Featuring data from the MAJIC-PV study, published in the *Journal of Clinical Oncology* 2023

Jakafi®
ruxolitinib (tablets)
5mg • 10mg • 15mg • 20mg • 25mg

For polycythemia vera (PV) in adults who have had an inadequate response to hydroxyurea (HU)[1]

INTERVENE

with Jakafi

to achieve durable count control

NCCN CLINICAL PRACTICE GUIDELINES IN ONCOLOGY (NCCN GUIDELINES®) RECOMMENDED

Ruxolitinib (Jakafi) is an NCCN Category 1* treatment option for patients with high-risk PV who have had an inadequate response or loss of response to cytoreductive therapy[2]

*Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.[2]
NCCN=National Comprehensive Cancer Network.

INDICATIONS AND USAGE

Jakafi® (ruxolitinib) is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.

IMPORTANT SAFETY INFORMATION

- Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary
- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi
- Severe neutropenia (ANC $<0.5 \times 10^9$/L) was generally reversible by withholding Jakafi until recovery

Please see related and other Important Safety Information on pages 16-17.
Please click here for Full Prescribing Information.

For your adult patients on HU and phlebotomy

Proactively identify the characteristics of advanced PV and treat differently

In a subset of patients, these characteristics may indicate advanced PV despite treatment with HU at the maximum tolerated dose and phlebotomy[3-6]

Hct ≥45% **PLUS** WBC count >11 × 10^9/L **OR** Disease-related symptoms

"If I have a patient who is encountering challenges strictly maintaining hematocrit levels below 45% and has leukocytosis, this tells me that the hydroxyurea is no longer sufficient."

— Andrew Kuykendall, MD, MPN Expert

Hct=hematocrit; WBC=white blood cell.

IMPORTANT SAFETY INFORMATION (continued)

Risk of infection

- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines
- Tuberculosis (TB) infection has been reported. Observe patients taking Jakafi for signs and symptoms of active TB and manage promptly. Prior to initiating Jakafi, evaluate patients for TB risk factors and test those at higher risk for latent infection. Consult a physician with expertise in the treatment of TB before starting Jakafi in patients with evidence of active or latent TB. Continuation of Jakafi during treatment of active TB should be based on the overall risk-benefit determination
- Progressive multifocal leukoencephalopathy (PML) has occurred with Jakafi treatment. If PML is suspected, stop Jakafi and evaluate
- Herpes zoster infection has been reported in patients receiving Jakafi. Advise patients about early signs and symptoms of herpes zoster and to seek early treatment. Herpes simplex virus reactivation and/or dissemination has been reported in patients receiving Jakafi. Monitor patients for the development of herpes simplex infections. If a patient develops evidence of dissemination of herpes simplex, consider interrupting treatment with Jakafi; patients should be promptly treated and monitored according to clinical guidelines
- Increases in hepatitis B viral load with or without associated elevations in alanine aminotransferase and aspartate aminotransferase have been reported in patients with chronic hepatitis B virus (HBV) infections. Monitor and treat patients with chronic HBV infection according to clinical guidelines

NCCN Guidelines® recommend

Actively monitoring patients' response and signs/symptoms of disease progression*

Potential indications for change of cytoreductive therapy for patients with symptomatic low-risk PV or high-risk PV are included in the NCCN Guidelines

NCCN GUIDELINES RECOMMENDED

Monitor patients for new thrombosis or bleeding, response* to cytoreductive therapy, and signs and symptoms* of disease progression[2]

Potential indications for change of cytoreductive therapy for patients with symptomatic low-risk PV or high-risk PV with no response or loss of response[2]

- **Intolerance or resistance to HU or interferons**
- **Disease-related symptoms (eg, pruritus, night sweats, fatigue)**
- **New thrombosis or disease-related major bleeding**
- **Progressive thrombocytosis and/or leukocytosis**
- **Frequent phlebotomy or intolerant of phlebotomy**
- **Splenomegaly**

FDA approved for use in adults with PV after inadequate response to or intolerance of HU[1]

- The phase 3 RESPONSE study defined inadequate response to include the maximum tolerated dose of HU, not just the ELN criteria of at least 2 g/d, after 3 months[7,8]
- RESPONSE was an open-label trial and, therefore, not designed to evaluate a difference in symptoms[1]
- The RESPONSE study did not evaluate the efficacy of Jakafi® (ruxolitinib) in reducing the risk of thrombosis[1]

*Every 3 to 6 months or more frequently as clinically indicated.[2]

ELN=European LeukemiaNet; RESPONSE=Randomized study of Efficacy and Safety in POlycythemia vera with JAK iNhibitor ruxolitinib verSus bEst available care.

"In my experience, the vast majority of patients are symptomatic, despite being on hydroxyurea."

—Ruben Mesa, MD, FACP, MPN Expert

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Jakafi® ruxolitinib (tablets)
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When PV advances beyond what HU can control, intervene with Jakafi® (ruxolitinib)

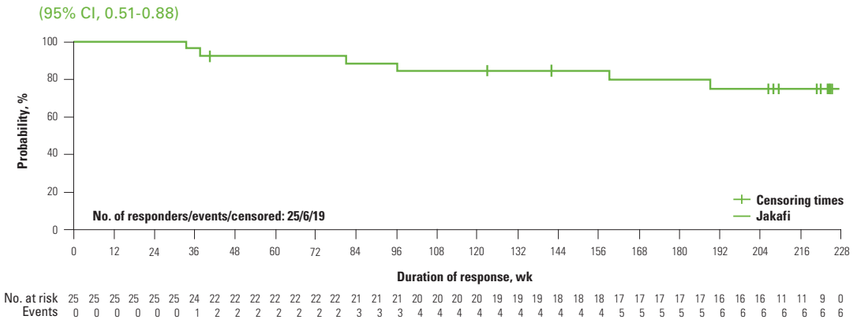
In the phase 3 RESPONSE* trial, Jakafi demonstrated superior results† vs BAT[1‡]

