Ruxolitinib for the Treatment of Acute Graft-Versus-Host Disease

Summary of Key Data

Ruxolitinib/Ruxolitinib XR Indication and Dosing

Indication and Dosing[1]

Ruxolitinib/Ruxolitinib XR is a kinase inhibitor indicated for treatment of steroid-refractory acute GVHD in adult and pediatric patients 12 years and older[a]

Recommended starting dose of ruxolitinib is:

5 mg ruxolitinib given orally twice daily[b] OR **11 mg** ruxolitinib XR given orally once daily

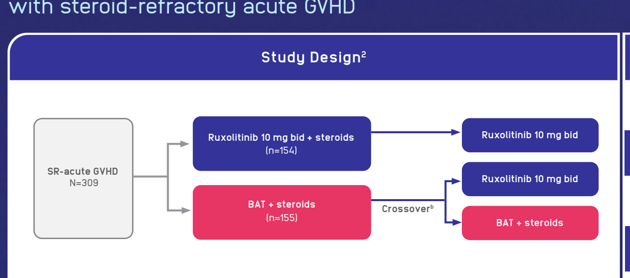
[a] The safety and effectiveness of ruxolitinib XR has been established from adequate and well-controlled studies of ruxolitinib in adult patients with myelofibrosis, polycythemia vera, and adult and pediatric patients with acute and chronic graft-versus-host-disease. [b] Consider increasing the dose to 10 mg twice daily after at least 3 days of treatment if the ANC and platelet counts are not decreased by 50% or more relative to the first day of dosing with ruxolitinib.

ANC, absolute neutrophil count; GVHD, graft-versus-host disease; XR, extended release.

REACH2 Overview: Efficacy and Safety

Phase 3, open-label, randomized study of ruxolitinib vs BAT in patients with steroid-refractory acute GVHD

Study Design[2]



Primary Endpoint: ORR (CR + PR) at day 28

Key Secondary Endpoints: Durable ORR at day 56

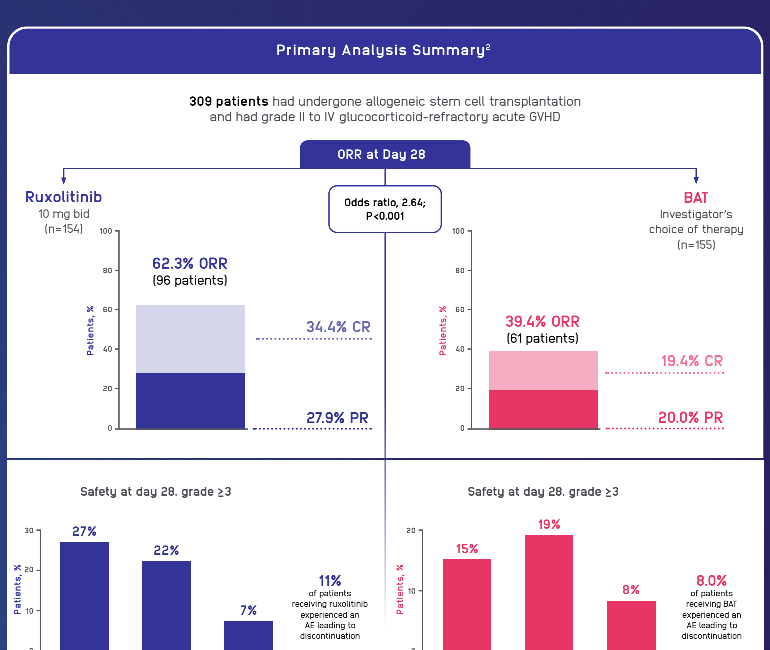
Secondary Endpoints: DOR, FFS, OS, disease relapse, NRM, cumulative steroid use, safety

BAT Medications[a]: ATG, Low-dose MTX, ECP, MMF, Etanercept, MSCs, Everolimus, Sirolimus, Infliximab

[a] Control was chosen by the investigator at the time of randomization. [b] Crossover to ruxolitinib therapy was permitted if patients did not have a response at day 28 or if they had a loss of response and received additional systemic therapy and did not have signs of chronic GVHD.

