SIMPLIFY-1 and SIMPLIFY-2:
Completed Phase 3 Studies of Momelotinib

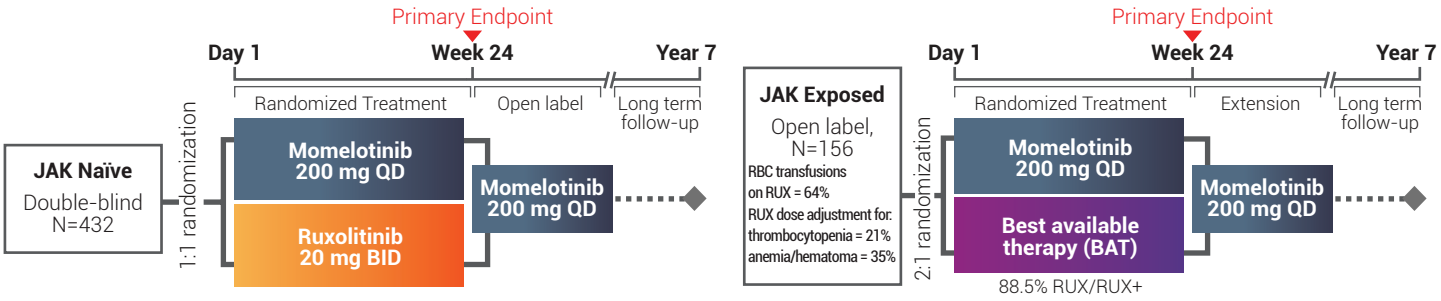
Study Designs

SIMPLIFY-1

Phase 3, randomized 1:1, double-blind, head-to-head, non-inferiority comparison of momelotinib (MMB) to ruxolitinib (RUX) in JAK inhibitor naïve myelofibrosis patients, N=432

SIMPLIFY-2

Phase 3, 2:1 randomized study comparing MMB to Best Available Therapy (BAT; ~90% RUX) in myelofibrosis patients previously treated with RUX, N=156



Primary endpoint: Splenic Response Rate (SRR)

Secondary endpoints: Total Symptom Score (TSS), Transfusion Independence Rate, Transfusion Dependence Rate, Red Blood Cell (RBC) Transfusion Rate

Overview of Results

	SIMPLIFY-1	SIMPLIFY-2
Primary endpoint: Splenic Response Rate	✓ Non-inferiority demonstrated	✗ Superiority was not demonstrated**
• **Total Symptom Score (TSS) Response Rate**	✗ Non-inferiority was not demonstrated*	✓ MMB higher than BAT (88.5% RUX)***
• **Transfusion Independence Rate**	✓ MMB higher than RUX***	✓ MMB higher than BAT (88.5% RUX)***
• **Transfusion Dependence Rate**	✓ MMB lower than RUX***	✓ MMB lower than BAT (88.5% RUX)***
• **RBC Transfusion Requirements**	✓ MMB lower than RUX***	✓ MMB lower than BAT (88.5% RUX)***

*Baseline TSS was not a stratification factor in SIMPLIFY-1 resulting in an inadvertent imbalance in baseline TSS strongly favoring RUX

**Prior RUX washout prohibited in SIMPLIFY-2, in contrast to other JAK inhibitor studies

***Due to failure of a higher level endpoint, these results can not be interpreted as showing superiority

Splenomegaly

MMB shows non-inferior splenic response to RUX in 1st-line.

SIMPLIFY-1
Non-inferiority demonstrated: 26.5% (MMB) vs. 29% (RUX), p=0.011

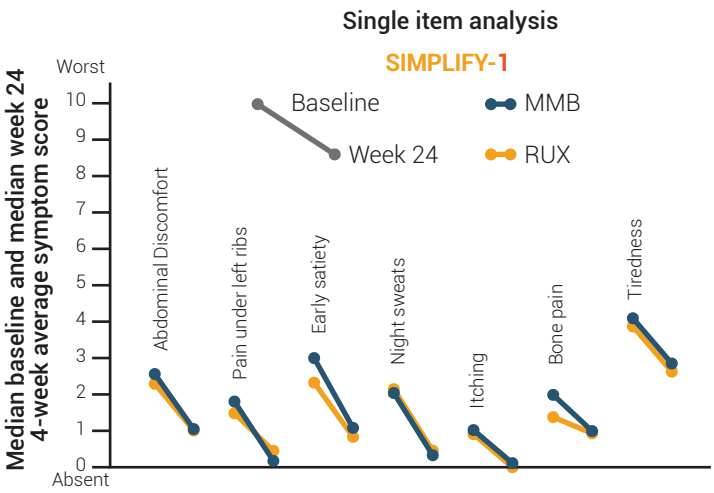
SIMPLIFY-2
Superiority not demonstrated, 6.7% (MMB) vs. 5.8% (BAT), likely due to lack of washout

