Poster 3646

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Characteristics of High-Risk Polycythemia Vera Patients With Suboptimal Response to First-Line Therapy Who Switched to Ruxolitinib vs Those Who Did Not Switch: Findings From PV-Switch, a Multinational, Retrospective Chart Review Study

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CONCLUSIONS

- This interim analysis shows the trending existence of clinical differences at baseline between switchers and non-switchers, including a milder comorbidity profile in switchers
- Although switchers experienced similar PV-related symptoms as non-switchers at baseline (ie, 12 months prior to the index date, which was defined as the time of suboptimal response to 1L therapy), switchers were more likely to have experienced persistence of PV-related symptoms or presence of new symptoms as their suboptimal response type
- Together, these two factors may have influenced clinicians' decisions to switch patients to ruxolitinib or continue 1L therapy
- Clinicians and patients may be more likely to switch to 2L therapy when the patient has fewer comorbidities and continues to be symptomatic

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INTRODUCTION

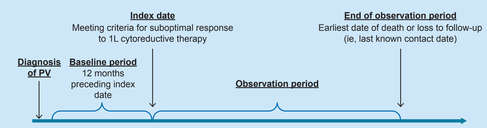
- Polycythemia vera (PV) is characterized by an abnormal increase in red cell mass and elevations in platelet and white blood cell counts[1] and is most commonly associated with mutations in the Janus kinase 2 (*JAK2*) gene (V617F or exon 12)[2,3]
- Cytoreductive therapy is recommended for patients with high-risk PV, with hydroxyurea and interferon often used as first-line (1L) therapy[4-6]
- However, nearly a quarter of patients discontinue therapy due to resistance or intolerance and require second-line (2L) therapy
- Ruxolitinib is approved by the US Food and Drug Administration and European Medicines Agency to treat hydroxyurea-resistant or -intolerant PV.[7] However, in real-world clinical practice, many patients continue 1L therapy after developing resistance or intolerance instead of switching to ruxolitinib as 2L therapy[5,8]
- The primary objective of this first-of-its-kind, multinational, retrospective chart review study is to assess the event-free survival rate of high-risk patients with PV who receive ruxolitinib as 2L therapy (switchers) vs those who continue receiving 1L therapy (non-switchers) after suboptimal response
- The current analysis describes the characteristics of an interim sample of ruxolitinib switchers and non-switchers following suboptimal response to 1L therapy

METHODS

Study design and population

- This is a multinational, retrospective chart review study with a recruitment target of 350 patients from 24 clinical sites across 9 countries. The study design is depicted in **Figure 1**
- The current analysis included an interim sample of eligible patients, with data extracted from February 2020 to June 2021

Figure 1. Study Design Scheme



PV, polycythemia vera.

- Eligible patients included those aged ≥18 years with *JAK2*-positive PV diagnosed in 2012 or later, a high-risk constellation with indication for cytoreductive therapy, suboptimal response to 1L therapy after ≥12 months of treatment, and ≥6 months of follow-up after suboptimal response except in the event of death. Patients were excluded if they initiated a PV treatment other than ruxolitinib after suboptimal response
- Suboptimal response is defined as meeting 1 of the following criteria:
  - Need for ≥3 phlebotomies within 1 year to maintain hematocrit <45%
  - Leukocyte count >15×10^9/L
  - Platelet count >600×10^9/L
  - Persistence of PV-related symptoms or presence of new PV-related symptoms
  - Cytopenias at lowest dose of cytoreductive therapy required to achieve a response
  - Failure to reduce splenomegaly by >50% as measured by palpation or progressive splenomegaly

Statistical analysis

- Patients were classified into two groups, switchers and non-switchers, based on whether they switched to ruxolitinib following first suboptimal response (ie, index date)
- Descriptive statistics were used to summarize patient demographics, criteria for suboptimal response, comorbidities (at any time prior to the index date), and PV-related symptoms and other clinical characteristics during the baseline period, for switchers and non-switchers, respectively