Primary Analysis Summary[2]

309 patients had undergone allogeneic stem cell transplantation and had grade II to IV glucocorticoid-refractory acute GVHD



Median dose intensity of ruxolitinib (interquartile range): 16.8 mg/day (11.9 to 19.6)

Adverse Events up to Day 28 in ≥8% of Patients Treated with Ruxolitinib[2]

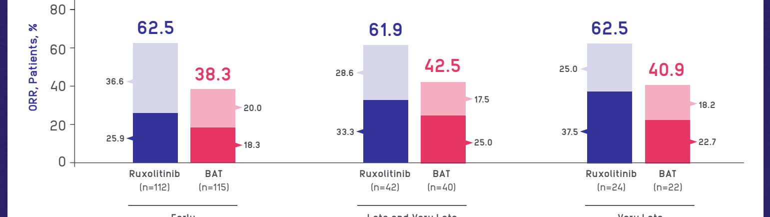
Event	Ruxolitinib (n= 152) Any grade	Ruxolitinib (n= 152) Grade ≥3	BAT (n=150) Any grade	BAT (n=150) Grade ≥3
	Number of patients (%)			
Any adverse event	145 (95)	118 (78)	140 (93)	117 (78)
Thrombocytopenia	50 (33)	41 (27)	27 (18)	23 (15)
Anemia	46 (30)	33 (22)	42 (28)	28 (19)
Cytomegalovirus infection	39 (26)	11 (7)	31 (21)	12 (8)
Peripheral edema	28 (18)	2 (1)	26 (17)	1 (1)
Platelet count decreased	26 (17)	22 (14)	21 (14)	20 (13)
Neutropenia	24 (16)	20 (13)	19 (13)	14 (9)
Hypokalemia	20 (13)	9 (6)	25 (17)	9 (6)
Hypertension	16 (11)	9 (6)	14 (9)	6 (4)
Hypoalbuminemia	16 (11)	6 (4)	15 (10)	10 (7)
Pyrexia	16 (11)	2 (1)	17 (11)	2 (1)
Hypomagnesemia	15 (10)	0	20 (13)	1 (1)
Diarrhea	14 (9)	7 (5)	15 (10)	5 (3)
White-cell count decreased	14 (9)	11 (7)	13 (9)	11 (7)
Nausea	13 (9)	0	9 (6)	0
Hypocalcemia	12 (8)	3 (2)	10 (7)	4 (3)
Hypophosphatemia	12 (8)	5 (3)	14 (9)	7 (5)

AE, adverse event; aGVHD, acute graft-versus-host disease; ATG, antithymocyte globulin; BAT, best available therapy; CMV, cytomegalovirus; CR, complete response; DOR, duration of response; ECP, extracorporeal photopheresis; FFS, failure-free survival; GVHD, graft-versus-host disease; MMF, mycophenolate mofetil; MSC, mesenchymal stromal cell; MTX, methotrexate; NRM, nonrelapse mortality; ORR, overall response rate; OS, overall survival; SR-GVHD, steroid refractory graft-versus-host disease; PR, partial response.

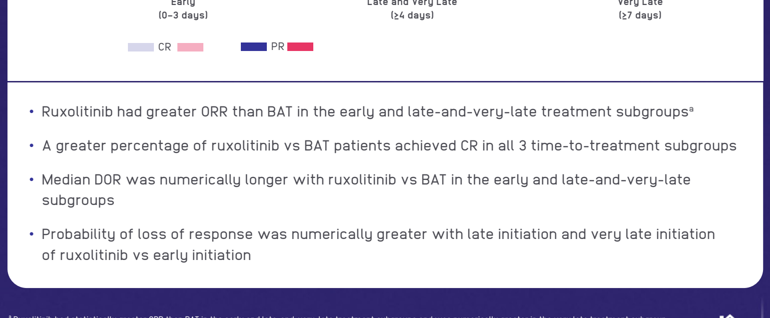
Early vs Late Treatment with Ruxolitinib

REACH2 post-hoc analyses: impact of the timing of ruxolitinib initiation on efficacy[3]

Days From Diagnosis of SR-Acute GVHD to REACH2 Randomization



Overall Response at Day 28



- Ruxolitinib had greater ORR than BAT in the early and late-and-very-late treatment subgroups[a]
- A greater percentage of ruxolitinib vs BAT patients achieved CR in all 3 time-to-treatment subgroups
- Median DOR was numerically longer with ruxolitinib vs BAT in the early and late-and-very-late subgroups
- Probability of loss of response was numerically greater with late initiation and very late initiation of ruxolitinib vs early initiation

[a] Ruxolitinib had statistically greater ORR than BAT in the early and late-and-very-late treatment subgroups and was numerically greater in the very late treatment subgroup.

