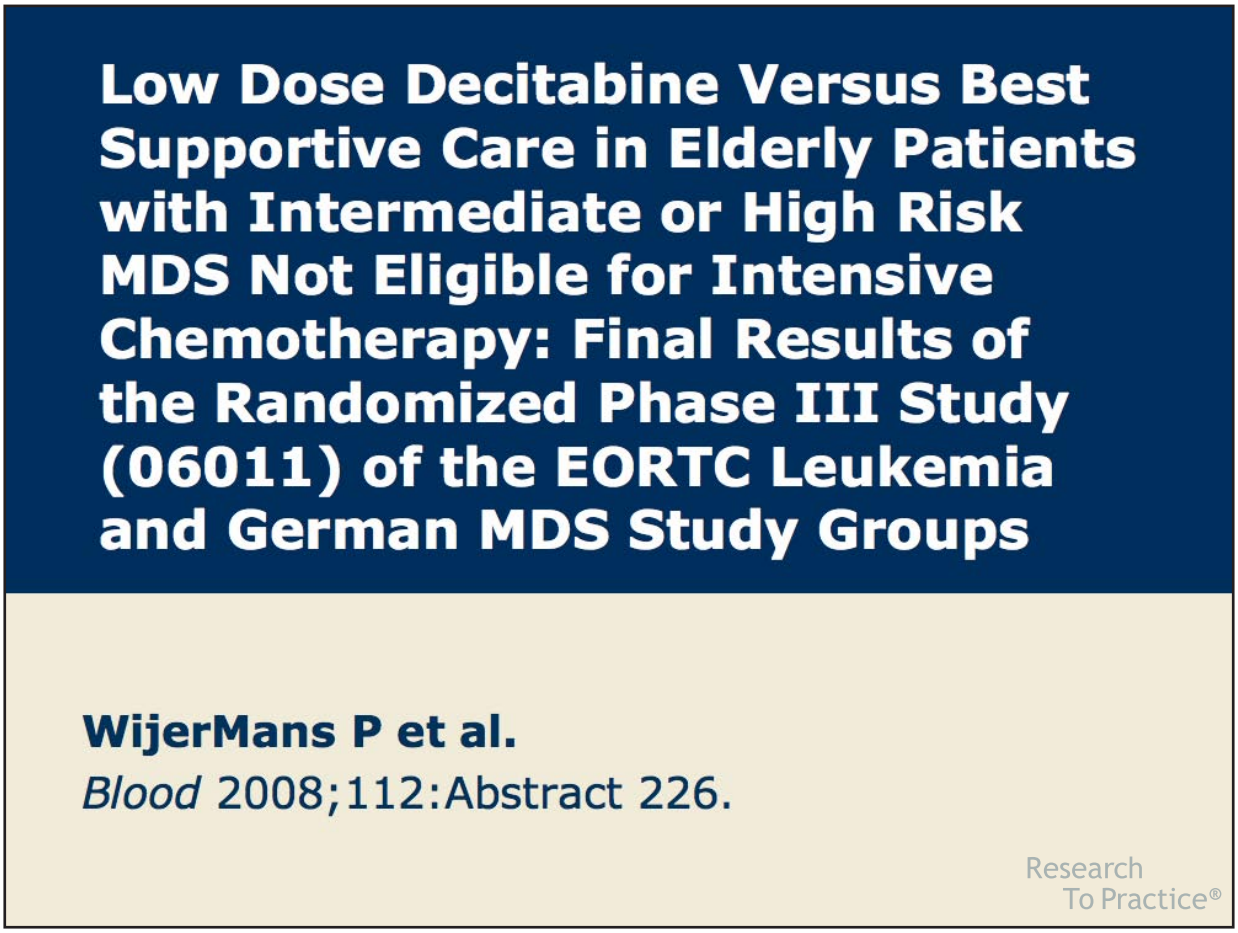
EORTC-06011: Low-Dose Decitabine versus Best Supportive Care for Elderly Patients with Intermediate- or High-Risk MDS

Presentation discussed in this issue:

WijerMans P et al. **Low dose decitabine versus best supportive care in elderly patients with intermediate or high risk MDS not eligible for intensive chemotherapy: Final results of the randomized phase III study (06011) of the EORTC Leukemia and German MDS Study Groups.** *Blood* 2008;**Abstract 226**.

Slides from journal article



Introduction

- Decitabine has demonstrated efficacy in patients with myelodysplastic syndrome (MDS) using two different dosing regimens.
  - Low-dose decitabine therapy (15 mg/m^2 q 8 hours x 3 days every six weeks) has demonstrated improved efficacy over supportive care (ORR 17% vs. 0%, p<0.001) (*Cancer* 2006;106:1794).
  - An alternative outpatient regimen of decitabine (20 mg/m^2 q day x 5 every four weeks) demonstrated a response in 70% of patients according to modified International Working Group criteria (*Cancer* 2007;109:265).
- **Current study objectives (n=233):**
  - To assess the safety and efficacy of low-dose decitabine therapy versus supportive care in elderly patients with MDS who are not eligible for intensive chemotherapy.

