Real-World Clinical Outcomes in Patients With Myelofibrosis With and Without Baseline Anemia in the Mass General Brigham Integrated Delivery Network

Gabriela Hobbs,[1] Nicole Niehoff,[2] Tom Liu,[2] Kalé Kponee-Shovein,[3] James Signorovitch,[3] Louise Yu,[3] Mingchen Ye,[3] Pangsibo Shen,[3] Gautam Sajeev,[3] Marlise R. Luskin[4]

[1]Mass General Brigham, Boston, MA, USA; [2]GSK, Collegeville, PA, USA; [3]Analysis Group, Boston, MA, USA; [4]Dana-Farber Cancer Institute, Boston, MA, USA

Digital poster — SCAN ME

Narrated poster — Audio File

Supplemental information — SCAN ME

Introduction

- Anemia is a major complication of myelofibrosis (MF) associated with reduced quality of life and shorter overall survival[1-4]
  - 38% of patients at MF diagnosis have hemoglobin (Hb) levels of <10 g/dL, increasing to almost 60% within the first year post diagnosis[5]
- While Janus kinase (JAK) inhibitor treatments are effective for managing spleen size and symptoms in MF, some JAK inhibitors such as ruxolitinib (RUX) can cause or worsen anemia[6-9]
- To date, there are limited real-world data comparing patient characteristics, clinical outcomes, and RUX treatment patterns in patients with MF with and without anemia
  - Using real-world data from the Mass General Brigham Research Patient Data Registry, this retrospective study described the patient characteristics, clinical outcomes, and treatment patterns of patients with MF by anemia status, overall and in RUX users

Methods

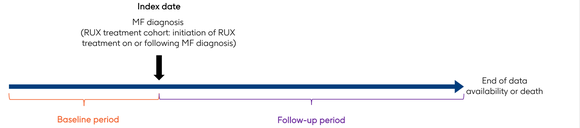
Study Design and Patients

- The data source for this study was the Mass General Brigham Research Patient Data Registry, which aggregates de-identified electronic health records from 9 major hospitals affiliated with the Harvard Medical School in Massachusetts
- A retrospective, observational, longitudinal, cohort study was conducted, including patients with a primary or secondary MF diagnosis (*ICD-10-CM* code, D47.4 or D75.81) in the database (1/1/2018 to 8/31/2023) (**Figure 1**)
- Patients were required to have ≥6 months of clinical activity data before (*baseline period*) the date of MF diagnosis (*MF index date*); this allowed sufficient time to gather data on baseline comorbidities and symptoms
  - Clinical outcomes were assessed during the *follow-up period* (from index date to the earlier of end of data availability or death)
- Analyses were conducted in the overall population regardless of treatment for MF as well as in the subcohort of patients treated with RUX; only RUX was analyzed as sample sizes in the database for fedratinib and pacritinib were low
  - In the RUX treatment cohort, the index date was defined as the date of initiation of RUX treatment on or following the first-observed MF diagnosis during the study period
  - RUX treatment patterns were assessed during the first RUX treatment episode on or after the MF diagnosis; both prevalent and incident RUX users were included

Variable Definitions/Sources

- Anemia: Hb of <10 g/dL from laboratory assessments or *ICD-10-CM* codes
- Thrombocytopenia: platelet (PLT) counts of <150×10^9/L from laboratory assessments or *ICD-10-CM* codes
- Comorbidities, symptoms, thrombosis, and leukemic transformation: *ICD-10-CM* codes
- Red blood cell (RBC) transfusions: *ICD-10-PCS* codes and curated transfusion data
- Treatment patterns: treatment prescription data

Figure 1: **Study Design**



MF, myelofibrosis; RUX, ruxolitinib.

Statistical Analyses

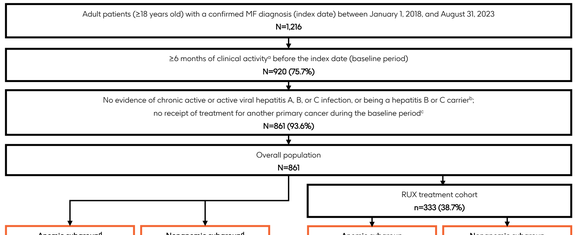
- All outcome measures were stratified by baseline anemia status (anemic vs nonanemic)
  - Baseline patient characteristics and clinical outcomes were described as frequency count and percentage or mean (SD)/median (IQR)
  - Incidence of clinical outcomes and treatment patterns were described during the follow-up period and evaluated using summary statistics and the Kaplan-Meier method
    - Treatment patterns were summarized for RUX dose, RUX duration, RUX combination treatments, and anemia supportive therapies
  - Differences were compared between patients with and without anemia
    - For binary variables, *P* values were calculated using χ^2 tests; Fisher exact test was used if the expected frequency was <5
    - For continuous variables, *P* values were calculated using *t* tests
    - RBC transfusion rates were summarized per patient-year using a univariable Poisson regression model

