SUPPLEMENTARY INFORMATION

Integrated safety analysis of ritlecitinib, an oral JAK3/TEC family kinase inhibitor, for the treatment of alopecia areata from the ALLEGRO clinical trial program

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Brett King,[1] Jennifer Soung,[2] Christos Tziotzios,[3] Lidia Rudnicka,[4] Pascal Joly,[5] Melinda Gooderham,[6] Rodney Sinclair,[7] Natasha A. Mesinkovska,[8] Carle Paul,[9] Yankun Gong,[10] Susan D. Anway,[11] Helen Tran,[10] Robert Wolk,[11] Samuel H. Zwillich,[11] Alexandre Lejeune[12]

1. Yale School of Medicine, New Haven, CT, USA
2. Southern California Dermatology, Santa Ana, CA, USA
3. St John's Institute of Dermatology, King's College London, London, UK
4. Department of Dermatology, Medical University of Warsaw, Warsaw, Poland
5. Rouen University Hospital, INSERM 1234, Normandie University, Rouen, France
6. Skin Centre for Dermatology, Canada Probity Medical Research, Waterloo, ON, Canada
7. Sinclair Dermatology, Melbourne, VIC, Australia
8. Department of Dermatology and Dermatopathology, School of Medicine, University of California, Irvine, CA, USA
9. Department of Dermatology, Toulouse University and INSERM infinity U1291, Toulouse, France
10. Pfizer Inc, New York, NY, USA
11. Pfizer Inc, Groton, CT, USA
12. Pfizer Inc, Paris, France

Corresponding author

Alexandre Lejeune, PhD

Pfizer Inc

alexandre.lejeune@pfizer.com

Table S1. Summary of clinical trials included in this integrated analysis. Studies in shaded cells were included in the placebo-controlled pool

Trial Name (ClinicalTrials.gov Identifier)	**Study Design**	**Key Inclusion Criteria**	**Treatment/Duration**	**Number of Patients (Safety Population)**
ALLEGRO phase 2a (NCT02974868)	Phase 2a, randomized, double-blind, placebo-controlled, multicenter study in adult patients	• Age 18-75 years • ≥50% scalp hair loss • Current AA episode duration of 6 months to 7 years	Treatment duration: up to 48 weeks[a] 24-week double-blind period + 48-week single-blind extension[b] • Ritlecitinib 200 mg/50 mg QD[c] • Placebo (ritlecitinib group) • Extension: Ritlecitinib 200 mg/50 mg QD	N=142[d] n=48 n=24 n=33

Phase 2a safety (NCT04517864)	Phase 2a, randomized, double-blind, placebo-controlled safety study with active extension in adult patients	• Age 18-50 years • ≥25% scalp hair loss • Normal hearing and normal brainstem auditory evoked potentials	Treatment duration: 24 months 9-month double-blind period + extension up to 15 months • Ritlecitinib 200 mg/50 mg QD • Placebo → 200 mg/ritlecitinib 50 mg QD	N=71 n=36 n=35

ALLEGRO phase 2b/3 (NCT03732807)	Phase 2b/3, randomized, double-blind, placebo-controlled, dose-ranging study in adult and adolescent patients	• Age 12-75 years • ≥50% scalp hair loss • Current AA episode duration of 6 months to 10 years	Treatment duration: 48 weeks 24-week double-blind period + 24-week extension • Ritlecitinib 200 mg/50 mg QD[c] • Ritlecitinib 200 mg/30 mg QD[e] • Ritlecitinib 50 mg QD • Ritlecitinib 30 mg QD • Ritlecitinib 10 mg QD • Placebo → ritlecitinib 200 mg/50 mg QD[f] • Placebo → ritlecitinib 50 mg QD[f]	N=715 n=131 n=129 n=130 n=132 n=62 n=65 n=66
ALLEGRO-LT (NCT04006457; ongoing)	Phase 3, open-label, multicenter, long-term study in adult and adolescent patients	• Age ≥12 years • ≥25% scalp hair loss (de novo patients) • Current AA episode duration of 6 months to 10 years (de novo patients)	Treatment duration: 36 months Open-label 36 months • Ritlecitinib 200 mg/50 mg QD (de novo patients) • Ritlecitinib 50 mg QD (rollover patients[g])	N=1052

AA, alopecia areata; QD, once daily.