RESPONSE Composite Primary Endpoint

23% **(25/110) of patients receiving Jakafi achieved Hct control and ≥35% spleen volume reduction at week 32 vs <1% (1/112) of patients receiving BAT (*P*<0.0001)[1§]**

Kaplan-Meier Estimate: Durability of Primary Response at 5 Years

74% **Probability of Maintaining the Primary Response at 5 Years[9]**



The median duration of primary response was not reached.[9]

Reprinted from *The Lancet Haematology,* Vol 7, Kiladjian J-J, Zachee P, Hino M, et al, Long-term efficacy and safety of ruxolitinib versus best available therapy in polycythaemia vera (RESPONSE): 5-year follow up of a phase 3 study, e226-e237, Copyright 2020, with permission from Elsevier.

- Analysis was conducted in week 32 primary responders, beginning at week 32[9]
- Progression was defined as: the first of 2 consecutive Hct assessments that confirmed phlebotomy eligibility, a spleen volume assessment that was reduced by <35% from the baseline AND that was ≥25% increased at the time of the best-documented spleen volume response, death, or development of MF or acute leukemia[10]

66% (72 of 110) **of patients in the Jakafi arm completed 5 YEARS OF ON-STUDY TREATMENT[9]**

"For patients with PV, we know that suboptimal control of hematocrit, which is anything greater than 45%, is associated with significant risks, even if the Hct is 47% or 48%. So, to protect my patients, I typically intervene slightly below 45%."

—Ruben Mesa, MD, FACP, MPN Expert

*The RESPONSE trial was a randomized, open-label, active-controlled phase 3 trial comparing Jakafi with BAT in 222 patients with PV. Patients enrolled in the study had been diagnosed with PV for at least 24 weeks, had an inadequate response to or were intolerant of HU, required phlebotomy for Hct control, and exhibited splenomegaly. All patients were required to demonstrate Hct control between 40% and 45% prior to randomization. After week 32, patients on BAT were able to cross over to Jakafi treatment.[1,8]

†The composite primary endpoint was defined as Hct control without phlebotomy eligibility and a ≥35% spleen volume reduction as measured by CT or MRI. To achieve the Hct control endpoint, patients could not become eligible for phlebotomy between weeks 8 and 32. Phlebotomy eligibility was defined as Hct >45% that is ≥3 percentage points higher than baseline or Hct >48% (lower value).[1,8]

‡BAT included HU (60%), interferon/pegylated interferon (12%), anagrelide (7%), pipobroman (2%), lenalidomide/thalidomide (5%), and observation (15%).[1]

§Jakafi: 95% CI, 0.15-0.32; BAT: 95% CI, 0.00-0.05.[1]

BAT=best available therapy; CI=confidence interval; CT=computed tomography; MF=myelofibrosis; MRI=magnetic resonance imaging.

Individual component of the primary endpoint

More patients achieved Hct control with Jakafi in the absence of phlebotomy eligibility

In the RESPONSE trial, patients on Jakafi achieved a higher rate of Hct control vs BAT[1]

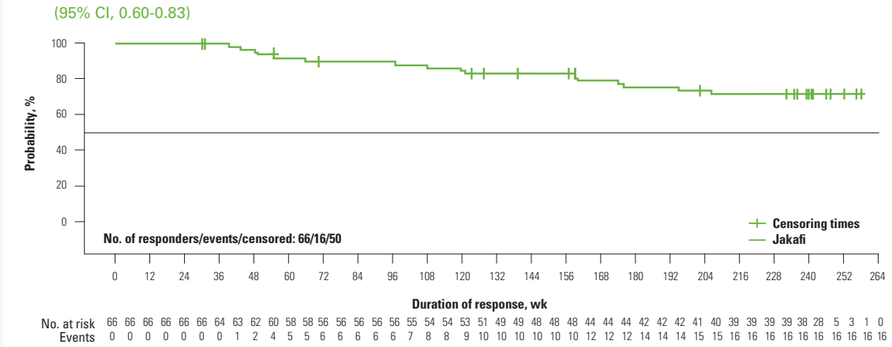
60% **(66/110) of patients receiving Jakafi achieved Hct control at week 32 vs 19% (21/112) of patients receiving BAT[1]**

- To achieve the Hct control endpoint, patients could not become eligible for phlebotomy between weeks 8 and 32. Phlebotomy eligibility was defined as Hct >45% that is ≥3 percentage points higher than baseline or Hct >48% (lower value)[1,8]

Kaplan-Meier Estimate: Durability of Hct Control at 5 Years

73% **Probability of Maintaining Hct Control[a] at 5 Years[9]**

[a]Absence of phlebotomy eligibility.



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- Analysis was conducted in week 32 Hct control responders, beginning at week 32[9]
- Progression events for the evaluation of duration of absence of phlebotomy eligibility included the first of 2 consecutive Hct assessments that confirmed phlebotomy eligibility, death, or development of MF or acute leukemia[10]

BAT=best available therapy.

