Long-term Efficacy and Safety of Ritlecitinib in Adults and Adolescents with Alopecia Areata: 3-year Results from the ALLEGRO-LT Phase 3, Open-label Study

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INTRODUCTION

- Alopecia areata (AA) is an autoimmune disease characterized by patchy or complete nonscarring hair loss on the scalp, with or without additional loss of facial and/or body hair[1]
- In the ALLEGRO phase 2b/3 study (ALLEGRO-2b/3; NCT03732807), ritlecitinib, a selective dual Janus kinase 3 (JAK3)/tyrosine kinase expressed in hepatocellular carcinoma (TEC) kinase family inhibitor, demonstrated efficacy and safety up to 48 weeks in patients with AA[2]

OBJECTIVE

- To investigate the efficacy and safety of ritlecitinib up to 3 years in patients with AA from ALLEGRO-2b/3 and the ongoing, phase 3, open-label 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
- Patients received ritlecitinib 50 mg once daily (QD) in ALLEGRO-2b/3 and continued the same dosage in the ALLEGRO-LT study (**Figure 1**)
  - Adolescents in ALLEGRO-LT were required to have an improvement in Severity of Alopecia Tool (SALT) score of ≥50% at Month 3 from baseline in ALLEGRO-2b/3 and a SALT score of ≤20 by Month 6 to continue in ALLEGRO-LT

Figure 1. Study design

Ritlecitinib 50 mg combined | Groups not assessed in this analysis

	ALLEGRO phase 2b/3 (NCT03732807)				ALLEGRO-LT (NCT04006457)
	Loading (4 weeks)	Maintenance (20 weeks)	Extension (24 weeks)		Long-term study (60 months)
Group A (n=131)	200 mg	50 mg	50 mg		50 mg
Group B (n=129)	200 mg	30 mg	30 mg		50 mg
Group C (n=130)	50 mg	50 mg	50 mg		50 mg
Group D (n=132)	30 mg	30 mg	30 mg		50 mg
Group E (n=61)	10 mg	10 mg	10 mg		50 mg
Group F (n=63)	Placebo	Placebo	200 mg	50 mg	50 mg
Group G (n=61)	Placebo	Placebo	50 mg		50 mg
			De novo group (N=447)	200 mg	50 mg

Outcomes

- Proportion of patients treated with ritlecitinib 50 mg QD with response through 3 years was assessed based on:
  - SALT score ≤20
  - SALT score ≤10
  - Patient Global Impression of Change (PGI-C) score of "moderately improved" or "greatly improved" from baseline
- Safety: incidence of adverse events (AEs), serious AEs (SAEs), and severe AEs

Statistical analyses

- Efficacy data are presented as:
  - Observed data
  - Imputed data (last observation carried forward [LOCF]), to account for missing data values
- Data while on placebo were not included in this analysis; data from patients in Group G were re-baselined from the start of treatment with ritlecitinib at Week 24 of the ALLEGRO-2b/3 study
- Visits were calculated as time since the first ritlecitinib dose, thus resulting in different months for some visits
  - The "Month 36" timepoint includes patients in Group C (n=130) who had a scheduled visit at Month 24 of ALLEGRO-LT and patients in Group G (n=61) who had a scheduled visit at Month 32 of ALLEGRO-LT, after rolling over from the ALLEGRO-2b/3 study
- Timepoints presented in this summary are those where all groups in the cohort had planned assessments for the efficacy endpoint under analysis
- Data are reported to the cutoff date of June 25, 2024

RESULTS

Baseline characteristics and patient disposition

- 191 patients were included in the **ritlecitinib 50 mg combined group** (**Table 1**)

Table 1. Demographic and baseline characteristics[3]

	Ritlecitinib 50 mg (N=191)
Age (years)	
Median (range)	31.0 (12.0-65.0)
12-17 years, n (%)	27 (14.1)
≥18 years, n (%)	164 (85.9)
≥65 years, n (%)	6 (3.1)
Female, n (%)	107 (56.0)
White, n (%)	123 (64.4)
AT/AU,* n (%)	86 (45.0)
SALT score among non-AT/AU patients, mean (SD)	83.3 (15.4)
Duration of AA since diagnosis (years), median (range)	6.9 (0.3-58.2)
Duration of current AA episode (years), median (range)	2.2 (0.0-10.0)
Prior pharmacological treatment for AA, n (%)	145 (75.9)

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; SALT, Severity of Alopecia Tool; SD, standard deviation.
Interim results are subject to change as additional data are collected and analyzed in the ongoing study.
*Patients in the AT/AU group had a SALT score of 100 at baseline.