[a] Crossover, open label extension period is not included.

[b] Single-blind extension noted here only includes the nonresponder segment.

[c] 200-mg loading dose first 4 weeks, 50-mg maintenance dose for 20 weeks.

[d] Includes patients in the brepocitinib (TYK2/JAK1 inhibitor) group, who are not included in this analysis; therefore, the total number of patients is greater than the placebo and ritlecitinib groups combined.

[e] 200-mg loading dose first 4 weeks, 30-mg maintenance dose for 20 weeks.

[f] Patients received placebo until Week 24 and then switched to ritlecitinib treatment (200 mg/50 mg QD or 50 mg QD).

[g] Rollover patients were eligible following completion of 48 weeks of treatment in either ALLEGRO phase 2a (NCT02974868) or ALLEGRO phase 2b/3 (NCT03732807).

Table S2. Detailed inclusion and exclusion criteria of the four clinical trials included in this integrated analysis

	Inclusion Criteria	**Exclusion Criteria**
ALLEGRO phase 2a (NCT02974868)	• Age 18-75 years • ≥50% scalp hair loss • Current AA episode duration of 6 months to 7 years	• Other types of alopecia or active inflammatory disease involving the scalp • History of HIV or positive HIV serology at screening • Infected with HBV or HCV • Evidence of active or latent or inadequately treated infection with TB • Use of an oral or topical JAK inhibitor within 12 weeks of the first dose of the study drug, a biologic within 12 weeks or 5 half-lives (whichever is longer), systemic or intralesional treatment that could affect AA within 8 weeks or 5 half-lives, phototherapy within 4 weeks, or a topical treatment that could affect AA within 2 weeks

Phase 2a safety (NCT04517864)	• Age 18-50 years • Diagnosis of AA with ≥25% scalp hair loss • Normal hearing and BAEP • Normal neurological exam	• Current hearing loss or current disease that could affect hearing, including disorders associated with progressive hearing loss in adults • Current or history of clinically significant central or peripheral neurological disease or first-degree family history of hereditary neuropathy • Active or chronic infection • Previous use of a JAK inhibitor

ALLEGRO phase 2b/3 (NCT03732807)	• Age ≥12 years
	  o <18 years if permitted by the sponsor, local competent authority, and IRB/IEC
	  o Within EU, VHP countries: age 18-74 years (inclusive)
	• Meet reproductive criteria, including relevant contraceptive methods
	• Not pregnant or breastfeeding
	• Meet the following AA criteria:
	  o Clinical diagnosis of AA with no other etiology of hair loss
	  o ≥50% hair loss of the scalp, including AT and AU, without evidence of terminal hair regrowth within 6 months at both Screening and BL visits
	  o Current episode of hair loss ≤10 years
		• Other types of alopecia, scalp disease, or active systemic disease
		• Any psychiatric condition, including recent or active suicidal ideation or behavior that meets any of the listed protocol criteria
		• Auditory conditions considered acute, fluctuating, or progressive
		• Known immunodeficiency disorder, including positive serology for HIV at Screening
		• Present/past malignancies, except for adequately treated or excised nonmetastatic basal cell or squamous cell cancer of the skin or cervical carcinoma in situ
		• Past/present lymphoproliferative disorder, lymphoma, or leukemia
		• History (single episode) of disseminated HZ or disseminated herpes simplex or recurrent (≥1 episode of) localized dermatomal HZ
		• Current/recent history of clinically significant severe, progressive, or uncontrolled renal, hepatic, hematologic, gastrointestinal, metabolic, endocrine, pulmonary, cardiovascular, psychiatric, immunological/rheumatological, or neurological disease

