Sustained hair regrowth with ritlecitinib to Week 48 in patients with alopecia areata: post hoc analysis of the ALLEGRO phase 2b/3 study

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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 ranging from small patches to complete scalp, face, and/or body hair loss[1]
- Ritlecitinib, an oral JAK3/TEC family inhibitor, demonstrated efficacy and safety in patients aged ≥12 years with AA and ≥50% scalp hair loss in the ALLEGRO phase 2b/3 trial (NCT03732807)[2]
  - Significant improvements in the proportion of patients with Severity of Alopecia Tool (SALT) score ≤20 (≤20% of scalp without hair) at Week 24 (primary endpoint) were observed in the 50 mg and 30 mg ritlecitinib treatment groups (+/- 200 mg loading dose) vs placebo (P<0.001)
  - Significant improvements in the proportions of patients with SALT score ≤10 (≤10% of scalp without hair) with ritlecitinib vs placebo were also seen at Week 24 (secondary endpoint)

OBJECTIVE

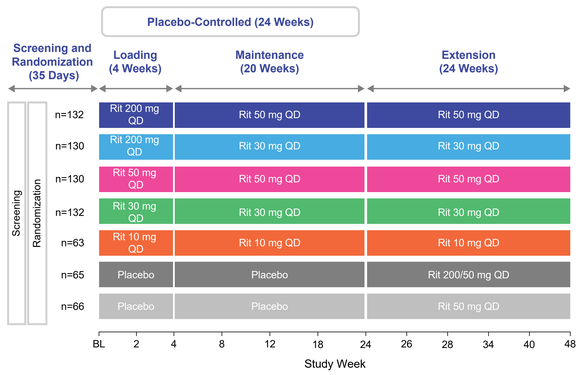
- To evaluate the maintenance of efficacy from Week 24 to Week 48 in patients with AA and ≥50% scalp hair loss treated with ritlecitinib

METHODS

Study design

- The ALLEGRO phase 2b/3 trial was an international, randomized, double-blind, placebo-controlled, combined dose-ranging and pivotal study (**Figure 1**)
- Patients initially received daily ritlecitinib (± a 4-week 200-mg daily loading dose): 200/50, 200/30, 50, 30, or 10 mg (10 mg assessed for dose ranging only) or placebo for 24 weeks
- During the 24-week extension period, ritlecitinib groups continued on 50-, 30-, or 10-mg maintenance doses, and patients initially assigned to placebo switched to 200/50 or 50 mg daily

Figure 1. ALLEGRO-2b/3 Study Design



BL, baseline; QD, once daily; Rit, ritlecitinib. No other therapies were allowed during the study.

Study population

- Inclusion criteria included:
  - Age ≥12 years
  - Diagnosis of AA
  - ≥50% scalp hair loss, including patients with AT and AU
  - Current AA episode duration of 6 months to 10 years
- Patients with other causes of alopecia or previous use of any JAK inhibitor were excluded
- This post hoc analysis included patients who received ritlecitinib 200/50, 200/30, 50, or 30 mg and had a SALT ≤20 or ≤10 response at Week 24

Outcomes

- The proportions of ritlecitinib-treated patients with clinical response at Week 24, based on SALT score ≤20 or SALT score ≤10, who sustained this response through Week 48, were assessed in this post-hoc analysis
- Definition of sustained response included:
  - Response at Week 24 and Week 48, based on SALT score ≤20 or ≤10, and
  - No loss of response (defined as SALT score >20 or >10) at any time point between Weeks 24 and 48 (Weeks 28, 34, or 40)
- Patients with missing SALT score data at Weeks 28, 34, or 40 were included in the analysis if they had observed SALT data at Week 48; patients with missing data at Week 48 were excluded from the analysis

Statistical analysis

- Descriptive analyses were used to evaluate the proportion of ritlecitinib-treated patients with SALT score ≤20 or SALT score ≤10 response at Week 24, who sustained this response through Week 48
- 95% CIs were calculated based on normal approximation

