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

Highlights from the REACH2 Study

Ruxolitinib Indication and Dosing

Indication and Dosing[1]	
Ruxolitinib is indicated for treatment of steroid-refractory acute graft-versus-host disease (GVHD) in adult and pediatric patients 12 years and older	The approved starting dose of ruxolitinib in acute GVHD is **5 mg** orally twice daily[a]

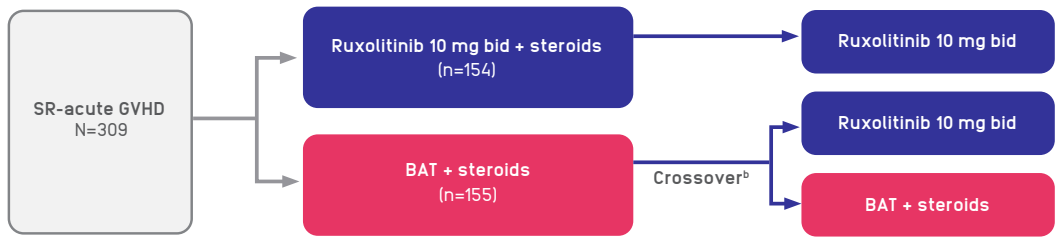
[a] Consider increasing the dose to 10 mg twice daily after at least 3 days of treatment if the ANC and platelet counts are not decreased by 50% or more relative to the first day of dosing with ruxolitianib.

ANC, absolute neutrophil count.

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]



BAT Medications[a]

- ATG
- Low-dose MTX
- ECP
- MMF
- Etanercept
- MSCs
- Everolimus
- Sirolimus
- Infliximab

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

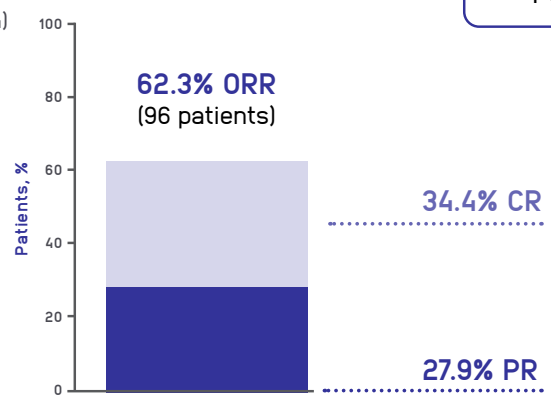
[a] Control was chosen by the investigator at the time of randomization. [b] Crossover to ruxolitinib therapy was permitted if patients did not have a response at day 28 or if they had a loss of response and received additional systemic therapy and did not have signs of chronic GVHD.

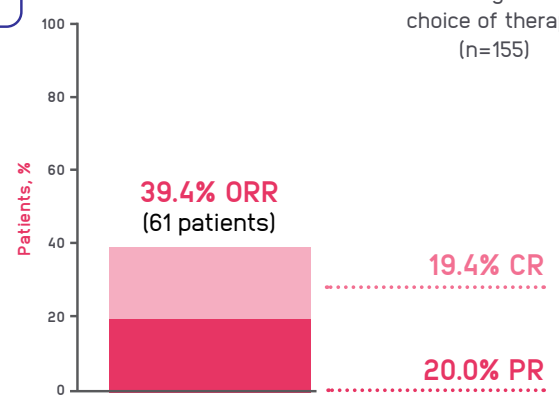
Primary Analysis Summary[2]