		• Age 12 to <18 years without a documented history of VZV vaccination or presence of VZV IgG Ab
		• History of systemic infection, active acute or chronic infection, or infection with HBV or HCV
		• Received any of the treatment regimens in the specified time frames
		  ○ At any time: previous use of any JAK inhibitor in any disease indication or any non–B-cell selective lymphocyte-depleting agent (eg, alefacept, alemtuzumab)
		  ○ Within 6 months of first dose of study drug or five half-lives (if known), or until lymphocyte count returns to normal, whichever is longer: any B-cell–depleting agents, including but not limited to rituximab
		  ○ Within 12 weeks of first dose of study drug or five half-lives (if known), whichever is longer: other immunomodulatory biologic agents
		  ○ Within 8 weeks of first dose of study drug or within 5 half-lives (if known), whichever is longer: other systemic treatments that could affect AA

ALLEGRO-LT (NCT04006457; ongoing)	• Age ≥12 years
	  ○ <18 years if permitted by the sponsor, local competent authority, and IRB/IEC
	• Agree to avoid prolonged sun exposure and not use tanning booths, sun lamps, or other UV light sources during the study
	• Meet reproductive criteria, including relevant contraceptive methods
	• Rollover patients from NCT03732807 must have completed ≥34 weeks of study intervention
	• De novo or rollover patients >30 days from the first study visit of study and the last dose in studies NCT02974868 or NCT03732807 had to meet the following AA criteria:
	  ○ Clinical diagnosis of AA with no other etiology of hair loss; androgenetic alopecia coexistent with AA was
		• Other scalp disease or active systemic disease
		• Any psychiatric condition, including recent or active suicidal ideation or behavior that meets any of the listed protocol criteria
		• Auditory conditions considered acute, fluctuating, or progressive
		• Known immunodeficiency disorder, including positive serology for HIV at Screening
		• Present/past malignancies, except for adequately treated or excised nonmetastatic basal cell or squamous cell cancer of the skin or cervical carcinoma in situ
		• Past/present lymphoproliferative disorder, lymphoma, or leukemia
		• History (single episode) of disseminated HZ or disseminated herpes simplex, or recurrent (≥1 episode of) localized, dermatomal HZ
		• Current/recent history of clinically significant severe, progressive, or uncontrolled renal, hepatic, hematologic, gastrointestinal, metabolic, endocrine, pulmonary, cardiovascular, psychiatric, immunological/rheumatological, or neurological disease
		• Age 12 to <18 years without a documented history of VZV vaccination or presence of VZV IgG Ab

	allowed provided the below threshold for hair loss due to AA was met ○ Hair loss carefully reviewed to verify the required percentage of terminal scalp hair loss is due to AA ▪ ≥25% hair loss of the scalp, including AT and AU ▪ No evidence of terminal hair regrowth within 6 months at both Screening and BL visits (de novo only) ▪ Current episode of hair loss ≤10 years (de novo only)	• History of systemic infection, active acute or chronic infection, or infection with HBV or HCV • History of systemic infection requiring hospitalization within 6 months; active acute or chronic infection requiring treatment with oral antibiotics, antivirals, antiparasitics, antiprotozoals, or antifungals within 4 weeks prior to Day 1; history of either untreated or inadequately treated latent or treated for active TB infection • Anticipated treatment with prohibited concomitant medication(s) during the course of the study. Participation in studies other than NCT02974868 or NCT03732807 involving investigational drug(s) within 8 weeks (12 weeks for JAK inhibitors other than ritlecitinib received in NCT02974868 or NCT03732807) or within 5 half-lives (if known), whichever is longer, prior to study entry and/or during study participation • Received other treatment regimens in the specified time frames (as listed above for NCT03732807)

AA, alopecia areata; Ab, antibody; AT, alopecia totalis; AU, alopecia universalis; BAEP, Brainstem auditory evoked potentials; BL, baseline; HBV, hepatitis B virus; HCV, hepatitis C virus; HZ, herpes zoster; IgG, immunoglobulin G; TB, tuberculosis; VHP, Voluntary Harmonisation Procedure; VZV, varicella-zoster virus.

