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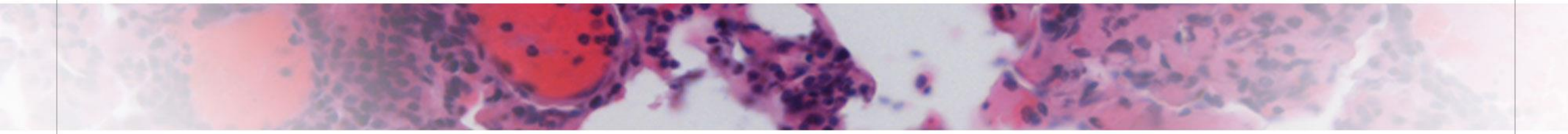

Updated Results from the Momentum Phase 3 Study of Momelotinib (MMB) Versus Danazol (DAN) in Symptomatic and Anemic Myelofibrosis (MF) Patients Previously Treated with a JAK Inhibitor

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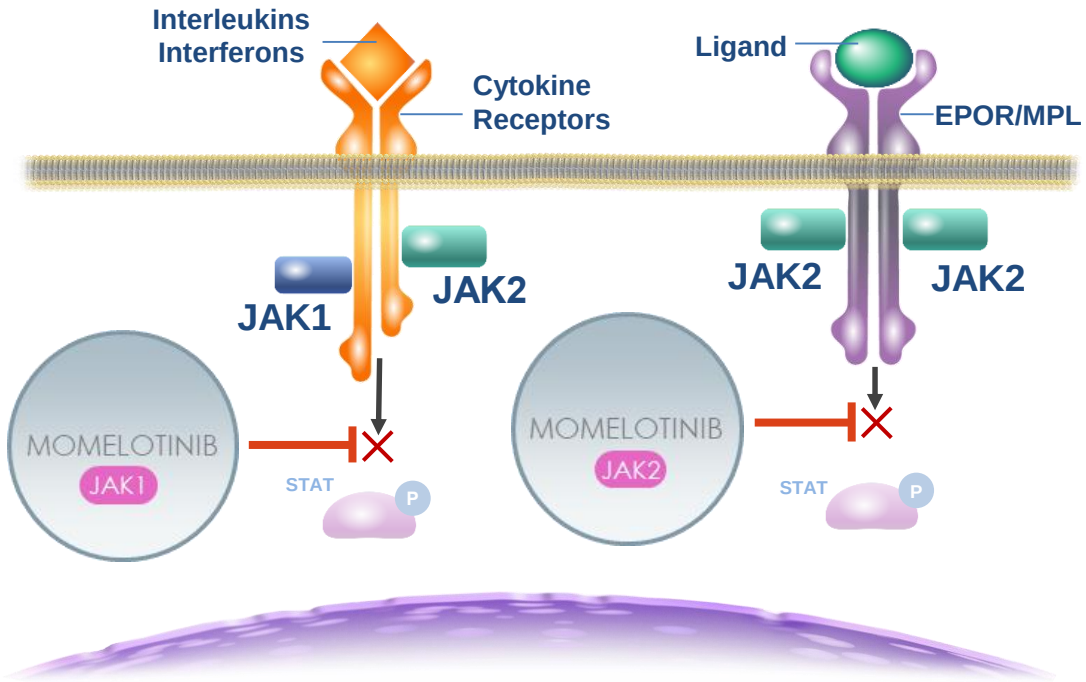
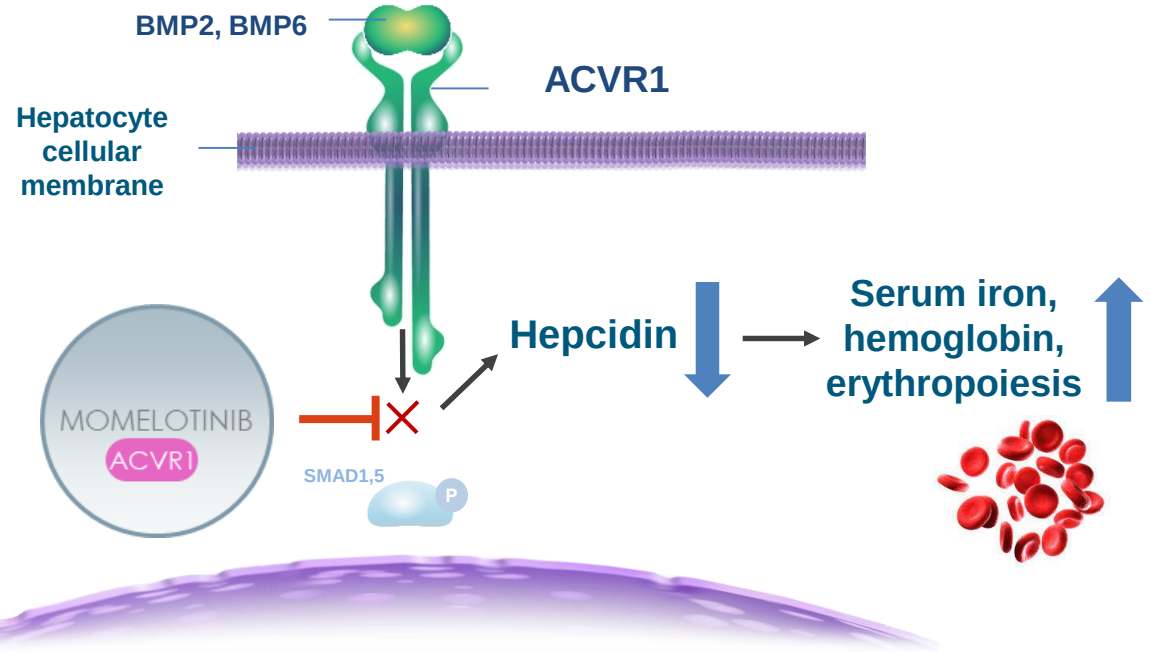
Momelotinib Inhibits JAK1, JAK2, and ACVR1 to Address MF Symptoms, Spleen, and Anemia



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]

ACVR1, activin A receptor type 1; BMP, bone morphogenetic protein; EPOR, erythropoietin receptor; JAK, Janus kinase; MF, myelofibrosis; MPL, myeloproliferative leukemia protein; SMAD1/5, mothers against decapentaplegic homolog 1/5; STAT, signal transducer and activator of transcription.

1. Chifotides HT, et al. *J Hematol Oncol*. 2022;15(1):7. 2. Verstovsek S, et al. *Future Oncol*. 2021;17(12):1449-1458. 3. Asshoff M, et al. *Blood*. 2017;129(13):1823-1830. 4. Oh ST, et al. *Blood Adv*. 2020;4(18):4282-4291.

