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The Impact of New or Worsening Anemia on Clinical Outcomes in 2233 Patients With Myelofibrosis Treated With Ruxolitinib: Results From the Expanded-Access JUMP Study

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Introduction

- Myelofibrosis (MF) is a myeloproliferative neoplasm characterized by cytopenias, splenomegaly, debilitating symptoms, and poor overall survival (OS)[1,2]
- Ruxolitinib is a potent and selective Janus kinase (JAK)1/JAK2 inhibitor approved for the treatment of patients with intermediate- or high-risk MF[3]
- Transient dose-dependent anemia is a known consequence of ruxolitinib treatment and can influence decisions regarding initiation, dosing, and discontinuation of therapy[3]
- In a post hoc analysis of data from the pivotal phase 3 COMFORT-I/II trials, new or worsening anemia did not impact the clinical outcomes of spleen volume response or symptom control[4]

Objective

- To validate findings from the post hoc COMFORT analysis using data from JUMP, the largest ruxolitinib trial in patients with MF to date

Methods

Study Design and Patients

- JUMP was a global, single-arm, phase 3b, expanded-access trial that provided ruxolitinib treatment of MF in a setting similar to that of routine clinical practice
- Eligible patients were ≥18 years old with a diagnosis of primary or secondary MF and high-, intermediate (Int)-2, or Int-1 risk using International Prognostic Scoring System (IPSS) criteria
  - Int-1-risk patients were required to have palpable splenomegaly ≥5 cm from the costal margin
- All patients received ruxolitinib twice daily: starting dose, 5 mg (platelet count 50–<100 × 10^9/L), 15 mg (100–200 × 10^9/L), or 20 mg (>200 × 10^9/L)
- In this post hoc analysis, patients were stratified based on baseline anemia and transfusion status: nonanemic (hemoglobin [Hb] >100 g/L), transfusion-requiring anemia (TRA; Hb <100 g/L, received ≥2 units of red blood cells over 8 weeks before first ruxolitinib dose), or non–transfusion-requiring anemia (NTRA)

Assessments

- Spleen length response (SLR), defined as ≥50% reduction from baseline at Weeks 24 or 48 assessed with manual palpation
- Symptom response as assessed by ≥6.5-point increase in Functional Assessment of Cancer Therapy–Lymphoma total score (FACT-Lym TS response) from baseline at Weeks 24 and 48
- OS defined as time from study initiation to death due to any cause

Statistical Analyses

- Outcomes were stratified by presence or absence of new or worsening anemia following ruxolitinib initiation (Hb decrease of ≥15 g/L or new transfusion requirement at Week 4, 8, or 12)
- OS was assessed using proportional hazard regression adjusted for age and Hb at baseline

Results

Patients

- All 2233 patients enrolled in JUMP were included in the analysis (**Table 1**)

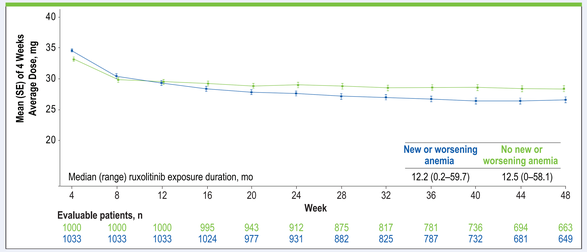
Table 1. Patient Demographics and Baseline Characteristics

Variable	New/Worsening Anemia up to Week 12 (n=1117)	No New/Worsening Anemia up to Week 12 (n=1116)	*P* Value	Total (N=2233)
Age, median (range), y	68.0 (18–89)	66.0 (20–89)	<0.0001	67.0 (18–89)
<65 y, n (%)	387 (34.6)	512 (45.9)	<0.0001	899 (40.3)
≥65 y, n (%)	730 (65.4)	604 (54.1)	–	1334 (59.7)
Male, n (%)	574 (51.4)	643 (57.6)	0.0127	1217 (54.5)
BMI, median (range), kg/m^2	23.8 (14–39.9)	24.2 (14.2–42.8)	0.1194	24.1 (14.0–42.8)
Time since initial diagnosis, median (range), mo*	24.9 (0–456)	26.9 (0–444)	0.9227	25.8 (0–456)
DIPSS risk status, n (%)				
High	98 (8.8)	96 (8.6)	0.7658	194 (8.7)
Intermediate-2	367 (32.9)	388 (34.8)	–	755 (33.8)
Intermediate-1	441 (39.5)	394 (35.3)	–	835 (37.4)
Low	29 (2.6)	31 (2.8)	–	60 (2.7)
Missing	182 (16.3)	207 (18.5)	–	389 (17.4)
Palpable spleen, n (%)	1048 (93.8)	1039 (93.1)	0.9560	2087 (93.5)
Length, median (range), cm	12.0 (1–40)	12.8 (0.5–45)	0.3031	12.0 (0.5–45)
Platelet count, median (range), 10^9/L	265.0 (55–2341)	243.0 (47–3062)	0.6807	254.0 (47–3062)
<100	53 (4.7)	85 (7.6)	0.0534	138 (6.2)
100–<200	332 (29.7)	357 (32.0)	–	689 (30.9)
≥200	726 (65.0)	672 (60.2)	–	1398 (62.6)
Baseline anemia status, n (%)				
Nonanemic	756 (67.7)	630 (56.5)	<0.0001	1386 (62.1)
Anemic NTRA	201 (18.0)	320 (28.7)	–	521 (23.3)
Anemic TRA	160 (14.3)	166 (14.9)	–	326 (14.6)
Hb, mean (SD), g/L	107.3 (17.3)	111.2 (27.3)	0.0003	109.3 (22.9)
<100, n (%)	367 (32.9)	489 (43.8)	<0.0001	856 (38.3)
≥100, n (%)	745 (66.7)	625 (56.0)	–	1370 (61.4)
Baseline Hb by baseline anemia status, mean (SD), g/L†				
Nonanemic	115.7 (13.6)	131.7 (18.4)	–	122.9 (17.8)
Anemic NTRA	91.9 (6.8)	88.3 (7.9)	–	89.7 (7.7)
Anemic TRA	87.2 (8.7)	79.9 (10.6)	–	83.7 (10.3)