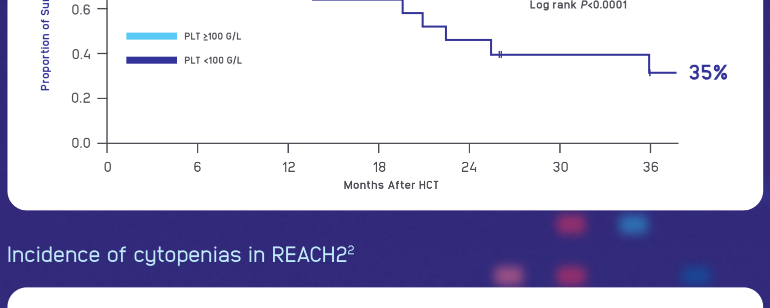
OR, odds ratio.

Cytopenias in REACH2

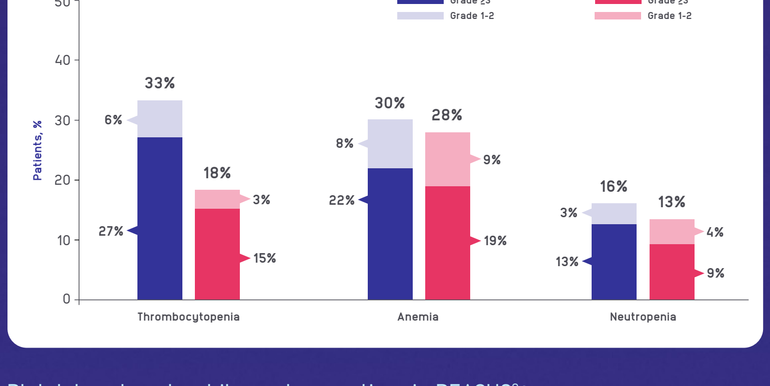
Background

GVHD promotes cytopenias after HSCT via loss or inhibition of hematopoietic cells or cells that comprise the hematopoietic niche (eg, MSCs, osteoblastic progenitor cells)[4,5]

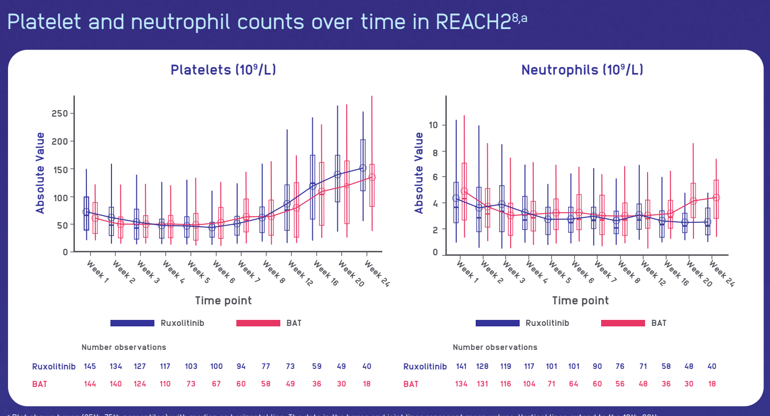
Low Platelet Count at Onset of GVHD Is Significantly Associated with Increased NRM and Worse Survival[6]



Incidence of cytopenias in REACH2[2]

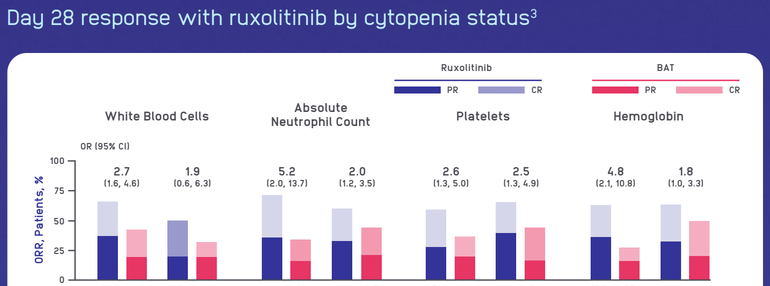


Platelet and neutrophil counts over time in REACH2[8,a]



[a] Plot shows boxes (25th-75th percentiles) with median as horizontal line. The dots in the boxes and joint lines represent mean values. Vertical lines extend to the 10th-90th percentiles. Values outside this range are not displayed.

