# Real-world clinical outcomes in patients with myelofibrosis previously treated with ruxolitinib

MPN-070

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## Introduction

- Myelofibrosis (MF) is a hematologic malignancy characterized by splenomegaly and debilitating symptoms;[1] thrombocytopenia is a common disease-related feature of MF associated with a poor prognosis[2-5]
- The first approved *JAK1*/*JAK2* inhibitor, ruxolitinib (RUX), is commonly used as a first-line (1L) treatment for MF; however, its use is limited by the risk of severe thrombocytopenia[6]
- In recent years, two newer JAK inhibitors have received approval from the US Food and Drug Administration (FDA) for treatment of MF
  - In August 2019, fedratinib (FEDR) was approved for the treatment of MF[7]
    - The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) include FEDR as an initial therapy option, as well as a second-line option after no response or loss of response to initial treatment, for patients with intermediate-2- and high-risk MF with a platelet count ≥ 50 × 10⁹/L who are not transplant candidates[8]
  - In February 2022,[9] pacritinib (PAC) was approved for the treatment of adults with intermediate-2- or high-risk primary or secondary MF with a platelet count < 50 × 10⁹/L
- To date, there is limited real-world evidence on the comparative efficacy of these newer JAK inhibitors in patients with MF previously treated with RUX

## Objective

- To characterize the real-world clinical outcomes of patients with MF who received FEDR, PAC, or other MF therapies after discontinuing RUX treatment in US clinical practice

## Methods

### Data source

- This was a retrospective US observational cohort study of patients with MF treated in a network of primarily community oncology practices using the Integra Connect PrecisionQ Database, which contains electronic health records, practice management, and administrative claims data
- This data source includes > 1 million oncology-based patient records from some of the country's largest community oncology programs on the east and west coasts of the USA, representing > 1000 physicians enrolled in the program

### Study design

- Study observation period: earliest data available – March 31, 2023
- Study population: patients with MF who actively received any systemic treatments for MF between August 16, 2018 and September 30, 2022; eligibility criteria included:
  - Adults ≥ 18 years of age at first treatment
  - ≥ 2 MF diagnoses based on International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM; 289.83) or International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM; D75.81) codes and 2 documented visits between August 16, 2018 and September 30, 2022
  - Received RUX treatment and had ≥ 1 documented visit ≥ 6 months before RUX initiation
  - ≥ 1 documented visit ≥ 6 months after the index date unless the patient had died
- Patients were classified into 3 treatment groups based on therapies received post-RUX
  - FEDR group
  - PAC group
  - Other MF therapies group
- Index date: date of initial treatment with FEDR, PAC, or other therapies following treatment with RUX
- Baseline period: 6 months before the index date
- Follow-up period: from index date to the end of study observation period, death, or the last contact date, whichever comes first

### Data curation process

- The curation prioritized patients with MF who initiated FEDR after August 16, 2019 (US FDA approval date) or PAC after February 28, 2022 (US FDA approval date) with prior RUX treatment
  - Once all those patients were curated, patients who initiated other MF treatment after August 16, 2018 (1 year prior to US FDA approval date of FEDR) were prioritized
  - Once these patients were curated, a random sample of patients with MF who had received RUX were curated
- Curation audits were performed by quality auditors at Integra Connect; rebuttals were reviewed and reverted as required, and any errors were corrected by the curator within 48 hours

### Characteristics and outcomes

- Patient demographics, and clinical, diagnostic, and treatment characteristics were captured
- Clinical outcomes included:
  - Time on treatment (TOT): time from initiation of index treatment to discontinuation of index treatment
  - Overall survival (OS): time from initiation of index treatment to death

### Statistical analysis

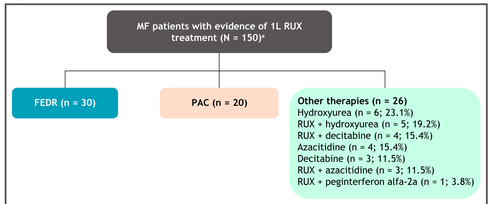
- Descriptive analyses of patient characteristics were reported as proportions for categorical variables and as mean (standard deviation [SD]) or median (range, interquartile range) as appropriate for continuous variables
- Kaplan-Meier analyses were conducted for TOT and OS in each post-RUX treatment group incorporating associated time of follow-up and censoring rules
  - TOT was censored on the last date a patient was known to be still on the index treatment
  - OS was censored on the last date a patient was known to be alive
  - Patients who were lost to follow-up were censored on the last contact date for both TOT and OS
- Subgroup analyses were performed among patients with thrombocytopenia (platelet count < 150 × 10⁹/L) and patients with platelet counts < 150 × 10⁹/L and ≥ 50 × 10⁹/L; patients without baseline laboratory values were not included in this analysis
- Statistical analyses were performed using SAS® 9.4 and Python 3.9 software

