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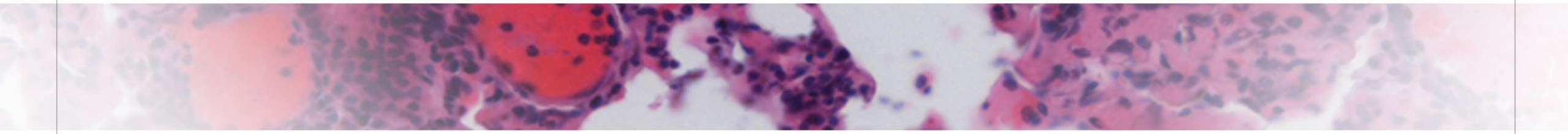

Momelotinib's Spleen, Symptom and Anemia Efficacy is Maintained in Intermediate/High Risk Myelofibrosis Patients With Thrombocytopenia

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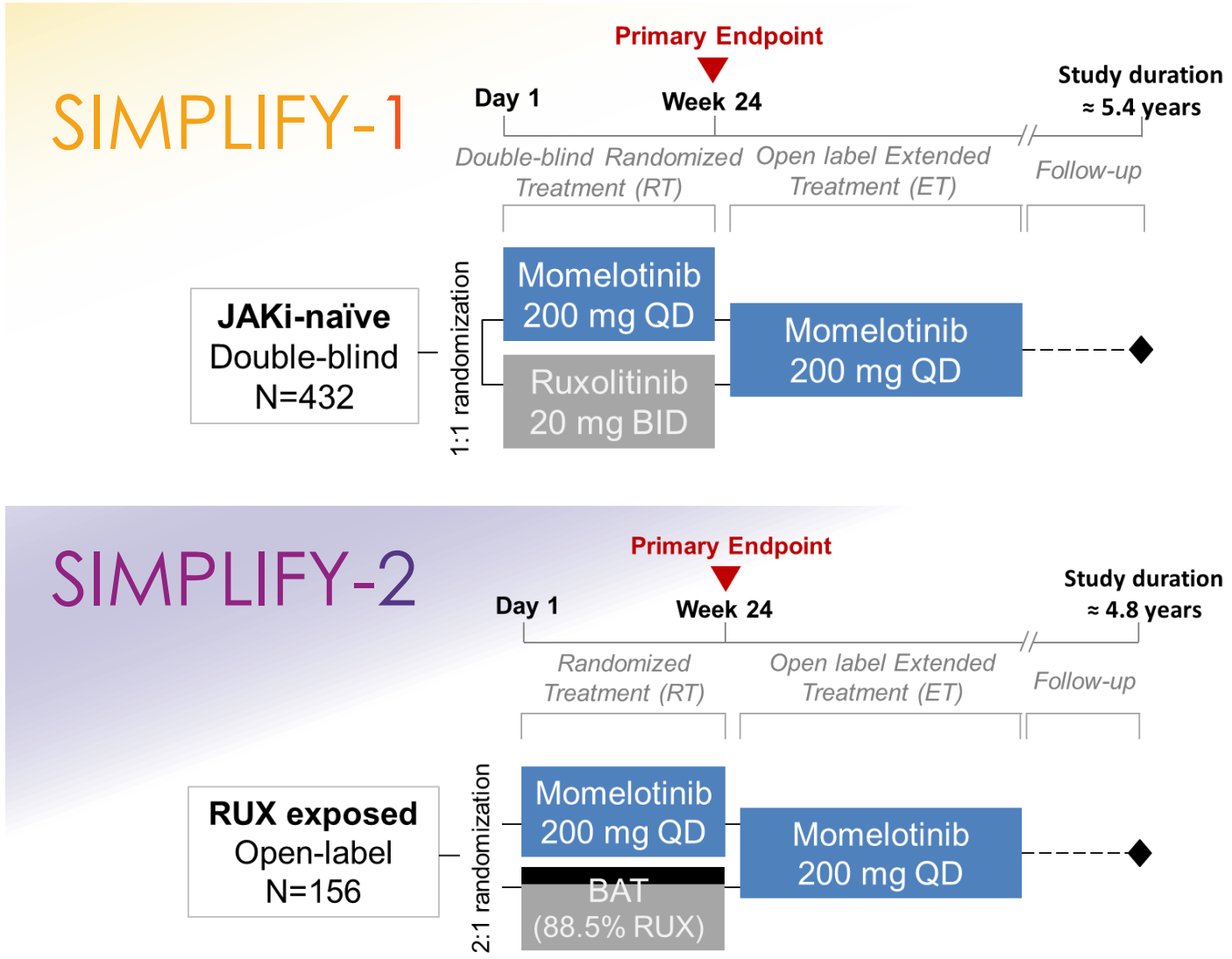
Background and Methods

