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Abstract #3088

Treatment with Imetelstat Improves Myelofibrosis-Related Symptoms and Other Patient-Reported Outcomes in Patients with Relapsed or Refractory Higher-Risk Myelofibrosis

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Disclosure

- **Presenter:** Jean-Jacques Kiladjian, MD, PhD
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- **Disclosure:**
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Background

- Myelofibrosis (MF) is a life-threatening myeloproliferative neoplasm characterized by splenomegaly and debilitating symptoms, such as fatigue, pruritus, night sweats, fever, bone pain, and weight loss that impact quality of life (QoL).
- Imetelstat, a 13-mer oligonucleotide that specifically targets the RNA template of human telomerase, is a potent competitive inhibitor of telomerase enzymatic activity.
- Imetelstat has demonstrated clinical benefit in terms of symptom response and potential improvement in OS in IMbark, a phase 2 study in MF patients (pts) relapsed or refractory (R/R) to a janus associated kinase inhibitor (JAKi).¹
- IMbark (MYF2001; NCT02426086) was a 2-dose, randomized, single-blinded, phase 2 study of imetelstat in R/R intermediate-2/high-risk MF pts, who received imetelstat 9.4 mg/kg or 4.7 mg/kg

1. Mascarenhas J et al, Imetelstat is effective treatment for patients with intermediate 2 or high-risk myelofibrosis who have relapsed on or are refractory to janus kinase inhibitor therapy: results of a phase 2 randomized study of two dose levels. *Blood*. 2018;132:68.5.



Methods

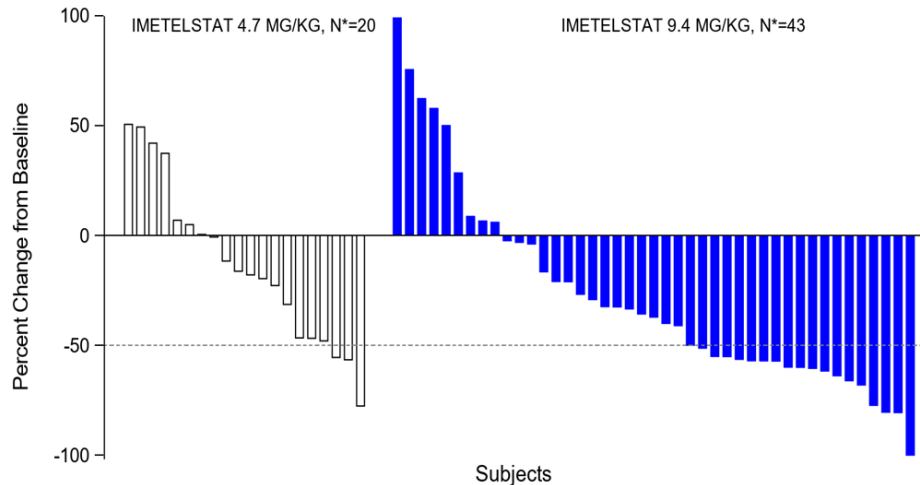
- The effects of imetelstat on MF symptom burden and QoL in IMbark were assessed, and the correlations of myelofibrosis-related symptoms measured by modified Myelofibrosis Symptom Assessment Form (MFSAF) 2.0 and other patient-reported outcome (PRO) endpoints were evaluated.
- Symptom response, one of the co-primary endpoints, was defined as $\geq 50\%$ reduction in total symptom score (TSS) from baseline to Week 24 as measured by the modified MFSAF 2.0 e-diary.
- The TSS was calculated as the 7-day average of daily TSS, which is the summation of 6 individual symptom scores (night sweats, itchiness, abdominal discomfort, pain under ribs on left side, early satiety, bone or muscle pain).
- Correlation of TSS with other PROs was explored: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 (EORTC QLQ-C30), Brief Pain Inventory (BP-I), and Patient Global Impression of Change (PGIC).
- All correlative analyses performed were not pre-specified and are exploratory.