## Results

### Cohort overview

- The patient population included 150 patients treated with 1L RUX (**Figure 1**)
  - 30/150 (20.0%) patients received FEDR post RUX
  - 20/150 (13.3%) patients received PAC post RUX
  - 26/150 (17.3%) patients received other therapies post RUX (13 [50.0%] of whom received RUX retreatment combined with other therapies)
- **Table 1** provides an overview of the 3 post-RUX treatment groups

**Figure 1. Study cohort**




[a]Among the 74 patients not included in any of the 3 post-RUX treatment groups, 66 patients were still on 1L RUX and 8 patients initiated RUX retreatment combined with other therapies before August 16, 2018 (and were not eligible for inclusion in the post-RUX treatment groups).

**Table 1. Cohort overview[a]**

| | Post-RUX therapy | | |
|---|---|---|---|
| | FEDR (n = 30) | PAC (n = 20) | Other therapies (n = 26)[b] |
| **Duration of prior RUX therapy, median (range), months** | 15 (2-100) | 20 (2-86) | 27 (2-102) |
| **Follow-up time from post-RUX index therapy, median (range), months** | 18 (5-41) | 6 (0-11) | 11 (1-39) |
| **Time from MF diagnosis to initiation of post-RUX index therapy, median (range), months** | 51 (5-306) | 28 (4-189) | 39 (3-26) |
| **Year post-RUX therapy was initiated, n (%)** | | | |
| 2019 | 8 (26.7) | 0 | 1 (4.8) |
| 2020 | 12 (40.0) | 0 | 15 (57.7) |
| 2021 | 5 (16.7) | 0 | 6 (23.1) |
| 2022 | 5 (16.7) | 18 (90.0) | 4 (15.4) |
| 2023 | 0 | 2 (10.0) | 0 |

[a]Percentages may not total 100% due to rounding; [b]13 patients (50.0%) received RUX retreatment combined with other therapies, 6 (23.1%) received hydroxyurea, 4 (15.4%) received azacitidine, 3 (11.5%) received decitabine.

### Demographics and clinical characteristics

- Patient demographic characteristics at baseline are presented in **Table 2**
  - Median age (range) across treatment groups appeared similar (FEDR: 75 [56-88]; PAC: 76 [51-89]; and other therapies: 76 [59-88] years)
  - The majority of patients were treated in the community practice setting, although 35.0% of patients in the PAC group were treated in the academic practice setting

**Table 2. Baseline patient demographic characteristics[a]**

| | FEDR (n = 30) | PAC (n = 20) | Other therapies (n = 26) |
|---|---|---|---|
| **Age, years** | | | |
| Mean (SD) | 73.6 (8.3) | 75.3 (9.2) | 75.9 (7.8) |
| Median (range) | 75 (56-88) | 76 (51-89) | 76 (59-88) |
| **Sex, n (%)** | | | |
| Male | 17 (56.7) | 14 (70.0) | 13 (50.0) |
| **Race, n (%)** | | | |
| White | 17 (56.7) | 14 (70.0) | 18 (69.2) |
| Black or African American | 4 (13.3) | 1 (5.0) | 1 (3.8) |
| Asian | 0 | 0 | 0 |
| Other[b] | 9 (30.0) | 5 (25.0) | 7 (26.9) |
| American Indian or Alaska Native | 0 | 0 | 0 |
| **Ethnicity, n (%)** | | | |
| Hispanic or Latino | 2 (6.7) | 0 | 1 (3.8) |
| Not Hispanic or Latino | 21 (70.0) | 18 (90.0) | 20 (76.9) |
| Other[b] | 7 (23.3) | 2 (10.0) | 5 (19.2) |
| **Insurance type, n (%)** | | | |
| Commercial | 3 (10.0) | 6 (30.0) | 3 (11.5) |
| Medicare/Medicaid | 12 (40.0) | 8 (40.0) | 13 (50.0) |
| Self-pay | 1 (3.3) | 0 | 0 |
| Other[b] | 14 (46.7) | 5 (25.0) | 9 (34.6) |
| Missing | 0 | 1 (5.0) | 1 (3.8) |
| **Practice setting, n (%)** | | | |
| Academic | 2 (6.7) | 7 (35.0) | 1 (3.8) |
| Community | 26 (86.7) | 12 (60.0) | 24 (92.3) |
| Combined[c] | 2 (6.7) | 1 (5.0) | 1 (3.8) |

[a]Percentages may not total 100% due to rounding; [b]Patients who did not fit in the standard, structured fields were identified as other; [c]Patients treated by multiple practices in academic and community settings.

