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Characteristics and Clinical Outcomes in Patients With Polycythemia Vera Receiving Ruxolitinib After Hydroxyurea: A Longitudinal Analysis From the Prospective Observational Study of Patients With Polycythemia Vera in US Clinical Practices Trial (REVEAL)

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Introduction

- Polycythemia vera (PV) is a Philadelphia-negative myeloproliferative neoplasm characterized by clonal proliferation of hematopoietic progenitor cells leading to elevated peripheral blood count[1,2]
- PV is also associated with splenomegaly and substantial symptom burden with an increased risk of thrombotic events and transformation to myelofibrosis or acute leukemia[3]
- The main goals of treatment are to control PV-related symptoms and to prevent thrombotic events[4]
- Resistance or intolerance to first-line hydroxyurea (HU) occurs in approximately 24% of patients with PV[5]
- Ruxolitinib (RUX), a Janus kinase inhibitor, is approved for the treatment of patients with PV who have an inadequate response to, or are intolerant of, HU therapy[6]
- In the large, real-world, multicenter, p**R**ospective Obs**E**rvational Study of Patients with Polycythemia **VE**ra in US Clinic**AL** Practices (REVEAL; NCT02252159), demographics, disease burden, clinical management, and patient-reported outcomes data were collected from 2510 patients across 227 community or academic centers between 2014 and 2019[4]

Objective

- To describe the characteristics and clinical outcomes of patients with PV enrolled in REVEAL who switched to RUX after HU treatment

Methods

Study Design

- REVEAL is a multicenter, noninterventional, prospective, observational study in patients with PV enrolled from US community practices and academic centers (**Figure 1**; **Table 1**)
- Data collection timepoints included at diagnosis, a 6-month period before, and during follow-up after enrollment (up to 3 years from last patient enrollment)
  - Data were collected between July 2014 and August 2019

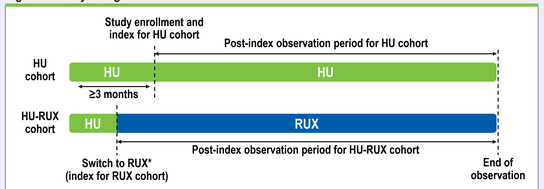
Table 1. Key Eligibility Criteria

Key Inclusion Criteria	The following cohorts were analyzed:
• ≥18 years of age • Clinical diagnosis of PV per physician judgment • Under physician supervision for management of PV	**HU Cohort** • Patients with PV treated with HU ≥3 months before study enrollment ***and*** did not switch to an alternative therapy during the observation period* • **Index:** study enrollment date
Key Exclusion Criteria • Life expectancy <6 months • History of/planning to undergo allogeneic hematopoietic stem cell transplantation • Splenectomy	**HU-RUX Cohort** • Patients with PV treated with HU and switched to RUX treatment for ≥3 months • **Index:** RUX initiation date

PV, polycythemia vera.

*Patients receiving HU did not have to be on HU for the duration of study. However, those receiving HU did not receive other PV medications such as RUX for the duration of study.
HU, hydroxyurea; PV, polycythemia vera; RUX, ruxolitinib.

Figure 1. Study Design



Note: Figure is for illustration purpose only.
*The actual time point of switching to RUX varied among patients and could take place anytime from index to end of observation minus 3 months.
HU, hydroxyurea; RUX, ruxolitinib.

Statistics

- Descriptive statistics were used to describe demographics, disease characteristics, and treatment patterns
- Blood count, Myeloproliferative Neoplasm–Symptom Assessment Form total symptom score (MPN-SAF TSS), and spleen length measurements were analyzed for the time period of at index and at 3 and 12 months post-index for patients who switched to RUX

