PREDICTORS OF RESPONSE TO SECOND-LINE MOMELOTINIB AFTER RUXOLITINIB FAILURE: AN INDEPENDENT COOPERATIVE STUDY

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Introduction

Momelotinib (MMB), a JAK1/JAK2/ACVR1 inhibitor, is approved for treating patients with myelofibrosis presenting splenomegaly, symptoms and anemia.[1]

Objectives

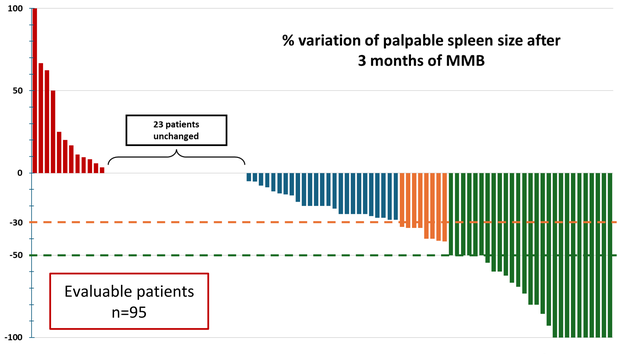
To evaluate Spleen Response (SR), Symptoms Response (SyR) and Anemia Response (AR) with MMB at 3 and 6 months (m) and identify predictors of response.

Methods

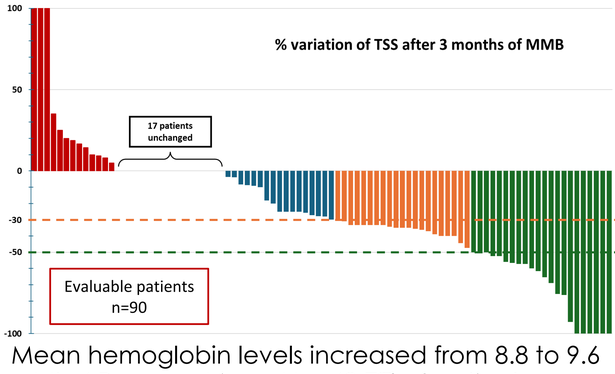
Real-world analysis of 156 patients who received momelotinib outside clinical trials after ruxolitinib failure. SR: spleen length reduction by 30% (SR30) or 50% (SR50) in patients with baseline splenomegaly. SyR: Total Symptoms Score reduction by 30% (SyR30) or 50% (SyR50). Anemia Response, AR: 50% reduction of transfusion need/Hb increase >1.5 g/dL.

Results

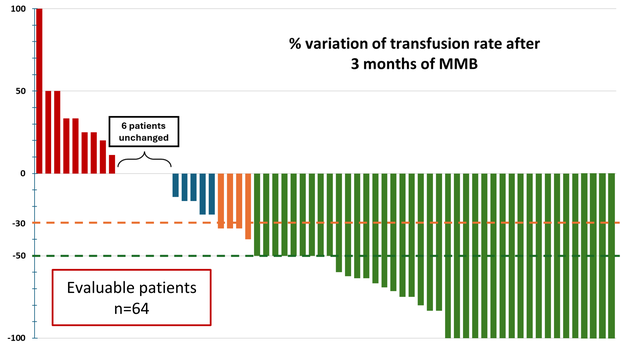
Mean ruxolitinib and momelotinib duration were 2.7yrs and 7.3m, respectively. During the first 6 months of ruxolitinib, 50.5% of patients achieved SR50 and 44% required RBC transfusions. Characteristics at MMB start were: mean age 72.4 yrs; male sex, 58.3%; primary myelofibrosis, 62.2%; hemoglobin <10 g/dL, 78.9%; RBC transfusion need, 78.9%; dependency (TD), 29.5%; platelets <100 x10^9/L, 45.5%; cytopenic phenotype (hemoglobin <10g/dL and/or platelet <100 x10^9/L), 88.5%; palpable spleen, 83.3% (large spleen, ≥10cm BCM, 39.7%); symptomatic patients (TSS>0), 84.0%.

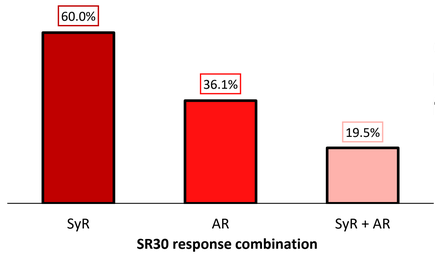


At 3 months, response rates were: SR30, 36.8%; SR50, 28.4%; SyR30, 50.0%, SyR50, 24.4%.
One out of 26 patients without baseline splenomegaly developed palpable spleen during the first 6 months of momelotinib.



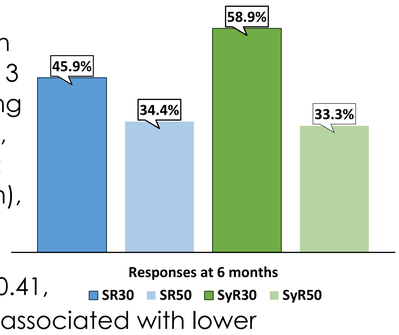
Mean hemoglobin levels increased from 8.8 to 9.6 g/dL. AR was achieved by 43.7% of patients.

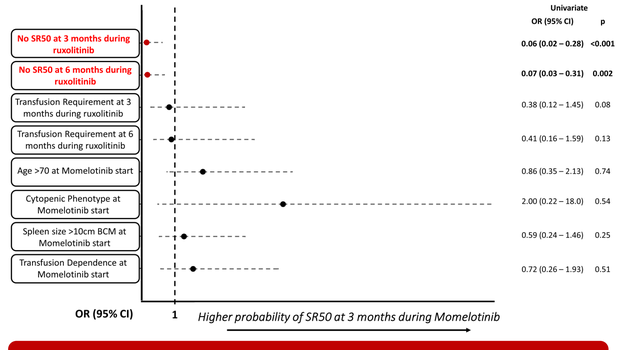




Combined response rates for SR30 patients at 3 months

Responses rates at 6 months are represented in the graph on the right.
In logistic regression analysis, noSR50 at 3 and 6 months during ruxolitinib (OR: 0.06, p<0.001 at 3m; OR: 0.07, p=0.002 at 6m), but not transfusion need (OR: 0.38, p=0.08 at 3m; OR: 0.41, p=0.13 at 6m) was associated with lower probability of SR50 at 3 months in momelotinib. Age, cytopenic phenotype, large spleen, and TD at momelotinib start were not associated with lower SR50.





Discussion

Despite advanced disease, >30% of patients achieved an SR50 to second-line momelotinib. Absence of SR50 in the first 6 months of ruxolitinib correlated with lower SR to momelotinib and may identify patients with suboptimal sensitivity to JAKi monotherapy. Cytopenias did not negatively impact momelotinib response, supporting its role as a viable treatment option in this difficult-to-treat population.

References

1.Verstovsek S, Mesa R, Gupta V, et al. Momelotinib long-term safety and survival in myelofibrosis: integrated analysis of phase 3 randomized controlled trials. Blood Adv. 2023;7(14):3582-3591.

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