INTRODUCTION

• Percentage of BMBL is the prognostic variable with the greatest impact on outcome in MDS at diagnosis and subsequent time points.
• Current composite response criteria (2006 IWG) do not consistently correlate with OS.
• Treatment impact of BMBL as an independent response criterion has not been adequately evaluated.

METHODS

• Evaluated correlation between OS and BMBL in pts with higher-risk MDS from 4 datasets from 7 studies with 887 pts total:
  o ONTIME – a Phase III randomized study of second-line rigosertib (RIG, N=199) vs best supportive care (BSC, N=100)²
  o 4 Phase II/II studies of RIG in pts with MDS/AML³
  o AZA-001, a Phase III study of azacitidine (AZA) vs 3 conventional care regimens (N=358)⁴,⁵
  o Cancer & Leukemia Group B (CALGB) Study 9221, a Phase II, randomized trial of 1st-line support care (BSC, N=100)²
  o AZA vs BSC (N=191)⁶
• Change in blasts was defined similarly: BM complete response is BMBL ≤5% and ≥50% decrease from baseline; BM partial response is ≥50% decrease from baseline, but BMBL still >5%; stable disease is <50% decrease or increase from baseline.

RESULTS

ONTIME: Landmark time-dependent analyses showed correlation of BMBL response/stabilization with OS at 4 weeks (P=0.011) and 12 weeks (p<0.001).

Study AZA-001: Time-dependent analysis of BMBL stabilization was associated with a significantly reduced risk of death in both treatment cohorts (p<0.001).

CONCLUSION

These studies, spanning more than a decade with different therapeutic agents and settings, demonstrate a consistent positive correlation between BMBL response and OS in pts with HR-MDS, including pts on supportive care. This suggests that use of reduction/stabilization in BMBL can serve as:
• a new early response parameter
• an intermediate clinical endpoint for evaluation of new agents
• a biomarker for disease progression in HR-MDS itself.

REFERENCES