Long-Term Efficacy of Ritlecitinib up to Month 24 From the ALLEGRO Phase 2b/3 and Long-Term Phase 3 Clinical Studies in Alopecia Areata

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BACKGROUND

- Alopecia areata (AA) is an autoimmune disease with an underlying immuno-inflammatory pathogenesis characterized by nonscarring hair loss ranging from small patches of hair loss to complete loss of scalp, face, and/or body hair[1]
- In the ALLEGRO phase 2b/3 study (NCT03732807), the oral JAK3/TEC family kinase inhibitor, ritlecitinib, demonstrated efficacy and acceptable safety in patients aged ≥12 years with AA[2]
- ALLEGRO-LT (NCT04006457) is an ongoing, phase 3, open-label study investigating the long-term safety and efficacy of ritlecitinib in AA

OBJECTIVE

- We report updated interim efficacy results of ritlecitinib up to Month 24 from the ALLEGRO phase 2b/3 study and ALLEGRO-LT study

METHODS

Study design and patients

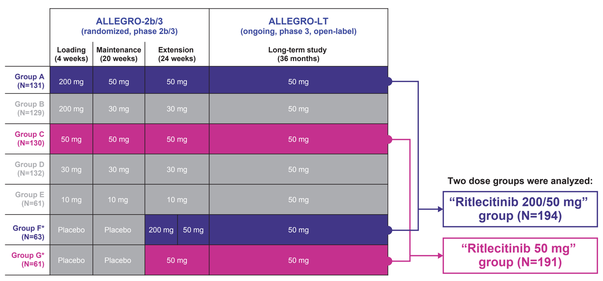
Key inclusion criteria in ALLEGRO-2b/3:

- Patients aged ≥12 years
- Diagnosis of AA with ≥50% scalp hair loss due to AA (including alopecia totalis [AT] and alopecia universalis [AU])
- Maximum duration of current episode of hair loss ≤10 years

This analysis of ALLEGRO-2b/3 and ALLEGRO-LT includes (**Figure 1**):

- Patients who received an initial 4-week loading dose of 200 mg ritlecitinib once daily (QD) followed by ritlecitinib 50 mg QD
- Patients who received 50 mg ritlecitinib QD without a loading dose

Figure 1. ALLEGRO-2b/3 and ALLEGRO-LT study designs and patients included in the long-term efficacy analysis



*Data while on placebo were not included in this analysis; data from patients in Groups F and G were re-baselined from the start of treatment with ritlecitinib.

Outcomes

- Proportion of patients with response through Month 24 based on:
  - Severity of Alopecia Tool (SALT) score ≤20
  - SALT score ≤10
  - Patients' Global Impression of Change (PGI-C) score of "moderately improved" or "greatly improved" from baseline
- Proportion of patients who sustained SALT ≤20 response from Month 12 through Month 24
- Safety: adverse events (AEs), serious AEs (SAEs), events of interest

Statistical analyses

- Efficacy data are presented as:
  - Observed data
  - Imputed data (last observation carried forward [LOCF]), to account for missing data values
    - LOCF was applied to each visit for all participants with missing data, except for those who have not yet reached that analysis visit
- Data are reported to the cutoff date of December 9, 2022
  - Efficacy data are shown up to Month 24 due to missing data at later timepoints

RESULTS

- The ritlecitinib 200/50 mg and 50 mg groups included 194 and 191 patients, respectively; 127 (65.5%) and 111 (58.1%) were ongoing at the data cutoff (**Table 1**)
- Baseline characteristics were generally similar and well balanced between the treatment groups (**Table 2**)

Table 1. Patient disposition

	Ritlecitinib 200/50 mg (N=194)	Ritlecitinib 50 mg (N=191)
Ongoing at the data cut date, n (%)	127 (65.5)	111 (58.1)
Completed, n (%)	7 (3.6)	9 (4.7)
Discontinued, n (%)	60 (30.9)	71 (37.2)
Adverse event	7 (3.6)	18 (9.4)
Lack of efficacy	12 (6.2)	14 (7.3)
Lost to follow-up	7 (3.6)	7 (3.7)
Non-compliance with study drug	0	0
Physician decision	0	2 (1.0)
Pregnancy	2 (1.0)	0
Withdrawal by patient	20 (10.3)	19 (9.9)
No longer meets eligibility criteria	9 (4.6)	6 (3.1)
Other	3 (1.5)	5 (2.6)

Continuation criteria for adolescents (aged 12-17 years) in ALLEGRO-LT required ≥50% improvement in Severity of Alopecia Tool (SALT) score by Month 3 for rollover patients from ALLEGRO-2b/3 and SALT score ≤20 by Month 6 in ALLEGRO-LT.