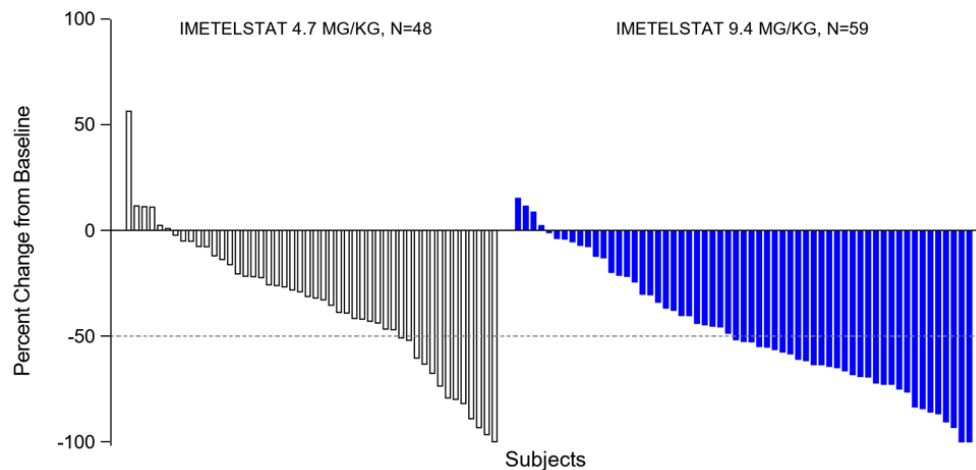
Results: Dose-Related Improvements in TSS

- All 107 patients enrolled in IMbark were symptomatic, with baseline mean TSS scores of 25.7 in the 9.4 mg/kg arm (N=59) and 24.6 in the 4.7 mg/kg arm (N=48), indicating a high symptom burden. Pts in both arms had $\geq 96.5\%$ mean compliance rates with completion of the e-diary.
- Treatment with imetelstat demonstrated a statistically significant dose-related improvement in symptom response rate at Week 24 for 9.4 mg/kg vs 4.7 mg/kg (32.1% vs 6.3%, $p=0.001$) and at any time (52.5% vs 27.1%, $p=0.010$).

Dose-dependent TSS change at week 24



Dose-dependent TSS change at any time

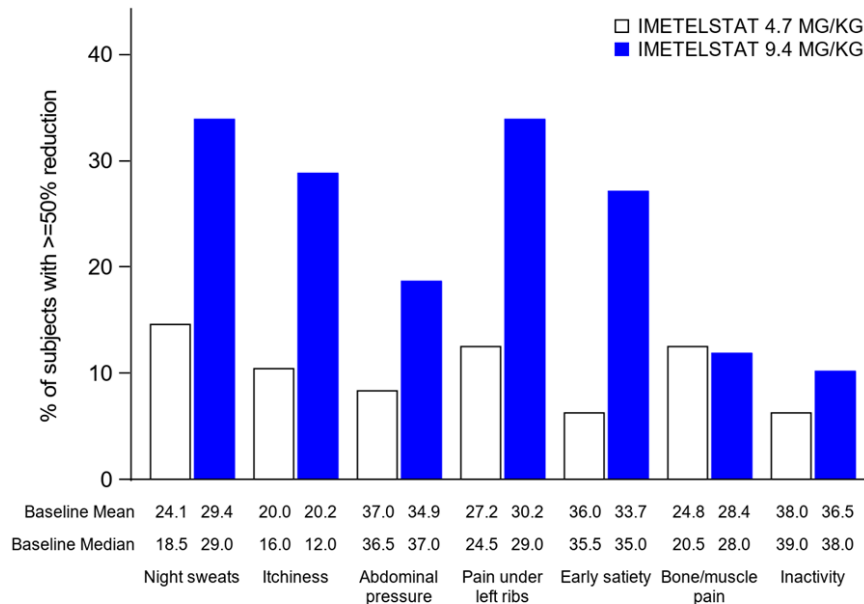


N* the number of subjects who had TSS data at both week 24 and baseline
Symptom response: $\geq 50\%$ total symptom score (TSS) reduction at week 24



