

# When to expect scalp hair regrowth during treatment of severe alopecia areata with baricitinib: insights from trajectories analyses of patients enrolled in two phase III trials

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## Abstract

**Background** Baricitinib is approved for the treatment of adults with severe alopecia areata (AA). In the absence of robust data on the patterns of regrowth during treatment of severe AA, there is a gap in the knowledge regarding treatment expectations.

**Objectives** To examine whether different clinical response subgroups could be identified in baricitinib-treated patients with severe AA and factors that contribute to these subgroups.

**Methods** The BRAVE-AA1 and BRAVE-AA2 phase III trials enrolled patients with severe AA [Severity of Alopecia Tool (SALT) score  $\geq 50$  ( $\geq 50\%$  scalp hair loss)]. Patients randomized to baricitinib 4 mg or 2 mg retained their treatment allocation for 52 weeks. Based on patterns identified through growth mixture modelling (GMM), patients were categorized into responder subgroups according to when they first achieved  $\geq 30\%$  improvement from baseline in SALT score (SALT<sub>30</sub>). For each responder subgroup, trajectories of response (i.e. achievement of a SALT score  $\leq 20$ , SALT score  $\leq 10$  and  $\geq 50\%$  change from baseline in SALT score) and baseline disease characteristics are reported.

**Results** Respectively, 515 and 340 patients were randomized to once-daily baricitinib 4 mg and 2 mg at baseline; 69% and 51%, respectively, achieved SALT<sub>30</sub> at least once by week 52. Based on GMM findings, we identified three responder subgroups: early (SALT<sub>30</sub> by week 12), gradual (SALT<sub>30</sub> after week 12–week 36) and late (SALT<sub>30</sub> after week 36–week 52). The proportions of early, gradual and late responders and nonresponders were, respectively, 33%, 28%, 8% and 31% among patients treated with baricitinib 4 mg, and 20%, 23%, 9% and 49%, respectively, among those treated with baricitinib 2 mg. Early responders had a shorter trajectory to maximal clinical outcomes (e.g.  $> 78\%$  achieved a SALT score  $\leq 20$  by week 36) vs. gradual or late responders. Early responders were more frequent among patients with baseline severe AA (SALT score 50 to  $< 95$ ) vs. very severe AA (SALT score 95–100). Overall, responders (early to late) were more frequent in patients with short ( $< 4$  years) episodes of hair loss.

**Conclusions** These analyses identified early, gradual and late responder subgroups for scalp hair regrowth in baricitinib-treated patients with severe AA, and that these subgroups are influenced by baseline characteristics. Findings from these analyses will help to inform treatment expectations for scalp hair regrowth.

### What is already known about this topic?

- Baricitinib is a systemic therapy approved for the treatment of severe alopecia areata (AA) in the USA, Europe, Japan and Australia.
- There is limited literature on the trajectory of hair regrowth in patients with severe AA in response to systemic therapy. Therefore, it remains difficult for clinicians to set expectations with patients and to predict the amount of time necessary to observe terminal hair regrowth during treatment.
- There is an incomplete understanding of the extent to which baseline disease characteristics (e.g. severity of hair loss and/or duration of current disease episode) can influence response to treatment.

Accepted: 19 July 2023

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**What does this study add?**

- This post hoc analysis of 52-week data from two pivotal phase III clinical trials shows that patients with severe AA treated with baricitinib 2 mg or 4 mg once-daily follow three distinct hair-regrowth response patterns – early, gradual and late – based on their time to scalp hair regrowth, as measured by changes in Severity of Alopecia Tool (SALT) scores.
- The analysis shows that baseline disease severity influences the response pattern.
- This analysis can be applied in routine clinical practice to help inform treatment expectations with baricitinib and decisions about patient management.

Alopecia areata (AA) is an autoimmune disease characterized by nonscarring hair loss involving any hair-bearing site; it ranges in severity from one or a few patches to total loss of hair on the scalp and/or body.<sup>1</sup> The loss of the hair follicle immune privilege leads to premature termination of the anagen phase and entry into catagen phase.<sup>2</sup> By blocking intracellular signalling of key cytokines involved in the immunopathogenesis of AA, including interferon- $\gamma$  and interleukin (IL)-15, Janus kinase (JAK) inhibitors promote hair regrowth.<sup>3,4</sup>

Unlike other immune-mediated dermatoses (e.g. psoriasis or atopic dermatitis) where treatment benefits are often seen early during treatment, hair regrowth in AA can take much longer.<sup>5</sup> While it is established that baseline disease characteristics can influence response to treatment in AA, there is still a gap in the knowledge regarding patterns of hair regrowth.<sup>5–7</sup> This, together with a general unfamiliarity regarding successful treatment of severe AA, makes it challenging for clinicians to understand treatment responses, much less be able to guide expectations in patients.