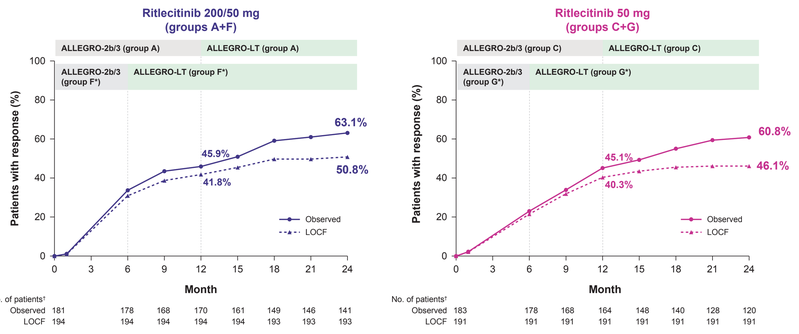
Table 2. Baseline characteristics

	Ritlecitinib 200/50 mg (N=194)	Ritlecitinib 50 mg (N=191)
Age		
Mean (SD), years	34.0 (14.6)	33.2 (14.4)
12-17 years, n (%)	30 (15.5)	27 (14.1)
≥18 years, n (%)	164 (84.5)	164 (85.9)
Female, n (%)	125 (64.4)	107 (56.0)
White, n (%)	137 (70.6)	123 (64.4)
AT/AU*, n (%)	92 (47.4)	86 (45.0)
SALT score among all patients, mean (SD)	91.9 (13.4)	90.8 (14.1)
Duration of AA since diagnosis, mean years (SD)	9.8 (10.6)	9.8 (10.5)
Duration of current AA episode, mean years (SD)	3.3 (2.8)	3.3 (2.8)

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; SALT, Severity of Alopecia Tool; SD, standard deviation.
*Participants in the AT/AU category had a SALT score of 100% at baseline (regardless of the category in the AA history CRF).

- SALT ≤20 response rates in the 200/50 mg and 50 mg groups increased from Month 12 (45.9% and 45.1% [observed]; 41.8% and 40.3% [LOCF]) to Month 24 (63.1% and 60.8% [observed]; 50.8% and 46.1% [LOCF]) (**Figure 2**)

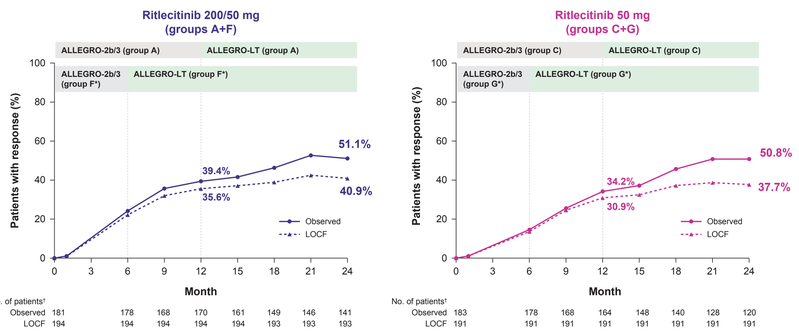
Figure 2. SALT score ≤20 over time



LOCF, last observation carried forward; SALT, Severity of Alopecia Tool.
*Data while on placebo were not included in this analysis; data from patients in Groups F and G were re-baselined from the start of treatment with ritlecitinib.
†Number of patients with valid data at that analysis visit.

- SALT ≤10 response rates increased between Months 12 and 24 for the 200/50 mg group (39.4% to 51.1% [observed]; 35.6% to 40.9% [LOCF]) and 50 mg group (34.2% to 50.8% [observed]; 30.9% to 37.7% [LOCF]) (**Figure 3**)

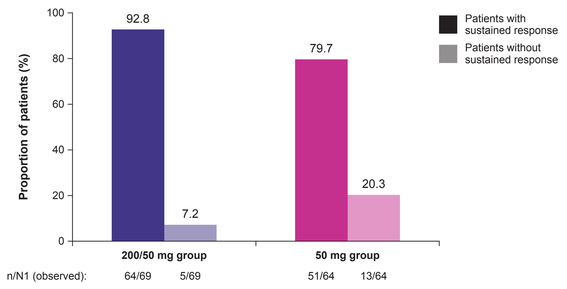
Figure 3. SALT score ≤10 over time



LOCF, last observation carried forward; SALT, Severity of Alopecia Tool.
*Data while on placebo were not included in this analysis; data from patients in Groups F and G were re-baselined from the start of treatment with ritlecitinib.
†Number of patients with valid data at that analysis visit.