MOMENTUM Is an Ongoing Phase 3 Study of Momelotinib Versus DAN in Symptomatic, Anemic, JAKi-Experienced Patients

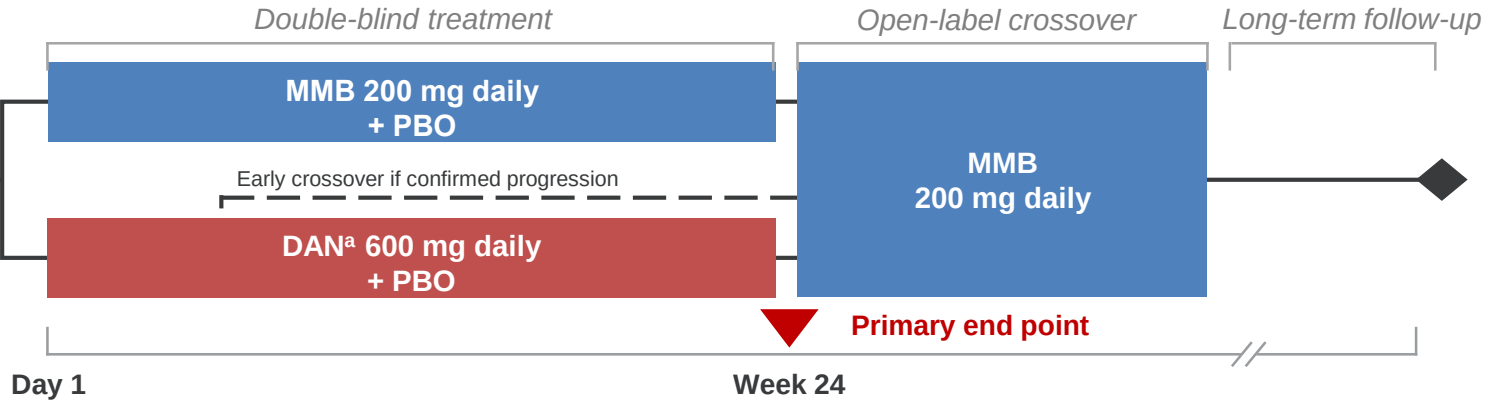
Previously treated with JAKi
Symptomatic (TSS ≥10)
Anemic (Hgb <10 g/dL)
Platelets ≥25×10^9/L

Stratification:
- TSS
- Palpable spleen length
- Transfused units in prior 8 weeks
- Study site

Patients
N=195

2:1 randomization
JAKi taper/washout ≥21 days

Planned enrollment: 180
FPE Apr 2020
LPE Jun 2021
Database lock Dec 2021



MOMENTUM Topline Results at Week 24: All Primary and Key Secondary End Points Met[1,2]

	MFSAF TSS[b] response rate (primary end point)	TI response[c] rate	SRR[d] (35% reduction)
MMB (N=130)	32 (24.6%)	40 (30.8%)	30 (23.1%)
DAN (N=65)	6 (9.2%)	13 (20.0%)	2 (3.1%)
	P=.0095 (superior)	1-sided *P*=.0064 (noninferior)	*P*=.0006 (superior)

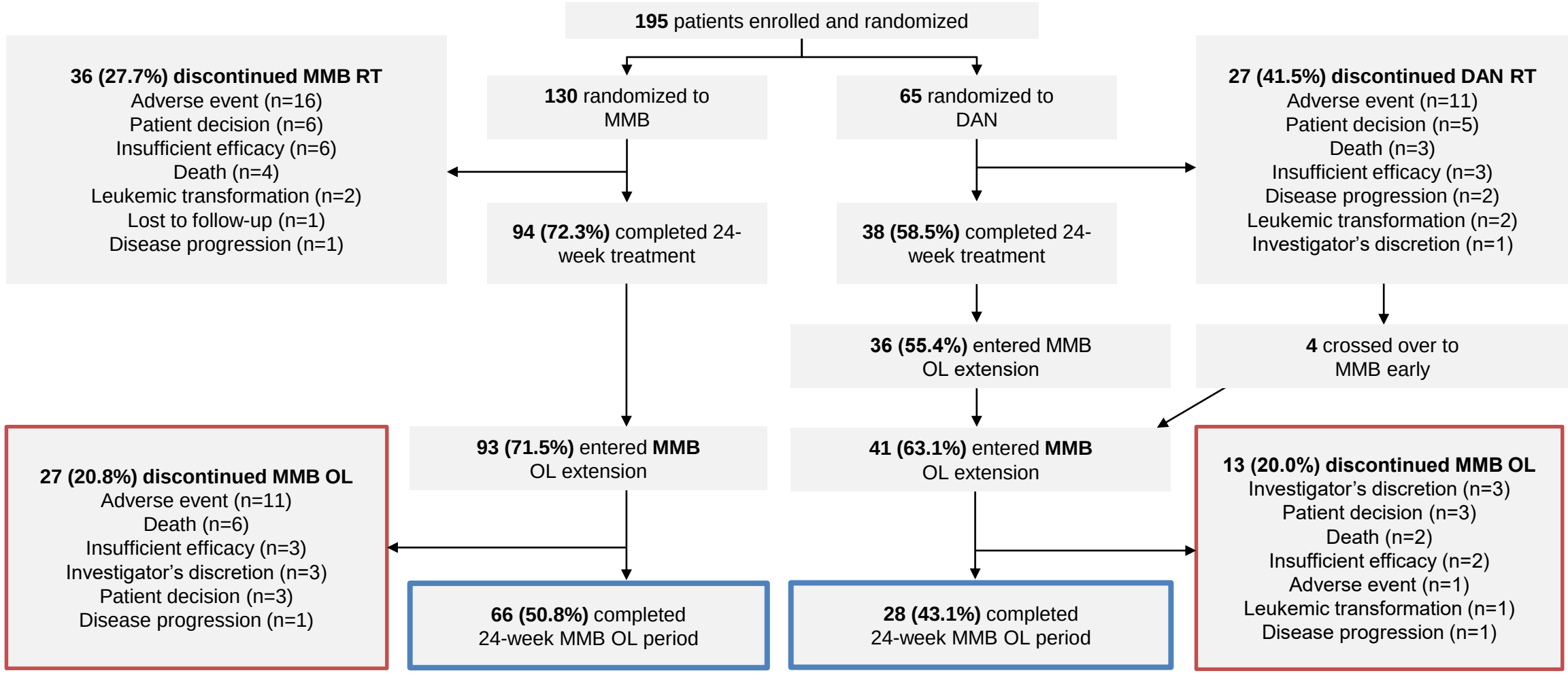
ClinicalTrials.gov: NCT04173494.
[a]Danazol was selected as an appropriate comparator given its use to ameliorate anemia in patients with MF.[3-5] [b]TSS response defined as achieving ≥50% reduction in TSS over the 28 days immediately before the end of week 24 compared with baseline. [c]TI response defined as not requiring red blood cell transfusion in the last 12 weeks of the 24-week randomized period, with all Hgb levels during the 12-week interval of ≥8 g/dL. [d]SRR defined as achieving a ≥25% or ≥35% reduction in spleen volume from baseline.
DAN, danazol; FPE, first patient enrolled; Hgb, hemoglobin; JAKi, Janus kinase inhibitor; LPE, last patient enrolled; MF, myelofibrosis; MFSAF, Myelofibrosis Symptom Assessment Form; MMB, momelotinib; PBO, placebo; SRR, splenic response rate; TI, transfusion independence; TSS, total symptom score.
1. Mesa R, et al. Abstract presented at: 2022 ASCO Annual Meeting; June 3-6, 2022; Chicago, IL and Virtual. Abstract 7002. 2. Verstovsek S, et al. Abstract presented at: 2022 EHA Congress; June 9-12; 2022; Vienna, Austria and Virtual. Abstract S195. 3. Chifotides HT, et al. *J Hematol. Oncol.* 2022;15(1):7. 4. Naymagon L, et al. *Hemasphere*. 2017;1(1):e1. 5. Vannucchi AM, et al. *Ann Oncol*. 2015;26(suppl 5):v85-v99.