The oral JAK1/JAK2 reversible inhibitor baricitinib, at a dose of 2 mg or 4 mg once daily, has shown efficacy vs. placebo in eyebrow, eyelash and scalp hair regrowth in two 36-week placebo-controlled phase III clinical trials (BRAVE-AA1 and BRAVE-AA2) and is approved for the treatment of adults with severe AA.<sup>8,9</sup> During these trials, patients randomized to baricitinib at baseline remained on the same dose for 52 weeks, with no rescue with other medications. We observed that while most responses were observed during the first months of treatment, response rates continued to increase over the 52-week period as some patients had a delayed response.<sup>10</sup>

To better characterize patterns of response to treatment with baricitinib for patients enrolled in BRAVE-AA1 and BRAVE-AA2, we used a two-step approach. Firstly, we used growth mixture modelling (GMM) of patients' scalp hair loss over time, as assessed by changes in the Severity of Alopecia Tool (SALT)<sup>11</sup> score, to identify different patterns of response. Three response patterns emerged and provided the rationale for the second step, which was to further describe the patterns based on time to initial clinical response. We report here the trajectories for key clinical endpoints, as well as the baseline disease characteristics for each subgroup of responders. The results from these analyses provide a resource for patients and clinicians to inform treatment expectations in patients with severe AA treated with baricitinib.

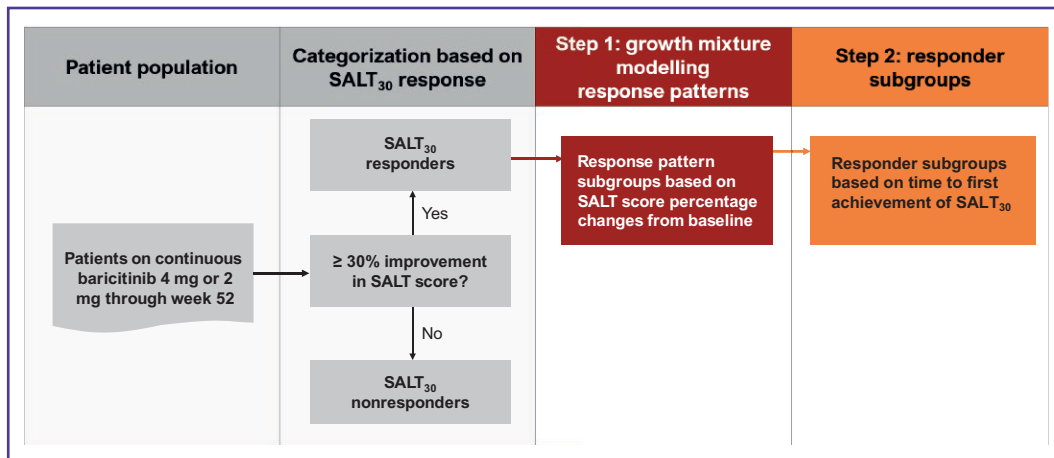
**Patients and methods****Study population**

This was a post hoc analysis of the phase III portion of the adaptive phase II–III trial BRAVE-AA1 (NCT03570749) and the phase III trial BRAVE-AA2 (NCT03899259), two double-blind, parallel-group, randomized, placebo-controlled trials conducted at 169 centres in 10 countries. The trials have identical eligibility criteria and design for the first 52 weeks. The trial protocols have been reported previously.<sup>8–10</sup> Briefly, enrolled patients were aged 18–60 years (men) and 18–70 (women), with a SALT score  $\geq 50$  ( $\geq 50\%$  scalp hair loss) and a current AA episode lasting  $> 6$  months to  $< 8$  years without spontaneous improvement (i.e.  $\leq 10$ -point reduction in SALT score) over the 6 months prior to screening. Patients were randomized 3 : 2 : 2 to receive once-daily baricitinib 4 mg, baricitinib 2 mg or placebo for 52 weeks, with placebo nonresponder patients rescued at week 36. All patients who completed the 36-week placebo-controlled period entered an extension phase for up to 68 weeks of additional treatment. This analysis focuses on patients randomized at baseline to receive baricitinib 2 mg or 4 mg who maintained the same dose through to week 52.

**Identification of response patterns and clinical subgroups****Step 1**

Patients who received continuous baricitinib 2 mg or baricitinib 4 mg for 52 weeks were first categorized into responders and nonresponders based on the achievement of a  $\geq 30\%$  improvement in SALT score (SALT<sub>30</sub>) at any point within the 52 weeks (Figure 1). The SALT<sub>30</sub> response has previously been used to define initial response in phase II clinical trials, including as a component of the BRAVE-AA1 phase II trial to select doses for the phase III components of BRAVE-AA1 and BRAVE-AA2.<sup>8,9,12</sup>

GMM is an unsupervised machine learning technique used to cluster patients into different subgroups based on similar trajectories.<sup>13</sup> We applied GMM to the SALT<sub>30</sub> responder population, to identify different treatment response patterns, using the individual patient trajectories for percentage change of SALT score from baseline over 52 weeks (Figure S1; see [Supporting Information](#)). GMM revealed three response patterns characterized by different speeds of onset of efficacy (Figures S2, S3; see [Supporting Information](#)).



**Figure 1** Overview of the two-step process toward defining responder subgroups. SALT, Severity of Alopecia Tool; SALT<sub>30</sub>, ≥30% improvement from baseline in SALT score.