Results

Baseline Characteristics

- Of 861 eligible patients, 300 (34.8%) had anemia at baseline (**Figure 2**). Median follow-up for all patients was 2.2 years (IQR, 0.8-4.2 years)

Figure 2: **Sample Selection of Patients**



MF, myelofibrosis; RUX, ruxolitinib.
[a] *Clinical activity was defined as a record associated with a diagnosis, laboratory test, procedure, medication, vitals measure, or patient visit.* [b] *Hepatitis exclusion was to align with momelotinib clinical trial enrollment criteria in preparation for a future analysis.* [c] *Primary cancer excluded basal and squamous cell carcinoma and acute myeloid leukemia.* [d] *Patients in the anemic and nonanemic subgroups in the overall population might have received RUX or therapies for MF other than RUX during the observation period.*

Overall Population

- In the overall population, patients with anemia generally had more comorbidities, constitutional symptoms, and thrombocytopenia than patients without anemia (**Table 1**)

Table 1: **Baseline Characteristics, Clinical Outcomes, and Laboratory Measures by Anemia Status (Overall Population)**

	Anemic (n=300)	Nonanemic (n=561)
Age at first-observed MF diagnosis, mean (SD), years*	70.7 (12.4)	66.1 (12.7)
Male, n (%)	173 (57.7)	303 (54.0)
Primary MF, n (%)	176 (58.7)	354 (63.1)
Secondary MF, n (%)	124 (41.3)	207 (36.9)
Constitutional symptoms, n (%)		
Weight loss*	33 (11.0)	15 (2.7)
Fever*	31 (10.3)	13 (2.3)
Night sweats	3 (1.0)	2 (0.4)
Signs and symptoms at MF diagnosis in >5% of patients, n (%)		
Splenomegaly*	74 (24.7)	85 (15.2)
Bone pain*	35 (11.7)	41 (7.3)
Fatigue*	35 (11.7)	31 (5.5)
Patients with Hb test results available, n (%)[a]	264 (88.0)	398 (70.9)
Hb, mean (SD), g/dL*	8.5 (1.0)	12.4 (1.7)
Transfusion dependent, n (%)[b]	111 (37.0)	4 (0.7)
Patients with PLT count test results available, n (%)*	279 (93.0)	398 (70.9)
PLT count, mean (SD), ×10^9/L*	246.1 (250.2)	313.7 (242.4)
Thrombocytopenia, n (%)*	141 (47.0)	110 (19.6)
Mild (PLTs 100×10^9/L to <150×10^9/L)*	29 (27.7)	56 (50.9)
Moderate (PLTs 50×10^9/L to <100×10^9/L)	50 (35.5)	34 (30.9)
Severe (PLTs <50×10^9/L)*	46 (32.6)	15 (13.6)
Unknown severity	6 (4.3)	5 (4.5)
Patients with WBC count test results available, n (%)*	280 (93.3)	398 (70.9)
WBC count, mean (SD), ×10^9/L	15.1 (29.3)	13.1 (14.8)
MF-related comorbidities in >5% of patients, n (%)		
Cardiovascular disease*	140 (46.7)	131 (23.4)
Acute myeloid leukemia	20 (6.7)	22 (3.9)
Thrombosis*	23 (7.7)	12 (2.1)
CCI score during 6-month baseline, mean (SD)*	1.6 (2.1)	0.8 (1.5)
Select CCI components in >20% of patients, n (%)		
Any malignancy, except malignant neoplasm of skin*	71 (23.7)	94 (16.8)
Renal disease*	63 (21.0)	29 (5.2)
Other comorbidities, n (%)		
Hypertension*	104 (34.7)	107 (19.1)
Dyslipidemia*	69 (23.0)	76 (13.5)
Pulmonary disease*	63 (21.0)	50 (8.9)

*Indicates P<.05.
CCI, Charlson Comorbidity Index; Hb, hemoglobin; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; MF, myelofibrosis; PLT, platelet; RBC, red blood cell; WBC, white blood cell.
[a] *Anemia status was based on Hb of <10 g/dL from laboratory assessments or ICD-10-CM codes; Hb values were not available for 36 patients in the anemic subgroup and 163 patients in the nonanemic subgroup.* [b] *Transfusion dependent was defined as ≥4 units of RBC transfusions or Hb of <8 g/dL during the 12-week period prior to or on the index date.*