Symptom Endpoints

SIMPLIFY-1
Pre-specified TSS analysis: 28.4% (MMB) vs. 42.2% (RUX); non-inferiority not demonstrated on this endpoint.

Despite failure to achieve the prespecified TSS response rate, single item analysis (figure) demonstrates clinically similar symptom responses.

SIMPLIFY-2
TSS Response Rate at Week 24 was higher with MMB compared to BAT (~90% RUX): 26.2% vs. 5.9% (nominal p< 0.001).



Anemia Endpoints

	SIMPLIFY-1	SIMPLIFY-2
Transfusion Independence, Week 24	66% vs. 49% (p<0.001)‡	43% vs. 21% (p=0.001)‡
Transfusion Independence in Transfusion Dependent subset†	49% vs. 29% (p=0.030)‡	47% vs. 19% (p=0.005)‡

- Reduced transfusion burden vs. RUX
- Long-term, maintained hemoglobin (Hgb) increase

†Transfusion independence period of ≥ 12 weeks; Sierra post-hoc analysis

‡Nominal p-value due to failure of a higher level endpoint

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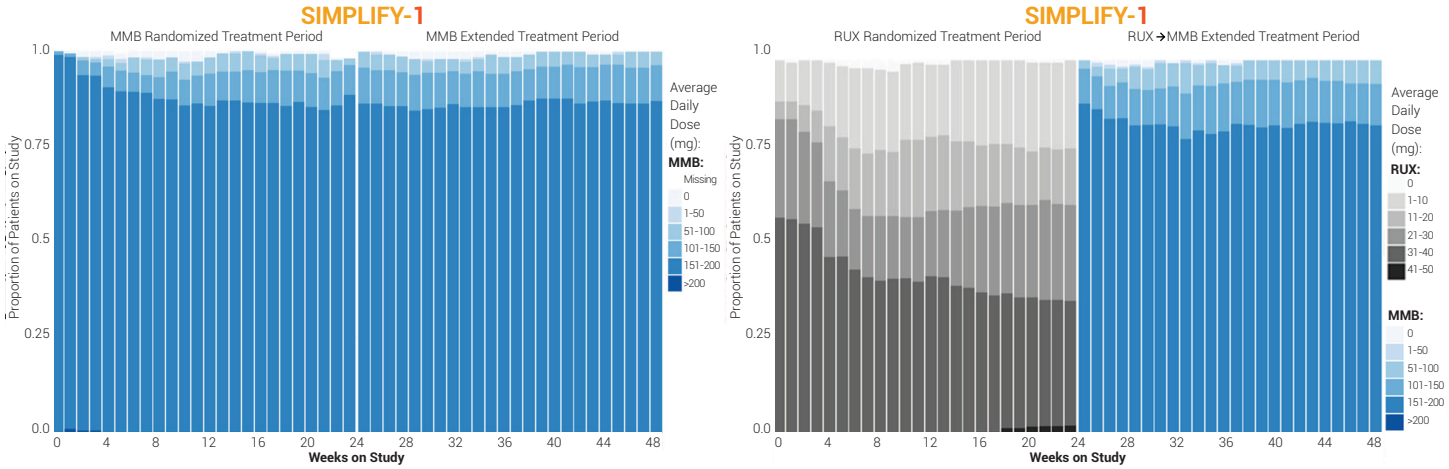
Dose Intensity

High MMB dose-intensity is maintained throughout treatment course, including in patients who switch from RUX to MMB, in contrast to a substantial loss of RUX dose intensity.



A similar pattern was seen in SIMPLIFY-2, with high MMB dose intensity maintained throughout treatment course.