Table S3. Serious adverse event definition

Definition of serious adverse event	
Serious	Results in death, is life threatening (immediate risk of death), requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions), or results in congenital anomaly/birth defect, and is an important medical event based on investigator judgment

Table S4. Disposition events summary for the placebo-controlled pool

n (%)	Placebo (n=213)	Ritlecitinib QD				
		10 mg (n=62)	All 30 mg[a] (n=261)	50/50 mg (n=130)	200/50 mg (n=215)	All 50 mg[b] (n=345)
Discontinued	20 (9.4)	4 (6.5)	20 (7.7)	9 (6.9)	14 (6.5)	23 (6.7)
Reasons for discontinuation						
Adverse event	3 (1.4)	2 (3.2)	4 (1.5)	2 (1.5)	5 (2.3)	7 (2.0)
Lack of efficacy	1 (0.5)	0	0	0	0	0
Lost to follow-up	0	1 (1.6)	2 (0.8)	1 (0.8)	2 (0.9)	3 (0.9)
Noncompliance with study drug	0	0	0	0	1 (0.5)	1 (0.3)
Physician decision	1 (0.5)	0	6 (2.3)	2 (1.5)	0	2 (0.6)
Pregnancy	1 (0.5)	0	0	0	1 (0.5)	1 (0.3)
Protocol deviation	1 (0.5)	0	0	0	1 (0.5)	1 (0.3)
Withdrawal by participant	11 (5.2)	1 (1.6)	8 (3.1)	4 (3.1)	4 (1.9)	8 (2.3)

No longer meets eligibility criteria	1 (0.5)	0	0	0	0	0
Refused further treatment	1 (0.5)	0	0	0	0	0

QD, once daily.

[a] Ritlecitinib all 30 mg includes patients from ritlecitinib 200/30 mg and 30/30 mg groups combined.

[b] Ritlecitinib all 50 mg includes patients from ritlecitinib 200/50 mg and 50/50 mg groups combined.

Table S5. Summary of ritlecitinib exposure for all-exposure pool

	All-exposure pool	
	Ritlecitinib 50 mg ± 200-mg loading dose[a] (n=1228)	**Any ritlecitinib (n=1294)**
Duration of treatment		
Median (IQR), days	547.0 (366.0-716.0)	624.0 (407.0-792.0)
Mean (SD), days	539.5 (244.93)	590.4 (266.29)
Range, days	1-1181	1-1181
Total patient-years	1813.7	2091.7
Cumulative exposure, n (%)		
≥6 months	1132 (92.2)	1200 (92.7)
≥12 months	974 (79.3)	1052 (81.3)
≥18 months	776 (63.2)	897 (69.3)
≥24 months	362 (29.5)	533 (41.2)
≥30 months	139 (11.3)	251 (19.4)
≥36 months	26 (2.1)	56 (4.3)

[a] Patients received ritlecitinib 50 mg once daily (QD) with or without an initial 4-week 200-mg QD loading dose.

Table S6. Disposition events summary for the all-exposure pool

n (%)	All-exposure pool	
	Ritlecitinib 50 mg ± 200-mg loading dose[a] (n=1228)	**Any ritlecitinib (n=1294)**
Discontinued	320 (26.1)	367 (28.4)
Reasons for discontinuation		
Adverse event	57 (4.6)	66 (5.1)
Death	2 (0.2)	2 (0.2)
Lack of efficacy	80 (6.5)	84 (6.5)
Lost to follow-up	33 (2.7)	40 (3.1)
Noncompliance with study drug	6 (0.5)	7 (0.5)
Physician decision	5 (0.4)	14 (1.1)
Pregnancy	11 (0.9)	12 (0.9)
Protocol deviation	1 (<0.1)	1 (<0.1)
Withdrawal by participant	70 (5.7)	83 (6.4)
No longer meets eligibility criteria	47 (3.8)	47 (3.6)
Other	8 (0.7)	11 (0.9)

[a] Patients received ritlecitinib 50 mg once daily (QD) with or without an initial 4-week 200-mg QD loading dose.

