MOMENTUM: Phase 3 randomized study of momelotinib versus danazol in symptomatic and anemic myelofibrosis patients previously treated with a JAK inhibitor

Poster number: 115

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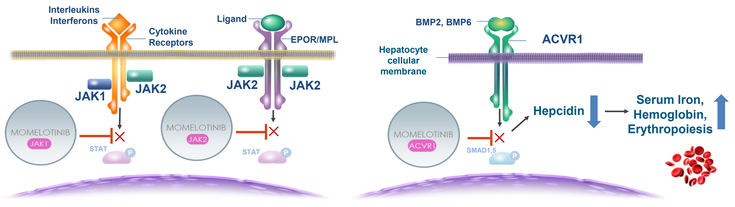
BACKGROUND

- Momelotinib (MMB) inhibits JAK1, JAK2 and ACVR1 to address MF symptoms, spleen, and anemia:

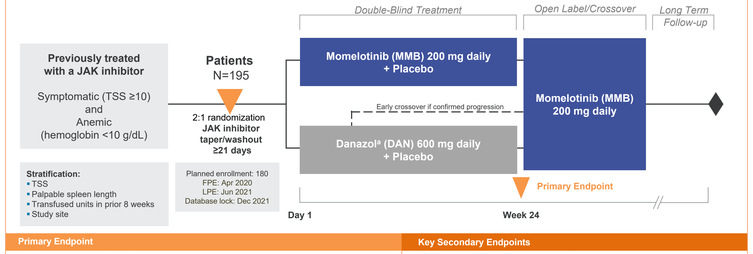


Dysregulated **JAK-STAT signaling** in MF drives overproduction of inflammatory cytokines, **bone marrow fibrosis, systemic symptoms,** and clonal proliferation resulting in extramedullary hematopoiesis and **splenomegaly**.[1,2]

Chronic inflammation also drives hyperactivation of **ACVR1**, elevated **hepcidin**, dysregulated iron metabolism, and **anemia** of MF.[3,4]

- The Phase 3 SIMPLIFY studies in JAK inhibitor–naive and post-ruxolitinib patients with MF demonstrated momelotinib benefits on symptoms, spleen, and anemia[5-7]
  - **TSS response rates** (≥50 reduction) with momelotinib were:
    - 28% in SIMPLIFY-1 (JAK inhibitor–naive)
    - 26% in SIMPLIFY-2 (post-ruxolitinib, no washout)
  - **Splenic response rate** (≥35% reduction) was 26.5% with momelotinib vs 29.0% with ruxolitinib in SIMPLIFY-1 (proportion difference, 0.09 [95% CI, 0.02-0.16]; *P*=.011 [noninferior])
  - **Cumulative transfusion burden** was lower in patients receiving momelotinib vs those receiving ruxolitinib in SIMPLIFY-1 (hazard ratio, 0.522; nominal *P*<.0001)
- Here we report the results of the phase 3 MOMENTUM study of momelotinib vs danazol (DAN) in symptomatic and anemic MF patients previously treated with a JAK inhibitor

MOMENTUM Study Design



Primary Endpoint	Key Secondary Endpoints
• TSS response rate at week 24	• Transfusion independence rate at week 24 • Splenic response rate at week 24

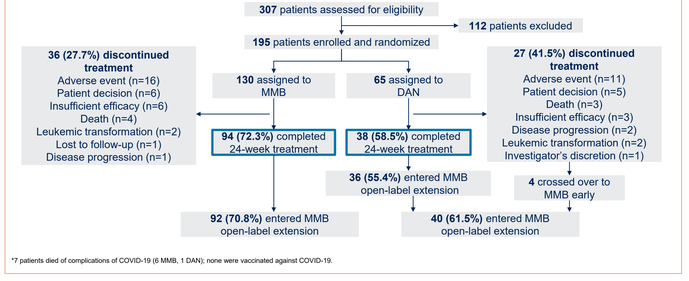
ClinicalTrials.gov: **NCT04173494**
[a] Danazol was selected as an appropriate comparator given its use to ameliorate anemia in MF patients, as recommended by guidelines.
TSS response defined as achieving ≥50% reduction in TSS over the 28 days immediately prior to the end of week 24 compared to baseline.
Transfusion independence defined as not requiring red blood cell transfusion in the last 12 weeks of the 24-week randomized period, with all hemoglobin levels during the 12-week interval of ≥8 g/dL.
Splenic response rate defined as achieving a **≥25%** or **≥35%** reduction in spleen volume from baseline.

