Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

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SUPPLEMENTARY APPENDIX

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SUPPLEMENTARY METHODS

Sample Size Calculation

The target accrual was 308 randomized patients, which would provide 90% power to test the primary end point (response at Day 28) and approximately 90% power to test the secondary end point (rate of durable response at Day 56). The family-wise error rate was controlled at 0.025 overall for the two comparisons. The efficacy objective would be met if there was a significant treatment effect observed for the primary end point at a one-sided $\alpha = 0.025$. Conditional to significance for the primary end point, the key secondary end point would be tested at a one-sided $\alpha = 0.025$.

The expected distribution of acute graft-versus-host disease (aGvHD) grades II:III:IV was 0.2:0.4:0.4. The expected response at Day 28 in the best available therapy (BAT) arm was 58% (see Martin et al.[1]). An expected increase in the response rate with ruxolitinib of 18% (i.e., an expected odds ratio of 2.25) would correspond to an increase in response rate to 75%. Power for the Cochran–Mantel–Haenszel test, stratifying by aGvHD grade, was calculated using the software package East V6 (Cytel). With 154 patients in each treatment arm (308 in total), an observed odds ratio ≥1.63 would achieve statistical significance for the primary end point. If the observed response rates for patients with grades II/III/IV aGvHD in the BAT arm were assumed to be 69%/59%/50% (overall, 57%), then observed response rates ≥ 78%/70%/62% (overall, 68%) in the ruxolitinib arm would achieve statistical significance.

Staging of aGvHD

(Derived from Harris et al.[2])

Organ Staging

Stage	**Skin (active erythema only)**	**Liver (bilirubin, mg/dL)**	**Upper GI**	**Lower GI (stool output per day)**
0	No active (erythematous) GvHD rash	<2	No or intermittent nausea, vomiting, or anorexia	Adult: <500 mL/day or <3 episodes/day Child: <10 mL/kg/day or <4 episodes/day
1	Maculopapular rash <25% BSA	2–3	Persistent nausea, vomiting, or anorexia	Adult: 500–999 mL/day or 3–4 episodes/day Child: 10–19.9 mL/kg/day or 4–6 episodes/day
2	Maculopapular rash 25–50% BSA	3.1–6	-	Adult: 1000–1500 mL/day or 5–7 episodes/day Child: 20–30 mL/kg/day or 7–10 episodes/day
3	Maculopapular rash >50% BSA	6.1–15	-	Adult: >1500 mL/day or >7 episodes/day Child: >30 mL/kg/day or >10 episodes/day
4	Generalized erythroderma	>15	-	Severe abdominal pain with or without ileus or grossly

	(>50% BSA) plus bullous formation and desquamation >5% BSA			bloody stool (regardless of stool volume)

BSA denotes body surface area; GI, gastrointestinal; GvHD, graft-versus-host disease.

Overall Clinical Grade

(Based on most severe target organ involvement)

Grade	**Description**
0	No stage 1–4 or any organ
I	Stage 1–2 skin without liver, upper GI or lower GI involvement.
II	Stage 3 rash and/or stage 1 liver and/or stage 1 upper GI and/or stage 1 lower GI
III	Stage 2–3 liver and/or stage 2–3 lower GI with stage 0–3 skin and/or stage 0–1 upper GI
IV	Stage 4 skin, liver or lower GI involvement, with stage 0–1 upper GI

GI denotes gastrointestinal.

Response Definitions

(Derived from Harris et al.[2])

Response	Description
Complete response	Score of 0 for aGvHD grading in all evaluable organs, indicating complete resolution of all signs and symptoms of aGvHD in all evaluable organs without administration of additional systemic therapies for any earlier progression, mixed response, or non-response of aGvHD
Partial response	Improvement of 1 stage in 1 or more organs involved with aGvHD signs or symptoms without progression in other organs or sites without administration of additional systemic therapies for an earlier progression, mixed response, or non-response of aGvHD
No response	Absence of improvement in any organ involved with aGvHD, without worsening in any involved organ
Mixed response	Improvement of at least 1 stage in the severity of aGvHD in at least 1 organ accompanied by progression in another organ or development of signs or symptoms of aGvHD in a new organ
Progression	Worsening in 1 or more organs by 1 or more stages without improvement in any involved organ

aGvHD denotes acute graft-versus-host disease.

Response rate is defined as the proportion of patients with complete or partial response.

Lack of response is defined as no response, mixed response, or progression.

Ruxolitinib Dose Modifications

Dose Reduction Steps

Current dose	First dose reduction step	Second dose reduction step
10 mg BID	5 mg BID	5 mg QD
5 mg BID	5 mg QD	Discontinue

BID denotes twice a day; QD, once a day.

Dose Re-Escalation Steps

Current dose	First dose escalation step	Second dose escalation step
5 mg QD	5 mg BID	10 mg BID
5 mg BID	10 mg BID	-

BID denotes twice a day; QD, once a day.

Dose Modifications for Adverse Events

Worst toxicity	**Ruxolitinib dose modification for events* suspected to be drug-related**
Neutropenia	
Grade 1 (ANC <LLN–1500/mm^3)	**Recommendation:** Maintain dose level
Grade 2 (ANC <1500–1000/mm^3)	**Recommendation:** Maintain dose level
Grade 3 (ANC <1000–750/mm^3)	**Recommendation:** Maintain dose level
Grade 3 (ANC <750–500/mm^3)	**Mandatory:** ↓ 1 dose level, monitor ANC daily until resolved to grade ≤2, then resume initial dose level
Grade 4 (ANC <500/mm^3)	**Mandatory:** Hold dose, monitor ANC daily until resolved to grade ≤3, then resume ↓ 1 dose level. If resolves to grade ≤2, can resume initial dose level. If not resolved in ≤14 days, treatment must be discontinued
Febrile neutropenia (ANC <750/mm^3, fever ≥38.5°C)	**Mandatory:** Hold dose until resolved, then restart at ↓ 1 dose level
Thrombocytopenia	
Grade 1 (PLT <LLN–75,000/mm^3)	**Recommendation:** Maintain dose level
Grade 2 (PLT <75,000–50,000/mm^3)	**Recommendation:** Maintain dose level
Grade 3 (PLT <50,000–25,000/mm^3)	**Recommendation:** Maintain dose level
Grade 4 (PLT <25,000–20,000/mm^3)	**Recommendation:** Maintain dose level

Worst toxicity	**Ruxolitinib dose modification for events* suspected to be drug-related**
Grade 4 (PLT <20,000–15,000/mm^3)	**Mandatory:** ↓ 1 dose level until resolved to ≥20,000/mm^3. If resolved in ≤7 days, then resume initial dose level. If resolved in >7 days, then maintain ↓ 1 dose level
Grade 4 (PLT <15,000/mm^3)	**Mandatory:** Hold dose until resolved to ≥20,000/mm^3, then resume at ↓ 1 dose level. If resolves to grade ≤3, can resume initial dose level. If not resolved in ≤14 days, treatment must be discontinued
Serum creatinine elevated	
Grade 1 (>ULN–1.5 × ULN)	**Recommendation:** Maintain dose level
Grade 2 (>1.5–3.0 × ULN)	**Mandatory:** ↓ 1 dose level until resolved to grade ≤1 or baseline, then resume initial dose level
Grade 3 (>3.0–6.0 × ULN)	**Mandatory:** Hold dose until resolved to grade ≤2, then restart at ↓ 1 dose level. If resolves to grade ≤1, can resume initial dose level
Grade 4 (>6.0 × ULN)	**Mandatory:** Hold dose and discontinue patient from study treatment
Total bilirubin elevated	
>ULN–1.5 × ULN	**Recommendation:** Maintain dose level
>1.5–3.0 × ULN	**Recommendation:** Maintain dose level
>3.0–5.0 × ULN‡	**Mandatory:** ↓ 1 dose level until resolved to ≤3.0 × ULN. Monitor LFTs† weekly, or more frequently if clinically indicated, until resolved to ≤3.0 × ULN:

Worst toxicity	**Ruxolitinib dose modification for events* suspected to be drug-related**
	If resolved in ≤14 days, then increase by one dose level If resolved in >14 days, then maintain the decreased dose level
>5.0–10.0 × ULN‡	**Mandatory:** Hold dose. Monitor LFTs† weekly, or more frequently if clinically indicated, until resolved to ≤3.0 × ULN: If resolved in ≤14 days, then resume same dose level If resolved in >14 days, then resume at ↓ 1 dose level
>10.0 × ULN‡	**Mandatory:** Hold dose. Monitor LFTs† weekly, or more frequently if clinically indicated, until resolved to ≤3.0 × ULN: If resolved in ≤14 days, then resume at ↓ 1 dose level If resolved in >14 days, then discontinue patient from study treatment. The patient should be monitored weekly (including LFTs†), or more frequently if clinically indicated, until total bilirubin has resolved to baseline or stabilization over 4 weeks
AST or ALT elevated	
>ULN–3.0 × ULN	**Recommendation:** Maintain dose level
≤3.0 × ULN	**Recommendation:** Maintain dose level. Repeat LFTs† as soon as possible, preferably within 48–72 hours from awareness of the abnormal results; if