- Momelotinib (MMB), a JAK1, JAK2 and ACVR1 inhibitor, which has shown activity against constitutional symptoms and splenomegaly across prior clinical studies
- Retrospective analysis of the W24 landmark symptom, transfusion independence (TI) and splenic response rates by baseline PLT strata in 2 previously completed studies:
- **SIMPLIFY-1 (S1),** a double-blind Phase 3 study in JAK-naïve patients with MF, comparing MMB vs RUX.
  Baseline PLTs ≥50 × 10^9/L were required.
- **SIMPLIFY-2 (S2),** a Phase 3 study in patients who previously received RUX for MF, comparing MMB vs best available therapy (BAT; 88% of which was RUX).
  There was no lower PLT limit.



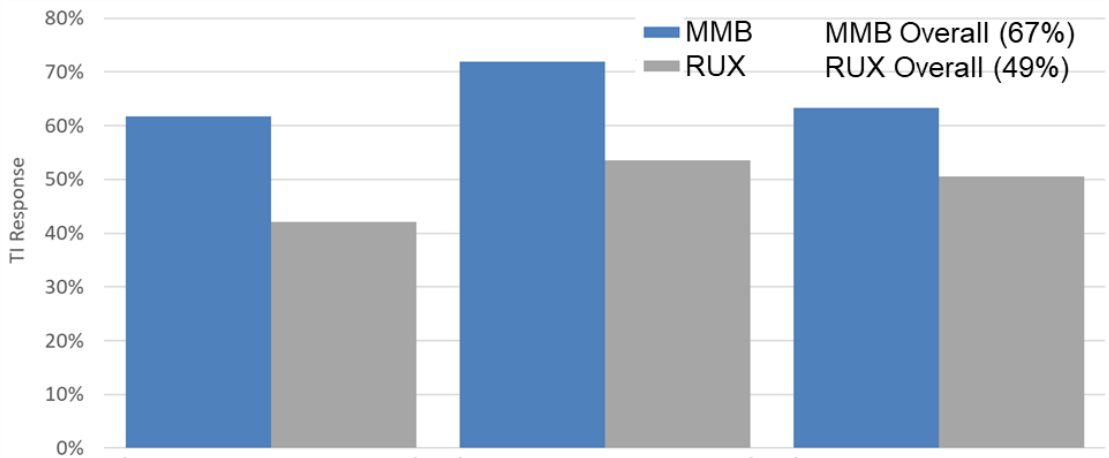
Results: Safety Profile and Durability of Dosing

- On momelotinib, safety in patients with low PLTs is comparable to safety in the overall momelotinib population:
  - Rates of treatment-emergent adverse events (TEAEs) on momelotinib were generally similar between the overall safety population and subjects with baseline PLTs <150 in both SIMPLIFY studies
  - However in SIMPLIFY-1, nausea, fatigue and anemia were more common in those with PLTs <150 vs the overall population (21-23% vs 15-16%)

- In SIMPLIFY-1, momelotinib dose intensity was maintained with 88.6% receiving a daily dose of 151 - 200 mg at the end of the randomized period
- By contrast, 36.9% were receiving 20 or 25 mg BID ruxolitinib dose by the end of the randomized period (EHA 2020)