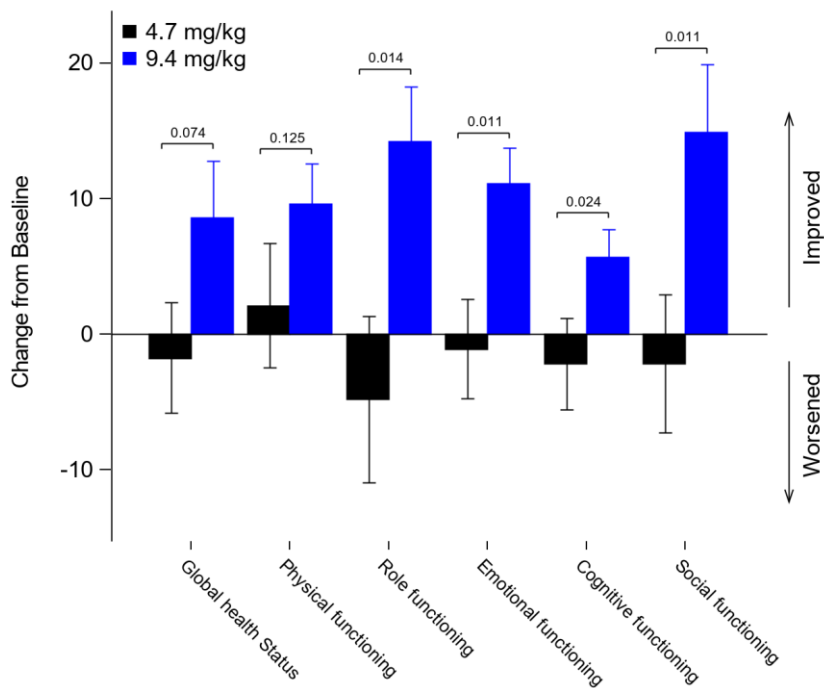
Results: Dose-Related Improvements in Individual Symptom

A higher proportion of pts in the 9.4 mg/kg arm than in the 4.7 mg/kg arm achieved $\geq 50\%$ reduction in 5 individual symptom including night sweats, itchiness, abdominal pressure, pain under left ribs, and early satiety

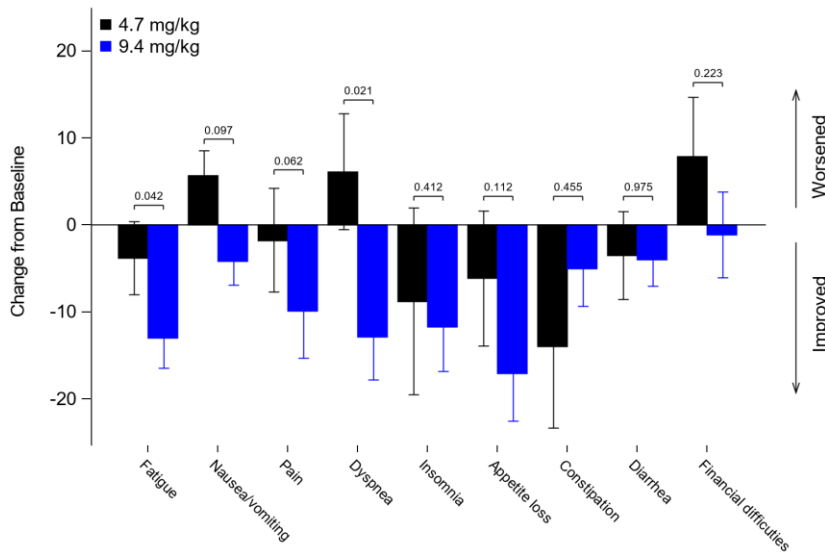


Dose-Related Improvements in EORTC QLQ-C30

Improvement in EORTC QLQ-C30 Global Health Status and Functional Scales at Week 24