MOMENTUM Was Conducted in Symptomatic Anemic, Post-RUX Patients With MF and a Heavy Transfusion Burden

Baseline characteristics	MMB (N=130)	DAN (N=65)
Mean age, y	69.85	71.46
Male, %	60.8	67.7
PMF/PPV-MF/PET-MF, %	60.0/20.8/19.2	70.8/16.9/12.3
DIPSS Int-1/Int-2/High, %	5.4/55.4/38.5	4.6/61.5/29.2
Mean prior JAKi therapy, y	2.7	2.4
Mean Hgb, g/dL	8.1	7.9
Hgb <8 g/dL, %	47.7	49.2
TI,[a] %	13.1	15.4
TR,[b] %	38.5	32.3
TD,[c] %	48.5	52.3
Mean platelets, $\times 10^9$/L	151.7	130.7

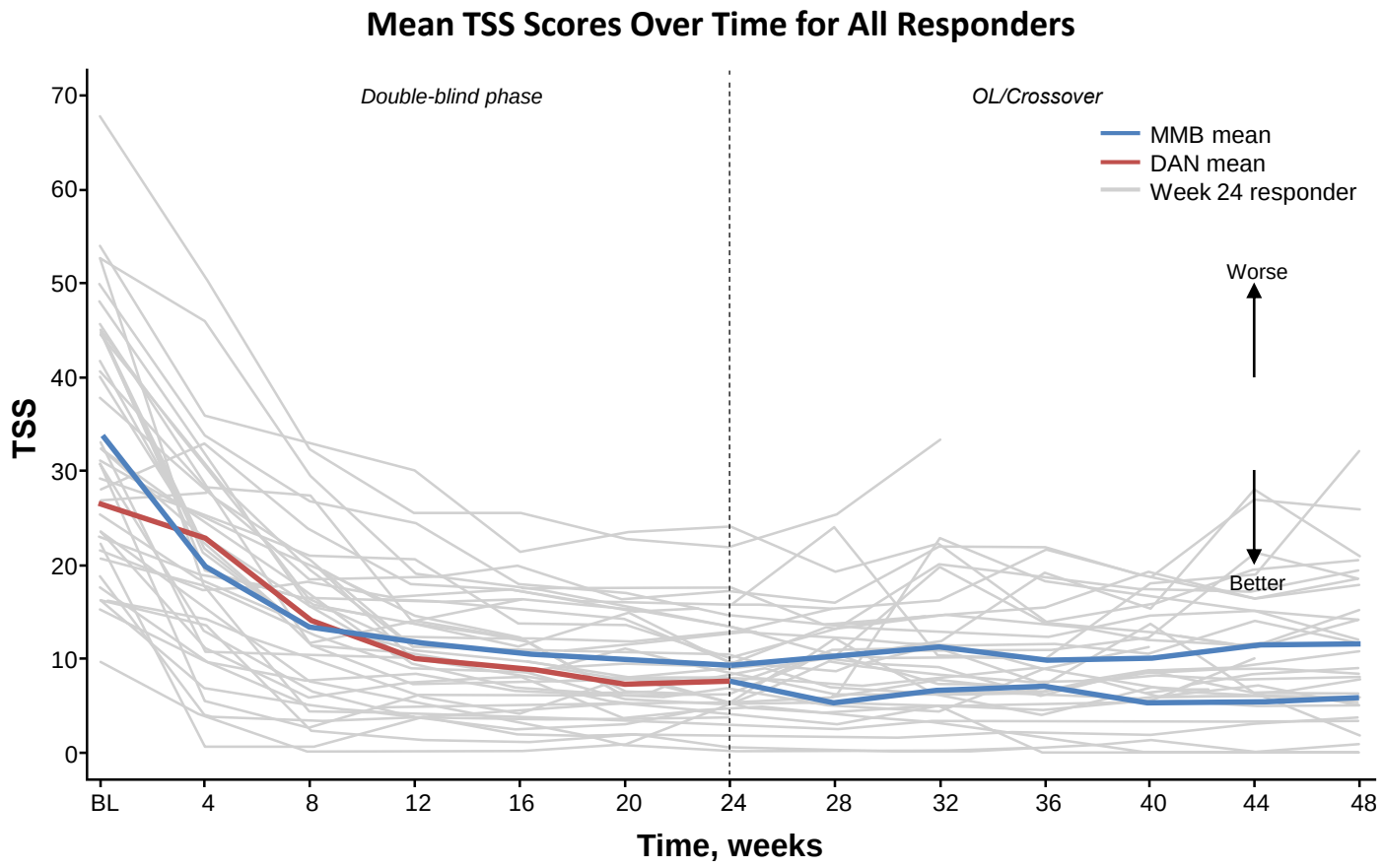
[a]TI defined as not requiring RBC transfusion for ≥12 weeks, with Hgb levels ≥8 g/dL. [b]TR defined as patients who required transfusions but did not meet the criteria for TD. [c]TD defined as requiring RBC transfusion ≥4 units in the 8 weeks before randomization.
DAN, danazol; DIPSS; Dynamic International Prognostic Scoring System; Hgb, hemoglobin; Int, intermediate; JAKi, Janus kinase inhibitor; MF, myelofibrosis; MMB, momelotinib; PET, post-essential thrombocythemia; PMF, primary myelofibrosis; PPV, post-polycythemia vera; RBC, red blood cell; RUX, ruxolitinib; TD, transfusion dependence; TI, transfusion independence; TR, transfusion-requiring.

