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Timing of Patient-Reported Outcome Response and Clinical Response: Results of an ALLEGRO 2b/3 Post-Hoc Analysis

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BACKGROUND

- Alopecia areata (AA) is an autoimmune disease characterized by hair loss on the scalp, face, and/or body
- Ritlecitinib is a dual JAK3/TEC family kinase inhibitor that is approved (50 mg once daily) to treat severe AA in adults and adolescents ≥12 years old
- Understanding the timing of patient-reported improvement and/or satisfaction with hair regrowth and how it relates to initial scalp hair regrowth is important for setting patient and provider expectations during treatment

OBJECTIVE

- To characterize the timing between initial clinical scalp hair regrowth and two patient-reported outcomes (PROs), Patient Global Impression of Change (PGI-C) and Patient Satisfaction With Hair Growth (P-Sat overall), using integrated ALLEGRO trial data

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 (36 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

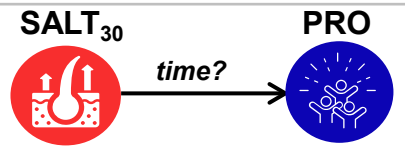
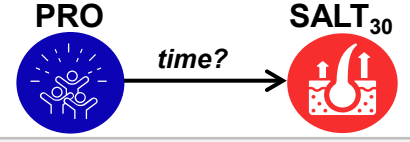
*Ritlecitinib dosing was once daily, at the doses indicated.
†This group is a subset of the ALLEGRO-LT *de novo* group; patients who had similar baseline characteristics as those in ALLEGRO-2b/3 were included in this analysis (≥50% scalp hair loss and without known etiology of hair loss).
n's represent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

- **Timing** was evaluated between clinical response as measured by ≥30% improvement from baseline in Severity of Alopecia Tool score ($SALT_{30}$) and each of the two **PROs**:
  - Patient Global Impression of Change (PGI-C) response†
  - Patient Satisfaction With Hair Growth (P-Sat overall) response‡

First $SALT_{30}$ response to PRO response	
First PRO response to $SALT_{30}$ response	
Overall and by first response timing (**early** [≤24 weeks], **middle** [25 to <48 weeks]), and **late** [≥48 weeks])	

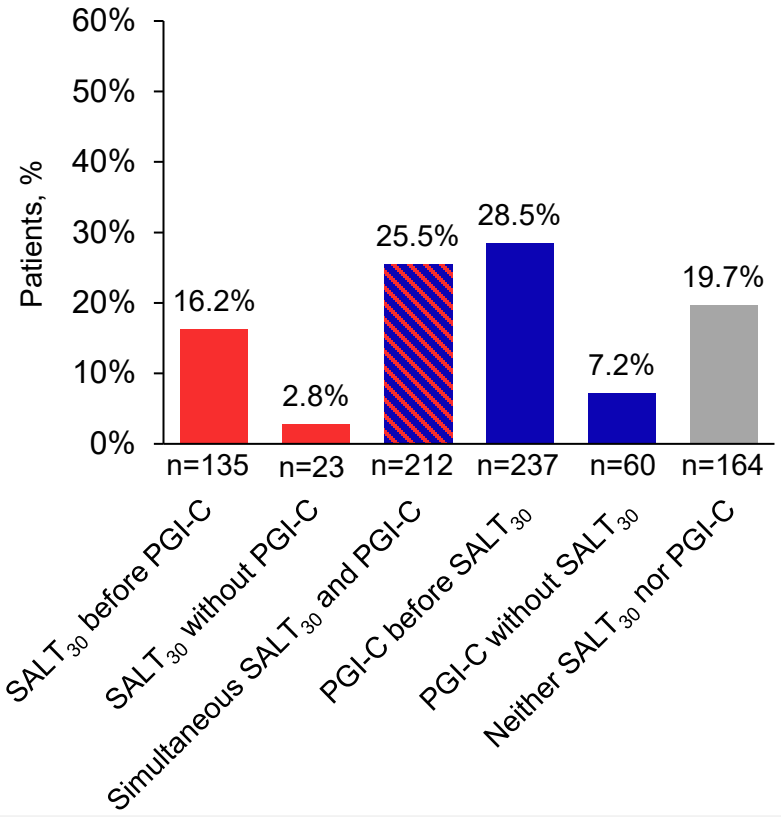
†PGI-C response defined as PGI-C score of "moderately improved" or "greatly improved".
‡P-Sat item response defined as "very satisfied", "moderately satisfied", or "slightly satisfied".

