# Anemia burden in patients with myelofibrosis treated with ruxolitinib: data from the Veterans Affairs Corporate Data Warehouse

MPN-203

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## Introduction

- Myelofibrosis (MF) is a hematologic malignancy characterized by splenomegaly and debilitating symptoms; anemia is common among patients with MF and is associated with a poor prognosis[1,2]
- Anemia is associated with fatigue, lower quality of life, excess morbidity, and cardiovascular mortality[3]
- Anemia is often managed with red blood cell (RBC) transfusions, but patients may become transfusion dependent (TD), which can worsen with time and carries the additional risk of iron overload[3]
- Ruxolitinib (RUX), the first approved JAK1/JAK2 inhibitor for patients with MF, is commonly used as a first-line (1L) treatment for MF; however, its myelosuppressive effect often comes with persistent or worsening anemia[3]
- To date, there are limited data on the real-world clinical management of anemia in patients with MF treated with RUX

## Objective

- To describe the real-world characteristics and anemia burden in patients with MF and anemia who have received RUX in clinical practice in the United States (US)

## Methods

### Data source

- This retrospective observational study used the Veterans Affairs Corporate Data Warehouse (VACDW), an enterprise-level health data warehouse of the US Veterans Health Administration containing claims data and electronic health records
- The de-identified data from the VACDW were accessed through the VA Informatics and Computing Infrastructure (VINCI) with appropriate regulatory approvals
- VINCI is an initiative to improve researchers' access to VA data and to facilitate analyses of those data while ensuring veterans' privacy

### Study design

- Study observation period: earliest data available to December 31, 2023
- Study population: patients with MF and anemia treated with RUX
  - Adults ≥ 18 years of age
  - ≥ 1 inpatient or ≥ 2 outpatient claims on different dates for MF
  - ≥ 1 inpatient or ≥ 2 outpatient claims on different dates for anemia between 3 months prior to the initial MF diagnosis through the end of the study period
  - ≥ 6 months of data prior to the initial diagnosis of MF
  - Received RUX as the first JAK inhibitor for MF between January 1 2013, and December 31, 2023
  - No other primary cancer diagnosis within 1 year before the initial MF diagnosis
  - No prior participation or concurrent enrollment in any interventional clinical trials
  - ≥ 6 months of follow-up data after initiation of RUX except for death
- Index date: the date of RUX initiation
- Follow-up period: from the index date to the end of the study observation period or death, whichever came first
- Patients were classified into 2 groups based on the TD status at index date
  - TD: had ≥ 1 unique date with RBC transfusion in the 6 weeks on or before RUX initiation
  - Non-TD (NTD): had 0 RBC transfusions in the 6 weeks on or before RUX initiation

### Variables and statistical analysis

- Demographic and clinical characteristics included age, sex, race/ethnicity, marital status, US region, MF type, Charlson Comorbidity Index (CCI) score, hemoglobin (Hb) level, and platelet count
- Treatment patterns included RUX treatment duration, RUX dosing patterns, and use of anemia supportive care (danazol, erythropoiesis-stimulating agents [ESAs], immunomodulatory imide drug [IMiD] agents, RBC transfusions)
- Characteristics and treatment patterns were analyzed using descriptive statistics

## Results

### Study population

- A total of 629 patients met the eligibility criteria and were included in the study (**Table 1**)
  - 122 (19.4%) were TD at RUX initiation
  - 507 (80.6%) were NTD at RUX initiation

### Demographic and clinical characteristics at RUX initiation

- Demographic characteristics were similar between patients who were TD or NTD at RUX initiation (**Table 1**)
  - For TD patients, the median age was 71 years, 96.7% were male, 77.1% were White, and 89.3% were non-Hispanic
  - For NTD patients, the median age was 72 years, 96.3% were male, 78.9% were White, and 92.5% were non-Hispanic
  - More than half of the patients had primary MF (TD: 62.3%; NTD: 60.2%)
- Patients who were TD at RUX initiation tended to have more comorbidities, and worse anemia and thrombocytopenia than NTD patients (**Table 1**)
  - For TD patients, 50.9% had a CCI score of ≥ 3, 95.9% had an anemia diagnosis on or before RUX initiation, 94.3% had an Hb level < 10 g/dL, and 42.1% had a platelet count < 150 × $10^9$/L
  - For NTD patients, 38.1% had a CCI score of ≥ 3, 61.3% had an anemia diagnosis on or before RUX initiation, 32.6% had an Hb level < 10 g/dL, and 24.2% had a platelet count < 150 × $10^9$/L
- Median time from initial MF diagnosis to RUX initiation was 10.9 months overall and similar between TD and NTD patients
- Median follow-up time from RUX initiation was 24.7 months overall, 15.7 months for TD patients, and 26.8 months for those who were NTD at RUX initiation