Day 28 response with ruxolitinib by cytopenia status[3]



- Presence of underlying cytopenia does not impact response rates
- Among day 28 responders, durable responses at day 56 were observed across all subgroups

*Low blood counts were defined as WBC <5 x10⁹ cells/L, ANC <1x10⁹ cells/L, PLT <30x10⁹ cells/L, and Hb <8 g/dL.

ANC, absolute neutrophil count; Hb, hemoglobin; HCT, hematopoietic cell transplantation; HSCT, hematopoietic stem cell transplantation; PLT, platelet count; WBC, white blood cell.

Drug-Drug Interactions

REACH2 post hoc analysis: use of azoles in patients with acute GVHD

Use of Concomitant Azoles in REACH2

More than two-thirds of patients in REACH2 received concomitant azoles[9]

Most Common Azoles in the Safety Analysis Set (N=302)[10]

Azole Received[a], %	Ruxolitinib (n=152)	BAT (n=150)
Posaconazole	52.0	46.0
Voriconazole	25.0	14.7
Fluconazole	11.8	11.3

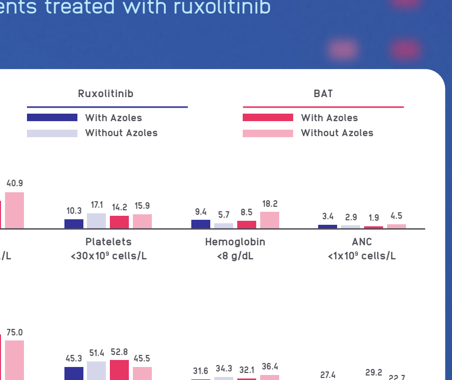
Effect of concomitant azoles on ruxolitinib treatment patterns[9]

- Fewer dose modifications were seen in ruxolitinib-treated patients who were not treated with azoles
- Mean and median ruxolitinib dose intensity up to day 28 were similar in patients with vs without concomitant administration of azoles

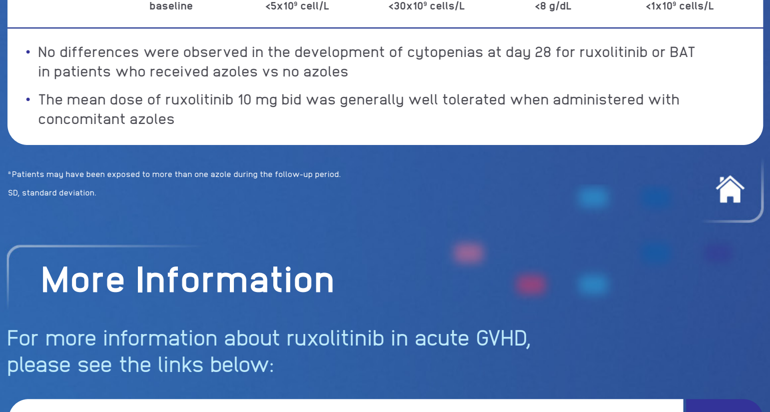
	Ruxolitinib (n=152) With Azoles (n=117)	Ruxolitinib (n=152) Without Azoles (n=35)
Ruxolitinib dose intensity up to day 28, mg/day		
Mean (SD)	18.1 (3.0)	18.6 (2.7)
Median (range)	20.0 (9.0-21.0)	20.0 (8.4-20.0)
Ruxolitinib dose modifications, n (%)	97 (82.9)	21 (60.0)
Ruxolitinib discontinuations, n (%)	108 (92.3)	33 (94.3)

Impact of concomitant azoles on ruxolitinib efficacy[9]

- Ruxolitinib had significantly greater ORR vs BAT in patients that received concomitant azoles
- The ORR with ruxolitinib was numerically higher vs BAT in patients who did not receive azoles
- Duration of response was numerically longer with ruxolitinib vs BAT regardless of azole subgroup



Incidence of cytopenias in patients treated with ruxolitinib and BAT by azole subgroup[9]



- No differences were observed in the development of cytopenias at day 28 for ruxolitinib or BAT in patients who received azoles vs no azoles
- The mean dose of ruxolitinib 10 mg bid was generally well tolerated when administered with concomitant azoles

[a] Patients may have been exposed to more than one azole during the follow-up period.

SD, standard deviation.

