PRM-151 in Myelofibrosis: Durable Efficacy and Safety at 72 Weeks

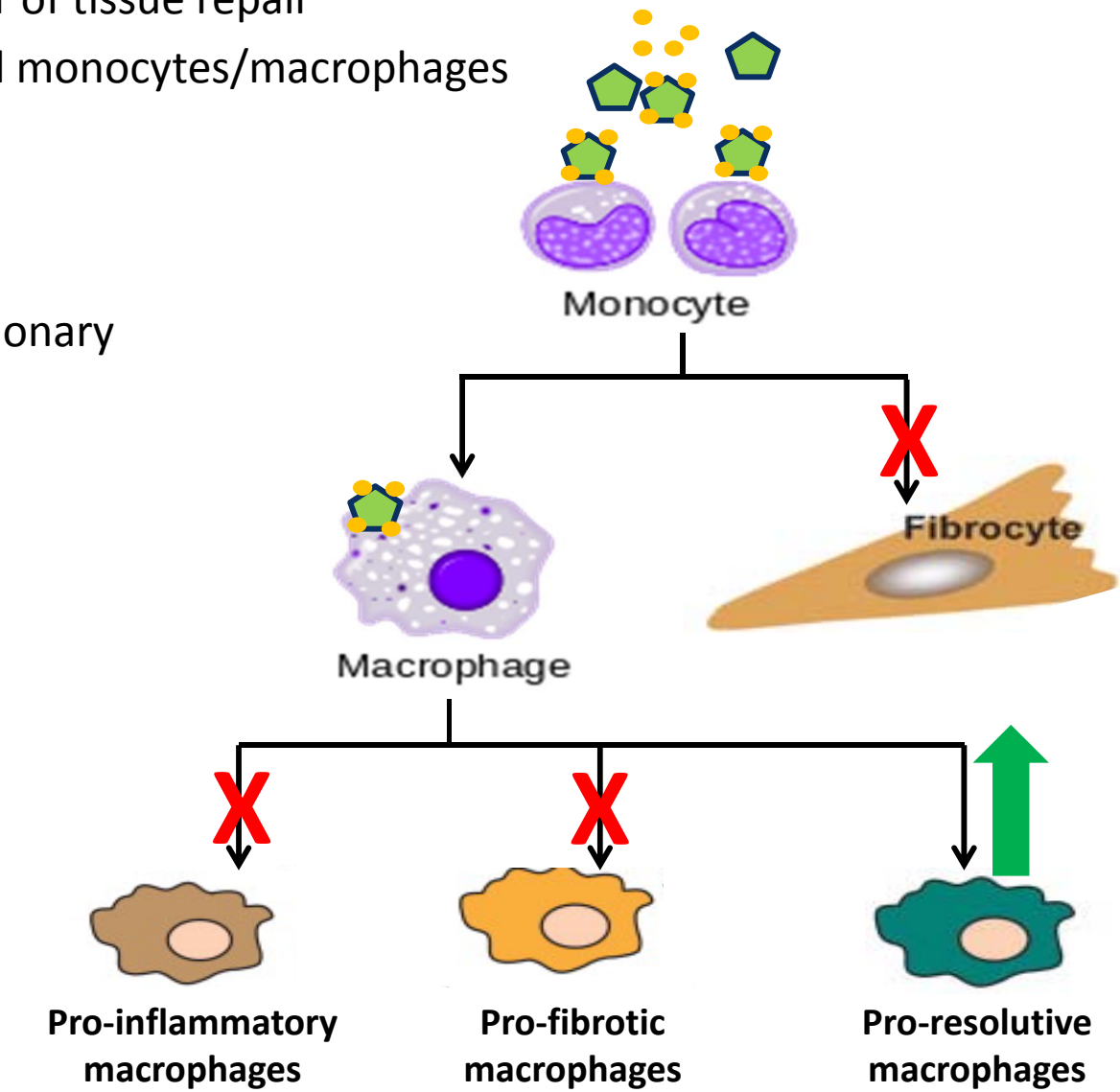
Srdan Verstovsek[1], Olga Pozdnyakova[2],Robert Hasserjian[3], Mohamed Salama[4], Ruben Mesa[5], Lynda Foltz[6], Vikas Gupta[7], John Mascarenhas[8], Ellen Ritchie[9], Ronald Hoffman[8], Richard Silver[9], Marina Kremyanskaya[8], Zeev Estrov[1], Elizabeth Trehu[10], Hagop Kantarjian[1], Jason Gotlib[11]