### Step 2

For the majority of patients, the response patterns revealed by GMM aligned with the timing of their first reported SALT<sub>30</sub> response. Therefore, the clinical criterion of time to first achievement of SALT<sub>30</sub> was applied to the responder population, leading to identification of the following three responder subgroups: early responders who first achieved SALT<sub>30</sub> within 12 weeks; gradual responders who first achieved SALT<sub>30</sub> after week 12 and up to week 36; and late responders who first achieved SALT<sub>30</sub> after week 36 and up to week 52.

### Main outcomes and measures

Among SALT<sub>30</sub> nonresponders and each of the responder subgroups, the proportions of patients who achieved the following clinical outcomes for scalp hair regrowth are reported through to week 52: SALT score ≤ 10, SALT score ≤ 20 and ≥ 50% improvement from baseline in SALT score (SALT<sub>50</sub>). In addition, baseline demographics and disease characteristics, including the proportion of patients with severe (SALT 50 to < 95) vs. very severe (SALT score 95–100) AA<sup>11</sup> and duration of current episode (< 4 years vs. ≥ 4 years), are reported.

### Statistical analysis

The full analysis set for patients randomized to baricitinib 2 mg or baricitinib 4 mg was considered in these analyses. Data were censored after permanent study drug discontinuation or if collected remotely due to the COVID-19 pandemic. The modified last observation carried forward method was applied to impute missing data. Statistical analyses were performed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

## Results

### Patient demographics

Among those enrolled in the BRAVE-AA1 and BRAVE-AA2 trials, 515 and 340 patients were randomized to receive

baricitinib 4 mg and baricitinib 2 mg, respectively, of whom 461 (89.5%) and 297 (87.3%) completed week 52. Patient demographics and baseline characteristics were comparable across the baricitinib 4-mg and 2-mg treatment arms (overall population; Table 1). In the baricitinib 4-mg and baricitinib 2-mg groups, respectively, mean patient age was 37.1 and 38.4 years, 60% and 62% were female, 52% and 54% were White, 35% and 37% were Asian and 9% and 6% were Black or African American. Also, the duration of current episode at baseline was 3.68 and 4.10 years, with 36% and 32% having a duration of ≥ 4 years, respectively. Mean baseline SALT score was 85.1 and 86.3, respectively, with 52% and 57% of patients, respectively, reported as having a very severe AA (SALT score 95–100) at baseline.

Based on the achievement of SALT<sub>30</sub> at any point within 52 weeks, 355 (68.9%) patients receiving baricitinib 4 mg and 174 (51.2%) receiving baricitinib 2 mg were classified as responders.

### Identification of different responder subgroups based on growth mixture modelling findings

The respective numbers of early, gradual and late responders were 168 (32.6%), 146 (28.3%) and 41 (8.0%) among the 515 patients treated with baricitinib 4 mg, and 67 (19.7%), 78 (22.9%) and 29 (8.5%) of the 340 treated with baricitinib 2 mg (Figures 2, 5). Representative photographs of patients treated with baricitinib 4 mg in each responder subgroup are shown in Figure 3.

### Trajectories of response for each responder subgroup

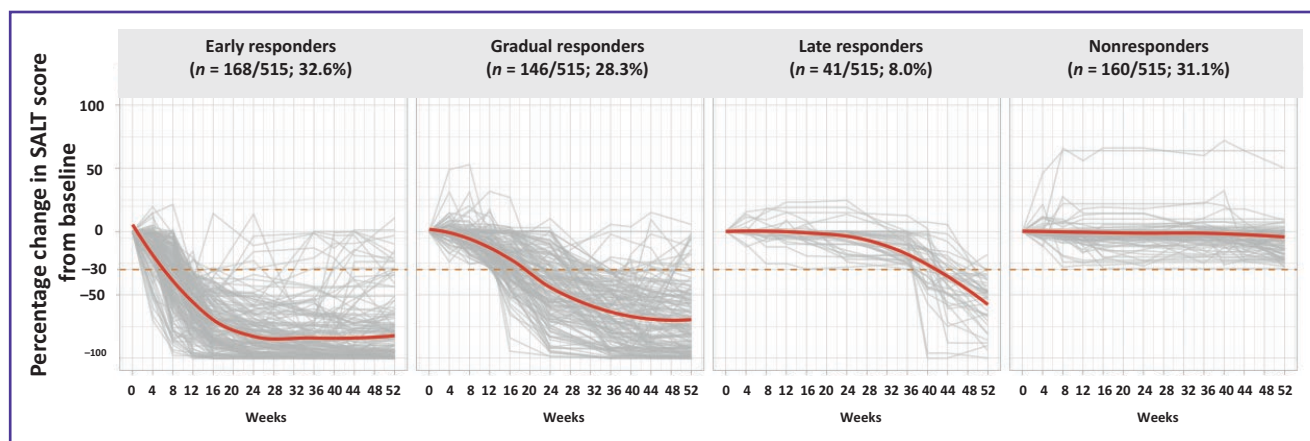
When examining trajectories of response, >80% of early responders treated with baricitinib 4 mg achieved a SALT<sub>50</sub> response by week 16 and >70% achieved a SALT score ≤ 20 as early as week 24, with up to 62% achieving a SALT score ≤ 10 by week 52. Among the baricitinib 4-mg gradual responders, 79% achieved SALT<sub>50</sub>, 51% achieved a SALT score ≤ 20 and 34% achieved a SALT score ≤ 10 by week 52. Among the late responders, 51% achieved SALT<sub>50</sub>, 20% achieved a SALT score ≤ 20 and 10% achieved a SALT score ≤ 10 by week 52 (Figure 4). Among patients treated with baricitinib 2 mg, response rates for SALT<sub>50</sub>, SALT score ≤ 20 and SALT score ≤ 10 across the three responder