Worst toxicity	**Ruxolitinib dose modification for events* suspected to be drug-related**
	abnormal lab values are confirmed upon the repeat test, ↓ 1 dose level until resolved to ≤3.0 × ULN. Monitor LFTs† weekly, or more frequently if clinically indicated, until resolved to ≤3.0 × ULN: If resolved in ≤14 days, then then increase by one dose level If resolved in >14 days, then continue at the ↓ 1 dose level
>3.0–5.0 × ULN	**Recommendation:** Maintain dose level. Monitor LFTs† weekly, or more frequently if clinically indicated, until resolved to ≤baseline
>5.0–10.0 × ULN	**Mandatory:** Hold dose. Repeat LFTs† as soon as possible, preferably within 48–72 hours from awareness of the abnormal results; monitor LFTs† weekly, or more frequently if clinically indicated, until resolved to ≤5.0 × ULN Then: If resolved in ≤14 days, then resume same dose level If resolved in >14 days, then resume at ↓ 1 dose level
>10.0–20.0 × ULN	**Mandatory:** Hold dose. Repeat LFTs† as soon as possible, preferably within 48–72 hours from awareness of the abnormal results; monitor LFTs† weekly, or more frequently if clinically indicated, until

Worst toxicity	**Ruxolitinib dose modification for events* suspected to be drug-related**
	resolved to ≤5.0 × ULN. Then resume at ↓ 1 dose level
>20.0 × ULN and deriving clinical benefit upon investigator's judgment	**Mandatory:** Hold dose. Repeat LFTs† as soon as possible, preferably within 48–72 hours from awareness of the abnormal results; monitor LFTs† weekly, or more frequently if clinically indicated, until resolved to ≤3 × ULN (or ≤5 × ULN for patients with baseline value >3.0–5.0 × ULN), then resume treatment at ↓ 1 dose level. Only 1 dose reduction is allowed; if reoccurs at >5 × ULN, discontinue study treatment
For all other patients with >20.0 × ULN	**Mandatory:** Discontinue patient from study treatment. Repeat LFTs† as soon as possible, preferably within 48–72 hours from awareness of the abnormal results; monitor LFTs† weekly, or more frequently if clinically indicated, until resolved to baseline or stabilization over 4 weeks
Asymptomatic amylase and/or lipase elevation§	
Grade 1 (>ULN–1.5 × ULN)	**Recommendation:** Maintain dose level
Grade 2 (>1.5–2.0 × ULN)	**Recommendation:** Maintain dose level
Grade 3 (>2.0–5.0 × ULN)	**Recommendation:** Hold dose of until resolved to grade ≤2, then:

Worst toxicity	**Ruxolitinib dose modification for events* suspected to be drug-related**
	If resolved in ≤7 days, then resume same dose level If resolved in >7 days, then resume at ↓ 1 dose level
Grade 4 (>5.0 × ULN)	**Recommendation:** Hold dose and discontinue patient from study treatment
Hypertension	
CTCAE grade 3	**Recommendation:** ↓ 1 dose level until resolved to grade ≤2, then increase by 1 dose level
CTCAE grade 4	**Mandatory:** Hold dose and discontinue patient from study treatment
Pancreatitis	
Grade 2	**Recommendation:** Maintain dose level
Grade ≥3	**Mandatory:** Hold dose and discontinue study treatment
Diarrhea¶	
Grade 1	**Recommendation:** Maintain dose level. May initiate anti-diarrhea treatment
Grade 2	**Recommendation:** Maintain dose level. May initiate anti-diarrhea treatment
Grade 3	**Recommendation:** ↓ 1 dose level until resolved to grade ≤2, then increase by 1 dose level
Grade 4	**Mandatory:** Hold dose. Discontinue patient from study treatment
Rash/photosensitivity	

Worst toxicity	**Ruxolitinib dose modification for events* suspected to be drug-related**
Grade 1	**Recommendation:** Maintain dose level
Grade 2	**Recommendation:** Maintain dose level
Grade 3	**Recommendation:** ↓ 1 dose level until resolved to grade ≤2, then: If resolved in ≤7 days, then increase by 1 dose level If resolved in >7 days, then maintain the ↓ dose level
Grade 4	**Mandatory:** Hold dose. Discontinue study treatment
Other adverse events	
Grade 1 or 2	**Recommendation:** Maintain dose level
Grade 3	**Recommendation:** ↓ 1 dose level until resolved to Grade ≤2 **Recommendation:** Hold dose for grade ≤3 vomiting or grade 3 nausea only if the vomiting or nausea cannot be controlled with optimal antiemetic (as per local practice)
Grade 4	**Recommendation:** Hold dose and then discontinue study treatment

All dose modifications should be based on the worst preceding toxicity.

" ↓ " denotes reduce or reduction; ALT, alanine aminotransferase; ANC, absolute neutrophil count; AST, aspartate aminotransferase; CT, computed tomography; CTCAE, Common Terminology Criteria for Adverse Events; GGT, gamma-glutamyltransferase; LFTs, liver function tests; LLN, lower limit of normal; PLT, platelet count; ULN, upper limit of normal.

* CTCAE version 4.03.

† Core LFTs consist of ALT, AST, GGT, total bilirubin (fractionated [direct and indirect], if total bilirubin >2.0 × ULN), and alkaline phosphatase (fractionated [quantification of isoforms], if alkaline phosphatase >2.0 × ULN).

‡ If total bilirubin >3.0 × ULN is due to the indirect (non-conjugated) component only, and hemolysis as the etiology has been ruled out as per institutional guidelines (e.g., review of peripheral blood smear and haptoglobin determination), then ↓ 1 dose level and continue treatment at the discretion of the investigator.

§ A CT scan or other imaging study to assess the pancreas, liver, and gallbladder must be performed within 1 week of the first occurrence of any grade ≥3 amylase and/or lipase. If asymptomatic grade 2 elevations of lipase and/or amylase occur again at the reduced dose, patients will be discontinued permanently from study treatment.

¶ Antidiarrheal medication is recommended at the first sign of abdominal cramping, loose stools, or overt diarrhea.

SUPPLEMENTARY RESULTS

Figure S1. Number and Type of BAT Used.

BAT denotes best available therapy. Number of patients who received more than one BAT at once was 17. BAT 1 is BAT initiated at time of randomization. BAT 2 or 3 may be either replacing BAT1 or in combination with the ongoing BAT.