[1]MD Anderson Cancer Center, Houston, TX, [2]Brigham and Women's Hospital, Boston, MA, [3]Massachusetts General Hospital, Boston, MA, [4]University of Utah, Salt Lake City, UT, [5]Mayo Clinic, Scottsdale, AZ, [6]St. Paul's Hospital, University of British Columbia, BC, CA, [7]Princess Margaret Hospital, Toronto, ON, CA, [8]Mt Sinai Medical Center, New York, NY, [9]Weill Cornell Medical Center, New York, NY, , [10]Promedior, Inc., Lexington, MA, [11]Stanford Cancer Institute, Stanford, CA

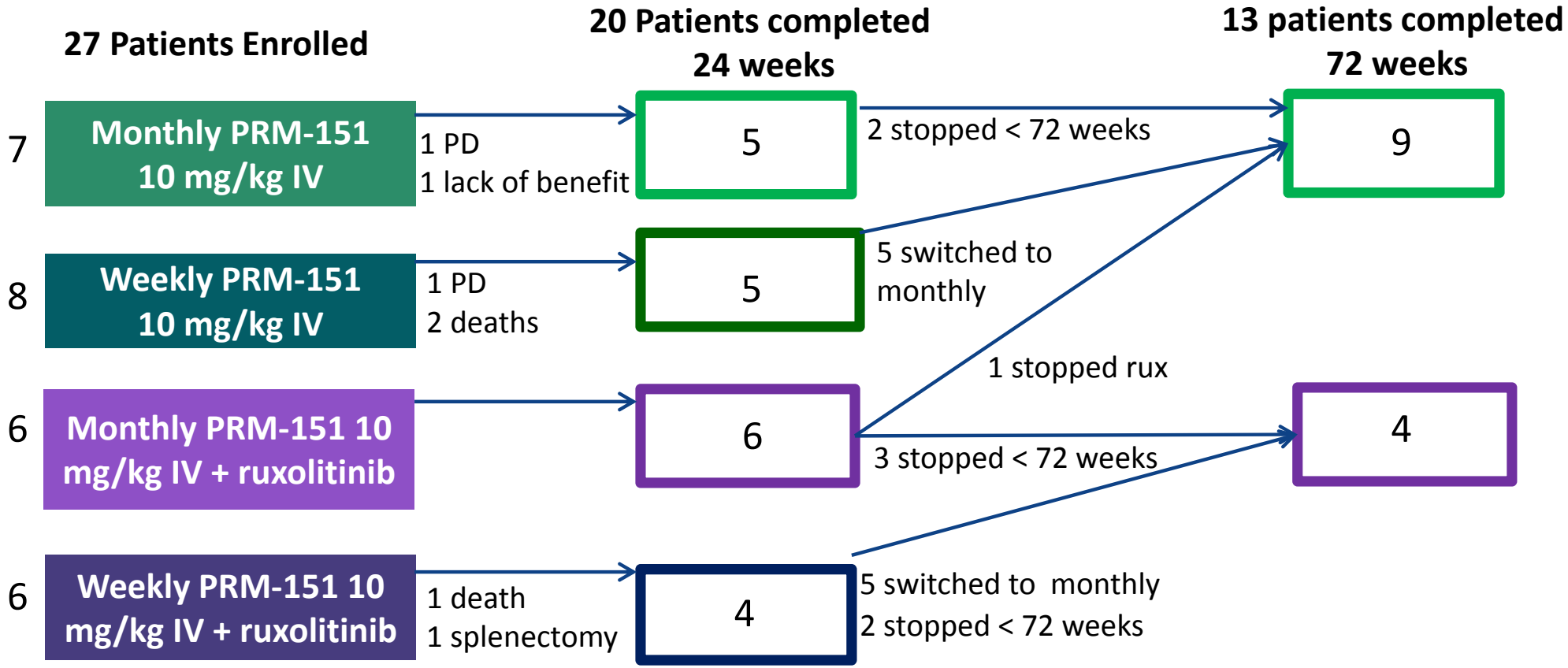
PRM-151: Recombinant Human Pentraxin-2 (PTX-2)