**Table 1** Baseline characteristics of patients in the phase III BRAVE-AA1 and BRAVE-AA2 trials treated with baricitinib 4 mg and baricitinib 2 mg once daily, overall, in SALT<sub>30</sub> nonresponders and by different responder subgroups

Response	Baricitinib 4 mg					Baricitinib 2 mg				
	Early (n = 168)	Gradual (n = 146)	Late (n = 41)	Nonresponders (n = 160)	Overall (n = 515)	Early (n = 67)	Gradual (n = 78)	Late (n = 29)	Nonresponders (n = 166)	Overall (n = 340)
Age (years), mean (SD)	37.7 (12.8)	36.2 (12.5)	37.7 (14.9)	37.1 (13.2)	37.1 (13.0)	37.7 (11.1)	38.2 (13.8)	37.8 (14.1)	38.9 (13.0)	38.4 (12.9)
Female sex	109 (64.9)	85 (58.2)	26 (63.4)	89 (55.6)	309 (60.0)	38 (56.7)	47 (60.3)	21 (72.4)	106 (63.9)	212 (62.4)
Race										
White	94 (56.0)	76 (52.1)	20 (48.8)	77 (48.1)	267 (51.8)	38 (56.7)	40 (51.3)	20 (69.0)	87 (52.4)	185 (54.4)
Asian	57 (33.9)	57 (39.0)	17 (41.5)	50 (31.2)	181 (35.1)	29 (43.3)	29 (37.2)	7 (24.1)	60 (36.1)	125 (36.8)
Black or African American	10 (6.0)	10 (6.8)	3 (7.3)	23 (14.4)	46 (8.9)	0 (0)	3 (3.8)	2 (6.9)	14 (8.4)	19 (5.6)
Duration of current AA episode (years)										
Mean (SD)	3.43 (3.06)	3.08 (2.76)	3.11 (3.59)	4.63 (3.91)	3.68 (3.37)	3.28 (4.42)	3.26 (3.69)	3.89 (5.48)	4.87 (6.24)	4.10 (5.38)
< 4	119 (70.8)	105 (71.9)	29 (70.7)	76 (47.5)	329 (63.9)	52 (77.6)	60 (76.9)	20 (69.0)	98 (59.0)	230 (67.6)
≥ 4	49 (29.2)	41 (28.1)	12 (29.3)	84 (52.5)	186 (36.1)	15 (22.4)	18 (23.1)	9 (31.0)	68 (41.0)	110 (32.4)
Duration since AA onset (years), mean (SD)	10.0 (10.2)	10.4 (10.2)	12.7 (12.4)	14.8 (11.8)	11.8 (11.1)	9.20 (8.67)	11.5 (10.5)	14.3 (12.5)	14.1 (11.0)	12.6 (10.7)
Baseline AA severity										
Severe (SALT score 50 to < 95)	122 (72.6)	68 (46.6)	14 (34.1)	44 (27.5)	248 (48.2)	54 (80.6)	34 (43.6)	10 (34.5)	49 (29.5)	147 (43.2)
Very severe (SALT score 95–100)	46 (27.4)	78 (53.4)	27 (65.9)	116 (72.5)	267 (51.8)	13 (19.4)	44 (56.4)	19 (65.5)	117 (70.5)	193 (56.8)
SALT score, mean (SD) <sup>a</sup>	78.1 (18.1)	84.8 (18.4)	90.0 (15.9)	91.4 (15.7)	85.1 (18.1)	73.3 (18.0)	85.9 (18.3)	86.1 (19.8)	91.7 (14.7)	86.3 (18.0)

AA, alopecia areata; SALT, Severity of Alopecia Tool. <sup>a</sup>SALT scores range from 0 to 100, with 0 representing no scalp hair loss and 100 complete hair loss.