Patient Disposition: Data Cutoff May 17, 2022



DAN, danazol; MMB, momelotinib; OL, open-label; RT, randomized treatment.

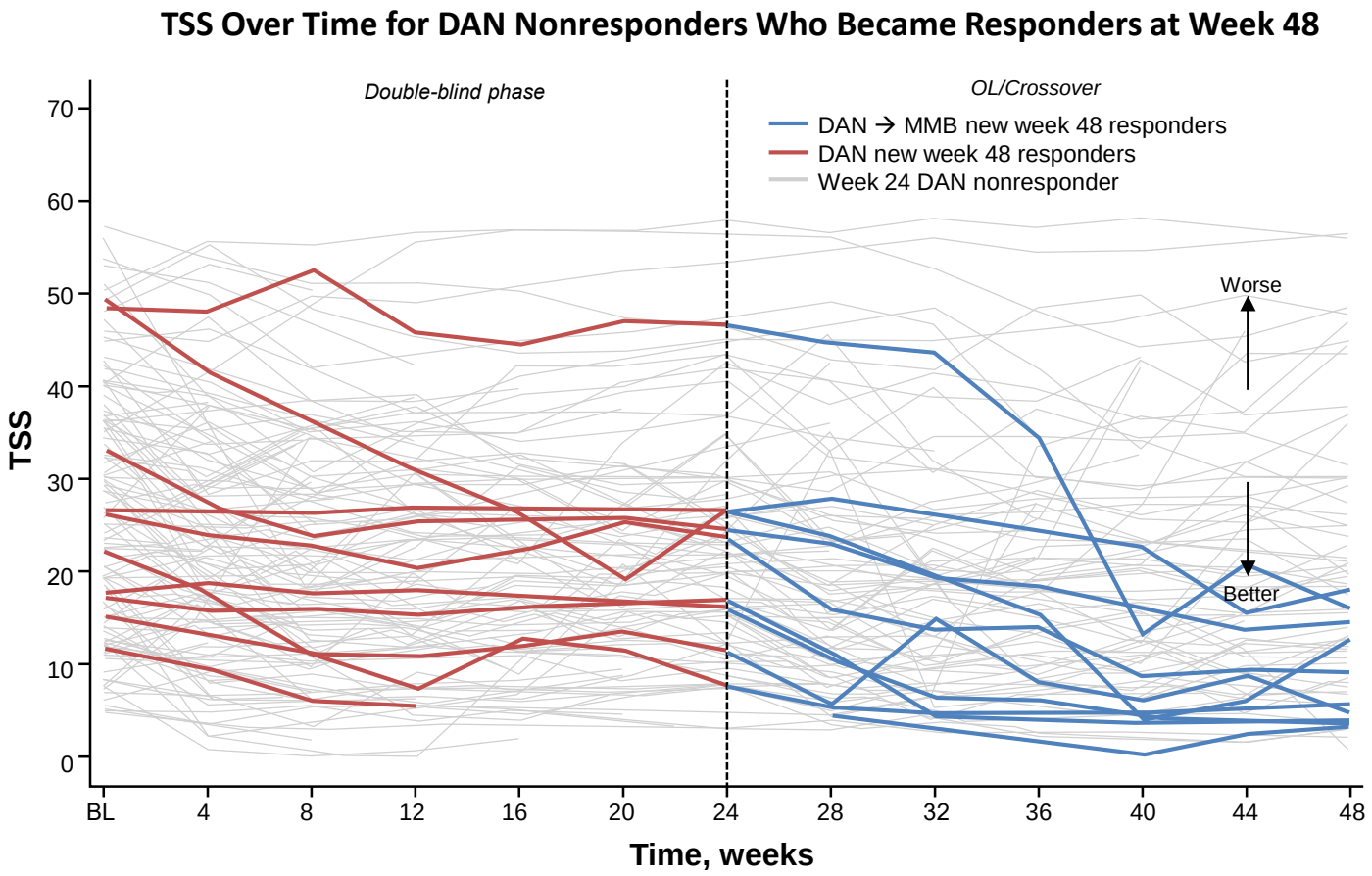
Week 24 Symptom Responses[a] Were Sustained Through Week 48



- Week 24 TSS response was 25% in the MMB group and 9% in the DAN group
- Week 24 TSS response was maintained in 31 of 32 (97%) MMB→MMB and 6 of 6 (100%) DAN→MMB patients

[a]Defined as the proportion of patients who achieve ≥50% reduction in TSS over the 28 days immediately before the end of week 24 compared with baseline.
DAN, danazol; MMB, momelotinib; OL, open-label; TSS, total symptom score.

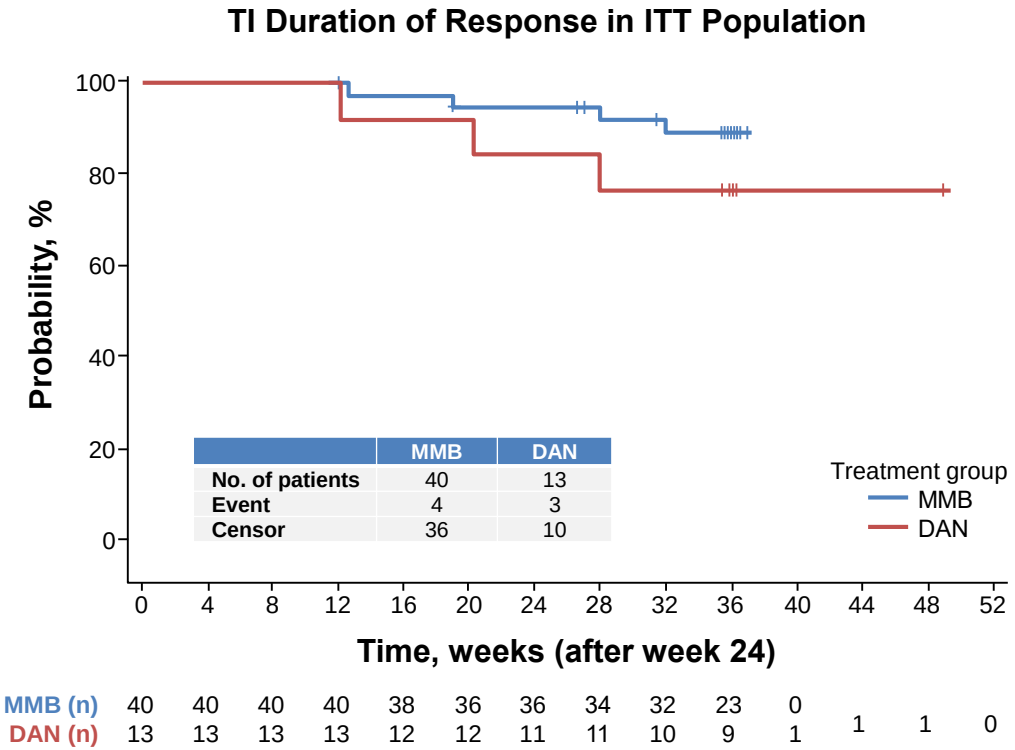
New Week 48 TSS Responses Were Observed for Week 24 Danazol Nonresponders[a]