More Information

For more information about ruxolitinib in acute GVHD, please see the links below:

- **Ruxolitinib for Glucocorticoid-Refractory Acute Graft-Versus-Host Disease** — Zeiser R, et al. *N Engl J Med.* 2020;382:1800-1810. LEARN MORE
- **Impact of Concomitant Azoles on Ruxolitinib Treatment in Patients With GVHD: Post Hoc Analyses of REACH2 and REACH3** — Mahmoudjafari Z, et al. *Blood Adv.* 2025 Aug 26;9:4206-4216. LEARN MORE
- **Impact Of Cytopenias And Early Versus Late Treatment With Ruxolitinib In Patients With Steroid-Refractory Acute Or Chronic Graft-Versus-Host Disease** — Mahmoudjafari Z, et al. *Bone Marrow Transplant.* 2025 Jan;60:69-78. LEARN MORE

For more information, please see the Full Prescribing Information, and Patient Information.

1. Jakafi/Jakafi XR (ruxolitinib). Prescribing information. Incyte Corporation; May 2026. 2. Zeiser R, et al. *N Engl J Med.* 2020;382:1800-1810. 3. Mahmoudjafari Z, et al. *Bone Marrow Transplant.* 2024 Nov 6. doi: 10.1038/s41409-024-02445-6. Online ahead of print. 4. von Bonin M Corporation; Bornh auser M. Stem Cells. 2014;32:1420-1428. 5. Muskens KF, et al. Cells. 2021;10(8):2051. 6. Pulanic D, et al. Bone Marrow Transplant. 2009;44:393-403. 7. Kuzmina Z, et al. Leukemia. 2012;26:746-756. 8. Data on File; Incyte Corporation. 9. Mahmoudjafari Z, et al. Blood Adv. 2025 Aug 26;9:4206-4216. 10. Kintsch E et al. Hematology/Oncology Pharmacy Association Annual Conference 2025. Poster 64.

FOR MEDICAL INFORMATION PURPOSES ONLY. NOT FOR PROMOTIONAL USE. DO NOT COPY, DISTRIBUTE, OR OTHERWISE REPRODUCE.

Incyte and the Incyte logo are registered trademarks of Incyte.
Jakafi is a registered trademark of Incyte.
Jakafi XR is a trademark of Incyte.
© 2026, Incyte. MSL-RUX-US-0103 06/26

Warnings, Precautions, and Specific Populations

Thrombocytopenia, Anemia and Neutropenia

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

CBC, complete blood count

Risk of Infection

- Serious bacterial, mycobacterial, fungal and viral infections have occurred. Delay starting therapy with Jakafi/Jakafi XR until active serious infections have resolved. Observe patients receiving Jakafi/Jakafi XR for signs and symptoms of infection and manage promptly. Use active surveillance and prophylactic antibiotics according to clinical guidelines

Tuberculosis

- Tuberculosis infection has been reported in patients receiving Jakafi. Observe patients receiving Jakafi/Jakafi XR for signs and symptoms of active tuberculosis and manage promptly
- Prior to initiating Jakafi/Jakafi XR, patients should be evaluated for tuberculosis risk factors, and those at higher risk should be tested for latent infection. Risk factors include, but are not limited to, prior residence in or travel to countries with a high prevalence of tuberculosis, close contact with a person with active tuberculosis, and a history of active or latent tuberculosis where an adequate course of treatment cannot be confirmed
- For patients with evidence of active or latent tuberculosis, consult a physician with expertise in the treatment of tuberculosis before starting Jakafi/Jakafi XR. The decision to continue Jakafi/Jakafi XR during treatment of active tuberculosis should be based on the overall risk-benefit determination

PML

- PML has occurred with Jakafi treatment. If PML is suspected, stop Jakafi/Jakafi XR and evaluate

Herpes Zoster and Herpes Simplex

- Herpes zoster infection has been reported in patients receiving Jakafi
- Advise patients about early signs and symptoms of herpes zoster and to seek treatment as early as possible if suspected
- 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/Jakafi XR; patients should be promptly treated and monitored according to clinical guidelines

Hepatitis B

- Hepatitis B viral load (HBV-DNA titer) increases, with or without associated elevations in alanine aminotransferase and aspartate aminotransferase, have been reported in patients with chronic HBV infections taking Jakafi. The effect of Jakafi/Jakafi XR on viral replication in patients with chronic HBV infection is unknown. Patients with chronic HBV infection should be treated and monitored according to clinical guidelines

