Timing of Initial Hair Regrowth and Clinical Trial-Defined Response Following Ritlecitinib Treatment in Patients With Alopecia Areata

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BACKGROUND

- 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]
- Ritlecitinib is an oral, selective, dual inhibitor of JAK3 and the TEC family kinases that was approved for treatment of severe AA in adults and adolescents aged ≥12 years in June 2023
- With the recent approval of ritlecitinib, understanding the timeline for therapeutic benefit after initial hair regrowth is crucial for patient management
- This post-hoc analysis evaluated the time to clinical trial-defined scalp hair regrowth following initial signs of scalp hair regrowth in patients with AA using data from the ALLEGRO clinical trial program, which evaluated the efficacy and safety of ritlecitinib, an oral JAK3/TEC family kinase[2]

OBJECTIVE

- To evaluate the time from initial scalp hair regrowth, defined as 30% improvement in Severity of Alopecia Tool score from baseline ($SALT_{30}$), to the primary clinical trial endpoint of SALT score ≤20 (≤20% scalp hair loss) while receiving ritlecitinib

METHODS

STUDY DESIGN

- Post hoc analysis using integrated data from the ALLEGRO-2b/3 (NCT03732807) and ALLEGRO-LT (NCT04006457) trials of ritlecitinib in AA
- Patients receiving active ritlecitinib doses, ritlecitinib 50 mg or 30 mg once daily with or without a 4-week 200 mg loading dose, were included in this analysis (**Figure 1**)
- Patients in groups E, F, and G were not included in this analysis (**Figure 1**)

Figure 1. Study design

	ALLEGRO phase 2b/3*			ALLEGRO-LT*
	Loading (4 weeks)	Maintenance (20 weeks)	Extension (24 weeks)	Long-term study (48 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=63)	10 mg	10 mg	10 mg	50 mg
Group F (n=65)	Placebo	Placebo	200 mg (4 wks) 50 mg	50 mg
Group G (n=66)	Placebo	Placebo	50 mg	50 mg
Modified de novo group† (n=309)				200 mg (4 wks) 50 mg

Key inclusion criteria (ALLEGRO-2b/3):

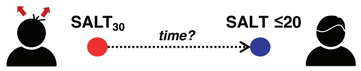
- Patients aged **≥12 years**
- Diagnosis of AA with **≥50% scalp hair loss due to AA** (including alopecia totalis and alopecia universalis)
- Maximum duration of current episode of hair loss **≤10 years**

*Ritlecitinib dosing was once daily, at the doses indicated.
†This group is a subset of the ALLEGRO-LT de novo group; patients who had similar baseline characteristics as those in ALLEGRO-2b/3 were included in this analysis (≥50% scalp hair loss and without known etiology of hair loss). n's represent number of patients included in this analysis.

ASSESSMENTS & STATISTICAL ANALYSIS

- The time between $SALT_{30}$ response and achievement of SALT score ≤20 was evaluated (**Figure 2**)

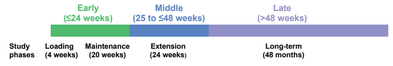
Figure 2. Timing between $SALT_{30}$ and SALT ≤20



SALT, Severity of Alopecia Tool; $SALT_{30}$, 30% improvement in SALT score from baseline.

- Results were analyzed overall and by when $SALT_{30}$ was achieved (**early**, **middle**, **late**) (**Figure 3**)

Figure 3. Timing of early, middle, and late $SALT_{30}$ response



SALT, Severity of Alopecia Tool; $SALT_{30}$, 30% improvement in SALT score from baseline.

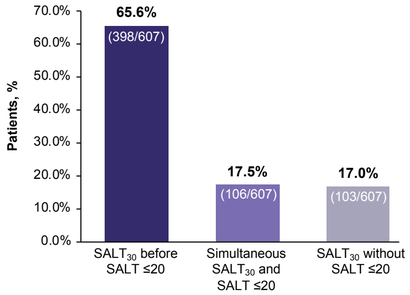
- The proportions of patients who achieved $SALT_{30}$ before, simultaneously with, or without SALT score ≤20 were calculated
- Kaplan-Meier method was used to calculate the **median time-to-event** with corresponding 95% confidence intervals and the **restricted mean survival times (RMST)** to event with corresponding standard errors
- Missing data were not imputed

RESULTS

Proportions of patients achieving $SALT_{30}$ response and SALT ≤20 response

- Among the 831 patients included in the analysis, 607 (73.0%) achieved a $SALT_{30}$ response
- Most of the 607 patients who achieved $SALT_{30}$ response also achieved SALT ≤20 response, and the majority of those achieved $SALT_{30}$ before SALT ≤20 (**Figure 4**)

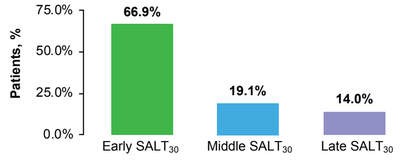
Figure 4. Proportions of patients who achieved $SALT_{30}$ before, simultaneously with, or without SALT ≤20



SALT, Severity of Alopecia Tool; SALT30, 30% improvement in SALT score from baseline.