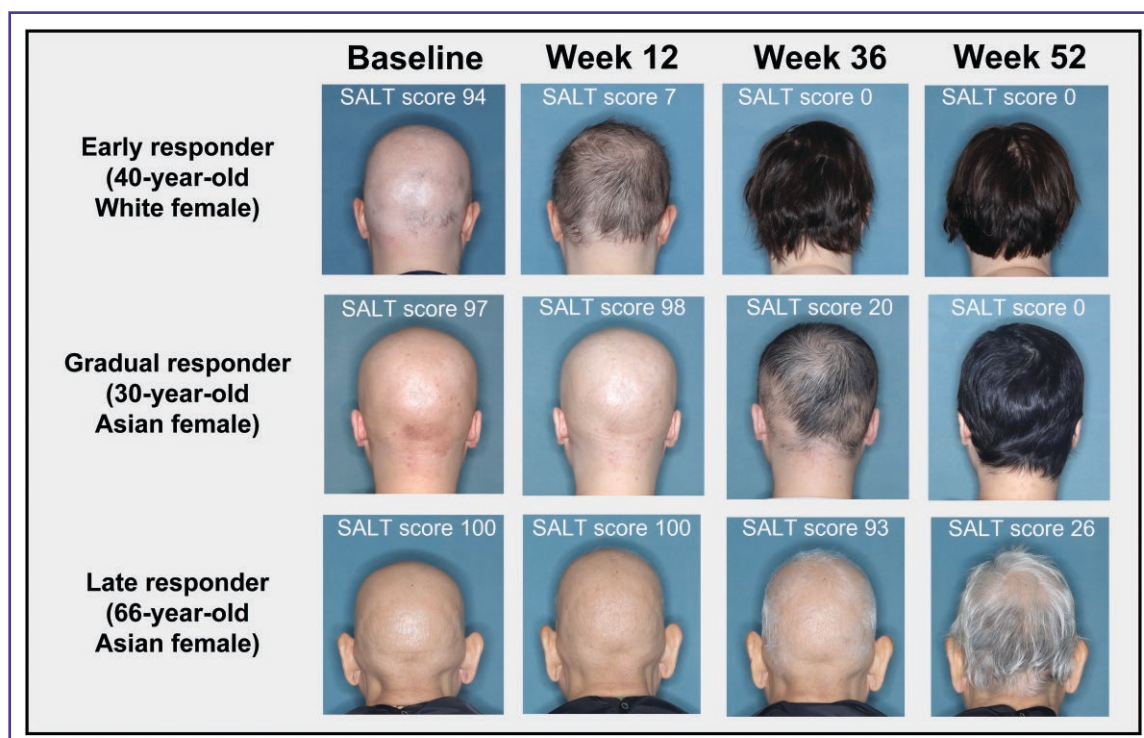
**Figure 2** Percentage change in Severity of Alopecia Tool (SALT) score from baseline through to week 52 for SALT<sub>30</sub> ( $\geq 30\%$  improvement from baseline in SALT score) early, gradual, late and nonresponders treated with baricitinib 4 mg. The grey lines indicate individual patients, the thick red lines are the smoothing lines using local polynomial regression fitting and the red dotted line indicates SALT<sub>30</sub>. Data were censored after permanent study drug discontinuation or data collected via remote visits due to the COVID-19 pandemic. Missing data were imputed using a modified last observation carried forward method.

subgroups followed similar trajectories as those for patients treated with baricitinib 4 mg, although with a slightly lower proportion of patients (Figure 6).

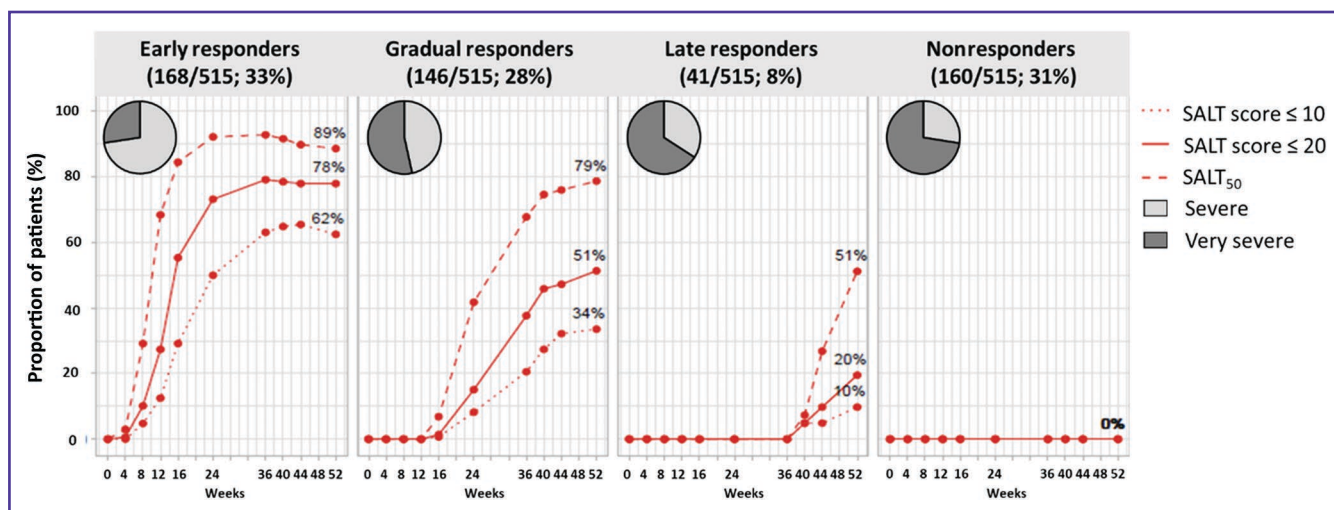
Baseline patient demographics did not differ across the different responder subgroups or in comparison with the nonresponder groups on both doses (Table 1). There was a trend for a slightly higher proportion of Black/African American patients among the nonresponder groups, but this observation should be interpreted with caution considering the overall small size of this subpopulation in the trials.