**Table 1. Patient demographic and clinical characteristics at RUX initiation**

| Characteristic | RUX patients (N = 629) | TD at RUX initiation (n = 122; 19.4%) | NTD at RUX initiation (n = 507; 80.6%) |
|---|---|---|---|
| **Age, median (range), years** | 72 (29-96) | 71 (66-77) | 72 (67-78) |
| **Male sex, n (%)** | 606 (96.3) | 118 (96.7) | 488 (96.3) |
| **Race, n (%)** | | | |
| White | 494 (78.5) | 94 (77.1) | 400 (78.9) |
| Black or African American | 97 (15.4) | 19 (15.6) | 78 (15.4) |
| Asian | 2 (0.3) | 0 | 2 (0.4) |
| Other[a] | 8 (1.3) | 1 (0.8) | 7 (1.4) |
| Unknown/missing | 28 (4.5) | 8 (6.6) | 20 (3.9) |
| **Ethnicity, n (%)** | | | |
| Hispanic or Latino | 33 (5.3) | 8 (6.6) | 25 (4.9) |
| Not Hispanic | 578 (91.9) | 109 (89.3) | 469 (92.5) |
| Unknown/missing | 18 (2.9) | 5 (4.1) | 13 (2.6) |
| **Marital status, n (%)** | | | |
| Married | 352 (56.0) | 60 (49.2) | 292 (57.6) |
| Divorced | 162 (25.8) | 43 (35.3) | 119 (23.5) |
| Other[b] | 113 (18.0) | 18 (14.8) | 95 (18.7) |
| Unknown/missing | 2 (0.3) | 1 (0.8) | 1 (0.2) |
| **US region, n (%)** | | | |
| Continental | 106 (16.9) | 21 (17.2) | 85 (16.8) |
| Midwest | 159 (25.2) | 29 (23.8) | 130 (25.6) |
| North Atlantic | 129 (20.5) | 27 (22.1) | 102 (20.1) |
| Pacific | 108 (17.2) | 21 (17.2) | 87 (17.2) |
| Southeast | 127 (20.2) | 24 (19.7) | 103 (20.3) |