- At the date of data cutoff, 27 (14.1%) patients were ongoing, and 62 (32.5%) patients had completed the study (**Table 2**)

Table 2. Patient disposition

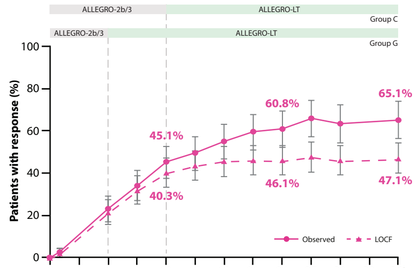
	Ritlecitinib 50 mg (N=191)
Ongoing at the date of datacut	27 (14.1)
Completed	62 (32.5)
Completed the study	9 (4.7)
Removed from study per protocol as commercial drug became available	53 (27.8)
Discontinued	102 (53.4)
Adverse event*	21 (11.0)
Lack of efficacy	17 (8.9)
Lost to follow-up	8 (4.2)
Physician decision	3 (1.6)
Pregnancy	1 (0.5)
Protocol deviation	0
Withdrawal by subject	35 (18.3)
No longer meets eligibility criteria†	6 (3.1)
Other	11 (5.8)

AE, adverse event; SAE, serious adverse event; SALT, Severity of Alopecia Tool.
Interim results are subject to change as additional data are collected and analyzed in the ongoing study. Data are presented as n (%).
*Treatment discontinuation and participant withdrawal from the study were required in the study protocol 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. †Adolescents (n=5) who did not meet the protocol continuation criteria in ALLEGRO-LT (i.e., did not achieve a ≥50% improvement in SALT score at Month 3 from baseline in ALLEGRO 2b/3 or a SALT score of ≤20 at Month 6) and one adult who was diagnosed with scarring alopecia.

SALT ≤20 response over time

- 65.1% (71/109 observed) and 47.1% (90/191 LOCF) of patients had SALT score ≤20 at Month 36 (**Figure 2**)

Figure 2. SALT ≤20 response over time



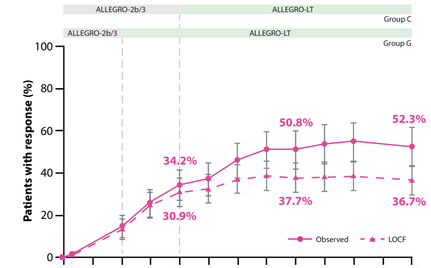
No. of patients†											
Observed	183	178	168	164	148	140	128	120	114	112	109
LOCF	191	191	191	191	191	191	191	191	191	191	191

LOCF, last observation carried forward; SALT, Severity of Alopecia Tool.
Interim results are subject to change as additional data are collected and analyzed in the ongoing study.
*To align timepoints across groups for summarization, visits are calculated as time since the first ritlecitinib dose; e.g., the "Month 36" timepoint includes patients in Group C (n=130) who had a scheduled visit at Month 24 of ALLEGRO-LT and patients in group G (n=61) who had a scheduled visit at Month 32 of ALLEGRO-LT, after rolling over from the ALLEGRO-2b/3 study. †Number of patients with valid data at that analysis visit.

SALT ≤10 response over time

- 52.3% (57/109 observed) and 36.7% (70/191 LOCF) of patients had SALT score ≤10 at Month 36 (**Figure 3**)

Figure 3. SALT ≤10 response over time



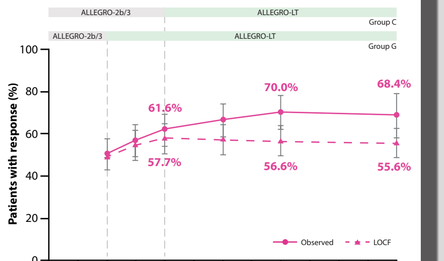
No. of patients†											
Observed	183	178	168	164	148	140	128	120	114	112	109
LOCF	191	191	191	191	191	191	191	191	191	191	191

LOCF, last observation carried forward; SALT, Severity of Alopecia Tool.
Interim results are subject to change as additional data are collected and analyzed in the ongoing study.
*To align timepoints across groups for summarization, visits are calculated as time since the first ritlecitinib dose; e.g., the "Month 36" timepoint includes patients in Group C (n=130) who had a scheduled visit at Month 24 of ALLEGRO-LT and patients in group G (n=61) who had a scheduled visit at Month 32 of ALLEGRO-LT, after rolling over from the ALLEGRO-2b/3 study. †Number of patients with valid data at that analysis visit.