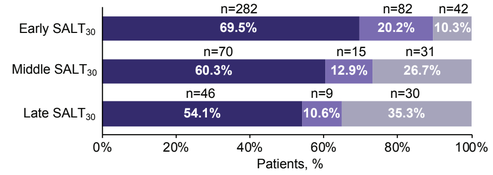
- Among the 607 patients who achieved $SALT_{30}$, most (66.9%) achieved early $SALT_{30}$ response (within 24 weeks) (**Figure 5**)
- A higher proportion of patients with a late $SALT_{30}$ response did not reach SALT ≤20 (35.3%) compared with those with an early or middle $SALT_{30}$ response (10.3% and 26.7%, respectively) (**Figure 6**)

Figure 5. Proportions of patients who achieved early, middle, and late $SALT_{30}$



SALT, Severity of Alopecia Tool; SALT30, 30% improvement in SALT score from baseline.

Figure 6. Proportions of patients who achieved $SALT_{30}$ and SALT ≤20 by early, middle, and late $SALT_{30}$

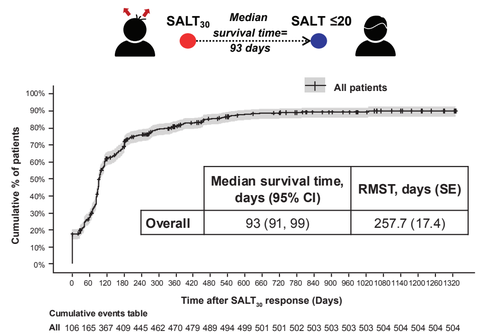


SALT, Severity of Alopecia Tool; $SALT_{30}$, 30% improvement in SALT score from baseline.

Time to SALT score ≤20 after $SALT_{30}$ response

- The overall median survival time from $SALT_{30}$ response to SALT ≤20 was 93 days, with a RMST of 258 days (**Figure 7**)

Figure 7. Overall time to SALT ≤20 after $SALT_{30}$



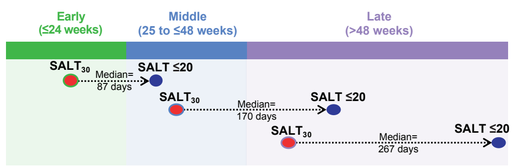
Cumulative events table

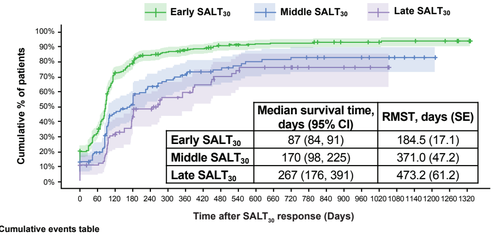
All	106	165	367	409	445	462	470	479	489	494	499	501	501	502	503	503	503	503	504	504	504	504	504		

Shaded areas represent the 95% confidence intervals.
CI, confidence interval; RMST, restricted mean survival time; SALT, Severity of Alopecia Tool; $SALT_{30}$, 30% improvement in SALT score from baseline; SE, standard error.

- The median survival time to SALT ≤20 was shorter for patients achieving early $SALT_{30}$ vs those with middle or late $SALT_{30}$ response (**Figure 8**)

Figure 8. Time to SALT ≤20 after early, middle, and late $SALT_{30}$ response





Cumulative events table

Early SALT30	82	134	290	317	337	345	348	352	358	359	361	362	362	362	363	363	363	363	364	364	364	364	364		
Middle SALT30	15	22	51	57	69	73	76	78	79	81	83	84	84	85	85	85	85	85	85	85	85	85	85		
Late SALT30	9	9	26	35	39	44	46	49	52	54	55	55	55	55	55	55	55	55	55	55	55	55	55		

Shaded areas represent the 95% confidence intervals.
CI, confidence interval; RMST, restricted mean survival time; SALT, Severity of Alopecia Tool; $SALT_{30}$, 30% improvement in SALT score from baseline; SE, standard error.

LIMITATIONS

- Patient visit schedule is not uniform, and measurement is less precise at later time points throughout the study due to less frequent visits
  - Therefore, time to event is likely overestimated in patients who achieve initial response later in the study
- Analyses are unadjusted; comparisons between patients achieving early, middle, and late $SALT_{30}$ response should be interpreted with caution
- RMST is sensitive to outlier values, thus median times are reported

CONCLUSIONS

- Considerable variability in the timing was observed in the overall cohort, though patients with early initial hair regrowth ($SALT_{30}$) achieved the clinically meaningful target of SALT ≤20 response in shorter median time than patients with later initial hair regrowth
- These results can help inform treatment expectations and goal setting between patients and their clinicians considering ritlecitinib therapy

REFERENCES

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

DISCLOSURES

This study was funded by Pfizer Inc. *KA Hansen is a former employee of Pfizer Inc. and was a consultant for Pfizer at the time of this analysis. G Bonfanti is an employee of Engineering Ingegneria Informatica and a paid sub-contractor to Health Services Consulting Corporation, in conjunction with this analysis. R.A. Edwards is an employee of Health Services Consulting Corporation and received consultancy fees from Pfizer Inc in connection with this study. P Farrant is a consultant for Pfizer and Eli Lilly and clinical trial investigator for Pfizer. A Mostaghimi has received personal fees from Hims and Hers Health, AbbVie, SUN Pharma, Pfizer, Digital Diagnostics, Eli Lilly, Equillium, ASLAN Pharmaceuticals, Boehringer Ingelheim, Acorn Healthcare, Otplex, and Legacy Healthcare. D Wajsbrot, A Lejeune, H Tran, and EH Law are employees of Pfizer Inc. and may hold stock/stock options in Pfizer. Support for third-party medical-writing assistance, provided by Nucleus Global, was funded by Pfizer Inc.

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