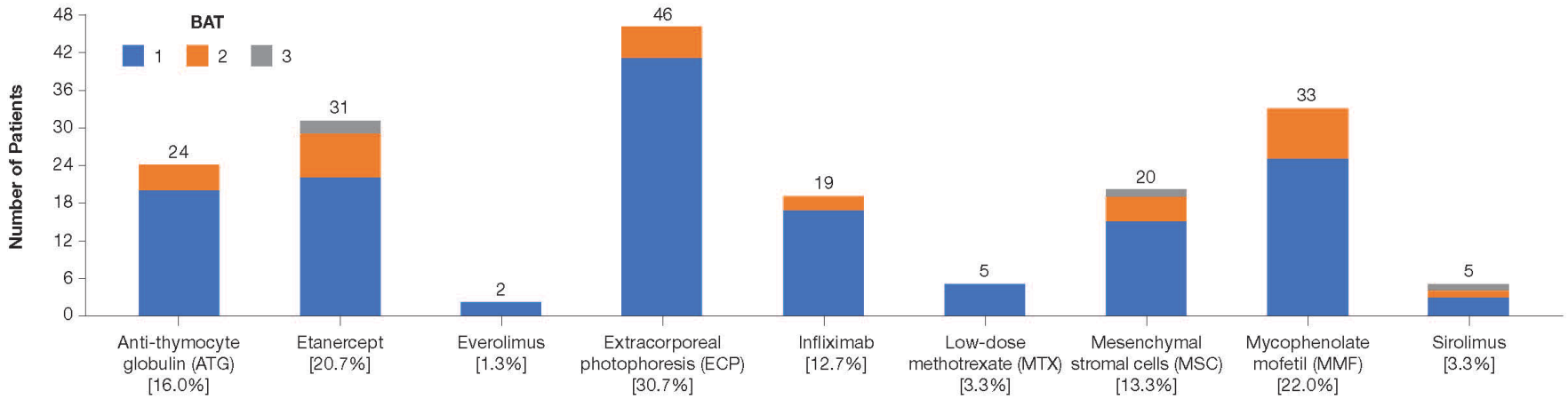
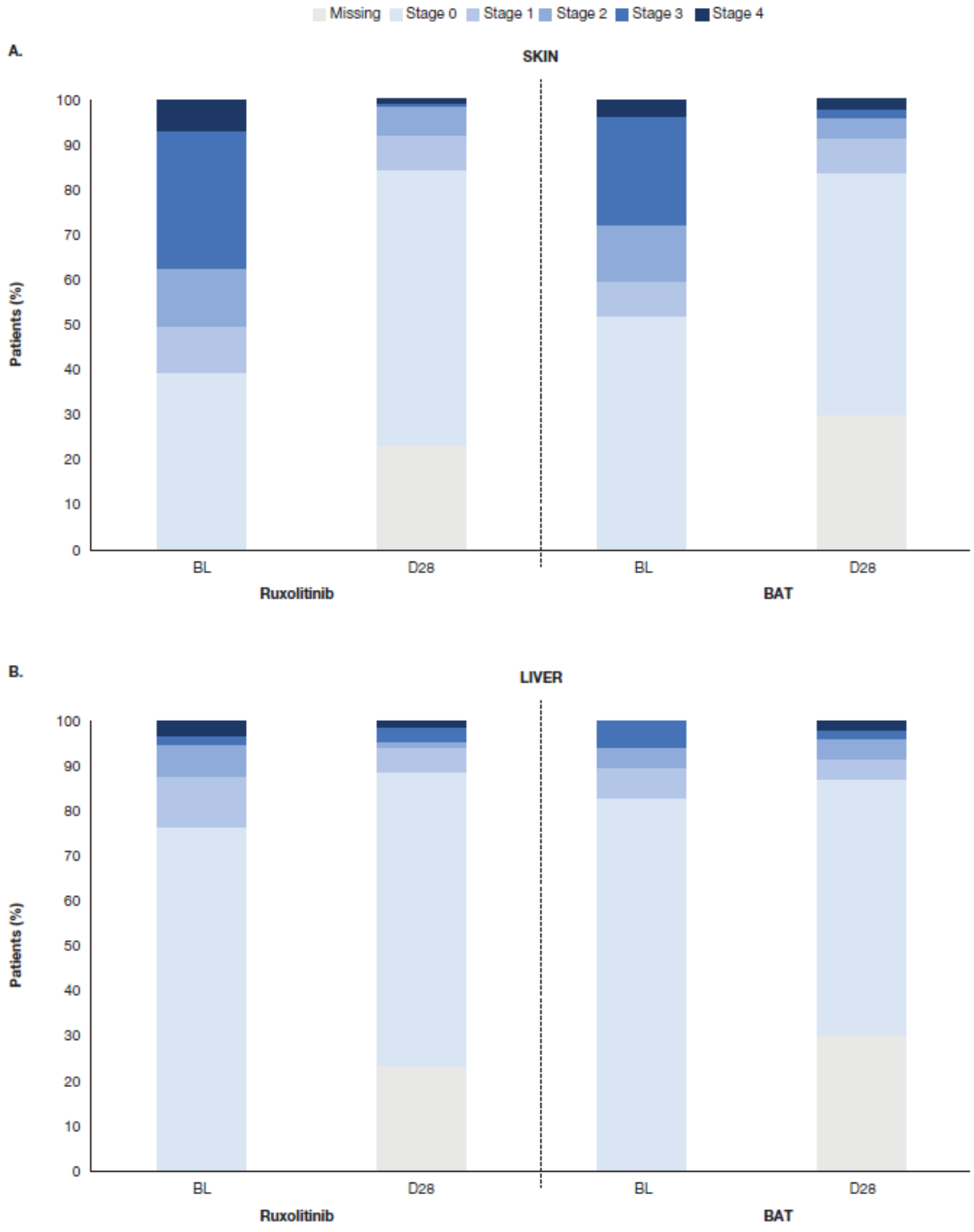
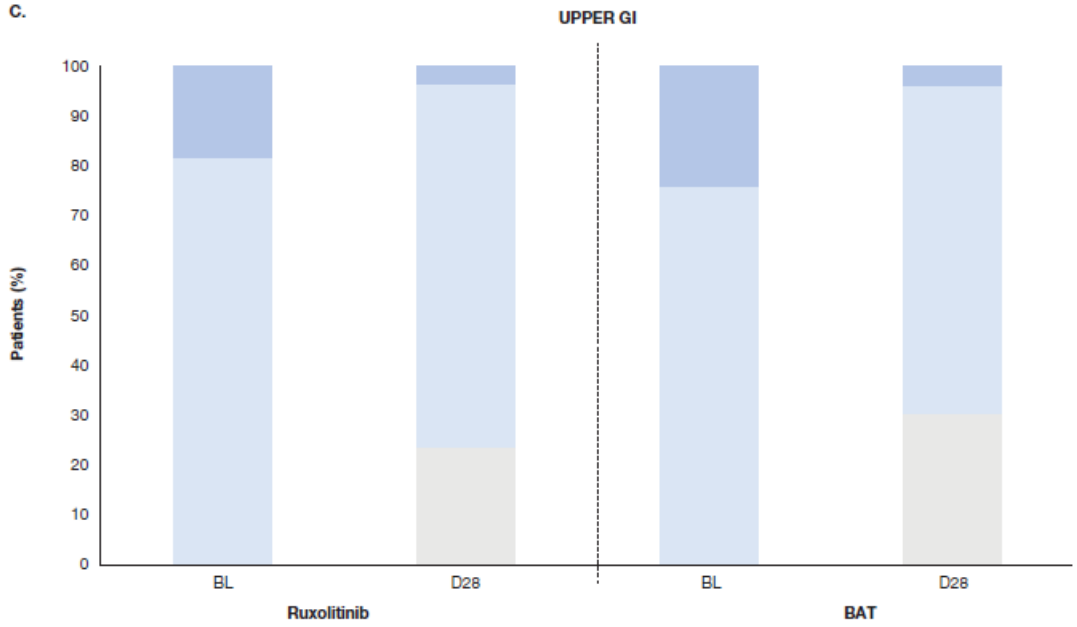


Figure S2. Shift in aGvHD Organ Staging From Baseline to Day 28 for Ruxolitinib and BAT for Skin (Panel A), Liver (Panel B), Upper GI (Panel C), and Lower GI (Panel D) Involvement.

aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; BL, baseline; D28, Day 28; GI, gastrointestinal.



C.


UPPER GI
Patients (%)
100
90
80
70
60
50
40
30
20
10
0
BL
D28
BL
D28
Ruxolitinib
BAT

D.

