In the phase 2 part of the IMerge study, patients with LR-MDS who were heavily RBC transfusion dependent, R/R to or ineligible for ESAs, were randomized 1:1 to receive imetelstat 42 mg/d administered as needed on study per investigator discretion or placebo capsule matched for appearance and taste. Treatment was continued until disease progression, unacceptable toxicity, or the patient elected to discontinue treatment. Baseline characteristics and disease characteristics are summarized in Table 1A. Baseline transfusion burden prior to randomization was 4-6 U every 8 weeks in 59% of patients, >6 U every 8 weeks in 32%, and 1-3 U every 2-3 weeks in 9% of patients. Baseline mean Hb level was 8 g/dL and median platelet count was 119,000/mL. Baseline IPSS risk category was low in 34% of patients, intermediate in 44%, intermediate-1 in 17%, and high in 5% of patients. The median number of prior lines of treatment was 5 (range, 3-8) and 6 (range, 2-9) in the imetelstat and placebo groups, respectively.

**RESULTS**

**Hematologic Improvement and Erythroid Response**

A primary endpoint of 8-week RBC-TI rate was significantly higher with imetelstat vs placebo (42% vs 3%, P < .001) (Figure 3A). Cytopenias were of short duration and were manageable (Table 2B). Cytopenias were of short duration and were manageable (Table 2B). No severe clinical consequences from grade 3-4 cytopenias were noted in the imetelstat group or placebo group. Treatment ongoing, n (%)

- Imetelstat: 39 (32) vs 42 (71)
- Placebo: 30 (50) vs 29 (49)

**Per IWG 2006 criteria.**

**Duration of Transfusion Independence**

Duration of transfection independence was calculated by Kaplan-Meier method and compared via the stratified log-rank test. The median duration of TI in the imetelstat group was 34 weeks (95% CI, 26-62 weeks) compared with 8 weeks (95% CI, 3-16 weeks) in the placebo group (HR, 0.41; 95% CI, 0.21-0.80; P = .009) (Figure 3B).

**Mean Changes in Hb Level Over Time**

Mean changes from the minimum Hb levels of the values that were after 14 days of transfusions in the 8 weeks before the first dosedate were 0.21 g/dL (95% CI, 0.10-0.31 g/dL) for the imetelstat group and 0.03 g/dL (95% CI, 0.00-0.06 g/dL) for the placebo group (P < .001) (Figure 3C). Treatment discontinuation due to TEAE occurred in 7 of 118 patients (5.9%) treated with imetelstat and 1 of 59 patients (1.7%) treated with placebo. The most common adverse events leading to treatment discontinuation were related to transfection burden.

**CONCLUSIONS**

In this heavily transfusion-dependent LR-MDS population in need of novel therapy, imetelstat demonstrated a higher 8-week RBC-TI rate vs placebo. Transfusion burdens were markedly reduced in patients treated with imetelstat (42 mg/d), and the median duration of TI was 34 weeks vs 8 weeks in the placebo group. Hematologic improvements were sustained over time. Cytopenias were of short duration and manageable with dose modification in both groups. Treatment discontinuation due to adverse events was not noted in the placebo group. These results provide clinical evidence for the potential role of imetelstat in transfusion-dependent LR-MDS.