RESULTS

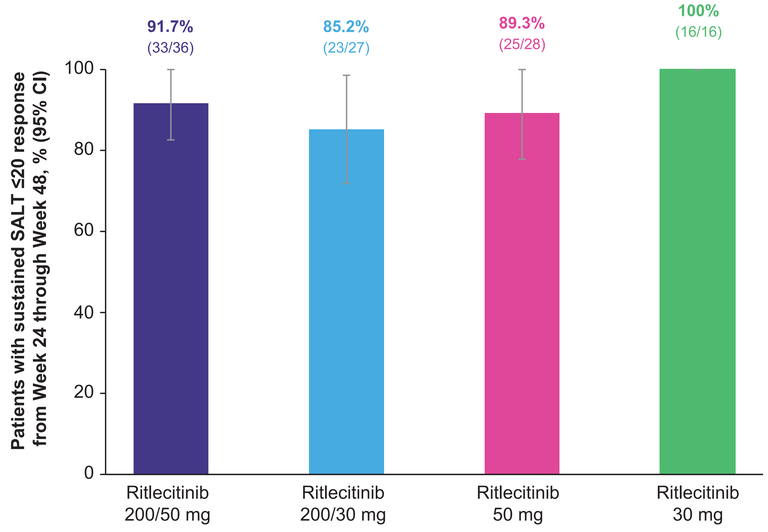
Table 1. Baseline characteristics of patients with SALT score ≤20 response at Week 24

	Ritlecitinib QD			
	200/50 mg (n=38)	200/30 mg (n=27)	50 mg (n=29)	30 mg (n=17)
Age				
Mean (SD), years	33.7 (14.2)	31.8 (12.2)	34.0 (14.5)	36.9 (14.7)
12-17 years, n (%)	5 (13.2)	3 (11.1)	4 (13.8)	3 (17.6)
≥18 years, n (%)	33 (86.8)	24 (88.9)	25 (86.2)	14 (82.4)
Female, n (%)	28 (73.7)	21 (77.8)	25 (86.2)	11 (64.7)
White, n (%)	25 (65.8)	16 (59.3)	18 (62.1)	12 (70.6)
Patients with AT/AU*, n (%)	8 (21.1)	7 (25.9)	4 (13.8)	4 (23.5)
Baseline SALT score, mean (SD)†	84.4 (16.0)	80.9 (18.2)	78.9 (16.9)	77.6 (19.2)
Duration of disease since AA diagnosis, mean (SD), years	9.9 (8.5)	9.2 (8.0)	7.1 (8.9)	6.9 (5.9)
Duration of current AA episode, mean (SD), years	2.5 (2.2)	3.1 (2.4)	2.4 (2.5)	2.1 (2.6)

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; QD, once daily; SALT, Severity of Alopecia Tool.
*Patients in the AT/AU category had a SALT score of 100 at baseline (regardless of the category in the AA history case report form).
†Mean (SD) baseline SALT score for all patients including patients with AT/AU.

- In the 200/50, 200/30, 50, 30 mg ritlecitinib treatment groups, 36/132, 27/130, 28/130, and 16/132 patients, respectively, had a SALT score ≤20 response at Week 24 and had SALT data at Week 48
  - Of these, 85% to 100% had a sustained response through Week 48 (**Figure 2**)

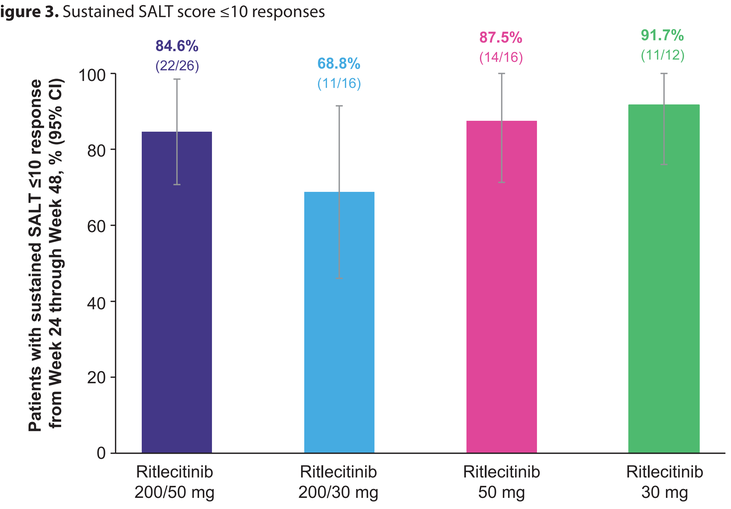
Figure 2. Sustained SALT score ≤20 responses



SALT, Severity of Alopecia Tool.

- Similarly, 26/132, 16/130, 16/130, and 12/132 patients in the 200/50, 200/30, 50, 30 mg groups, respectively, had a SALT score ≤10 response at Week 24 and had SALT data at Week 48
  - Of these, 69% to 92% had a sustained response through Week 48 (**Figure 3**)

Figure 3. Sustained SALT score ≤10 responses



SALT, Severity of Alopecia Tool.

