Evaluation of Response to Ritlecitinib Treatment Based on SALT Improvement Scores 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 immunoinflammatory pathogenesis and is characterized by nonscarring hair loss ranging from small bald patches to complete loss of scalp, face, and/or body hair[1]
- Ritlecitinib, an oral JAK3/TEC inhibitor, demonstrated efficacy and safety in patients aged ≥12 years with AA 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% scalp without hair) at Week 24 (primary endpoint) were observed in active ritlecitinib treatment groups vs placebo ($P<0.001$)[1]
  - Ritlecitinib was also found to have significantly higher SALT score ≤10 (10% scalp without hair) response rates than placebo at Week 24 (secondary endpoint)

OBJECTIVE

- To evaluate responses to ritlecitinib treatment based on predefined SALT improvement categories from baseline to Weeks 24 and 48

METHODS

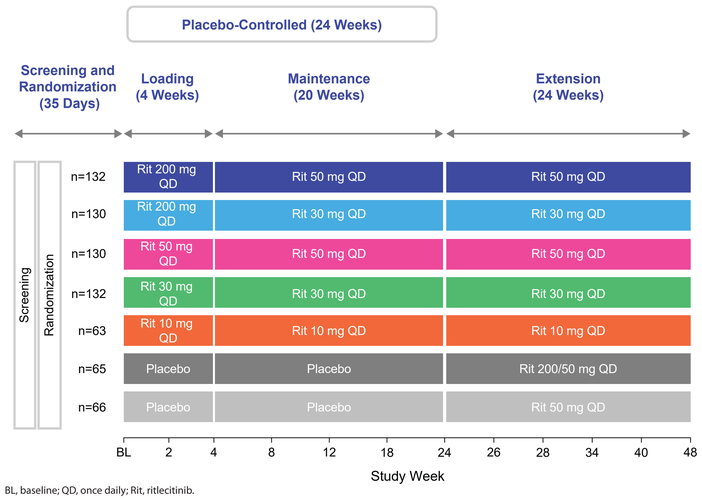
Study design

- 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

Key eligibility criteria

- Patients were aged ≥12 years with a diagnosis of AA and ≥50% scalp hair loss, including alopecia totalis and alopecia universalis, and a current AA episode duration of 6 months to 10 years

Figure 1. Study design



BL, baseline; QD, once daily; Rit, ritlecitinib.

Outcomes

- In this post hoc analysis, the proportions of patients with 50%, 75%, 90%, and 100% improvement from baseline in SALT score ($SALT_{50}$, $SALT_{75}$, $SALT_{90}$, $SALT_{100}$, respectively) were assessed at Weeks 24 and 48
  - **SALT score** assesses the amount of scalp hair loss with scores ranging from 0 (no scalp hair loss) to 100 (complete scalp hair loss)
  - **$SALT_x$** denotes X% improvement in SALT score from baseline

Statistical analysis

- Descriptive analyses were used to evaluate proportions of patients with $SALT_{50}$, $SALT_{75}$, $SALT_{90}$, and $SALT_{100}$ at Weeks 24 and 48
- 95% CIs were calculated based on normal approximation
- Patients with missing data due to COVID-19–related reasons at specified time points were excluded; patients with missing data due to reasons unrelated to COVID-19 were considered nonresponders

RESULTS

- At baseline, mean SALT scores ranged from 90.0 to 93.0 and were generally consistent across treatment groups (**Table 1**)

