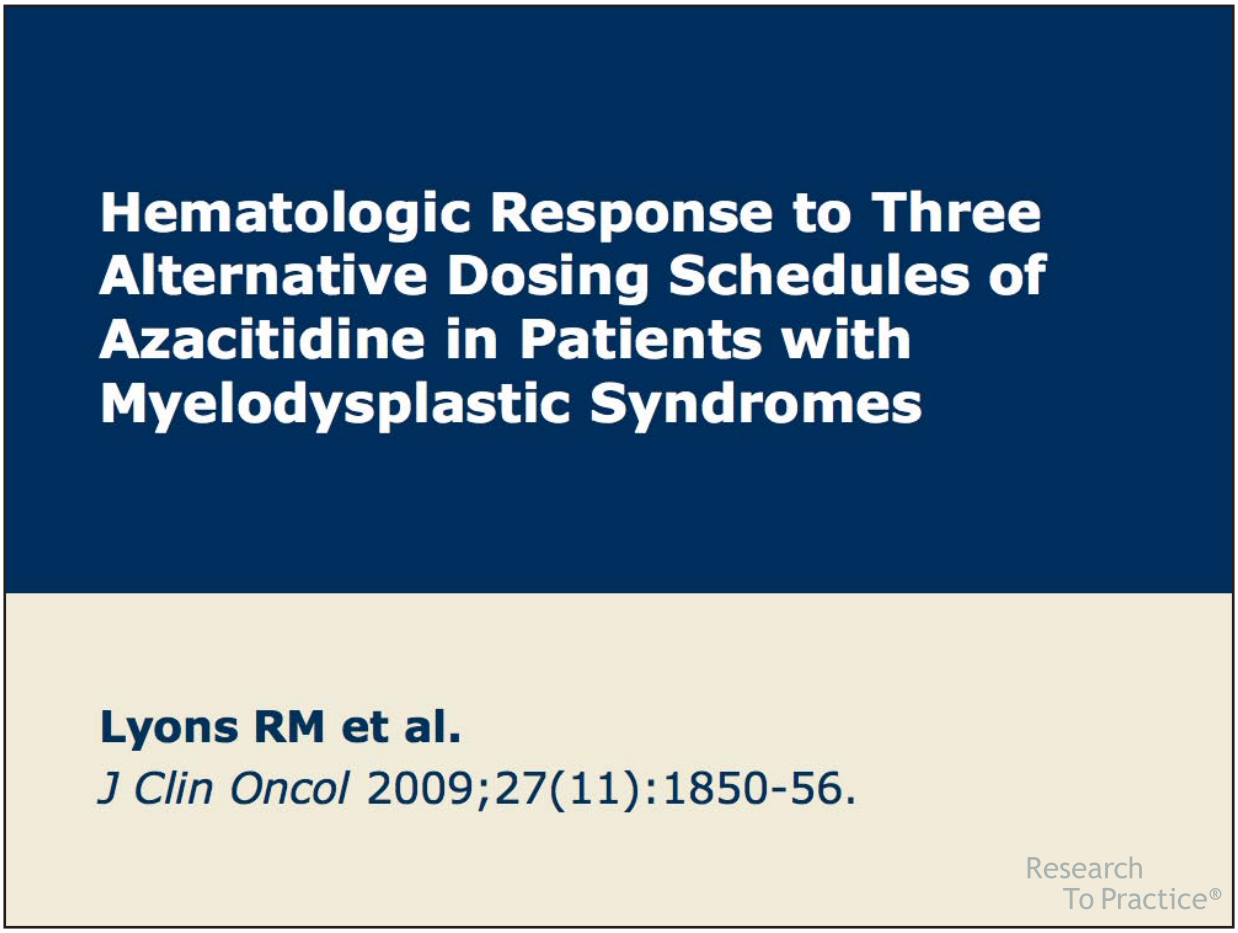
Three Alternate Dosing Schedules of Azacitidine for MDS

Presentation discussed in this issue:

Lyons RM et al. **Hematologic response to three alternative dosing schedules of azacitidine in patients with myelodysplastic syndromes.** *J Clin Oncol* 2009;27(11):1850-6. **Abstract**