IMPORTANT SAFETY INFORMATION (continued)

Risk for symptom exacerbation following interruption or discontinuation of Jakafi

- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering Jakafi, evaluate and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi without consulting their physician. When discontinuing or interrupting Jakafi for reasons other than thrombocytopenia or neutropenia, consider gradual tapering rather than abrupt discontinuation

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Significantly more patients

Achieved complete hematologic remission with Jakafi® (ruxolitinib)

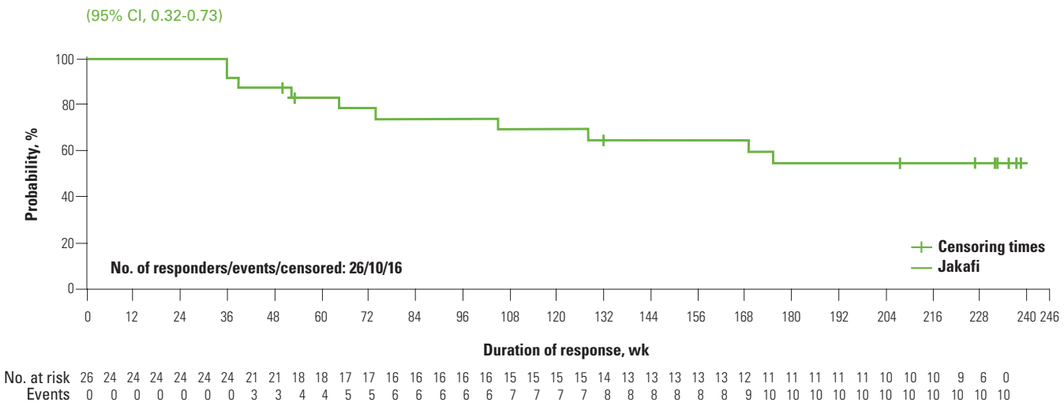
Patients on Jakafi demonstrated significantly higher rates of complete hematologic remission (CHR)* vs BAT[1]

RESPONSE Secondary Endpoint

24% (26/110) of patients receiving Jakafi achieved CHR at week 32 vs 8% (9/112) of patients receiving BAT (*P*=0.0016)[1†]

Kaplan-Meier Estimate: Durability of CHR at 5 Years

55% Probability of Maintaining CHR at 5 Years[9]



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- Analysis was conducted in week 32 CHR responders, beginning at week 32[9]
- Progression events for the evaluation of duration of CHR included first of 2 consecutive Hct assessments that confirmed phlebotomy eligibility, first of 2 contiguous visits during which platelet count was >400 × 10^9/L or WBC count was >10 × 10^9/L, death, or development of MF or acute leukemia[10]

*CHR was defined as achieving Hct control (as specified in the primary endpoint), platelet count ≤400 × 10^9/L, and WBC count ≤10 × 10^9/L.[1]
†Jakafi: 95% CI, 0.16-0.33; BAT: 95% CI, 0.04-0.15.[1]

BAT=best available therapy.

IMPORTANT SAFETY INFORMATION (continued)

Other important safety considerations

- Non-melanoma skin cancers (NMSC) including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations
- Treatment with Jakafi has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiating Jakafi. Monitor and treat according to clinical guidelines for the management of hyperlipidemia

Individual component of complete hematologic remission

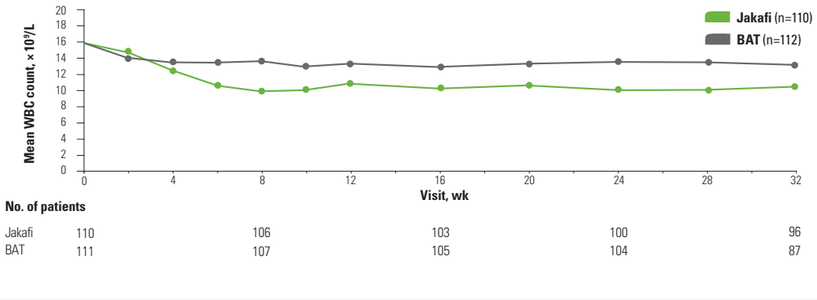
Jakafi reduced mean WBC counts

"It's important in patients with polycythemia vera to establish what their baseline white blood cell count is. Ideally, we want this number to be at or below 11,000 because we understand there's some risk associated with a higher baseline white blood cell count."

— Andrew Kuykendall, MD, MPN Expert

Exploratory analyses from the RESPONSE trial: WBC count data

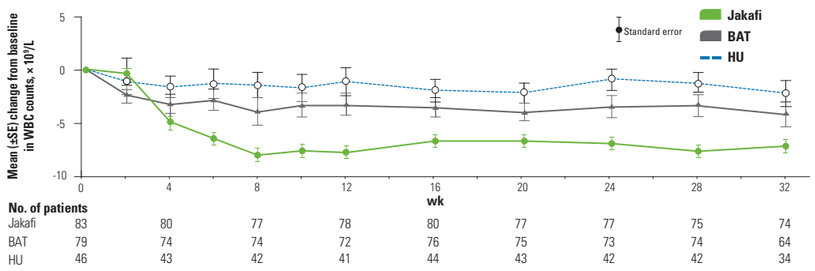
Mean WBC Counts Over Time[8]



From *The New England Journal of Medicine,* Vannucchi AM, Kiladjian JJ, Griesshammer M, et al, Ruxolitinib versus standard therapy for the treatment of polycythemia vera, 372, 426-435. Copyright © 2015 Massachusetts Medical Society. Reprinted with permission from Massachusetts Medical Society.

- As shown below, data for patients treated with HU were included in the group of patients receiving BAT[11]

Mean Change From Baseline in WBC Counts for Patient Subgroups With WBC Counts ≥11 × 10^9/L[11]



Comprehensive haematological control with ruxolitinib in patients with polycythaemia vera resistant to or intolerant of hydroxycarbamide, Harrison CN, Griesshammer M, Miller C, et al. Copyright © 2018 John Wiley & Sons Ltd, *British Journal of Haematology.* Reproduced with permission of John Wiley & Sons Ltd.

- At baseline, 75.5% of patients (n=83) receiving Jakafi and 71.4% of patients (n=80) receiving BAT had WBC counts ≥11 × 10^9/L[11]

BAT=best available therapy.

