

# Differential Impact of Thrombocytopenia and Anemia on Myelofibrosis Symptom Burden

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## BACKGROUND

- Cytopenias are associated with poor survival and increased symptom burden in patients with myelofibrosis (MF).<sup>1</sup>
- Patients with MF and thrombocytopenia (platelet count <100x10<sup>9</sup>/L) report worse fatigue, inactivity, early satiety, and quality of life compared to patients with higher platelet counts.<sup>1</sup>
- Because thrombocytopenia and anemia frequently co-occur in MF,<sup>1</sup> the relative impact of thrombocytopenia and anemia on MF symptoms is unknown.
- Understanding whether anemia is the major driver of disease-related symptoms in cytopenic patients could help physicians determine appropriate goals of therapy for patients with MF.

## AIM

- To describe the differential impact of thrombocytopenia and anemia on symptom burden by analyzing symptom data from patients with MF who have isolated thrombocytopenia versus isolated anemia.

## METHODS

- Baseline data from PERSIST-1<sup>2</sup> and PAC203<sup>3</sup> studies were included, as these trials enrolled patients with MF regardless of platelet count or hemoglobin.
  - Patients who received ruxolitinib within the 30 days prior to randomization were excluded, as the presence or withdrawal of ruxolitinib could impact baseline symptom scores.
- TSS version 1.0 was employed in 55% of patients initially enrolled on PERSIST-1, and v2.0 was used for the remainder of PERSIST-1 and all PAC203 patients.
  - For symptoms assessed in TSS v1.0 and v2.0 see **Figure 1**.
- Scores were reported separately by study due to differences in eligible patient population.
  - PERSIST-1 enrolled JAK inhibitor naïve patients while PAC203 enrolled patients resistant to or intolerant of ruxolitinib.

**Figure 1: TSS Version 1 and Version 2 - Symptoms**

	Tiredness /Fatigue	Early Satiety	Abdominal discomfort	Left rib pain	Night Sweats	Itching	Bone pain
TSS v1.0	✓	✓	✓		✓	✓	✓
TSS v2.0	✓	✓	✓	✓	✓	✓	✓

- Patients were included in the **low platelets only** group if they had platelet count <100 x 10<sup>9</sup>/L and hemoglobin ≥8 g/dL.
- Patients were included in the **low hemoglobin only** group if they had platelet count ≥100x10<sup>9</sup>/L and hemoglobin <8 g/dL.
- A difference in total score of 4.3 was considered the minimal clinically important difference.<sup>4</sup>

## Patient Characteristics

- Compared to patients with low platelets only, those with low hemoglobin only had higher rates of RBC transfusion dependence, higher DIPSS risk scores, and smaller spleens based on palpation (**Table 1**).
- Age and percentage with prior JAK2 inhibitor exposure was similar between groups.

**Table 1: Baseline Characteristics**

	Low Platelets Only N=113	Low Hemoglobin Only N=20
Median age, years	69	69
DIPSS high risk, n (%)	34 (30)	10 (50)
Median platelet count x 10 <sup>9</sup> /L	46	165
Median hemoglobin, g/dL	9.5	7.1
RBC-TD, n (%)	26 (23)	10 (50)
Prior JAK2 inhibitor, n (%)	27 (24)	5 (25)
Median spleen length, cm	15	11
Study and TSS version		
PERSIST-1 TSS v1.0, n	54	4
PERSIST-1 TSS v2.0, n	32	11
P203 TSS v2.0, n	27	5

DIPSS=Dynamic International Prognostic Scoring System; JAK=Janus associated kinase; RBC-TD, red blood cell transfusion-dependent; TSS, total symptom score.