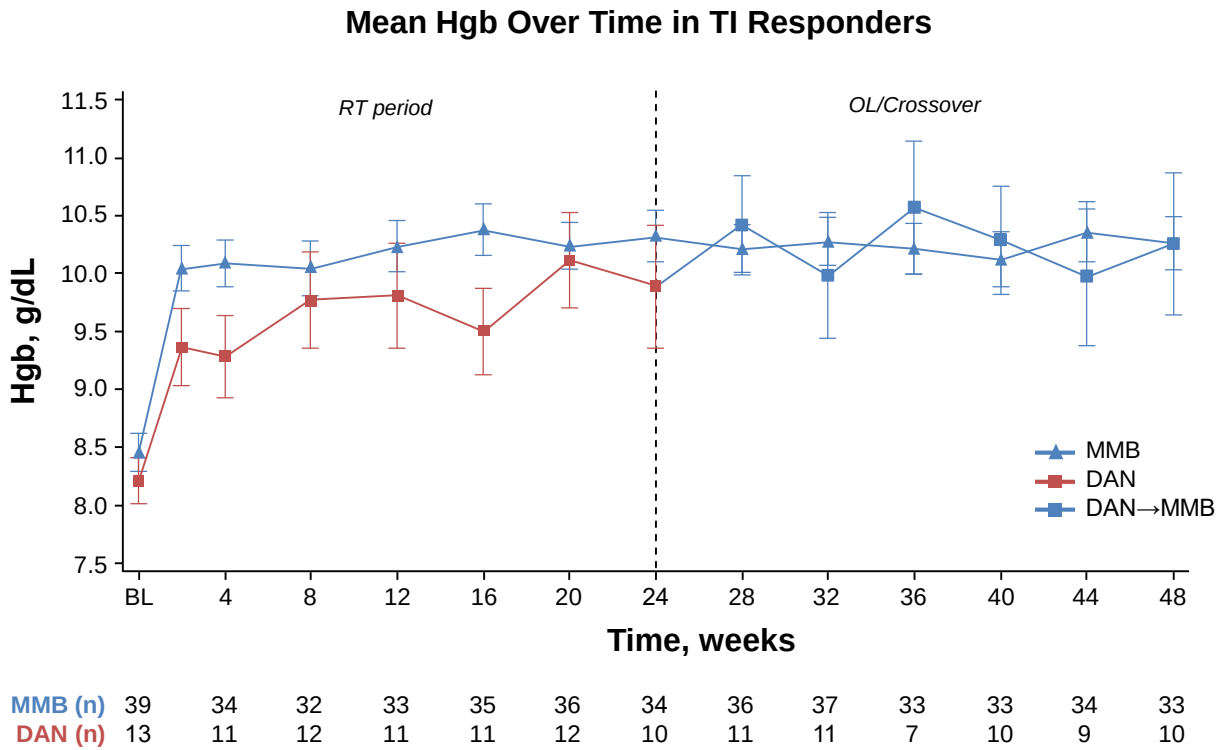


- 10 of 35 (29%) DAN → MMB week 24 TSS nonresponders were new responders at week 48
- 12 of 61 (20%) MMB → MMB week 24 TSS nonresponders were also new responders at week 48 (not shown)

[a]Defined as the proportion of patients who achieve <50% reduction in TSS over the 28 days immediately before the end of week 24 compared with baseline.
DAN, danazol; MMB, momelotinib; OL, open-label; TSS, total symptom score.

Week 24 TI Responses[a] Were Sustained Through Week 48

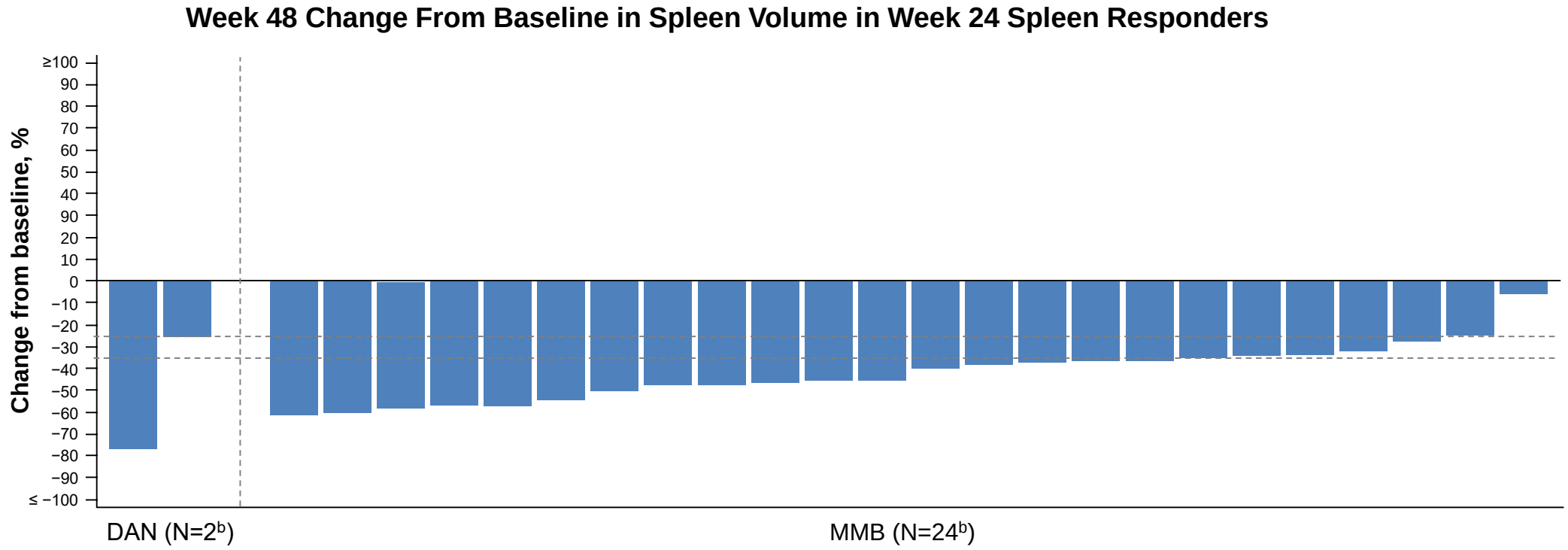




- Week 24 TI response was 31% in the MMB group and 20% in the DAN group
  - Consecutive 12-week TI-R[b] was 44.6% in the MMB group and 29.2% in the DAN group (Poster #3028)
- Week 24 TI response was maintained in 36 of 40 (90%) MMB→MMB and 10 of 13 (77%) DAN→MMB patients

[a]Defined as not requiring RBC transfusion in the prior 12 weeks and Hgb levels ≥8 g/dL; [b]Consecutive 12-week TI-R (defined as absence of RBC transfusions and no Hgb measurement below 8 g/dL over any 12-week period through week 24)
BL, baseline; DAN, danazol; Hgb, hemoglobin; ITT, intention-to-treat; MMB, momelotinib; OL, open-label; RBC, red blood cell; RT, randomized treatment; TI, transfusion independence.

