

Phase II Study of Maintenance Treatment with 5-Azacitidine for Patients with MDS or Post-MDS AML

Presentation discussed in this issue:

Grövdal M et al. Maintenance treatment with 5-azacitidine for patients with high risk myelodysplastic syndrome (MDS) or acute myeloid leukemia following MDS (MDS-AML) in complete remission (CR) after induction chemotherapy. *Blood* 2008;112;Abstract 223.

Slides from a presentation at ASH 2008

Maintenance Treatment with 5-Azacitidine for Patients with High Risk Myelodysplastic Syndrome (MDS) or Acute Myeloid Leukemia Following MDS (MDS-AML) in Complete Remission (CR) after Induction Chemotherapy

Grövdal M et al.

Blood 2008;112:Abstract 223.

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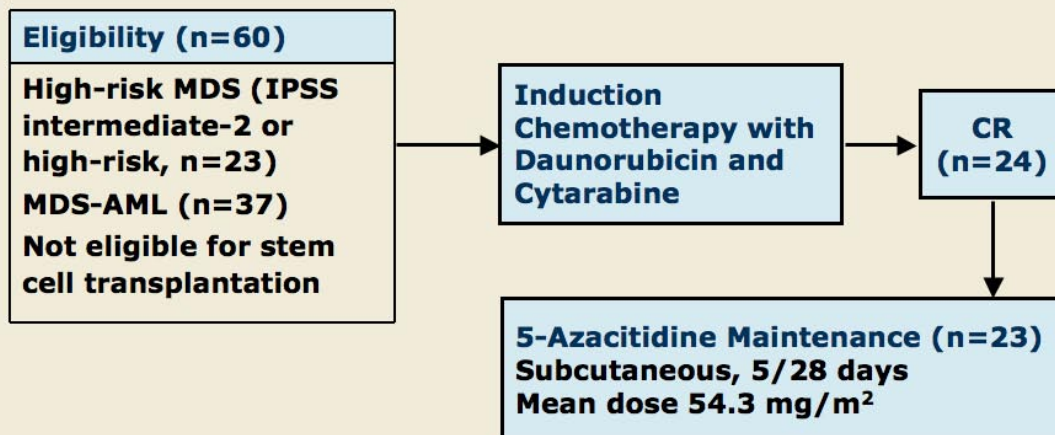
Introduction

- Approximately 50% of patients with high-risk MDS or MDS-AML achieve CR after administration of induction chemotherapy.
- However, the duration of CR and of overall survival (OS) is frequently short.
- **Study objectives:**
 - Assess the clinical feasibility and utility of long-term maintenance treatment with 5-azacitidine in patients with high risk MDS or MDS-AML who achieve CR after induction chemotherapy.

Source: Grövdal M et al. *Blood* 2008;112:Abstract 223.

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Phase II Multicenter Study of Long-Term Maintenance with 5-Azacitidine in Patients with MDS or MDS-AML



Promoter methylation status of the P15^{ink4b} (P15), E-cadherin (CDH) and hypermethylated in cancer 1 (HIC) genes was assessed at study start, at CR, and for some patients during follow-up.

Source: Grövdal M et al. *Blood* 2008;112:Abstract 223.

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Results Summary

- The median CR duration in patients receiving 5-azacitidine maintenance therapy (n=23) was 13.5 months.
 - Four of 23 patients (17%) had a CR exceeding 24 months.
 - Two patients with *CDH* hypermethylation at baseline had CR durations of two and five months, respectively.
- The probability of reaching CR was negatively correlated to hypermethylation of the *CDH* promoter ($p=0.008$).
- The median survival was 20 months in patients receiving 5-azacitidine maintenance therapy.
- In the whole group, survival was shorter in patients with hypermethylation of the *CDH* gene (3 months vs 9 months, $p=0.005$).
 - Baseline methylation status of *p15* did not affect CR duration or overall survival.
- No side effects were reported in 52% of the patients receiving 5-azacitidine maintenance therapy.

Source: Grövdal M et al. *Blood* 2008;112:Abstract 223.

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Summary and Conclusions

- 5-azacitidine maintenance therapy after induction chemotherapy is feasible in patients with high-risk MDS or MDS-AML.
 - Median duration of CR was 13.5 mos.
 - Mild adverse events were reported.
- 5-azacitidine maintenance therapy, however, does not appear to prevent relapse in the majority of patients.
- Hypermethylation of multiple genes is a strong negative factor for probability of CR, duration of CR and survival.
 - The probability of achieving CR was negatively correlated to *CDH* promoter hypermethylation ($p=0.008$), and none of the six patients with all three genes hypermethylated achieved CR ($p=0.03$).
 - Two patients with baseline hypermethylation of the *CDH* gene had CR durations of only 2 and 5 months, respectively.
 - Survival was shorter in patients with hypermethylation of the *CDH* gene than in patients lacking it (9 mos vs 3 mos, $p=0.005$).

Source: Grövdal M et al. *Blood* 2008;112:Abstract 223.

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