- PTX-2 ( ) is an endogenous regulator of tissue repair
- PTX-2 binds to damaged tissue ( ) and monocytes/macrophages
- PTX-2 prevents and reverses fibrosis in pre-clinical models
- PTX-2 levels are low in MF patients
  - Also low in patients with renal, pulmonary and liver fibrosis

<u>Hypothesis</u>:
Reduction of bone marrow fibrosis will restore hematopoiesis and improve cytopenias



PRM-151G-101 Stage 1 and Extension



- 24 week treatment period
  - Patients with clinical benefit may continue beyond 24 weeks
- PRM-151 + RUX: stable RUX dose ≥3 months with no decrease in splenomegaly for ≥ 4 weeks
- No eligibility restrictions for anemia, thrombocytopenia, leukopenia, or spleen size

Patient Demographics (n=13)

Median Age, Years (range)	60 (51-76)
Median Years Since Diagnosis (range)	2 (0-9)
DIPSS Stage[1] (n, %) Intermediate 1/Intermediate 2	6/7 (46/54)
Fibrosis Grade by central pathologist s (n, %) MF 3/2/1	5/6/2 (38/46/15)
Median number of prior therapies (#, range)	2 (0-6)
Mean weeks since last prior therapy, pts not on rux (#, range)	20 (3-60)
Prior or current JAK Inhibitor (n, %)	9 (69)
Mean duration of ongoing RUX, Years (range)	1.5 (0.6-2.2)
Hgb < 100 g/L (n, %)	5 (38)
Patients receiving RBC transfusions (n, %)	5 (38)
Platelets <50 x 10^9/L (n, %)	5 (38)
Platelets < 100 x 10^9/L (n, %)	9 (69)
Patients receiving Platelet transfusions (n, %)	4 (31)
Patients with palpable spleen (n, %)	10 (77)
Mean MPN-SAF Total Symptom Score[2] (#, range)	20 (4-47)

