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**

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.


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

**Eligibility (n=60)**
- High-risk MDS (IPSS intermediate-2 or high-risk, n=23)
- MDS-AML (n=37)
- Not eligible for stem cell transplantation

**Induction Chemotherapy with Daunorubicin and Cytarabine**

**CR (n=24)**

**5-Azacitidine Maintenance (n=23)**
- Subcutaneous, 5/28 days
- Mean dose 54.3 mg/m²

*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.*

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.


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).