BMI, body mass index; DIPSS, Dynamic International Prognostic Scoring System; Hb, hemoglobin; NTRA, non–transfusion-requiring anemia; TRA, transfusion-requiring anemia.
* New/worsening anemia, n=1114; no new/worsening anemia, n=1115.
† New/worsening anemia: nonanemic, n=697; anemic NTRA, n=185; anemic TRA, n=146; no new/worsening anemia: nonanemic, n=575; anemic NTRA, n=286; anemic TRA, n=137.

Treatment Exposure

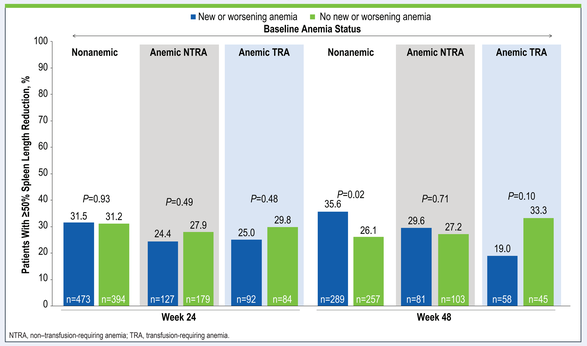
Figure 1. Mean Dose of Ruxolitinib in Patients With vs Without New or Worsening Anemia



Spleen Length Response

- SLR rates at Weeks 24 and 48 among patients with new or worsening anemia were similar to or better than those without new or worsening anemia (**Figure 2**)
- In the post hoc analysis of pooled COMFORT data, spleen volume response rates at Weeks 24 and 48 were similar between patients with and without new or worsening anemia, regardless of anemia and transfusion status at baseline (all *P* values >0.05)[4]

Figure 2. Percentage of Patients With ≥50% Spleen Length Reduction

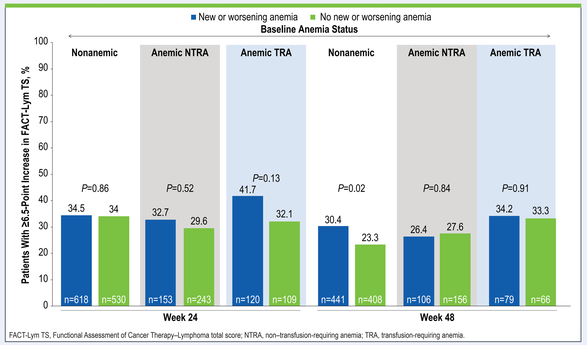


NTRA, non–transfusion-requiring anemia; TRA, transfusion-requiring anemia.

Symptom Response

- At Weeks 24 and 48, symptom improvement among patients with new or worsening anemia was similar to or better than those without new or worsening anemia (**Figure 3**)
- A similar finding was reported in the post hoc COMFORT analysis; there was no significant difference in the percentage of patients achieving a ≥6.5-point increase in FACT-Lym TS or ≥50% improvement in the MF Symptom Assessment Form total symptom score at Week 24 among those with vs without new or worsening anemia regardless of anemia and transfusion status at baseline (all *P* values >0.05)[4]

Figure 3. Percentage of Patients Achieving ≥6.5-Point Increase in FACT-Lym TS



FACT-Lym TS, Functional Assessment of Cancer Therapy–Lymphoma total score; NTRA, non–transfusion-requiring anemia; TRA, transfusion-requiring anemia.