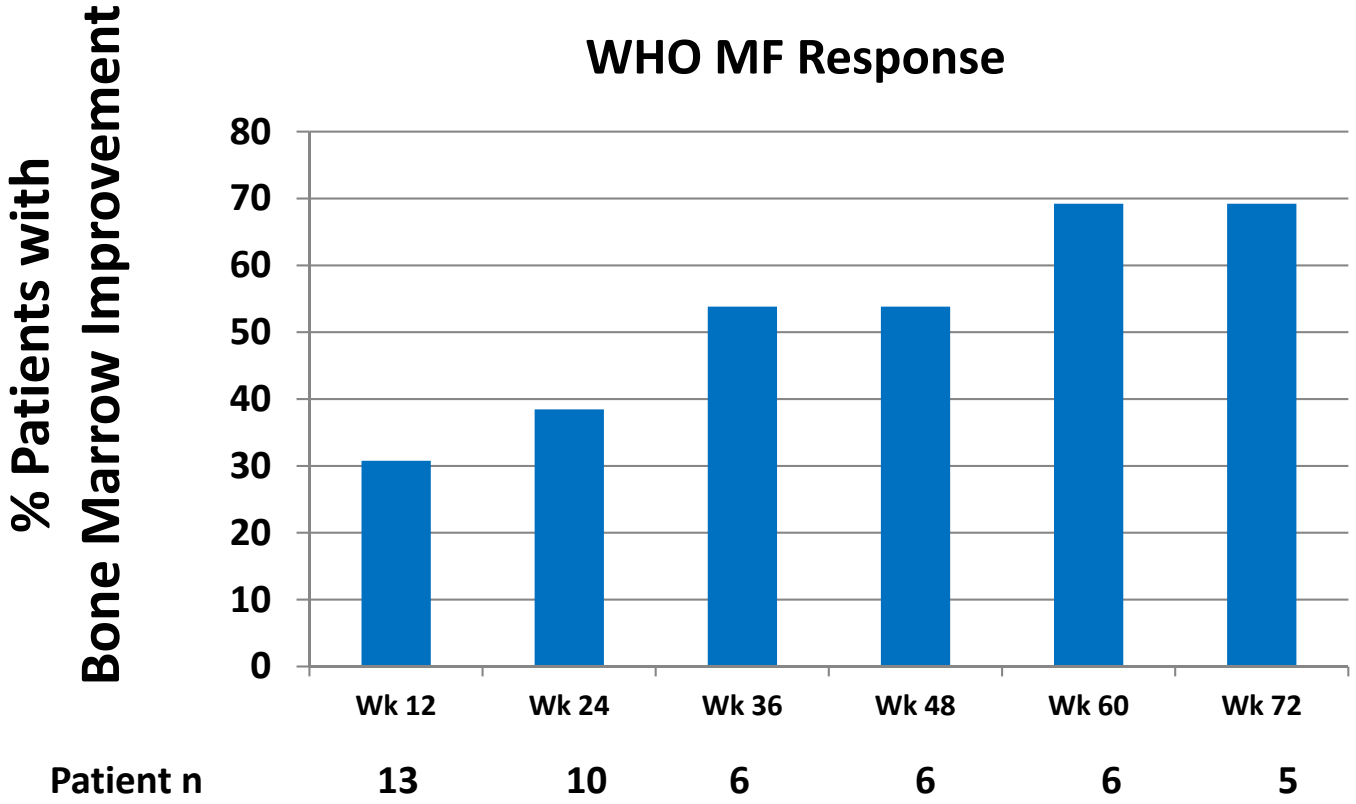
1. Passamonti et al, *Blood* 2010 ; (115): 1703-1708.
2. Emmanuel et al, J Clin Oncol 2012; (30): 4098-4103.

All Possibly Related Adverse Events Through 72 Weeks (n=13)

Adverse Event	Grade 1	Grade 2	Grade 3	Total
ANKLE SWELLING	1			1
DIARRHEA	1			1
ANEMIA			1	1
COUGH NONPRODUCTIVE	1			1
HYPERURICEMIA	1			1
BLURRED VISION	1			1
FATIGUE	2			2
TOOTH INFECTION	1			1
SKIN INFECTION	1			1
HSV INFECTION		1		1
HOT FLASHES	1			1
SWEATING	1			1

6 SAEs in 4 patients - none related: wound infection, multiple fractures, bladder rupture, bowel obstruction, focal pneumonia, and unspecified infection