### *Distinct baseline demographics across each responder group*

Baseline disease characteristics differed across responder groups. The duration of current episode had an impact on the likelihood of achieving a SALT<sub>30</sub> response vs. nonresponse, with 69–77% of the responders across both treatment arms having a duration of current episode of hair loss of  $\leq 4$  years. In contrast, for nonresponders, between 48% and 59% had a shorter duration of current episode. Duration of current episode did not appear to influence whether the patient was



**Figure 3** Representative photographs of early-, gradual- and late-responder patients treated with baricitinib 4 mg through to week 52. The duration of current episode of alopecia areata was  $< 4$  years in all patients at baseline. SALT, Severity of Alopecia Tool. Copyright © 2023. Eli Lilly and Company. All rights reserved. Permission for any use should be sought from Eli Lilly and Company.



**Figure 4** Severity of Alopecia Tool (SALT) score  $\leq 10$ , SALT score  $\leq 20$  and SALT<sub>50</sub> ( $\geq 50\%$  improvement from baseline in SALT score) response trajectories over time by different responder subgroups among patients treated with baricitinib 4 mg. The insets show the proportion of patients with baseline severe (SALT score 50 to  $< 95$ ) and very severe (SALT score 95–100) alopecia areata in each responder subgroup. Data were censored after permanent study drug discontinuation or data collected via remote visits due to the COVID-19 pandemic. The modified last observation carried forward method was applied to impute missing data.

an early, gradual or late responder. Instead, baseline severity influenced responder subgroups. Among baricitinib 4-mg and baricitinib 2-mg early responder groups, respectively, 73% and 81% had severe AA (SALT score 50 to  $< 95$ ) at baseline. Conversely, the population with very severe AA accounted for about two-thirds of the late responders.

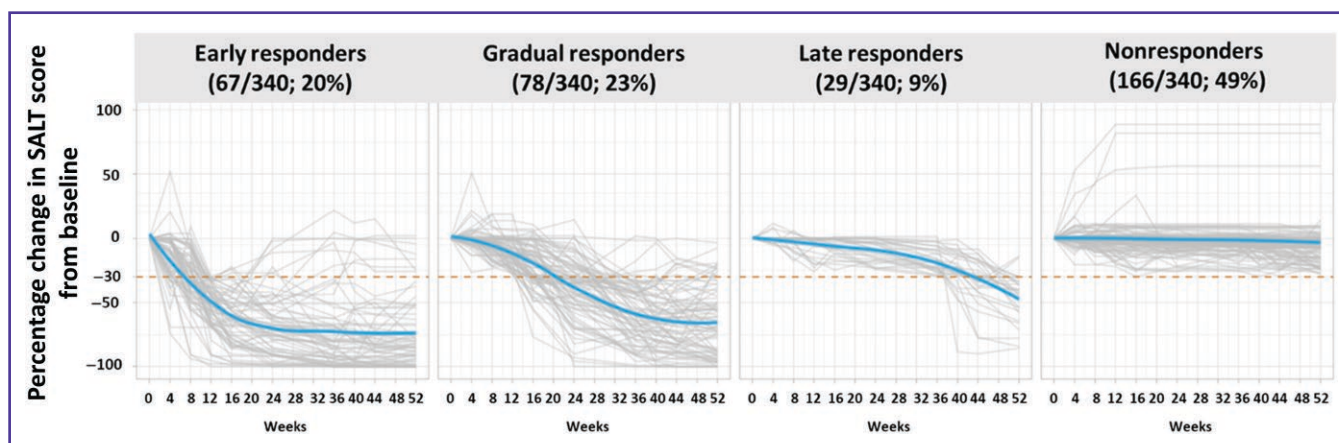
## Discussion

Here we report different responder subgroups among patients with severe AA treated with baricitinib, and their corresponding trajectories of scalp hair regrowth. The identification of three responder subgroups to baricitinib treatment, and the observation that segregation into these responder subgroups is influenced by baseline disease severity, adds