Week 24 Spleen Responses[a] Were Sustained Through Week 48



- Week 24 SRR35 response was 23% in the MMB group and 3% in the DAN group
- All SRR35 responders at week 24 maintained spleen volume below baseline (24 of 24 MMB→MMB and 2 of 2 DAN→MMB patients)

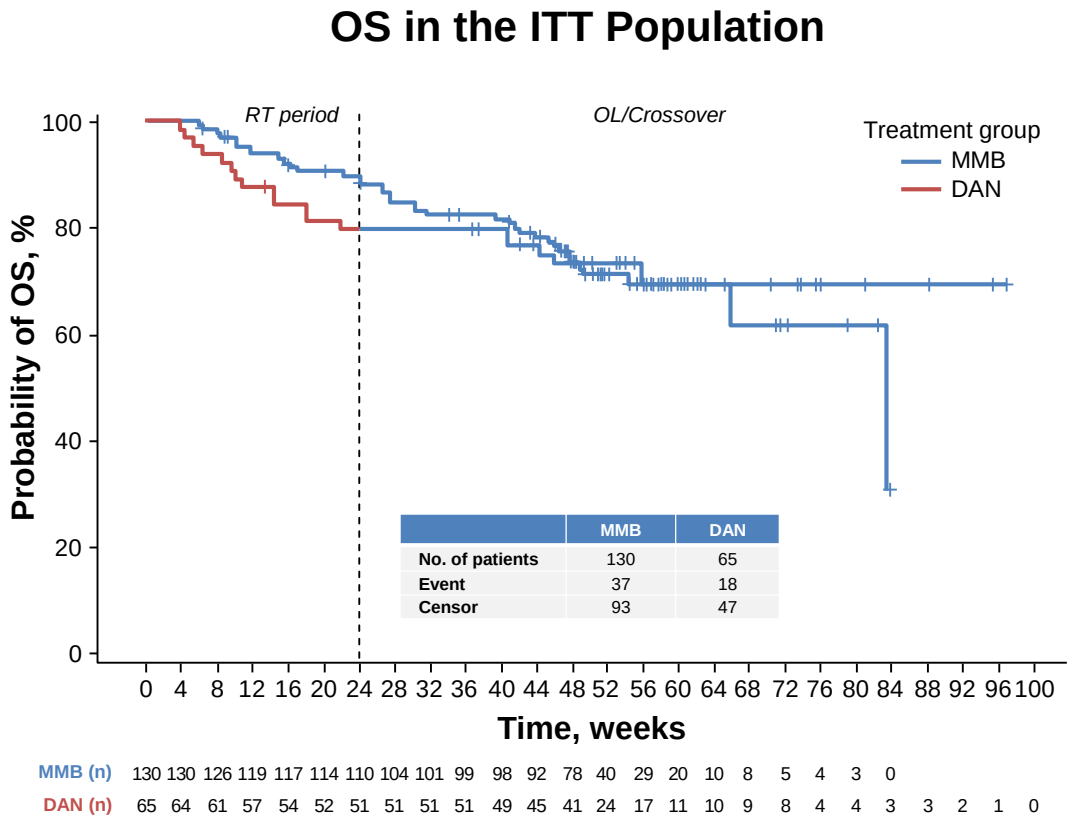
[a]Defined as the proportion of patients who have a reduction in spleen volume of ≥35% from baseline. [b]N is the number of patients with percent change in spleen volume at week 48 available.
DAN, danazol; MMB, momelotinib; SRR35, splenic response rate >35%.

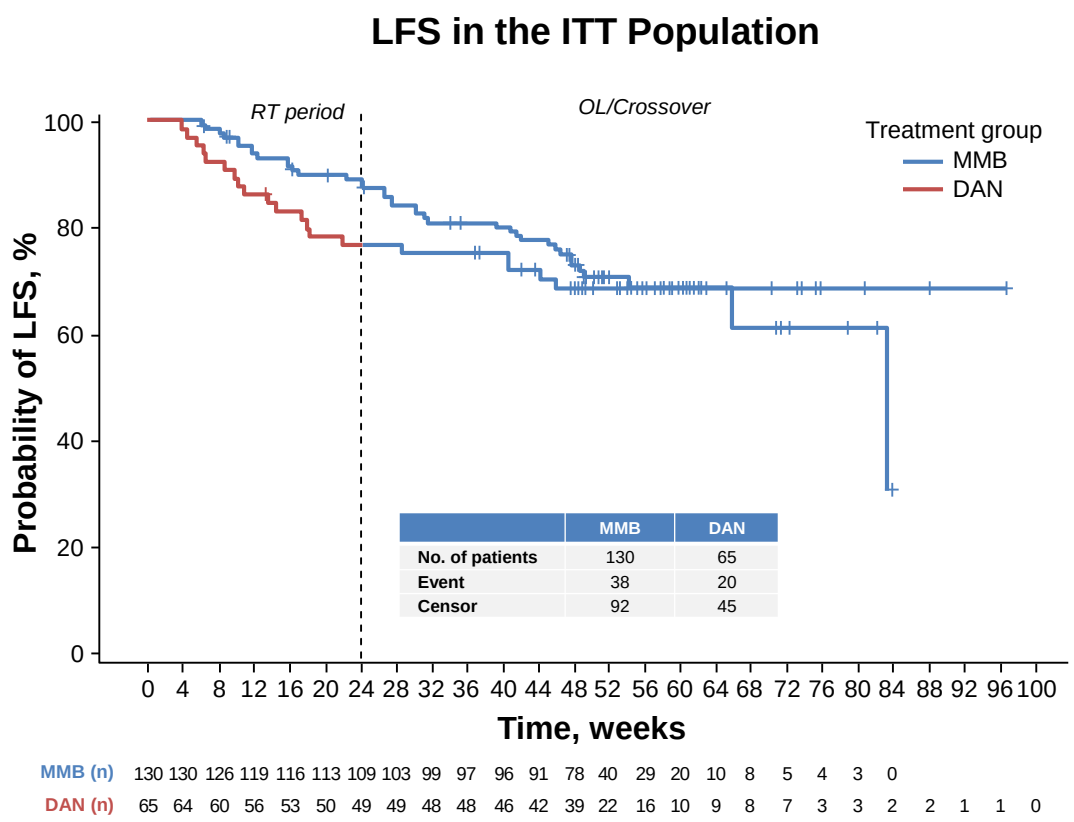
TEAEs in ≥10% of Patients During OL MMB Treatment with No New Safety Signals Detected