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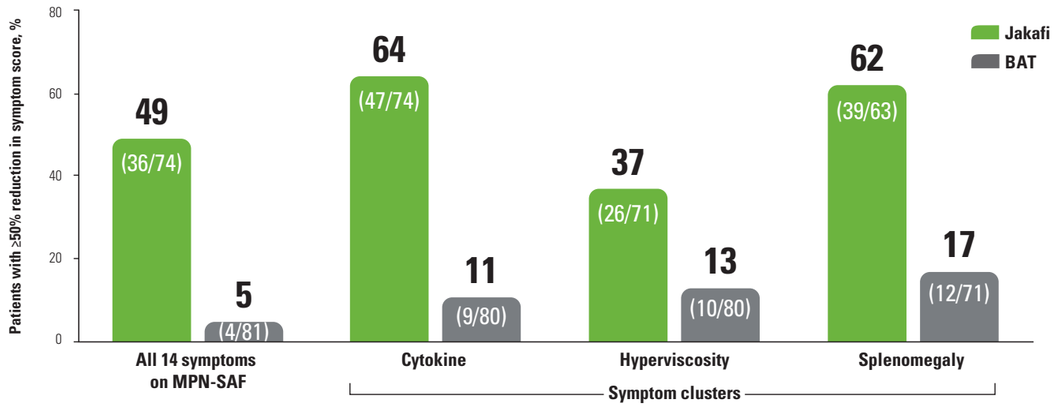
Jakafi® (ruxolitinib) symptom data

Exploratory endpoint from the RESPONSE trial

- At week 32, 49% of patients receiving Jakafi and 5% of patients receiving BAT had at least a 50% reduction in the 14-item Myeloproliferative Neoplasm Symptom Assessment Form (MPN-SAF) Total Symptom Score[8]
- RESPONSE was an open-label trial and, therefore, not designed to evaluate differences in symptoms[1]
- Patient-reported outcomes were assessed using the MPN-SAF symptom diary. The MPN-SAF diary was administered daily in an electronic diary format to score 14 disease-related symptoms on a scale of 0 (absent) to 10 (worst possible). At baseline, median Total Symptom Score was 23.4 (range, 0-106) in the group receiving Jakafi and 33.3 (range, 0-118) in the group receiving BAT[8,10]

Patients Achieving ≥50% Reduction in MPN-SAF Total Symptom Score at Week 32[8,a]



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[a] Higher symptom score indicates greater severity of symptoms. Cytokine symptom cluster includes tiredness, itching, muscle ache, night sweats, and sweating while awake; hyperviscosity symptom cluster includes vision problems, dizziness, concentration problems, headache, numbness or tingling in the hands or feet, ringing in the ears, and skin redness; and splenomegaly symptom cluster includes abdominal discomfort and early satiety. Patients with data at both baseline (value >0) and week 32 were included in this analysis.[8]

BAT=best available therapy.

IMPORTANT SAFETY INFORMATION (continued)

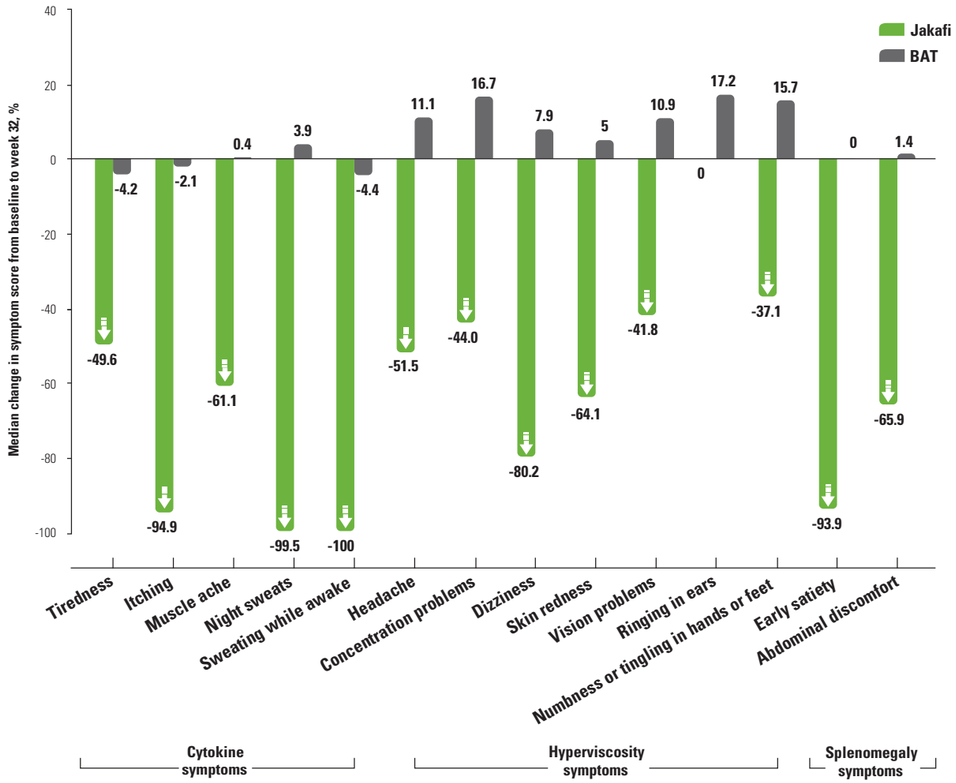
Other important safety considerations (continued)

- Another JAK-inhibitor has increased the risk of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, and stroke (compared to those treated with tumor TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur

Exploratory endpoint from the RESPONSE trial

- Patients receiving Jakafi had greater reductions in all symptom clusters reported, whereas patients receiving BAT had an increase in scores of many symptoms[8]

Median Percent Change in Symptom Score From Baseline to Week 32[8,a]



This analysis is exploratory in nature and these results should be interpreted with caution.