OBJECTIVE

- To evaluate the efficacy and safety of MMB vs DAN in previously treated, symptomatic, and anemic patients with MF

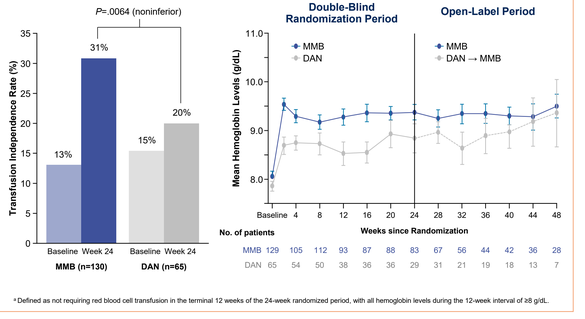
RESULTS

Patient Disposition



[a]7 patients died of complications of COVID-19 (6 MMB, 1 DAN); none were vaccinated against COVID-19.

Transfusion Independence[a] Rate at Week 24 and Mean Hemoglobin Over Time



[a] Defined as not requiring red blood cell transfusion in the terminal 12 weeks of the 24-week randomized period, with all hemoglobin levels during the 12-week interval of ≥8 g/dL.

Adverse Events in ≥10% of Patients in Either Treatment Group During 24-Week Randomized Treatment

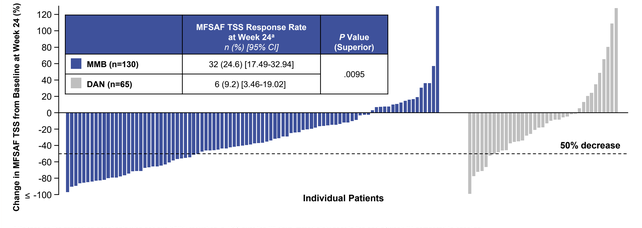
	MMB (n=130)		DAN (n=65)	
	% of patients			
Grade ≥3 adverse events	53.8		64.6	
Serious adverse events	34.6		40.0	
	Any Grade	Grade ≥3	Any Grade	Grade ≥3
Nonhematologic (preferred term)				
Diarrhea	22.3	0	9.2	1.5
Nausea	16.2	2.3	9.2	3.1
Blood creatinine increased	7.7	0.8	15.4	3.1
Asthenia	13.1	0.8	9.2	1.5
Dyspnea	7.7	2.3	13.8	1.5
Peripheral edema	7.7	1.5	13.8	0
Acute kidney injury	4.6	3.1	12.3	9.2
Fatigue	6.2	0.8	10.8	3.1
Pruritus	10.8	1.5	10.8	0
Weight decreased	10.8	0	6.2	0
Hematologic abnormalities[a]				
Anemia	99.2	60.8	100	75.4
Thrombocytopenia	76.2	27.7	61.5	26.2
Neutropenia	29.2	12.3	26.2	9.2

[a] Hematologic abnormalities are based on laboratory values. Data shown are for events of the worst grade during the randomized treatment phase, regardless of whether this grade was a change from baseline.
Adverse event of prior interest: Peripheral neuropathy occurred in 4% with MMB and 2% with DAN; all cases were low grade and did not prompt study drug discontinuation.