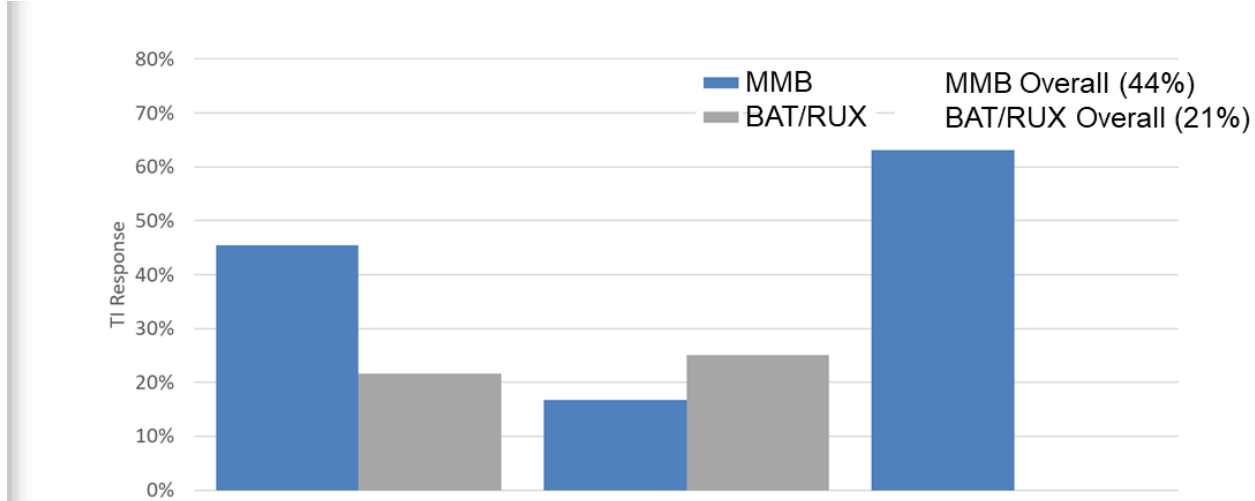
Results: TI Rates Compared by Baseline PLT Strata

1A: SIMPLIFY-1: W24 Anemia (TI) Response



PLTs (×10⁹/L)	50-150		>150-300		>300	
# in stratum	n=47	n=57	n=89	n=71	n=79	n=89
% Response	62%	42%	72%	54%	63%	51%

1B: SIMPLIFY-2: W24 Anemia (TI) Response



PLTs (×10⁹/L)	≤150		>150-300		>300	
# in stratum	n=66	n=37	n=18	n=12	n=19	n=3
% Response	45%	22%	17%	25%	63%	0%

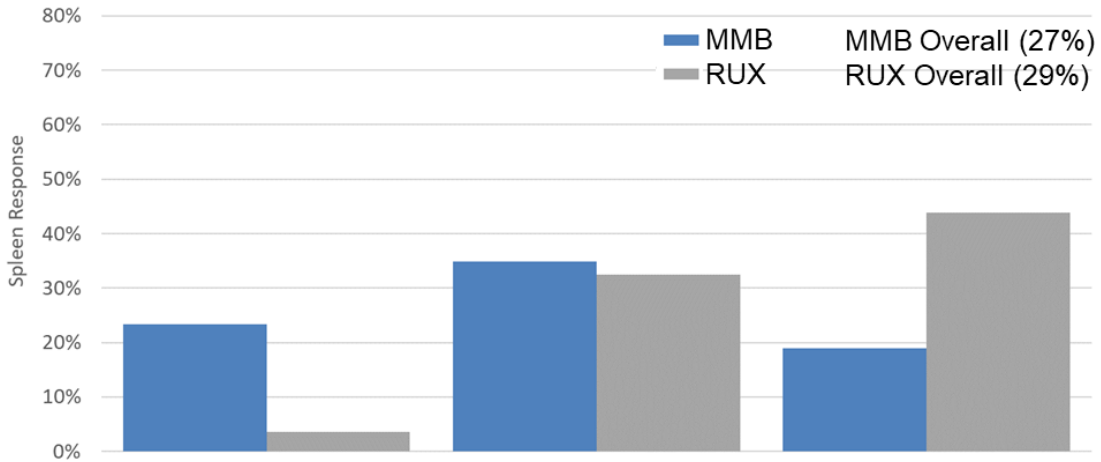
- In S1 (JAKi-naïve patients), MMB treatment elicited a TI response rate greater than 60% in each baseline PLT stratum in comparison to rates of 42%-54% for RUX (Figure 1A)

- In S2 (RUX-exposed patients), the TI rate on MMB was preserved in those with lower PLTs at baseline (Figure 1B)
- Overall TI response rates in the BAT (RUX) arm in S2 were low (Figure 1B)