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[a] Patients with data at both baseline (value >0) and week 32 were included in this analysis. Negative values indicate a reduction in the severity of symptoms.[8]

BAT=best available therapy.

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Safety profile for Jakafi® (ruxolitinib) in PV

RESPONSE nonhematologic adverse reactions[1]

Adverse Reactions (Incidence ≥5%)	Jakafi (n=110)		BAT (n=111)	
	All Grades,[a] %	Grades 3 and 4, %	All Grades, %	Grades 3 and 4, %
Diarrhea	15	0	7	<1
Dizziness[b]	15	0	13	0
Dyspnea[c]	13	3	4	0
Muscle spasms	12	<1	5	0
Constipation	8	0	3	0
Herpes zoster[d]	6	<1	0	0
Nausea	6	0	4	0
Weight gain[e]	6	0	<1	0
Urinary tract infections[f]	6	0	3	0
Hypertension	5	<1	3	<1

[a]National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0.
[b]Includes dizziness and vertigo.
[c]Includes dyspnea and dyspnea exertional.
[d]Includes herpes zoster and postherpetic neuralgia.
[e]Includes weight increased and abnormal weight gain.
[f]Includes urinary tract infection and cystitis.

BAT=best available therapy.

IMPORTANT SAFETY INFORMATION (continued)

Other important safety considerations (continued)

- Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. In patients with myelofibrosis (MF) and polycythemia vera (PV) treated with Jakafi in clinical trials, the rates of thromboembolic events were similar in Jakafi and control treated patients. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately
- Another JAK-inhibitor has increased the risk of lymphoma and other malignancies excluding NMSC (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi, particularly in patients with a known secondary malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers

Clinically relevant laboratory abnormalities[1]

Laboratory Parameter[a]	Jakafi (n=110)			BAT (n=111)		
	All Grades,[b] %	Grade 3, %	Grade 4, %	All Grades, %	Grade 3, %	Grade 4, %
Hematology						
Anemia	72	<1	<1	58	0	0
Thrombocytopenia	27	5	<1	24	3	<1
Neutropenia	3	0	<1	10	<1	0
Chemistry						
Hypercholesterolemia	35	0	0	8	0	0
Elevated ALT	25	<1	0	16	0	0
Elevated AST	23	0	0	23	<1	0
Hypertriglyceridemia	15	0	0	13	0	0

[a]Presented values are worst grade values regardless of baseline.
[b]National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE), version 3.0.

Thromboembolic events[8]

Patients, n (%)	Jakafi (n=110)		BAT (n=111)	
	All Grades	Grade 3/4	All Grades	Grade 3/4
All thromboembolic events	1 (0.9)	1 (0.9)	6 (5.4)[a]	2 (1.8)[a]

[a]One patient in the BAT group had both myocardial infarction and pulmonary embolism.

- Discontinuation for adverse events, regardless of causality, was observed in 4% of patients treated with Jakafi[1]

ALT=alanine transaminase; AST=aspartate transaminase; BAT=best available therapy.

Please see related and other Important Safety Information on pages 16-17.
Please click here for Full Prescribing Information.

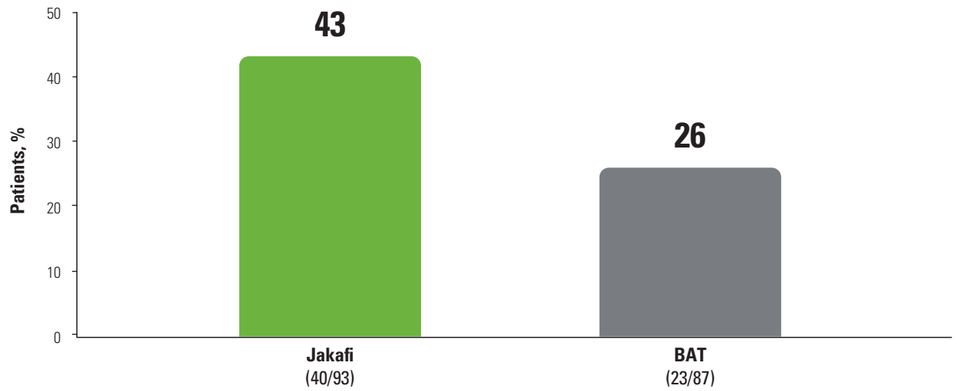
Significantly more patients on Jakafi® (ruxolitinib) achieved a complete response vs BAT[12]

MAJIC-PV study design[12]

- MAJIC-PV was an open-label, phase 2, randomized, controlled trial of Jakafi vs BAT* conducted in patients with high-risk PV meeting criteria for being resistant/intolerant to HU (N=180)
- There was no per-protocol crossover of BAT patients to Jakafi†
- Primary endpoint was complete response (CR) rate within 12 months as defined by ELN criteria: Hct <45% without phlebotomy for 3 months; platelets ≤400 × 10^9/L; WBC count ≤10 × 10^9/L, and normal spleen size
- Apart from the primary endpoint, all additional endpoints were exploratory and unpowered

MAJIC-PV Primary Endpoint: Achievement of CR Within 12 Months[12]

OR, 2.12 (90% CI, 1.25-3.60; *P*=0.02)



*BAT included HU (32%), interferon (15%), HU/interferon (11%), anagrelide/HU (10%), anagrelide (3%), anagrelide/interferon (3%), anagrelide/HU/interferon (3%), busulfan/interferon (2%), interferon/ruxolitinib (2%), HU/interferon/ruxolitinib (3%), anagrelide/ruxolitinib (1%), anagrelide/interferon/ruxolitinib (1%), anagrelide/HU/interferon/ruxolitinib (1%), busulfan/HU/interferon (1%), busulfan/ruxolitinib (1%), HU/ruxolitinib (1%), interferon/pipobroman (1%), 32P (1%), busulfan (1%), 32P/HU (1%), 32P/anagrelide/interferon (1%).