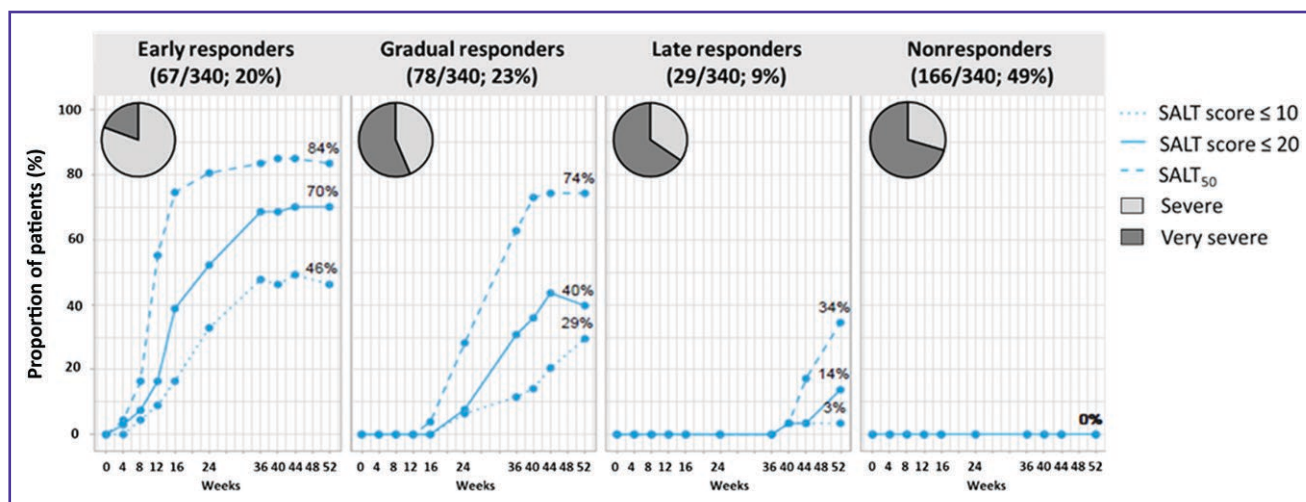
to our understanding of the disease and may help to guide expectations at the time of initiating treatment. Indeed, the time point at which a SALT<sub>30</sub> response is achieved could be used in clinical practice to predict when near-complete or complete hair regrowth is likely to occur.

Overall, a higher proportion of patients on baricitinib 4 mg were early and gradual responders vs. patients on baricitinib 2 mg, and a higher proportion of patients on baricitinib 4 mg also achieved clinically meaningful scalp hair regrowth (SALT score  $\leq 20$ ) vs. those on baricitinib 2 mg.

The analyses presented here confirm that baseline disease characteristics impact on treatment outcomes. Shorter duration of current episode of hair loss (i.e.  $< 4$  years) influenced the likelihood of response but did not determine whether a patient was an early, gradual or late responder. However, baseline disease severity influenced whether a



**Figure 5** Percentage change in Severity of Alopecia Tool (SALT) score from baseline through to week 52 for SALT<sub>30</sub> ( $\geq 30\%$  improvement from baseline in SALT score) early, gradual, late and nonresponders treated with baricitinib 2 mg. The thin grey lines indicate individual patients, the thick blue lines are the smoothing lines using local polynomial regression fitting and the red dotted lines indicate SALT<sub>30</sub>. Data were censored after permanent study drug discontinuation or data collected via remote visits due to the COVID-19 pandemic. Missing data were imputed using a modified last observation carried forward method.



**Figure 6** Severity of Alopecia Tool (SALT) score  $\leq 10$ , SALT score  $\leq 20$  and SALT<sub>50</sub> ( $\geq 50\%$  improvement from baseline in SALT score) response trajectories over time by different responder subgroups among patients treated with baricitinib 2 mg. The insets indicate the proportion of patients with baseline severe (SALT score 50 to  $< 95$ ) vs. very severe (SALT score 95–100) alopecia areata in each responder subgroup. Data were censored after permanent study drug discontinuation or data collected via remote visits due to the COVID-19 pandemic. The modified last observation carried forward method was applied to impute missing data.

patient was an early, gradual or late responder (and the likelihood of response). Specifically, patients with severe AA (SALT score 50 to  $< 95$ ) had a higher chance of being an early responder than patients with very severe AA (SALT score 95–100). While it was expected that patients with complete or near-complete scalp hair loss (i.e. very severe AA) would take more time to achieve regrowth than those with less severe AA, these data indicate that they are also more likely to have a delayed onset of response to therapy. This is particularly important as the absence of visible hair regrowth over the first months of treatment could lead to premature discontinuation in this subset of patients. The pathophysiology that might explain the different patterns of response is unclear, but there are biologic differences among patients with AA.

Early responders who received either baricitinib 4 mg or 2 mg achieved the greatest benefits in clinical outcomes during their first year of treatment. In this group, response rates for SALT score  $\leq 20$  and SALT score  $\leq 10$  maximized and appeared to plateau by about 36 weeks. In comparison, no plateau was evident in gradual responders during the 52-week treatment period, particularly in the baricitinib 4-mg treatment arm. This was also true of late responders. The proportion of patients who achieved scalp hair regrowth was lower among late responders than in the other subgroups; however, response rates appeared to be on an upward trajectory after week 40. A longer period of observation is required to confirm the optimal duration of treatment for gradual and late responders to achieve the maximal benefit. Importantly, the analyses presented here do not include response patterns for eyebrow and eyelash involvement, which will need to be examined in the future, to provide a more holistic view of hair regrowth across hair-bearing sites.