TI = transfusion independence, PLT = platelets

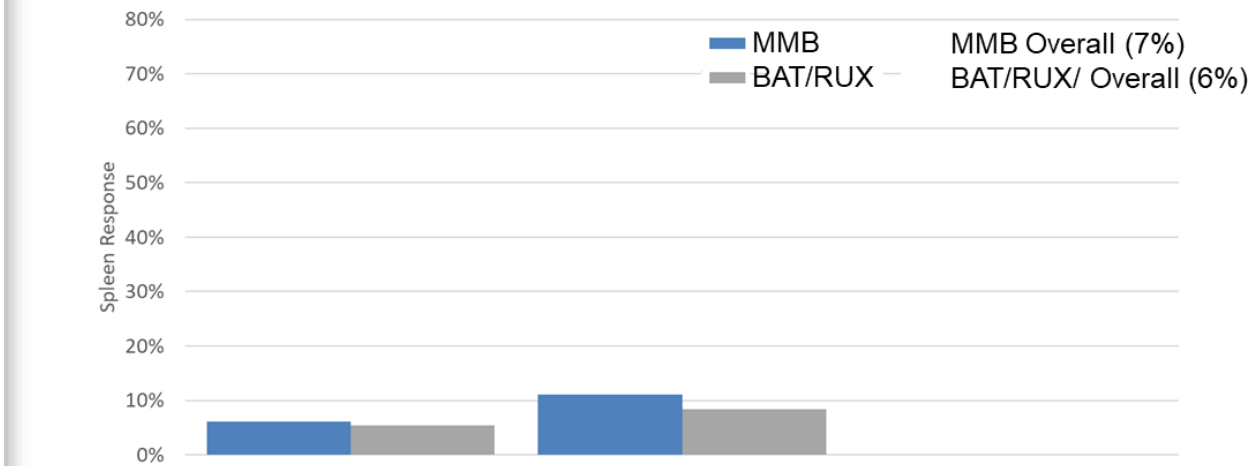
Results: SRRs Compared by Baseline PLT Strata

1C: SIMPLIFY-1: W24 Splenic Response



PLTs (×10⁹/L)	50-150		>150-300		>300	
# in stratum	n=47	n=57	n=89	n=71	n=79	n=89
% Response	23%	4%	35%	32%	19%	44%

1D: SIMPLIFY-2: W24 Splenic Response



PLTs (×10⁹/L)	≤150		>150-300		>300	
# in stratum	n=66	n=37	n=18	n=12	n=19	n=3
% Response	6%	5%	11%	8%	0%	0%

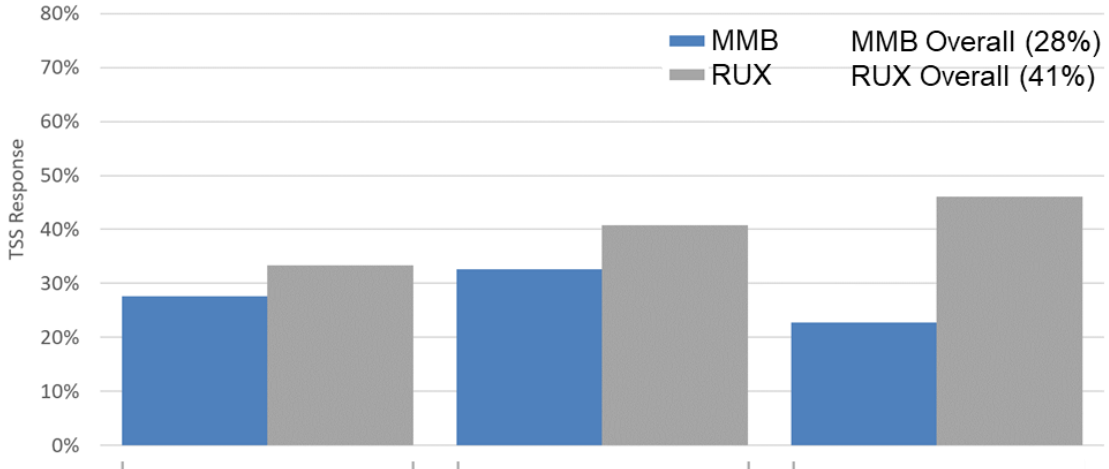
- In S1 (JAKi-naïve patients), the splenic response rate (SRR) was maintained in all baseline PLT strata with MMB whereas a marked reduction in SRR was observed for patients with lower baseline PLTs on RUX (Figure 1C)

- In S2 (RUX-exposed patients), overall SRRs in both MMB and BAT arms were low, likely due to a lack of mandatory washout from prior JAKi therapy (Figure 1D)