RESULTS

Baseline demographic characteristics

- A total of 137 patients were included in the interim sample; 44 patients (32.1%) were classified as switchers and 93 (67.9%) as non-switchers (**Table 1**)
- Switchers tended to be younger than non-switchers at PV diagnosis (mean [SD], 66.5 [12.0] vs 70.2 [8.5] years) and at index date (68.9 [11.9] vs 73.0 [8.7] years) and were more likely male (52.3% vs 47.3%)
- Half of switchers had never smoked, while only 37.6% of non-switchers had never smoked
- Baseline body mass index (BMI) was comparable between the two groups
- Switchers were more likely than non-switchers to have been enrolled in an interventional clinical trial for an investigational PV treatment (6.8% vs 3.2%)

Table 1. Patient Baseline Demographic Characteristics[a]

	Switch n=44	Non-switch n=93
Age at PV diagnosis, years		
Mean (SD) [median]	66.5 (12.0) [70.5]	70.2 (8.5) [70.0]
Age at index date, years		
Mean (SD) [median]	68.9 (11.9) [72.2]	73.0 (8.7) [73.7]
Sex, n (%)		
Male	23 (52.3)	44 (47.3)
Female	21 (47.7)	49 (52.7)
Smoking status, n (%)		
Current smoker	4 (9.1)	6 (6.5)
Former smoker	13 (29.5)	23 (24.7)
Never smoker	22 (50.0)	35 (37.6)
Unknown	5 (11.4)	29 (31.2)
BMI		
BMI available, n (%)	38 (86.4)	50 (53.8)
Mean (SD)	27.5 (5.0)	27.4 (5.6)
Median (IQR)	25.9 (23.7-30.9)	26.2 (23.5-30.1)
Previous enrollment in interventional clinical trial for an investigational PV treatment, n (%)	3 (6.8)	3 (3.2)

BMI, body mass index; IQR, interquartile range; PV, polycythemia vera.
[a]Baseline period: 12 months prior to index date (ie, time of suboptimal response to 1L therapy)

Baseline clinical characteristics

- More switchers (54.4%) than non-switchers (31.2%) had a history of thrombosis at time of PV diagnosis (**Table 2**)
- Comorbidities tended to be less prevalent in switchers than in non-switchers prior to the index date
  - Commonly reported comorbidities in switchers vs non-switchers, respectively, included hypertension (43.2% vs 66.7%), cardiac conditions (18.2% vs 29.0%), hypercholesterolemia (9.1% vs 25.8%), and diabetes (2.3% vs 16.1%)
  - Switchers had a higher proportion of obesity than non-switchers (15.9% vs 7.5%)
- In both groups, fatigue (18.2% switchers vs 16.1% non-switchers) and pruritus (15.9% vs 14.0%) were the most observed PV-related symptoms in the baseline period; proportions were similar between groups
- Fewer switchers (36.4%) than non-switchers (60.2%) received phlebotomies in the baseline period, while the mean (SD) number of procedures was similar (3.8 [2.3] vs 3.9 [2.8]) between groups

Table 2. Patient Baseline Clinical Characteristics[a]