Table S7. Summary of treatment-emergent serious adverse events (all causalities) in the all-exposure pool by System Organ Class and Preferred Term

System organ class and preferred term	**Any ritlecitinib (n=1294)**	
	n (%)	**IR (95% CI)[a]**
Patients with SAEs	57 (4.4)	2.6 (2.0, 3.4)
Cardiac disorders	2 (0.2)	0.09 (0.01, 0.31)
Acute myocardial infarction	1 (0.1)	0.05 (0.00, 0.23)
Cardio-respiratory arrest	1 (0.1)	0.05 (0.00, 0.23)
Eye disorders	1 (0.1)	0.05 (0.00, 0.23)
Retinal artery occlusion	1 (0.1)	0.05 (0.00, 0.23)
Gastrointestinal disorders	2 (0.2)	0.09 (0.01, 0.31)
Ileus	1 (0.1)	0.05 (0.00, 0.23)
Upper gastrointestinal hemorrhage	1 (0.1)	0.05 (0.00, 0.23)
General disorders and administration site conditions	1 (0.1)	0.05 (0.00, 0.23)

Cyst rupture	1 (0.1)	0.05 (0.00, 0.23)
Hepatobiliary disorders	1 (0.1)	0.05 (0.00, 0.23)
Cholelithiasis	1 (0.1)	0.05 (0.00, 0.23)
Immune system disorders	2 (0.2)	0.09 (0.01, 0.31)
Anaphylactic reaction	1 (0.1)	0.05 (0.00, 0.23)
Hypersensitivity	1 (0.1)	0.05 (0.00, 0.23)
Infections and infestations	14 (1.1)	0.64 (0.36, 1.06)
Appendicitis	5 (0.4)	0.23 (0.07, 0.51)
Covid-19	2 (0.2)	0.09 (0.01, 0.31)
COVID-19 pneumonia	2 (0.2)	0.09 (0.01, 0.31)
Diverticulitis	1 (0.1)	0.05 (0.00, 0.23)
Empyema	1 (0.1)	0.05 (0.00, 0.23)
Pyelonephritis	1 (0.1)	0.05 (0.00, 0.23)
Sepsis	1 (0.1)	0.05 (0.00, 0.23)
Septic shock	1 (0.1)	0.05 (0.00, 0.23)
Staphylococcal sepsis	1 (0.1)	0.05 (0.00, 0.23)
Vulval abscess	1 (0.1)	0.05 (0.00, 0.23)
Injury, poisoning and procedural complications	6 (0.5)	0.27 (0.11, 0.58)

Chemical poisoning	1 (0.1)	0.05 (0.00, 0.23)
Joint dislocation	1 (0.1)	0.05 (0.00, 0.23)
Ligament rupture	1 (0.1)	0.05 (0.00, 0.23)
Meniscus injury	1 (0.1)	0.05 (0.00, 0.23)
Subdural hematoma	1 (0.1)	0.05 (0.00, 0.23)
Tendon rupture	1 (0.1)	0.05 (0.00, 0.23)
Thermal burn	1 (0.1)	0.05 (0.00, 0.23)
Musculoskeletal and connective tissue disorders	4 (0.3)	0.18 (0.05, 0.45)
Flank pain	1 (0.1)	0.05 (0.00, 0.23)
Foot deformity	1 (0.1)	0.05 (0.00, 0.23)
Intervertebral disc protrusion	2 (0.2)	0.09 (0.01, 0.31)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	8 (0.6)	0.37 (0.17, 0.70)
Basal cell carcinoma	1 (0.1)	0.05 (0.00, 0.23)
Breast cancer	3 (0.2)	0.14 (0.03, 0.38)
Invasive lobular breast carcinoma	1 (0.1)	0.05 (0.00, 0.23)

