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RESEARCH ARTICLE

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Real-world treatment patterns and health outcomes for patients with myelofibrosis treated with fedratinib

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ABSTRACT

Aim: Assess real-world fedratinib (FEDR) treatment patterns and clinical outcomes in patients with primary or secondary myelofibrosis following discontinuation of ruxolitinib (RUX).

Patients & Methods: This study was a retrospective, noninterventional medical record review of patients in Canada, Germany, and the United Kingdom (UK). A total of 70 physicians (primarily hematologist-oncologists [78.6%]) provided data for 196 eligible patients.

Results: Patients were mostly male (62.8%) with primary myelofibrosis (76.5%) and initiated FEDR at a mean age of 67.7 years. Median treatment duration was 11.5 months (median follow-up, 13.8 months), and nearly half (49.5%) of patients initiated FEDR at the label-indicated dose of 400 mg daily. Six months post-initiation, 77.7% and 66.8% of patients experienced symptom and spleen response, respectively. Kaplan-Meier estimates of median progression-free and overall survival from initiation were 23.8 months (95% CI, 21.1–27.6) and 29.8 months (95% CI, 23.9-NE), respectively.

Conclusion: These findings demonstrate real-world FEDR effectiveness among patients with myelofibrosis who discontinued RUX.

PLAIN LANGUAGE SUMMARY

What is this summary about?

Myelofibrosis (MF) is a rare blood cancer that can cause unhealthy spleen growth and symptoms, such as feeling tired, loss of appetite, bone pain, and fever. This is a summary of an article that reviewed medical records of patients with MF from treatment centers in Canada, Germany, and the United Kingdom (UK). The study looked at people who had been taking a medication called fedratinib (FEDR) for their MF after they had stopped taking a different medication called ruxolitinib (RUX). Many of the people stopped taking RUX because their MF got worse within a few years. The study wanted to see if taking FEDR reduced symptoms and spleen size for people with MF after they stopped taking RUX.

What were the results?

After at least 6 months of taking FEDR, 77.7% of the people in the study had fewer symptoms, and 66.8% of people in the study had a decrease in spleen size or no spleen growth. Additionally, most people taking FEDR after discontinuing RUX went nearly 2 years without their MF symptoms or illness getting worse.

What do the results mean?

These results suggest that FEDR is an effective treatment for people with MF who have stopped taking RUX.

ARTICLE HISTORY
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KEYWORDS
Myelofibrosis; fedratinib; ruxolitinib; real-world evidence; survival analysis; medical record review

1. Introduction

Myeloproliferative neoplasms (MPNs) are rare and heterologous conditions caused by proliferation of clonal hematopoietic stem cells [1,2]. Though clinical presentation is variable, MPNs often have common genetic characteristics, including a prevalent mutation to the gene encoding Janus kinase 2 (JAK2) [3]. The 3 main types of MPNs are primary myelofibrosis (MF), polycythemia vera (PV), and essential thrombocythemia (ET). PV and ET may progress into post-polycythemia vera (PPV) and post-essential thrombocythemia (PET), conditions collectively referred to as secondary MF. MF is characterized by bone marrow fibrosis, splenomegaly, and anemia, as well as debilitating constitutional symptoms, such as fatigue, early satiety, fever, bone pain, and pruritus [1,4,5]. Median overall survival (OS) for individuals with MF is 5–7 years [6–9]. The only curative treatment for MF is allogenic hematopoietic stem-cell transplantation (allo-HSCT); however, allo-HSCT is associated with high morbidity and mortality risks that leave only a minority of individuals with MF eligible for the therapy [5,10]. Other treatments for MF are therefore limited to symptom control, decreasing spleen volume, improving quality of life, and increasing survival.

The development of targeted, life-prolonging therapies over the last decade has changed the treatment landscape, especially for people with MF who are ineligible for allo-HSCT. Increased

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Article highlights

Myelofibrosis (MF) is a blood cancer with limited treatment options

- MF is characterized by spleen enlargement and debilitating constitutional symptoms, and curative treatment options are limited. Ruxolitinib (RUX) was the only targeted, life-prolonging therapy for MF available before the approval of fedratinib (FEDR), but most patients discontinue RUX within 3 years due to adverse events, symptom progression, disease progression, or death.

FEDR is an effective treatment for people with MF who have discontinued RUX

- Forty-two percent of patients included in the study experienced complete symptom resolution of MF-related symptoms, and 66.8% experienced spleen size reduction during the first 6 months of FEDR initiation after RUX discontinuation. These findings align with clinical benefit of FEDR reported in the FREEDOM2 clinical trial as well as a US-based real-world study.

Future directions

- This study demonstrates a real-world clinical benefit of FEDR following RUX treatment failure for individuals with MF in Canada, Germany, and the UK. FEDR should be considered as a treatment option for patients with MF who discontinued RUX.

understanding of MPN and MF oncogenic drivers, such as *JAK2 V617F* mutation—observed in an estimated 45%-68% of individuals with MF—led to the development of JAK inhibitors ruxolitinib (RUX) and fedratinib (FEDR) approved by the European Medicines Agency (EMA) and United States (US) Food and Drug Administration for treatment of MF [1,11–14]. RUX was approved in 2012 by the EMA and was the only approved JAK inhibitor available before EMA approval of FEDR in 2021. In clinical practice, RUX treatment provided improvements in symptoms and quality of life for individuals with MF, but up to 89% of patients discontinued within 3 years for reasons, including toxicity or adverse events (e.g., thrombocytopenia, worsening of anemia), disease progression, or death [15,16].

FEDR is currently approved for treatment of adults with intermediate-2 or high-risk primary or secondary MF. Results from the FREEDOM2 clinical trial indicated superior performance of FEDR compared with best available therapy in reducing spleen volume and MF-related symptom burden among people with MF who were previously treated with RUX [17,18]. In a real-world, US-based study, FEDR therapy following RUX discontinuation was associated with decreased spleen size and MF-related symptoms after 3 months of treatment [19,20]. However, prior to this study, real-world evidence (RWE) on individuals with MF receiving FEDR after RUX failure in routine practice settings in Canada and Europe was limited. The objective of this study was to describe patient demographics, clinical characteristics, treatment patterns, and clinical outcomes of patients with primary or secondary MF who received FEDR after discontinuing RUX in clinical practice in Canada, Germany, and the United Kingdom (UK). Study results provide RWE to corroborate findings from the FREEDOM2 trial, provide insights on the use and effectiveness of FEDR in real-world practice, and inform providers and patients on treatment decisions.

2. Patients & methods

2.1. Study design

A retrospective, noninterventional review of data extracted from medical records was conducted to assess FEDR treatment patterns and clinical outcomes. Physicians from treatment centers in Canada, Germany, and the UK led data extraction from medical records of patients diagnosed with primary or secondary MF who received treatment with FEDR following discontinuation of RUX due to treatment refractoriness, relapse, or intolerance. Patients were required to have initiated FEDR from the date of first availability in each country (21 September 2020 [Canada], 9 February 2021 [Germany], or 1 November 2021 [UK]) to 6 months before initiation of data extraction (last extraction date: 31 August 2023) to allow for at least 6 months of follow-up opportunity for each patient (Supplemental Figure S1). In our study, eligible patients had initiated FEDR between 29 September 2020 and 2 September 2022, with initiation of FEDR defining the study index date.

An electronic data collection form (eDCF) was programmed and disseminated to physicians to screen physician and patient eligibility and to collect detailed information required to address study objectives. All patient data were deidentified, and data were collected from March through August 2023. Results were described for country-specific and pooled patient populations. RTI International's Institutional Review Board deemed the study exempt from full review, and the study was further reviewed and approved or exempted by country-specific ethics review committees.

