Sponsor

Novartis Pharmaceuticals

Generic Drug Name

Ruxolitinib

Trial Indication(s)

Polycythemia Vera

Protocol Number

CINC424B3001

Protocol Title

Ruxolitinib for the treatment of Polycythemia Vera in patients who are resistant to or intolerant of hydroxyurea: a retrospective non-interventional study using the US Optum electronic health record data base.

Clinical Trial Phase

NA

Phase of Drug Development

NA

Study Start/End Dates

Study start date: 27/11/2020

Study Completion date: 29/06/2021

Reason for Termination

NA

Study Design/Methodology

This was an analytical and descriptive, non-interventional, retrospective cohort study of PV patients aged ≥ 18 years in the US using a secondary data source, Optum EHR database.

The Optum EHR database was current up to 30-Jun-2020.

Identification period: From 01-Apr-2007 to 30-Jun-2019

Study period: From 01-Jan-2007 to 30-Jun-2020

Index date:

First evidence of resistance to or intolerance of HU treatment in patients with PV according to modified European Leukemia Net (ELN) criteria and defined as:

1) HCT ≥ 45% with phlebotomy (last phlebotomy within last 3 months) Or

2) Platelet count > 400 x 109/L and presence of palpable splenomegaly (palpable spleen up to 3 months after platelet count)

Pre-index period:

Patients had a minimum of 3 months pre-index data available.

Pre-index data availability was determined using the reported 'first month active' field.

Post-index period:

There was no minimum post-index period required. Each patient had a 'first month active' and 'last month active' reported within the database. As the 'last month active' was based on any activity in the database, including encounters such as letters and emails which occurred several months after the 'death_date' of the patient, using the 'last month active' can overestimate the follow-up for a given patient. For this reason, the end of follow-up for each patient was defined as the date of the last activity within the diagnosis, observations, prescriptions, laboratories, procedures tables or discharge date from the last visit within the visit table (whichever of these activities occurs latest). This underestimated the follow-up for some patients where they were not actively using healthcare resources.

Centers

Novartis Investigative Site

Objectives:

Primary objective(s)

- The primary objective of this study was to investigate differences in TEs between those treated with BAT compared to those treated with RUX in PV patients resistant to or intolerant of HU and identify subgroups of patients treated with BAT who might have had the greatest capacity to benefit from treatment with RUX

Secondary objective(s)

- To examine differences in the incidence rate of TEs and time to first TE in PV patients resistant to or intolerant of HU treated with BAT compared to those treated with RUX.
- To examine differences in the incidence rate of phlebotomies and time to phlebotomy in PV patients resistant to or intolerant of HU treated with BAT compared to those treated with RUX.
- To examine differences in the incidence rate of neoplasm transformations and time to neoplasm transformation in PV patients resistant to or intolerant of HU treated with BAT compared to those treated with RUX.
- To examine differences in treatment patterns in PV patients resistant to or intolerant of HU treated with BAT compared to those treated with RUX.
- To examine differences in healthcare resource utilization (HCRU) in PV patients resistant to or intolerant of HU treated with BAT compared to those treated with RUX.

Test Product (s), Dose(s), and Mode(s) of Administration

NA

Statistical Methods

Frequencies of TEs (total number of TEs during entire study period and at distinct dates (dates where multiple events occurred in a single day and counted as single event)) in PV patients in the BAT group and RUX group were calculated (TEs were defined as per codes in RESPONSE and GEMFIN studies). Frequency of TEs in both groups was a continuous variable, and was summarized using patient counts, missing counts,

and percentage, mean, standard deviation, median, range (minimum, maximum), and interquartile range (25%, 75%). A Wilcoxon-Mann-Whitney test was used to compare the difference of numbers of TEs in the two groups. The test statistic and p-value were reported.

Crude incidence rates of TEs, phlebotomies with corresponding 95% CI was calculated for PV patients in the BAT and RUX groups respectively. Descriptive statistics were used for comparing the time to first TE and phlebotomy in PV patients in the BAT group and in the RUX group. Time to the first TE was a continuous variable, and was summarized using patient count, mean, standard deviation, median, range (minimum, maximum), and interquartile range (25%, 75%).

