An Analysis of Ruxolitinib Dosing for Myelofibrosis in Real-World Practice

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CONCLUSIONS

- These real-world data suggest that a majority of patients starting ruxolitinib (RUX), including those with platelets >200x10^9/L, are initiated on ≤20 mg total daily dose, and the majority of patients are not titrated up to the doses tested in the pivotal studies that led to RUX approval.
- These data suggest that clinicians are hesitant to prescribe RUX at doses known to be clinically effective.[1] Together with the timing of dose modification, there may be concerns related to toxicity or treatment-related cytopenias.
- Recognizing that JAK2 inhibition remains an important part of managing myelofibrosis (MF) for patients, clinicians now have alternative treatment options. These newer treatments inhibit additional pathways (IRAK1/ACVR1), are less myelosuppressive, and can maintain dose intensity regardless of baseline platelet count.[2]

INTRODUCTION

- In patients with MF, worsening cytopenias are associated with poor survival.[3]
- The JAK1/2 inhibitor RUX is effective in decreasing splenomegaly and improving symptom control at starting doses of 30-40 mg total daily dose (TDD), though drug-induced cytopenias often lead to dose reductions.[4]
- Patients regardless of baseline platelet count are being treated with RUX ≤20 mg TDD. While there is insufficient data for non-cytopenic patients, cytopenic patients receiving lower average RUX TDD achieve lower rates of spleen and symptom responses.[5]
- Doses of ≤20 mg TDD are associated with decreased efficacy for spleen response, and doses of ≤10 mg TDD demonstrate minimal efficacy for spleen or symptom reduction.[1,5]
  - Cytopenic patients typically start on lower doses and have poorer outcomes than non-cytopenic patients treated at higher doses. Notably, even a modest reduction in dose can impact outcomes.[5]
- Treating with less clinically effective doses may not be optimal in light of newer, less myelosuppressive JAK2 inhibitors that can be administered without dose reduction, regardless of baseline cytopenias.
- This study describes RUX dosing patterns in real-world community practice.

OBJECTIVES

This study uses data from patients with MF treated in the real-world setting to better understand the:

1. Baseline and clinical characteristics of patients with MF treated with RUX, and
2. Treatment and starting dose patterns of RUX in relation to the platelet levels.

METHODS

- This retrospective, observational study included deidentified data of adult patients from the IntegraConnect PrecisionQ database (~80% community practice) with MF treated with RUX and with ≥2 office visits (with a criterion of 2 MF diagnosis codes reported within 180 days) from January 2016 to July 2022.
- Patients were stratified by baseline platelet count.
- Data on RUX TDD at initiation and at first dose modification were collected, with a focus on less clinically effective dosing of ≤20 mg TDD and ≤10 mg TDD.
- Inclusion and exclusion criteria are shown in **Table 1.**

Table 1: Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Patients with the following ICD10 codes of interest • Level 1 ○ D47.4 (osteomyelofibrosis) or ○ D75.81 (myelofibrosis) or • Level 2 ○ D47.1 (chronic myeloproliferative disease)	Patients with MF without adequate labs and treatment information to support the study
Require 2 diagnostic codes reported on two-separate days where second diagnosis is within 180 days after first diagnosis such that: • 2 diagnoses from Level 1 • 1 diagnosis from Level 2 PLUS a subsequent diagnosis from Level 1	
Patients with at least 2 visits documented in the EHR/EMR	

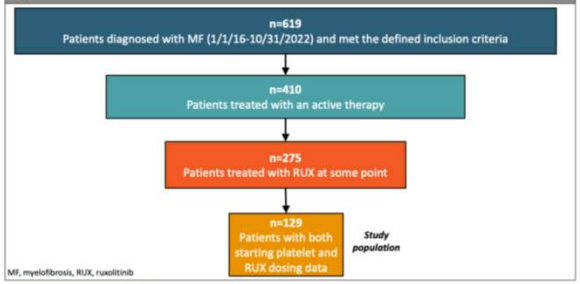
EHR, electronic health record; EMR, electronic medical record

RESULTS

Study Population

- Of 619 patients with MF identified from the IntegraConnect PrecisionQ database who met the defined inclusion criteria, 410 were treated with an active therapy.
- Of the 410 patients treated with an active therapy, 275 patients were treated with RUX at some point.
  - 245 of these patients received first-line therapy with RUX.
- The study population included 129 patients with MF treated with RUX in the real-world setting who had both starting platelet and RUX dosing data available (**Figure 1**).

Figure 1: Attrition



MF, myelofibrosis, RUX, ruxolitinib

Baseline Demographics

- Baseline demographics and clinical characteristics are shown in **Table 2.**
- The median (min, max) age was 73.0 (41, 89) years for patients treated with RUX at some point (n=275) and 75 (42, 89) years for those included in the final study population (n=129). In both groups, ~90% of patients were ≥65 years of age.
- Race was not documented for 42% of patients with both starting platelet and RUX data.