2.1.1. Physician and patient selection criteria

Qualifying physicians were required to be a practicing hematologist, oncologist, or hematologist-oncologist; to have treated at least 5 patients with primary or secondary MF in the year before data extraction (ensuring physicians have recent experience treating patients with MF with potentially diverse disease characteristics); and to have experience treating patients with FEDR. Patients eligible for inclusion had received FEDR for at least 28 days (i.e., 1 complete cycle), had intermediate-2 or high-risk MF at FEDR initiation or at initial MF diagnosis, and had their spleen size assessed via palpation at FEDR initiation and at least once during the first 6 months of FEDR treatment. Patients who received allo-HSCT after initial MF diagnosis or who participated in a clinical trial involving JAK2 inhibitors for the treatment of MF were excluded.

2.2. Study endpoints

2.2.1. Patient characteristics

Patient demographic characteristics were recorded at baseline and included age at initial diagnosis of primary or secondary MF, age at FEDR initiation, sex, race/ethnicity, vital status at the time of medical record extraction, and total duration of follow-up. Patient clinical characteristics were recorded at initial MF diagnosis and at FEDR initiation, periodic intervals during treatment, and discontinuation on the basis of data availability at each timepoint. Year of diagnosis; MF grade via bone marrow biopsy, if conducted; past or current MPNs or hematologic disorders; genetic mutation status; and unfavorable chromosomal abnormalities, if any, were recorded at the time of MF diagnosis. Disease type (i.e., primary or secondary MF) and

Dynamic International Prognostic Scoring System (DIPSS) or International Prognostic Scoring System (IPSS) risk category were recorded at initial diagnosis of MF and treatment initiation with FEDR [21]. Eastern Cooperative Oncology Group (ECOG) or Karnofsky score performance status (PS) and comorbidity burden – represented by Charlson Comorbidity Index score from the 12 months prior – were recorded at FEDR initiation [22]. Constitutional symptom presence, platelet counts, spleen size via palpation, and testing for thiamine (i.e., vitamin B_1) were recorded at FEDR initiation and periodically during treatment, including at FEDR discontinuation.

2.2.2. Treatment patterns

Characteristics of FEDR treatment assessed included time to initiation from initial MF diagnosis and RUX discontinuation; rationale for initiation; total duration of treatment; initial and last dose, including any dose modifications or therapy interruptions; and rationale for discontinuation, if applicable. Treatments or procedures prior to FEDR initiation were recorded, with detailed information on RUX therapy, including time from initial MF diagnosis to FEDR initiation; total duration of FEDR treatment; initial and last dose of FEDR, including any dose modifications; and reasons for FEDR discontinuation. Any treatments received concurrently with FEDR (e.g., therapy to prevent gastrointestinal toxicity, transfusions, and other supportive care) were also recorded.

2.2.3. Symptom and spleen response

The total number of constitutional symptoms (e.g., fatigue, early satiety, weight loss, night sweats, fever, bone pain, and pruritus) were assessed at baseline and at 3 and 6 months after FEDR initiation. Spleen size evaluation results were recorded at baseline and every month for 6 months after FEDR initiation. Symptom response, as measured by increase or decrease in the total number of constitutional symptoms compared with the symptoms recorded at the time of FEDR initiation, was assessed at 3 and 6 months after FEDR initiation. Spleen response was assessed as either no splenomegaly or decrease in spleen size as compared with the spleen size recorded at the time of FEDR initiation. Time to spleen response was defined as the time from FEDR initiation to first reported date of spleen size decrease (including no splenomegaly); patients with no change or an increase in spleen size were censored. The proportions of patients with no splenomegaly (spleen not palpable), mild splenomegaly (spleen barely palpable or palpable just below the costal margin [5–10 cm can be palpated]), moderate splenomegaly (spleen palpable between the costal margin and umbilicus [11–20 cm can be palpated]), or severe splenomegaly (spleen palpable near the umbilicus [>20 cm can be palpated]) were assessed at baseline and every month for 6 months after FEDR initiation.

2.2.4. Disease progression and survival outcomes

Date of clinician-determined disease progression and the criteria used for determination (including International Working Group-Myeloproliferative Neoplasms Research and Treatment [IWG-MRT] criteria, constitutional symptoms, spleen size/volume, blood tests), and date of death (if applicable) were recorded. Real-world progression-free survival (rw-PFS) was defined as time from FEDR initiation to disease progression (clinician determined, or FEDR discontinuation due to anemia, splenomegaly, or loss of response) with all-cause death as a competing event; patients who did not experience progression and/or were alive at the time of record extraction were censored at the end of available follow-up. OS was defined as time from FEDR initiation until all-cause death; patients alive at the time of record extraction were censored at the end of available follow-up.

2.3. Statistical analysis

All analyses were descriptive and performed using SAS statistical analysis software, version 9.4 (accessed through SAS Studio version 3.8, SAS Institute). Continuous variables of interest were summarized with mean values, medians, quartiles, ranges, and standard deviations (SDs). Categorical variables of interest were summarized with frequency distributions. Time-to-event outcomes (i.e., rw-PFS, OS, time to spleen response) were estimated using Kaplan-Meier analysis.

3. Results

3.1. Study population

A total of 70 physicians across Canada ($n = 21$), Germany ($n = 24$), and the UK ($n = 25$) provided data for 196 eligible patients with MF (Canada, $n = 45$ [23.0%]; Germany, $n = 86$ [43.9%]; UK, $n = 65$ [33.2%]). Most physicians (78.6%) were hematologist-oncologists in practice for an average of 16.7 years (SD, 7.1), and about two-thirds practiced in a large practice setting.

Demographic characteristics of the pooled and country-specific patient populations included in this study are detailed in Table 1. Among the pooled study cohort, mean (SD) age at initial primary or secondary MF diagnosis was 64.7 years (10.3) and at FEDR initiation was 67.7 years (9.6). Most of the pooled cohort was male (62.8%) and White (82.7%). Among country-specific cohorts, a greater proportion of individuals in the UK identified as male (70.8%) compared with Germany (65.1%) and Canada (46.7%), and a greater proportion of individuals in Germany identified as White (97.7%) compared with Canada (73.3%) and the UK (69.2%). At the time of medical record extraction, 78.1% of eligible patients were alive. Mean (SD) duration of follow-up for the pooled cohort was 14.0 months (5.5) (Canada, 17.2 months [8.4]; Germany, 13.4 months [4.1]; UK, 12.6 months [3.5]).

Baseline clinical characteristics at FEDR initiation are presented in Table 2 and Supplemental Table S1. At baseline, patients in the pooled cohort had a mean of 2.1 comorbidities (SD, 1.5) and mean Charlson Comorbidity Index score of 2.1 (SD, 1.3). The most common comorbidities included hypertension (50.0%), cardiovascular disease (37.2%), and diabetes without end organ damage (20.4%). The most commonly reported mutation was *JAK2 V617F* (56.1%), and nearly two-thirds of patients did not have any chromosomal abnormality (65.3%). Most (76.5%) of the pooled cohort had primary MF; 55.1% were considered intermediate-2 risk, and 22.4% were

Table 1. Demographic characteristics.