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

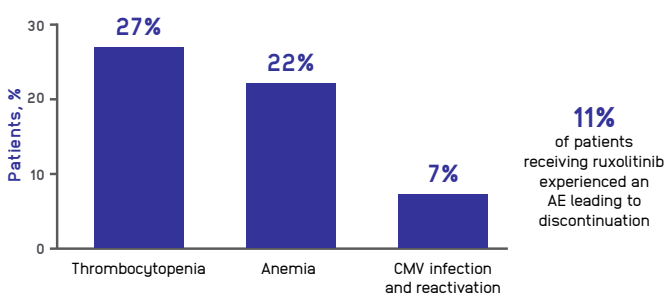
ORR at Day 28

Odds ratio, 2.64; P<0.001

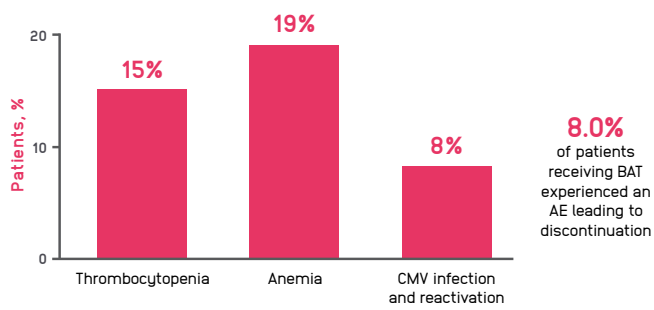




Safety at day 28. grade ≥3



Safety at day 28. grade ≥3



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

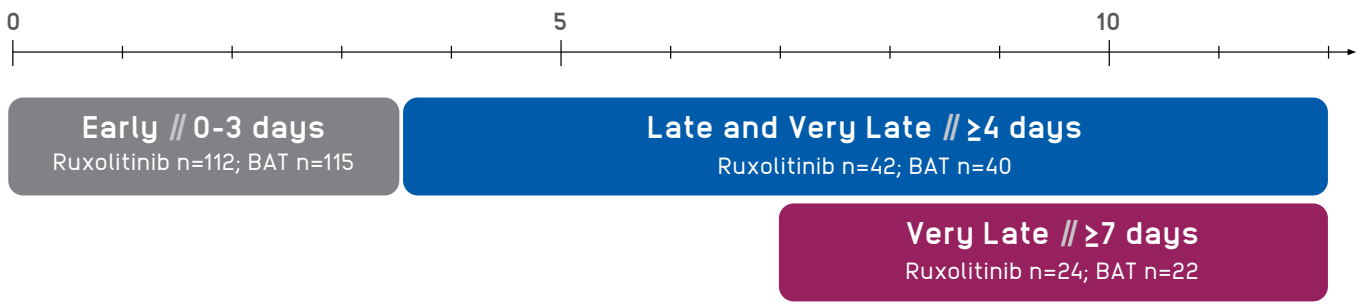
Adverse Events up to Day 28 in ≥8% of Patients Treated with Ruxolitinib[2]				
Event	Ruxolitinib (n= 152)		BAT (n=150)	
	Any grade	Grade ≥3	Any grade	Grade ≥3
	Number of patients (%)			
Any adverse event	145 (95)	118 (78)	140 (93)	117 (78)
Thrombocytopenia	50 (33)	41 (27)	27 (18)	23 (15)
Anemia	46 (30)	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.

