Integrated safety analysis of ritlecitinib in adolescent patients with alopecia areata from the randomized, placebo-controlled ALLEGRO phase 2b/3 and ongoing open-label phase 3 ALLEGRO-LT studies

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BACKGROUND

- Alopecia areata (AA) is an autoimmune disease that has an underlying immuno-inflammatory pathogenesis and is characterized by nonscarring hair loss of the scalp, face, and/or body[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]

OBJECTIVE

- To investigate the long-term safety of ritlecitinib in adolescents (aged 12-17 years) with AA based on integrated data from the ALLEGRO phase 2b/3 study and the open-label long-term ALLEGRO-LT phase 3 study

METHODS

Analysis populations

Two adolescent cohorts were analyzed:

A placebo-controlled cohort including adolescents from the 24-week placebo-controlled period of ALLEGRO-2b/3

- Patients in ALLEGRO-2b/3 had a diagnosis of AA with ≥50% scalp hair loss and current AA episode duration of 6 months to 10 years

An any-ritlecitinib cohort including adolescents who received 1 or more ritlecitinib doses in ALLEGRO-2b/3 and/or ALLEGRO-LT up to 36 months

- ALLEGRO-LT included:
  - Roll-over patients from ALLEGRO-2b/3
  - *De novo* patients with diagnosis of AA with ≥25% scalp hair loss and current AA episode duration of 6 months to 10 years
- Data are from the start of the patients' first dose of ritlecitinib

Any-ritlecitinib cohort (up to 36 months)

Placebo-controlled cohort (up to 24 weeks)

ALLEGRO-2b/3 (NCT03732807): Once-daily ritlecitinib 50 mg or 30 mg (±4-week 200 mg daily loading dose), 10 mg, or placebo for 24 weeks

Ritlecitinib for 24 weeks*

ALLEGRO-LT (NCT04006457)†

- ***De novo* patients**: 4-week 200mg daily loading dose then once-daily ritlecitinib 50 mg
- **Roll-over patients** (from ALLEGRO-2b/3): once-daily ritlecitinib 50 mg

*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 200/50 or 50 mg daily for 24 weeks.
†Adolescents must have had SALT score ≤20 by Month 6 to continue in the study. Roll-over adolescents must have also had improvement in SALT score of ≥50% from baseline in ALLEGRO-2b/3 at Month 3.

Statistical analyses

- Safety data were summarized descriptively using counts and percentages for adverse events (AEs) and lab abnormalities in each cohort
- The incidence rates of AEs within the any-ritlecitinib cohort were calculated using study-size weights and 95% CIs using the mid-p Gamma method

RESULTS

Patients

- 105 adolescents were included in the **placebo-controlled cohort** and 181 adolescents were included in the **any-ritlecitinib cohort** (76 de novo patients) (**Table 1**)

Table 1. Baseline characteristics

	Placebo-Controlled Cohort (N=105)						Any-Ritlecitinib Cohort (N=181)
	Placebo (n=19)	Ritle 10 mg (n=9)	Ritle 30 mg (n=20)	Ritle 50 mg (n=18)	Ritle 200/30 mg (n=19)	Ritle 200/50 mg (n=20)	
Age, mean (SD), y	14.2 (1.4)	15.4 (1.3)	15.1 (1.6)	15.3 (1.4)	14.7 (1.9)	15.0 (1.8)	14.9 (1.6)
Female, n (%)	12 (63.2)	6 (66.7)	9 (45.0)	6 (33.3)	14 (73.7)	7 (35.0)	98 (54.1)
Race, n (%)							
White	17 (89.5)	5 (55.6)	15 (75.0)	12 (66.7)	9 (47.4)	14 (70.0)	122 (67.4)
Asian	0	2 (22.2)	3 (15.0)	3 (16.7)	7 (36.8)	5 (25.0)	36 (19.9)
Black	2 (10.5)	2 (22.2)	1 (5.0)	3 (16.7)	1 (5.3)	1 (5.0)	15 (8.3)
Weight, mean (SD), kg	54.2 (12.5)	60.5 (18.3)	63.3 (15.6)	63.6 (17.8)	63.2 (21.0)	63.1 (16.0)	60.9 (15.5)
AT/AU, n (%)*	9 (47.4)	3 (33.3)	8 (40.0)	8 (44.4)	9 (47.4)	8 (40.0)	63 (34.8)

AT, alopecia totalis; AU, alopecia universalis; QD, once-daily; Ritle, ritlecitinib; SALT, Severity of Alopecia Tool.
*Participants in the AT/AU category had a SALT score of 100 (complete scalp hair loss) at baseline.
The any-ritlecitinib cohort includes patients from ALLEGRO-2b/3 and ALLEGRO-LT.