PLT = platelets

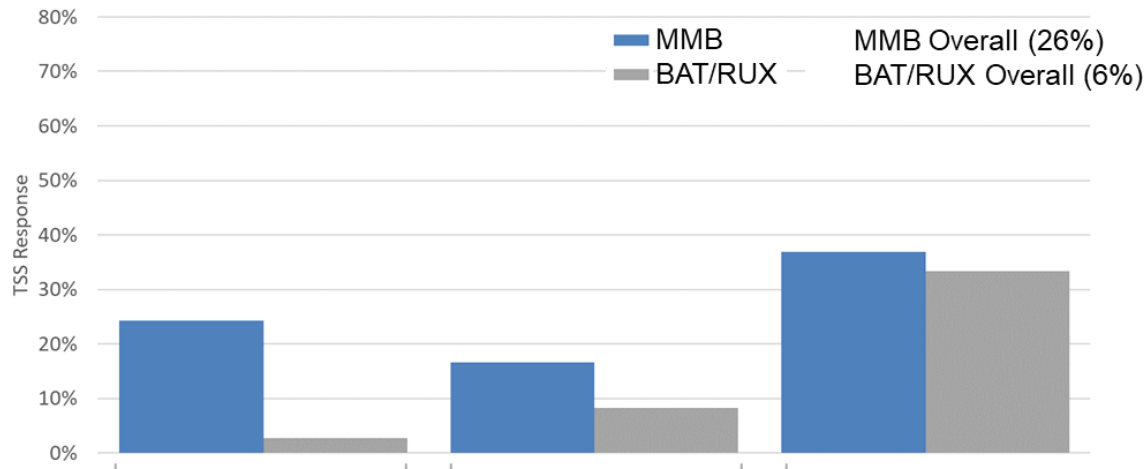
Results: TSS Response Rates Compared by Baseline PLT Strata

1E: SIMPLIFY-1: W24 Symptom (TSS) Response



PLTs (×10⁹/L)	50-150		>150-300		>300	
# in stratum	n=47	n=57	n=89	n=71	n=79	n=89
% Response	28%	33%	33%	41%	23%	46%

1F: SIMPLIFY-2: W24 Symptom (TSS) Response



PLTs (×10⁹/L)	≤150		>150-300		>300	
# in stratum	n=66	n=37	n=18	n=12	n=19	n=3
% Response	24%	3%	17%	8%	37%	33%

- In S1 (JAKi-naïve) and S2 (RUX-exposed), the TSS response rate was maintained on MMB in patients with lower baseline PLTs (Figure 1E and 1F)
- In comparison, in the RUX arm of S1 TSS response rates were lower with lower baseline PLTs (Figure 1E)

- In S2, MMB TSS response rates preserved across platelet strata (Figure 1F)
- TSS response rates were higher in the MMB arm compared to BAT in all strata (Figure 1F), consistent with the TSS response rates for MMB (26%) vs. RUX (6%) in the overall population

TSS = MFSAF Total Symptom Score, PLT = platelets

Summary

- SIMPLIFY-1 (JAKi naïve patients) summary:
  - In patients whose baseline platelet counts were:
    - ≤150 × 10^9/L, momelotinib achieved substantially higher TI and splenic response rates and a similar symptomatic response relative to ruxolitinib;
    - 150-300 × 10^9/L, generally similar splenic and symptom response rates and a higher TI response rate were achieved with momelotinib relative to ruxolitinib;
    - >300 × 10^9/L, higher splenic and symptom response rates at W24 were achieved with ruxolitinib than with momelotinib; the Week 24 TI rate remained higher with momelotinib.
- SIMPLIFY-2 (RUX-exposed patients) summary:
  - Momelotinib's response rates for the 3 response parameters remain very consistent with the overall (ITT) response rates in patients whose baseline platelets were ≤150 × 10^9/L
  - Momelotinib's symptomatic and anemia benefits were also preserved in patients whose baseline platelet counts were ≤50 and >50–100 × 10^9/L (data not shown)
- In both SIMPLIFY-1 and SIMPLIFY-2, rates of TEAEs on MMB were generally similar between the overall safety population and subjects with baseline PLTs <150 × 10^9/L

Conclusions

- These retrospective analyses of data from the two Phase 3 SIMPLIFY studies demonstrate that MMB's safety and activity profile do not appear to be affected by baseline PLT count.
  - In contrast, activity with ruxolitinib declined in patients with lower baseline platelet counts.
- Therefore, the relative benefit-risk profile of momelotinib and ruxolitinib is influenced by baseline platelet count, and is generally comparable or favorable in JAKi naïve patients whose baseline platelet count is at or below 300 x 10^9/L.
- These updated efficacy analyses complement previous findings highlighting the ability to initiate and maintain near-maximal momelotinib dose intensity irrespective of baseline PLT count, suggesting that this durable dosing contributes to the compound's efficacy profile.

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