Slides from journal article



Introduction

- Azacitidine has been shown to alter the natural history of myelodysplastic syndromes (MDS) (*J Clin Oncol* 2002;20:2429; *Lancet Oncol* 2009;10(3):223; *J Clin Oncol* 2002;20:2441)
  - Significant prolonged survival in higher-risk MDS and trend toward prolonged survival in all French-American-British (FAB) MDS subtypes; decreased risk of transformation to AML
  - Significant reduction in transfusion dependence in higher- and lower-risk MDS (*J Clin Oncol* 2002;20:2429; *J Clin Oncol* 2006;24:3895)
- The approved AZA regimen is 75 mg/m^2/d administered subcutaneously or intravenously for 7 days every 28 days and includes weekend dosing
- **Study Objective:**
  - Assess safety and efficacy, based on hematologic improvement and transfusion independence rates, of three azacitidine dosing schedule alternatives that eliminate weekend dosing, in a multicenter, community-based open-label study

Source: Lyons RM et al. *J Clin Oncol* 2009;27:1850-56.

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Phase II Trial of Alternative Dosing Schedules of Azacitidine (AZA) in Patients with MDS

Eligibility

Diagnosis of MDS:

Refractory anemia (RA) or RA with ringed sideroblasts (RARS) requiring a transfusion every 28 days or with thrombocytopenia or neutropenia

RA with excess blasts (RAEB)

RA with excess blasts in transformation (RAEB-T)

Chronic myelomonocytic leukemia (CMML)

R

AZA 5-2-2 (n=50)
AZA, 75 mg/m^2 SC, d1-5 → AZA, 75 mg/m^2, d8-9 q28d x 6

AZA 5-2-5 (n=51)
AZA, 50mg/m^2 SC, d1-5 → AZA, 50 mg/m^2, d8-12 q28d x 6

AZA 5 (n=50)
AZA, 75 mg/m^2 SC, d1-5 q28d x 6

SC = subcutaneous

Source: Lyons RM et al. *J Clin Oncol* 2009;27:1850-56.

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Hematologic Improvement (HI)

	AZA 5-2-2	AZA 5-2-5	AZA 5
Major or minor HI[1] (Intent-to-treat) (n=50, 51, 50)	44%	45%	56%
Onset of HI during first two cycles	82%	56%	90%
Major or minor HI, FAB lower-risk patients (n=33, 29, 32)	49%	41%	50%
Patients with multilineage cytopenias who experienced multilineage HI (n=32, 24, 30)	34%	21%	33%

[1]HI evaluated using International Working Group 2000 criteria

Source: Lyons RM et al. *J Clin Oncol* 2009;27:1850-56.

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Achievement of RBC Transfusion Independence (TI) Among Baseline RBC Transfusion-Dependent Patients

	AZA 5-2-2	AZA 5-2-5	AZA 5
Overall (intent-to-treat) (n=24, 22, 25)	50%	55%	64%
FAB lower-risk patients (n=17, 12, 18)	53%	50%	61%
Onset of TI within first two cycles	92%	75%	75%

Absence of baseline neutropenia or thrombocytopenia and lower transfusion requirements were predictive of higher rates of RBC transfusion independence.

Source: Lyons RM et al. *J Clin Oncol* 2009;27:1850-56.

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Selected Grade 3 or 4 Adverse Events

	AZA 5-2-2 (n = 50)	AZA 5-2-5 (n = 48)	AZA 5 (n = 50)
≥ 1 grade 3 or 4 adverse events	84%	77%	58%
Hematologic disorders	66%	50%	34%
Anemia	24%	15%	10%
Febrile neutropenia	8%	8%	2%
Leukopenia	14%	8%	8%
Neutropenia	42%	31%	22%
Thrombocytopenia	26%	15%	12%
Infections	22%	29%	10%

Source: Lyons RM et al. *J Clin Oncol* 2009;27:1850-56.

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Summary and Conclusions

- These three alternate dosing regimens demonstrated good activity and tolerability
  - HI, overall (intent-to-treat): 44%-56%
  - HI, lower-risk MDS: 41%-50%
  - Achievement of TI, overall (intent-to-treat): 50%-64%
  - Achievement of TI, lower-risk MDS: 50%-61%
- In all dosing arms, the onset of TI and HI was relatively rapid, occurring in the majority of patients within the first two dosing cycles (75%-92% for TI, 56%-90% for HI)
- Grade III/IV adverse events included hematologic disorders (34%-66%) and infections (10%-29%)
- The AZA 5 dosing regimen may be a better-tolerated and more convenient dosing schedule than the other two alternative dosing regimens.

Source: Lyons RM et al. *J Clin Oncol* 2009;27:1850-56.

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