Results

Patient Characteristics

- Out of 2510 patients enrolled in REVEAL, 1053 were eligible for this analysis and included 906 patients treated with HU and 147 who switched to RUX after previous HU treatment (**Table 2**)
- Median time to index date from PV diagnosis was 6.9 (range, 0.3-36.3) years in the HU-RUX cohort and 4.8 (range, 0.1-36.5) years in the HU cohort
- Median duration of HU treatment before index date was similar between the cohorts
- Patients who switched to RUX had higher mean MPN-SAF TSS vs the HU cohort, and there was a higher percentage of patients with a palpable spleen in the HU-RUX cohort

Table 2. Baseline Patient and Disease Characteristics

Variable	HU Cohort (N=906)	HU-RUX Cohort (N=147)
Age, median (range), y	70 (26-94)	67 (28-95)
Women, n (%)	469 (51.8)	65 (44.2)
Race, n (%)		
White	807 (89.1)	130 (88.4)
Other*	78 (8.6)	9 (6.1)
Risk status, n (%)		
Low risk†	139 (15.3)	27 (18.4)
High risk†	767 (84.7)	120 (81.6)
Duration of HU treatment before index date, median (range), mo	26.7 (3.0-435.6)	27.6 (0.1-221.0)
MPN-SAF TSS, mean (SD)	17.3 (15.1)	27.5 (17.7)
Palpable spleen, n/N (%)	84/906 (9.3)	40/98 (40.8)
Spleen length, mean (SD), cm‡	7.6 (7.3)	12.8 (8.7)
Laboratory values by index date		
WBC, ×10⁹/L, n/N	834/906	145/147
Mean (SD)	9.2 (6.2)	16.1 (16.3)
Hematocrit, L/L, n/N	834/906	145/147
Mean (SD)	0.43 (0.05)	0.42 (0.07)
Platelet, ×10⁹/L, n/N	833/906	144/147
Mean (SD)	345.6 (146.5)	411.7 (236.9)
No. of phlebotomies in last 6 months before index date, n/N	906/906	147/147
Mean (SD)	0.7 (1.5)	1.3 (2.3)
History of TEs before index date, n (%)	175 (19.3)	40 (27.2)
Most recent TE before index date, n/N (%)		
Arterial	74/175 (42.3)	16/40 (40.0)
Venous	101/175 (57.7)	24/40 (60.0)
Number of TEs before index date, mean (SD)	1.3 (0.6)	1.4 (0.8)

*Other includes Black/African American, Asian, Native Hawaiian/Pacific Islander, American Indian/Alaska Native, or unspecified. †Low risk = age at index ≤60 years and no history of TE; High risk = age at index >60 years or history of TE. ‡Analysis is limited to patients with spleen length measurements only (RUX, n=13; HU, n=28).
HU, hydroxyurea; MPN-SAF, Myeloproliferative Neoplasm–Symptom Assessment Form; RUX, ruxolitinib; SD, standard deviation; TE, thrombotic event; TSS, total symptom score; WBC, white blood cell.

- At index, a higher percentage of patients who switched to RUX (n=26 [18.1%]) vs treated with HU (n=65 [7.8%]) had an elevated white blood cell (WBC) count only
  - Patients who switched to RUX had a higher mean WBC count vs those treated with HU
- Mean number of phlebotomies in the 6 months before the index date was higher in the HU-RUX vs the HU cohort
- A higher percentage of patients who switched to RUX (27.2%) vs treated with HU (19.3%) had a history of thrombotic events
- Reasons for HU discontinuation before RUX treatment are shown in **Table 3**

Table 3. Reasons for HU Discontinuation Before RUX Treatment

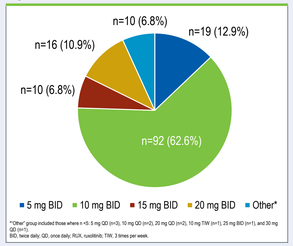
Variable, n (%)	HU-RUX Cohort (N=147)
Lack of efficacy	53 (36.1)
Adverse events	47 (32.0)
Disease progression	10 (6.8)
Others	21 (14.3)
Unreported	16 (10.9)

HU, hydroxyurea; RUX, ruxolitinib.