Table 1. Baseline characteristics

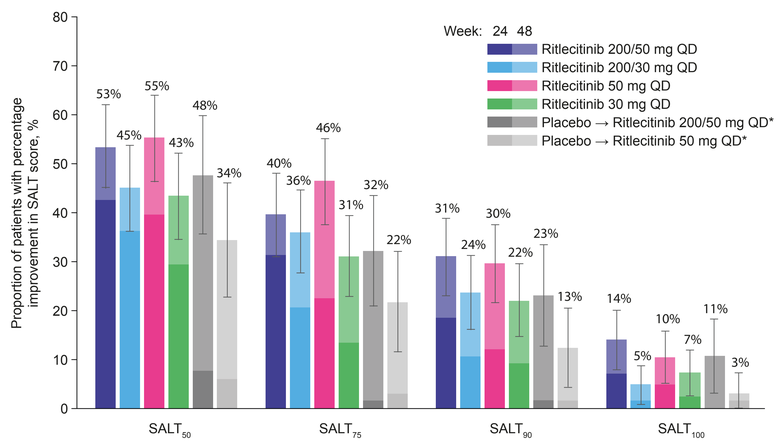
	Ritlecitinib QD*				
	200/50 mg (n=132)	200/30 mg (n=130)	50 mg (n=130)	30 mg (n=132)	Placebo† (n=131)
Age					
Mean (SD), years	35.5 (15.0)	34.4 (13.8)	32.4 (13.4)	33.7 (14.8)	34.0 (15.0)
12-17 years, n (%)	20 (15.2)	19 (14.6)	18 (13.8)	20 (15.2)	19 (14.5)
≥18 years, n (%)	112 (84.8)	111 (85.4)	112 (86.2)	112 (84.8)	112 (85.5)
Female, n (%)	81 (61.4)	85 (65.4)	71 (54.6)	80 (60.6)	86 (65.6)
White, n (%)	92 (69.7)	90 (69.2)	79 (60.8)	91 (68.9)	94 (71.8)
Patients with AT/AU, n (%)‡	60 (45.5)	60 (46.2)	60 (46.2)	60 (46.2)	60 (45.8)
Baseline SALT score, mean (SD)					
All patients	90.3 (15.1)	90.5 (14.3)	90.3 (14.7)	90.0 (15.1)	93.0 (11.5)
Non-AT/AU‡	82.2 (16.5)	82.4 (15.4)	82.0 (15.9)	81.5 (16.3)	87.0 (12.9)
Duration of current AA episode, mean (SD), years	3.4 (2.9)	3.4 (2.9)	3.2 (2.7)	3.6 (2.8)	3.2 (2.7)

AA, alopecia areata; AT, alopecia totalis; AU, alopecia universalis; QD, once daily; SALT, Severity of Alopecia Tool.
*Ritlecitinib 10 mg was assessed for dose ranging only; data are not shown.
†Placebo for 24 weeks and then ritlecitinib 200/50 mg or 50 mg QD.
‡Participants in the AT/AU category had SALT scores of 100 (complete scalp hair loss) at baseline (regardless of the category in the AA history case report form).

SALT score improvement from baseline up to Week 48

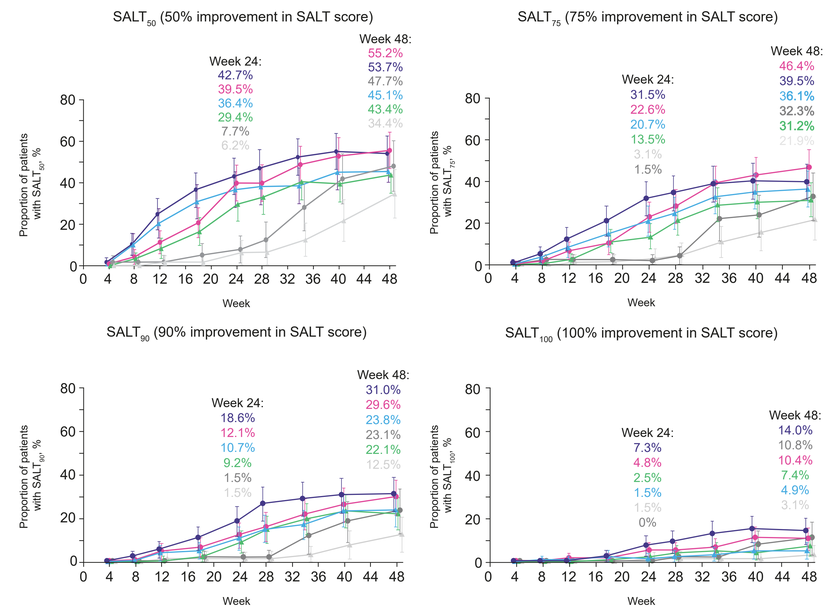
- Across all ritlecitinib dose regimens tested for efficacy (200/50 mg, 200/30 mg, 50 mg, and 30 mg), a greater proportion of patients had $SALT_{50}$, $SALT_{75}$, $SALT_{90}$, or $SALT_{100}$ response at Week 24 vs placebo (**Figure 2**)
  - At Week 24, 29-43% of patients in the ritlecitinib arms had a 50% improvement in SALT score, with some patients reaching 100% improvement
- The proportion of patients with SALT score improvements continued to increase through Week 48 (**Figures 2 and 3**)
  - At Week 48, 34-55% of patients had a 50% improvement in SALT score, and 3-14% of patients had a 100% improvement

