Updated Integrated Safety Analysis of Ritlecitinib Up to ~5 Years in Adolescents With Alopecia Areata From the ALLEGRO Clinical Trials

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SYNOPSIS

- Alopecia areata (AA) is an autoimmune disease that is characterized by patchy or complete nonscarring hair loss on the scalp, with or without additional loss of facial and/or body hair[1]
- Ritlecitinib, an oral, selective dual JAK3/TEC family kinase inhibitor, demonstrated efficacy and safety in patients ≥12 years of age with AA in the ALLEGRO phase 2b/3 study up to 48 weeks[2,3]

OBJECTIVE

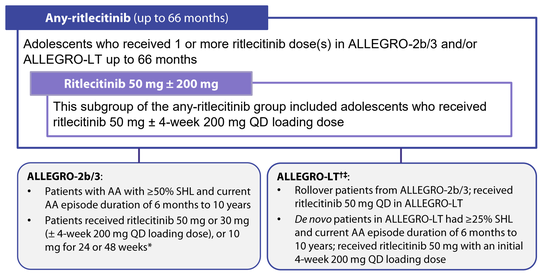
- This updated integrated safety analysis evaluated ritlecitinib treatment for up to ~5 years in adolescents with AA in the ALLEGRO phase 2b/3 (NCT3732807) study and/or ongoing ALLEGRO-LT phase 3 (NCT04006457) study

METHODS

Patients

- Adolescents (aged 12-17 years) who received 1 or more ritlecitinib dose(s) in ALLEGRO-2b/3 and/or ALLEGRO-LT up to ~5 years were included (**Figure 1**)
- Two adolescent treatment groups were analyzed:
  - **"Any-ritlecitinib" group:** Adolescents who received any ritlecitinib dose in ALLEGRO-2b/3 and/or ALLEGRO-LT (10 mg, 30 mg, 50 mg, 200/30 mg, or 200/50 mg once daily [QD])
  - **"Ritlecitinib 50-mg ± 200 mg" group:** Adolescents who received ritlecitinib 50 mg QD with or without an initial 4-week 200 mg QD loading dose in ALLEGRO-2b/3 and/or ALLEGRO-LT

Figure 1. Analysis populations



AA, alopecia areata; SALT, Severity of Alopecia Tool; SHL, scalp hair loss; QD, once daily.
*In ALLEGRO-2b/3, after week 24, ritlecitinib-groups continued their 50-, 30-, or 10-mg maintenance doses for another 24 weeks, and patients initially assigned to placebo switched to ritlecitinib 50 mg QD (±4-week 200 mg QD loading dose) at Week 24 for 24 weeks. †Data cutoff for the ongoing ALLEGRO-LT was 25 June 2024. ‡ALLEGRO-LT required ≥50% improvement in SALT score by Month 3 for rollover adolescents from ALLEGRO-2b/3 and SALT score ≤20 by Month 6 for all adolescents.

Statistical analyses

- Data are from the start of the patients' first dose of ritlecitinib
  - For all patients in the ritlecitinib 50 mg ± 200 mg group, Day 1 of exposure was the first day of the ritlecitinib 50 mg dose (or the 200 mg loading dose), even if some patients received placebo or other ritlecitinib doses in ALLEGRO-2b/3 before switching to ritlecitinib 50 mg
  - For patients in the any-ritlecitinib group, events were evaluated from the start of the patients' first dose of ritlecitinib
- The data cutoff date was 25 June 2024
- Safety data were summarized descriptively using counts and percentages for adverse events (AEs) and lab abnormalities in each analysis group
- The incidence rates (IRs) of AEs were calculated using study-size weights and 95% confidence intervals (CIs) using the mid-p Gamma method and are reported per 100 patient-years (PY)

RESULTS

Baseline characteristics and patient disposition

- The any-ritlecitinib group included 181 adolescents (76 de novo), of whom 172 were included in the ritlecitinib 50 mg ± 200 mg loading dose group (**Table 1**)

Table 1. Baseline characteristics

	Ritlecitinib 50 mg ± 200 mg*† (N=172)	Any-ritlecitinib† (N=181)
Age, mean (SD), years	14.8 (1.6)	14.9 (1.6)
Female, n (%)	92 (53.5)	98 (54.1)
Race, n (%)		
White	117 (68.0)	122 (67.4)
Asian	34 (19.8)	36 (19.9)
Black	14 (8.1)	15 (8.3)
Other	4 (2.3)	5 (2.8)
Not reported	3 (1.7)	3 (1.7)
Height, mean (SD), cm	164.1 (10.4)	164.2 (10.3)
Weight, mean (SD), kg	61.0 (15.5)	60.9 (15.5)
Patients with AT/AU, n (%)	60 (34.9)	63 (34.8)

AT, alopecia totalis; AU, alopecia universalis.
*Patients received ritlecitinib 50 mg once daily with or without an initial 4-week 200 mg loading dose. †The analysis groups are not additive and are overlapping populations, with the any-ritlecitinib group including all patients.