Characteristic	All countries (*N* = 196)	Canada (*n* = 45)	Germany (*n* = 86)	UK (*n* = 65)
Age at initial primary or secondary MF diagnosis, years				
n	196	45	86	65
Mean (SD)	64.7 (10.3)	62.5 (11.2)	67.4 (9.8)	62.6 (9.5)
Median (Q1, Q3)	65.8 (58.5, 72.4)	65.3 (55.1, 71.6)	69.5 (60.7, 75.1)	63.6 (57.9, 67.8)
Age at FEDR initiation, years				
N	196	45	86	65
Mean (SD)	67.7 (9.6)	67.7 (9.2)	69.9 (9.4)	64.8 (9.4)
Median	68.7	70.3	71.7	64.8
Sex, n (%)				
Male	123 (62.8)	21 (46.7)	56 (65.1)	46 (70.8)
Female	73 (37.2)	24 (53.3)	30 (34.9)	19 (29.2)
Race or ethnicity, n (%)[a]				
African/Black	13 (6.6)	3 (6.7)	0 (0.0)	10 (15.4)
East Asian[b]	3 (1.5)	2 (4.4)	0 (0.0)	1 (1.5)
South Asian[c]	8 (4.1)	2 (4.4)	0 (0.0)	6 (9.2)
Middle Eastern	8 (4.1)	3 (6.7)	2 (2.3)	3 (4.6)
White	162 (82.7)	33 (73.3)	84 (97.7)	45 (69.2)
Unknown/not documented	3 (1.5)	3 (6.7)	0 (0.0)	0 (0.0)
Vital status at medical record extraction, n (%)				
Alive	153 (78.1)	32 (71.1)	65 (75.6)	56 (86.2)
Deceased	42 (21.4)	13 (28.9)	21 (24.4)	8 (12.3)
Lost to follow-up/unable to contact	1 (0.5)	0 (0.0)	0 (0.0)	1 (1.5)
Total duration of follow-up, months[d]				
N	196	45	86	65
Mean (SD)	14.0 (5.5)	17.2 (8.4)	13.4 (4.1)	12.6 (3.5)
Median (Q1, Q3)	13.8 (10.4, 16.2)	15.3 (10.6, 24.7)	14.1 (12.0, 15.9)	12.9 (9.5, 15.0)

FEDR = fedratinib; MF = myelofibrosis; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; UK = United Kingdom.
[a]Multiple responses allowed; thus, rows may add up to greater than 100%.
[b]Mainland China, Hong Kong, Macau, Taiwan, Japan, Mongolia, North Korea, and South Korea.
[c]India, Pakistan, Bangladesh, Nepal, Bhutan, the Maldives, Sri Lanka.
[d]Length of follow-up is the duration of time between the date of initiation of FEDR (index date) and death or end of patient record.

considered high risk at FEDR initiation. A greater proportion of patients in the UK had primary MF (92.3%) compared with Canada (75.6%) and Germany (65.1%). Most patients were intermediate-2 risk in Germany (59.3%), the UK (55.4%), and Canada (46.7%), and the highest proportion of high-risk patients was in the UK (32.3% versus 16.3%-20.0%).

Among the 81.6% of patients across countries with a bone marrow biopsy at initial MF diagnosis, 60.0% had grade 2 bone marrow fibrosis. Most patients had moderate (56.1%) or severe (24.5%) splenomegaly at FEDR initiation. The most commonly reported MF-related symptoms at baseline were fatigue (65.3%), abdominal discomfort (56.1%), night sweats (32.7%), and unintentional weight loss (25.5%).

3.2. Treatment patterns

3.2.1. Treatments received prior to fedratinib initiation

Patients included in the study were required to have received and discontinued treatment with RUX prior to FEDR initiation. Characteristics of RUX treatment are detailed in Supplemental Table S2. Across countries, median time to RUX initiation from MF diagnosis was 1.5 months (interquartile range [IQR], 0.5–12.0) and median duration of RUX treatment was 15.0 months (IQR, 6.8–30.1). Patients in Canada had both longer median time to RUX initiation (3.4 months [IQR, 0.6–48.1]) and median duration of RUX treatment (31.1 months [IQR, 12.2–53.4]) compared with patients in the other countries (median initiation, 1.0–1.5 months; median duration, 8.5–16.3 months). For the pooled cohort, common reasons indicated for RUX discontinuation were relapse or disease progression (59.7%), intolerance to RUX (i.e., hematologic toxicity [e.g., anemia, thrombocytopenia], nonhematologic toxicity) (25.0%), and treatment refractoriness (19.9%). Relapse or disease progression was provided as rationale for discontinuation more often for patients in Canada (71.1%) and Germany (72.1%) than in the UK (35.4%), while intolerance was less common in Germany (14.0%) than other countries (31.1%-35.4%). Across countries, 27.6% of patients received no other therapies in addition to RUX prior to FEDR initiation; other treatments or procedures commonly received included red blood cell transfusion (27.6%), hydroxyurea (23.0%), and erythropoietin (12.2%).

3.2.2. Fedratinib treatment and concurrent supportive treatment

FEDR treatment characteristics are presented in Table 3 and Supplemental Table S3. Patients initiated FEDR an average of 2.9 (SD, 5.8) months after RUX discontinuation, most often for reasons of RUX failure (59.2%), FEDR efficacy (57.1%), splenomegaly (54.6%), and/or symptom control (48.5%). Overall, mean duration of FEDR treatment was 11.5 months (SD, 6.2) and 45.9% of the pooled cohort received FEDR for ≥12 months. Average duration of overall FEDR treatment was shorter for patients in the UK (8.1 months [SD, 4.3]) than for patients in Canada (14.0 months [SD, 8.5]) or Germany (12.7 months [SD, 4.7]). At the time of data extraction, 108 patients (55.1%) had ongoing treatment and 88 patients (44.9%) had discontinued FEDR (Supplemental Figure S2). Nearly 75% of patients in Germany had FEDR treatment ongoing at medical record extraction, while 48.9% of patients in Canada and 33.8% of patients in the UK had treatment ongoing. Across countries, the observed mean duration of treatment for those with

Table 2. Clinical characteristics at fedratinib initiation.

Characteristic	All countries (*N* = 196)	Canada (*n* = 45)	Germany (*n* = 86)	UK (*n* = 65)
MF type, n (%)				
Primary MF	150 (76.5)	34 (75.6)	56 (65.1)	60 (92.3)
Post-polycythemia vera (PPV) MF	31 (15.8)	9 (20.0)	18 (20.9)	4 (6.2)
Post-essential thrombocythemia (PET) MF	15 (7.7)	2 (4.4)	12 (14.0)	1 (1.5)
DIPSS or IPSS risk status, n (%)				
Intermediate-2 risk	110 (56.1)	16 (35.6)	52 (60.5)	42 (64.6)
High risk	86 (43.9)	29 (64.4)	34 (39.5)	23 (35.4)
MF-related symptoms, n (%)[a,b]				
Abdominal discomfort (feeling pressure or bloating)	110 (56.1)	29 (64.4)	51 (59.3)	30 (46.2)
Bone pain (diffuse, not joint pain or arthritis)	43 (21.9)	20 (44.4)	12 (14.0)	11 (16.9)
Concentration problems (compared with concentration prior to MF)	37 (18.9)	16 (35.6)	18 (20.9)	3 (4.6)
Early satiety (early feeling of fullness after eating)	61 (31.1)	26 (57.8)	17 (19.8)	18 (27.7)
Fatigue (weariness, tiredness)	128 (65.3)	40 (88.9)	58 (67.4)	30 (46.2)
Fever	27 (13.8)	15 (33.3)	8 (9.3)	4 (6.2)
Inactivity	41 (20.9)	10 (22.2)	24 (27.9)	7 (10.8)
Itching/pruritus	37 (18.9)	10 (22.2)	20 (23.3)	7 (10.8)
Night sweats	64 (32.7)	17 (37.8)	28 (32.6)	19 (29.2)
Numbness/tingling (in hands/feet)	11 (5.6)	5 (11.1)	5 (5.8)	1 (1.5)
Pain under ribs on left side	39 (19.9)	11 (24.4)	18 (20.9)	10 (15.4)
Weight loss (unintentional) in the last 6 months	50 (25.5)	19 (42.2)	18 (20.9)	13 (20.0)
No MF-related symptoms	9 (4.6)	0 (0.0)	2 (2.3)	7 (10.8)
MF-related symptoms not evaluated	11 (5.6)	0 (0.0)	0 (0.0)	11 (16.9)
Spleen size[b]				
Physical evaluation, n (%)	196 (100.0)	45 (100.0)	86 (100.0)	65 (100.0)
No splenomegaly, spleen not palpable	4 (2.0)	0 (0.0)	0 (0.0)	4 (6.2)
Spleen barely palpable or palpable just below the costal margin (very mild or mild splenomegaly: 5–10 cm can be palpated)	34 (17.3)	7 (15.6)	10 (11.6)	17 (26.2)
Spleen palpable between the costal margin and umbilicus (moderate splenomegaly: 11–20 cm can be palpated)	110 (56.1)	29 (64.4)	45 (52.3)	36 (55.4)
Spleen palpable near the umbilicus (severe splenomegaly: > 20 cm can be palpated)	48 (24.5)	9 (20.0)	31 (36.0)	8 (12.3)
Spleen palpable but other details unknown	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

CCI = Charlson Comorbidity Index; DIPSS = Dynamic International Prognostic Scoring System; ECOG = Eastern Cooperative Oncology Group; FEDR = fedratinib; IPSS = International Prognostic Scoring System; MF = myelofibrosis; Q1 = first quartile; Q3 = third quartile; PS = performance status; SD = standard deviation; UK = United Kingdom.
[a]Multiple responses allowed; thus, rows may add up to greater than 100%.
[b]At the evaluation closest to and before FEDR initiation.