Ritlecitinib exposure

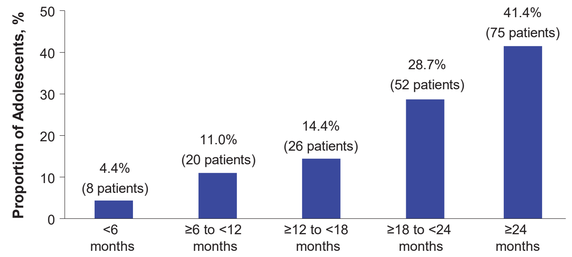
- Median exposure in the any-ritlecitinib cohort was 624 days (**Table 2**); 41.4% of patients had ≥24 months exposure (**Figure 1**)

Table 2. Exposure to study drug

	Placebo-Controlled Cohort (N=105)						Any-Ritlecitinib Cohort (N=181)
	Placebo (n=19)	Ritle 10 mg (n=9)	Ritle 30 mg (n=20)	Ritle 50 mg (n=18)	Ritle 200/30 mg (n=19)	Ritle 200/50 mg (n=20)	
Duration of exposure							
Median (range), days	170 (163-176)	169 (148-175)	169 (162-180)	172 (19-190)	171 (158-204)	170 (150-179)	624 (19-1077)
Mean (SD), days	170 (3)	168 (8)	170 (5)	162 (37)	172 (9)	170 (6)	602 (256)
Total patient-years	8.9	4.1	9.3	8.0	8.9	9.3	298.1

The any-ritlecitinib cohort includes patients from ALLEGRO-2b/3 and ALLEGRO-LT.

Figure 1. Exposure to study drug in the any-ritlecitinib cohort (N=181)



Adverse events overview

Table 3. AEs in the placebo-controlled cohort (up to 24 weeks) and any-ritlecitinib cohort (up to 36 months)

	Placebo-Controlled Cohort (N=105)						Any- Ritlecitinib Cohort (N=181)	
	Placebo (n=19)	Ritle 10 mg (n=9)	Ritle 30 mg (n=20)	Ritle 50 mg (n=18)	Ritle 200/30 mg (n=19)	Ritle 200/50 mg (n=20)	n (%)	IR (95% CI)
AE, n (%)	15 (78.9)	6 (66.7)	13 (65.0)	15 (83.3)	14 (73.7)	15 (75.0)	150 (82.9)	160.6 (136.4-187.9)
SAE, n (%)	0	2 (22.2)	0	0	0	0	7 (3.9)	2.3 (1.0-4.5)
Discontinued due to AE, n (%)	0	1 (11.1)	0	1 (5.6)	0	0	9 (5.0)	2.9 (1.4-5.3)
Most frequent AEs‡								
Acne, n (%)	1 (5.3)	1 (11.1)	3 (15.0)	2 (11.1)	3 (15.8)	3 (15.0)	36 (19.9)	13.7 (9.7-18.7)
Headache, n (%)	2 (10.5)	2 (22.2)	3 (15.0)	3 (16.7)	3 (15.8)	1 (5.0)	35 (19.3)	13.3 (9.4-18.3)
SARS-CoV-2 test positive, n (%)	0	0	0	0	0	0	25 (13.8)	8.4 (5.6-12.2)
Nasopharyngitis, n (%)	0	2 (22.2)	3 (15.0)	2 (11.1)	1 (5.3)	3 (15.0)	24 (13.3)	8.7 (5.7-12.8)
Upper respiratory tract infection, n (%)	3 (15.8)	1 (11.1)	1 (5.0)	0	1 (5.3)	0	20 (11.0)	6.8 (4.3-10.3)

AE, adverse event; IR, incidence rate; Ritle, ritlecitinib; SAE, serious adverse event.
*Most frequent AEs in the any-ritlecitinib cohort, >10% by preferred term.
The any-ritlecitinib cohort includes patients from ALLEGRO-2b/3 and ALLEGRO-LT.
IRs are per 100 patient-years.