Malignant melanoma	1 (0.1)	0.05 (0.00, 0.23)
Papillary thyroid cancer	1 (0.1)	0.05 (0.00, 0.23)
Testis cancer	1 (0.1)	0.05 (0.00, 0.23)
Nervous system disorders	2 (0.2)	0.09 (0.01, 0.31)
Bell's palsy	1 (0.1)	0.05 (0.00, 0.23)
Syncope	1 (0.1)	0.05 (0.00, 0.23)
Pregnancy, puerperium and perinatal conditions	3 (0.2)	0.14 (0.03, 0.38)
Abortion spontaneous	3 (0.2)	0.14 (0.03, 0.38)
Psychiatric disorders	6 (0.5)	0.27 (0.11, 0.57)
Bipolar I disorder	1 (0.1)	0.05 (0.00, 0.23)
Bipolar disorder	1 (0.1)	0.05 (0.00, 0.23)
Delirium	1 (0.1)	0.05 (0.00, 0.23)
Major depression	1 (0.1)	0.05 (0.00, 0.23)
Suicidal behavior	2 (0.2)	0.09 (0.01, 0.31)
Suicidal ideation	1 (0.1)	0.05 (0.00, 0.23)
Renal and urinary disorders	1 (0.1)	0.05 (0.00, 0.23)
Calculus urinary	1 (0.1)	0.05 (0.00, 0.23)

Reproductive system and breast disorders	2 (0.2)	0.09 (0.01, 0.31)
Cervical dysplasia	1 (0.1)	0.05 (0.00, 0.23)
Cervical polyp	1 (0.1)	0.05 (0.00, 0.23)
Respiratory, thoracic and mediastinal disorders	4 (0.3)	0.18 (0.05, 0.45)
Acute respiratory failure	3 (0.2)	0.14 (0.03, 0.38)
Pulmonary embolism	1 (0.1)	0.05 (0.00, 0.23)
Skin and subcutaneous tissue disorders	1 (0.1)	0.05 (0.00, 0.23)
Eczema	1 (0.1)	0.05 (0.00, 0.23)
Vascular disorders	3 (0.2)	0.14 (0.03, 0.38)
Aortic aneurysm	1 (0.1)	0.05 (0.00, 0.23)
Takayasu's arteritis	1 (0.1)	0.05 (0.00, 0.23)
Varicose vein	1 (0.1)	0.05 (0.00, 0.23)

[a] Study size–adjusted IRs per 100 PY and mid-p gamma CIs.

Patients may have experienced >1 event.

Table S8. Time to onset and duration of select treatment-emergent dermatological AEs

	All-exposure pool	
	Ritlecitinib 50 mg ± 200-mg loading dose[a] (n=1228)	**Any ritlecitinib (n=1294)**
Acne (including dermatitis acneiform)[b]		
Time to onset, median (range), weeks	21.7 (0.1-101.6)	22.1 (0.4-149.4)
Duration, median (range), days	146.0 (1-947)	151.0 (1-947)
Folliculitis[c]		
Time to onset, median (range), weeks	24.3 (0.6-111.1)	26.1 (0.6-121.0)
Duration, median (range), days	75.5 (1-677)	78.0 (1-820)
Rashes, eruptions, and exanthems[b]		
Time to onset, median (range), weeks	21.4 (0.1-103.1)	21.4 (0.1-103.1)
Duration, median (range), days	7.0 (1-372)	7.0 (1-372)

Urticarias[b]		
Time to onset, median (range), weeks	10.3 (1.6-101.1)	10.1 (0.3-145.1)
Duration, median (range), weeks	7.0 (1-655)	7.0 (1-1055)

AE, adverse event: MedDRA, Medical Dictionary of Regulatory Activities.