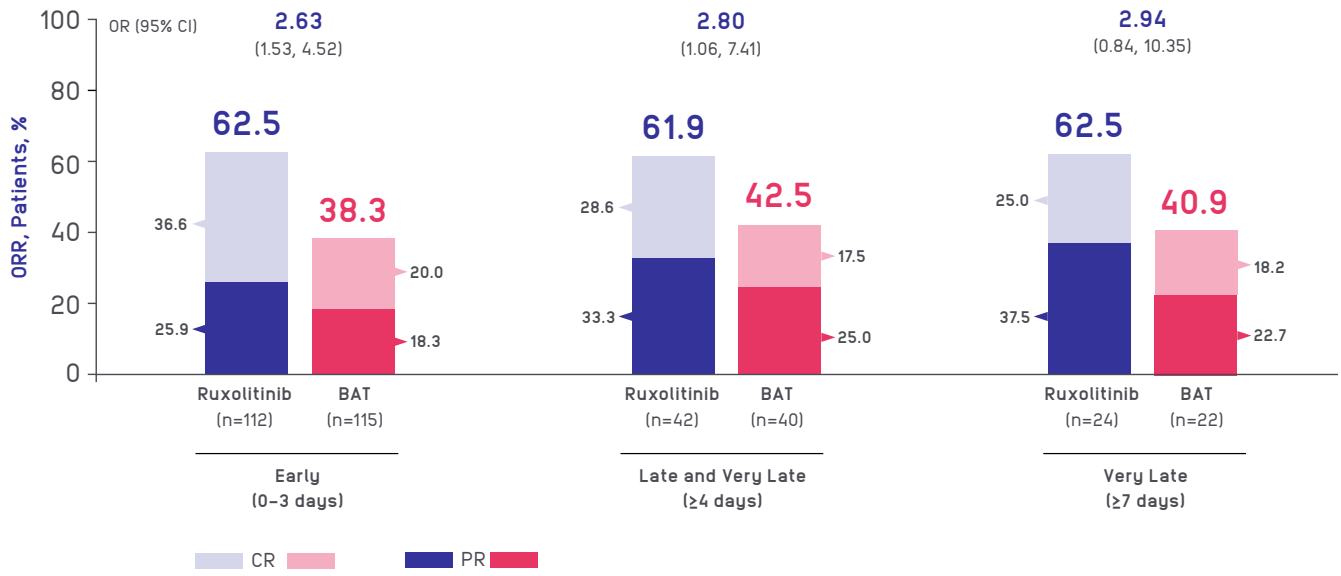
Early vs Late Treatment with Ruxolitinib

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.