RUX Treatment Cohort

- A total of 333 patients were treated with RUX, including a higher percentage of patients with anemia than in the overall population (RUX: anemic, n=191 [57.4%]; nonanemic, n=142 [42.6%]; overall: anemic, n=300 [34.8%]; nonanemic, n=561 [65.2%])
  - At baseline, RUX patients with anemia had a higher mean Charlson Comorbidity Index (CCI) score (1.5 vs 0.5; *P*<.001) and higher rates of splenomegaly (43.5% vs 30.3%; *P*=.014), hypertension (33.5% vs 17.6%; *P*=.001), and thrombocytopenia (49.7% vs 22.5%; *P*<.001) than RUX patients without anemia
  - Mean (SD) Hb was significantly lower among RUX patients with anemia compared to RUX patients without anemia (8.5 [0.9] vs 12.0 [1.4] g/dL; *P*<.001), while mean (SD) PLT counts were similar (anemic, 252.3 [276.3]; nonanemic, 259.4 [153.4] ×10^9/L; *P*=.774)

Treatment Patterns

Table 2: **Treatment Patterns by Baseline Anemia Status (RUX Treatment Cohort)**

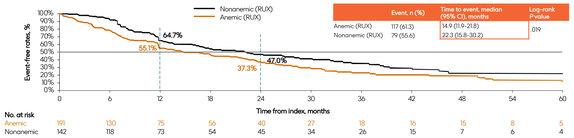
	Anemic (n=191)	Nonanemic (n=142)
RUX combination therapy, n (%)*[a]	93 (48.7)	26 (18.3)
RUX + supportive care for anemia*[b]: Erythropoiesis-stimulating agent*	33 (17.3) 28 (14.7)	2 (1.4) 2 (1.4)
Maximum RUX daily dosing <20 mg/day, n (%)*	40 (20.9)	17 (12.0)
Maximum RUX daily dosing ≥40 mg/day, n (%)*	156 (81.7)	92 (64.8)

*Indicates P<.001. †Indicates P<.05.
JAK, Janus kinase; MF, myelofibrosis; RBC, red blood cell; RUX, ruxolitinib.
[a] *Combination therapy was defined as initiation of any non–JAK inhibitor MF-directed treatments within 30 days before or after the initiation of RUX.* [b] *Supportive care for anemia included erythropoiesis-stimulating agents, immunomodulators, androgens, RBC transfusions, and other anemia treatments.*

RUX Dose Modifications by Baseline Anemia Status

- In the RUX treatment cohort, patients with anemia were more likely to have higher rates of any dose reductions (47.6% vs 35.2%; *P*=.023) and only dose reductions (23.0% vs 9.9%; *P*=.002) than patients without anemia during the RUX treatment episode

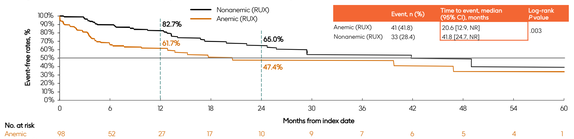
Figure 3: **RUX Treatment Duration by Baseline Anemia Status (RUX Treatment Cohort)[a]**



	Event, n (%)	Time to event, median (95% CI), months	Log-rank P value
Anemic (RUX)	117 (61.3)	14.9 (11.9-21.8)	.019
Nonanemic (RUX)	79 (55.6)	22.3 (15.8-30.2)	

RUX, ruxolitinib.
[a] *Duration of RUX treatment was defined as time from initiation of RUX to the earlier of treatment discontinuation or death. The discontinuation date was defined as the last day of supply prior to the 45-day treatment-free period. Patients who did not discontinue or die were censored at the earliest of allogeneic hematopoietic cell transplant, splenectomy, or end of data availability.*

Figure 4: **Time to Addition of Supportive Care for Anemia by Baseline Anemia Status (RUX Treatment Cohort)[a,b]**



	Event, n (%)	Time to event, median (95% CI), months	Log-rank P value
Anemic (RUX)	41 (41.8)	20.6 [12.9, NR]	.003
Nonanemic (RUX)	33 (28.4)	41.8 [24.7, NR]	