	MMB→MMB (n=93)		DAN→MMB (n=41)	
	% of patients			
Grade ≥3 adverse events	49.5		46.3	
Serious adverse events	31.2		29.3	
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Nonhematologic (preferred term)				
Weight decreased	7.5	0	14.6	0
Diarrhea	14.0	1.1	12.2	0
Pyrexia	14.0	0	7.3	0
Hypertension	3.2	0	12.2	2.4
Asthenia	11.8	3.2	0	0
Hematologic (preferred term)				
Thrombocytopenia	14.0	8.6	17.1	14.6
Anemia	10.8	8.6	7.3	2.4
Neutropenia	5.4	5.4	4.9	0
Other				
COVID-19 (pneumonia)	10.8	5.4	0	0
Peripheral sensory neuropathy	2.2	0	2.4	0

DAN, danazol; MMB, momelotinib; OL, open-label; TEAE, treatment-emergent adverse event.

OS and LFS Curves for MMB→MMB and DAN→MMB Converged After All Patients Crossed Over to OL MMB at Week 24[a]

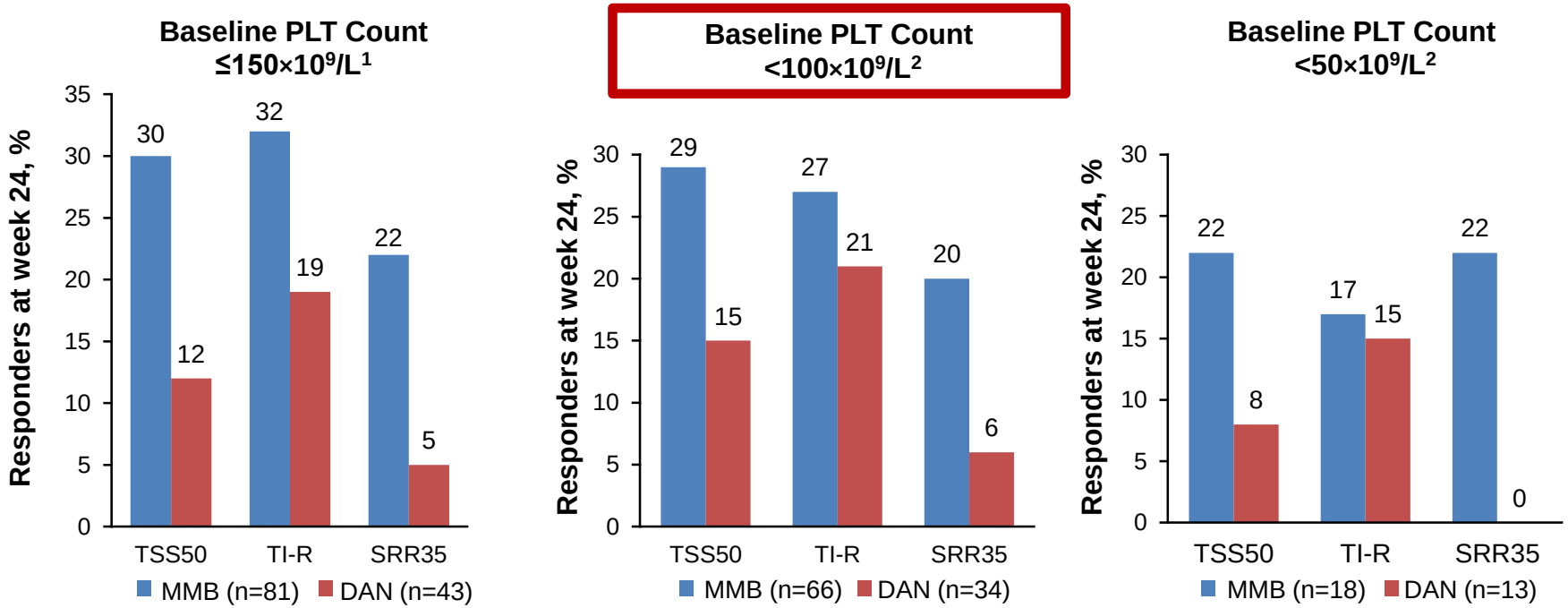




OS was significantly improved for MMB→MMB patients who achieved a week 24 TI response (Poster 3028)

[a]Median follow-up for OS was 51 weeks (range, 6-84 weeks) for MMB-treated and 53 weeks (range, 4-97 weeks) for DAN-randomized patients.
DAN, danazol; LFS, leukemia-free survival; MMB, momelotinib; OL, open-label; OS, overall survival; RT, randomized treatment.

Efficacy in Patients With Thrombocytopenia Was Consistent With the Overall ITT Patient Population



- For baseline PLTs <100×10⁹/L, week 24 responses were also well maintained during OL period:
  - TSS50 responders: 18 of 19 (95%) MMB→MMB and all (5 of 5; 100%) DAN→MMB patients maintained TSS responses
  - TI-R responders: 16 of 18 (89%) MMB→MMB and 5 of 7 (71%) DAN→MMB patients maintained TI responses
  - SRR35 responders: 13 of 13 (100%) MMB→MMB and 2 of 2 (100%) DAN→MMB patients maintained splenic responses

BL, baseline; DAN, danazol; Hgb, hemoglobin; ITT, intention-to-treat; MMB, momelotinib; OL, open-label; PLT, platelet; SRR35, splenic response rate ≥35%; TI-R, transfusion independence response; TSS50, total symptom score ≥50% response.

1. Gerds AT, et al. Abstract presented at: 2022 ASCO Annual Meeting; June 3-6, 2022; Chicago, IL and Virtual. Abstract 7061; 2. Gerds AT, et al. Poster presented at: 2022 ASCO Annual Meeting; June 3-6, 2022; Chicago, IL and Virtual. Poster 292.