PGI-C response over time

- 68.4% (52/76 observed) and 55.6% (105/189 LOCF) of patients reported "moderately" or "greatly" improved PGI-C response at Month 36 (**Figure 4**)

Figure 4. PGI-C response over time



No. of patients†											
Observed	183	179	166	164	140	120	76				
LOCF	191	189	189	189	189	189	189				

LOCF, last observation carried forward; PGI-C, Patient Global Impression of Change.
Interim results are subject to change as additional data are collected and analyzed in the ongoing study.
*To align timepoints across groups for summarization, visits are calculated as time since the first ritlecitinib dose; e.g., the "Month 36" timepoint includes patients in Group C (n=130) who had a scheduled visit at Month 24 of ALLEGRO-LT and patients in group G (n=61) who had a scheduled visit at Month 32 of ALLEGRO-LT, after rolling over from the ALLEGRO-2b/3 study. †Number of patients with valid data at that analysis visit.

Safety overview

- Ritlecitinib was generally well tolerated through Month 36 in patients with AA (**Tables 3 and 4**)
- The long-term safety profile of ritlecitinib 50 mg was consistent with that reported previously[3]

Table 3. Safety overview

	Ritlecitinib 50 mg (N=191)
AE	186 (97.4)
SAE	13 (6.8)
Most frequent AEs*	
SARS-CoV-2 test positive	46 (24.1)
Headache	38 (19.9)
Nasopharyngitis	34 (17.8)
Cough	30 (15.7)
Pyrexia	29 (15.2)
Upper respiratory tract infection	29 (15.2)
Oropharyngeal pain	26 (13.6)
Acne	23 (12.0)

AE, adverse event; SAE, serious adverse event.
Interim results are subject to change as additional data are collected and analyzed in the ongoing study. Data are presented as n (%).
*8 most frequent AEs by preferred term.

- The results represent a partial view of the overall safety profile that has been characterized in an integrated safety analysis of the ALLEGRO clinical program[4,5]

Table 4. AEs of special interest

	Ritlecitinib 50 mg (N=191)
Serious infections*	3 (1.6)
Opportunistic infections†	1 (0.5)
Herpes zoster	10 (5.2)
Malignances excluding NMSC†	3 (1.6)
Breast cancer†	2 (1.9)
MACE†‡	0
TE†	1 (0.5)

AE, adverse event; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; TE, thromboembolic event.
Interim results are subject to change as additional data are collected and analyzed in the ongoing study. Data are presented as n (%).
*Serious infections are defined as any serious adverse event in the infections and infestations system organ class.
†Adjudicated safety events. ‡MACE was defined as a composite of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke.

CONCLUSIONS

- Ritlecitinib 50-mg demonstrated meaningful clinician- and patient-reported efficacy up to 3 years
- These data are the longest duration of ritlecitinib treatment to be reported to date and support the long-term use of ritlecitinib in patients aged ≥12 years with AA

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DISCLOSURES

This study was sponsored by Pfizer Inc. M. Senna has served on advisory boards and/or is a consultant and/or is a clinical trial investigator or a speaker for Abbvie, Arena Pharmaceuticals, Concert Pharmaceuticals Inc, Eli Lilly and Company, Inmagene, LEO Pharma, Merck, Pfizer Inc, Sun Pharmaceutical, and Kintor. She is a scientific advisor for BiologicsMD. I. Figueras has served as an advisory board member, consultant, and/or investigator for AbbVie, Eli Lilly and Company, LEO Pharma, L'Oréal, Pfizer, Novartis, Sanofi, Celgene, Amgen, Galderma and Gebro Pharma, and speaker for AbbVie, Eli Lilly and Company, LEO Pharma, Pfizer, Sanofi, Novartis, Sobi, Pierre Fabre, La Roche Posay, Galderma and Gebro Pharma. M. Kinoshita-Ise is a clinical trial investigator for AbbVie, Eli Lilly Japan, Pfizer, Bristol Myers Squibb, and a speaker for Eli Lilly Japan and Pfizer. S. Hanna is a clinical trialist with Abbvie, Lilly, Lumenis, and Pfizer, and has received honoraria for speaking/consulting from AbbVie, Lilly, and Pfizer. W. Wu is a clinical trial investigator and a speaker for Abbvie, Eli Lilly and Pfizer. D. Wajsbrot, D. Woodworth, R. Wolk, A. Chaudhry, A. Lejeune, and H. Tran employees of, and may hold stock or stock options in Pfizer Inc. Third-party medical writing assistance, provided by Nucleus Global, an Inizio Company, was funded by Pfizer Inc.

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