NR, not reached; RBC, red blood cell; RUX, ruxolitinib.
[a] *Supportive care for anemia included erythropoiesis-stimulating agents, immunomodulators, androgens, RBC transfusions, and other anemia treatments.* [b] *Analyses were conducted among patients treated with RUX monotherapy. Time to addition of supportive care for anemia was defined as time from the initiation of RUX to the earliest addition of supportive medications for anemia or RBC transfusions. Patients who did not add supportive care for anemia were censored at the earliest of treatment discontinuation, allogeneic hematopoietic cell transplant, splenectomy, death, or end of data availability.*

Outcomes

Table 3: **Clinical Outcomes of Patients by Baseline Anemia Status**

	Overall population		RUX treatment cohort	
	Anemic (n=300)	Nonanemic (n=561)	Anemic (n=191)	Nonanemic (n=142)
Follow-up duration, mean (SD), years*	2.0 (1.8)	2.8 (2.0)	2.1 (1.8)	2.9 (1.8)
Incidence of anemia, n (%)*	–	343 (61.1)	–	105 (73.9)
Moderate (Hb 8 to <10 g/dL)	–	201 (58.6)	–	73 (69.5)
Severe (Hb <8 g/dL)	–	31 (9.0)	–	5 (4.8)
Unknown severity	–	111 (32.4)	–	27 (25.7)
Incidence of thrombocytopenia, n (%)*†	73 (45.9)	180 (39.9)	70 (72.9)	62 (56.4)
Mild (PLTs 100×10^9/L to <150×10^9/L)	55 (75.3)	126 (70.0)	58 (82.9)	46 (74.2)
Moderate (PLTs 50×10^9/L to <100×10^9/L)	10 (13.7)	29 (16.1)	8 (11.4)	5 (8.1)
Severe (PLTs <50×10^9/L)*	0 (0.0)	15 (8.3)	0 (0.0)	7 (11.3)
Unknown severity	8 (11.0)	10 (5.6)	4 (5.7)	4 (6.5)
Incidence of leukemic transformation, n (%)†	29 (10.4)	45 (8.3)	17 (9.8)	16 (11.9)
Incidence of thrombosis, n (%)†	23 (8.3)	46 (8.4)	17 (9.7)	13 (9.4)
RBC transfusions, PPY*‡	4.1	1.3	5.2	1.8

*Indicates P<.05 for overall population and RUX treatment cohort. †Indicates P<.05 for RUX treatment cohort only.
Hb, hemoglobin; PLT, platelet; PPY, per patient-year; RBC, red blood cell; RUX, ruxolitinib.
[a] *Patients in the overall population/RUX users without the following on the index date: anemia (n=561/n=142); thrombocytopenia (anemic, n=159/n=96; nonanemic, n=483/n=193); acute myeloid leukemia (anemic, n=280/n=172; nonanemic, n=536/n=264); and thrombosis (anemic, n=277/n=175; nonanemic, n=549/n=238).* [b] *Incidence of RBC transfusions PPY was calculated as the number of RBC transfusions during the observation period divided by the total number of person-years in the study population.*

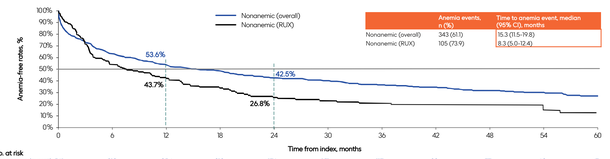
Conclusions

- This retrospective analysis of the Mass General Brigham Research Patient Data Registry suggests that most patients with MF will develop anemia over time, which is associated with substantial additional treatment and clinical burdens, including increased need for transfusions
  - Patients with anemia also had a higher incidence rate of thrombocytopenia (developing thrombocytopenia a median of approximately 2 years faster) than patients without anemia
- Consistent with previous studies, the burden of anemia in the RUX treatment cohort was higher than in the overall patient population
  - RUX-treated patients with baseline anemia had a significantly shorter duration of treatment, and median time to addition of supportive care for anemia was almost 2 years faster compared with patients without baseline anemia
- These findings highlight the challenges of RUX treatment in patients with anemia, underscoring the importance of incorporating effective anemia management into treatment strategies for MF

Limitations

- Differences between anemia status subgroups are not adjusted for potential confounders and should therefore be interpreted with caution
- *ICD-10-CM* and *ICD-10-PCS* codes were used to record MF-related comorbidities, symptoms, and RBC transfusions, which are subject to misspecification and potential data entry errors[10]
- The data source is limited to academic medical centers within Massachusetts, and patients in the Mass General Brigham system are more likely to be White and have higher socioeconomic status compared with the rest of the patient population in the state, limiting the generalizability of these results
- Treatment prescription data were used for analyses of treatment patterns but do not provide information on medication dispensing or treatment adherence and compliance