## Total Symptom Scores

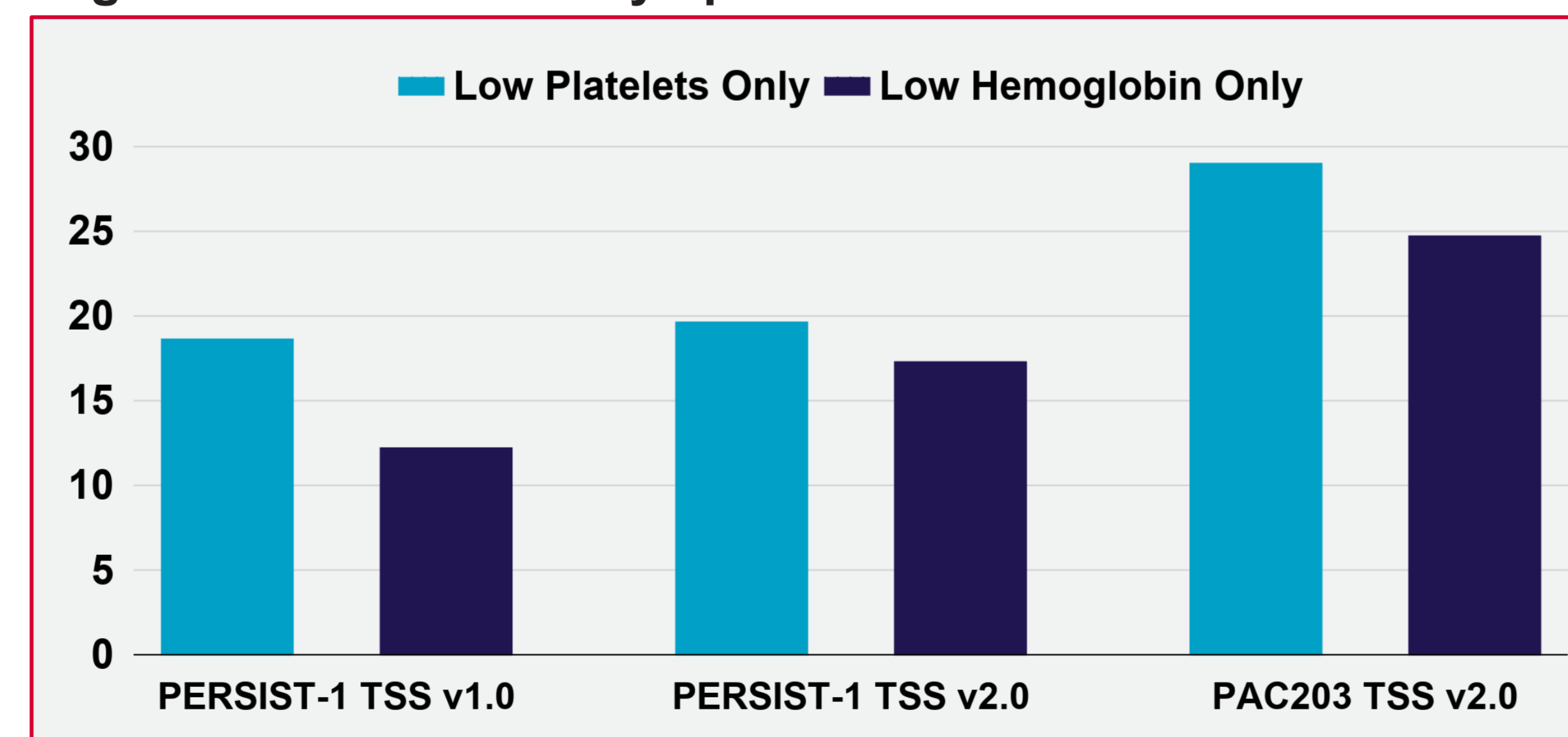
- Patients with low platelets only had worse TSS than patients with low hemoglobin only, indicating more severe MF symptoms (**Figure 2**).
  - A minimal clinically important difference in TSS was found in two of the tested groups (**Table 2**).