- Of SALT ≤20 responders at Month 12, 92.8% (200/50 mg) and 79.7% (50 mg) (observed) sustained this response through Month 24 (**Figure 4**)

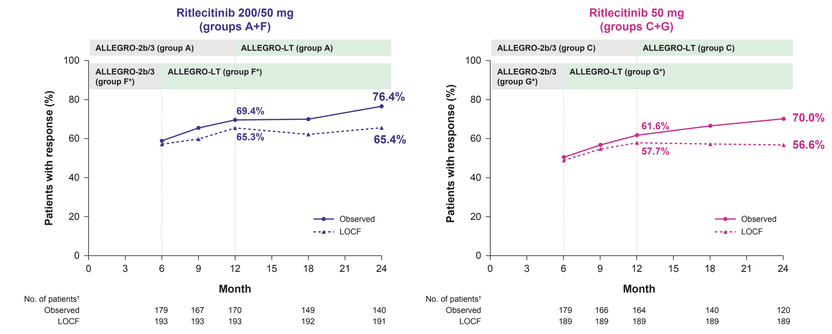
Figure 4. Sustained SALT ≤20 response at Month 24



SALT, Severity of Alopecia Tool.
Sustained response was defined as patients with SALT ≤20 response at Month 12 and Month 24, and patients who did not reach SALT >20 at any timepoint between Month 12 and Month 24.
Percentages are based on n/N1 where n = the number of patients with sustained response, and N1 = total number of patients with observed value at Month 24.
Observed data are presented.

- PGI-C response rates were maintained from Month 12 (200/50 mg: 69.4% [observed], 65.3% [LOCF]; 50 mg: 61.6% [observed], 57.7% [LOCF]) to Month 24 (200/50 mg: 76.4% [observed], 65.4% [LOCF]; 50 mg: 70.0% [observed], 56.6% [LOCF]) (**Figure 5**)

Figure 5. PGI-C response over time



LOCF, last observation carried forward; PGI-C, Patients' Global Impression of Change.
PGI-C response = score of "moderately" or "greatly" improved from baseline. The PGI-C asks the patient to evaluate the improvement or worsening of their AA compared with the start of the study.
*Data while on placebo were not included in this analysis; data from patients in Groups F and G were re-baselined from the start of treatment with ritlecitinib.
†Number of patients with valid data at that analysis visit.

- The safety profile was consistent with that seen in the primary ALLEGRO phase 2b/3 study (**Tables 3 and 4**)[2]

Table 3. Safety overview

n (%)	Ritlecitinib 200/50 mg (N=194)	Ritlecitinib 50 mg (N=191)	Any Ritlecitinib* (N=1294)
Patients with AEs	175 (90.2)	184 (96.3)	1125 (86.9)
Patients with SAEs	9 (4.6)	11 (5.8)	65 (5.0)
Patients with severe AEs	14 (7.2)	18 (9.4)	93 (7.2)
Patients discontinued from study or study drug due to AEs	9 (4.6)	20 (10.5)	92 (7.1)
Patients with temporary drug discontinuation due to AEs	57 (29.4)	63 (33.0)	344 (26.6)
AEs occurring in ≥5% of patients in any treatment group†			
Headache	41 (21.1)	37 (19.4)	258 (19.9)
SARS-CoV-2 test positive	37 (19.1)	46 (24.1)	250 (19.3)
Nasopharyngitis	33 (17.0)	27 (14.1)	181 (14.0)
Upper respiratory tract infection	37 (19.1)	25 (13.1)	157 (12.1)
Acne	18 (9.3)	22 (11.5)	141 (10.9)
Pyrexia	18 (9.3)	25 (13.1)	131 (10.1)
Cough	26 (13.4)	29 (15.2)	124 (9.6)
Oropharyngeal pain	18 (9.3)	26 (13.6)	112 (8.7)
Fatigue	18 (9.3)	17 (8.9)	109 (8.4)
Urticaria	15 (7.7)	16 (8.4)	93 (7.2)

AE, adverse event; SAE, serious adverse event. Includes patients from the start of their first dose of ritlecitinib.
*Includes patients with alopecia areata who received any dose of ritlecitinib in ALLEGRO-2a, ALLEGRO-2b/3, ALLEGRO-LT, and ALLEGRO-2a safety study from the start of their first dose of ritlecitinib.
†Ten most frequent AEs shown; other AEs (≥5% of patients in any treatment group) included COVID-19, folliculitis, urinary tract infection, diarrhea, nausea, blood creatine phosphokinase increased, back pain and myalgia.