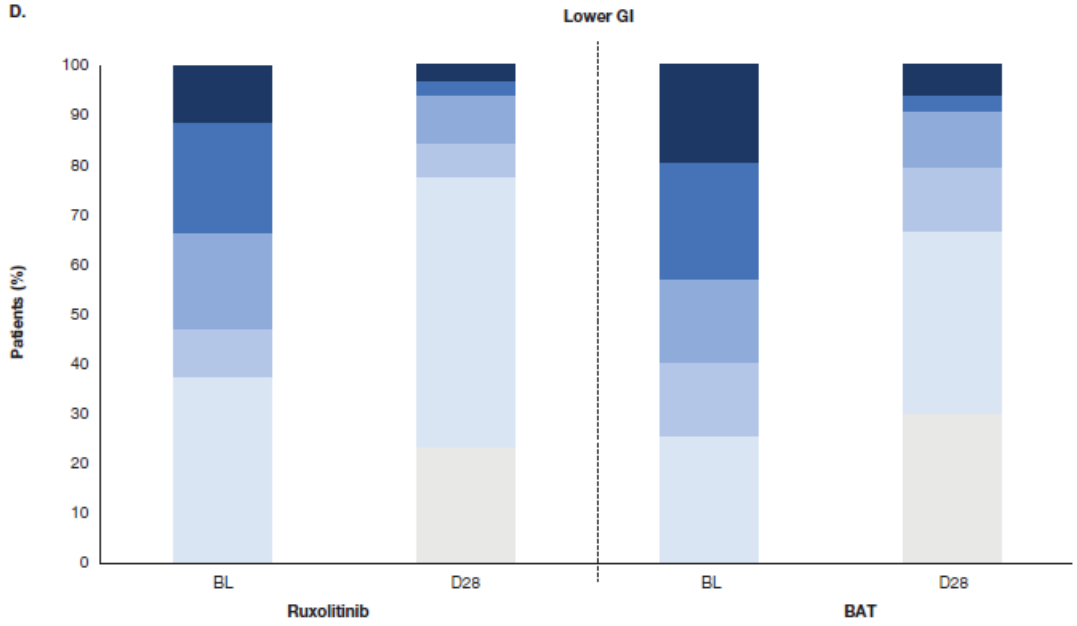
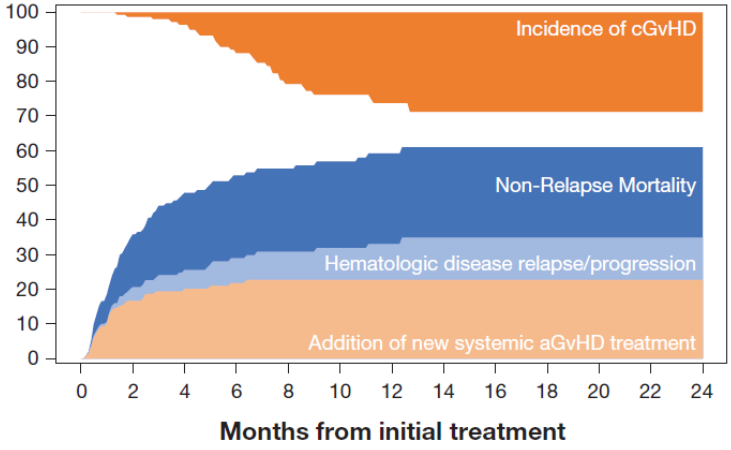

Lower GI
Patients (%)
100
90
80
70
60
50
40
30
20
10
0
BL
D28
BL
D28
Ruxolitinib
BAT

Figure S3. Median Failure-Free Survival in the Ruxolitinib Group (Panel A) and BAT Group (Panel B).

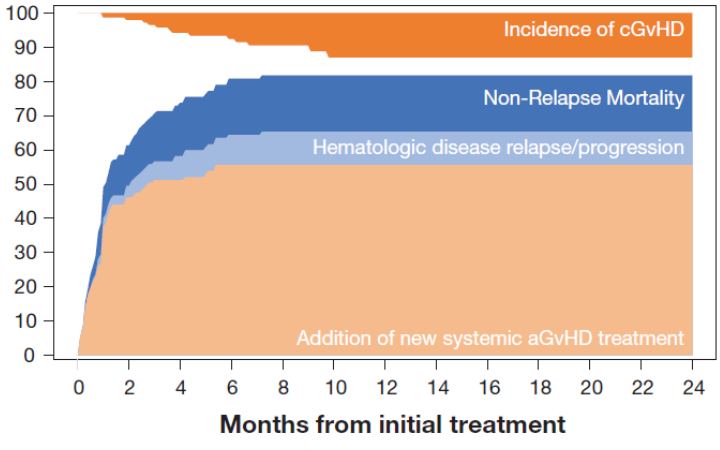
aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; cGvHD, chronic graft-versus-host disease. Events include hematologic disease relapse/progression, non-relapse mortality, or addition of systemic aGvHD treatment.

A.



Addition of new systemic aGvHD treatment	0%	17%	20%	22%	23%	23%	23%	23%	23%	23%	23%	23%	23%
Hematologic disease relapse/progression	0%	4%	5%	7%	8%	9%	10%	12%	12%	12%	12%	12%	12%
Non-Relapse Mortality	0%	15%	22%	24%	24%	25%	26%	26%	26%	26%	26%	26%	26%
Incidence of cGvHD	0%	1%	4%	12%	21%	24%	26%	29%	29%	29%	29%	29%	29%

B.



Addition of new systemic aGvHD treatment	0%	46%	51%	56%	56%	56%	56%	56%	56%	56%	56%	56%	56%
Hematologic disease relapse/progression	0%	3%	7%	9%	10%	10%	10%	10%	10%	10%	10%	10%	10%
Non-Relapse Mortality	0%	12%	16%	16%	16%	16%	16%	16%	16%	16%	16%	16%	16%
Incidence of cGvHD	0%	2%	6%	8%	9%	13%	13%	13%	13%	13%	13%	13%	13%

Figure S4. Cumulative Incidence of Malignancy Relapse/Progression.

BAT denotes best available therapy; NA, not applicable. Competing risk was malignancy relapse/progression.

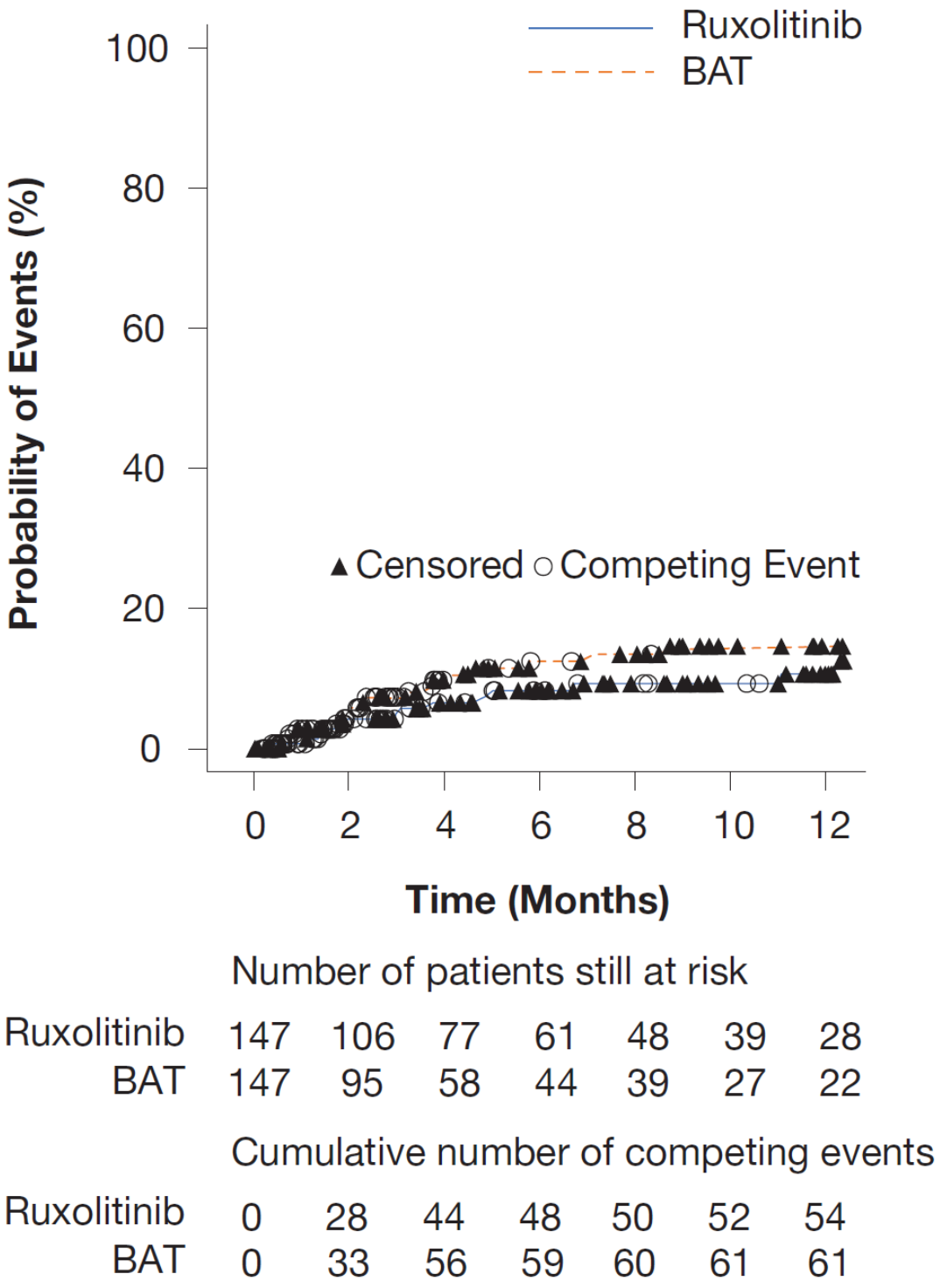
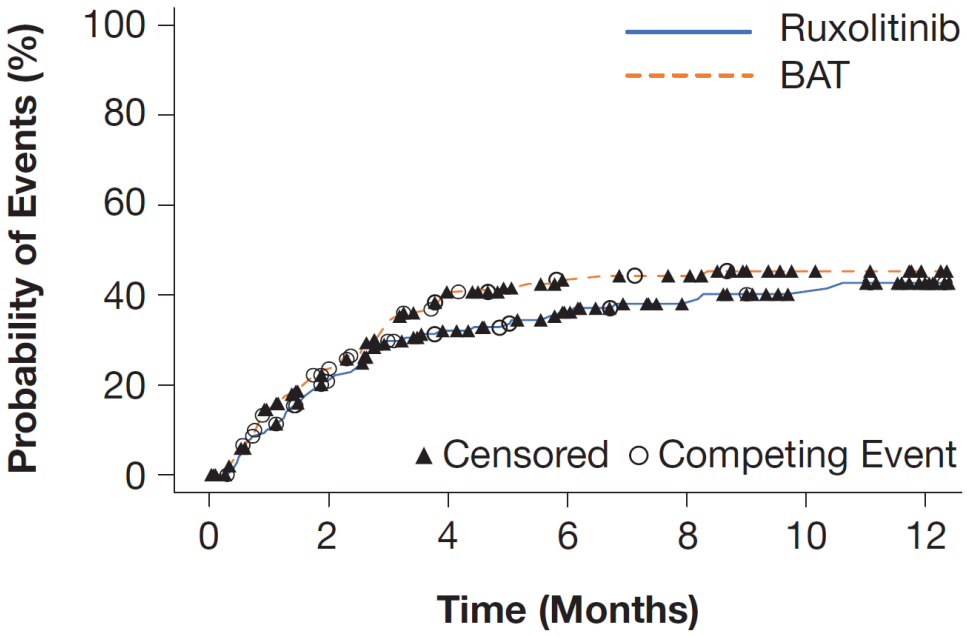