Safety in Patients With Thrombocytopenia (PLTs <100 × 10^9/L) Was Consistent With the ITT

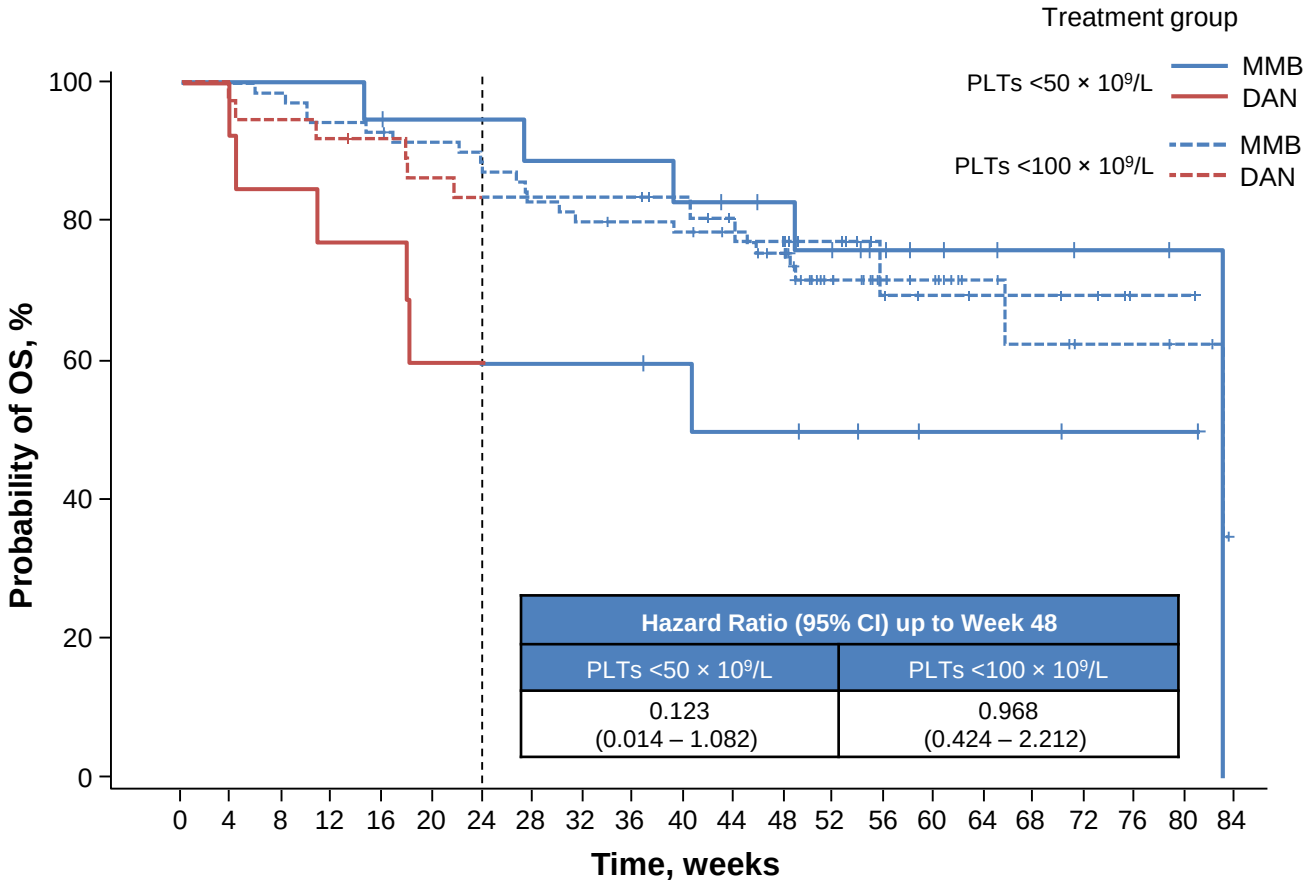
	MMB→MMB (N=46)		DAN→MMB (N=24)	
	% of patients			
Grade ≥3 adverse events	50.0		45.8	
Serious adverse events	32.6		25.0	
	Any grade	**Grade ≥3**	**Any grade**	**Grade ≥3**
Nonhematologic (preferred term)				
Diarrhea	15.2	0	12.5	0
Asthenia	15.2	2.2	0	0
Blood creatinine increased	8.7	0	12.5	0
Pyrexia	13.0	0	4.2	0
Fatigue	8.7	2.2	8.3	4.2
Hemorrhage (SMQ)[a]	34.8	15.2	33.3	4.2
MACE	6.5	6.5	0	0
Hematologic abnormalities[a]				
Thrombocytopenia	21.7	15.2	25.0	20.8
Neutropenia	8.7	8.7	8.3	0
Anemia	8.7	4.3	8.3	4.2

Grade ≥3 bleeding events occurred in 15% of MMB→MMB and 4% of DAN→MMB patients

MACE occurred in 7% of MMB→MMB patients and 0% of DAN→MMB patients

[a]Contusion, epistaxis, hematoma, traumatic hematoma, upper gastrointestinal hemorrhage, cerebral hemorrhage, eye contusion, gingival bleeding, hematochezia, hemorrhagic erosive gastritis, hyphema, injection site bruising, esophageal varices hemorrhage, optic disc hemorrhage, petechiae, spontaneous hematoma, or subdural hematoma.
DAN, danazol; ITT, intention-to-treat; MACE, major adverse cardiovascular events; MMB, momelotinib; OL, open-label; PLT, platelet; SMQ, standardized MedDRA queries.

Improved OS Was Observed in Patients With Baseline PLTs <50 × 10^9/L



PLTs <50 × 10⁹/L	MMB (n)	18	18	18	18	17	16	16	15	15	15	14	13	12	11	8	5	4	3	2	2	1	0
	DAN (n)	13	12	11	10	9	7	7	7	7	7	6	5	5	4	3	2	2	2	1	1	1	0
PLTs <100 × 10⁹/L	MMB (n)	66	66	65	62	61	59	57	53	51	50	49	47	43	26	18	14	8	6	4	4	3	0
	DAN (n)	34	33	32	31	30	28	27	27	27	27	25	22	21	13	8	6	5	5	4	1	1	0

- BL PLTs <100 × 10^9/L, median follow-up of 54 weeks for MMB→MMB patients and 53 weeks for DAN→MMB patients
- BL PLTs <50 × 10^9/L, median follow-up of 56 weeks for MMB→MMB patients and 54 weeks for DAN→MMB patients

BL, baseline; DAN, danazol; MMB, momelotinib; OS, overall survival; PLT, platelet; RT, randomized treatment.

Conclusions and Implications

- In this updated analysis, OL momelotinib maintained week 24 symptom, TI, and spleen responses with continued favorable survival and safety
- This study reports sustained TSS response through week 48, and new TSS responses beyond week 24 for the first time
- No new safety signals were detected beyond week 24
- Efficacy and safety results in patients with thrombocytopenia were consistent with the overall ITT population
- Momelotinib is the first and only JAK1 and JAK2 inhibitor that also decreases hepcidin through ACVR1 inhibition, thus providing benefit for patients with MF and anemia, which is an unmet need in MF treatment

These findings support the potential use of momelotinib as an effective treatment in patients with MF, particularly in patients with anemia and thrombocytopenia

ACVR1, activin A receptor type 1; ITT, intention-to-treat; JAK, Janus kinase; MF, myelofibrosis; OL, open-label; TI, transfusion independence; TSS, total symptom score.

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