HBV, hepatitis B virus; PML, progressive multifocal leukoencephalopathy

Symptom Exacerbation Following Interruption or Discontinuation of Treatment

- Following discontinuation of JAK-inhibitors, including Jakafi/Jakafi XR, signs and symptoms from myeloproliferative neoplasms may flare. Some patients with MF have experienced one or more of the following after discontinuing JAK-inhibitors: fever, respiratory distress, hypotension, disseminated intravascular coagulation, or multi-organ failure
- If one or more of these signs and symptoms occur after discontinuation of Jakafi/Jakafi XR, or while tapering the dose, evaluate for and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi/Jakafi XR. Instruct patients not to interrupt or discontinue therapy without consulting their healthcare provider. When discontinuing or interrupting therapy with Jakafi/Jakafi XR for reasons other than life-threatening toxicities, consider tapering the dose of Jakafi/Jakafi XR gradually rather than discontinuing abruptly.

DIC, disseminated intravascular coagulation; MF, myelofibrosis

NMSC

- NMSCs including basal cell, squamous cell, and Merkel cell carcinoma have occurred in patients treated with Jakafi/Jakafi XR. Perform periodic skin examinations

NMSC, non-melanoma skin cancer

Lipid Elevations

- Treatment with Jakafi has been associated with increases in lipid parameters including total cholesterol, low-density lipoprotein cholesterol, and triglycerides. The effect of these lipid parameter elevations on cardiovascular morbidity and mortality has not been determined in patients treated with Jakafi/Jakafi XR. Assess lipid parameters approximately 8-12 weeks following initiation of Jakafi/Jakafi XR therapy. Monitor and treat according to clinical guidelines for the management of hyperlipidemia

MACE

- Another JAK-inhibitor has increased the risk of MACE, including cardiovascular death, myocardial infarction, and stroke (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi/Jakafi XR is not indicated
- Consider the benefits and risks for the individual patient prior to initiating or continuing therapy with Jakafi/Jakafi XR 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

MACE, major adverse cardiovascular event

Thrombosis

- Another JAK-inhibitor has increased the risk of thrombosis, including deep venous thrombosis, pulmonary embolism, and arterial thrombosis (compared to those treated with TNF blockers) in patients with rheumatoid arthritis, a condition for which Jakafi/Jakafi XR is not indicated. In patients with MF and 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

TNF, tumor necrosis factor

Secondary Malignancies

- 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/Jakafi XR 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/Jakafi XR, 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

Pregnancy and Lactation

- There are no studies with the use of Jakafi/Jakafi XR in pregnant women to inform drug-associated risks
- Use of Jakafi/Jakafi XR during pregnancy is not recommended and should only be used if the potential benefit justifies the potential risk to the fetus
- Advise women not to breastfeed during treatment with Jakafi/Jakafi XR and for 2 weeks after the final dose

Pediatric Use

- The safety and effectiveness of Jakafi/Jakafi XR for treatment of chronic GVHD or steroid-refractory acute GVHD has not been established in pediatric patients younger than 12 years old

Renal Impairment

- Total exposure of ruxolitinib and its active metabolites increased with moderate and severe renal impairment, and end stage renal disease on dialysis
- Modify Jakafi/Jakafi XR dosage as recommended

Hepatic Impairment

- Exposure of ruxolitinib increased with mild (Child-Pugh A), moderate (Child-Pugh B) and severe (Child-Pugh C) hepatic impairment
- Reduce Jakafi/Jakafi XR dosage as recommended for patients with Stage 4 liver acute GVHD
- Monitor blood counts more frequently for toxicity and modify the Jakafi/Jakafi XR dosage for adverse reactions if they occur for patients with Score 3 liver chronic GVHD

Geriatric Use

- Clinical studies of Jakafi in patients with acute GVHD did not include sufficient numbers of subjects age 65 and over to determine whether they respond differently from younger subjects
- Of the total number of patients with chronic GVHD treated with Jakafi in clinical trials, 11% were 65 years and older. No overall differences in safety or effectiveness of Jakafi were observed between these patients and younger patients

FOR MEDICAL INFORMATION PURPOSES ONLY. NOT FOR PROMOTIONAL USE.
DO NOT COPY, DISTRIBUTE, OR OTHERWISE REPRODUCE.

Incyte and the Incyte logo are registered trademarks of Incyte
Jakafi is a registered trademark of Incyte
All rights reserved.
© 2020, Incyte. MSL-RUX-OS-0112-0620