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Timing of Initial Hair Regrowth and Clinical Trial-Defined Response: Results of an ALLEGRO 2b/3 Post-Hoc Analysis

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BACKGROUND

- Alopecia areata (AA) is an autoimmune disease characterized by nonscarring hair loss ranging from small bald patches to complete scalp, face, and/or body hair loss[1]
- With recently approved therapies for severe AA, 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

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

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 in groups E, F, G (figure below) were not included in this analysis

	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

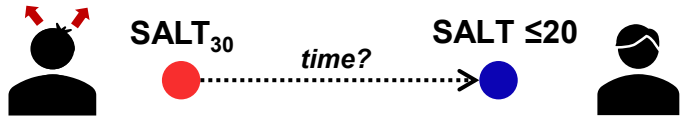
*Ritlecitinib dosing was once daily, at the doses indicated.
†This group is a subset of the ALLEGRO-LT *de novo* group; patients who had similar baseline characteristics as those in ALLEGRO-2b/3 were included in this analysis (≥50% scalp hair loss and without known etiology of hair loss).
n's represent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

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

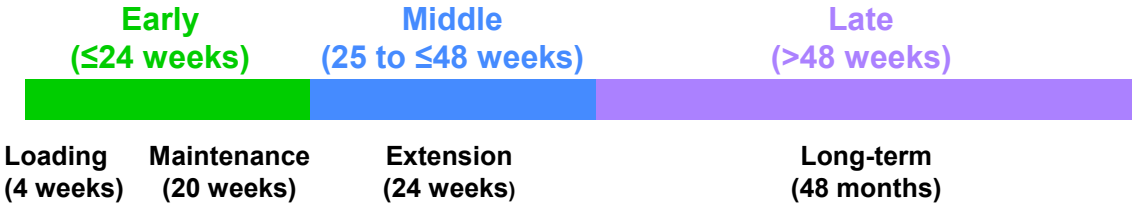
- Patients **aged ≥12 years**
- Diagnosis of AA with **≥50% scalp hair loss due to AA** (including alopecia totalis and alopecia universalis)
- Maximum duration of current episode of hair loss **≤10 years**

ASSESSMENTS & STATISTICAL ANALYSIS

- The time between $SALT_{30}$ response and achievement of SALT score ≤20 was evaluated



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



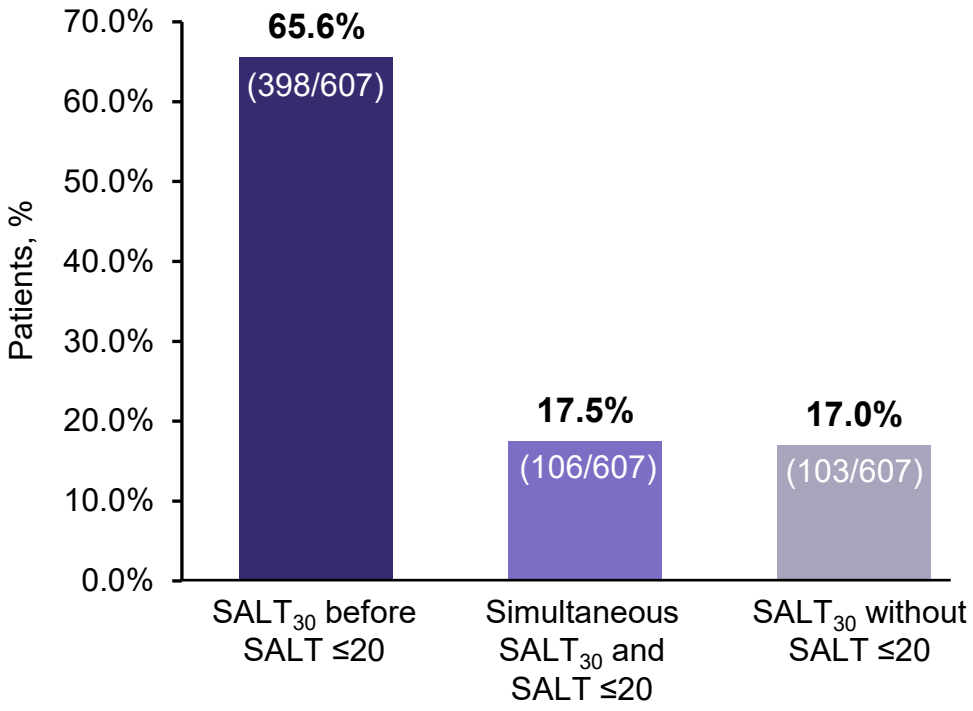
- The proportions of patients who achieved $SALT_{30}$ before, simultaneously with, or without SALT score ≤20 were calculated
- Kaplan-Meier method was used to calculate the **median time-to-event** with corresponding 95% confidence intervals and the **restricted mean survival times (RMST)** to event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