FEDR treatment ongoing at the time of extraction was 14.5 months (SD, 4.8), and for those who discontinued FEDR, it was 7.8 months (SD, 5.5). Patients in Canada had the longest mean treatment duration among those with FEDR treatment ongoing at the time of extraction (15.6 months [SD, 8.7]), followed by Germany (14.9 months [SD, 2.6]) and the UK (12.3 months [SD, 4.1]). Of those who discontinued FEDR, mean treatment duration was 12.5 months (SD, 8.3) in Canada, 6.3 months (SD, 3.3) in Germany, and 6.0 months (SD, 2.4) in the UK.

Nearly half of patients (49.5%) in the pooled cohort initiated FEDR at a daily dose of 400 mg, which increased to approximately 65% of patients at FEDR discontinuation. Though FEDR dose was not changed for most patients across countries (77.0%), patients with dose changes most often experienced one change (15.8%), and the change was most often for reasons of titration to therapeutic dose (82.2%). In the pooled cohort, 44.4% of patients received no other therapy along with FEDR. Among those receiving concomitant treatments or procedures with FEDR, many received erythropoiesis-stimulating agents (21.9%), corticosteroids (24.5%), thiamine (15.8%), and anti-gastrointestinal toxicity treatments (41.3%). Additional concurrent or supportive care, such as red blood cell transfusions, nonopioid analgesics, and antibiotics was received by 29.1%-52.0% of patients. Among the patients who discontinued FEDR, the most frequently reported reasons for discontinuation were improvement in patient's condition with no additional clinical benefit of continued treatment anticipated (25.0%), patient decision (21.6%), and death of patient (20.5%) (Table 3).

3.3. Clinical outcomes

3.3.1. MF-related symptom burden and symptom response during the first 6 months of fedratinib treatment

Data on MF-related symptom burden at baseline and symptom resolution at 3 and 6 months after FEDR initiation are presented in Table 4 and Figure 1(a). At FEDR initiation, patients had a mean (SD) of 3.5 (2.1) MF-related symptoms (Canada, 4.8 [2.7]; Germany, 3.3 [1.6]; UK, 2.9 [1.9]). The total number of symptoms decreased for 65.9% of the pooled cohort at 3 months (mean [SD] number of symptoms: Canada, 2.4 [1.6]; Germany, 2.3 [1.8]; UK, 1.7 [1.4]) and for 77.7% of the pooled cohort at 6 months (mean [SD] number of symptoms: Canada, 1.8 [2.0]; Germany, 1.4 [1.6]; UK, 0.8 [1.2]) of FEDR treatment. Resolution of at least 1 baseline symptom was reported for 73.4% of patients at 3 months and 82.2% of patients at 6 months after FEDR initiation, while complete resolution of baseline symptoms was reported for 15.6% of patients at 3 months and 42.0% of patients at 6 months after FEDR initiation. Higher proportions of patients in the UK had complete resolution of baseline symptoms at both 3 (28.6%) and 6 (46.9%) months of FEDR treatment compared

Table 3. Fedratinib treatment characteristics.

Characteristic	All countries (*N* = 196)	Canada (*n* = 45)	Germany (*n* = 86)	UK (*n* = 65)
Time from MF diagnosis to FEDR initiation, months				
Mean (SD)	36.8 (35.0)	62.7 (44.1)	30.4 (30.4)	27.4 (23.6)
Median (Q1, Q3)	24.9 (12.6, 49.1)	62.2 (29.3, 89.0)	23.7 (13.1, 35.9)	14.1 (11.5, 36.7)
Time from RUX discontinuation to FEDR initiation, months				
Mean (SD)	2.9 (5.8)	2.4 (5.0)	2.0 (6.0)	4.4 (5.9)
Median (Q1, Q3)	1.2 (0.5, 2.9)	0.7 (0.1, 2.1)	0.8 (0.5, 1.6)	3.4 (1.2, 6.4)
Rationale for initiating treatment with FEDR, n (%)[a,b]				
Treatment efficacy	112 (57.1)	23 (51.1)	49 (57.0)	40 (61.5)
Achieve symptom control	95 (48.5)	33 (73.3)	36 (41.9)	26 (40.0)
Splenomegaly	107 (54.6)	24 (53.3)	64 (74.4)	19 (29.2)
Anemia	24 (12.2)	4 (8.9)	13 (15.1)	7 (10.8)
Thrombocytopenia	33 (16.8)	11 (24.4)	18 (20.9)	4 (6.2)
RUX failure	116 (59.2)	23 (51.1)	69 (80.2)	24 (36.9)
Safety profile of FEDR	23 (11.7)	2 (4.4)	7 (8.1)	14 (21.5)
No other treatment available	27 (13.8)	9 (20.0)	14 (16.3)	4 (6.2)
Duration of FEDR treatment				
Overall, months[c]				
Mean (SD)	11.5 (6.2)	14.0 (8.5)	12.7 (4.7)	8.1 (4.3)
Median (Q1, Q3)	11.5 (6.5, 15.0)	11.3 (7.8, 21.1)	13.8 (10.9, 15.8)	7.2 (5.3, 10.2)
Among patients with ongoing treatment[c]				
n	108	22	64	22
Mean (SD)	14.5 (4.8)	15.6 (8.7)	14.9 (2.6)	12.3 (4.1)
Median (Q1, Q3)	14.3 (11.8, 16.4)	12.3 (9.0, 24.6)	14.6 (12.9, 16.3)	11.3 (9.1, 16.7)
Among patients who discontinued treatment[c,d]				
n	88	23	22	43
Mean (SD)	7.8 (5.5)	12.5 (8.3)	6.3 (3.3)	6.0 (2.4)
Median (Q1, Q3)	6.3 (4.4, 9.0)	11 (5.3, 21.1)	5.4 (3.9, 8.7)	5.9 (4.4, 7.6)
FEDR discontinuation				
Reason(s) for stopping treatment with FEDR, n (%)[a,b,d]				
Patient decision	19 (21.6)	7 (30.4)	6 (27.3)	6 (14.0)
Improvement in patients' condition, with no additional clinical benefit of continued treatment anticipated	22 (25.0)	4 (17.4)	2 (9.1)	16 (37.2)
Inadequate response	11 (12.5)	4 (17.4)	2 (9.1)	5 (11.6)
Progressive disease – anemia (including transformation to AML)	11 (12.5)	6 (26.1)	1 (4.5)	4 (9.3)
Progressive disease – splenomegaly	16 (18.2)	6 (26.1)	2 (9.1)	8 (18.6)
Loss of response[e]	17 (19.3)	8 (34.8)	2 (9.1)	7 (16.3)
Death	18 (20.5)	3 (13.0)	15 (68.2)	0 (0.0)

AML = acute myeloid leukemia; FEDR = fedratinib; MF = myelofibrosis; Q1 = first quartile; Q3 = third quartile; RUX = ruxolitinib; SD = standard deviation; UK = United Kingdom.
[a]Multiple responses allowed; thus, rows may add up to greater than 100%.
[b]Common responses (>10% for all countries) included.
[c]Time from FEDR initiation to discontinuation or last medical record date (if treatment ongoing) excluding treatment interruptions/holidays.
[d]Among patients who stopped treatment with FEDR.
[e]Worsening of symptoms, overall disease progression (blast phase or AML), and/or increase in spleen size or stable large spleen (≥10 cm).