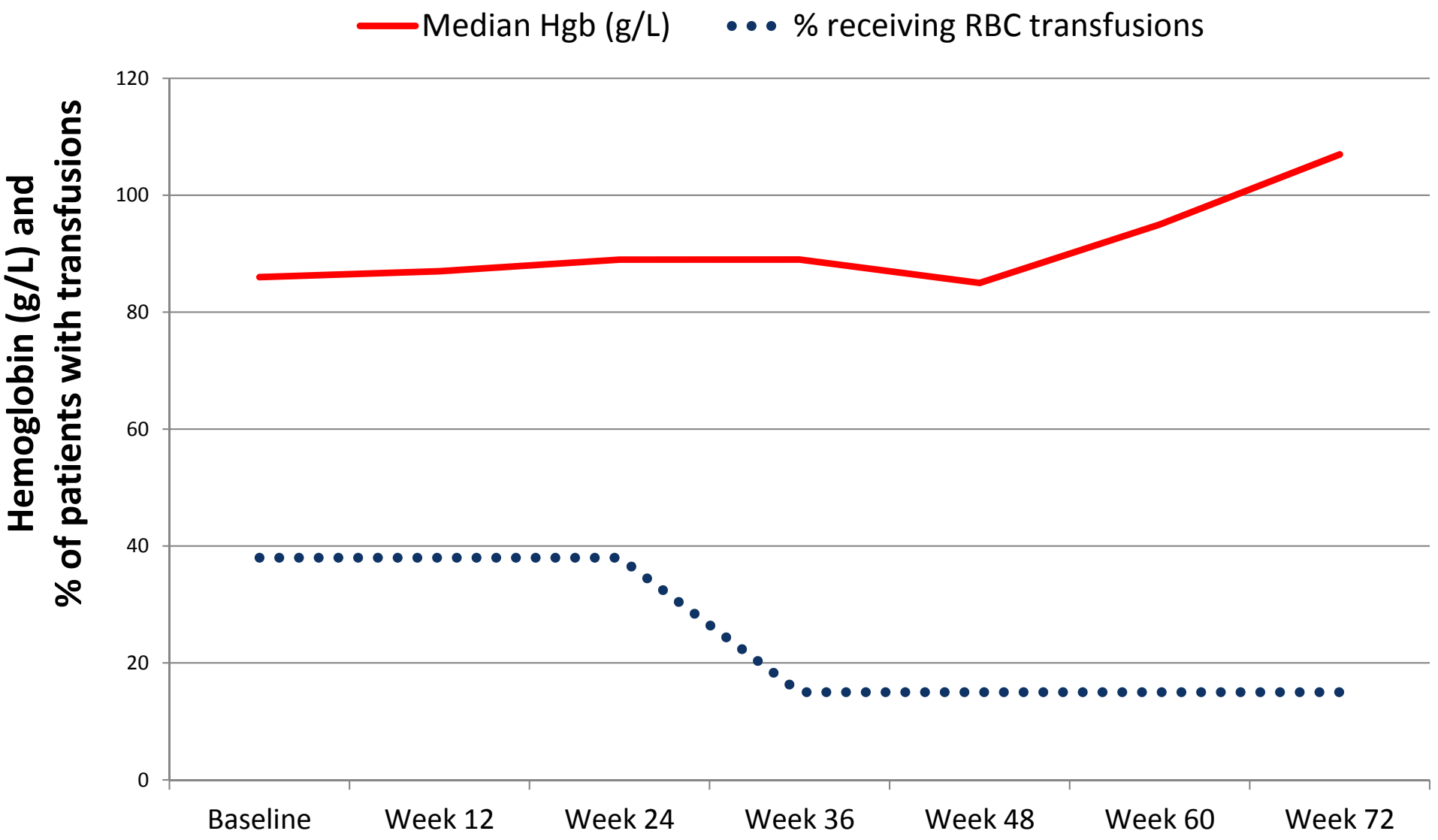
Bone Marrow Fibrosis Improvement as Measured by WHO Criteria



- Response assessment by central hematopathologists blinded to patient, treatment and time point. WHO MF Response = % of patients with ≥1 grade reduction in MF score at any time point
- Reduction in BM fibrosis was associated with normalization of bone marrow architecture: Normal erythroid clustering, Normal or decreased myeloid:erythroid ratio, Fewer paratrabecular megakaryocytes