The total number of patients who ever had any type of neoplasm transformation during the follow-up period was used for the calculation of the crude incidence rates of neoplasm transformation for PV patients in the BAT group and in the RUX group respectively. Descriptive statistics were used for comparing the time to first neoplasm transformation in PV patients in the BAT group and in the RUX group. Time to the first transformation was a continuous variable, and was summarized using patient count, mean, standard deviation, median, range (minimum, maximum), and interquartile range (25%, 75%).

Descriptive statistics was used to compare the number and proportion of patients using different PV-related treatments during follow-up, categorized by the BAT group and the RUX group. The BAT and RUX categories were further sub-categorized as HU, IFN, busulfan, imatinib, and RUX (only for RUX group). For each treatment category, descriptive statistics included patient counts and proportion of patients in that treatment group.

Mean duration of treatment was calculated for each treatment in the BAT group and the RUX group. Both groups were further sub categorized as HU, IFN, busulfan, imatinib, and RUX (only for RUX group).

Descriptive statistics were used to compare the number of patients who switched from BAT to RUX treatment during follow-up. Descriptive statistics included patient counts and proportion of patients in that treatment group.

Descriptive statistics were used to compare differences in HCRU between PV patients in the BAT group and in the RUX group, categorized by all-cause and PV-specific, for number of inpatient hospitalizations, number of outpatient visits, and number of emergency room visits. Descriptive statistics included patient counts, missing percentage, mean, standard deviation, median, range (minimum, maximum), and interquartile range (25%, 75%).

Study Population: Key Inclusion/Exclusion Criteria

Inclusion criteria

- With at least one International Classification of Diseases, 9th Revision, Clinical Modification/International Classification of Diseases,10th Revision, Clinical Modification code for PV in the identification period (01-Apr-2007 until 30-Jun-2019) that had non-missing sex and year of birth data and who were treated as part of the Integrated Delivery Network
- That were ≥ 18 years old at PV diagnosis
- With ≥ 2 prescriptions of HU
- That were classified as resistant to or intolerant of HU after a minimum of 3 months HU treatment (index date), defined as: HCT ≥ 45% with phlebotomy (last phlebotomy within last 3 months) or Platelet count > 400 x 109/L and presence of palpable splenomegaly (palpable spleen up to 3 months after platelet count). To identify patients in the RUX group: - With ≥ 2 prescriptions of RUX in the post-index period.

Exclusion criteria

- With a MF or AML diagnosis prior to a PV diagnosis.

Participant Flow

Overall, the population of PV patients in Optum EHR database with at least one ICD-9- CM/ICD-10-CM code in the identification period with no missing data of gender and year of birth was 78271. Out of which, 1576 PV patients met the eligibility criteria, and 1367 patients were in the BAT group and 209 patients were in the RUX group.

Attrition table for Polycythemia Vera cohort including patients diagnosed with Essential Thrombocythemia

Criteria number	Criteria	Best available therapy (BAT) group		Ruxolitinib (RUX) group	
		N	% excluded	N	% excluded
1	With at least one ICD-9-CM/ICD-10-CM code for Polycythemia Vera in the identification period (01-April-2007 until 31-March-2019) that have non-missing sex and year of birth data	78271	0%	78271	0%
2	Include patients with age >= 18 years at index	76563	2.18%	76563	2.18%
3	Polycythemia Vera patients with at least 3 months of hydroxyurea medication and >= 2 prescriptions of hydroxyurea	6453	91.57%	6453	91.57%
4	Include patients that are classified as resistant to or intolerant of hydroxyurea after a minimum of 3 months hydroxyurea treatment (index date)	1620	74.90%	1620	74.90%
5a*	Exclude patients with ≥2 prescriptions of Ruxolitinib in the post-index period	1394	13.95%		
5b**	Include patients with ≥2 prescriptions of Ruxolitinib in the post-index period			226	86.05%
6	Exclude patients with a diagnosis of Myelofibrosis or Acute Myeloid Leukemia prior to or on Polycythemia Vera diagnosis date	1367	1.94%	209	7.52%