Table 4. MF-Related symptom and spleen outcomes while on treatment with fedratinib.

	All countries (*N* = 196)	Canada (*n* = 45)	Germany (*n* = 86)	UK (*n* = 65)
MF-related symptoms				
Total number of symptoms				
At baseline, n[a]	183	45	85	53
Mean (SD)	3.5 (2.1)	4.8 (2.7)	3.3 (1.6)	2.9 (1.9)
Median (Q1, Q3)	3.0 (2.0, 5.0)	5.0 (3.0, 6.0)	3.0 (2.0, 4.0)	3.0 (2.0, 4.0)
At 3 months after initiation of treatment with FEDR, n[b]	173	44	80	49
Mean (SD)	2.1 (1.7)	2.4 (1.6)	2.3 (1.8)	1.7 (1.4)
Median (Q1, Q3)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	1.0 (1.0, 3.0)
At 6 months after initiation of treatment with FEDR, n[b]	157	37	71	49
Mean (SD)	1.3 (1.6)	1.8 (2.0)	1.4 (1.6)	0.8 (1.2)
Median (Q1, Q3)	1.0 (0.0, 2.0)	1.0 (1.0, 2.0)	1.0 (0.0, 2.0)	0.0 (0.0, 1.0)
Spleen response				
Time to response, months				
Spleen size decreased or no splenomegaly – event, n (%)	131 (66.8)	32 (71.1)	60 (69.8)	39 (60.0)
Kaplan-Meier estimates				
n	196	45	86	65
Median (95% CI)	4.0 (4.0–5.0)	4.0 (3.0–6.0)	3.0 (3.0–4.0)	5.0 (4.0-NE)

CI = confidence interval; FEDR = fedratinib; MF = myelofibrosis; NE = not estimable; Q1 = first quartile; Q3 = third quartile; SD = standard deviation; UK = United Kingdom.
[a]MF-related symptoms were not known/not evaluated for 13 patients at baseline.
[b]The denominator included eligible study sample at each timepoint defined as patients who had follow-up until the specified timepoint and had an evaluation of MF-related symptoms with known details at the specified timepoint.

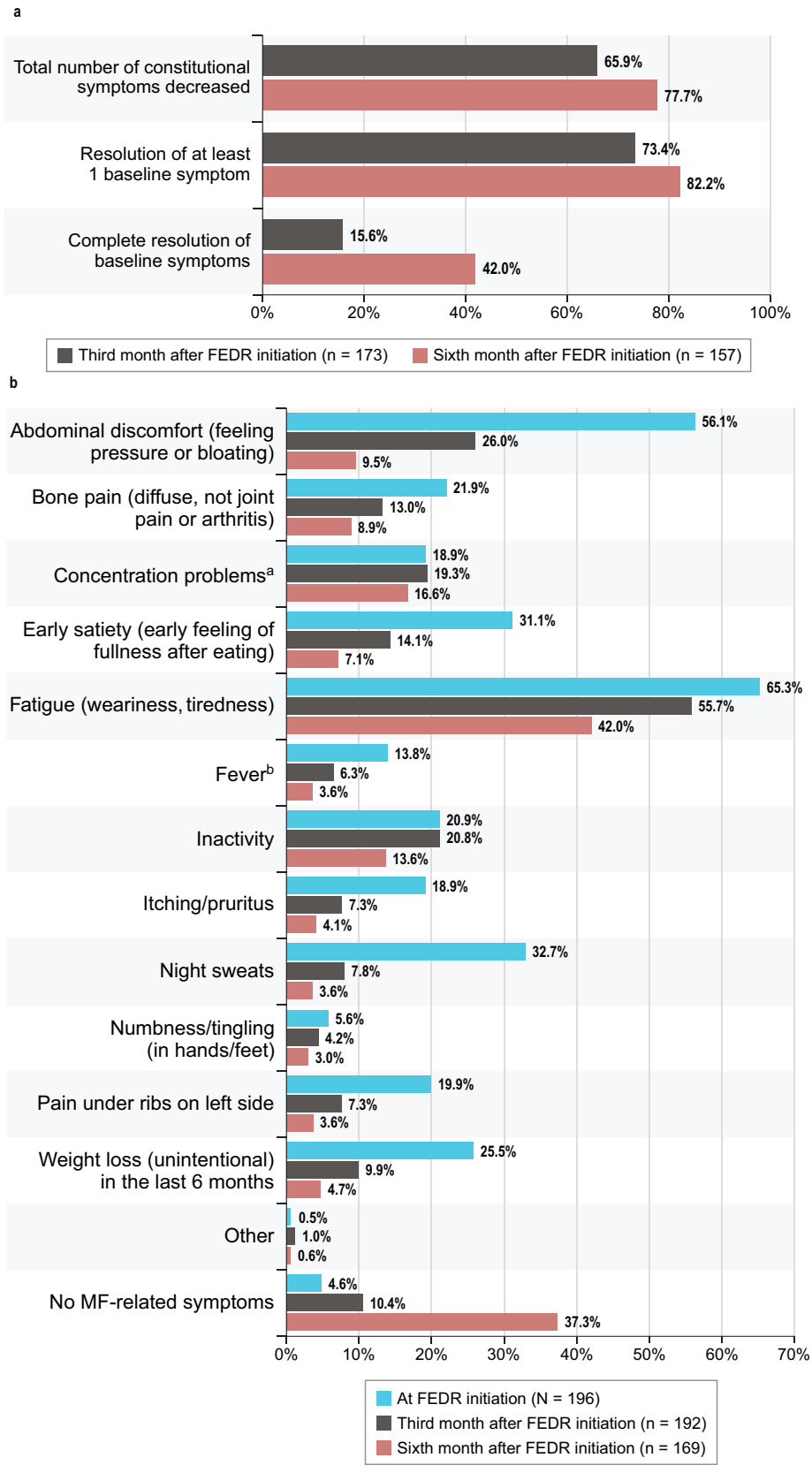

Figure 1. MF-Related symptoms while receiving FEDR treatment.

a. Resolution of MF-related symptoms during the first 6 months of fedratinib treatment.

b. Change in MF-related symptoms during the first 6 months of fedratinib treatment.

FEDR = fedratinib; MF = myelofibrosis; UK = United Kingdom.

[a]Compared with concentration prior to myeloproliferative disorder (i.e., MF).

[b]Mild: <38°C, Moderate: 38–39°C, Severe: >39°C.

with the other countries (3 months, 10.0%-11.4%; 6 months, 32.4%-43.7%).

MF-related symptoms and their prevalence reported at FEDR initiation, 3 months, and 6 months after FEDR initiation for the pooled cohort are presented in Figure 1(b) (see also Table 2). Prevalence of all symptoms decreased at 3 months (excepting concentration problems) and 6 months after FEDR initiation. At 6 months, fatigue remained a commonly reported symptom (42.0%), and concentration problems (16.6%) and inactivity (13.6%) were the next most common, while abdominal discomfort, bone pain, early satiety, fever, itching/pruritus, night sweats, numbness/tingling, and unintentional weight loss were reported by less than 10% of patients. No MF-related symptoms were reported for 4.6% of patients at FEDR initiation, 10.4% of patients at 3 months, and 37.3% of patients at 6 months of FEDR treatment.