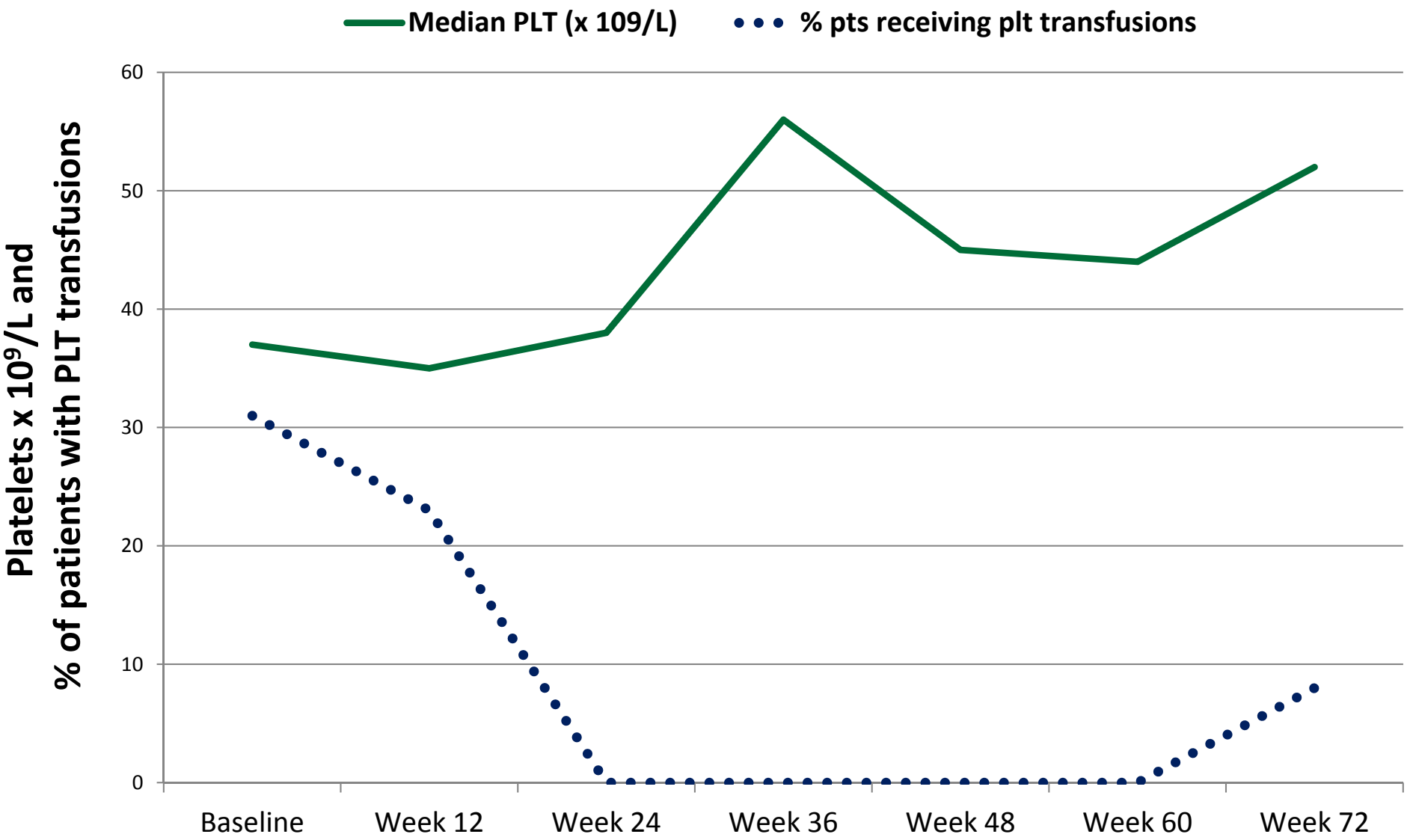
Hemoglobin and RBC Transfusions

Patients with baseline Hgb < 100 g/L who completed ≥ 72 weeks (n=5)