Safety

- Ritlecitinib was well tolerated up to Week 48 in patients with SALT score ≤20 response at Week 24; most adverse events (AEs) were mild or moderate in severity, 2 serious AEs were reported, and 2 patients permanently discontinued due to AEs (**Table 2**)

Table 2. Safety summary up to Week 48 in patients with SALT score ≤20 response at Week 24

	Ritlecitinib QD			
	200/50 mg (n=38)	200/30 mg (n=27)	50 mg (n=29)	30 mg (n=17)
Patients with AEs	35 (92.1)	20 (74.1)	27 (93.1)	14 (82.4)
Patients with SAEs*	0	1 (3.7)	1 (3.4)	0
Patients permanently discontinued due to AEs†	0	1 (3.7)	1 (3.4)	0
Most frequent AEs‡				
Upper respiratory tract infection	11 (28.9)	2 (7.4)	3 (10.3)	0
Headache	7 (18.4)	1 (3.7)	8 (27.6)	4 (23.5)
Nasopharyngitis	7 (18.4)	4 (14.8)	2 (6.9)	3 (17.6)

AE, adverse event; QD, once daily; SAE, serious adverse event; SALT, Severity of Alopecia Tool.
*SAEs were chemical poisoning and suicidal behavior in 1 patient in the 200/30 mg group and pulmonary embolism in 1 patient in the 50 mg group.
†Patients who had an AE record indicating that the patient was permanently discontinued from the study or study drug.
‡AEs occurring in ≥5% of patients in any treatment group by preferred term (all causalities).

CONCLUSIONS

- In this post hoc analysis, sustained scalp hair regrowth through Week 48 was observed in the majority of patients with AA who had a SALT score ≤20 or ≤10 response after Week 24 of ritlecitinib treatment
- The safety profile of ritlecitinib up to Week 48 in SALT ≤20 responders was consistent with that of the overall study population, which has been reported previously[3]

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REFERENCES

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2. King B, et al. Poster presented at: 30th Annual EADV Meeting; September 29-October 2, 2021.
3. King B, et al. Poster presented at: AAD Annual Meeting; March 25-29, 2022.

DISCLOSURES

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R. Wolk, S.H. Zwillich, H. Tran, F. Zhang, and L. Takiya are employees of Pfizer, Inc and hold stock or stock options in Pfizer, Inc. M. Piliang: consultant and/or investigator for Pfizer, Eli Lilly, and Proctor and Gamble. C. Lynde: speaker and/or consultant for AbbVie, Altius, Amgen, Aralez, Arcutis, Bausch Health, Bayer, Boehringer Ingelheim, BMS, Celgene, Cipher, Dermavant, Eli Lilly, Fresnius Kabi, GSK, Innovaderm, Intega Skin, Janssen, Kyowa, La Roche Posay, LEO Pharma, L'Oreal, Medexus, Merck, Proctor and Gamble, Pediapharm, Regeneron, Roche, Sanofi Genzyme, Sentrex, TEVA, Tribute, UCB, Valeant, and Viatris; principal investigator for AbbVie, Amgen, Aralez, Arcutis, Bausch Health, Bayer, Boehringer Ingelheim, BMS, Celgene, Cipher, Dermavant, Eli Lilly, GSK, Innovaderm, Janssen, Kyowa, LEO Pharma, L'Oreal, Merck, Pediapharm, Regeneron, Roche, Sanofi Genzyme, Tribute, UCB, and Valeant. B. King: honoraria and/or consultation fees from AbbVie, Aclaris Therapeutics, AltruBio, Almirall, Arena Pharmaceuticals, Bionz Therapeutics, BMS, Concert Pharmaceuticals, Dermavant Sciences, Eli Lilly, Incyte, LEO Pharma, Otsuka/Visterra, Pfizer, Regeneron, Sanofi Genzyme, Twi Biotechnology, and Viela Bio and speakers bureau fees from Pfizer Inc. P. Mirmirani: investigator grants and/or research funding from Concert Pharmaceuticals, Pfizer Inc, and Eli Lilly. R. Sinclair: professional services from AbbVie, Aerotech, Amgen, Arena, Arcutis, Aksebio, AstraZeneca, Ascend, Bayer, Boehringer Ingelheim, BMS, Celgene, Coherus Biosciences, Cutanea, Connect, Demira, Eli Lilly, Galderma, GSK, Janssen, LEO Pharma, MedImmune, Merck, MSD, Novartis, Oncobiologics, Pfizer, Regeneron, Reistone, Roche, Sanofi, Samson Clinical, Sun Pharma, and UCB.

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