The prevalence of commonly reported symptoms, such as fatigue, abdominal discomfort, and night sweats at baseline was generally lower for patients in the UK (29.2%-46.2%) than for those in Germany (32.6%-67.4%) and Canada (37.8%-88.9%). A similar pattern was observed after 6 months of FEDR treatment, where prevalence of symptoms was generally lower for patients in the UK (3.8%-34.0%) compared with Germany (3.9%-42.1%) and Canada (2.5%-52.5%). Corresponding with lower prevalence of symptoms, the proportion of patients reporting no MF-related symptoms was higher in the UK than in Germany or Canada both at baseline (UK, 10.8%; Germany, 2.3%; Canada, 0.0%) and after 6 months of FEDR treatment (UK, 50.9%; Germany, 36.8%; Canada, 20.0%) (Supplemental Figure S3A-B).

3.3.2. Spleen response and splenomegaly during the first 6 months of fedratinib treatment

Spleen response data are detailed in Table 4. During the study follow-up, spleen size decrease or no splenomegaly was reported for 66.8% of patients in the pooled cohort (UK, 60.0%; Germany, 69.8%; Canada, 71.1%). The median time to spleen response across countries was 4.0 months (95% confidence interval [CI], 4.0–5.0). Median time to spleen response was 3.0 months (95% CI, 3.0–4.0) in Germany, 4.0 months (95% CI, 3.0–6.0) in Canada, and 5.0 months (95% CI, 4.0-NE) in the UK. During the study follow-up, spleen size increase was reported for 12.2% of patients.

At FEDR initiation, moderate splenomegaly was reported for 56.1% of patients, which increased to 60.2% of patients at the first month – likely as patients with severe splenomegaly improved after FEDR initiation and moved into the moderate splenomegaly category – then subsequently decreased each month to 17.8% of patients at the sixth month of FEDR treatment (Figure 2; see also Table 2). Similar patterns of moderate splenomegaly prevalence were reported for patients in the UK (55.4% at initiation, 17.0% at 6 months) and Germany (52.3% at initiation, 15.8% at 6 months), while prevalence was higher among patients in Canada (64.4% at initiation, 22.5% at 6 months) (Supplemental Figure S4). The proportion of patients in Germany with moderate splenomegaly did not decrease below baseline until the fourth month of FEDR treatment.

Across all countries, severe splenomegaly was reported for 24.5% of patients at FEDR initiation and decreased each month to the fifth month (5.6%), followed by a small increase to 5.9% of patients at the sixth month of FEDR treatment (Figure 2). A higher proportion of patients in Germany had severe splenomegaly at initiation (36.0%) than did patients in Canada (20.0%) and the UK (12.3%) (Supplemental Figure S4). Severe splenomegaly prevalence steadily decreased to 1.9% of patients in the UK and 5.3% of patients in Germany at 6 months of FEDR treatment. For patients in Canada, prevalence decreased to 8.9% of patients at 3 months of FEDR treatment and subsequently increased to 12.5% of patients at 6 months of FEDR treatment.

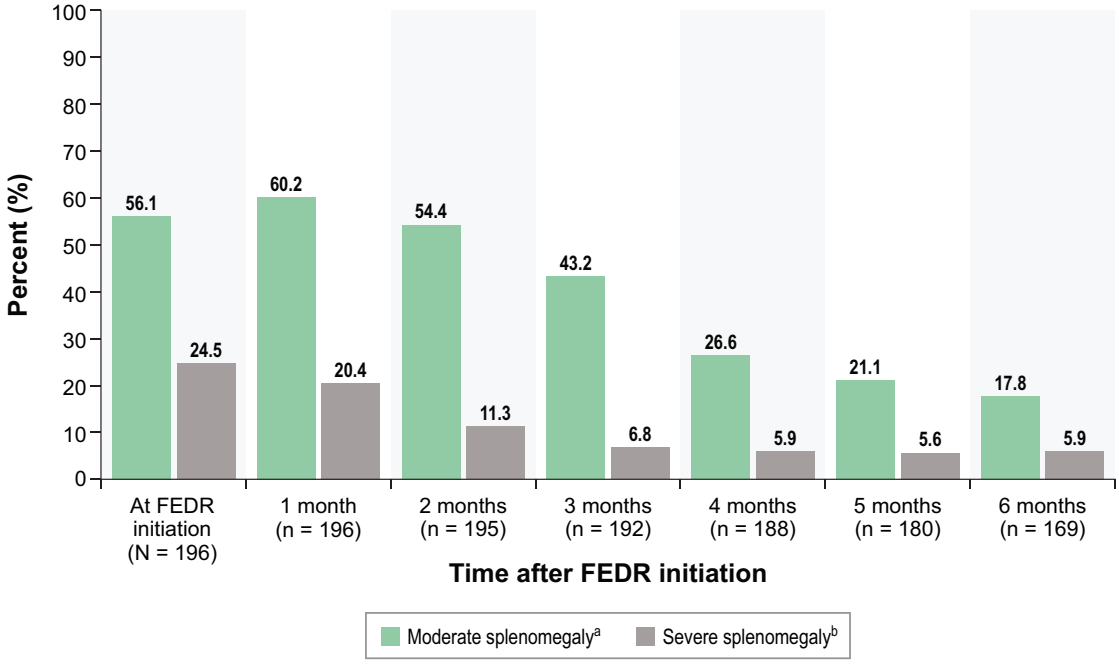

Figure 2. Change in spleen size while receiving fedratinib treatment.

FEDR = fedratinib; MF = myelofibrosis.

Table 5. Disease progression, rw-PFS, and OS while on treatment with fedratinib.

	All countries (*N* = 196)	Canada (*n* = 45)	Germany (*n* = 86)	UK (*n* = 65)
Inadequate response or disease progression while on FEDR treatment, n (%)				
Yes	48 (24.5)	14 (31.1)	16 (18.6)	18 (27.7)
No	148 (75.5)	31 (68.9)	70 (81.4)	47 (72.3)
Don't know	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Progression-free survival from FEDR initiation[a]				
Disease progression – event, n (%)	55 (28.1)	19 (42.2)	17 (19.8)	19 (29.2)
Deceased – event, n (%)	10 (5.1)	1 (2.2)	9 (10.5)	0 (0.0)
Kaplan-Meier estimates				
n	196	45	86	65
Median (95% CI)	23.8 (21.1–27.6)	22.4 (12.2–27.6)	23.8 (16.5-NE)	NE (9.9-NE)
Progression-free survival rate, % (SE)				
6 months	86.4 (2.5)	88.7 (4.8)	87.2 (3.6)	83.7 (4.8)
12 months	72.3 (3.5)	68.5 (7.7)	79.1 (4.4)	59.6 (8.4)
All-cause survival from FEDR initiation (months)				
Died, n (%)	42 (21.4)	13 (28.9)	21 (24.4)	8 (12.3)
Kaplan-Meier estimates				
N	196	45	86	65
Median (95% CI)	29.8 (23.9-NE)	29.8 (18.7-NE)	26.6 (NE-NE)	NE (NE-NE)
Survival rate, % (SE)				
6 months	95.9 (1.4)	100.0 (0.0)	90.7 (3.1)	100.0 (0.0)
12 months	85.9 (2.6)	92.6 (4.1)	81.3 (4.2)	87.2 (4.6)

CI = confidence interval; FEDR = fedratinib; MF = myelofibrosis; NE = not estimable; OS = overall survival; rw-PFS = real-world progression-free survival; SD = standard deviation; SE = standard error; UK = United Kingdom.

[a]Progression was defined as inadequate response or disease progression while on treatment with FEDR or FEDR treatment discontinuation due to disease progression due to anemia, splenomegaly, or loss of response.