Treatment response trajectories for patients with severe AA have not been described previously. Analyses of patients treated with baricitinib 4 mg and 2 mg in the BRAVE-AA trials revealed three responder subgroups – early, gradual and late – defined by the time taken to achieve SALT<sub>30</sub>,

which was employed in this analysis as a clinical response. Baseline disease characteristics (i.e. duration of current episode and severity) and dose (baricitinib 4 mg vs. 2 mg) influence both a patient's likelihood to be a responder and in which responder subgroup they find themselves in. These findings help us to understand treatment outcomes and, in turn, inform treatment expectations. Some patients, particularly those with near-complete or complete scalp hair loss, or those with longer duration of current episode of hair loss, may require a longer treatment course in order to attain meaningful scalp hair regrowth.

## Acknowledgements

We thank all the clinical trial participants and trial staff, without whom this work would not be possible. We would like to acknowledge and thank Jakub P. Jedynek PhD of Eli Lilly and Company for his support in creating graphics for the manuscript. Medical writing and editorial support were provided by Eric A. Rodriguez PhD of Eli Lilly and Company.

## Funding sources

Baricitinib is developed by Eli Lilly and Company, under license from Incyte Corporation. Eli Lilly and Company (Indianapolis, IN, USA) was involved in the study design, data collection, data analysis, data interpretation, manuscript preparation and publication decisions. All authors had full access to all data in the study and had final responsibility for the decision to submit for publication.

## Conflicts of interest

B.K. has served on advisory boards and/or is a consultant and/or is a clinical trial investigator for AbbVie, AltruBio, Almirall, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol Myers Squibb, Concert Pharmaceuticals, Equillum,



Horizon Therapeutics, Eli Lilly and Company, Incyte, Janssen Pharmaceuticals, LEO Pharma, Otsuka/Visterra, Pfizer, Regeneron, Sanofi-Genzyme, TWi Biotechnology and Viela Bio; and has served on speaker bureaus for AbbVie, Eli Lilly and Company, Incyte, Pfizer, Regeneron and Sanofi Genzyme. J.S. has received travel reimbursement and speaking honoraria from Eli Lilly and Company. M.O. has received lecture fees from Eli Lilly and Company and advisory fees from Eli Lilly and Company, Pfizer, Janssen Pharmaceuticals (Japan), Taisho Pharmaceutical, Maruho, Bristol Myers Squibb Japan, AbbVie and ROHTO Pharmaceutical; and grants/research funds from Shiseido, Maruho, Advantest and Sun Pharma Japan. He is a specialist associate editor of the *British Journal of Dermatology* and was excluded from all editorial decision-making related to the acceptance of this article for publication. A.E. has received research funding from Pfizer, Eli Lilly and Company, Novartis, Bristol Myers Squibb, Boehringer Ingelheim, AbbVie, Janssen Pharmaceuticals, Boehringer Ingelheim, the Danish National Psoriasis Foundation, the Simon Spies Foundation and the Kgl Hofbundtmager Aage Bang Foundation; and honoraria as a consultant and/or speaker from AbbVie, Amgen, Boehringer Ingelheim, LEO Pharma, Zuellig Pharma, Galápagos, Sun Pharmaceuticals, Samsung Bioepis, Pfizer, Eli Lilly and Company, Novartis, Union Therapeutics, Galderma, Dermavant, UCB, Mylan, Bristol Myers Squibb, McNeil Consumer Healthcare, Horizon Therapeutics, Boehringer Ingelheim and Janssen Pharmaceuticals. B.M.P. has received lecture fees from Eli Lilly and Company and Pfizer; consulting fees from Eli Lilly and Company, Pfizer, ISDIN, Amgen and Vichy; and has participated in advisory boards for Eli Lilly and Company and Pfizer. B.C. has received honoraria and/or fees from Eli Lilly and Company, Pfizer, Regeneron and Sanofi-Genzyme. R.S. reports serving as a consultant or paid speaker for or participating in clinical trials sponsored by LEO Pharma, Amgen, Novartis Pharmaceuticals, Merck & Co, Celgene, Coherus BioSciences, Janssen Global Services, Regeneron Pharmaceuticals, MedImmune, GlaxoSmithKline, Cutanea, Samson Clinical, Boehringer Ingelheim, Pfizer, Merck Sharpe & Dohme, Oncobiologics, F. Hoffmann-La Roche, Eli Lilly and Company, and Bayer; and is serving as the current President of the Australasian Hair and Wool Research Society. Y.-F.C., W.-S.W., Y.D., N.S. and Y.D. are employees of and shareholders in Eli Lilly and Company.

### Data availability

Lilly provides access to all individual participant data collected during the trial, after anonymization, with the exception of pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has received first regulatory authorization and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, and blank or annotated

case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at [www.vivli.org](http://www.vivli.org).

### Ethics statement

Both trials were conducted in accordance with the ethical principles of the Declaration of Helsinki and Good Clinical Practice guidelines, and the trial protocols were approved by the Institutional Review Board or ethics committee at each centre. All patients provided written informed consent for participation in the clinical studies.

### Supporting Information

Additional [Supporting Information](#) may be found in the online version of this article at the publisher's website.

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