Figure S5. Non-Relapse Mortality.

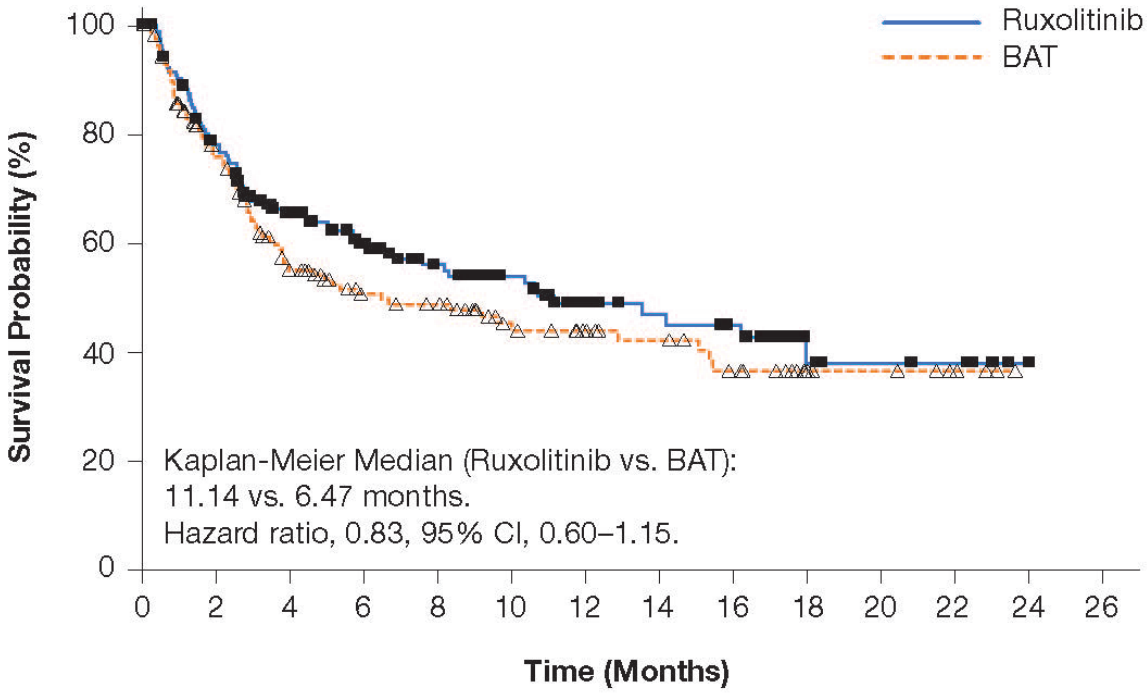
BAT denotes best available therapy; NA, not applicable. Competing risk was hematological disease relapse/progression.



	Number of patients still at risk						
Ruxolitinib	154	110	80	63	50	40	29
BAT	155	101	63	48	43	31	26
	Cumulative number of competing events						
Ruxolitinib	0	6	9	11	12	13	14
BAT	0	6	13	16	17	18	18

Figure S6. Overall Survival.

BAT denotes best available therapy; CI, confidence interval. For this analysis, the 49 patients in the BAT group who crossed over to receive ruxolitinib are included in the BAT group.



Number of patients still with response

Ruxolitinib	154	114	85	68	54	44	30	23	20	8	6	5	1	0
BAT	155	105	69	54	49	33	28	24	18	9	7	4	0	0

Table S1. Baseline Disease Characteristics.

Characteristic	Ruxolitinib (n = 154)	BAT (n = 155)	Total (N = 309)
Primary disease classification – no. (%)			
Malignant – leukemia/MDS	129 (83.8)	121 (78.1)	250 (80.9)
Malignant – lymphoproliferative	18 (11.7)	26 (16.8)	44 (14.2)
Non-malignant	1 (0.6)	5 (3.2)	6 (1.9)
Other	6 (3.9)	3 (1.9)	9 (2.9)
Diagnosis of underlying malignant disease – no. (%)			
Acute lymphoblastic leukemia (all)	25 (16.2)	16 (10.3)	41 (13.3)
Acute myelogenous leukemia	58 (37.7)	63 (40.6)	121 (39.2)
Chronic myelogenous leukemia	6 (3.9)	2 (1.3)	8 (2.6)
Excess blasts, developed from Fanconi Syndrome	1 (0.6)	0	1 (0.3)
Hodgkin lymphoma	6 (3.9)	2 (1.3)	8 (2.6)
Multiple myeloma	2 (1.3)	5 (3.2)	7 (2.3)
MDS	26 (16.9)	29 (18.7)	55 (17.8)
Non-Hodgkin lymphoma	9 (5.8)	19 (12.3)	28 (9.1)
Other acute leukemia	4 (2.6)	3 (1.9)	7 (2.3)
Other leukemia	6 (3.9)	8 (5.2)	14 (4.5)
Other	4 (2.6)	0	4 (1.3)
Diagnosis of underlying non-malignant disease – no. (%)			
Histiocytic disorders	0	1 (0.6)	1 (0.3)

Sickle cell disease	1 (0.6)	1 (0.6)	2 (0.6)
Other	0	3 (1.9)	3 (1.0)
Diagnosis of underlying disease, other – no. (%)			
Blastic neoplasm of plasmacytoid dendritic cells	0	1 (0.6)	1 (0.3)
Multiple myeloma and secondary acute myeloid leukemia	0	1 (0.6)	1 (0.3)
Myelofibrosis	2 (1.3)	0	2 (0.6)
Myeloma	0	1 (0.6)	1 (0.3)
Myeloproliferative neoplasm	1 (0.6)	0	1 (0.3)
Post-polycythemia vera myelofibrosis	1 (0.6)	0	1 (0.3)
Primary myelofibrosis	1 (0.6)	0	1 (0.3)
Septic granulomatosis	1 (0.6)	0	1 (0.3)
Time from diagnosis to screening, yr – mean (SD)	2.2 (3.2)	1.7 (2.2)	1.9 (2.7)
CIBMTR risk assessment – no. (%)			
Low	46 (29.9)	46 (29.7)	92 (29.8)
Intermediate	43 (27.9)	48 (31.0)	91 (29.4)
High	61 (39.6)	55 (35.5)	116 (37.5)
Unknown	4 (2.6)	6 (3.9)	10 (3.2)
Conditioning regimen type – no. (%)			
Myeloablative	85 (55.2)	65 (41.9)	150 (48.5)
Non-myeloablative	31 (20.1)	41 (26.5)	72 (23.3)
Reduced intensity	38 (24.7)	49 (31.6)	87 (28.2)