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

RESULTS

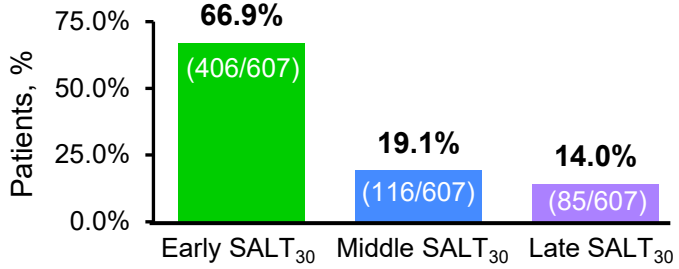
Proportions of patients who achieved $SALT_{30}$ before, simultaneously with, or without SALT ≤20

- 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**)



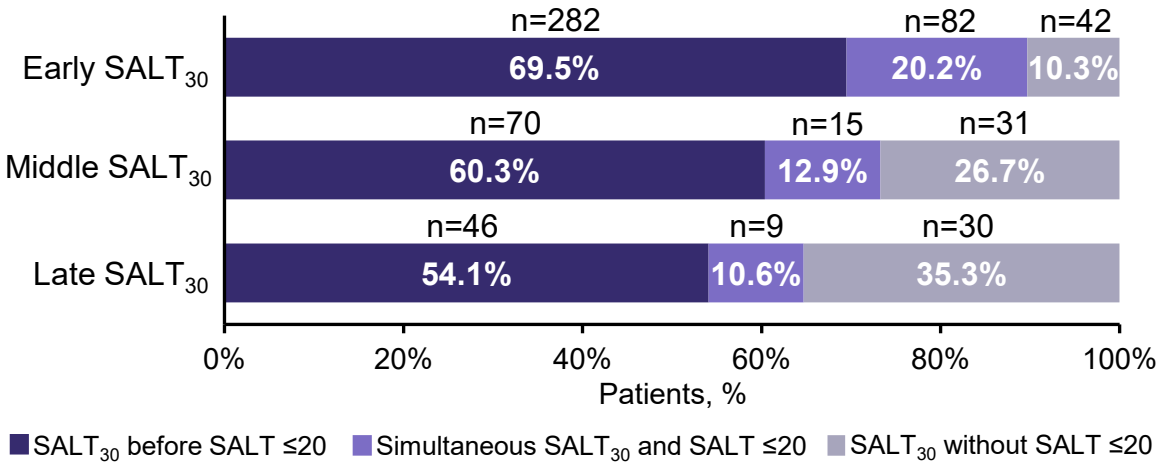
Proportions of patients who achieved early, middle, and late $SALT_{30}$

- Among the 607 patients who achieved $SALT_{30}$, most (66.9%) achieved early $SALT_{30}$ response (within 24 weeks)



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

- 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)

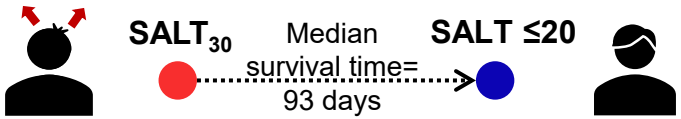


SALT, Severity of Alopecia Tool; $SALT_{30}$, 30% improvement in SALT score from baseline.

