DISEASE MODIFYING ACTIVITY OF IMETELSTAT IN PATIENTS WITH HEAVILY TRANSFUSED NON-DEL(5Q) LOWER-RISK MYELODYSPLASTIC NEOPLASMS RELAPSED/REFRACTORY/INELIGIBLE FOR ERYTHROPOIESIS-STIMULATING AGENTS IN IMERGE PHASE III

INTRODUCTION

- Hematologic and non-hematologic risk factors not related to transfusion burden, which are independent predictors of outcomes in patients with non-del(5q) myelodysplastic syndromes (MDS), including high transfusion burden, are associated with worse survival, suggesting the potential for disease-modifying activity.

AIM

- To evaluate the disease-modifying activity of imetelstat (S. NAVADA) in combination with standard-of-care erythropoiesis-stimulating agents (ESA) in patients with non-del(5q) lower-risk MDS who have received ≥50% transfusions per week without an increase in hemoglobin (Hb) ≥1.5 g/dL or transfusion independence (TI).

METHODS

- In the IMERGE phase II, 382 heavily transfused (50%), lower risk MDS patients were randomized to imetelstat (S. NAVADA) + ESA or placebo + ESA to determine disease-modifying activity.

RESULTS

- Hematologic improvement (HI) was achieved in 49% (95% CI: 42, 56) in the imetelstat (S. NAVADA) group compared to 31% (95% CI: 24, 40) in the placebo group (P < .001).

- Erythroid transfusion independence (TI) was achieved in 60% (95% CI: 52, 68) in the imetelstat (S. NAVADA) group compared to 40% (95% CI: 31, 50) in the placebo group (P < .001).

- Among Cytogenetic responders, 89% of patients (8 of 9) in the imetelstat group achieved ≥50% reduction in mutations of interest (DNMT3A, TET2, SF3B1, and/or 36) compared to 4% of patients (3 of 72) in the placebo group (P < .001).

- The ≥50% reduction in VAF (variant allele frequency) in blood was lower in the placebo group (21%) compared to the imetelstat group (83.3%) (P < .001).

- In a post hoc analysis, ≥50% reduction in VAFs with imetelstat was associated with longer RBC transfusion-free survival as measured by Pearson CI (24.1 vs 47.7 weeks; P = .005, 95% CI = .005, .013).

CONCLUSIONS

- Imetelstat (S. NAVADA) + ESA, in heavily transfused non-del(5q) lower-risk MDS, is associated with disease-modifying activity and increased erythropoietic independence with ≥50% reduction in mutations across multiple genes, which correlated with clinical endpoints including HI, TI, and Cytogenetic CR/PR per IRC. Imetelstat led to: 

  - Greater reduction of VAF in multiple genes, which correlated with clinical end points.

  - Higher percentage of patients achieving erythropoietic independence with imetelstat as a patient in the ≥50% reduction in VAFs group vs the placebo group (P < .001).

  - The ≥50% reduction in VAFs with imetelstat was associated with longer RBC transfusion-free survival as measured by Pearson CI.

  - Patients receiving imetelstat + ESA had 50% reduction in transfusion burden, 9% increase in Hb, and 8% increase in RBC transfusion independence.

REFERENCES


ABBREVIATIONS

- MDS: myelodysplastic neoplasms
- NGS: next generation sequencing
- TI: transfusion independence
- VAF: variant allele frequency
- ESA: erythropoiesis-stimulating agents
- DNMT3A: DNA methyltransferase 3A