Total HCT-specific co-morbidity index score – no. (%)			
0	70 (45.5)	63 (40.6)	133 (43.0)
1	30 (19.5)	27 (17.4)	57 (18.4)
2	24 (15.6)	19 (12.3)	43 (13.9)
3	9 (5.8)	26 (16.8)	35 (11.3)
4	12 (7.8)	6 (3.9)	18 (5.8)
≥5	6 (3.9)	6 (3.9)	12 (3.9)
Missing	3 (1.9)	8 (5.2)	11 (3.6)
Time from diagnosis to transplant, days – mean (SD)	713.1 (1156.5)	553.3 (786.0)	633.2 (990.4)
Time from transplant to randomization, days – mean (SD)	84.3 (71.9)	81.5 (66.8)	82.9 (69.3)
Stem cell type – no. (%)			
Bone marrow	19 (12.3)	30 (19.4)	49 (15.9)
Peripheral blood	134 (87.0)	118 (76.1)	252 (81.6)
Single cord blood	1 (0.6)	7 (4.5)	8 (2.6)
Source of graft – no. (%)			
Not related	107 (68.2)	100 (63.3)	207 (65.7)
Related	50 (31.8)	57 (36.1)	107 (34.0)
Missing	0	1 (0.6)	1 (0.3)
Cytomegalovirus positive at transplant – no. (%)	81 (52.6)	87 (56.1)	168 (54.4)
Donor cytomegalovirus positive at transplant – no. (%)	72 (45.9)	76 (48.1)	148 (47.0)

T-cell depleted – no. (%)			
No	138 (87.9)	128 (81.0)	266 (84.4)
Yes	17 (10.8)	22 (13.9)	39 (12.4)
Missing	0	3 (1.9)	3 (1.0)
Time from diagnosis of aGvHD grade II or higher to steroid refractory, days – mean (SD)	26.19 (43.16)	20.13 (30.83)	23.15 (37.55)
Steroid-refractory criteria – no. (%)			
Progression after at least 3 days	35 (22.7)	43 (27.7)	78 (25.2)
Failure to respond after 7 days	72 (46.8)	63 (40.6)	135 (43.7)
Failure during steroid taper	47 (30.5)	49 (31.6)	96 (31.1)
Overall aGvHD grade at baseline*– no. (%)			
Grade 0	4 (2.6)	1 (0.6)	5 (1.6)†
Grade I	2 (1.3)	0	2 (0.6)†
Grade II	50 (32.5)	54 (34.8)	104 (33.7)
Grade III	68 (44.2)	68 (43.9)	136 (44.0)
Grade IV	30 (19.5)	32 (20.6)	62 (20.1)
aGvHD organ involvement – no. (%)			
Skin	93 (60.4)	74 (47.7)	167 (54.0)
Liver	36 (23.4)	26 (16.8)	62 (20.1)
Upper GI	28 (18.2)	37 (23.9)	65 (21.0)
Lower GI	96 (62.3)	115 (74.2)	211 (68.3)
Missing	4 (2.6)	1 (0.6)	5 (1.6)
Steroid dose at randomization, mg/day – mean (SD)	132.3 (90.9)	126.5 (73.1)	129.4 (82.5)

aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; CIBMTR, Center for International Blood and Marrow Transplant Research; GI, gastrointestinal; HCT, hematopoietic cell transplantation; MDS, myelodysplastic syndrome; SD, standard deviation.

* Baseline defined as the last aGvHD assessment prior to or on randomization date + 3 days, but no later than the treatment start date.

† Protocol deviations.

Table S2A. Overall Response Rate at Day 28 (Full Analysis Set).

	Ruxolitinib (n = 154)		BAT (n = 155)			
	n (%)	95% CI	n (%)	95% CI	Odds Ratio (Ruxolitinib/BAT)	95% CI
Overall response						
Responders						
CR	53 (34.4)		30 (19.4)			
PR	43 (27.9)		31 (20.0)			
Non-responders						
No response	7 (4.5)		10 (6.5)			
Mixed response	10 (6.5)		17 (11.0)			
Progression	4 (2.6)		13 (8.4)			
Other*	1 (0.6)		7 (4.5)			
Unknown	36 (23.4)		47 (30.3)			
Death	15 (9.7)		22 (14.2)			

	Ruxolitinib (n = 154)		BAT (n = 155)			
	n (%)	95% CI	n (%)	95% CI	Odds Ratio (Ruxolitinib/BAT)	95% CI
Early discontinuation	17 (11.0)		16 (10.3)			
Missing visits	4 (2.6)		9 (5.8)			
Overall response rate (CR + PR)	**96 (62.3)**	**54.2–70.0**	**61 (39.4)**	**31.6–47.5**	**2.64**	**1.65–4.22**

aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method. Odds ratio and 95% CI were calculated using the stratified Cochran–Mantel–Haenszel test.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S2B. Overall Response Rate at Day 28 for Patients With aGvHD Grade II at Randomization*.

	Ruxolitinib (n = 53)		BAT (n = 53)			
	n (%)	95% CI	n (%)	95% CI	Odds Ratio (Ruxolitinib/BAT)	95% CI
Overall response						
Responders						
CR	27 (50.9)		14 (26.4)			
PR	13 (24.5)		13 (24.5)			
Non-responders						
No response	2 (3.8)		3 (5.7)			
Mixed response	2 (3.8)		4 (7.5)			
Progression	0		5 (9.4)			
Other†	0		2 (3.8)			
Unknown	9 (17.0)		12 (22.6)			
Death	2 (3.8)		2 (3.8)			

	Ruxolitinib (n = 53)		BAT (n = 53)			
	n (%)	95% CI	n (%)	95% CI	Odds Ratio (Ruxolitinib/BAT)	95% CI
Early discontinuation	4 (7.5)		6 (11.3)			
Missing visits	3 (5.7)		4 (7.5)			
Overall response rate (CR + PR)	**40 (75.5)**	**61.7–86.2**	**27 (50.9)**	**36.8–64.9**	**2.96**	**1.30–6.76**

aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method. Odds ratio and 95% CI were calculated using the stratified Cochran–Mantel–Haenszel test.

* Randomized as per Interactive Response Technology (IRT), includes 3 patients with identified protocol deviation for baseline aGvHD grading.

† Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S2C. Overall Response Rate at Day 28 for Patients With aGvHD Grade III at Randomization*.

	Ruxolitinib (n = 71)		BAT (n = 72)			
	n (%)	95% CI	n (%)	95% CI	Odds ratio (Ruxolitinib/BAT)	95% CI
Overall response						
Responders						
CR	20 (28.2)		12 (16.7)			
PR	20 (28.2)		15 (20.8)			
Non-responders						
No response	4 (5.6)		4 (5.6)			
Mixed response	6 (8.5)		11 (15.3)			
Progression	3 (4.2)		7 (9.7)			
Other†	0		3 (4.2)			
Unknown	18 (25.4)		20 (27.8)			
Death	9 (12.7)		14 (19.4)			

	Ruxolitinib (n = 71)		BAT (n = 72)			
	n (%)	95% CI	n (%)	95% CI	Odds ratio (Ruxolitinib/BAT)	95% CI
Early discontinuation	8 (11.3)		3 (4.2)			
Missing visits	1 (1.4)		3 (4.2)			
Overall response rate (CR + PR)	**40 (56.3)**	**44.0–68.1**	**27 (37.5)**	**26.4–49.7**	**2.15**	**1.10–4.20**

aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method. Odds ratio and 95% CI were calculated using the stratified Cochran–Mantel–Haenszel test.

* Randomized as per Interactive Response Technology (IRT), includes 2 patients with identified protocol deviations for baseline aGvHD grading.

† Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S2D. Overall Response Rate at Day 28 for Patients With aGvHD Grade IV at Randomization*.

	Ruxolitinib (n = 30)		BAT (n = 30)			
	n (%)	95% CI	n (%)	95% CI	Odds ratio (Ruxolitinib/BAT)	95% CI
Overall response						
Responders						
CR	6 (20.0)		4 (13.3)			
PR	10 (33.3)		3 (10.0)			
Non-responders						
No response	1 (3.3)		3 (10.0)			
Mixed response	2 (6.7)		2 (6.7)			
Progression	1 (3.3)		1 (3.3)			
Other†	1 (3.3)		2 (6.7)			
Unknown	9 (30.0)		15 (15.0)			
Death	4 (13.3)		6 (20.0)			

	Ruxolitinib (n = 30)		BAT (n = 30)			
	n (%)	95% CI	n (%)	95% CI	Odds ratio (Ruxolitinib/BAT)	95% CI
Early discontinuation	5 (16.7)		7 (23.3)			
Missing visits	0		2 (6.7)			
Overall response rate (CR + PR)	**16 (53.3)**	**34.3–71.7**	**7 (23.3)**	**9.9–42.3**	**3.76**	**1.24–11.38**

aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method. Odds ratio and 95% CI were calculated using the stratified Cochran–Mantel–Haenszel test.