Treatment Patterns in Patients Who Switched to RUX

- The median time from HU discontinuation to RUX initiation was 1 day (range, 0-930)
- Ninety-two patients (62.6%) received the recommended initial dose of RUX of 10 mg twice daily
  - Other initial doses received are shown in **Figure 2**
- Thirty-eight patients (25.9%) required a RUX dose modification during the study
  - Reasons for the first RUX dose change were lack of efficacy (n=12 [8.2%]), adverse events (n=10 [6.8%]), disease progression (n=1 [0.7%]), and other (n=15 [10.2%])
- At the end of study, 124 patients (84.4%) were still receiving RUX
  - Reasons for RUX discontinuation in the remaining 23 patients (15.6%) were lack of efficacy (n=6 [4.1%]), adverse events (n=4 [2.7%]), disease progression (n=1 [0.7%]), and other (n=12 [8.2%])
- The median RUX treatment duration was 22.6 (range, 3.0-54.5) months by the end of study follow-up
  - Most patients (89.1%) received RUX for ≥6 months

Figure 2. Initial Dose of RUX

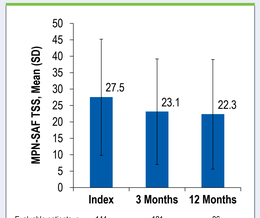


*"Other" group included those where x <5: 5 mg QD (n=3), 10 mg QD (n=2), 20 mg QD (n=2), 10 mg TIW (n=1), 25 mg BID (n=1), and 30 mg QD (n=1).
BID, twice daily; QD, once daily; RUX, ruxolitinib; TIW, 3 times per week.

Clinical Outcomes in Patients Who Switched to RUX

- Compared with index, MPN-SAF TSS (**Figure 3**), the proportion of patients with a palpable spleen (**Figure 4A**), and spleen length (**Figure 4B**) all decreased at the 3- and 12-month follow-up with RUX

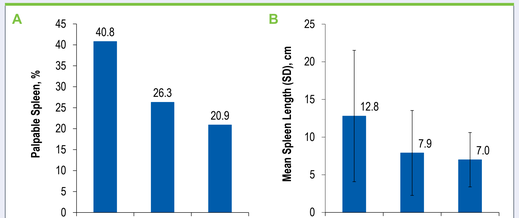
Figure 3. Symptoms by MPN-SAF TSS in Patients Who Switched to RUX



Evaluable patients, n	144	121	86
Change from index, mean (SD)	–	−5.0 (14.2)	−6.5 (14.4)

MPN-SAF, Myeloproliferative Neoplasm–Symptom Assessment Form; RUX, ruxolitinib; SD, standard deviation; TSS, total symptom score.

Figure 4. (A) Percentage of Patients With a Palpable Spleen and (B) Mean Spleen Length in Patients Who Switched to RUX

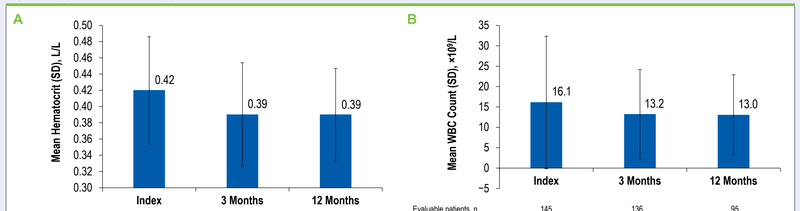


Evaluable patients, n	98	95	67
Evaluable patients, n	13	8	3

RUX, ruxolitinib; SD, standard deviation.