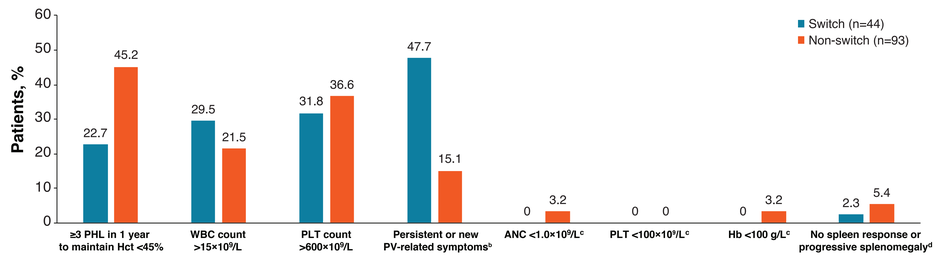
	Switch n=44	Non-switch n=93
History of thrombosis at time of PV diagnosis, n (%)	24 (54.5)	29 (31.2)
Comorbidities prior to the index date, n (%)		
Hypertension	19 (43.2)	62 (66.7)
Cardiac	8 (18.2)	27 (29.0)
Obesity	7 (15.9)	7 (7.5)
Hypercholesterolemia	4 (9.1)	24 (25.8)
Cancer	4 (9.1)	10 (10.8)
Diabetes	1 (2.3)	15 (16.1)
Other	9 (20.5)	39 (41.9)
None of the above	13 (29.5)	11 (11.8)
PV-related symptoms during the baseline period, n (%)		
Fatigue	8 (18.2)	15 (16.1)
Pruritus	7 (15.9)	13 (14.0)
Night sweats	3 (6.8)	3 (3.2)
Abdominal pain	2 (4.5)	4 (4.3)
Inactivity	1 (2.3)	0
Early satiety	0	3 (3.2)
Problems with concentration	0	2 (2.2)
Unintentional weight loss	0	2 (2.2)
Fever	0	1 (1.1)
Other	4 (9.1)	11 (11.8)
None of the above	32 (72.7)	66 (71.0)
Phlebotomies received during the baseline period, n (%)	16 (36.4)	56 (60.2)
Number of phlebotomies received, mean (SD) [median]	3.8 (2.3) [3.5]	3.9 (2.8) [3.0]

PV, polycythemia vera.
[a]Baseline period: 12 months prior to index date (ie, time of suboptimal response to 1L therapy)

Suboptimal response to first-line cytoreductive therapy on the index date

- The median (IQR) time from PV diagnosis to index date was shorter for switchers than non-switchers: 13.6 (12.3-22.3) vs 20.6 (14.7-37.0) months
- Distribution of suboptimal response criteria on the index date differed between the two groups (**Figure 2**)
  - For switchers, the most common criterion was "persistence of PV-related symptoms or presence of new PV-related symptoms," which was reported in 47.7% of patients; only 15.1% of non-switchers experienced this criterion
  - For non-switchers, the most common criterion was "need for ≥3 phlebotomies within 1 year to maintain hematocrit <45%," which was reported in 45.2% of patients; only 22.7% of switchers experienced this criterion

Figure 2. Suboptimal Response Criteria on the Index Date[a]

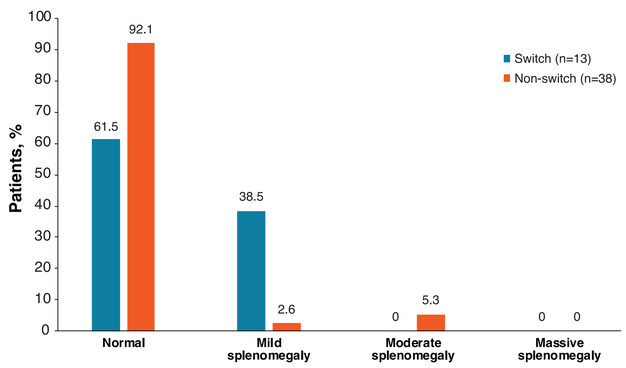


ANC, absolute neutrophil count; Hb, hemoglobin; Hct, hematocrit; PHL, phlebotomy; PLT, platelet; PV, polycythemia vera; WBC, white blood cell.
[a]Patients can experience >1 criterion defining suboptimal response. [b]PV-related symptoms include pruritus, fatigue, night sweats, fever, unintentional weight loss, abdominal pain, early satiety, problems with concentration, and inactivity. [c]Cytopenias at the lowest dose of cytoreductive therapy required to achieve a response; >1 cutoff can be used to diagnose cytopenias. [d]Spleen response was defined as a reduction in palpable splenomegaly of >50%.