Figure 2. Response based on % improvement from baseline in SALT score at Weeks 24 and 48



QD, once daily; SALT, Severity of Alopecia Tool; $SALT_{50/75/90/100}$, 50%/75%/90%/100% improvement from baseline in SALT score.
Percentages and error bars are 95% CI at Week 48.
*Patients received placebo until Week 24 and then received ritlecitinib treatment (200/50 or 50 mg QD) from Week 24 to Week 48.

Figure 3. Response based on % improvement from baseline in SALT scores over time



QD, once daily; SALT, Severity of Alopecia Tool; $SALT_{50/75/90/100}$, 50%/75%/90%/100% improvement from baseline in SALT score. N indicates the number of patients in each treatment group at baseline. Error bars are 95% CI.
*Patients received placebo until Week 24 and then received ritlecitinib treatment (200/50 or 50 mg QD) from Week 24 to Week 48.

Safety

- Over 48 weeks of treatment, the most frequent adverse events (AEs), with no evident dose response, were upper respiratory tract infection, nasopharyngitis, and headache
- Most AEs were mild or moderate in severity, 12 serious AEs were reported, and 26 patients permanently discontinued treatment due to AEs up to Week 48
- Overall, there were 8 cases of herpes zoster infection, 4 serious infections, 2 malignancies (both breast cancer), and 1 pulmonary embolism; no major adverse cardiovascular events, deaths, or opportunistic infections were reported

CONCLUSIONS

- Ritlecitinib treatment led to scalp hair regrowth over 48 weeks of treatment
  - At Week 24, up to 43% of patients had a 50% improvement in SALT score; a small proportion of patients had 100% improvement
  - Further improvements were seen after Week 24; by Week 48, up to 55% and 14% of patients showed a 50% and 100% improvement in SALT score, respectively
- Ritlecitinib had an acceptable safety profile over 48 weeks
- Various SALT improvement categories, including $SALT_{50}$, $SALT_{75}$, $SALT_{90}$, and $SALT_{100}$, may help facilitate discussion of treatment progress in patients with AA

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REFERENCES

1. Islam N, et al. *Autoimmun Rev*. 2015;14:81-89.
2. King B, et al. Poster presented at EADV 2021.

DISCLOSURES

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U.B.-P. has served as a consultant and/or participated in advisory boards for AbbVie, CeraVe, Dermocosmétique Vichy, Galderma, Lilly, Neuroderm, Pfizer, Sanofi Regeneron, and Boots Healthcare and is a clinical study investigator for Amryt, Bayer, Cassiopeia, Concert Pharmaceuticals, Pierre Fabre, Novartis, LEO Pharma, and Mayne Pharma. J.W.G.H. has served as a scientific advisor and/or clinical study investigator for Pfizer, Galderma, GSK, Eucerin, Johnson & Johnson, Janssen, Sanofi, BioNOOX, and Beiersdorf/Eucerin. Q.Y. declares no conflicts of interests. G.J.S. is a principal clinical trial investigator for Pfizer. M.K.H. declares receiving grant support from Concert Pharmaceuticals, Eli Lilly, and Pfizer, and consulting fees from ASLAN Pharmaceuticals, Bioniz, Cassiopeia, and Pulse Biosciences. G.M. declares no conflicts of interests. M.O. is a medical advisor for Pfizer Japan Inc, Taisho Pharmaceutical Co, Eli Lilly Japan KK, and ROHTO Pharmaceutical Co, and receives advisory fees; he also receives lecture fees from Eli Lilly Japan KK and research grants for projects not related to this study from Maruho Co, Sun Pharma Japan Ltd, and Shiseido Co. L.T., F.Z., G.S., R.W., and U.K. are employees of Pfizer and hold stock or stock options in Pfizer.

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