[a] Patients received ritlecitinib 50 mg once daily (QD) with or without an initial 4-week 200-mg QD loading dose.

[b] MedDRA high-level term.

[c] MedDRA preferred term.

Table S9. Details of patients who reported serious adverse events adjudicated as malignancies

Baseline Age, years	**Race**	**Sex**	**Preferred Term**	**Dose at Time of Onset**	**Event Start Day**	**Event End Day**	**Risk Factors and Medical History**	**Event Outcome**	**Causality Assessment**
64	Asian	Female	Breast cancer (spindle cell carcinoma)	50 mg	90	353	- History of alcohol use - Nonsmoker, no HRT, and no family history of breast cancer	Fatal	Not related (per investigator and per sponsor)
66	White	Female	Breast cancer	50 mg	124	–	- Current smoker - Mild alcohol use - Sedentary lifestyle (BMI: 30.4 kg/m^2) - Estrogen hormone therapy for 5 years - Family history of breast cancer (great aunt)	Ongoing	Related to the study intervention (per investigator and per sponsor)

58	White	Female	Breast cancer	50 mg	195	566	- History of smoking and alcohol use - No HRT or any known family history of breast cancer	Recovered/ resolved	Related to the study intervention (per investigator) Not related (per sponsor)
46	White	Female	Invasive lobular breast carcinoma	50 mg	68	–	- History of smoking and alcohol use	Ongoing	Not related (per investigator and per sponsor)

21	Multiracial	Male	Testicular cancer	50 mg	217	223	None	Recovered/ resolved	Related to the study intervention (per investigator) Not related (per sponsor)
26	White	Male	Papillary thyroid cancer	50 mg	116	–	None	Not recovered/ not resolved	Not related (per investigator and per sponsor)
50	White	Female	Malignant melanoma	50 mg	314	–	- Fair skinned with blond hair and blue eyes - Current smoker - Previous sunburn - Left shin atypical squamoproliferative lesion	Ongoing	Related to the study intervention (per investigator and per sponsor)

BMI, body mass index; HRT, hormone replacement therapy.

Table S10. Details of patients who reported serious adverse events adjudicated as MACE or VTE

Baseline Age, years	Race	Sex	Preferred Term	Dose at Time of Onset	Event Start Day	Event End Day	Risk Factors and Medical History	Event Outcome	Causality Assessment
51	White	Female	Acute respiratory failure, cardiorespiratory arrest	50 mg	234	234	• Asthma • Prior history of smoking • AE of acute bronchitis (Day 84; resolved)	Fatal	Not related (per investigator and per sponsor)
49	Unknown	Male	Acute myocardial infarction	50 mg	384	–	• Current smoker • Hyperlipidemia • Diabetes	Ongoing	Not related (per investigator and per sponsor)

48	White	Female	Retinal artery occlusion	50 mg	442	445	• Congenital arterial malformation (pulsating lesion right carotid congenital anomaly) • Family history of atrial septal defect • Family history of SLE and colon cancer	Recovered/ resolved with sequelae	Not related (per investigator and per sponsor)

54	White	Female	Pulmonary embolism	50 mg	169	178	• SARS-CoV-2 positive test (Day 60; resolved) • Monoclonal gammopathy • Morbid obesity (BMI: 46.09 kg/m^2) • Sleep apnea • Cardiovascular disease (hypertension, hyperlipidemia)	Recovered/ resolved	Not related (per investigator) Related (per sponsor)

AE, adverse event; BMI, body mass index; MACE, major adverse cardiovascular events; SLE; systemic lupus erythematosus; VTE, venous thromboembolic event.