Safety

- 550 patients received MMB at any time (as randomized or following cross-over) in the SIMPLIFY-1 and -2 studies.
- During the randomized treatment period in SIMPLIFY-1, rates of anemia were lower with MMB, 6.1% vs. 22.7%.
- No new safety signals or cumulative toxicity were observed during extended MMB dosing.*
- Peripheral neuropathy was infrequent, of low grade, and not progressive.

*Patients in both arms of each study could receive extended treatment with MMB after Week 24.

Grade 3/4 Adverse Events Randomized and Extended Treatment Phase (Overall Exposure*)

SIMPLIFY-1 Gr3/4 TEAEs†† by PT	RT Period MMB (N=214)	RT Period RUX (N=216)	Overall MMB exposure* in RT and ET (N=411)
Number of patients with any Gr3/4 TEAE, n (%)	74 (34.6%)	94 (43.5%)	251 (61.1%)
Thrombocytopenia	15 (7.0%)	10 (4.6%)	55 (13.4%)
Anemia	13 (6.1%)	49 (22.7%)	48 (11.7%)
Pneumonia	5 (2.3%)	3 (1.4%)	30 (7.3%)
SIMPLIFY-2 Gr3/4 TEAEs†† by PT	**RT Period MMB (N=104)**	**RT Period BAT (N=52)**	**Overall MMB exposure* in RT and ET (N=144)**
Number of patients with any Gr3/4 TEAE, n (%)	57 (54.8%)	22 (42.3%)	104 (72.2%)
Anemia	14 (13.5%)	9 (17.3%)	33 (22.9%)
Thrombocytopenia	11 (10.6%)	3 (5.8%)	22 (15.3%)
Asthenia	5 (4.8%)	1(1.9%)	11 (7.6%)
Neutropenia	5 (4.8%)	1 (1.9%)	9 (6.3%)
Pneumonia	2 (1.9%)	1 (1.9%)	9 (6.3%)

††Most Frequent Grade 3 or 4 Treatment Emergent Adverse Events by Preferred Term

Momelotinib Survival Data

A log-rank analysis of data from the SIMPLIFY-1 and SIMPLIFY-2 studies showed robust survival in both JAK inhibitor-naïve and previously treated patients, regardless of original randomization*.

*Patients in both arms of each study could receive extended treatment with MMB after Week 24.

SIMPLIFY-1

- Equivalently robust OS was observed in both treatment arms.
- Median OS of 53.1 months was observed in RUX → MMB crossover patients, and was not reached in originally MMB-randomized patients.

SIMPLIFY-2

- Median OS of 37.5 months was observed in BAT → MMB crossover patients, and 34.3 months for originally MMB-randomized patients.
- These data compare favorably to historical survival data reported in patients previously treated with RUX.

Conclusion

Data from Phase 1, 2, and 3 clinical trials demonstrate potential clinical activity and support further clinical development of momelotinib.

References:

1. Mesa et al. Simplify-1: A phase III randomized trial of momelotinib versus ruxolitinib in janus kinase inhibitor–naïve patients with myelofibrosis. J Clin Oncol. 2017;35(34):3844–50.
2. Harrison et al. Momelotinib versus best available therapy in patients with myelofibrosis previously treated with ruxolitinib (SIMPLIFY 2): a randomised, open-label, phase 3 trial. Lancet Haematol. 2018;5(2):e73–81.
3. Gupta et al. Momelotinib Dose-Intensity is Maintained in JAK Inhibitor Naïve and Previously JAK Inhibitor Treated Intermediate/High Risk Myelofibrosis Patients. EHA Poster. 2020.
4. Verstovsek et al. Robust Overall Survival and Sustained Efficacy Outcomes during Long Term Exposure to Momelotinib in JAK Inhibitor Naïve and Previously JAK Inhibitor Treated Intermediate/High Risk Myelofibrosis Patients. ASH 2020.

5-9. Kuykendall et al. 2017; Mehra et al. 2016; Newberry et al. 2017; Palandri et al. 2018; Mascarenhas et al 2018.

FOR INFORMATIONAL AND EDUCATIONAL PURPOSES ONLY; Momelotinib is an investigational agent not yet approved by the US FDA or any regulatory authority

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