*Criteria 5a applies to the BAT group only

**Criteria 5b applies to the RUX group only

Baseline Characteristics

Baseline characteristics for the overall Polycythemia Vera cohort and for the BAT and RUX groups

Characteristic	Variable	Statistic	Overall cohort		Best available therapy		Ruxolitinib		
			N	%	n	%	n	%	p-value
Total cohort		n, %	1576	100%	1367	100%	209	100%	-
Age (continuous)		N	1576	100%	1367	100%	209	100%	0.02
		% missing	0	0	0	0	0	0	
		Min	24		24		25		
		percentile_25	60		60		58		
		Mean	67.05		67.29		65.43		
		Median	68		69		67		
		percentile_75	76		76		73		
		SD	11.26		11.28		11.03		
		Max	88		88		87		
Age (categorical)	≤ 60	n, %	385	24.43 %	326	23.85 %	59	28.23 %	0.17
	> 60	n, %	1191	75.57 %	1041	76.15 %	150	71.77 %	
Sex	Female	n, %	724	45.94 %	618	45.21 %	106	50.72 %	0.14
	Male	n, %	852	54.06 %	749	54.79 %	103	49.28 %	
Race	African American	n, %	90	5.71 %	79	5.78 %	11	5.26 %	0.13

Characteristic	Variable	Statistic	Overall cohort		Best available therapy		Ruxolitinib		
			N	%	n	%	n	%	p-value
	Asian	n, %	15	0.95 %	10	0.73 %	5	2.39 %	
	Caucasian	n, %	1398	88.71 %	1213	88.73 %	185	88.52 %	
Ethnicity	Hispanic	n, %	36	2.28 %	32	2.34 %	4	1.91 %	0.58
	Not Hispanic	n, %	1441	91.43 %	1246	91.15 %	195	93.30 %	
	Unknown	n, %	99	6.28 %	89	6.51 %	10	4.78 %	
Smoking Status	Current smoker	n, %	144	9.14 %	127	9.29 %	17	8.13 %	0
	Former smoker	n, %	522	33.12 %	453	33.14 %	69	33.01 %	
	Never smoker	n, %	504	31.98 %	411	30.07 %	93	44.50 %	
	Other smoker	n, %	79	5.01 %	68	4.97 %	11	5.26 %	
	Unknown	n, %	327	20.75 %	308	22.53 %	19	9.09 %	

Body Mass Index (continuous)		N	1518	96.32 %	1311	95.90 %	207	99.04 %	0
		% missing	58	3.68 %	56	4.10 %	2	0.96 %	
		Min	12.50		12.50		15.90		
		percentile_25	23.70		23.80		23		
		Mean	27.64		27.84		26.39		
		Median	27.03		27.30		25.80		
		percentile_75	30.50		30.90		29.10		
		SD	5.83		5.89		5.33		
		Max	63.70		63.70		49.50		
Body Mass Index (categorical)	Missing/Unknown	n, %	58	3.68 %	56	4.10 %	2	0.96 %	0.01
	Normal Weight	n, %	481	30.52 %	403	29.48 %	78	37.32 %	
	Obese	n, %	427	27.09 %	386	28.24 %	41	19.62 %	

	Overweight	n, %	573	36.36 %	491	35.92 %	82	39.23 %	
	Underweight	n, %	37	2.35 %	31	2.27 %	6	2.87 %	
Systolic blood pressure		N	1546	98.10 %	1339	97.95 %	207	99.04 %	0.0719
		% missing	30	1.90 %	28	2.05 %	2	0.96 %	
		Min	83		83		85		
		percentile_25	120		120		117.28		
		Mean	131.14		131.46		129.07		
		Median	130		130		129		
		percentile_75	141		141.50		141		
		SD	17.82		17.82		17.75		
		Max	219		219		183		
Follow up time (in days) (continuous)		N	1576	100%	1367	100%	209	100%	0
		% missing	0	0%	0	0%	0	0%	
		Min	0		0		19		
		percentile_25	644.50		667		426		
		Mean	1252.01		1292.07		990.01		
		Median	1102		1128		914		
		percentile_75	1737.50		1785		1501		
		SD	806.35		822.46		633.60		