Table S11. Summary of select laboratory abnormalities

Evaluation	Placebo-controlled pool (n=881)			All-exposure pool (n=1294)	
	Placebo (n=212)	**Ritlecitinib 30 mg[a] (n=257)**	**Ritlecitinib 50 mg[b] (n=344)**	**Ritlecitinib 50 mg ± 200-mg loading dose[b] (n=1228)**	**Any ritlecitinib (n=1294)**
Anemia (hemoglobin), n/N1 (%)[c]					
Grade 2 (8.0 to <10.0 g/dL)	2/212 (0.9)	1/257 (0.4)	0	11/1224 (0.9)	13/1286 (1.0)
Grade 3 (<8.0 g/dL)	0	0	0	1/1224 (<0.1)	1/1286 (<0.1)
Neutrophils, n/N1 (%)[c]					
Grade 2 (1000 to <1500/mm^3)	6/212 (2.8)	12/257 (4.7)	6/344 (1.7)	51/1224 (4.2)	66/1286 (5.1)
Grade 3 (500 to <1000/mm^3)	0	0	0	9/1224 (0.7)	10/1286 (0.8)
Lymphocytes, n/N1 (%)[c]					
Grade 2 (500 to <800/mm^3)	5/212 (2.4)	16/257 (6.2)	22/344 (6.4)	201/1224 (16.4)	212/1286 (16.5)

Grade 3 (200 to <500/mm^3)	0	2/257 (0.8)	4/344 (1.2)	25/1224 (2.0)	27/1286 (2.1)
Grade 4 (<200/mm^3)	0	0	1/344 (0.3)	1/1224 (<0.1)	1/1286 (<0.1)
Platelets, n/N1 (%)[c]					
Grade 2 (50.0 to <75.0 × 10^3/mm^3)	0	0	0	0	0
CPK, n/N1 (%)[c]					
Grade 2 (>2.5×-5× ULN)	3/211 (1.4)	4/257 (1.6)	9/342 (2.6)	64/1222 (5.2)	70/1284 (5.5)
Grade 3 (>5×-10× ULN)	1/211 (0.5)	3/257 (1.2)	11/342 (3.2)	37/1222 (3.0)	37/1284 (2.9)
Grade 4 (>10× ULN)	1/211 (0.5)	4/257 (1.6)	5/342 (1.5)	28/1222 (2.3)	39/1284 (3.0)
HDL cholesterol (mg/dL), n/N1 (%)					
<0.8 × LLN	0	1/256 (0.4)	3/304 (1.0)	5/1146 (0.4)	7/1211 (0.6)
LDL cholesterol (mg/dL), n/N1 (%)					
>1.2 × ULN	0	1/255 (0.4)	2/304 (0.7)	16/1146 (1.4)	19/1210 (1.6)

Triglycerides (mg/dL), n/N1 (%)					
>1.3 × ULN	8/174 (4.6)	13/255 (5.1)	11/304 (3.6)	83/1146 (7.2)	99/1210 (8.2)
ALT (U/L), n/N1 (%)					
>3.0 × ULN	0	3/256 (1.2)	3/342 (0.9)	28/1222 (2.3)	32/1283 (2.5)
AST (U/L), n/N1 (%)					
>3.0 × ULN	0	2/256 (0.8)	2/342 (0.6)	23/1222 (1.9)	30/1283 (2.3)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatine phosphokinase; CTCAE, Common Terminology Criteria for Adverse Events; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LLN, lower limit of normal; ULN, upper limit of normal.

Percentages are n/N1. N1 = total number of patients with at least one postbaseline observation of the given laboratory test for each treatment group while on study treatment or during lag time (35 days); n = number of patients meeting each CTCAE grade criteria or with a laboratory abnormality meeting specified criteria while on study treatment or during lag time (35 days).

[a] Patients received ritlecitinib 30 mg once daily (QD) with or without an initial 4-week 200-mg QD loading dose.

[b] Patients received ritlecitinib 50 mg QD with or without an initial 4-week 200-mg QD loading dose.

[c] Grade indicates the worst CTCAE (version 5.0) grade in patients who experienced a treatment-emergent increase in grade while on study treatment or during lag time (35 days).