**Table 1. Patient demographic and clinical characteristics at RUX initiation (cont.)**

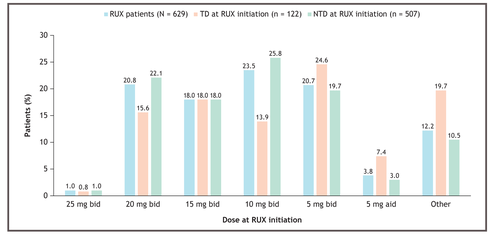
| Characteristic | RUX patients (N = 629) | TD at RUX initiation (n = 122; 19.4%) | NTD at RUX initiation (n = 507; 80.6%) |
|---|---|---|---|
| **MF type, n (%)** | | | |
| Primary MF | 381 (60.6) | 76 (62.3) | 305 (60.2) |
| Secondary MF | 248 (39.4) | 46 (37.7) | 202 (39.8) |
| **CCI score, median (IQR)** | 2 (0-3) | 3 (1-5) | 2 (0-3) |
| **CCI score, n (%)** | | | |
| 0 | 170 (27.0) | 20 (16.4) | 150 (29.6) |
| 1-2 | 204 (32.4) | 40 (32.8) | 164 (32.3) |
| 3-4 | 142 (22.6) | 24 (19.7) | 118 (23.3) |
| ≥ 5 | 113 (18.0) | 38 (31.2) | 75 (14.8) |
| **Anemia diagnosis before RUX initiation, n (%)** | 428 (68.0) | 117 (95.9) | 311 (61.3) |
| **Hb level at RUX initiation, n (%)[c]** | | | |
| N | 518 | 119 | 399 |
| Normal | 88 (17.0) | 0 | 88 (22.1) |
| Grade 1 | 188 (36.3) | 7 (5.9) | 181 (45.4) |
| Grade 2 | 170 (32.9) | 57 (47.9) | 113 (28.3) |
| Grade 3 | 58 (11.2) | 41 (34.6) | 17 (4.3) |
| Grade 4 | 14 (2.7) | 14 (11.8) | 0 |
| **Platelet count at RUX initiation, n (%)[d]** | | | |
| N | 506 | 119 | 387 |
| Normal | 362 (71.5) | 69 (58.0) | 293 (75.7) |
| Grade 1a | 61 (12.1) | 16 (13.5) | 45 (11.6) |
| Grade 1b | 38 (7.5) | 10 (8.4) | 28 (7.2) |
| Grade 2 | 23 (4.6) | 11 (9.2) | 12 (3.1) |
| Grade 3 | 14 (2.8) | 9 (7.6) | 5 (1.3) |
| Grade 4 | 8 (1.6) | 4 (3.4) | 4 (1.0) |
| **Time from initial MF diagnosis to RUX initiation, median (IQR), months** | 10.9 (1.4-35.5) | 10.4 (1.0-35.5) | 11.1 (1.4-35.6) |
| **Follow-up time from RUX initiation, median (IQR), months** | 24.7 (12.2-45.4) | 15.7 (6.7-31.2) | 26.8 (13.4-47.7) |
| **Year of RUX initiation, n (%)** | | | |
| 2012-2016 | 141 (22.4) | 33 (27.5) | 108 (21.3) |
| 2017-2020 | 304 (48.3) | 53 (43.4) | 251 (49.5) |
| 2021-2023 | 184 (29.3) | 36 (29.5) | 148 (29.2) |
| **Line of RUX treatment, n (%)** | | | |
| 1L | 397 (63.1) | 80 (65.6) | 317 (62.5) |
| 2L | 225 (35.8) | 39 (32.0) | 186 (36.7) |
| 3L+ | 7 (1.1) | 3 (2.5) | 4 (0.8) |

Totals may not sum to 100% due to rounding. [a]Patients who did not fit in the standard, structured fields were identified as other; [b]Other includes patients who were never married, separated, or widowed; [c]Grade 1, Mild: ≥ 10, < 12 g/dL for women and ≥ 10, < 13.5 g/dL for men; Grade 2, Moderate: ≥ 8, < 10 g/dL; Grade 3, Severe: ≥ 6.5, < 8 g/dL; Grade 4, Life-threatening: < 6.5 g/dL; [d]Grade 1a: ≥ 100, < 150 × $10^9$/L; Grade 1b: ≥ 75, < 100 × $10^9$/L; Grade 2: ≥ 50, < 75 × $10^9$/L; Grade 3: ≥ 25, < 49 × $10^9$/L; Grade 4: < 25 × $10^9$/L. 2L, second line; 3L+, third line and beyond; IQR, interquartile range.

### RUX treatment patterns

- Median duration of RUX treatment was shorter among patients who were TD (8.9 months; IQR, 2.6-18.9 months) at RUX initiation versus NTD patients (17.2 months; IQR, 7.4-34.9 months)
- Overall, approximately half of patients had a RUX dose reduction (51.5%, n = 324); 43.4% (n = 53) for TD patients, and 53.5% (n = 271) for NTD patients
- Fewer patients in the TD group (32.8%; n = 40) achieved maximum RUX total daily dose ≥ 40 mg than patients who were NTD at RUX initiation (40.6%; n = 206)
- Overall, ≤ 1% of patients started RUX at a dose of 25 mg twice daily (bid) (**Figure 1**)
  - The most common RUX starting dose was 5 mg bid for TD patients (24.6%) and 10 mg bid for NTD patients (25.8%)

**Figure 1. Dosing at RUX initiation**




### Anemia supportive care

- More patients in the TD group received anemia supportive care as drug treatment or RBC transfusion than patients who were NTD at RUX initiation (**Table 2**)
  - For TD patients, 91.0% received an RBC transfusion with a median time from RUX initiation to first RBC transfusion of 1 month, and 38.5% received an anemia supportive drug after RUX initiation (18.0% danazol, 27.1% ESAs, and 4.9% IMiD agents) with a median time from RUX initiation to first anemia supportive drug of 2 months
  - For NTD patients, 36.5% received an RBC transfusion with a median time from RUX initiation to first RBC transfusion of 8 months, and 18.5% received an anemia supportive drug after RUX initiation (6.9% danazol, 12.0% ESAs, and 2.8% IMiD agents) with a median time from RUX initiation to the anemia supportive drug of 5.7 months