**Table 2: Median Total Symptom Scores**

	Low Platelets Only	Low Hemoglobin Only
<b>Total Score</b>		
PERSIST-1 TSS v1.0	18.6 <sup>a</sup>	12.2
PERSIST-1 TSS v2.0	19.6	17.3
P203 TSS v2.0	29.0 <sup>a</sup>	24.7

<sup>a</sup>Difference in score between Low Platelets Only and Low Hemoglobin Only exceeds the MCID. MCID= minimal clinically important difference; TSS=total symptom score.

**Figure 2: Median Total Symptoms Score**



## RESULTS

### Individual Symptom Scores

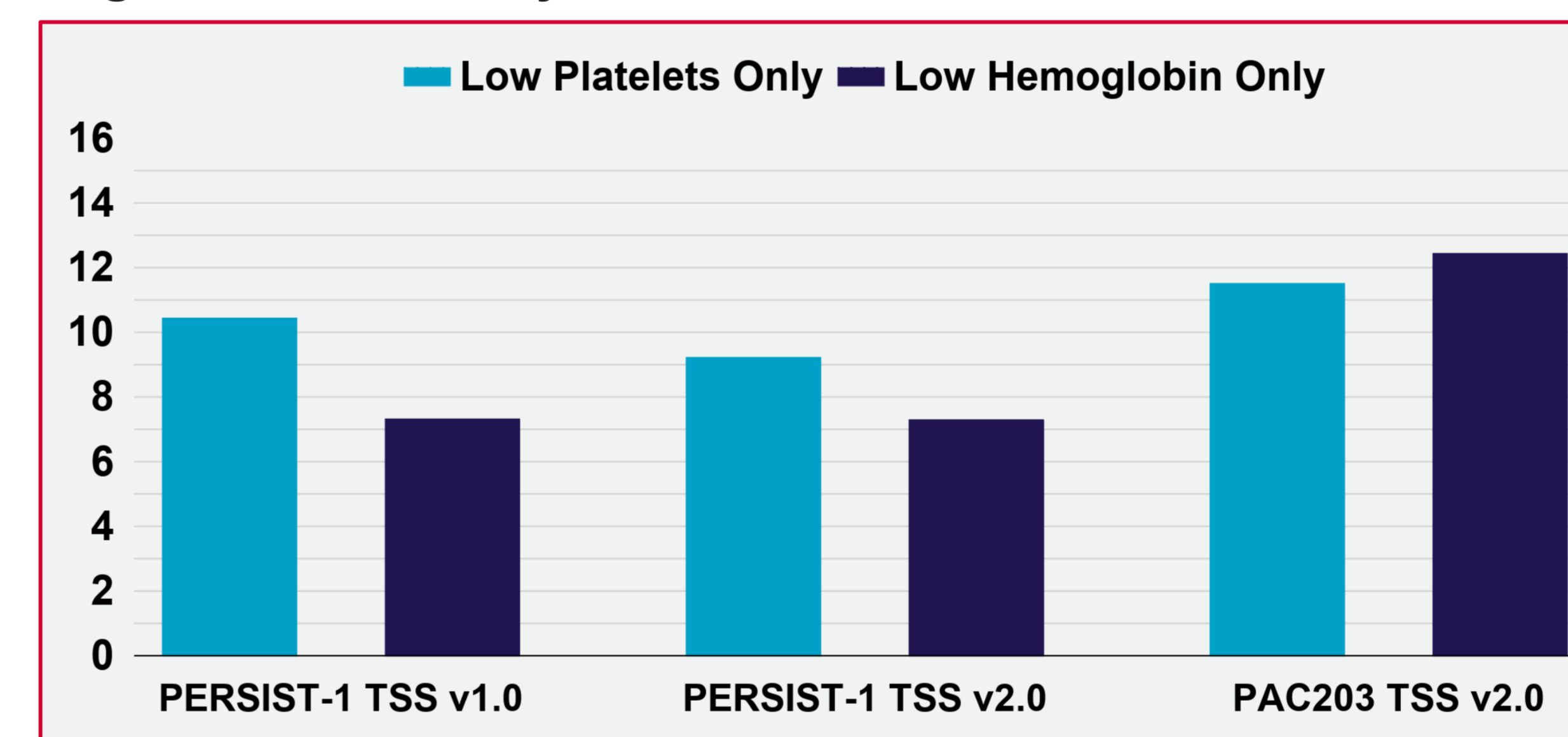
- Patients with low platelets only reported more fatigue and inactivity than patients with low hemoglobin only (**Table 3**).