Improvement in EORTC QLQ-C30 Symptom Scales and Single Items at Week 24

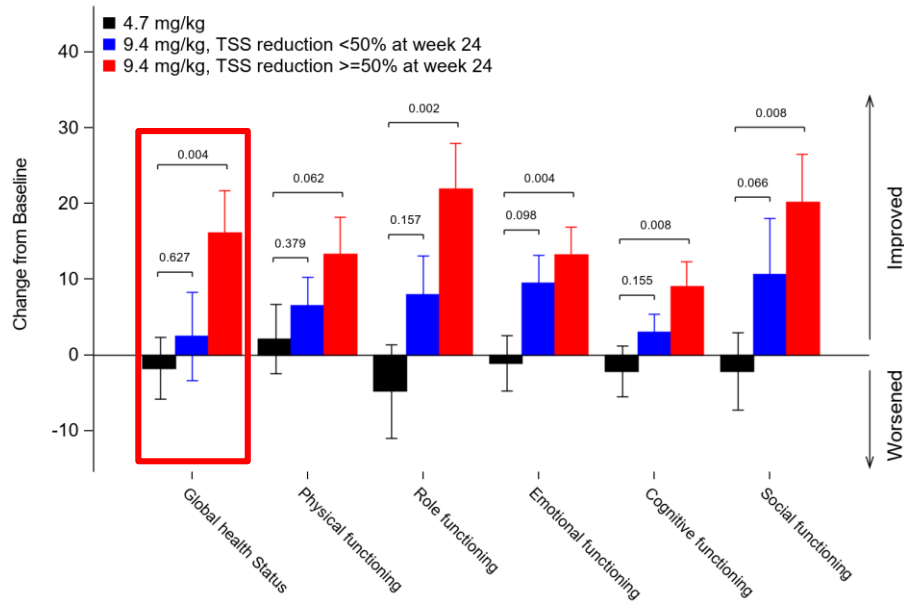


Notably for fatigue (a common MF symptom which was not measured in MFSAF v2.0), patients in the 9.4 mg/kg arm had improvement at Week 24 relative to baseline, compared to the pts in the 4.7 mg/kg arm (LS means -13.3 vs -3.1, $p=0.042$).



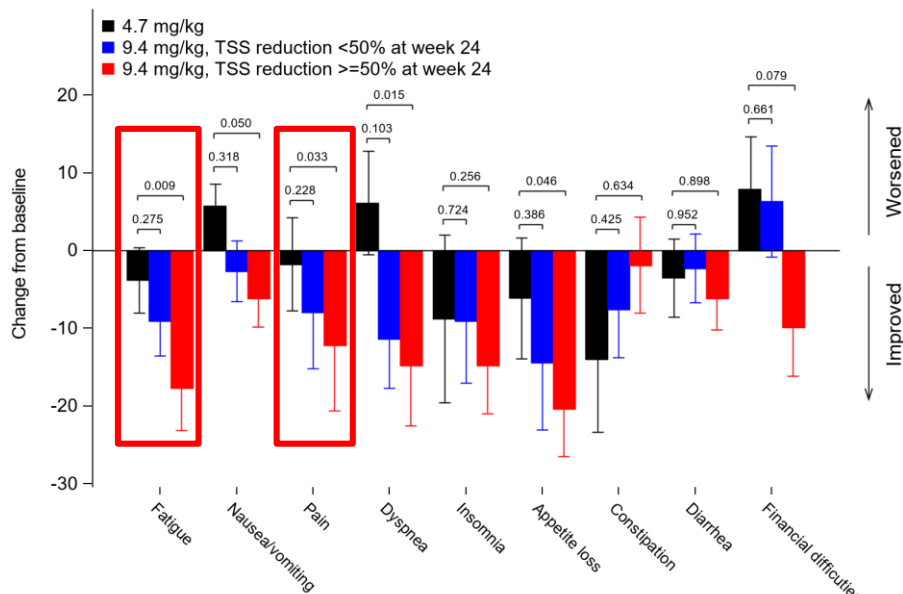
TSS Response Correlate with EORTC QLQ-C30

High correlation between TSS improvement and EORTC QLQ-C30 GHS and functional scales



Compared to pts in the 4.7 mg/kg arm, TSS symptom responders in the 9.4 mg/kg arm achieved significantly greater improvements in the global health status ($p=0.004$), and most of the functional scales in EORTC QLQ-C30

High correlation between TSS improvement and EORTC QLQ-C30 symptom scales and single items



Compared to pts in the 4.7 mg/kg arm, TSS symptom responders in the 9.4 mg/kg arm achieved significantly greater improvements in fatigue ($p=0.009$), pain ($p=0.033$)



TSS Response Correlate with BP-I and PGIC

- Pain scores per the modified MFSAF v2.0 correlated with BP-I (correlation coefficients 0.5-0.6).
- More than 90% of TSS symptom responders in the 9.4 mg/kg arm also characterized their condition as having had either “very much improvement” (36.4%) or “somewhat improvement” (54.6%) in PGIC.



Conclusions

- These data show a dose-related, clinically meaningful improvement in overall and individual MF symptoms as measured by MFSAF 2.0 with imetelstat treatment in pts who are JAK inhibitor R/R.
- TSS symptom responders treated with imetelstat 9.4 mg/kg also had improvement in QoL as measured by EORTC QLQ-C30.
- The data further support the robustness of overall and individual symptom improvement in pts with MF as evidenced by the correlation of modified MFSAF v2.0 with other PROs such as EORTC QLQ-C30, PGIC, and BP-I.
- Further data on PRO will be collected in the upcoming Phase 3 trial in refractory MF (IMpactMF).