3.3.3. Disease progression, rw-PFS, and OS while on treatment with fedratinib

Disease progression and survival data are presented in Table 5. An inadequate response or disease progression while on FEDR treatment – commonly determined by MF-related symptoms (79.2%) or spleen size or volume (58.3%) criteria – was reported for 24.5% of patients in the pooled cohort (Canada, 31.1%; UK, 27.7%; Germany, 18.6%). In rw-PFS evaluation, 33.2% of patients experienced disease progression or all-cause death (Canada, 44.4%; Germany, 30.3%; UK, 29.2%). Across countries, median rw-PFS from FEDR initiation was 23.8 months (95% CI, 21.1–27.6) (Figure 3(a)). Median rw-PFS was 22.4 months (95% CI, 12.2–27.6) in Canada, 23.8 months (95% CI, 16.5-NE) in Germany, and not reached in the UK (Supplemental Figure S5). The estimated 12-month rw-PFS rate was 72.3% (standard error [SE], 3.5%) for the pooled cohort (Germany, 79.1% [SE, 4.4%]; Canada, 68.5% [SE, 7.7%]; UK, 59.6% [SE, 8.4%]).

At the time of medical record extraction, 21.4% of patients in the pooled cohort were deceased (Canada, 28.9%; Germany, 24.4%; UK, 12.3%); commonly reported reasons for death were progression of MF (28.6%) and progression to myeloid leukemia (23.8%). Across countries, median OS from the time of FEDR initiation was 29.8 months (95% CI, 23.9-NE) (Figure 3(b)). Median OS was 29.8 months (95% CI, 18.7-NE) in Canada, 26.6 months (95% CI, NE-NE) in Germany, and not reached in the UK (Supplemental Figure S6). The estimated 12-month OS rate was 85.9% (SE, 2.6%) for the pooled cohort (Canada, 92.6% [SE, 4.1%]; UK, 87.2% [SE, 4.6%]; Germany, 81.3% [SE, 4.2%]).

4. Discussion

This real-world, observational study assessed characteristics and diverse clinical outcomes among patients with primary or secondary MF who received FEDR after discontinuation of RUX treatment in Canada, Germany, and the UK. Key findings demonstrate real-world effectiveness of FEDR following RUX discontinuation. Overall, the prevalence of MF-related symptoms and proportion of patients with moderate and severe splenomegaly decreased during the first 6 months of FEDR treatment. Across countries, about two-thirds of patients experienced a reduction in spleen size a median of 4.0 months after FEDR initiation. Among the pooled cohort, median rw-PFS was 23.8 months (95% CI, 21.1–27.6) from FEDR initiation, with a 12-month rw-PFS rate of 73%, and median OS was 29.8 months (95% CI, 23.9-NE) from FEDR initiation, with a 12-month OS rate of 86%. Regarding treatment patterns, 49.5% of patients initiated therapy at the label-indicated dose (400 mg daily), and most patients had no changes in dose. Of those who had a dosage change, it was most often (82.2%) to titrate to therapeutic dose.

In addition to pooled analyses, results were derived for each of the 3 included countries, which allows for observation of differences in certain measures and outcomes. Notably, our findings highlight differences in FEDR prescribing and treatment patterns between countries. Among patients in Canada, median time to FEDR initiation from MF diagnosis was 62.2 months, compared with 23.7 months and 14.1 months for patients in Germany and in the UK, respectively. Healthcare system differences between Canada, Germany, and the UK may contribute to these observed variations in time to FEDR initiation after MF diagnosis or RUX discontinuation; for instance, Canada has complex and rigorous approval and reimbursement processes that contribute to delays in drug access [23,24]. Further, the proportions of patients with ongoing FEDR treatment differed at the end of follow-up (Canada, 48.9%; Germany, 74.4%; UK, 33.8%), which may be attributable to differences in total duration of FEDR treatment, as well as variability in practice patterns and overall disease management between countries. Compared with patients in Germany or the UK, a larger proportion of patients in Canada experienced a decrease in their total number of

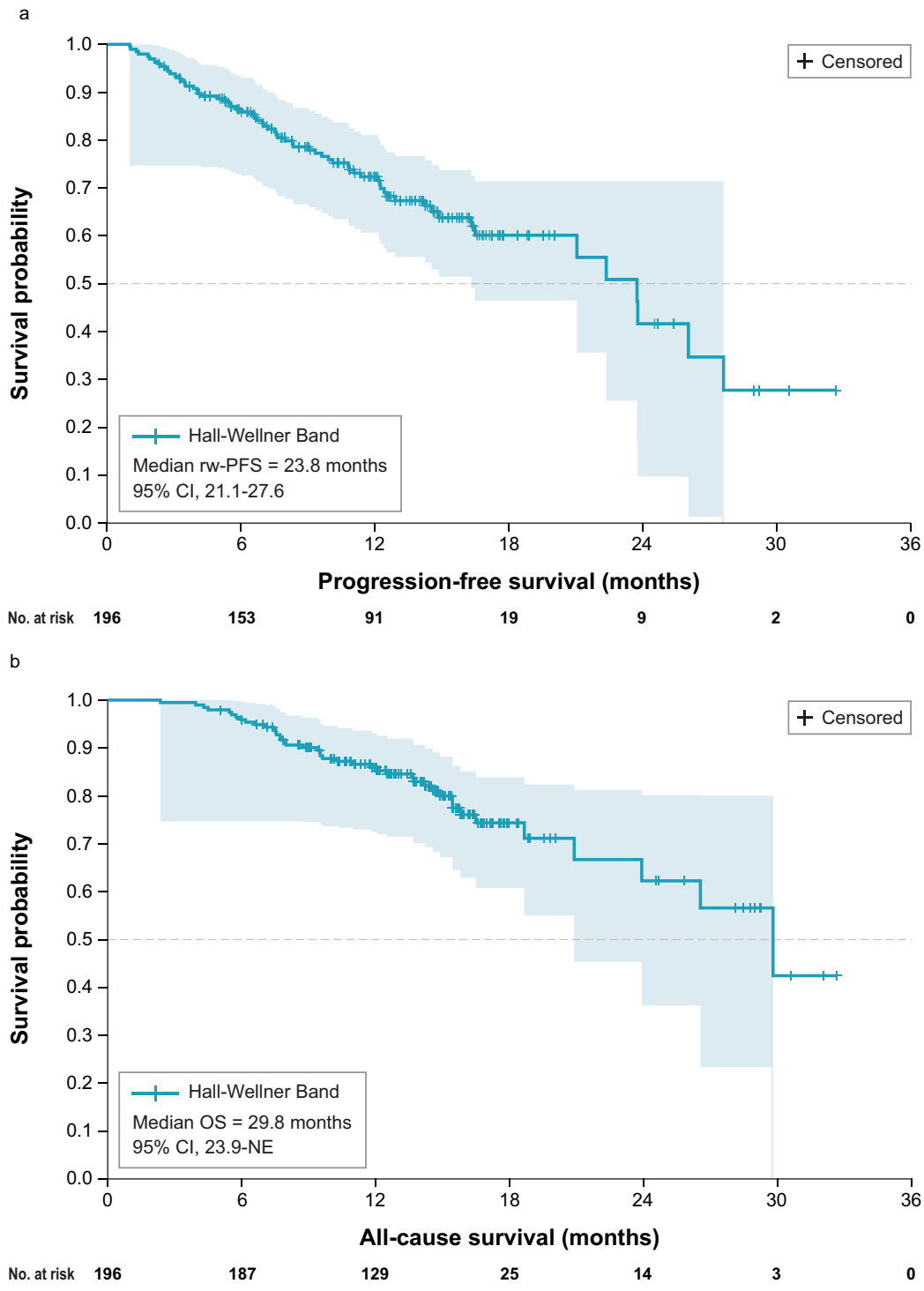

Figure 3. Kaplan-Meier analyses of rw-PFS and OS from fedratinib initiation.

