

Improved Transfusion Independence Rates for Momelotinib vs Ruxolitinib in Anemic JAKi Naïve Myelofibrosis Patients are Independent of Baseline Platelet or Transfusion Status



Jean-Jacques Kiladjian¹, Uwe Platzbecker², Jiří Mayer³, Árpád Illés⁴, Witold Prejzner⁵, Tomasz Woźny⁶, Nikolay Tzvetkov⁷, Alessandro M Vannucchi⁸, Ilya Kirgner⁹, Zsolt Nagy¹⁰, Sebastian Grosicki¹¹, Åsa Derolf¹², Mihaela Cornelia Lazaroiu¹³, Sung-Soo Yoon¹⁴, Yeow Tee Goh¹⁵, Nikolas von Bubnoff¹⁶, Ruben Mesa¹⁷, Barbara J Klencke¹⁸, Rafe Donahue¹⁸, Srdan Verstovsek¹⁹

¹Saint-Louis Hospital (AP-HP), Paris, France; ²Leipzig University Hospital, Leipzig, Germany; ³Masaryk University Hospital Brno, Brno, Czechia; ⁴Department of Hematology, Faculty of Medicine, University of Debrecen, Hungary; ⁵Department of Hematology and Transplantology, Medical University of Gdansk, Gdansk, Poland; ⁶Department of Hematology, Szpital MSWiA w Poznaniu, Poland; ⁷University Multiprofile Hospital For Active Treatment, Bulgaria; ⁸Center Research and Innovation of Myeloproliferative Neoplasms, AOU Careggi, University of Florence, Italy; ⁹Division of Hematology, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; ¹⁰Semmelweis University, Budapest, Hungary; ¹¹Medical University of Silesia, Katowice, Poland; ¹²Department of Medicine, Division of Hematology, Karolinska University Hospital Solna, Karolinska Institutet; ¹³Policlinica de Diagnostic Rapid Brasov, Romania; ¹⁴Seoul National University Hospital, Seoul, Korea; ¹⁵Singapore General Hospital, Singapore; ¹⁶Department of Hematology and Oncology, Medical Center, University of Schleswig Holstein, Lübeck / Department of Medicine I (Hematology, Oncology and Stem Cell Transplantation), Medical Center, Faculty of Medicine, University of Freiburg / German Cancer Consortium (DKTK) partner site Freiburg and German Cancer Research Center (DKFZ), Heidelberg, Germany; ¹⁷UT Health San Antonio Cancer Center, San Antonio, United States; ¹⁸Sierra Oncology Inc., Vancouver, Canada; ¹⁹The University of Texas MD Anderson Cancer Center, Houston, United States