- The proportions of patients with unique PRO-$SALT_{30}$ sequences were calculated
- Kaplan-Meier method was used to calculate the **restricted mean survival times (RMST)** to event with corresponding standard errors and **median time-to-event** with corresponding 95% confidence intervals
- Missing data were not imputed

RESULTS: Timing between patient-reported improvement and $SALT_{30}$

Proportion of patients with PGI-C response *before or after* $SALT_{30}$ response

- Of the 831 patients included in the analysis, most achieved **PGI-C** response *before* (28.5%) or *simultaneous* (25.5%) with $SALT_{30}$ response

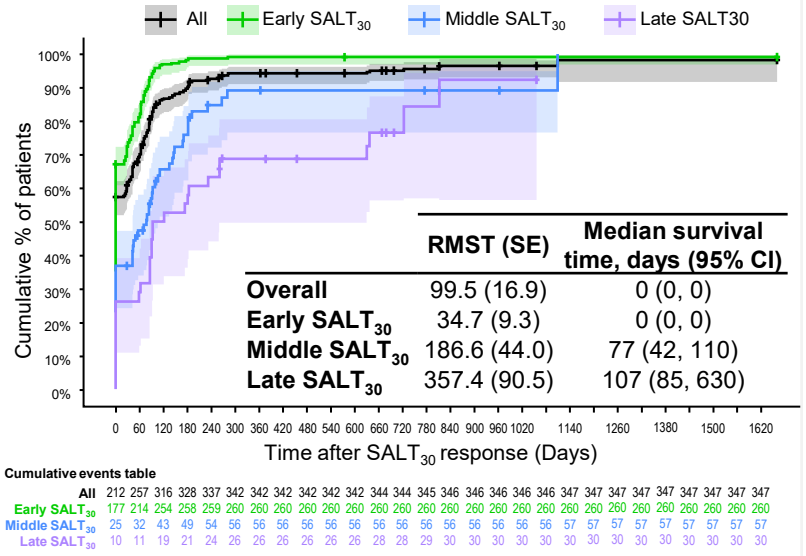


Time to PGI-C response *after* $SALT_{30}$ response

$SALT_{30}$ → ? → PGI-C

- Overall RMST to **PGI-C** response after first $SALT_{30}$ response was **99.5 days**
- Among early, middle, and late **$SALT_{30}$ responders**, RMST to PGI-C response after first $SALT_{30}$ response was 34.7, 186.6, and 357.4 days

Cumulative probability of achieving PGI-C response after $SALT_{30}$ response



	RMST (SE)	Median survival time, days (95% CI)
Overall	99.5 (16.9)	0 (0, 0)
Early $SALT_{30}$	34.7 (9.3)	0 (0, 0)
Middle $SALT_{30}$	186.6 (44.0)	77 (42, 110)
Late $SALT_{30}$	357.4 (90.5)	107 (85, 630)

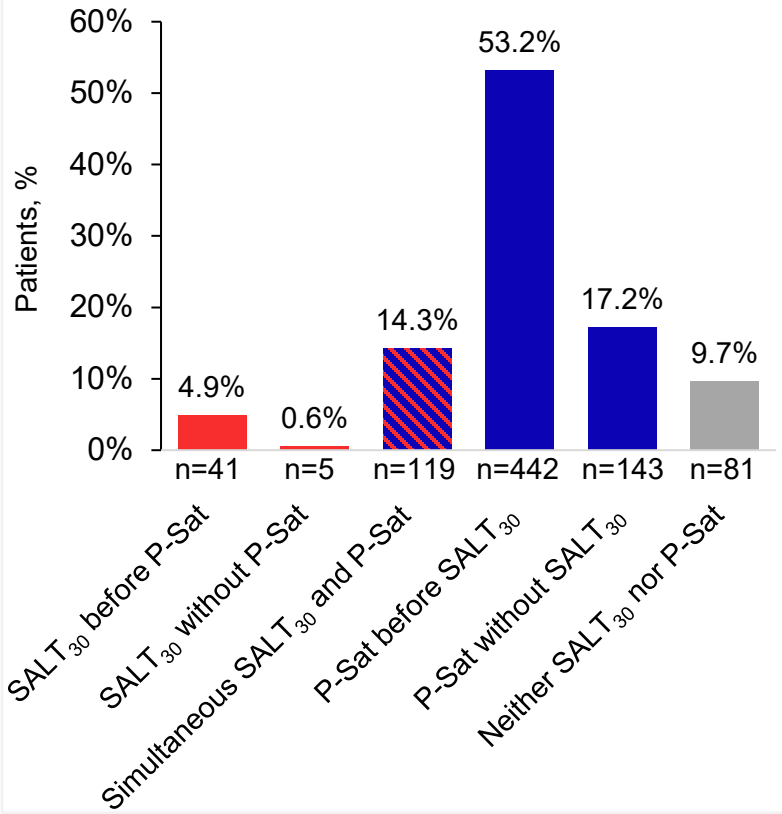
Cumulative events table

| | | |

RESULTS: Timing between patient-reported improvement and $SALT_{30}$

Proportion of patients with P-Sat response *before or after* $SALT_{30}$ response

- Of the 831 patients included in the analysis, the majority (53.2%) achieved **P-Sat (overall) response** *before* $SALT_{30}$ response