**Table 3: Median Physical Function Symptoms**

	Low Platelets Only	Low Hemoglobin Only
<b>Tiredness/Fatigue</b>		
PERSIST-1 TSS v1 (fatigue)	5.4	4.0
PERSIST-1 TSS v2.0 (tired)	4.8	3.6
P203 TSS v2.0 (tired)	6.9	6.0
<b>Inactivity</b>		
PERSIST-1 TSS v1.0	5.0	3.3
PERSIST-1 TSS v2.0	4.1	3.3
P203 TSS v2.0	5.1	6.6

- Physical function domain scores (sum of tiredness/fatigue and inactivity) were worse in patients with low platelets only in two of the tested groups (**Figure 3**).

**Figure 3: Median Physical Function Scores**



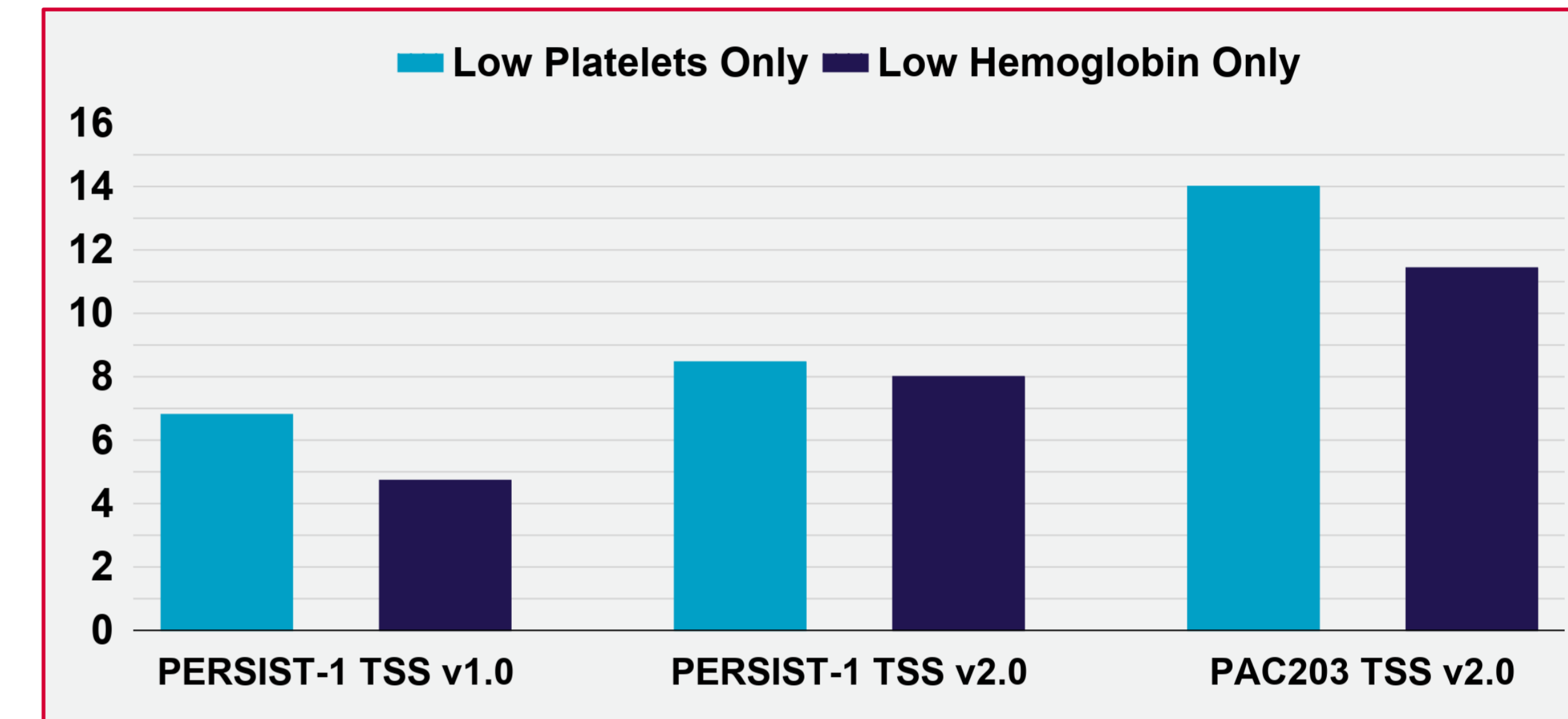
- Patients with low platelets only reported more severe symptoms of splenomegaly than patients with low hemoglobin only (**Table 4**).