Follow up time (in days) (categorical)	0	n %	2	0.13 %	2	0.15 %	0	0%	0
	1-30	n %	11	0.70 %	8	0.59 %	3	1.44 %	
	31-90	n %	28	1.78 %	22	1.61 %	6	2.87 %	
	91-182	n %	43	2.73 %	31	2.27 %	12	5.74 %	
	183-273	n %	41	2.60 %	30	2.19 %	11	5.26 %	
	274-365	n %	44	2.79 %	36	2.63 %	8	3.83 %	
	366-730	n %	306	19.42 %	260	19.02 %	46	22.01 %	
	731-1094	n %	307	19.48 %	276	20.19 %	31	14.83 %	
	>1094	n %	794	50.38 %	702	51.35 %	92	44.02 %	

Note: Chi-square test was used for categorical variables, t-test was used for continuous variables, between BAT group and RUX groups.

Results

Descriptive statistics:

- A total of 1576 PV patients met the eligibility criteria. Out of these, 1367 patients were in the BAT group and 209 patients were in the RUX group.
- Majority of the patients were elderly (>60 years of age), females and Caucasians. More than 50% (50.38%) patients followed-up for >1094 days.
- Approximately 75% of patients experienced hypertension and up to 50% patients experienced fatigue ever during the study period. Greater than 95% of patients had laboratory results for hematocrit, hemoglobin, RCD width and platelet count variables retrieved from Optum HER database, which were crucial in assessing risk and severity of PV. But, while comparing the data for the above-mentioned laboratory values between the BAT and RUX treatment groups, no significant differences were observed.

Primary Outcome Result(s)

Analysis of Primary objective:

- No significant difference was found between the BAT and the RUX groups in terms of the number of TEs experienced during the follow-up (p=0.304), in post-index period (p=0.25) and at distinct dates (p=0.24) using TE codes consistent with RESPONSE. Similarly, no significant differences were observed between the BAT and the RUX groups in terms of TEs experienced during the follow-up (p=0.852), in post-index period (p=0.91) and at distinct dates (p=0.71) using TE codes consistent with GEMFIN.

CART analysis:

- Of the 1367 patients included in the BAT group, and therefore eligible for CART analysis, the following characteristics were identified as risk factors of TEs. BAT patients with a lymphocyte count ≥ 7.85 and hematocrit value of < 51.55 (n=957) were at lower risk (<1 TE per year) of experiencing a TE. The remaining 410 patients whose lymphocyte count was ≥ 7.85 and a hematocrit value of ≥51.55 were at higher risk of experiencing a TE (≥1 TE per year).
- In high-risk subgroup (in analyses performed using TE codes consistent with RESPONSE), a significantly a lower incidence rate of TEs was reported in the RUX group (165.26) compared to the BAT group (304.08) during the study period. In contrast, the incidence rate of TEs in low-risk subgroup was higher in the RUX group (142.92) compared to the BAT group (73.48).
- At distinct dates, the incidence rates in the BAT versus the RUX groups were 202.94 vs. 92.48 respectively, in high-risk patients and 53.42 vs. 97.88, respectively in low-risk patients.
- The incidence rates of TEs during post –index period in the RUX vs BAT group was 10.94 vs 9.85 in high-risk patients and 9.63 vs. 5.59 in the low risk patients.

Thromboembolic events in overall Polycythemia Vera cohort and in the BAT and RUX groups

		TEs-RESPONSE							TEs-GEMFIN						
Variables	**Statistic**	**Overall cohort**		**Best available therapy**		**Ruxolitinib**		**p-value**	**Overall cohort**		**Best available therapy**		**Ruxolitinib**		**p-value**
		n	**%**	**n**	**%**	**n**	**%**		**n**	**%**	**n**	**%**	**n**	**%**	
Total cohort	N	1576	100%	1367	100%	209	100%		1576	100%	1367	100%	209	100%	
Any TE	N	385	24.43%	328	23.99%	57	27.27%	0.304	854	54.19%	742	54.28%	112	53.59%	0.852
Any TE (post-index)	N	1576	100%	1367	100%	209	100%		1576	100%	1367	100%	209	100%	
	Min	0		0		0			0		0		0		
	percentile_25	0		0		0			0		0		0		
	Mean	1.50		1.46		1.76		0.25	5.71		5.56		6.63		0.91
	Median	0		0		0			0.35		0.38		0.20		
	percentile_75	0		0		0.34			4.73		4.61		5.15		