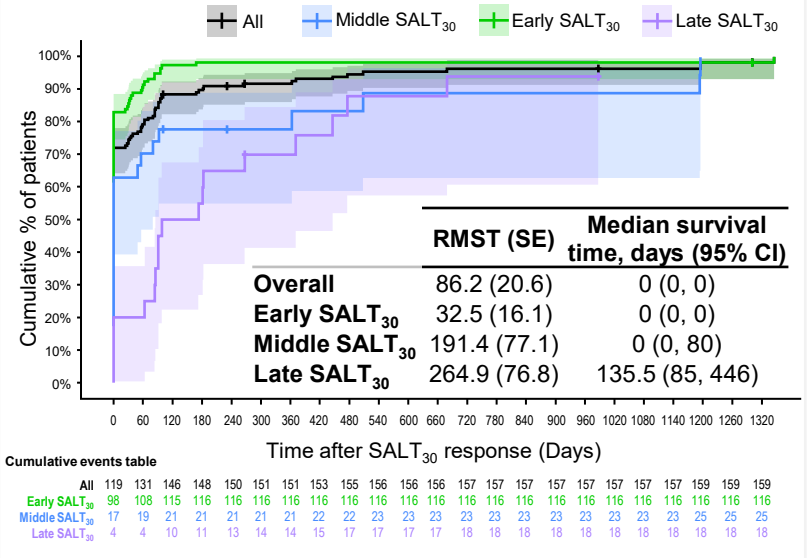


Time to P-Sat response *after* $SALT_{30}$ response

$SALT_{30}$ → ? → P-Sat

- Overall RMST to **P-Sat** response after $SALT_{30}$ response was **86.2 days**
- Among early, middle, and late **$SALT_{30}$ responders**, RMST to P-Sat response after $SALT_{30}$ response was 32.5, 191.4, and 264.9 days

Cumulative probability of achieving P-Sat overall response after $SALT_{30}$ response

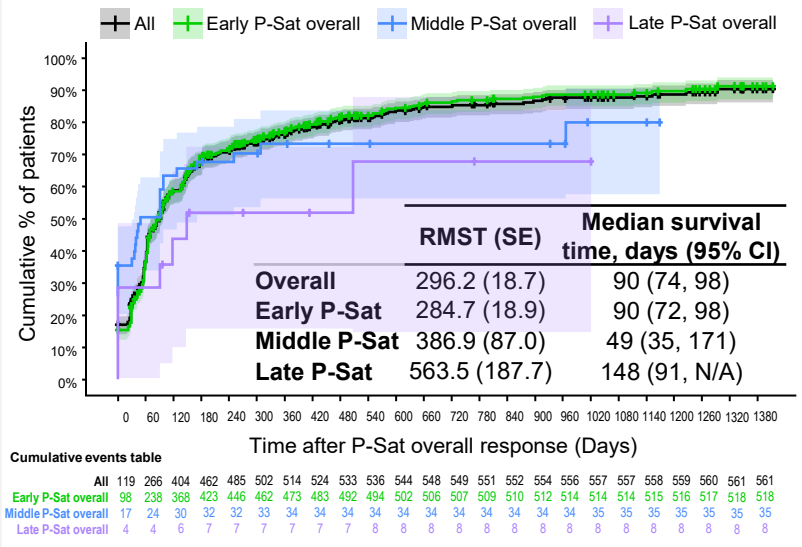


Time to $SALT_{30}$ response *after* P-Sat response

P-Sat → ? → $SALT_{30}$

- Overall RMST to $SALT_{30}$ response after **P-Sat** response was **296.2 days**
- Among early, middle, and late **P-Sat responders**, RMST to $SALT_{30}$ response after P-Sat response was 284.7, 386.9, and 563.5 days

Cumulative probability of achieving $SALT_{30}$ response after P-Sat overall response



Shaded areas represent the 95% confidence intervals. P-Sat item response defined as “very satisfied”, “moderately satisfied”, or “slightly satisfied”. P-Sat (overall), Patient Satisfaction with overall hair regrowth; RMST, restricted mean survival time; $SALT_{30}$, 30% improvement in Severity of Alopecia Tool from baseline; SE, standard error.

LIMITATIONS & CONCLUSIONS

LIMITATIONS

- SALT measurements and PRO measurements were not collected on the same schedule
  - Time to event may be overestimated in periods where there is a SALT measurement, but no PRO measurement
- 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; therefore, comparisons between early, middle, and late responders should be interpreted with caution
- RMST is sensitive to outlier values, thus median times are reported to provide additional information



CONCLUSIONS

- These findings indicate variability in the timing of initial PRO response and initial hair regrowth
- A large proportion of patients achieve PRO response *before* $SALT_{30}$ response, particularly for P-Sat
  - This suggests that many patients receiving ritlecitinib perceive therapeutic benefit before clinical response as defined by $SALT_{30}$