**Table 4: Median Spleen-Related Symptoms**

	Low Platelets Only	Low Hemoglobin Only
<b>Early Satiety</b>		
PERSIST-1 TSS v1.0	3.9	1.6
PERSIST-1 TSS v2.0	3.9	3.0
P203 TSS v2.0	5.7	4.7
<b>Abdominal discomfort</b>		
PERSIST-1 TSS v1.0	3.3	3.2
PERSIST-1 TSS v2.0	3.1	3.0
P203 TSS v2.0	4.1	3.6
<b>Left Rib Pain</b>		
PERSIST-1 TSS v1.0	N/A	N/A
PERSIST-1 TSS v2.0	2.0	2.1
P203 TSS v2.0	4.7	2.9

- Spleen-related symptom scores (sum of early satiety, abdominal discomfort, and left rib pain) were worse in patients with low platelets only in all tested groups (**Figure 4**).

**Figure 4: Median Spleen-Related Symptom Scores**



- Cytokine-related symptoms occurred with similar severity in patients with low platelets only and low hemoglobin only (**Table 5**).

**Table 5: Median Cytokine-Related Symptoms**

	Low Platelets Only	Low Hemoglobin Only
<b>Night Sweats</b>		
PERSIST-1 TSS v1.0	1.2	2.4
PERSIST-1 TSS v2.0	2.8	3.3
P203 TSS v2.0	1.3	1.9
<b>Itching</b>		
PERSIST-1 TSS v1.0	0.5	1.1
PERSIST-1 TSS v2.0	1.8	1.9
P203 TSS v2.0	3.1	1.0
<b>Bone pain</b>		
PERSIST-1 TSS v1.0	1.9	0.0
PERSIST-1 TSS v2.0	1.7	2.8
P203 TSS v2.0	3.0	4.0

## CONCLUSIONS

- In this retrospective analysis, patients with isolated thrombocytopenia had more severe symptom burden than those with isolated anemia, particularly with physical function- and spleen-related symptoms.
- These data suggest that anemia is not the sole driver of symptom burden among patients with cytopenic MF.
- While amelioration of anemia is an important therapeutic goal for patients with cytopenic MF, additional efforts aimed at control of platelet count and underlying disease should be implemented to achieve optimal symptom control.

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**PLEASE NOTE:** Some data have been updated for increased precision since original abstract publication.

**REFERENCES:** 1. Scotch AH et al. *Leuk Res*. 2017; 63:34-40. 2. Mesa RA et al. *Lancet Hematol*. 2017;4(5):e225-e236. 3. Gerds AT et al. *Blood Adv*. 2020; 4(22):5825-5835. 4. Mesa RA et al. *J Clin Oncol*. 2013;31(10):1285-1292.