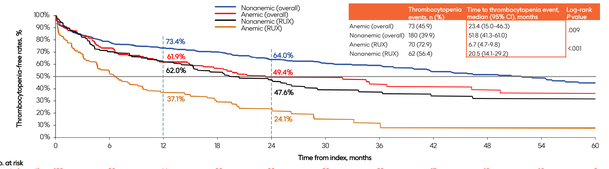
Figure 5: **Incidence of Anemia Among Patients Without Anemia at Baseline[a]**



	Anemia events, n (%)	Time to anemia event, median (95% CI), months
Nonanemic (overall)	343 (61.1)	15.3 (11.5-19.8)
Nonanemic (RUX)	105 (73.9)	8.3 (5.0-12.4)

MF, myelofibrosis; RUX, ruxolitinib.
[a] *Time to incident anemia was defined as time from the index date to first-observed manifestation of anemia. Patients without an anemia event were censored at the earlier of death or end of data availability. For the overall population, the index date was defined as the date of MF diagnosis from January 1, 2018, to August 31, 2023. For the RUX cohort, the index date was defined as the date of RUX initiation on or following MF diagnosis.*

Figure 6: **Incidence of Thrombocytopenia Among Patients Without Baseline Thrombocytopenia by Baseline Anemia Status[a]**



	Thrombocytopenia, n/n-1, n (%)	Time to thrombocytopenia event, median (95% CI), months	Log-rank P value
Anemic (overall)	73 (45.9)	23.4 (15.0-46.3)	.009
Nonanemic (overall)	180 (39.9)	51.8 (41.3-61.0)	
Anemic (RUX)	70 (72.9)	6.7 (4.7-9.8)	<.001
Nonanemic (RUX)	62 (56.4)	20.6 (14.1-29.2)	

MF, myelofibrosis; RUX, ruxolitinib.
[a] *Time to incident thrombocytopenia was defined as time from the index date to first-observed manifestation of thrombocytopenia. Patients without a thrombocytopenia event were censored at the earlier of death or end of data availability. For the overall population, the index date was defined as the date of MF diagnosis from January 1, 2018, to August 31, 2023. For the RUX cohort, the index date was defined as the date of RUX initiation on or following MF diagnosis.*

Abbreviations

CCI, Charlson Comorbidity Index; Hb, hemoglobin; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; ICD-10-PCS, International Classification of Diseases, Tenth Revision, Procedure Coding System; JAK, Janus kinase; MF, myelofibrosis; NR, not reached; PLT, platelet; PPY, per patient-year; RBC, red blood cell; RUX, ruxolitinib; WBC, white blood cell.

References

1. Naymagon L, Mascarenhas J. *Hemasphere.* 2017;1(1):e1.
2. Mesa R, et al. *ASCO* 2023. Poster 7066.
3. Nicolaou M, et al. *Leukemia.* 2018;32(5):1254-1258.
4. Gerds AT, et al. *ASH* 2022. Poster 1729.
5. Tefferi A, et al. *Mayo Clin Proc.* 2012;87(1):25-33.
6. Passamonti F, et al. *Crit Rev Oncol Hematol.* 2022;180:103862.
7. Maffioli M, et al. *Blood Adv.* 2022;6(6):1855-1864.
8. Verstovsek S, et al. *N Engl J Med.* 2012;366(9):799-807.
9. Harrison CN, et al. *Leukemia.* 2016;30(8):1701-1707.
10. Mainor AJ, et al. *Med Care.* 2019;57(7):e42-e46.

Acknowledgments

This analysis was supported by GSK.

Medical writing support was provided by Gabriella Florence, MS, of Nucleus Global, an Inizio company, and funded by GSK.

Disclosures

GH reports consulting fees from AbbVie, BMS, Pfizer, Novartis, GSK, and Incyte, payment or honoraria from PharmaEssentia, and stock/stock options from Regeneron and is a member of Cogent. **NN** reports employment with GSK and stock/stock options from McKesson. **TL** reports employment with GSK. **KKS**, **JS**, **LY**, **MY**, **PS**, and **GS** report employment with Analysis Group, Inc., which received funding from GSK to conduct the present analysis. **MRL** reports consulting fees from Pfizer, Novartis, Kite, and Jazz and payment or honoraria from Pfizer and Jazz.

Society of Hematologic Oncology 2024 Annual Meeting | September 4-7, 2024 | Houston, TX, USA

Corresponding author: Nicole Niehoff, nicole.m.niehoff@gsk.com