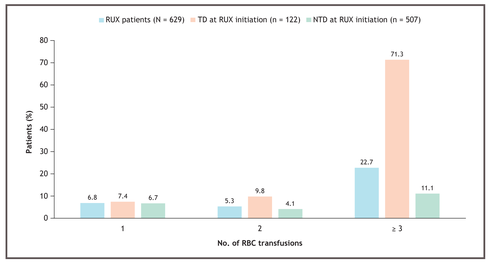
**Table 2. Anemia supportive care use**

| | RUX patients (N = 629) | TD at RUX initiation (n = 122) | NTD at RUX initiation (n = 507) |
|---|---|---|---|
| **Received RBC transfusion after RUX initiation, n (%)** | 296 (47.1) | 111 (91.0) | 185 (36.5) |
| No. of RBC transfusions within 1 year after RUX initiation, median (IQR) | 5 (2-11) | 10 (3-18) | 3 (1-6) |
| No. of RBC transfusions within 1 year after RUX initiation, PPPM | 0.5 (0.2-1.4) | 1.1 (0.5-2.1) | 0.3 (0.1-0.6) |
| **Time from RUX initiation to first RBC transfusion, median (IQR), months** | 3.0 (1.0-12.3) | 1.0 (0.2-1.1) | 8.0 (3.6-20.9) |
| **Received anemia supportive drug after RUX initiation, n (%)** | 141 (22.4) | 47 (38.5) | 94 (18.5) |
| Danazol | 57 (9.1) | 22 (18.0) | 35 (6.9) |
| ESAs | 94 (14.9) | 33 (27.1) | 61 (12.0) |
| Darbepoetin alfa | 53 (8.4) | 18 (14.8) | 35 (6.9) |
| Epoetin alfa | 38 (6.0) | 15 (12.3) | 23 (4.5) |
| Epoetin alfa-epbx | 19 (3.0) | 4 (3.3) | 15 (3.0) |
| IMiD agents | 20 (3.1) | 6 (4.9) | 14 (2.8) |
| Lenalidomide | 14 (2.2) | 4 (3.3) | 10 (2.0) |
| Thalidomide | 7 (1.1) | 3 (2.5) | 4 (0.8) |
| Pomalidomide | 1 (0.2) | 0 | 1 (0.2) |
| **Time from RUX initiation to first anemia supportive drug, median (IQR), months** | 4.7 (1.3-13.6) | 2.0 (0.7-5.6) | 5.7 (1.9-23.5) |

PPPM, per-patient-per-month.

- Overall, the median number of RBC transfusions received within 1 year after RUX initiation was 10 for patients who were TD at RUX initiation and 3 for NTD patients (**Table 2**)
  - For TD patients, 71.3% had ≥ 3 RBC transfusions within 1 year after RUX initiation (**Figure 2**)
  - For NTD patients, 11.1% had ≥ 3 RBC transfusions within 1 year after RUX initiation (**Figure 2**)

**Figure 2. Number of RBC transfusions within 1 year after RUX initiation**




## Limitations

- This study used the Veterans Health Administration data set where the majority of patients were male; therefore, the study results may not be generalizable to the broader US population or other countries
- These data describe anemia-related treatment patterns only for patients with anemia who have received RUX as their first JAK inhibitor; the results may not be applicable to the broader MF treatment population
- Factors related to physician prescribing behaviors or patient preference (eg, anemia supportive drug discontinuation reason) were not available
- There was a potential misclassification of TD status as this study used a simplified definition of TD due to unavailability of transfusion unit/volume in the VACDW

## Conclusions

- This retrospective real-world analysis showed a substantial burden of RBC transfusions for patients with MF and anemia treated with RUX
  - Anemia supportive drug use is not as prevalent as use of RBC transfusions regardless of high transfusion burden
  - The majority of patients who were TD at RUX initiation remained TD through the study period
  - Approximately one-quarter of patients who were NTD at RUX initiation received RBC transfusions within 1 year after RUX initiation
- Patients who were TD at RUX initiation were less likely to achieve maximum RUX total daily dose of ≥ 40 mg than NTD patients and had a shorter duration of treatment, illustrating the potential impact of anemia on clinical management of spleen size and symptoms for patients with MF

## References

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