Abstract: S184

Title: OVERALL SURVIVAL, CLINICAL BENEFIT, AND DURABLE TRANSFUSION INDEPENDENCE WITH IMETELSTAT IN THE IMERGE PHASE 3 TRIAL OF RED BLOOD CELL-TRANSFUSION DEPENDENT LOWER-RISK MYELODYSPLASTIC SYNDROMES

Abstract Type: Oral Presentation

Session Title: Immune and targeted therapies in MDS

Background:

In the IMerge phase 3 study (NCT02598661), imetelstat, a first-in-class telomerase inhibitor, resulted in significantly higher rates of RBC-TI for ≥8 weeks, ≥24 weeks, and ≥1 year (39.8%, 28.0%, and 17.8%) than placebo (15.0%, 3.3%, and 1.7%) in patients with non-del(5q) lower risk-myelodysplastic syndromes (LR-MDS) that were red blood cell (RBC)-transfusion dependent (TD), relapsed/refractory to or ineligible for erythropoiesis-stimulating agents, and naïve to lenalidomide or hypomethylating agents (Platzbecker U, et al. *Lancet* 2024;403:249-60).

Aims:

To report initial assessment of overall survival (OS) and clinical benefit of durable RBC-TI with imetelstat in IMerge.

Methods:

IMerge is a global, double-blind, randomized, placebo-controlled, phase 3 trial of imetelstat versus placebo in RBC-TD patients with non-del(5q) LR-MDS. The primary endpoint was ≥8-week RBC-TI; key secondary endpoints included ≥24-week RBC-TI, duration of TI, hemoglobin (Hb) rise, OS and safety. Duration of RBC-TI and OS were calculated by Kaplan-Meier method and compared by stratified log-rank test. Cutoff date was Oct 2022 for the primary analysis, Oct 2023 for ≥1-year RBC-TI, and Jan 2024 for OS.

Results:

Among patients achieving ≥8-week RBC-TI, median duration of TI was 52 weeks for the 47/118 patients in the imetelstat group vs 13 weeks for the 9/60 patients in the placebo group (P<.001) and median increase from baseline in central Hb level was 3.6 g/dL vs 0.8 g/dL, respectively. Of imetelstat-treated patients in this subset, 70% remained RBC-TI for ≥24 weeks and 64% of these ≥24-week responders remained RBC-transfusion free for ≥1 year. Among ≥24-week RBC-TI responders, median duration of TI was 80 weeks for the 33/118 patients in the imetelstat group vs 78 weeks for the 2/60 patients in the placebo group (P<.001) and median increase in central Hb was 4.2 g/dL vs 1.1 g/dL, respectively. In the ≥1-year RBC-TI responders, median duration of TI was 132 weeks for the 21/118 patients in the imetelstat group vs 131 weeks for the 1/60 patients in the placebo group; median increase in central Hb with imetelstat vs placebo was 5.2 g/dL vs 1.7 g/dL. In a separate assessment, ≥8-week, ≥24-week, and ≥1-year RBC-TI with concurrent Hb rise of ≥1.5 g/dL with imetelstat vs placebo occurred in 28% vs 2%, 23% vs 0%, and 17% vs 0% of patients, respectively (all P<.001). As of Jan 2024, 55 (47%) and 26 (43%) patients were in follow-up in the imetelstat and placebo groups, respectively. Median duration of follow-up was 32 months for imetelstat and 28 months for placebo. Median OS was 40.4 months with imetelstat and not estimable with placebo (HR, 0.98; 95% CI, 0.526-1.823). In the imetelstat group, 2-year OS rate was 78% overall, 81% in ≥8-week TI responders, and 75% in nonresponders (Figure). In the placebo group, 2-year OS rate was 74%.

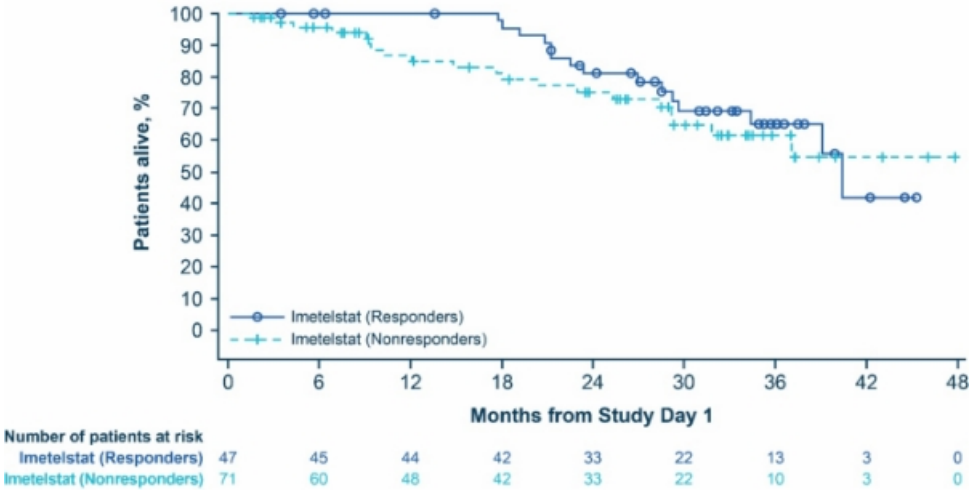
Summary/Conclusion:

Results from these updated analyses confirm that achievement of RBC-TI with imetelstat was durable and associated with improvement in Hb level. Additionally, preliminary OS analysis suggests no detriment with

imetelstat vs placebo.

VS/RSK and AMZ/UP contributed equally.

Figure. OS in Imetelstat 8-week RBC-TI Responders vs Nonresponders



Number of patients at risk									
Imetelstat (Responders)	47	45	44	42	33	22	13	3	0
Imetelstat (Nonresponders)	71	60	48	42	33	22	10	3	0

Keywords: Transfusion, Myelodysplastic syndrome, Survival