Lenalidomide in Transfusion-Dependent, Low-Risk, and Intermediate-1-Risk Myelodysplastic Syndromes with Karyotypes Other Than Deletion 5q

Raza A et al.

Blood 2008;111(1):86-93.

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Erythroid Response to Lenalidomide in Patients Lacking 5q Deletion

	Daily dosing 10 mg/day (n=100)	21-day dosing 10 mg/day (n=114)	All patients (n=214)
Erythroid response[1]			
Total transfusion response TI + ≥ 1 g/dL Hb increase ≥ 50% ↓ no. of transfusions	42% 27% 15%	45% 25% 19%	43% 26% 17%
Median time to TI	7.4 wk	4.1 wk	4.8 wk
Hemoglobin			
Baseline, median Response, median Increase, median	7.9 g/dL 11.6 g/dL 3.3 g/dL	8.1 g/dL 11.0 g/dL 3.1 g/dL	8.0 g/dL 11.6 g/dL 3.2 g/dL

TI, transfusion independence; Hb, hemoglobin.
[1]Erythroid response measured according to modified International Working Group 2000 criteria.

Source: Raza A et al. *Blood* 2008;111(1):86-93.

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Summary and Conclusions

- A Phase II, multicenter trial (n=214) evaluating lenalidomide therapy in patients with a long-standing diagnosis of MDS (median 2.2 years) that is low- or intermediate-1-risk, with substantial RBC transfusion requirements (median 4 units/8 weeks) and without del 5q.
- In the ITT population, 26% of patients achieved transfusion independence (TI) after median 4.8 weeks of lenalidomide treatment.
  - Median TI duration was 41 weeks and 36% or responders remained transfusion-free for at least one year (median TI duration for MDS del 5q responders was > 2 years)
  - A reduction in the need for transfusion was seen in 43% of patients.
  - Median rise in hemoglobin was 3.2 g/dL from baseline
- Lenalidomide demonstrated clinically meaningful activity in patients with transfusion-dependent, low- or intermediate-1-risk MDS without deletion 5q.

Source: Raza A et al. *Blood* 2008;111(1):86-93.

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