Source: WijerMans P et al. *Blood* 2008;112:Abstract 226.

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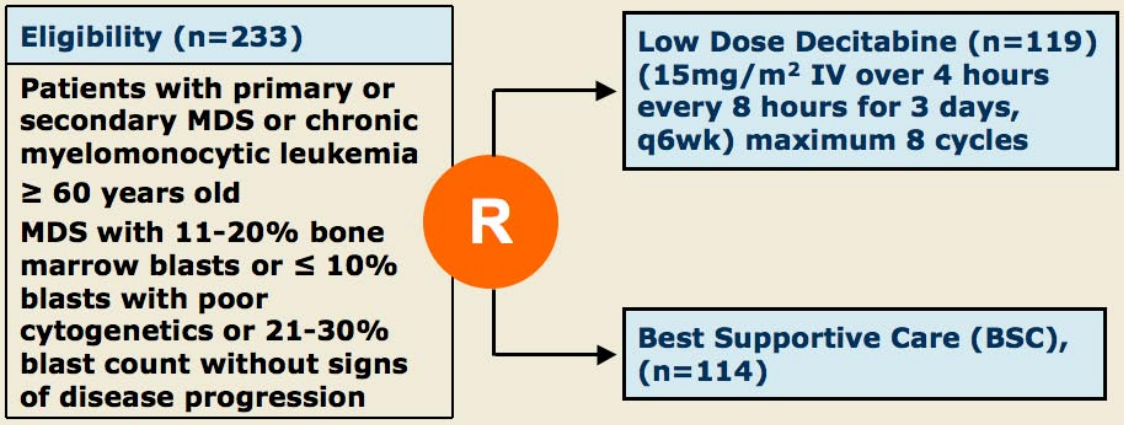
Phase III Randomized, Open-Label, Multicenter Trial of Low Dose Decitabine Versus Supportive Care



Patients stratified according to cytogenetics risk group, IPSS, primary or secondary MDS, and study center

Source: WijerMans P et al. *Blood* 2008;112:Abstract 226.

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Patient Characteristics and Decitabine Treatment Courses

Patient Characteristics (n=233)	
Median age, n (range)	70 (60-90)
IPPS intermediate-2	55%
IPPS high	38%
Poor-risk cytogenetics	46%
Subsequent treatment therapy Transplant Induction chemotherapy	 10% 11%
Median number of decitabine cycles administered	4
Patients receiving ≤ 2 cycles of decitabine	40%

Source: WijerMans P et al. *Blood* 2008;112:Abstract 226.

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Response: Decitabine Versus BSC in Elderly Patients with Intermediate/High Risk MDS

	Decitabine (n=119)	BSC (n=114)
Complete Response (CR)	13%	0%
Partial Response (PR)	6%	0%
Hematological Improvement (HI)[1]	15%	2%
Stable Disease	14%	22%
Overall Response Rate (CR+PR+HI)	34%	2%
Median Time to Response (CR/PR/HI)	0.32 yrs	
Response Duration	0.72 yrs	

[1]Patients in the decitabine arm with HI (n=18) showed the following responses: 3-lineage (n=7), 2-lineage (n=5), and 1-lineage (n=6).

Source: WijerMans P et al. *Blood* 2008;112:Abstract 226.

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Survival: Decitabine Versus BSC in Elderly Patients with Intermediate/High Risk MDS

	Decitabine (n=119)	BSC (n=114)	Hazard ratio	p-value
Median OS (months)	10.1	8.5	0.88	0.38
Median PFS (months)	6.6	3.0	0.68	0.004
Median time to AML/death (months)	8.8	6.1	0.85	0.24

OS = overall survival; PFS = progression-free survival; AML = acute myelogenous leukemia.

Source: WijerMans P et al. *Blood* 2008;112:Abstract 226.

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Adverse Events

Adverse Event	Decitabine (n= 119)	BSC (n=114)
Febrile neutropenia (Grades 3/4)	26%	7%
Infection (Grades 3/4)	59%	47%
Nausea (Grades 1/2)	28%	16%
Vomiting (Grade 1/2)	16%	9%

Toxicity-related deaths (n): Decitabine = 9, BSC = 0

Source: WijerMans P et al. *Blood* 2008;112:Abstract 226.

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Summary and Conclusions

- Low-dose decitabine therapy resulted in significant response rates in elderly patients with intermediate- or high-risk MDS.
  - ORR: 34% (versus BSC, 2%)
- Nine patients experienced toxicity-related deaths with decitabine (vs. none on best supportive care)
- There was not a significant difference in the time to AML transformation/death (decitabine, 8.8 mos; BSC, 6.1 mos) or in median overall survival (decitabine, 10.1 mos; BSC, 8.5 mos) between the two study arms
  - Lack of effect on overall survival may be due to the limited number of decitabine cycles (median 4 cycles) or to subsequent treatments administered after disease progression.
- The alternative outpatient regimen of decitabine should be investigated for its effect on survival.

Source: WijerMans P et al. *Blood* 2008;112:Abstract 226.

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