Background and Methods

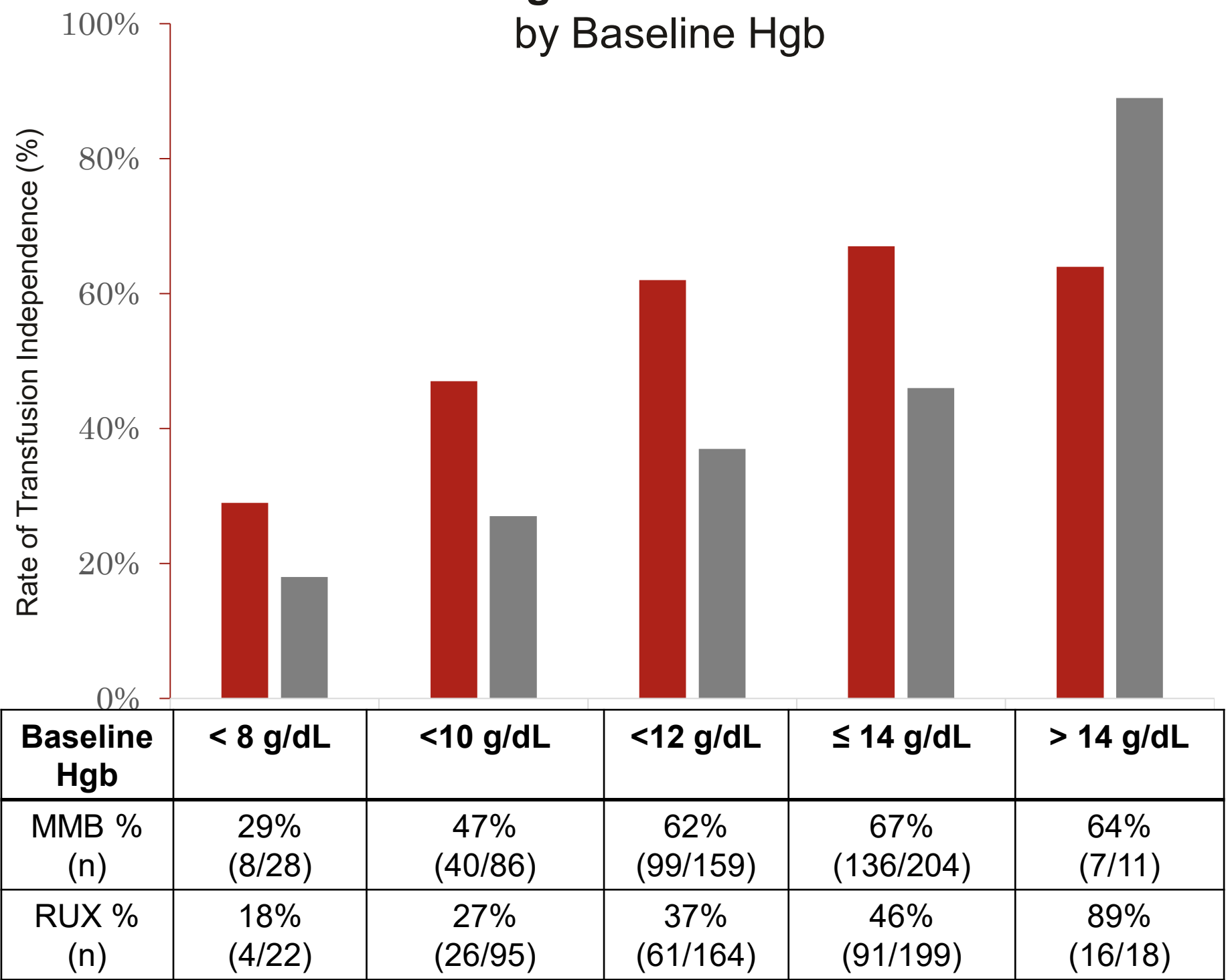
- Momelotinib (MMB) is a JAK1, JAK2 and ACVR1/ALK2 inhibitor with clinical activity against the hallmark features of myelofibrosis (MF), namely anemia, constitutional symptoms and splenomegaly, across the continuum of JAKi naïve or previously JAKi treated patients.
- Inhibition of ACVR1/ALK2 reduces hepcidin; elevated levels of hepcidin cause an iron-restricted anemia of inflammation shortening survival in patients with MF.
- Progressive anemia is common in MF and an important negative prognostic factor, with nearly all patients requiring transfusions as their disease advances.
- SIMPLIFY-1 (S1) was a Phase 3 trial in JAKi naïve patients with MF (n=432) double-blind randomized 1:1 to MMB or ruxolitinib (RUX).
- Given the positive impact of transfusion independence (TI) on survival in patients receiving MMB (Mesa et al, EHA 2021 presentation S202), we expanded the previously reported retrospective platelet (PLT) subset analysis to explore the Week 24 (W24) TI response rates for MMB and RUX randomized patients in S1 by baseline (BL) hemoglobin (Hgb) and PLT levels and transfusion status.

Relevant previously reported results:

- The overall W24 TI response rate on MMB in S1 was 67% vs 49% for RUX (nominal *P*<0.001).
- MMB demonstrated a statistically non-inferior splenic response rate (SRR) to RUX at the W24 landmark analysis in S1 but did not meet significance for total symptom score (TSS) response (Mesa et al, JCO. 2017).
- Robust survival was demonstrated in the final analysis of S1 with a median overall survival of 53 months in patients randomized to RUX for 24 weeks followed by MMB, and not reached in patients randomized to MMB (Verstovsek et al, ASH 2020 Oral Presentation).

Results

Fig 1: W24 TI Rate by Baseline Hgb



Hgb=hemoglobin, MMB=momelotinib, PLT=platelet, RUX=ruxolitinib, TD=transfusion dependent (≥4 units of RBCs or Hgb level, ≤ 8 g/dL in the 8 weeks prior to randomization), TI=transfusion independent (absence of RBC transfusions and no Hgb < 8 g/dL in the 12 weeks prior to randomization), TR=transfusion requiring (neither TD nor TI)

- Treatment with MMB resulted in higher TI rates vs RUX in all patient subsets with BL Hgb ≤ 14 g/dL (Fig 1), and all subsets defined by BL PLTs (Fig 2) and BL transfusion status (Fig 3).
- Patient subsets with BL Hgb ≤ 14 g/dL account for 93% of patients in S1, representing a population where the majority have some degree of anemia.