Spleen assessments on the index date

- Data from spleen size assessment by palpation were available for 13 switchers (29.5%) and 38 non-switchers (40.9%) on the index date (**Figure 3**)
- On the index date, switchers tended to have a lower proportion of normal spleen size (61.5% vs 92.1%) and a higher proportion of mild or moderate splenomegaly (38.5% vs 7.9%) than non-switchers
- Spleen length assessments revealed the following results:
  - 20 switchers (45.5%) and 14 non-switchers (15.1%) had available spleen length results
  - The mean (SD) spleen lengths were 15.6 (5.0) and 13.8 (2.6) cm, respectively, which further supported the findings from palpation
  - Almost all spleen lengths were assessed by ultrasound

Figure 3. Spleen Size Assessed by Palpation on the Index Date



The types of spleen assessment (ie, spleen length and spleen size) are not mutually exclusive categories. If data from the index date are unavailable, then the data from the most recent date prior to the index date are reported.

Disclosures

M.W. Zuurman, **C. Paley**, and **G. Gilotti** have employment relationships with Novartis Pharmaceuticals Corporation. **W.Y. Cheng**, **C. Gao**, **M. Cheng**, **M. Wu**, and **M.S. Duh** are employees of Analysis Group, a consulting firm that received funding from Novartis Pharmaceuticals Corporation to conduct this study. **S. Koschmieder** received honoraria for consulting for Novartis, Bristol Myers Squibb Company, AOP Orphan Pharmaceuticals GmbH, Janssen Pharmaceuticals, Inc, Geron, Pfizer Inc, Incyte Corporation, Ariad Pharmaceuticals, Celgene Corporation, Shire, and Roche; served on advisory committees and other for Novartis, Bristol Myers Squibb Company, AOP Orphan Pharmaceuticals GmbH., Janssen Pharmaceuticals, Inc, Geron, Pfizer Inc, Incyte Corporation, Ariad Pharmaceuticals, Celgene Corporation, CTI BioPharma, Roche, Baxalta, and Sanofi; and received travel support from Alexion Pharmaceuticals, Karthos, Imago BioSciences, and AbbVie Inc. **E. von der Heyde** is a consultant for Novartis, Bristol Myers Squibb Company, Boehringer Ingelheim International GmbH, Ipsen Pharma, AstraZeneca Pharmaceuticals LP, and Merck.

T. Devos is a consultant for Novartis, Bristol Myers Squibb Company, Celgene Corporation, AbbVie Inc, and Incyte Corporation and has membership on Board of Directors or advisory committees for Alexion Pharmaceuticals and AstraZeneca Pharmaceuticals LP. **C. Schulte**, **L. Busque**, and **F. Boyer-Perrard** are consultants for Novartis. **F. Passamonti** has membership on Board of Directors or advisory committees and speakers bureau for Novartis, Celgene Corporation, Bristol Myers Squibb Company, Janssen Pharmaceuticals, Inc, and AbbVie Inc. **C. Harrison** has membership on Board of Directors or advisory committees and speakers bureau for Novartis, Celgene Corporation, CTI BioPharma, Gilead Sciences, Inc, Shire, Roche, Janssen Pharmaceuticals, Inc, Promedior, Inc, AOP Orphan Pharmaceuticals GmbH, Incyte Corporation, AbbVie Inc, Bristol Myers Squibb Company, Geron, Galecto, Inc, and Keros Therapeutics; receives research funding from Constellation Pharmaceuticals; and received honoraria for consulting for Sierra Oncology.

References

1. Vannucchi AM. *Blood*. 2014;124(22):3212-3220; **2.** Adamson JW, et al. *N Engl J Med*. 1976;295(17):913-916; **3.** Tefferi A, et al. *Leukemia*. 2013;27(9):1874-1881; **4.** Barbui T, et al. *J Clin Oncol*. 2011;29(6):761-770; **5.** Marchioli R, et al. *Thrombosis*. 2011;2011:794240; **6.** Marchioli R, et al. *N Engl J Med*. 2013;368(1):22-33; **7.** Jakavi (ruxolitinib). Prescribing information. Novartis; 2021; **8.** Landolfi R, et al. *N Engl J Med*. 2004;350(2):114-124.