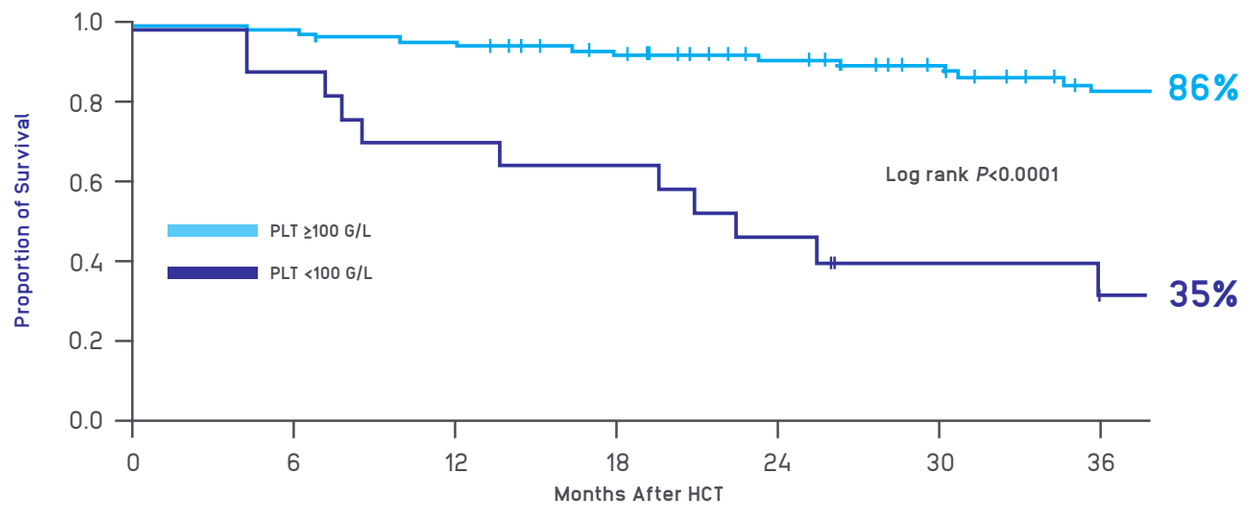
Cytopenias in REACH2

Background

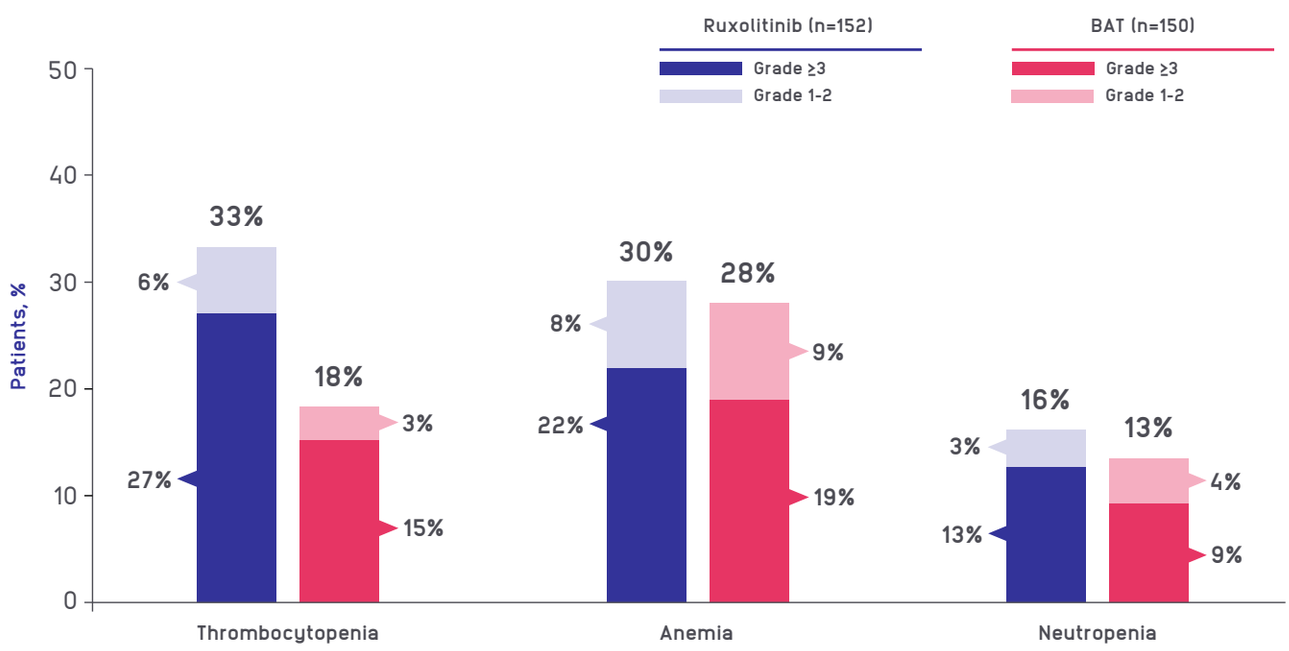
GVHD promotes cytopenias after HSCT via loss or inhibition of hematopoietic cells or cells that comprise the hematopoetic niche (eg, MSCs, osteoblastic progenitor cells)[4,5]

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

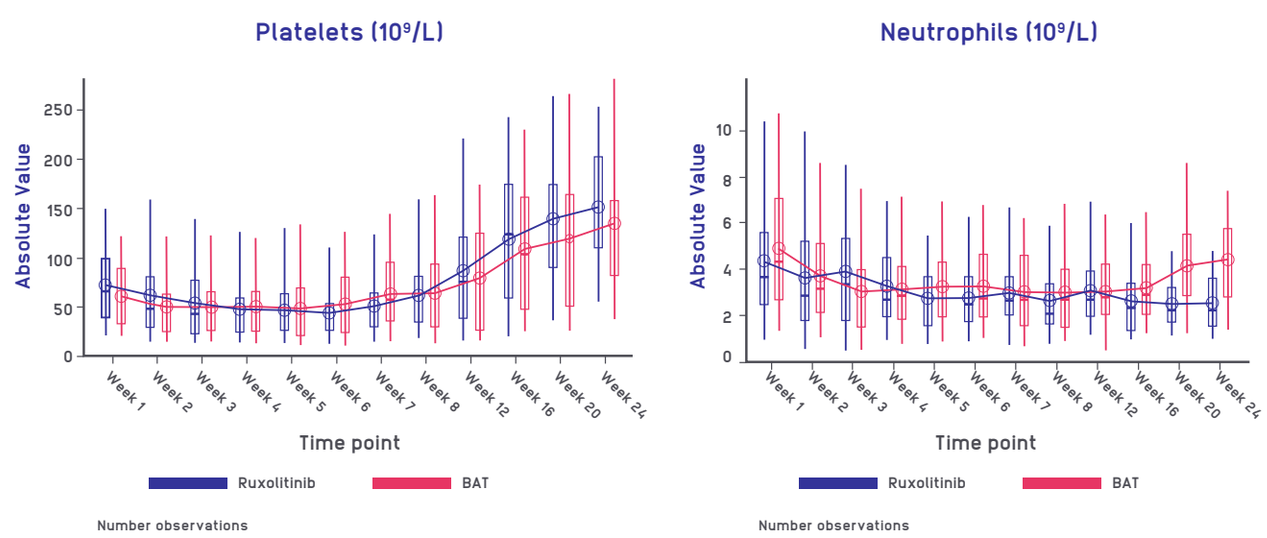
Probability of survival according to platelet counts at diagnosis[7]