Fig 2: W24 TI Rate by Baseline PLT

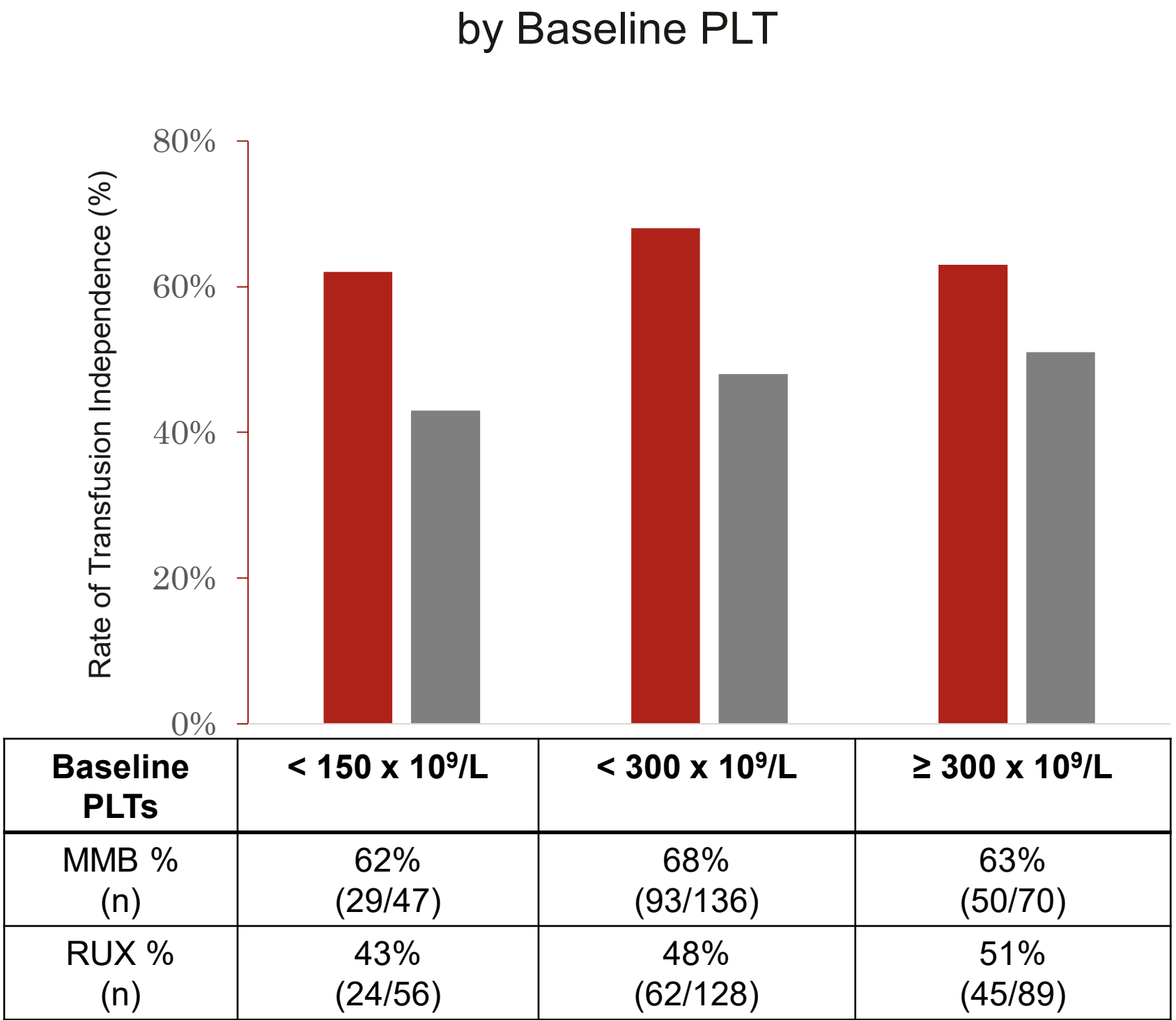
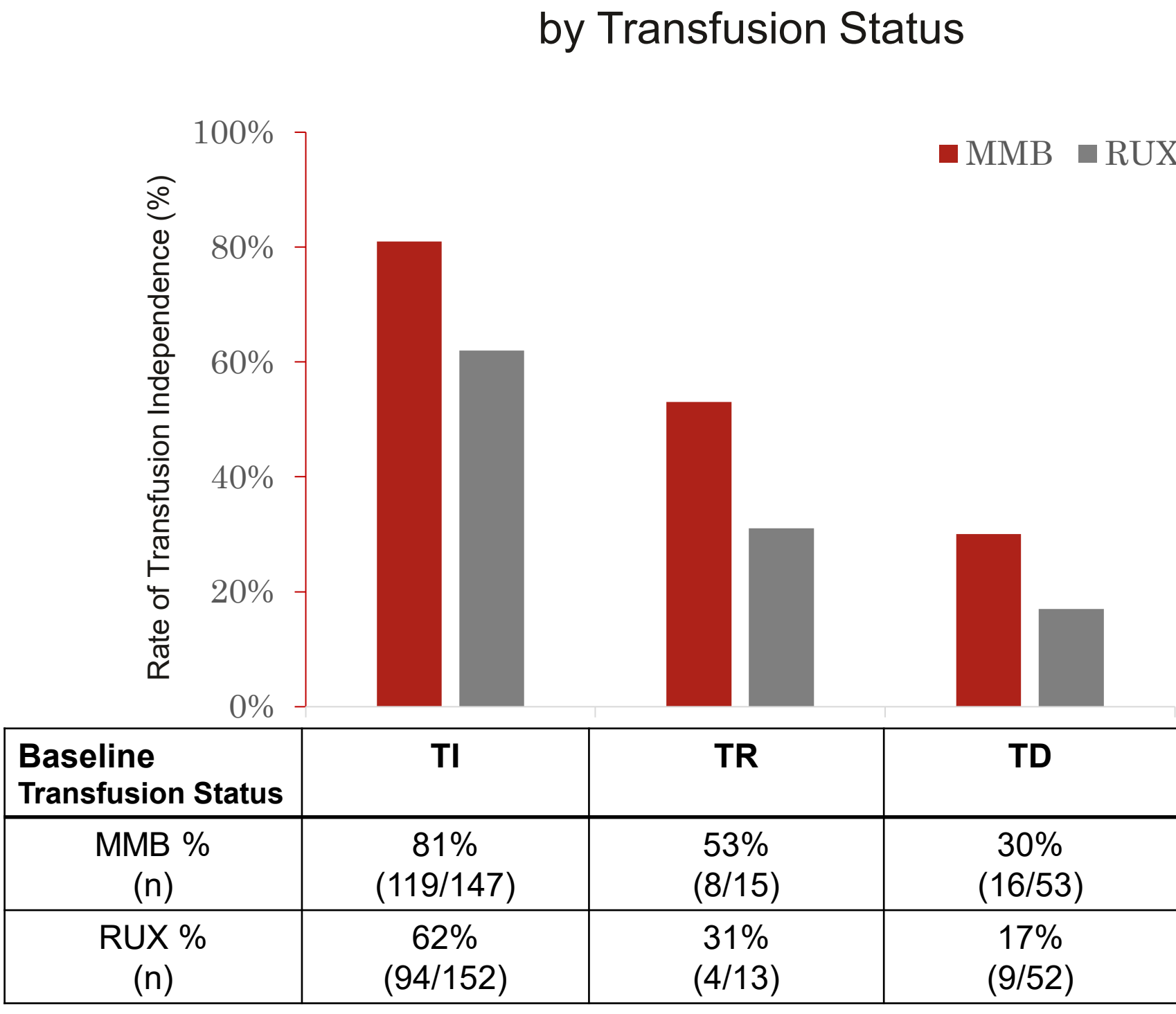


Fig 3: W24 TI Rate by Transfusion Status



Conclusions and Clinical Relevance

- The data presented here support the breadth of W24 TI benefit for patients receiving MMB, irrespective of the degree of baseline anemia, baseline PLT count, or baseline transfusion status.
- In addition, data suggest that an MMB-mediated TI response at W24 is associated with a survival advantage (Mesa et al, EHA 2021 presentation S202).
- Taken together, these data further support the potential benefit of MMB's ACVR1/ALK2 inhibitor activity in addition to inhibiting JAK1 and JAK2, leading to improved TI rates and overall survival
- As a result, MMB has the potential to become a preferred treatment for patients with MF who are anemic or who are at risk of myelosuppression as a result of treatment with currently available JAKi.

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