* Randomized as per Interactive Response Technology (IRT), includes 2 patients with identified protocol deviations for baseline aGvHD grading.

† Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3A. Overall Response Rate at Day 28 for Patients Receiving ATG (BAT).

	ATG (N = 20)	
	n (%)	**95% CI**
Overall response		
Responders		
CR	3 (15.0)	
PR	3 (15.0)	
Non-responders		
No response	2 (10.0)	
Mixed response	5 (25.0)	
Progression	3 (15.0)	
Other*	0	
Unknown	4 (20.0)	
Death	2 (10.0)	
Early discontinuation	2 (10.0)	

	ATG (N = 20)	
	n (%)	**95% CI**
Missing visits	0	
Overall response rate (CR + PR)	**6 (30.0)**	**11.9–54.3**

ATG denotes anti-thymocyte globulin; BAT, best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3B. Overall Response Rate at Day 28 for Patients Receiving Etanercept (BAT).

	Etanercept (N = 22)	
	n (%)	**95% CI**
Overall response		
Responders		
CR	6 (27.3)	
PR	4 (18.2)	
Non-responders		
No response	0	
Mixed response	2 (9.1)	
Progression	3 (13.6)	
Other*	1 (4.5)	
Unknown	6 (27.3)	
Death	4 (18.2)	
Early discontinuation	1 (4.5)	

	Etanercept (N = 22)	
	n (%)	95% CI
Missing visits	1 (4.5)	
Overall response rate (CR + PR)	**10 (45.5)**	**24.4–67.8**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3C. Overall Response Rate at Day 28 for Patients Receiving Everolimus (BAT).

	Everolimus (N = 2)	
	n (%)	95% CI
Overall response		
Responders		
CR	0	
PR	0	
Non-responders		
No response	0	
Mixed response	1 (50.0)	
Progression	0	
Other*	0	
Unknown	1 (50.0)	
Death	0	
Early discontinuation	0	

	Everolimus (N = 2)	
	n (%)	**95% CI**
Missing visits	1 (50.0)	
Overall response rate (CR + PR)	**0**	**0–84.2**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3D. Overall Response Rate at Day 28 for Patients Receiving ECP (BAT).

	ECP (N = 41)	
	n (%)	**95% CI**
Overall response		
Responders		
CR	8 (19.5)	
PR	10 (24.4)	
Non-responders		
No response	2 (4.9)	
Mixed response	4 (9.8)	
Progression	3 (7.3)	
Other*	0	
Unknown	14 (34.1)	
Death	6 (14.6)	
Early discontinuation	4 (9.8)	

	ECP (N = 41)	
	n (%)	95% CI
Missing visits	4 (9.8)	
Overall response rate (CR + PR)	**18 (43.9)**	**28.5–60.3**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; ECP, extracorporeal photopheresis; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3E. Overall Response Rate at Day 28 for Patients Receiving Infliximab (BAT).

	Infliximab (N = 17)	
	n (%)	**95% CI**
Overall response		
Responders		
CR	2 (11.8)	
PR	4 (23.5)	
Non-responders		
No response	2 (11.8)	
Mixed response	2 (11.8)	
Progression	1 (5.9)	
Other*	0	
Unknown	6 (35.3)	
Death	2 (11.8)	
Early discontinuation	2 (11.8)	

	Infliximab (N = 17)	
	n (%)	95% CI
Missing visits	2 (11.8)	
Overall response rate (CR + PR)	**6 (35.3)**	**14.2–61.7**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3F. Overall Response Rate at Day 28 for Patients Receiving Low-Dose MTX (BAT).

	Low-dose MTX (N = 5)	
	n (%)	95% CI
Overall response		
Responders		
CR	2 (40.0)	
PR	0	
Non-responders		
No response	0	
Mixed response	0	
Progression	0	
Other*	1 (20.0)	
Unknown	2 (40.0)	
Death	0	
Early discontinuation	1 (20.0)	

	Low-dose MTX (N = 5)	
	n (%)	95% CI
Missing visits	1 (20.0)	
Overall response rate (CR + PR)	**2 (40.0)**	**5.3–85.3**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; MTX, methotrexate; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3G. Overall Response Rate at Day 28 for Patients Receiving MSC (BAT).

	MSC (N = 15)	
	n (%)	95% CI
Overall response		
Responders		
CR	3 (20.0)	
PR	6 (40.0)	
Non-responders		
No response	1 (6.7)	
Mixed response	1 (6.7)	
Progression	1 (6.7)	
Other*	1 (6.7)	
Unknown	2 (13.3)	
Death	1 (6.7)	
Early discontinuation	1 (6.7)	

	MSC (N = 15)	
	n (%)	95% CI
Missing visits	0	
Overall response rate (CR + PR)	**9 (60.0)**	**32.3–83.7**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; MSC, mesenchymal stromal cells; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3H. Overall Response Rate at Day 28 for Patients Receiving MMF (BAT).

	MMF (N = 25)	
	n (%)	95% CI
Overall response		
Responders		
CR	4 (16.0)	
PR	4 (16.0)	
Non-responders		
No response	3 (12.0)	
Mixed response	2 (8.0)	
Progression	2 (8.0)	
Other*	4 (16.0)	
Unknown	6 (24.0)	
Death	4 (16.0)	
Early discontinuation	2 (8.0)	

	MMF (N = 25)	
	n (%)	95% CI
Missing visits	0	
Overall response rate (CR + PR)	**8 (32.0)**	**14.9–53.5**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; MMF, mycophenolate mofetil; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S3l. Overall Response Rate at Day 28 for Patients Receiving Sirolimus (BAT).

	Sirolimus (N = 3)	
	n (%)	95% CI
Overall response		
Responders		
CR	2 (66.7)	
PR	0	
Non-responders		
No response	0	
Mixed response	0	
Progression	0	
Other*	0	
Unknown	1 (33.3)	
Death	1 (33.3)	
Early discontinuation	0	

	Sirolimus (N = 3)	
	n (%)	95% CI
Missing visits	0	
Overall response rate (CR + PR)	**2 (66.7)**	**9.4–99.2**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; MMF, mycophenolate mofetil; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method.

* Other: patients with additional systemic therapies along with CR/PR per investigator assessment.

Table S4. Best Overall Response by Day 28.

	Ruxolitinib (n = 154)		BAT (n = 155)			
	n (%)	95% CI	n (%)	95% CI	Odds ratio (Ruxolitinib/BAT)	95% CI
Overall response						
Responders						
CR	67 (43.5)		42 (27.1)			
PR	59 (38.3)		52 (33.5)			
Non-responders						
No response	13 (8.4)		21 (13.5)			
Mixed response	7 (4.5)		14 (9.0)			
Progression	4 (2.6)		10 (6.5)			
Unknown	4 (2.6)		16 (10.3)			
Death	2 (1.3)		6 (3.9)			
Early discontinuation	2 (1.3)		4 (2.6)			

	Ruxolitinib (n = 154)		BAT (n = 155)			
	n (%)	95% CI	n (%)	95% CI	Odds ratio (Ruxolitinib/BAT)	95% CI
Missing visits	0		6 (3.9)			
Overall response rate (CR + PR)	**126 (81.8)**	**74.8–87.6**	**94 (60.6)**	**52.5–68.4**	**3.07**	**1.80–5.25**

BAT denotes best available therapy; CI, confidence interval; CR, complete response; N, the total number of subjects in the treatment group and the denominator for the percentage (%) calculation; n, number of patients who were in the corresponding category; PR, partial response. The 95% CI for the response rate was calculated using the Clopper–Pearson exact method. Odds ratio, and 95% CI were calculated using the stratified Cochran–Mantel–Haenszel test.

Table S5. Duration of Response.

	Ruxolitinib (n = 96)	BAT (n = 61)
Number of patients with events	9 (9.4)	21 (34.4)
Number of patients with competing risks	53 (55.2)	23 (37.7)
Death	28 (29.2)	12 (19.7)
Incidence of cGvHD	25 (26.0)	11 (18.0)
Number of patients censored	34 (35.4)	17 (27.9)
Estimated cumulative incidence and 95% CI at:		
1 month	2.08 (0.40–6.65)	11.54 (5.03–21.03)
2 months	5.37 (1.98–11.30)	20.13 (11.02–31.19)
6 months	9.65 (4.39–17.40)	38.98 (25.54–52.19)
12 months	11.76 (5.51–20.57)	NE (NE–NE)

aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; cGvHD, chronic graft-versus-host disease; CI, confidence interval; CR, complete response; N, the number of subjects whose overall response is CR or PR at Day 28; NE, non-evaluable; PR, partial response; Q1–Q3, interquartile range. The start date was the date of first documented response of CR or PR,

which could be prior to or at Day 28. The event was defined as the progression of aGvHD or addition of systemic therapies for aGvHD after Day 28. The competing risks included death without prior observation of aGvHD progression and onset of cGvHD. Duration of response was censored at the last response assessment.