Incidence of cytopenias in REACH2[2]



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

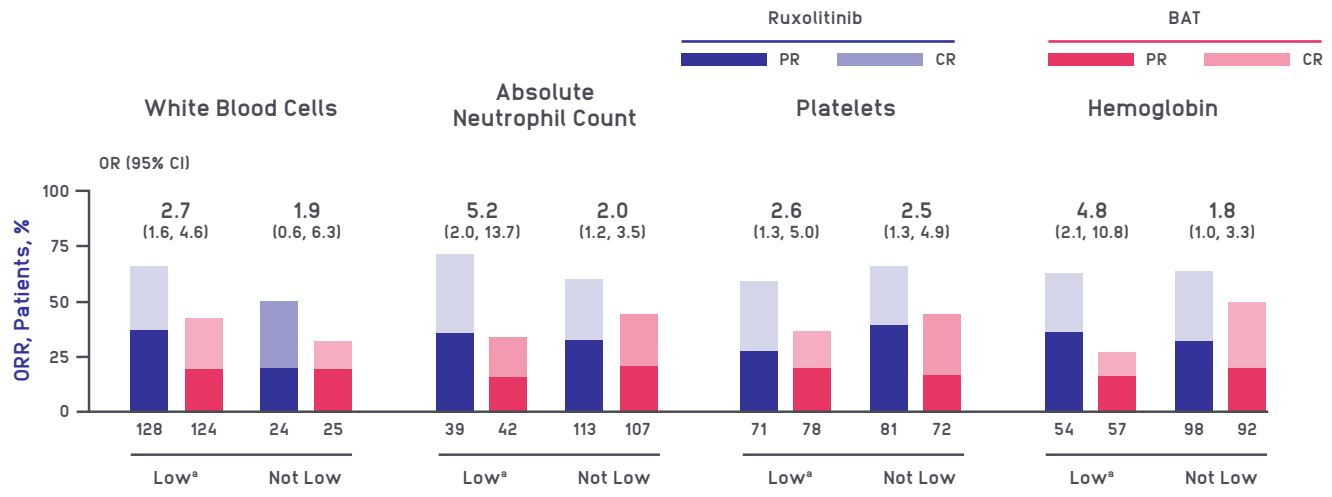


Ruxolitinib	145	134	127	117	103	100	94	77	73	59	49	40
BAT	144	140	124	110	73	67	60	58	49	36	30	18

Ruxolitinib	141	128	119	117	101	101	90	76	71	58	48	40
BAT	134	131	116	104	71	64	60	56	48	36	30	18

[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

[a] Low blood counts were defined as WBC <5 x10^9 cells/L, ANC <1x10^9 cells/L, PLT <30x10^3 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