Overall Survival

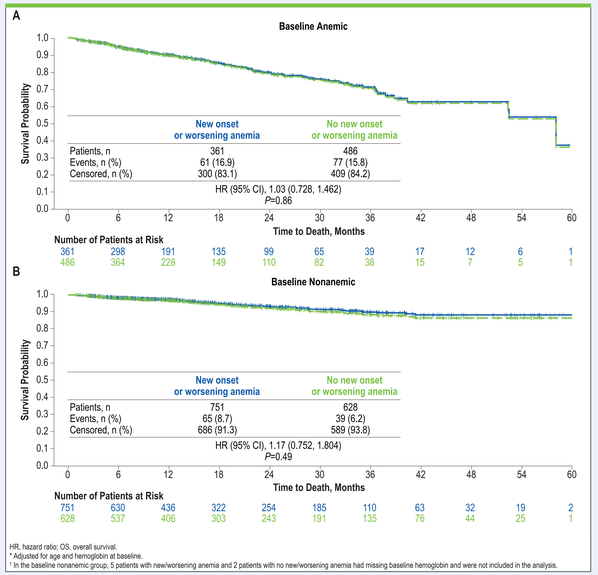
- In patients without anemia at baseline, those that developed new or worsening anemia had evidence of higher-risk disease at enrollment, including older age and lower Hb (**Table 2**)
- When adjusted for age and Hb at baseline, no difference in OS was observed between those with vs without new or worsening anemia among patients with or without anemia at baseline (**Figure 4**)
- In the post hoc COMFORT analysis, OS was similar between patients with vs without new or worsening anemia

Table 2. Baseline Characteristics in the OS Patient Subgroups

	Baseline Anemic			Baseline Nonanemic		
Baseline characteristics	New/Worsening Anemia (n=361)	No New/Worsening Anemia (n=486)	*P* Value	New/Worsening Anemia (n=756)	No New/Worsening Anemia (n=630)	*P* Value
Age, median (range), y	69.0 (33–89)	68.0 (31–89)	0.7286	68.0 (18–88)	64.0 (20–85)	<0.0001
≥65 y, n (%)	247 (68.4)	302 (62.1)	0.1667	483 (63.9)	302 (47.9)	<0.0001
Int-2 DIPSS risk status, n (%)	192 (53.2)	290 (59.7)	0.1693	175 (23.1)	98 (15.6)	0.0019
Hb*, mean (SD), g/L	89.7 (8.2)	85.5 (9.7)	<0.0001	115.8 (13.8)	131.1 (18.4)	<0.0001
Ruxolitinib exposure duration, mean (SD), mo	15.9 (13.0)	14.0 (12.1)	0.09	18.2 (14.3)	20.5 (15.6)	0.02

DIPSS, Dynamic International Prognostic Scoring System; Hb, hemoglobin; Int, intermediate; OS, overall survival.
*In the baseline nonanemic group, 5 patients with new/worsening anemia and 2 patients with no new/worsening anemia had missing baseline hemoglobin.

Figure 4. OS* of Patients With vs Without New or Worsening Anemia Who Were (A) Anemic and (B) Nonanemic† at Baseline



HR, hazard ratio; OS, overall survival.
* Adjusted for age and hemoglobin at baseline.
† In the baseline nonanemic group, 5 patients with new/worsening anemia and 2 patients with no new/worsening anemia had missing baseline hemoglobin and were not included in the analysis.

Conclusions

- **The onset of new or worsening anemia post-baseline did not diminish clinical benefit of ruxolitinib treatment vs that observed in patients without new or worsening anemia**
- **Ruxolitinib was associated with a reduction in spleen volume and a reduction in symptoms associated with MF regardless of baseline anemia and transfusion status**
- **When controlled for baseline risk factors, no difference in OS was observed between patients with vs without new or worsening anemia regardless of baseline anemia status**
- **The results are consistent with an analysis of pooled COMFORT-I/II data, reporting similar findings for spleen volume, symptom response, and OS in patients with anemia at baseline**
- **These results from JUMP based on a broad population in a real-world setting, including those with platelet count <100 × 10^9/L and lower-risk MF, support the use of ruxolitinib in patients with MF regardless of baseline anemia or development of treatment-related anemia**

Disclosures

VG reports consultancy for Novartis, Constellation Biopharma, and Sumitomo Pharm; consultancy and participation on a data safety monitoring board or advisory board for BMS Celgene, Sierra Oncology, Pfizer, and CTI Biopharma; consultancy, participation on a data safety monitoring board or advisory board, and honoraria for AbbVie; consultancy, honoraria, support for attending meetings and/or travel for GSK Pharma; participation on a data safety monitoring board or advisory board for Roche. PG has served on speaker bureaus and membership on the board of directors or advisory committees for Novartis and AbbVie, and speaker bureaus for GSK. JEH-M and EB are employees and shareholders of Incyte. HKA-A has served as a consultant for AOP, Novartis, BMS, GSK, AbbVie, and BluePrint and has received research funding from BMS and Incyte.

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References

1. Tefferi A. *Am J Hematol*. 2021;96(1):145-162. **2.** Szuber N, et al. *Mayo Clin Proc*. 2019;94(4):599-610. **3.** JAKAFI® (ruxolitinib). Full Prescribing Information, Incyte Corporation, Wilmington, DE, 2023. **4.** Al-Ali HK, et al. Effect of new or worsening anemia on clinical outcomes in patients with myelofibrosis treated with ruxolitinib: a post hoc analysis of the COMFORT-I and -II trials. Presented at: Society of Hematologic Oncology (SOHO) Annual Meeting; September 6-9, 2023; Houston, TX.

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