- Mean hematocrit levels decreased from index to 3 months and were maintained at 12 months (**Figure 5A**)
  - The percentage of patients with hematocrit >0.45 L/L decreased from index to 3 months and was approximately maintained at 12 months
- Mean WBC counts decreased from index to 3 months and 12 months (**Figure 5B**)
  - The percentage of patients with WBC counts >15×10⁹/L decreased from index to 3 months and was approximately maintained at 12 months
- Patients with controlled hematocrit/WBC more likely had no blood count test at follow-up and therefore were not included in the assessment

Figure 5. (A) Hematocrit and (B) WBC Count in Patients Who Switched to RUX



Evaluable patients, n	145	134	93
Change from index, mean (SD)	—	−0.04 (0.06)	−0.04 (0.06)
≤0.45 L/L, n (%)	96 (66.2)	115 (85.8)	77 (83.8)
>0.45 L/L, n (%)	49 (33.8)	19 (14.2)	16 (17.2)

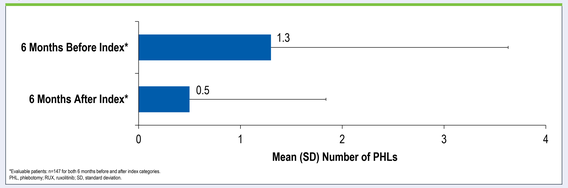
Evaluable patients, n	145	136	95
Change from index, mean (SD)	—	−3.0 (10.6)	−3.2 (14.5)
≤10×10⁹/L, n (%)	58 (40.0)	70 (51.5)	47 (49.5)
>10 to ≤15×10⁹/L, n (%)	39 (26.9)	37 (27.2)	24 (25.3)
>15×10⁹/L, n (%)	48 (33.1)	29 (21.3)	24 (25.3)

RUX, ruxolitinib; SD, standard deviation; WBC, white blood cell.

Phlebotomy Outcomes in Patients Who Switched to RUX

- The mean (standard deviation) number of phlebotomies was decreased from 1.3 at 6 months before index to 0.5 at 6 months after index (**Figure 6**)
- Most patients (n=110; 74.8%) no longer required phlebotomy 12 months after index

Figure 6. Number of PHLs in Patients Who Switched to RUX

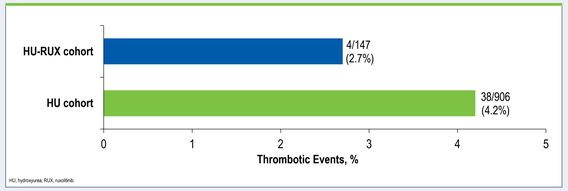


*Evaluable patients: n=147 for both 6 months before and after index categories.
PHL, phlebotomy; RUX, ruxolitinib; SD, standard deviation.

Thrombotic Events

- The thrombotic event rate after index was numerically lower in the HU-RUX vs the HU cohort (**Figure 7**) after a median follow-up of 26 and 44 months, respectively

Figure 7. Thrombotic Events After Index



HU, hydroxyurea; RUX, ruxolitinib.

Conclusions

- **This analysis of REVEAL demonstrated that among patients who were treated with HU before study enrollment, those who switched from HU to RUX had more severe disease burden than those who were treated with HU**
- **After switching from HU, RUX treatment resulted in significant improvements in PV-related symptoms, correlating with reduction in spleen size and sustained improvement in hematologic parameters**
- **This resulted in a reduction in phlebotomy within 6 months, with most patients becoming phlebotomy-free at 12 months after index**
- **There was also a trend towards lower rates of thrombotic events with RUX**
- **This longitudinal analysis validates the efficacy of RUX for the treatment of PV after HU exposure in the real-world**
- **Furthermore, our analysis suggests that the monitoring of patients with PV receiving HU would identify those who are likely to benefit from transition to RUX in order to meet treatment goals and become phlebotomy-free**

Disclosures

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References

1. Barbui T, *et al. Blood.* 2013;122:2176-2184. **2.** Barbui T, *et al. Blood Cancer J.* 2018;8:15. **3.** Coltoff A, *et al. Clin Lymphoma Myeloma Leuk.* 2020;20:697-703. **4.** Grunwald MR, *et al. Clin Lymphoma Myeloma Leuk.* 2020;20:219-225. **5.** Alvarez-Larran A, *et al. Blood.* 2012;119:1363-1369. **6.** Barbui T, *et al. Leukemia.* 2018;32:1057-1069.

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