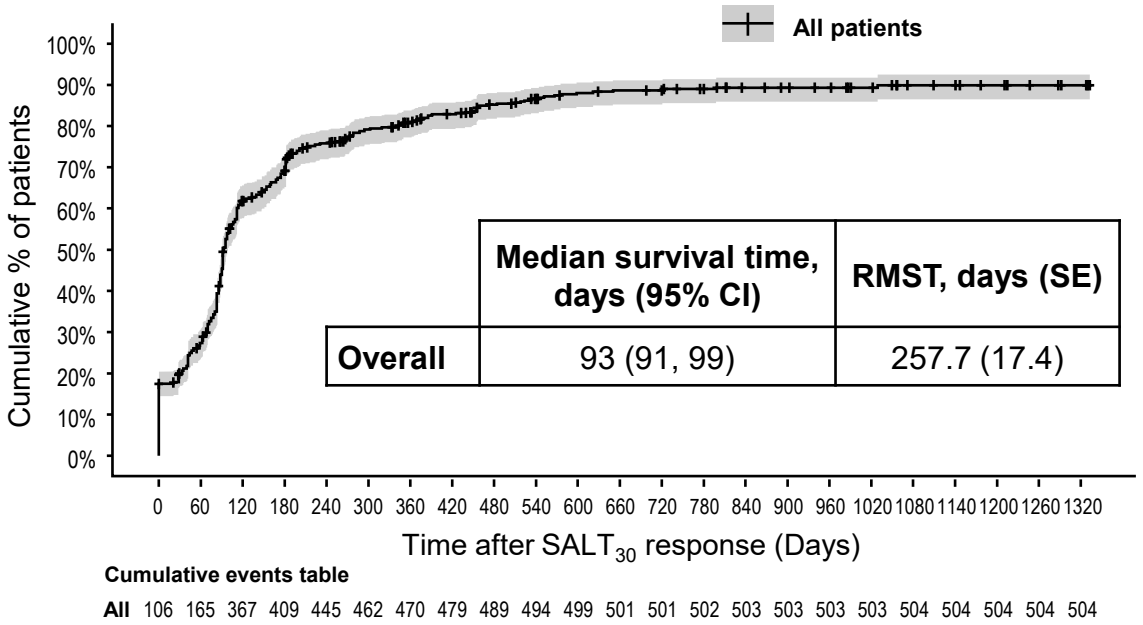
RESULTS

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



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



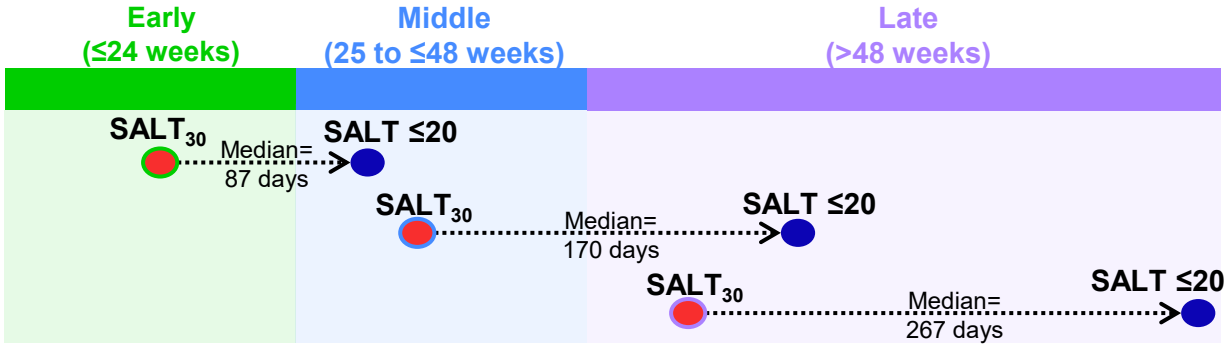
	Median survival time, days (95% CI)	RMST, days (SE)
Overall	93 (91, 99)	257.7 (17.4)

Cumulative events table

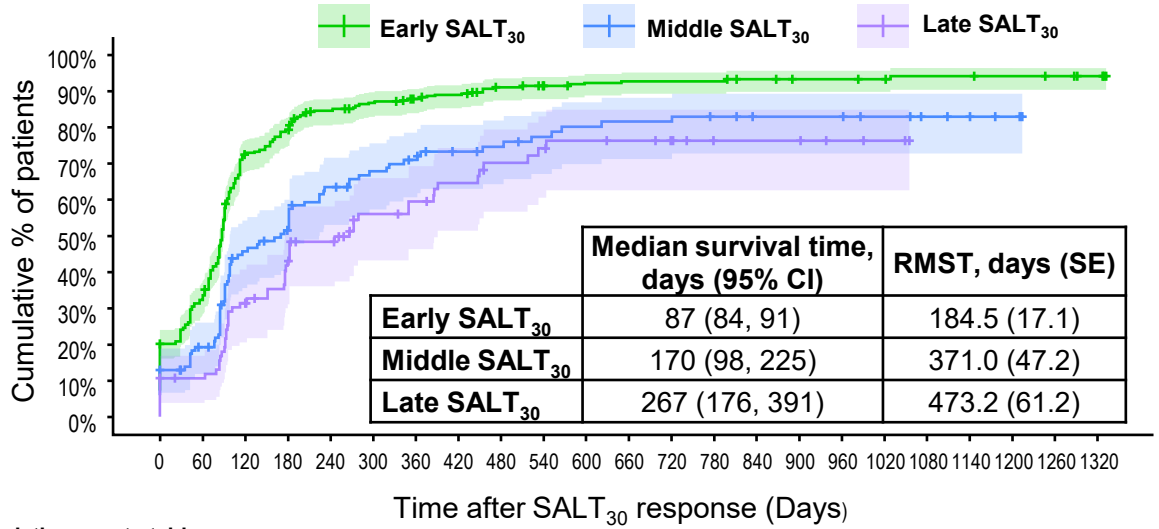
All	106	165	367	409	445	462	470	479	489	494	499	501	501	502	503	503	503	503	504	504	504	504	504	504

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



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



	Median survival time, days (95% CI)	RMST, days (SE)
Early $SALT_{30}$	87 (84, 91)	184.5 (17.1)
Middle $SALT_{30}$	170 (98, 225)	371.0 (47.2)
Late $SALT_{30}$	267 (176, 391)	473.2 (61.2)

Cumulative events table

Early $SALT_{30}$	82	134	290	317	337	345	348	352	358	359	361	362	362	362	363	363	363	363	364	364	364	364	364	364
Middle $SALT_{30}$	15	22	51	57	69	73	76	78	79	81	83	84	84	85	85	85	85	85	85	85	85	85	85	85
Late $SALT_{30}$	9	9	26	35	39	44	46	49	52	54	55	55	55	55	55	55	55	55	55	55	55	55	55	55

LIMITATIONS & CONCLUSIONS

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