- Patient clinical characteristics at baseline are presented in **Table 3**
  - Hb levels were < 8 g/dL in 30.0% of patients who received FEDR and in 25.0% and 30.8% of patients who received PAC and other therapies, respectively
  - Platelet counts were > 100 × 10⁹/L in 56.6% of patients who received FEDR, and in 25.0% and 42.3% of patients who received PAC and other therapies, respectively
  - 70.0%, 65.0%, and 57.7% of patients were *JAK2* mutation positive in the FEDR, PAC, and other therapies groups, respectively

### TOT

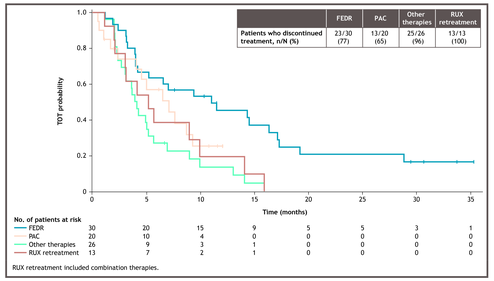
- For patients who received FEDR, median TOT was numerically longer (11.0 months) than in those who received PAC (7.0 months; $P = 0.155$) and significantly longer than in those who received other therapies (3.9 months, including 5.1 months for patients on RUX retreatment) ($P < 0.001$) (**Figure 2**)
- The probability of remaining on FEDR over time was numerically higher than for PAC, other therapies, or RUX retreatment
  - At 3 months, 90% of FEDR patients, 74% of PAC patients, and 65% of other therapies patients (including 71% of the RUX retreatment group) remained on post-RUX treatment
  - At 6 months, 63% of FEDR patients, 57% of PAC patients, and 27% of other therapies patients (including 36% of the RUX retreatment group) remained on post-RUX treatment
- Among patients with thrombocytopenia (platelet count < 150 × 10⁹/L; 18 FEDR patients, 14 PAC patients, and 14 other therapies patients), median TOT was numerically longer in patients who received FEDR (7.0 months) than in those who received PAC and other therapies (6.5 and 4.2 months, respectively)
- Among patients with platelet counts between < 150 × 10⁹/L and ≥ 50 × 10⁹/L (13 FEDR patients, 7 PAC patients, and 6 other therapies patients), median TOT was numerically longer in patients who received FEDR (7.0 months) than in those who received PAC and other therapies (2.3 and 3.1 months, respectively)