		TEs-RESPONSE							TEs-GEMFIN						
Variables	**Statistic**	**Overall cohort**		**Best available therapy**		**Ruxolitinib**		**p-value**	**Overall cohort**		**Best available therapy**		**Ruxolitinib**		**p-value**
		n	**%**	**n**	**%**	**n**	**%**		**n**	**%**	**n**	**%**	**n**	**%**	
Thromboembolic event (dates) - continuous	SD	5.83		5.70		6.64			16.22		16.40		14.98		
	Max	91.29		91.29		59.19			314.31		314.31		101.94		
	N	1576	100%	1367	100%	209	100%		1576	100%	1367	100%	209	100%	
	Min	0		0		0			0		0		0		
	percentile_25	0		0		0			0		0		0		
	Mean	1.02		1		1.16			3.57		3.46		4.25		
	Median	0		0		0		0.24	0.31		0.33		0.20		0.71
	percentile_75	0		0		0.34			3.04		2.95		4.19		
	SD	3.70		3.69		3.74			10.59		10.85		8.65		
	Max	54.81		54.81		30.35			264.31		264.31		57.66		

Secondary Outcome Result(s)

Analysis of Secondary objective 1:

- The crude incidence rate was higher in those treated with RUX compared to those treated with BAT in analyses using TE codes consistent with RESPONSE or TE codes consistent with GEMFIN estimated for entire study period and at distinct dates. During post-index period, the observed difference for the incidence rates of TE between the BAT therapy and RUX treatment was only significant when analyzed using TE codes consistent with RESPONSE.

Incidence rate of thromboembolic event and time to first thromboembolic event

		Thromboembolic event codes consistent with RESPONSE			Thromboembolic event codes consistent with GEMFIN		
Variables	**Statistic**	**Overall cohort**	**Best available therapy**	**Ruxolitinib**	**Overall cohort**	**Best available therapy**	**Ruxolitinib**
Incidence rate of thromboembolic events (all events)	IR	139.09	137.80	150.12	443.64	437.91	492.52
	95%CI lower	135.96	134.51	140.20	438.04	432.04	474.42
	95%CI upper	142.27	141.14	160.55	449.29	443.85	511.13
Incidence rate of thromboembolic events (dates)	IR	95.23	95.12	96.14	279.88	274.99	321.58
	95%CI lower	92.64	92.39	88.24	275.43	270.34	306.99
	95%CI upper	97.87	97.91	104.56	284.37	279.70	336.69
Incidence rate of thromboembolic events (ever had a TE in post-index)	IR	7.12	6.78	10.05	15.80	15.33	19.76
	95%CI lower	6.43	6.06	7.62	14.76	14.25	16.27
	95%CI upper	7.87	7.55	13.03	16.89	16.48	23.77
Time to first TE (days)	N	385	328	57	854	742	112
	Min	0	0	0	0	0	0
	percentile_25	22	22	37	12	13	11.25
	mean	475.21	494.50	364.21	333.21	344.32	259.57
	median	201	211.50	166	105	109.50	67
	percentile_75	673	741	503	433.25	445.75	339.25

		Thromboembolic event codes consistent with RESPONSE			Thromboembolic event codes consistent with GEMFIN		
Variables	Statistic	Overall cohort	Best available therapy	Ruxolitinib	Overall cohort	Best available therapy	Ruxolitinib
	SD	615.36	636.12	467.93	512.22	524.03	420.36
	max	3890	3890	2070	3141	3141	2070

Analysis of secondary objective 2:

- A significantly lower rate of phlebotomy procedures was observed in the RUX group (IR: 51.69) compared to the BAT group (IR:198.80). Similarly, lower incidence rate of phlebotomy procedures in distinct dates was observed in RUX group (51.69) compared to BAT group (198.80) and a lower incidence rate of phlebotomies during post-index period were observed in RUX group (13.23) compared to BAT group (22.84)

Incidence rate of phlebotomy procedures and time to first phlebotomy procedure

Variables	Statistic	Overall cohort	Best available therapy	Ruxolitinib
Incidence rate of phlebotomy procedures (all events)	IR	183.37	198.80	51.69
	95%CI lower	179.78	194.85	45.94
	95%CI upper	187.02	202.81	57.96
Incidence rate of phlebotomy procedures (dates)	IR	183.37	198.80	51.69
	95%CI lower	179.78	194.85	45.94
	95%CI upper	187.02	202.81	57.96
Incidence rate of phlebotomy procedures (ever had a phlebotomy in post-index)	IR	21.83	22.84	13.23
	95%CI lower	20.60	21.51	10.41
	95%CI upper	23.11	24.22	16.58
Time to first phlebotomy procedure (days)	N	1180	1105	75
	Min	0	0	0
	percentile_25	0	0	8.5
	Mean	50.29	43.15	155.41
	Median	0	0	40
	percentile_75	14	8	154
	SD	170.85	160.37	263.47
	Max	2138	2138	1289

Analysis of secondary objective 3:

The incidence rate of neoplasm transformations was significantly higher in RUX group (13.94) compared to the BAT group (2.07). The mean (SD) number of days taken for neoplasm transformations was 723.72 (788.89) and 258.29 (481.05) in overall cohort, BAT group and RUX group respectively

Incidence rate of neoplasm transformations and time to first neoplasm transformation

Variables	Statistic	Overall cohort	Best available therapy	Ruxolitinib
Incidence rate of neoplasm transformations	IR	3.31	2.07	13.94
	95%CI lower	2.84	1.68	11.03
	95%CI upper	3.83	2.51	17.37
Time to neoplasm transformation (days)	N	179	100	79
	Min	0	0	0
	percentile_25	7	93	0
	Mean	518.31	723.72	258.29
	Median	224	463	16
	percentile_75	785	1005	300.5
	SD	707.99	788.89	481.05
	Max	2885	2765	2885

Analysis of secondary objective 4:

- Most received treatment was hydroxyurea (93.34%) followed by interferons (1.68%), busulfan (1.32%) and imatinib (0.15%) in BAT group. The treatment pattern in RUX group was hydroxyurea (58.85%), interferons (3.83%), and imatinib (1.44%). The mean length of treatment for hydroxyurea was 901.23 days for patients in the BAT group and 227.56 days in RUX group.

Treatment patterns in Polycythemia Vera patients in the BAT group and the RUX group

		Length of treatment (days)					
		Overall cohort		Best available therapy		Ruxolitinib	
Variables	Statistic	N	%	n	%	N	%
Total	n, %	1495	94.86%	1286	94.07%	209	100%
	Min	0		0		1	
	25% Percentile	276.5		277.5		273	
	Mean	902.88		913.51		833.29	
	Median	729		736		701	
	75% Percentile	1365.50		1371.50		1272	
	SD	776.33		795.47		634.43	
	Max	4607		4607		3009	
Hydroxyurea	n, %	1399	88.77%	1276	93.34%	123	58.85%
	Min	0		0		0	
	25% Percentile	105.75		265.5		0	
	Mean	811.89		901.23		227.56	
	Median	623		728		0	
	75% Percentile	1278.25		1366		212	
	SD	790.83		794.58		440.22	
	Max	4607		4607		1869	
Ruxolitinib	n, %					209	100%
	Min					1	
	25% Percentile					230	
	Mean					759.50	
	median					584	
	75% Percentile					1216	
	SD					629.95	
	Max					2887	
Interferon	n, %	31	1.97%	23	1.68%	8	3.83%
	Min	0		0		0	
	25% Percentile	0		0		0	
	Mean	10.93		10.45		14.10	
	median	0		0		0	
	75% Percentile	0		0		0	
	SD	102.04		101.58		105.21	
	Max	1525		1525		1093	