†Patients receiving BAT were permitted to change therapy; 66% (57 of 87) continued with HU as BAT. Ten patients received Jakafi treatment in the BAT arm.[12]

32P=radiophosphorus 32; BAT=best available therapy; CI=confidence interval; HU=hydroxyurea; OR=odds ratio.

IMPORTANT SAFETY INFORMATION (continued)

Other important safety considerations (continued)

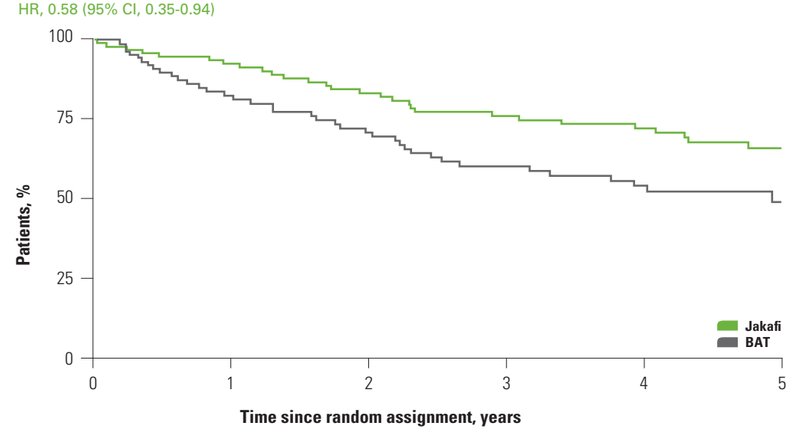
- In myelofibrosis and polycythemia vera, the most common nonhematologic adverse reactions (incidence ≥15%) were bruising, dizziness, headache, and diarrhea. In acute graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >50%) were infections (pathogen not specified) and edema. In chronic graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >20%) were infections (pathogen not specified) and viral infections

MAJIC-PV secondary endpoint

Jakafi EFS and thrombosis-free survival vs BAT[12]

Kaplan-Meier Analysis: Event-Free Survival[12]

HR, 0.58 (95% CI, 0.35-0.94)



42%
Reduction in the risk of an event with Jakafi[12]

EFS was a composite of major thrombosis, major hemorrhage, transformation, or death.

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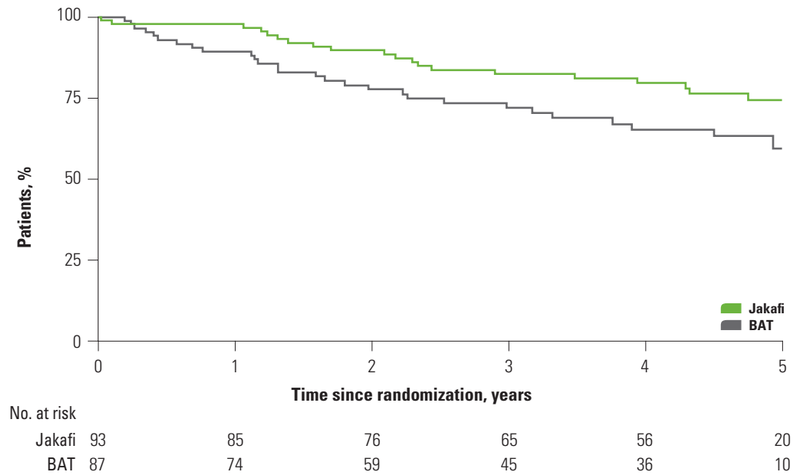
Kaplan-Meier Analysis: Thrombosis-Free Survival[12]

HR, 0.56 (95% CI, 0.32-1.00)



44%
Reduction in the risk of major thrombosis with Jakafi[12]

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BAT=best available therapy; CI=confidence interval; EFS=event-free survival; HR=hazard ratio.

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Jakafi® (ruxolitinib) safety data: MAJIC-PV trial[12]

MAJIC-PV adverse events[12]

Toxicity (Events [Patients]) (≥5 patients in either arm)	Jakafi (n=93)		BAT (n=87)	
	Grade 3	Grade 4	Grade 3	Grade 4
Blood and lymphatic system disorders	16 (11)	0 (0)	4 (3)	0 (0)
Anemia	12 (7)	0 (0)	2 (1)	0 (0)
Gastrointestinal disorders	12 (9)	0 (0)	9 (6)	3 (3)
General disorders and administration site conditions	6 (6)	0 (0)	6 (5)	0 (0)
Hepatobiliary disorders	0 (0)	0 (0)	5 (5)	0 (0)
Infections and infestations[a]	18 (14)	2 (2)	4 (4)	7 (4)
Injury, poisoning and procedural complications	9 (6)	1 (1)	4 (4)	0 (0)
Investigations (abnormal laboratory results)	11 (9)	1 (1)	2 (2)	0 (0)
Metabolism and nutrition disorders	8 (6)	1 (1)	6 (4)	1 (1)
Musculoskeletal and connective tissue disorders	10 (6)	0 (0)	2 (2)	0 (0)

[a]Malignancies and infections were deemed adverse events of special interest and have been presented separately. See MAJIC supplementary information.

BAT=best available therapy.