**Table 3. Baseline patient clinical characteristics[a]**

| | FEDR (n = 30) | PAC (n = 20) | Other therapies (n = 26) |
|---|---|---|---|
| **Anemia, n (%)** | | | |
| Normal | 2 (6.7) | 0 | 0 |
| G1 (mild: Hb 10-12 g/dL women; 10-14 g/dL men) | 4 (13.3) | 3 (15.0) | 8 (30.8) |
| G2 (moderate: Hb 8 to < 10 g/dL | 13 (43.3) | 8 (40.0) | 8 (30.8) |
| G3 (severe: Hb 6.5 to < 8 g/dL | 7 (23.3) | 4 (20.0) | 6 (23.1) |
| G4 (life-threatening: Hb < 6.5 g/dL) | 2 (6.7) | 1 (5.0) | 2 (7.7) |
| Missing or not tested | 2 (6.7) | 4 (20.0) | 2 (7.7) |
| **Thrombocytopenia, n (%)** | | | |
| Normal | 10 (33.3) | 2 (10.0) | 8 (30.8) |
| G1a (PLT count 101-150 × 10⁹/L) | 7 (23.3) | 3 (15.0) | 3 (11.5) |
| G1b (PLT count 75-100 × 10⁹/L) | 2 (6.7) | 1 (5.0) | 2 (7.7) |
| G2 (PLT count 50-74 10⁹/L) | 4 (13.3) | 3 (15.0) | 1 (3.8) |
| G3 (PLT count 25-49 10⁹/L) | 3 (10.0) | 4 (20.0) | 4 (15.4) |
| G4 (PLT count < 25 × 10⁹/L) | 2 (6.7) | 3 (15.0) | 4 (15.4) |
| Missing or not tested | 2 (6.7) | 4 (20.0) | 4 (15.4) |
| **Age-adjusted CCI, n (%)** | | | |
| 0-1 | 1 (3.3) | 1 (5.0) | 1 (3.8) |
| 2-3 | 11 (36.7) | 3 (15.0) | 6 (23.1) |
| ≥ 4 | 18 (60.0) | 16 (80.0) | 19 (73.1) |
| **ECOG PS, n (%)** | | | |
| 0 | 5 (16.7) | 0 | 3 (11.5) |
| 1 | 12 (40.0) | 2 (10.0) | 9 (34.6) |
| 2 | 1 (3.3) | 3 (15.0) | 0 |
| 3 | 1 (3.3) | 0 | 2 (7.7) |
| Missing | 11 (36.7) | 15 (75.0) | 12 (46.2) |
| ***JAK2* mutation, n (%)** | | | |
| Positive | 21 (70.0) | 13 (65.0) | 15 (57.7) |
| Negative | 8 (26.7) | 6 (30.0) | 10 (38.5) |
| Missing or not tested | 1 (3.3) | 1 (5.0) | 1 (3.8) |
| ***CALR* mutation, n (%)** | | | |
| Positive | 4 (13.3) | 4 (20.0) | 3 (11.5) |
| Negative | 13 (43.3) | 11 (55.0) | 14 (53.8) |
| Missing or not tested | 13 (43.3) | 5 (25.0) | 9 (34.6) |
| ***MPL* mutation, n (%)** | | | |
| Positive | 4 (13.3) | 3 (15.0) | 2 (7.7) |
| Negative | 6 (20.0) | 9 (45.0) | 15 (57.7) |
| Missing or not tested | 20 (66.7) | 8 (40.0) | 9 (34.6) |

[a]Percentages may not total 100% due to rounding.
CCI, Charlson Comorbidity Index; ECOG PS, Eastern Cooperative Oncology Group performance status, Hb, hemoglobin; PLT, platelet.

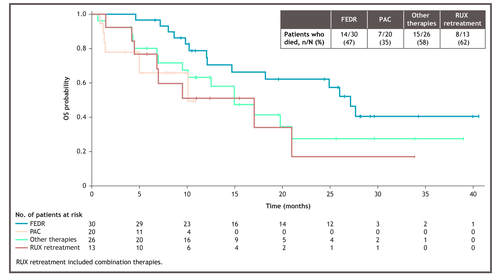
**Figure 2. TOT for patients treated with FEDR, PAC, other therapies, and RUX retreatment**




### OS

- Median OS was numerically longer in patients who received FEDR (27.1 months) than in those who received PAC (10.1 months; $P = 0.032$) and than in those who received other therapies or RUX retreatment (14.9 and 17.0 months, respectively) ($P = 0.106$) (**Figure 3**)
- The probability of survival over time was numerically higher in patients receiving FEDR than PAC, other therapies, or RUX retreatment
  - At 6 months, 97%, 65%, and 80% of patients were alive in the FEDR, PAC, and other therapies (including 77% of the RUX retreatment group), respectively
  - At 12 months, 79%, 50%, and 63% of patients were alive in the FEDR, PAC, and other therapies (including 51% of the RUX retreatment group), respectively

**Figure 3. OS for patients treated with FEDR, PAC, other therapies, and RUX retreatment**




- Among patients with thrombocytopenia (platelet count < 150 × 10⁹/L; 18 FEDR patients, 14 PAC patients, and 14 other therapies patients), median OS was numerically longer in patients who received FEDR (24.9 months) than in those who received PAC and other therapies (10.1 and 19.8, respectively)
- Among patients with platelet counts between < 150 × 10⁹/L and ≥ 50 × 10⁹/L (13 FEDR patients, 7 PAC patients, and 6 other therapies patients), median OS was numerically longer in patients who received FEDR (26.0 months) than in those who received other therapies (12.5 months); median OS not reached for PAC group

## Limitations

- The results should be interpreted in the context of the study sample selection criteria and limited sample size
- This study is descriptive rather than comparative in nature, and findings may be susceptible to unadjusted confounders
- These data describe outcomes only for patients who, by design, have initiated RUX as their 1L therapy
- Factors related to physician prescribing behaviors or patient preference (eg, treatment discontinuation reasons) were unavailable

## Conclusions

- Although limited by sample size, this real-world US study demonstrated that TOT and OS were longer with FEDR in the post-RUX setting than other commercially available options
- In the smaller subset of patients with thrombocytopenia at baseline, patients remained on treatment longer and lived longer with FEDR than other options

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