		Length of treatment (days)					
		Overall cohort		Best available therapy		Ruxolitinib	
Variables	Statistic	N	%	n	%	N	%
Busulfan	n, %	18	1.14%	18	1.32%	-	0%
	Min	0		0		0	
	25% Percentile	0		0		0	
	Mean	2.78		3.20		0	
	median	0		0		0	
	75% Percentile	0		0		0	
	SD	56.76		60.94		0	
	Max	1699		1699		0	
Imatinib	n, %	5	0.32%	2	0.15%	3	1.44%
	Min	0		0		0	
	25% Percentile	0		0		0	
	Mean	0.65		0.69		0.39	
	median	0		0		0	
	75% Percentile	0		0		0	
	SD	17.39		18.59		4.56	
	Max	594		594		65	

Analysis of secondary objective 5:

Overall, most of the patient visits were outpatient both in case of all-cause (overall: 98.86%; 98.68% in the BAT group vs. 100% in the RUX group) and in PV-specific scenarios (overall: 74.05%; 74.40% in BAT group vs. 71.77% in RUX group)

Healthcare resource utilization in polycythemia vera patients in the BAT group and RUX group

		All-cause						PV-specific					
		Overall cohort		Best available therapy		Ruxolitinib		Overall cohort		Best available therapy		Ruxolitinib	
Variables	Statistic	n	%	n	%	n	%	n	%	n	%	n	%
	n, %	556	35.28%	478	34.97%	78	37.32%	127	8.06%	101	7.39%	26	12.44%

		All-cause						PV-specific					
		Overall cohort		Best available therapy		Ruxolitinib		Overall cohort		Best available therapy		Ruxolitinib	
Variables	Statistic	n	%	n	%	n	%	n	%	n	%	n	%
Inpatient hospitalizations	Min	0		0		0		0		0		0	
	25% Percentile	0		0		0		0		0		0	
	Mean	0.93		0.91		1.07		0.11		0.10		0.18	
	Median	0		0		0		0		0		0	
	75% Percentile	1		1		1		0		0		0	
	SD	2.06		2.04		2.27		0.43		0.41		0.57	
	Max	39		39		17		4		4		4	
	n, %	1558	98.86%	1349	98.68%	209	100%	1167	74.05%	1017	74.40%	150	71.77%
Outpatient visits	Min	0		0		1		0		0		0	
	25% Percentile	39		38		41		0		0		0	
	Mean	133.30		130.27		153.06		23.13		23.19		22.73	
	Median	88		85		109		11		11		11	
	75% Percentile	175		168.50		199		31		31		32	
	SD	146.18		143.21		163.31		34.08		33.16		39.65	
	Max	1079		968		1079		424		334		424	
	n, %	617	39.15%	541	39.58%	76	36.36%	85	5.39%	70	5.12%	15	7.18%
Emergency room visits	Min	0		0		0		0		0		0	
	25% Percentile	0		0		0		0		0		0	
	Mean	1.21		1.23		1.09		0.07		0.07		0.08	
	Median	0		0		0		0		0		0	
	75% Percentile	1		1		1		0		0		0	

Safety Results
Not applicable.

Other Relevant Findings
NA

Conclusion
Although there was no significant difference in the number of TEs between patients on RUX treatment compared to BAT in the overall population, these results should be interpreted with caution due to the small number of patients in the RUX group and differences in baseline patient characteristics between the RUX and BAT groups. The CART analysis identified a sub-group of patients relapsed/refractory to HU, at higher risk of a TE that may have a greater capacity to benefit from treatment with RUX based on lymphocyte count and hematocrit percentage. Analysis of the high risk sub-group demonstrated lower incidence of TEs in patients treated with RUX compared with BAT over the entire study period. Given the retrospective nature and considering the inherent limitations of this type of analysis, these results should be interpreted with caution, especially in light of the small number of patients in the RUX group, and differences in baseline patient characteristics between RUX and BAT

Date of Clinical Study Report
22 March, 2022