Serious adverse events

- In the placebo-controlled cohort, SAEs were suicidal behavior and eczema (in 1 patient each receiving ritlecitinib 10 mg) (**Table 3**)
- In the any-ritlecitinib cohort, SAEs were appendicitis in 2 adolescents; COVID-19 pneumonia, septic shock, delirium, and acute respiratory failure in 1 adolescent; miscarriage in 1 adolescent; bipolar disorder and suicidal ideation in 1 adolescent; suicidal behavior in 1 adolescent; and eczema in 1 adolescent

Serious infections

- There were no serious infections in the placebo-controlled cohort
- There were 3 adolescents (1.7%) with serious infection in the any-ritlecitinib cohort (IR: 1.0 per 100 PY [95% CI: 0.2-2.6]): appendicitis in 2 adolescents, and COVID-19 pneumonia and septic shock in 1 adolescent
  - All serious infections recovered/resolved

AEs of special interest

- No deaths, opportunistic infections, herpes zoster, malignancies, cardiovascular, or thrombotic events were reported in adolescent patients
- There were no AEs related to growth disturbance; changes in height and weight were within normal growth parameters

Laboratory abnormalities

Table 4. CTCAE Grade 2 or higher decreases in neutrophil and lymphocyte counts in the placebo-controlled cohort (up to 24 weeks) and any-ritlecitinib cohort (up to 36 months)

	Placebo-Controlled Cohort (N=105)						Any-Ritlecitinib Cohort (N=181)
	Placebo (n=19)	Ritle 10 mg (n=9)	Ritle 30 mg (n=20)	Ritle 50 mg (n=18)	Ritle 200/30 mg (n=19)	Ritle 200/50 mg (n=20)	
Neutrophil count decreased							
Grade 2 (<1500-1000/mm³)	3 (15.8)	3 (33.3)	2 (10.0)	1 (5.6)	2 (10.5)	3 (15.0)	14 (7.7)
Grade 3 (<1000-500/mm³)	0	0	0	0	0	0	3 (1.7)
Lymphocyte count decreased							
Grade 2 (<800-500/mm³)	0	1 (11.1)	0	0	0	1 (5.0)	20 (11.0)
Grade 3 (<500-200/mm³)	0	0	0	0	0	1 (5.0)	3 (1.7)

CTCAE, Common Terminology Criteria for Adverse Events; Ritle, ritlecitinib.
There were no cases of Grade 2 or higher decreases in platelets (<75,000/mm³) and no cases of Grade 3 or higher anemia (hemoglobin <8.0 g/dL) in adolescent patients. Three adolescents (1.7%) in the any-ritlecitinib cohort and none in the placebo-controlled cohort had Grade 2 anemia (hemoglobin <10.0-8.0 g/L).
The any-ritlecitinib cohort includes patients from ALLEGRO-2b/3 and ALLEGRO-LT.

- Three adolescents in the placebo-controlled cohort and 12 adolescents in the any-ritlecitinib cohort experienced creatine kinase values >5x the upper limit of normal (**Table 5**)
  - There were no cases of rhabdomyolysis

Table 5. Laboratory test abnormalities in the placebo-controlled cohort (up to 24 weeks) and any-ritlecitinib cohort (up to 36 months)

	Placebo-Controlled Cohort (N=105)						Any-Ritlecitinib Cohort (N=181)
	Placebo (n=19)	Ritle 10 mg (n=9)	Ritle 30 mg (n=20)	Ritle 50 mg (n=18)	Ritle 200/30 mg (n=19)	Ritle 200/50 mg (n=20)	
Aspartate aminotransferase >3x ULN	0	0	0	0	0	0	5 (2.8)
Alanine aminotransferase >3x ULN	0	0	0	0	0	0	3 (1.7)
Creatine kinase (U/L) >5x ULN	0	0	2 (10.0)	1 (5.6)	0	0	12 (6.6)
HDL cholesterol (mg/dL) <0.8x LLN	0	0	0	0	0	1 (5.0)	2 (1.1)*
LDL cholesterol (mg/dL) >1.2x ULN	0	0	0	0	0	1 (5.0)	4 (2.2)†

HDL, high-density lipoprotein; LDL, low density lipoprotein; LLN, lower limit of normal; Ritle, ritlecitinib; ULN, upper limit of normal.
*Of the 2 adolescents with an HDL reading <0.8x LLN during the study, 1 had an HDL level below the normal range at baseline (24 mg/dL).
†Of the 4 adolescents with an LDL reading >1.2x ULN during the study, 2 had LDL levels above the normal range at baseline (155 and 195 mg/dL).
The any-ritlecitinib cohort includes patients from ALLEGRO-2b/3 and ALLEGRO-LT.

CONCLUSIONS

- Long-term treatment with ritlecitinib in adolescents with AA was well tolerated and demonstrated no new safety signals compared with prior ritlecitinib studies

REFERENCES

1. Islam N, et al. *Autoimmun Rev*. 2015;14:81-89.
2. King B, et al. *Lancet* 2023;401:1518-1529.

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