Table 4. AEs of special interest

n (%)	Ritlecitinib 200/50 mg (N=194)	Ritlecitinib 50 mg (N=191)	Any Ritlecitinib* (N=1294)
Serious infections	4 (2.1)	2 (1.0)	16 (1.2)
Opportunistic infections†	0	0	1 (<0.1)
Herpes zoster	5 (2.6)	8 (4.2)	25 (1.9)
Herpes simplex	7 (3.6)	5 (2.6)	40 (3.1)
Malignancies (excluding NMSC)†	2 (1.0)	3 (1.6)	9 (0.7)
NMSC†	1 (0.5)	0	3 (0.2)
MACE†‡	0	0	5 (0.4)
Thromboembolic events†	0	1 (0.5)	1 (<0.1)
Death	0	0	2 (0.2)

AE, adverse event; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer. Includes patients from the start of their first dose of ritlecitinib.
*Includes patients with alopecia areata who received any dose of ritlecitinib in ALLEGRO-2a, ALLEGRO-2b/3, ALLEGRO-LT, and ALLEGRO-2a safety study from the start of their first dose of ritlecitinib.
†Adjudicated safety events.
‡ MACE was defined as defined as a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

CONCLUSIONS

- Ritlecitinib 50 mg (with or without a 200 mg loading dose) demonstrated clinically meaningful and sustained clinician- and patient-reported efficacy through Month 24
- Ritlecitinib was well tolerated over 24 months; the safety profile was consistent with the primary ALLEGRO phase 2b/3 study
- These data support the long-term use of ritlecitinib in patients aged ≥12 years with severe AA

REFERENCES

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

ABBREVIATIONS

AA, alopecia areata; AE, adverse event; AT, alopecia totalis; AU, alopecia universalis; JAK3, Janus kinase 3; LOCF, last observation carried forward; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PGI-C, Patients' Global Impression of Change; QD, once daily; SAE, serious AE; SALT, Severity of Alopecia Tool; SD, standard deviation; TEC, tyrosine kinase expressed in hepatocellular carcinoma.

CONFLICTS OF INTEREST

We thank all investigators, participants, and their families. This study was supported by Pfizer

M. Piliang: speaker, consultant, and/or investigator for Pfizer, Eli Lilly, and Proctor & Gamble. J. Soung: speaker for Celgene, Regeneron/Sanofi, and Ortho Dermatologics: speaker and investigator for Amgen, AbbVie, and Pfizer; speaker, investigator, and advisor for Eli Lilly; investigator and advisor for LEO Pharma; investigator, speaker, and consultant for Novartis; investigator for UCB, Janssen, Kyowa Kirin, KoBio Labs, and Castel Biosciences; investigator and consultant for Dermavant; speaker and consultant for Bristol Myers Squibb, speaker, investigator, and consultant for Arcutis. B. King: AbbVie, AltruBio, Almirall, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol-Meyers Squibb, Concert Pharmaceuticals, Equillium, Horizon Therapeutics, Eli Lilly, Incyte, Janssen Pharmaceuticals, LEO Pharma, Otsuka/Visterra, Pfizer, Regeneron, Sanofi Genzyme, TWi Biotechnology, and Viela Bio, and on the speakers bureau for Pfizer. J. Shapiro: consultant for Pfizer and Eli Lilly and clinical trial investigator for Pfizer. L. Rudnicka: speaker for AbbVie, L'Oreal, LEO Pharma, Novartis, Pierre Fabre, Pfizer, and advisory board member for LEO Pharma, Janssen, L'Oreal, Novartis, Pfizer, Sanofi, and UCB. P. Farrant: consultant for Eli Lilly; advisory board member and clinical trial investigator for Pfizer. N. Magnolo: honoraria for participation in advisory boards, speaker and/or consultancy for AbbVie, Almirall, Amgen, BMS, Boehringer Ingelheim, Celgene, Dr. Wolff, Eli Lilly, Janssen, La Roche-Posay, LEO Pharma, Novartis, Pfizer, and UCB Pharma. B. Piraccini: consultant for Almirall, Pfizer, Eli Lilly, Pierre Fabre-Ducray, Cantabria-Difa Cooper, Dercos-L'Oreal, ISDIN, Legacy Healthcare. X. Luo, D. Woodworth, G. Schaefer, A. Lejeune, and R. Wolk are employees of, and hold stock or stock options in, Pfizer Inc.

Medical writing and editorial support was provided by Nucleus Global, which was funded by Pfizer

Presented at the Winter Clinical Dermatology Conference - Hawaii®; January 12-17, 2024; Maui, HI