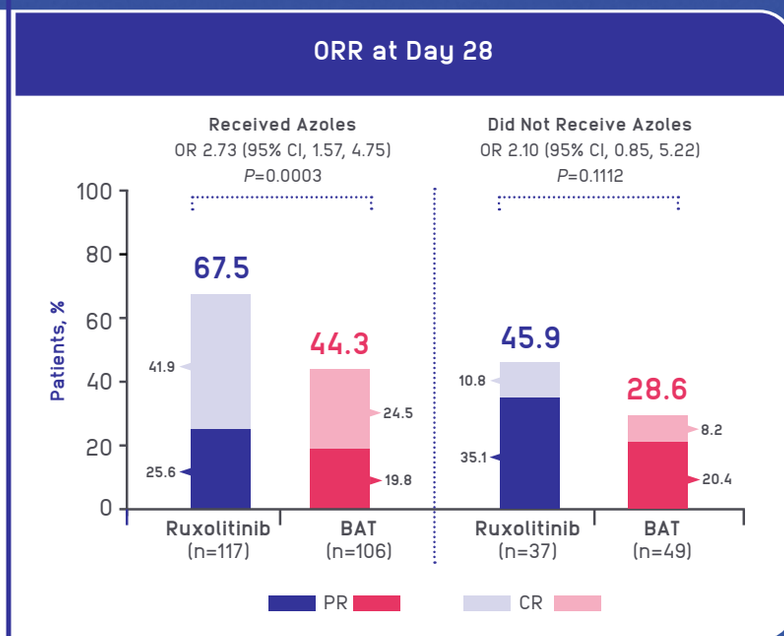
Effect of concomitant azoles on ruxolitinib treatment patterns[9]

- 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

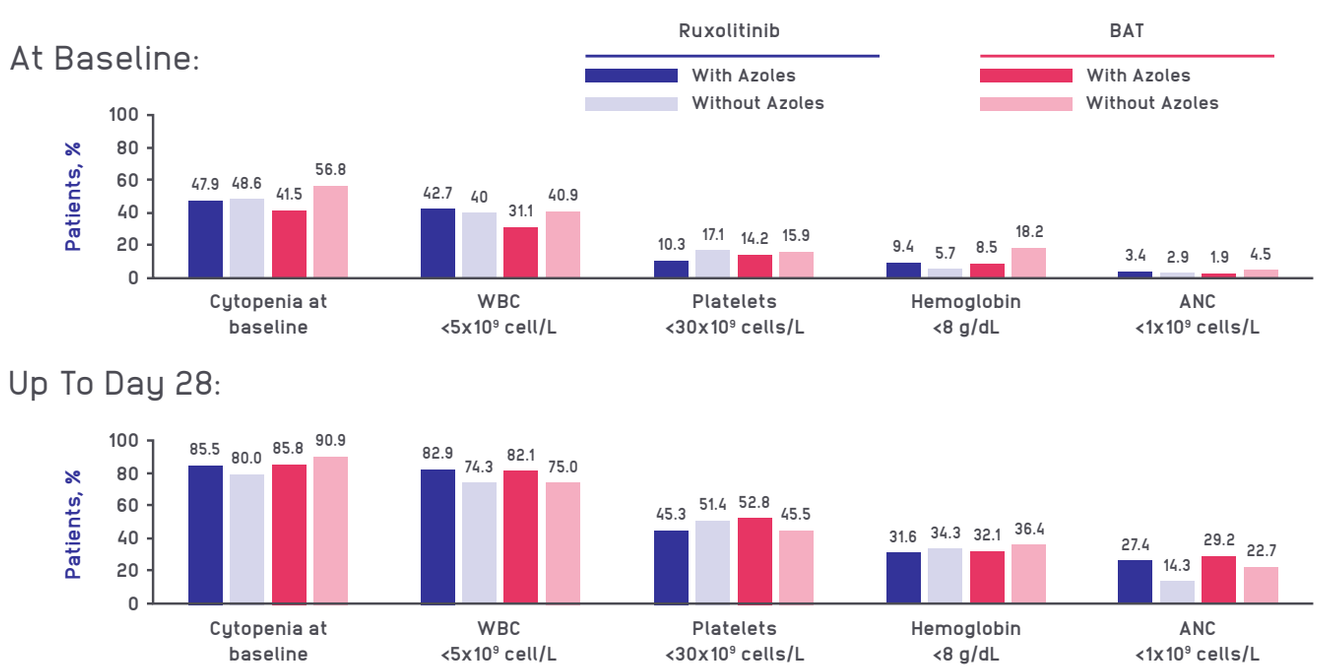
	Ruxolitinib (n=152)	
	With Azoles (n=117)	Without Azoles (n=35)
Ruxolitinib dose intensity up to day 28, mg/day		
Mean (SD)	18.1 (3.0)	18.6 (2.7)
Median (range)	20.0 (9.0-21.0)	20.0 (8.4-20.0)
Ruxolitinib dose modifications, n (%)	97 (82.9)	21 (60.0)
Ruxolitinib discontinuations, n (%)	108 (92.3)	33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