A. rw-PFS from fedratinib initiation.

B. OS from fedratinib initiation.

CI = confidence interval; NE = not estimable; OS = overall survival; rw-PFS = real-world progression-free survival.

symptoms; this may be due to patients in Canada having a higher median number of MF-related symptoms at FEDR initiation compared with patients in the other countries (5.0 versus 3.0). Moreover, consequential to a greater number of symptoms at baseline, a smaller proportion of patients in Canada experienced complete baseline symptom resolution 6 months after FEDR initiation compared with patients in the other countries (UK, 46.9%; Germany, 43.7%; Canada, 32.4%). Similar proportions of patients across countries (60.0%-71.1%) experienced a decrease in spleen size, though the proportions of patients with moderate or severe splenomegaly 6 months after FEDR initiation were lower in the UK (moderate, 17.0%; severe, 1.9%) and Germany (moderate, 15.8%; severe, 5.3%) than in Canada (moderate, 22.5%; severe, 12.5%). These findings suggest

patients in Canada in this study may have had a greater MF-related disease burden compared with patients in Germany and the UK, which may impact symptom and spleen response to FEDR treatment. We additionally observed the proportions of patients who did not have a bone marrow biopsy reported at initial MF diagnosis differed between countries (Canada, 0.0%; Germany, 11.6%; UK, 33.8%), which in part reflects variation in practice patterns regarding MF diagnosis across countries. Importantly, when excluding patients missing a bone marrow biopsy (no/unknown biopsy status, $n = 36$ [18.4%]) in sensitivity analyses, we found overall findings were largely consistent, suggesting the presence or absence of bone marrow biopsy did not contribute to observed differences in outcomes (Supplemental Table S4).

The real-world findings reported in this study help corroborate clinical trial evidence and contribute to the body of RWE supporting the clinical benefit of FEDR for individuals with MF previously treated with RUX. Overall, our findings are consistent with the phase 3 FREEDOM2 trial, which demonstrated both decreases in spleen volume and MF-related symptom burden for patients treated with FEDR after RUX discontinuation due to resistance or intolerance [17]. Characteristics of the cohort in the present study are generally similar to those of the FREEDOM2 trial population, and in comparison, we found that overall median duration of FEDR treatment was slightly longer in our study (11.5 months versus 10.8 months) [17]. Findings described in this study of treatment patterns, symptom response, and spleen response are also consistent with those from a US-based real-world study of clinical outcomes after 3 and 6 months of FEDR therapy following RUX treatment failure [20]. The duration of FEDR treatment was longer in our study than in the US study among patients with ongoing treatment (14.3 months versus 4.4 months) [20]. This could be due to differences in the follow-up opportunity between studies – the minimum follow-up opportunity in our study was 6 months, whereas minimum follow-up in the US study was 90 days [20]. Moreover, although similar proportions of patients at FEDR initiation had high-risk MF between our study and that of the US study (43.9% versus 43.3%) and overall rates of FEDR discontinuation were similar (44.9% versus 44.7%), greater proportions of patients in the latter study had an ECOG PS ≥ 2 at FEDR initiation (33.8% versus 54.7%) and discontinued FEDR due to progressive disease (30.7% versus 43.3%) [20]. Disease progression was the most common reason for discontinuation in the US study, while no additional clinical benefit and patient decision – likely including for reasons of tolerability – were reported most frequently in our study.

In addition to describing FEDR treatment patterns and outcomes, findings from our study add to the body of evidence describing therapy for individuals with MF following RUX discontinuation [25,26]. In addition to initiating FEDR for reasons of treatment efficacy (57.1%), splenomegaly (54.6%), and achieving symptom control (48.5%), more than half of the patients in our study (59.2%) initiated FEDR due to RUX treatment failure. The criteria of RUX treatment failure are poorly defined and heterogenous and may include resistance, loss of response, intolerance, or progressive disease during treatment [15,27,28]. Of all patients who discontinued RUX, 59.7% discontinued due to relapse or disease progression, 25.0% discontinued due to RUX intolerance, and 19.9% discontinued due to treatment refractoriness or suboptimal response to RUX.

This study has a number of strengths. Physicians in Canada, Germany, and the UK led data extraction of patient medical records to allow for a comprehensive evaluation of patients' demographic and clinical characteristics, FEDR treatment patterns, and longitudinal evaluation of changes in MF-related disease burden. Moreover, the extraction was completed using a customized eDCF allowing for the collection of important clinical measures that may have involved the clinician's interpretation or that are typically not available in preexisting secondary data sources, as well as extraction of data in a uniform structure across all practices and geographic locations. This allowed our assessment of a pooled cohort to support greater generalizability, as well as the comparison of differences between countries. Though clinical trials and real-world observational studies have evaluated treatment patterns and symptom and/or spleen response, evidence of survival outcomes related to FEDR treatment following RUX failure is limited; to date, no other real-world study in Canada or Europe has estimated rw-PFS or OS for patients receiving FEDR after previous RUX treatment.

Certain limitations should be considered when interpreting the findings of this study, including those inherent to observational studies. Patient medical records were obtained from eligible physicians who were willing to participate in the study; therefore, selection bias is possible, patients selected for study inclusion represented a convenience sample, and this sample may not be generalizable for each country. Though several logic checks were included in the eDCF to potentially minimize errors and inaccuracies, data entered directly by the treating physicians or their designated clinical staff may be subject to entry errors and resulting inaccuracies in reporting. Although not directly related, receipt of supportive care (e.g., corticosteroids) may impact the tolerability of FEDR and thereby influence patient outcomes. Moreover, use of over-the-counter medications, treatments prescribed by other physicians, and any other treatments not regularly documented in medical records may be underreported. For information that is not explicitly recorded in patient medical records, certain measures (e.g., reasons for treatment initiation or discontinuation) may be subject to physician recall bias. Additionally, although we observed differences between countries, we did not perform country-specific adjustments for baseline characteristics, and analyses considering potential imbalances in future studies are warranted. Furthermore, evaluation of factors or predictors associated with survival outcomes while on FEDR were not evaluated in the current study but should be assessed in future studies. Despite these limitations, this study provides important RWE describing treatment patterns and clinical outcomes in 3 countries that support FEDR effectiveness in clinical practice and further provides insights to inform providers and patients on treatment decisions.

5. Conclusions

This study illustrates the real-world clinical benefit of FEDR following RUX treatment failure for individuals with MF in

Canada, Germany, and the UK. Patients included in the study experienced MF-related symptom burden reduction, spleen size reduction, and improved survival outcomes. These real-world results align with RWE reported from clinical practice in a different geographic location, as well as findings observed in a clinical trial setting.

Author contributions

Conceptualization: SK, RCP, MC, AY, KLD, SS; methodology: SK, RCP, MC, AY, SS; data curation: SK, RCP, JR; formal analysis: SK, RCP; writing – original draft: SK, RCP; writing – reviewing and editing: FP, SK, RCP, MC, AY, JR, SJ, DZ, KLD, SS; supervision: KLD, SS.

Disclosure statement

MC, AY, SJ, DZ, and SS are employees of Bristol Myers Squibb. SK, RCP, JR, and KLD are full-time employees of RTI Health Solutions, an independent nonprofit research organization, which was retained by Bristol Myers Squibb to conduct the research that is the subject of this manuscript. Their compensation is unconnected to the studies on which they work. Medical writing support was provided by Gabrielle Dardis, PhD, and Madison Walker, MPH, of RTI Health Solutions, and editing support was provided by John Forbes of RTI Health Solutions, as part of a contract with Bristol Myers Squibb.

Ethical declaration

This study was conducted in accordance with ethical principles originating from the Declaration of Helsinki, with International Society for Pharmacoepidemiology (ISPE) Guidelines for Food Epidemiology Practices, and with local standards in Canada, Germany, and the UK. RTI Health Solutions worked with Bristol Myers Squibb and Klinikos, a third-party contractor specializing in ethics review board approval, to submit the necessary ethics review board applications. For Germany, ethics submission required additional support from a designated lead site principal investigator. The RTI International Institutional Review Board deemed this study exempt from full review. Due to use of deidentified/pseudonymized data, informed patient consent was not required.

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Data sharing statement

Data are not publicly available but may be made available on a case-by-case basis, upon request.

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