Table 2: Baseline Demographics

	Patients treated with RUX at some point n=275	Patients with both starting platelet and RUX data n=129
Age at diagnosis, years		
Mean (SD)	72.3 (9.7)	73.5 (9.8)
Median (min, max)	73.0 (41, 89)	75 (42, 89)
Age at diagnosis, n (%)		
Age <65 years	33 (12.0%)	12 (9.3%)
Age ≥65 years	242 (88.0%)	117 (90.7%)
Gender, n (%)		
Female	121 (44.0%)	58 (45.0%)
Male	152 (55.3%)	70 (54.3%)
Not documented	2 (0.7%)	1 (0.8%)
Race, n (%)		
Asian	9 (3.3%)	5 (3.9%)
Black or African American	8 (2.9%)	4 (3.1%)
White	134 (48.7%)	66 (51.12%)
Not documented/Unknown/Other	128 (46.5%)	54 (41.9%)
Payer group, n (%)		
Medicare/Medicaid	66 (24.0%)	54 (41.9%)
Commercial	94 (34.2%)	25 (19.9%)
Other	75 (27.3%)	45 (34.9%)
Not reported	6 (2.2%)	4 (3.1%)
ECOG at MF diagnosis, n (%)		
No. of pts w/ ECOG data available	n=107	n=78
0	44 (41.1%)	29 (37.2%)
1	50 (46.7%)	38 (48.7%)
2	12 (11.2%)	10 (12.8%)
3	1 (0.9%)	1 (1.3%)
Median follow-up, days (IQR)	596 (281, 1078)	485 (232, 881)

ECOG, Eastern Cooperative Oncology Group; IQR, interquartile range; MF, myelofibrosis; max, maximum; min, minimum; SD, standard deviation

Starting Dose and Dose Modification

- Across all platelet strata, 88% (n=114) of patients were initiated on RUX at a TDD of ≤20 mg; 51% (n=66) were started at a TDD ≤10 mg.
- Nearly half of patients with higher baseline platelet counts (>100 x 10^9/L) were started on doses ≤10 mg TDD (**Figure 2**).
- Among 79 patients with platelets >200x10^9/L, the starting RUX TDD was ≤20 mg in 87% (n=69) and ≤10 mg in 43% (n=34).
- Among the 24 patients with platelets of 100 - 200x10^9/L, the starting RUX TDD was ≤20 mg in 87.5% patients (n=21) and a TDD of ≤10 mg 50.0% patients (n=12).

Figure 2: Starting Dose of RUX by Baseline Platelet Count

Pt numbers	All pts	>200	151-200	100-150	50-99	<50
>20 mg TDD	15	10	2	1	1	1
>10 mg to 20 mg TDD	48	35	4	5	2	2
≤10 mg TDD	66	34	5	7	10	10
Total patients	129	79	11	13	13	13

pt, patient; RUX, ruxolitinib; TDD, total daily dose

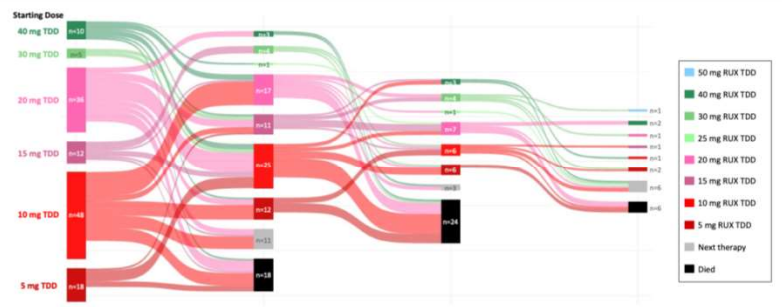
Table 3: Starting RUX Dose and Dose Modification by Baseline Platelet Count

	Platelet >200x10^9/L	Platelet 100 to ≤200x10^9/L	Platelet <100x10^9/L
Starting RUX TDD, n (%)	n=79	n=24	n=26
≤20 mg	69 (87%)	21 (87.5%)	24 (86%)
≤10 mg	34 (43%)	12 (50%)	20 (77%)
Dosing details after the first dose Δ, n (%)	n=49	n=12	n=12
>20 mg TDD	5 (10%)	3 (25%)	0 (0%)
≤20 mg TDD	44 (90%)	9 (75%)	12 (100%)
≤10 mg TDD	21 (43%)	7 (58%)	9 (75%)

Δ, modification; max, maximum; min, minimum; RUX, ruxolitinib; TDD, total daily dose

- Of patients with platelets >200x10^9/L, 49 patients underwent dose modification, with 19 dose increases and 30 dose decreases for the first dose modification from baseline.
  - The median time to dose modification (min, max) was 47 (10, 1336) days.
  - Of patients whose dose increased, only 4 escalated to a TDD >20 mg. Some patients who started on a TDD >20 mg may have remained on a TDD >20 mg.
  - Despite dose modification, RUX TDD remained ≤20 mg in 44 of 49 (90%) patients and ≤10 mg in 21 of 49 (43%) patients at the end of follow-up (**Table 3**).
- In this dataset, 88% of patients stayed on doses ≤20 mg (**Figure 3**).

Figure 3: Sankey Diagram of Patients with Dose Modifications, Subsequent Treatment, or Death



Δ, modification; RUX, ruxolitinib; TDD, total daily dose

Note: Not all patients who failed to have a dose change remained on the initial dose; some were lost to follow-up.

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DISCLOSURES

JR is a consultant for, has membership on the Board of Directors, and is a member on advisory committees or speakers bureau for CTI BioPharma Corp., AbbVie, and IntegraConnect. **JR** has membership on the Board of Directors and advisory committees for the Leukemia and Lymphoma Society. **JR** is a member of a speakers bureau for the MPN Support Group. **RC** is a consultant for IntegraConnect. **P. Davis** is an equity holder in Eli Lilly and Company and ended employment in the past 24 months and a former employee of CTI Biopharma Corp., a Sobi company. **PS** is an employee of Sobi Inc. and have received payment of unvested equity awards from CTI Biopharma Corp., a Sobi company, following its acquisition in June 2023 by Sobi US Holding, which is wholly owned by Sobi AB. **AV, P. Davé, VV, BW,** and **HK** are employees of IntegraConnect.