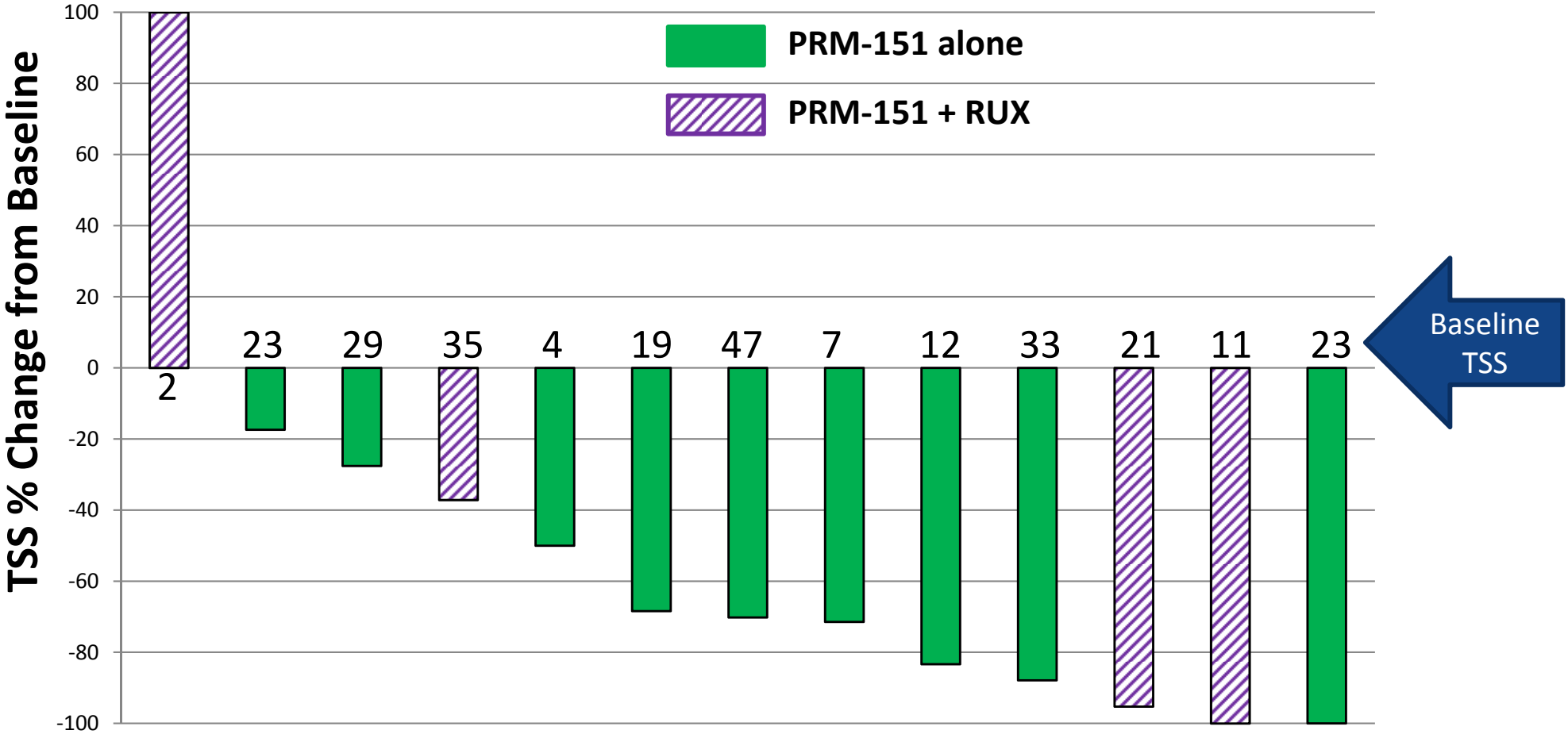
Platelets and Platelet Transfusions

Patients with Baseline Platelets < 100 x 10^9/L who completed ≥ 72 weeks (n=9)