IMPORTANT SAFETY INFORMATION (continued)

Other important safety considerations (continued)

- Avoid concomitant use with fluconazole doses greater than 200 mg. Dose modifications may be required when administering Jakafi with fluconazole doses of 200 mg or less, or with strong CYP3A4 inhibitors, or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy
- Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breastfeed during treatment and for 2 weeks after the final dose

MAJIC-PV adverse events (continued)[12]

Toxicity (Events [Patients]) (≥5 patients in either arm)	Jakafi (n=93)		BAT (n=87)	
	Grade 3	Grade 4	Grade 3	Grade 4
Neoplasms benign, malignant, and unspecified (including cysts and polyps)[a]	7 (6)	1 (1)	3 (3)	1 (1)
Nervous system disorders	9 (7)	0 (0)	8 (7)	1 (1)
Respiratory, thoracic, and mediastinal disorders	8 (5)	1 (1)	4 (4)	2 (2)
Skin and subcutaneous tissue disorders	13 (10)	0 (0)	1 (1)	0 (0)
Vascular disorders	14 (8)	0 (0)	7 (6)	1 (1)

[a]Malignancies and infections were deemed adverse events of special interest and have been presented separately. See MAJIC supplementary information.

- No grade 5 events occurred in the Jakafi arm, and 3 grade 5 events (1 intracranial hemorrhage and 2 vascular disorders) occurred in the BAT arm[12]
- Squamous cell skin cancer was reported more commonly with Jakafi compared with BAT (11 vs 0 events, respectively)[12]

In the overall MAJIC-PV population, the safety profile was generally consistent with previous reports for Jakafi

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IMPORTANT SAFETY INFORMATION

- Treatment with Jakafi® (ruxolitinib) can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated
- Manage thrombocytopenia by reducing the dose or temporarily interrupting Jakafi. Platelet transfusions may be necessary
- Patients developing anemia may require blood transfusions and/or dose modifications of Jakafi
- Severe neutropenia (ANC <0.5 × 10^9/L) was generally reversible by withholding Jakafi until recovery
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines
- Tuberculosis (TB) infection has been reported. Observe patients taking Jakafi for signs and symptoms of active TB and manage promptly. Prior to initiating Jakafi, evaluate patients for TB risk factors and test those at higher risk for latent infection. Consult a physician with expertise in the treatment of TB before starting Jakafi in patients with evidence of active or latent TB. Continuation of Jakafi during treatment of active TB should be based on the overall risk-benefit determination
- Progressive multifocal leukoencephalopathy (PML) has occurred with Jakafi treatment. If PML is suspected, stop Jakafi and evaluate
- Herpes zoster infection has been reported in patients receiving Jakafi. Advise patients about early signs and symptoms of herpes zoster and to seek early treatment. Herpes simplex virus reactivation and/or dissemination has been reported in patients receiving Jakafi. Monitor patients for the development of herpes simplex infections. If a patient develops evidence of dissemination of herpes simplex, consider interrupting treatment with Jakafi; patients should be promptly treated and monitored according to clinical guidelines
- Increases in hepatitis B viral load with or without associated elevations in alanine aminotransferase and aspartate aminotransferase have been reported in patients with chronic hepatitis B virus (HBV) infections. Monitor and treat patients with chronic HBV infection according to clinical guidelines
- When discontinuing Jakafi, myeloproliferative neoplasm-related symptoms may return within one week. After discontinuation, some patients with myelofibrosis have experienced fever, respiratory distress, hypotension, DIC, or multi-organ failure. If any of these occur after discontinuation or while tapering Jakafi, evaluate and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi without consulting their physician. When discontinuing or interrupting Jakafi for reasons other than thrombocytopenia or neutropenia, consider gradual tapering rather than abrupt discontinuation
- Non-melanoma skin cancers (NMSC) including basal cell, squamous cell, and Merkel cell carcinoma have occurred. Perform periodic skin examinations
- Treatment with Jakafi has been associated with increases in total cholesterol, low-density lipoprotein cholesterol, and triglycerides. Assess lipid parameters 8-12 weeks after initiating Jakafi. Monitor and treat according to clinical guidelines for the management of hyperlipidemia

IMPORTANT SAFETY INFORMATION (continued)

- Another JAK-inhibitor has increased the risk of major adverse cardiovascular events (MACE), including cardiovascular death, myocardial infarction, and stroke (compared to those treated with tumor TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi particularly in patients who are current or past smokers and patients with other cardiovascular risk factors. Patients should be informed about the symptoms of serious cardiovascular events and the steps to take if they occur
- Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis (DVT), pulmonary embolism (PE), and arterial thrombosis (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. In patients with myelofibrosis (MF) and polycythemia vera (PV) treated with Jakafi in clinical trials, the rates of thromboembolic events were similar in Jakafi and control treated patients. Patients with symptoms of thrombosis should be promptly evaluated and treated appropriately
- Another JAK-inhibitor has increased the risk of lymphoma and other malignancies excluding NMSC (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi is not indicated. Patients who are current or past smokers are at additional increased risk. Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi, particularly in patients with a known secondary malignancy (other than a successfully treated NMSC), patients who develop a malignancy, and patients who are current or past smokers
- In myelofibrosis and polycythemia vera, the most common nonhematologic adverse reactions (incidence ≥15%) were bruising, dizziness, headache, and diarrhea. In acute graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >50%) were infections (pathogen not specified) and edema. In chronic graft-versus-host disease, the most common nonhematologic adverse reactions (incidence >20%) were infections (pathogen not specified) and viral infections
- Avoid concomitant use with fluconazole doses greater than 200 mg. Dose modifications may be required when administering Jakafi with fluconazole doses of 200 mg or less, or with strong CYP3A4 inhibitors, or in patients with renal or hepatic impairment. Patients should be closely monitored and the dose titrated based on safety and efficacy
- Use of Jakafi during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus. Women taking Jakafi should not breastfeed during treatment and for 2 weeks after the final dose