Table 2. Patient disposition

	Ritlecitinib 50 mg ± 200 mg*† (N=172)	Any-ritlecitinib† (N=181)
Ongoing at the data cut date	26 (15.1)	26 (14.4)
Completed		
Completed the study	3 (1.7)	7 (3.9)
Removed from the study per protocol as commercial drug became available	60 (34.9)	60 (33.1)
Discontinued	83 (48.3)	88 (48.6)
No longer meets eligibility criteria‡	43 (25.0)	43 (23.8)
AE§	10 (5.8)	11 (6.1)
Lack of efficacy	9 (5.2)	9 (5.0)
Lost to follow-up	8 (4.7)	9 (5.0)
Withdrawal by patient	7 (4.1)	8 (4.4)
Pregnancy	3 (1.7)	3 (1.7)
Physician decision	1 (0.6)	3 (1.7)
Non-compliance with study drug	1 (0.6)	1 (0.6)
Other	1 (0.6)	1 (0.6)

AE, adverse event; SAE, serious adverse event.*Patients received ritlecitinib 50 mg once daily with or without an initial 4-week 200 mg loading dose.
†The analysis groups are not additive and are overlapping populations, with the any ritlecitinib group including all patients. ‡Per study protocol, continuation criteria for adolescents in ALLEGRO-LT required ≥50% improvement in SALT score by Month 3 for rollover adolescents and SALT score ≤20 by Month 6 for all adolescents.
§Per study protocol, treatment discontinuation and participant withdrawal from the study were required for the following AEs: serious infections (defined as any infection requiring parenteral antimicrobial therapy or hospitalization for treatment or meeting other criteria that require the infection to be classified as a SAE); treatment-related SAEs, or other SAEs or severe AEs (at the discretion of the investigator or sponsor); clinically meaningful and treatment-emergent declines in hearing from baseline were discussed with the sponsor for possible withdrawal from study.

Duration of ritlecitinib exposure

- In the ritlecitinib 50 mg ± 200 mg group, median ritlecitinib exposure was 1111.5 days (427.2 total PY) (**Table 3**)

Table 3. Duration of ritlecitinib treatment

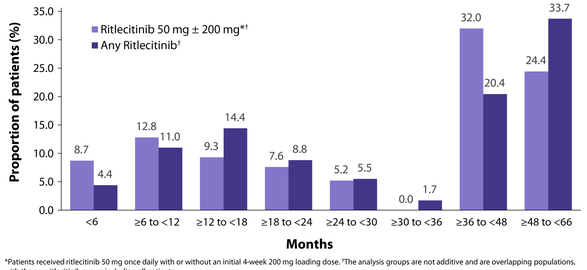
	Ritlecitinib 50 mg ± 200 mg*† (N=172)	Any-ritlecitinib† (N=181)
Mean (SD), days	907.2 (525.8)	950.5 (531.0)
Median (Q1, Q3), days	1111.5 (360.5, 1333.5)	1169.0 (420.0, 1434.0)
Range, days	19.0-1775.0	19.0-1778.0
Total PY	427.2	471

PY, patient years; Q1, first quartile; Q3 third quartile.
*Patients received ritlecitinib 50 mg once daily with or without an initial 4-week 200 mg loading dose. †The analysis groups are not additive and are overlapping populations, with the any ritlecitinib group including all patients.

Ritlecitinib exposure by month

- For the ritlecitinib 50 mg ± 200 mg group, 56.4% of adolescents were exposed for ≥36 months and 24.4% for ≥48 months (**Figure 2**)

Figure 2. Ritlecitinib exposure by month



*Patients received ritlecitinib 50 mg once daily with or without an initial 4-week 200 mg loading dose. †The analysis groups are not additive and are overlapping populations, with the any ritlecitinib group including all patients

Adverse events

- **Serious infections:** In the any-ritlecitinib group, serious infections were appendicitis (2 patients; 1 on 30 mg and 1 on 50 mg), COVID-19 pneumonia and septic shock (1 patient, 50 mg), osteomyelitis (1 patient, 50 mg), latent tuberculosis (1 patient, 50 mg), urinary tract infection (1 patient, 50 mg)
- All serious infections recovered/resolved
- No deaths, opportunistic infections, herpes zoster, malignancies, cardiovascular, or thrombotic events were reported in adolescent patients
- The median change from baseline in standard deviation scores for BMI was zero and ranged from -0.3 to 0.3 for the ritlecitinib 50 mg ± 200 mg group and -0.4 to 0.3 for the any ritlecitinib group at 2 years (Day 720), indicating that changes in BMI were small and age and gender appropriate