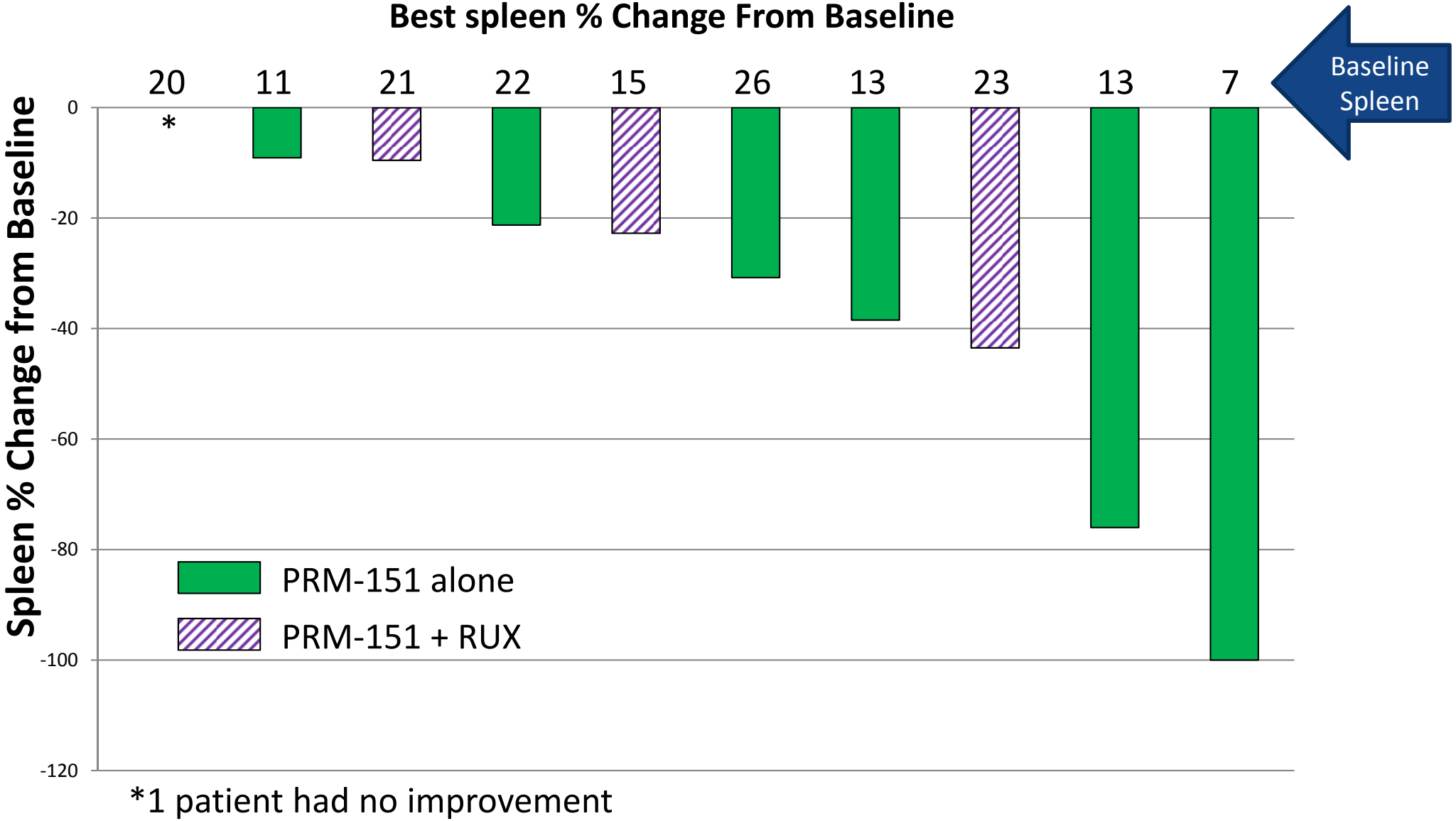
Symptom Improvements

MPN-SAF TSS Best % Change from Baseline (n=13)



Spleen Reductions

Patients with palpable spleen at baseline (n = 10)



*1 patient had no improvement

Conclusions

- 13 patients have completed 72 weeks of PRM-151 treatment
- Reductions in bone marrow fibrosis have been accompanied by
  - Median increase in Hgb in patients with baseline Hgb < 100 g/L
  - Decreased RBC transfusions
  - Median increase in PLT in patients with baseline PLT < 100 x 10^9/L
  - Decreased PLT transfusions
  - > 50% reduction in symptoms in 62% of patients
  - > 50% reduction in splenomegaly in 2 patients on PRM-151 alone
- PRM-151 was well-tolerated
  - 13 related adverse events, 11 Grade 1
  - 6 SAEs, none related

Next Steps

- **Stage 2 of this adaptive study is now enrolling:**
  - Single agent PRM-151 Q4W x 36 weeks: blinded randomization to 1 of 3 doses
  - Patients may continue beyond 36 weeks in open label extension
  - Eligibility
    - DIPSS Intermediate -1, Intermediate-2, or High Risk
    - WHO Grade 2 or 3 myelofibrosis
  - Patients not candidates for ruxolitinib based on:
    - **EITHER** Hgb < 100 g/L, requiring ≥ 2 units RBC in prior 12 weeks, and intolerance of or inadequate response to ruxolitinib
    - **AND/OR** Platelet count < 50 x 10^9/L