References: 1. Jakafi [package insert]. Wilmington, DE: Incyte Corporation. **2.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Myeloproliferative Neoplasms V.1.2023. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed May 22, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **3.** Verstovsek S, Passamonti F, Rambaldi A, et al. A phase 2 study of ruxolitinib, an oral JAK1 and JAK2 inhibitor, in patients with advanced polycythemia vera who are refractory or intolerant to hydroxyurea. *Cancer.* 2014;120(4):513-520. **4.** Marchioli R, Finazzi G, Specchia G, et al; for CYTO-PV Collaborative Group. Cardiovascular events and intensity of treatment in polycythemia vera. *N Engl J Med.* 2013;368(1):22-33. **5.** Barbui T, Masciulli A, Marfisi MR, et al. White blood cell counts and thrombosis in polycythemia vera: a subanalysis of the CYTO-PV study. *Blood.* 2015;126(4):560-561. **6.** Emanuel RM, Dueck AC, Geyer HL, et al. Myeloproliferative neoplasm (MPN) symptom assessment form total symptom score: prospective international assessment of an abbreviated symptom burden scoring system among patients with MPNs. *J Clin Oncol.* 2012;30(33):4098-4103. **7.** Barbui T, Barosi G, Birgegard G, et al. Philadelphia-negative classical myeloproliferative neoplasms: critical concepts and management recommendations from European LeukemiaNet. *J Clin Oncol.* 2011;29(6):761-770. **8.** Vannucchi AM, Kiladjian JJ, Griesshammer M, et al. Ruxolitinib versus standard therapy for the treatment of polycythemia vera. *N Engl J Med.* 2015;372(5):426-435. Supplementary appendix available at: https://www.nejm.org/doi/suppl/10.1056/NEJMoa1409002/suppl_file/nejmoa1409002_appendix.pdf. **9.** Kiladjian J-J, Zachee P, Hino M, et al. Long-term efficacy and safety of ruxolitinib versus best available therapy in polycythaemia vera (RESPONSE): 5-year follow up of a phase 3 study. *Lancet Haematol.* 2020;7(3):e226-e237. Supplementary appendix available at: doi:10.1016/S2352-3026(19)30207-8. **10.** Data on file. Incyte Corporation. Wilmington, DE. **11.** Harrison CN, Griesshammer M, Miller C, et al. Comprehensive haematological control with ruxolitinib in patients with polycythaemia vera resistant to or intolerant of hydroxycarbamide. *Br J Haematol.* 2018;182(2):279-284. Supplemental information available at: https://onlinelibrary.wiley.com/doi/10.1111/bjh.14764. **12.** Harrison CN, Nangalia J, Boucher R, et al. Ruxolitinib versus best available therapy for polycythemia vera intolerant or resistant to hydroxycarbamide in a randomized trial. *J Clin Oncol.* doi:10.1200/JCO.22.01935. Supplemental information available at: https://ascopubs.org/doi/suppl/10.1200/JCO.22.01935. **13.** Rumi E, Cazzola M. Diagnosis, risk stratification, and response evaluation in classical myeloproliferative neoplasms. *Blood.* 2017;129(6):680-692. **14.** Parasuraman S, DiBonaventura M, Reith K, Naim A, Concialdi K, Sarlis NJ. Patterns of hydroxyurea use and clinical outcomes among patients with polycythemia vera in real-world clinical practice: a chart review. *Exp Hematol Oncol.* doi:10.1186/s40164-016-0031-8. **15.** Mascarenhas J. A concise update on risk factors, therapy, and outcome of leukemic transformation of myeloproliferative neoplasms. *Clin Lymphoma Myeloma Leuk.* 2016;16(suppl):S124-S129. **16.** Barosi G, Birgegard G, Finazzi G, et al. A unified definition of clinical resistance and intolerance to hydroxycarbamide in polycythaemia vera and primary myelofibrosis: results of a European LeukemiaNet (ELN) consensus process. *Br J Haematol.* 2010;148(6):961-963. **17.** Michiels JJ, Berneman Z, Schroyens W, Lam KH, De Raeve H. PVSG and WHO vs European Clinical, Molecular and Pathological Criteria for prefibrotic myeloproliferative neoplasms. *World J Hematol.* 2013;2(3):71-88.

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For adults with PV who have had an inadequate response to HU[1]

Intervene with Jakafi® (ruxolitinib) to achieve durable count control

PV is a hematologic malignancy that can become advanced in a subset of patients[6,13-17]

Proactively identify the subset of patients with characteristics of advanced PV despite treatment with HU at the maximum tolerated dose and phlebotomy, and treat differently[3-6]

Hct ≥45% **PLUS** WBC count >11 × 10^9/L **OR** Disease-related symptoms

"I think it's important to identify patients who may be appropriate for Jakafi. These may be patients who are struggling to maintain hematocrit less than 45% and/or having leukocytosis. In addition, for those patients who also have disease-related symptoms such as fatigue, pruritus, night sweats at the maximum tolerated dose of hydroxyurea, and frequent phlebotomies, I typically intervene with Jakafi."

— ***Andrew Kuykendall, MD, MPN Expert***

Indications and Usage

Jakafi is indicated for treatment of polycythemia vera (PV) in adults who have had an inadequate response to or are intolerant of hydroxyurea.

Important Safety Considerations

- Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia, which are each dose-related effects. Perform a pre-treatment complete blood count (CBC) and monitor CBCs every 2 to 4 weeks until doses are stabilized, and then as clinically indicated. In patients with cytopenias, consider dose reductions, temporarily interrupting Jakafi or transfusions, as clinically indicated
- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting Jakafi until active serious infections have resolved. Observe patients receiving Jakafi for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines

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