Baseline Characteristics

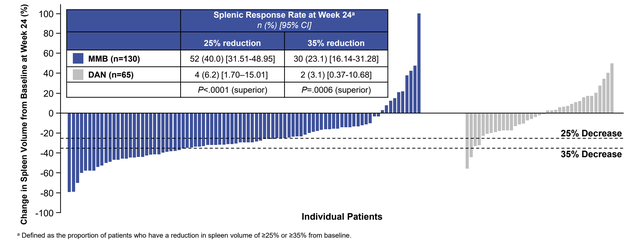
	MMB (n=130)	DAN (n=65)
Age, median, years	71.0	72.0
Male, %	60.8	67.7
White, %	82.3	76.9
MF subtype, %		
Primary	60.0	70.8
Post-PV	20.8	16.9
Post-ET	19.2	12.3
DIPSS risk category, %		
Int-2	55.4	61.5
High	38.5	29.2
***JAK2* V617F–mutation positive, %**	74.6	78.5
ECOG PS, %		
1	62.8	52.3
2	23.8	24.6
Mean prior JAK inhibitor duration, weeks	138.5	124.8
Mean TSS	28.0	25.7
Mean hemoglobin, g/dL	8.1	7.9
Transfusion independent, %	13.1	15.4
Transfusion dependent, %	48.5	52.3
Mean central spleen volume, cm³	2367	2288
Mean platelet count, ×10⁹/L	151.7	130.7

MFSAF TSS Response Rate[a] at Week 24



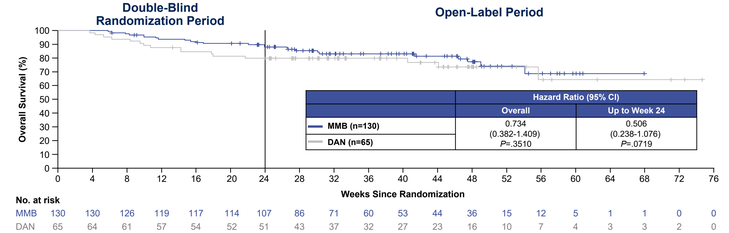
[a] Defined as the proportion of patients who achieve ≥50% reduction in TSS over the 28 days immediately prior to the end of week 24 compared to baseline.

Splenic Response Rate[a] at Week 24



[a] Defined as the proportion of patients who have a reduction in spleen volume of ≥25% or ≥35% from baseline.

Overall Survival



CONCLUSIONS

- In the phase 3 MOMENTUM study, all prespecified primary and key secondary endpoints were met
  - Significant improvements in symptoms, spleen size, and anemia measures were observed with momelotinib vs danazol
  - Momelotinib was associated with a favorable safety profile and trend towards improved overall survival
- Momelotinib is the first and only JAK1 and JAK2 inhibitor that also decreases hepcidin through ACVR1 inhibition
  - This may contribute to rapid and sustained improvements in hemoglobin levels and transfusion requirements
- Momelotinib exhibits a consistent profile across thrombocytopenic subgroups, as described on a separate poster at this meeting
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- These findings support the future use of momelotinib as an effective treatment in MF patients, especially those with anemia

Presented at

14th International Congress on Myeloproliferative Neoplasms
October 27-28, 2022; Brooklyn, NY

The data described in this poster were previously presented at the ASCO Annual Meeting; June 3-7, 2022; Chicago (abstract 7002)

Abbreviations

ACVR1, activin A receptor type 1; BMP, bone morphogenic protein; COVID-19, coronavirus disease 2019; DAN, danazol; DIPSS, Dynamic International Prognostic Scoring System; ECOG PS, Eastern Cooperative Oncology Group performance status; EPOR, erythropoietin receptor; ET, essential thrombocythemia; FPE, first patient enrolled; Int, intermediate; JAK, Janus kinase; LPE, last patient enrolled; MF, myelofibrosis; MFSAF, Myelofibrosis Symptom Assessment Form; MMB, momelotinib; MPL, myeloproliferative leukemia protein; PV, polycythemia vera; STAT, signal transducer and activator of transcription; TSS, Total Symptom Score.

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