Table S6. Failure-Free Survival.

	Ruxolitinib (n = 154)	BAT (n = 155)
Patients with events – no. (%)	84 (54.5)	119 (76.8)
Patients with competing risks – no. (%)	30 (19.5)	14 (9.0)
Patients censored – no. (%)	40 (26.0)	22 (14.2)
Estimated cumulative incidence and 95% CI at:		
1 month	18.47 (12.74–25.04)	49.13 (40.94–56.80)
2 months	35.83 (28.22–43.50)	61.32 (53.00–68.61)
6 months	52.85 (44.24–60.74)	80.86 (72.95–86.67)
12 months	59.20 (50.01–67.26)	81.83 (73.93–87.53)
18 months	61.02 (51.36–69.34)	81.83 (73.93–87.53)

aGvHD denotes acute graft-versus-host disease; BAT, best available therapy; cGvHD, chronic graft-versus-host disease; CI, confidence interval. The competing risk included onset of cGvHD. Failure-free survival included hematologic disease relapse/progression, non-relapse mortality, or addition of new systemic aGvHD treatment.

Table S7. Incidence of Malignancy Relapse/Progression.

	Ruxolitinib (n = 147)	BAT (n = 147)
Patients with events – no. (%)	14 (9.5)	20 (13.6)
Patients with competing risks – no. (%)	56 (38.1)	62 (42.2)
Patients censored – no. (%)	77 (52.4)	65 (44.2)
Estimated cumulative incidence and 95% CI at:		
1 month	0.69 (0.06–3.51)	2.80 (0.92–6.54)
2 months	4.23 (1.73–8.49)	4.30 (1.76–8.63)
6 months	8.28 (4.36–13.80)	12.45 (7.40–18.88)
12 months	10.65 (5.84–17.11)	14.62 (8.96–21.60)
18 months	12.56 (6.84–20.08)	19.04 (11.36–28.23)
24 months	12.56 (6.84–20.08)	NE (NE–NE)

BAT denotes best available therapy; CI, confidence interval; N, the number of patients with underlying hematologic malignant disease; NE, non-evaluable. The competing risk includes death with non-relapse mortality for patients with underlying hematologic malignant disease.

Table S8. Non-Relapse Mortality.

	Ruxolitinib (n = 154)	BAT (n = 155)
Patients with events – no. (%)	60 (39.0)	66 (42.6)
Patients with competing risks – no. (%)	15 (9.7)	20 (12.9)
Patients censored – no. (%)	79 (51.3)	69 (44.5)
Estimated cumulative incidence and 95% CI at:		
1 month	9.96 (5.83–15.39)	14.52 (9.45–20.64)
2 months	20.75 (14.64–27.60)	23.60 (17.09–30.73)
6 months	36.18 (28.28–44.12)	43.34 (34.89–51.48)
12 months	42.67 (33.84–51.19)	45.33 (36.67–53.57)
18 months	49.38 (36.37–61.12)	50.77 (40.73–59.96)
24 months	49.38 (36.37–61.12)	NE (NE–NE)

BAT denotes best available therapy; CI, confidence interval; NE, non-evaluable. The competing risk included hematologic disease relapse/progression.

Table S9. Overall Survival.

	Ruxolitinib (n = 154)	BAT (n = 155)
Patients who died – no. (%)	72 (46.8)	79 (51.0)
Patients who are censored – no. (%)	82 (53.2)	76 (49.0)
Hazard ratio (ruxolitinib/BAT) (95% CI)	0.83 (0.60–1.15)	
Kaplan–Meier median, months	11.14	6.47
Kaplan–Meier estimates and 95% CI of overall survival of:		
0 to <1 month	90.04 (84.02–93.87)	85.48 (78.79–90.19)
1 to <2 months	77.91 (70.36–83.75)	75.62 (67.83–81.78)
2 to <6 months	59.54 (50.92–67.14)	50.36 (41.61–58.47)
6 to <12 months	48.69 (39.35–57.38)	43.64 (34.60–52.32)
12 to <18 months	37.69 (25.24–50.07)	36.18 (26.37–46.05)
18 to <24 months	NE (NE–NE)	NE (NE–NE)
24 to <48 months	NE (NE–NE)	NE (NE–NE)

BAT denotes best available therapy; CI, confidence interval; NE, non-evaluable. Hazard ratio and 95% CI were obtained from the stratified Cox proportional hazards model using the Wald test. For this analysis, the 49 patients in the BAT group who crossed over to receive ruxolitinib are included in the BAT group.

Table S10. Overview of Infections up to Day 28 Visit, by Type and Maximum Severity Grade.

Type of Infection, Maximum severity grade	Ruxolitinib (n = 152) n (%)	BAT (n = 150) n (%)
Number of patients with at least 1 event	93 (61.2)	82 (54.7)
Grade 1	17 (11.2)	15 (10.0)
Grade 2	42 (27.6)	38 (25.3)
Grade 3	34 (22.4)	28 (18.7)
Missing	0	1 (0.7)
Fungal infections	13 (8.6)	6 (4.0)
Grade 1	4 (2.6)	3 (2.0)
Grade 2	2 (1.3)	0
Grade 3	7 (4.6)	3 (2.0)
Viral infections	65 (42.8)	50 (33.3)
Grade 1	15 (9.9)	11 (7.3)
Grade 2	37 (24.3)	27 (18.0)
Grade 3	13 (8.6)	12 (8.0)
Bacterial infections	45 (29.6)	48 (32.0)
Grade 1	17 (11.2)	10 (6.7)
Grade 2	10 (6.6)	25 (16.7)
Grade 3	18 (11.8)	13 (8.7)
Unknown	13 (8.6)	8 (5.3)
Grade 1	1 (0.7)	1 (0.7)

Grade 2	8 (5.3)	2 (1.3)
Grade 3	4 (2.6)	4 (2.7)
Missing	0	1 (0.7)
Other	4 (2.6)	1 (0.7)
Grade 1	3 (2.0)	0
Grade 2	1 (0.7)	1 (0.7)

BAT denotes best available therapy; n, counts of patients. A patient with multiple severity grades for an adverse event is only counted under the maximum grade. Adverse events occurring outside the on-randomized-treatment period or after Day 31 are not summarized.

Table S11. Infections by Type and Maximum Infection Severity Grade up to the Data Cut Off.

Type of Infection. **Maximum severity grade**	**Ruxolitnib (n = 152) n (%)**	**BAT (n = 150) n (%)**
Number of patients with at least one event	121 (79.6)	104 (69.3)
Grade 1	14 (9.2)	21 (14.0)
Grade 2	50 (32.9)	41 (27.3)
Grade 3	56 (36.8)	42 (28.0)
Missing	1 (0.7)	0
Fungal infections	26 (17.1)	13 (8.7)
Grade 1	7 (4.6)	5 (3.3)
Grade 2	4 (2.6)	2 (1.3)
Grade 3	13 (8.6)	6 (4.0)
Missing	2 (1.3)	0
Viral infections	87 (57.2)	65 (43.3)
Grade 1	19 (12.5)	18 (12.0)
Grade 2	48 (31.6)	30 (20.0)
Grade 3	19 (12.5)	16 (10.7)
Missing	1 (0.7)	1 (0.7)
Bacterial infections	73 (48.0)	68 (45.3)
Grade 1	18 (11.8)	12 (8.0)

Grade 2	22 (14.5)	33 (22.0)
Grade 3	33 (21.7)	23 (15.3)
Unknown	28 (18.4)	21 (14.0)
Grade 1	4 (2.6)	4 (2.7)
Grade 2	15 (9.9)	8 (5.3)
Grade 3	9 (5.9)	8 (5.3)
Missing	0	1 (0.7)
Other	5 (3.3)	3 (2.0)
Grade 1	2 (1.3)	1 (0.7)
Grade 2	1 (0.7)	1 (0.7)
Grade 3	2 (1.3)	1 (0.7)

BAT denotes best available therapy; n, counts of patients. A patient with multiple severity grades for an adverse event is only counted under the maximum grade. Adverse events occurring outside the on-randomized-treatment period are not summarized.

SUPPLEMENTARY REFERENCES

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