Effects Of Concomitant Azoles On Ruxolitinib Treatment In Patients With Acute Graft-versus-host Disease: A Post Hoc Analysis From The Randomized Phase 3 REACH2 Study
Mahmoudjafari Z, et al. Transplantation & Cellular Therapy Meeting of ASTCT and CIBMTR 2024. Poster 387.
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.* 2024 Nov 6. doi: 10.1038/s41409-024-02445-6. Online ahead of print.
LEARN MORE

For more information, please see the Full Prescribing Information.

1. Jakafi (ruxolitinib). Prescribing Information. Incyte Corporation; January 2023. 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.user M. *Stem Cells.* 2014;32:1420-1428. 5. Müskens 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. Transplantation & Cellular Therapy Meeting of ASTCT and CIBMTR 2024. Poster 387. 10. Kintsch E et al. Hematology/Oncology Pharmacy Association Annual Conference 2024. 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.
© 2025, Incyte. MI-RUX-US-0523 04/25

Warnings, Precautions, and Specific Populations

Thrombocytopenia, Anemia and Neutropenia

- Treatment with Jakafi can cause thrombocytopenia, anemia and neutropenia
- 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 less than 0.5×10^9/L) was generally reversible by withholding Jakafi until recovery
- Perform a pre-treatment complete blood count 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 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

- Tuberculosis infection has been reported in patients receiving Jakafi. Observe patients receiving Jakafi for signs and symptoms of active tuberculosis and manage promptly
- Prior to initiating Jakafi, 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. The decision to continue Jakafi 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 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; 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 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 with Jakafi

- Following discontinuation of Jakafi, symptoms from myeloproliferative neoplasms may return to pretreatment levels over a period of approximately one week. Some patients with MF have experienced one or more of the following adverse events after discontinuing Jakafi: fever, respiratory distress, hypotension, DIC, or multi-organ failure. If one or more of these occur after discontinuation of, or while tapering the dose of Jakafi, evaluate for and treat any intercurrent illness and consider restarting or increasing the dose of Jakafi. Instruct patients not to interrupt or discontinue Jakafi therapy without consulting their physician. When discontinuing or interrupting therapy with Jakafi for reasons other than thrombocytopenia or neutropenia, consider tapering the dose of Jakafi 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. 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. Assess lipid parameters approximately 8-12 weeks following initiation of Jakafi 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 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

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 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 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

TNF, tumor necrosis factor.

Pregnancy and Lactation

- There are no studies with the use of Jakafi in pregnant women to inform drug-associated risks
- Advise women not to breastfeed during treatment with Jakafi and for at least 2 weeks after the final dose

Pediatric Use

- The safety and effectiveness of Jakafi for treatment of chronic GVHD or 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 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 dosage as recommended for patients with Stage 4 liver acute GVHD
- Monitor blood counts more frequently for toxicity and modify the Jakafi 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

Jakafi (ruxolitinib). Prescribing Information. Incyte Corporation; January 2023.

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.
© 2025, Incyte. MI-RUX-US-0523 04/25