Table 4. Overview of AEs

	Ritlecitinib 50 mg ± 200 mg*† (N=172)			Any-ritlecitinib† (N=181)		
	n (%)	PY	IR‡ (95% CI)	n (%)	PY	IR‡ (95% CI)
Participants with AEs	144 (83.7)	98.5	146.3 (123.8, 171.7)	158 (87.3)	99.4	158.9 (135.5, 185.2)
Participants with SAEs	10 (5.8)	473.1	2.3 (1.2, 4.2)	13 (7.2)	477.8	2.7 (1.5, 4.5)
Most frequent AEs (in >10% of patients)						
Headache	32 (18.6)	362.3	8.7 (6.1, 12.2)	41 (22.7)	386	10.6 (7.7, 14.3)
Acne	33 (19.2)	355.9	9.4 (6.6, 13.1)	40 (22.1)	390.4	10.3 (7.4, 13.8)
SARS-CoV-2 test positive	34 (19.8)	373.2	9.10 (6.4, 12.6)	34 (18.8)	417.9	8.1 (5.7, 11.2)
Nasopharyngitis	25 (14.5)	387.3	6.5 (4.3, 9.5)	29 (16.0)	414.2	7.0 (4.8, 9.9)
Oropharyngeal pain	23 (13.4)	401.4	5.7 (3.7, 8.5)	27 (14.9)	437.8	6.2 (4.1, 8.9)
Upper respiratory tract infection	22 (12.8)	400.4	5.6 (3.5, 8.4)	24 (13.3)	439.9	5.5 (3.6, 8.0)
Pyrexia	20 (11.6)	406.1	5.0 (3.1, 7.6)	21 (11.6)	450.3	4.7 (3.0, 7.0)
Nausea	20 (11.6)	401.7	5.0 (3.1, 7.6)	21 (11.6)	445.1	4.7 (3.0, 7.1)
AEs of special interest						
Serious infections	5 (2.9)	440	1.1 (0.4, 2.5)	6 (3.3)	481.3	1.3 (0.5, 2.6)

AE, adverse event; IR, incidence rate; PY, patient years; SAE, serious adverse event.
*Patients received ritlecitinib 50 mg once daily with or without an initial 4-week 200 mg QD loading dose. †The analysis groups are not additive and are overlapping populations, with the any ritlecitinib group including all patients. ‡Study-size adjusted results per 100 PY and mid-p gamma intervals.

Laboratory measures

Table 5. CTCAE grade ≥2 hematological parameters

Parameter, CTCAE grade, n (%)		Ritlecitinib 50 mg ± 200 mg*† (N=172)	Any-ritlecitinib† (N=181)
Anemia (hemoglobin)	Grade 2: <8.0-10.0 g/dL	5 (2.9)	5 (2.8)
Neutrophil count decreased	Grade 2: <1000-1500/mm³	10 (5.8)	16 (8.8)
	Grade 3: <500-1000/mm³	3 (1.7)	3 (1.7)
Lymphocyte count decreased	Grade 2: <500-800/mm³	26 (15.1)	28 (15.5)
	Grade 3: <200-500/mm³	3 (1.7)	3 (1.7)

CTCAE, Common Terminology Criteria for Adverse Events.
*Patients received ritlecitinib 50 mg once daily with or without an initial 4-week 200 mg loading dose. †The analysis groups are not additive and are overlapping populations, with the any ritlecitinib group including all patients.

Table 6. Laboratory test abnormalities (without regard to baseline abnormality)

n (%)	Ritlecitinib 50 mg ± 200 mg*† (N=172)	Any-ritlecitinib† (N=181)
AST >5x ULN	2 (1.2)	2 (1.1)
ALT >5x ULN	2 (1.2)	3 (1.7)
HDL cholesterol (mg/dL), <0.8x LLN	1 (0.6)	2 (1.1)
LDL cholesterol (mg/dL), >1.2x ULN	6 (3.5)	6 (3.3)
CPK (U/L), >5x ULN-10x ULN	6 (3.5)	7 (3.9)
CPK (U/L), >10.0x ULN	6 (3.5)	7 (3.9)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatinine phosphokinase; HDL, high-density lipoprotein; LDL, low-density lipoprotein; LLN, lower limit of normal; ULN, upper limit of normal.
*Patients received ritlecitinib 50 mg once daily with or without an initial 4-week 200 mg loading dose. †The analysis groups are not additive and are overlapping populations, with the any ritlecitinib group including all patients.

CONCLUSIONS

- Longer-term use of ritlecitinib for up to ~5 years in adolescents with AA was well tolerated
- The updated, longer-term cumulative safety data in adolescents demonstrated no new safety signals compared to the previously presented data cut and support ritlecitinib use in adolescents

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DISCLOSURES

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