Evidence-Based Data on How Long to Treat to Achieve Treatment Response With Baricitinib in Severe Alopecia Areata

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OBJECTIVE

- In this post hoc analysis, we evaluated patients achieving at least 30% improvement ($SALT_{30}$), and their ultimate achievement of 20% or less hair loss (SALT score ≤20) to better characterize the optimal length of time required to treat individual patients with severe AA

CONCLUSIONS

- These post hoc data from the BRAVE-AA trials can help answer 2 important clinical questions
- **Clinical Question #1:** What treatment duration is required to observe meaningful improvement predicting success?
  - $SALT_{30}$ improvement can be used to predict those for whom ongoing treatment will have greatest benefit
  - Most patients with severe AA (SALT score 50-94) showed $SALT_{30}$ improvement by 6 months of treatment
  - In those with very severe AA (SALT score 95-100), $SALT_{30}$ improvement rates continued to increase through 1 year of treatment
- **Clinical Question #2:** If I observe a clinical change that indicates treatment is working in my patients, how many will achieve treatment success?
  - Most patients with severe AA (SALT score 50-94), who showed objective improvement at 6 months, achieved SALT score ≤20 within 1 year of treatment
  - Patients with very severe AA (SALT score 95-100) continued to show increases in absolute numbers of $SALT_{30}$ improvers and SALT score ≤20 responders up to at least 1 year
- The results of this analysis are applicable to baricitinib 4-mg monotherapy, and not to treatment with baricitinib 2-mg, where up-titration to baricitinib 4-mg and/or the addition of other therapies may be a consideration

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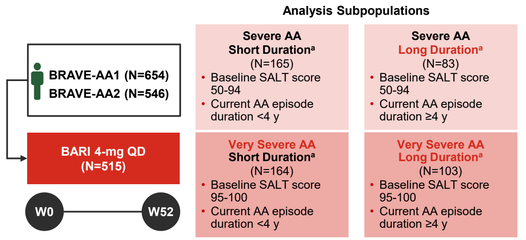
BACKGROUND

- AA is an autoimmune, non-scarring hair loss disorder that most often affects the scalp but can develop on any hair-bearing site, including eyebrows and eyelashes[1]
- Baricitinib 4-mg or 2-mg showed efficacy vs. placebo in hair regrowth in 2 Phase 3 trials (BRAVE-AA1 and BRAVE-AA2) and is an approved systemic therapy (selective JAK inhibitor) for treatment of severe AA in adults[1,2]
- Hair regrowth in response to treatment can be variable, with the timing and likelihood of treatment response being affected by baseline disease severity and by duration of current episode[3]
- The speed of hair regrowth is slow unlike the more rapid responses to treatment observed with other dermatoses, and clinicians are continuing to learn about what to expect from treatment
- At least 30% improvement ($SALT_{30}$) has previously been shown to be a predictor of future achievement of 20% or less hair loss (SALT score ≤20)[3]
- To appropriately counsel patients and to make decisions on when to stop or switch therapy, clinicians continue to seek data on how long to optimally treat patients to achieve a response

STUDY DESIGN

BRAVE-AA1 and BRAVE-AA2

- This analysis included patients who continued to receive baricitinib 4-mg from randomization through to Week 52



[a]Of current AA episode.
Note: Figure is not the full BRAVE-AA1 and BRAVE-AA2 program.

Assessments and Statistical Analyses

- Proportion of patients achieving *meaningful improvement* in SALT score ($SALT_{30}$) for each subpopulation
- Proportion of patients achieving SALT score ≤20 through Week 52 among patients who achieved $SALT_{30}$ at Weeks 24, 36, and 52
- Visits after permanent study drug discontinuation were excluded with non-responder imputation for $SALT_{30}$ and SALT score ≤20

STUDY QUESTIONS

What treatment duration is required to observe meaningful improvement predicting success? → Time to observe at least 30% improvement ($SALT_{30}$)

If I observe this clinical change, how likely is it that my patient will achieve treatment success? → Treatment success: SALT score ≤20 at Week 52 among those achieving $SALT_{30}$ at each time point (Weeks 24, 36, 52)

KEY RESULTS

Clinical characteristics can guide treatment decisions

Patient presentation	Baseline Severe AA (SALT score 50-94)		Baseline Very Severe AA (SALT score 95-100)		Therapy must be continued beyond these time points to achieve treatment success
Treatment duration for meaningful improvement?	Most **signal** improvement ($SALT_{30}$) by 06 MONTHS		Patients continue to **signal** improvement ($SALT_{30}$) through 12 MONTHS		
	Current Episode Duration <4 years	Current Episode Duration ≥4 years	Current Episode Duration <4 years	Current Episode Duration ≥4 years	
Number of patients achieving treatment success[a]?	74-77%	63-69%	58-66%	43-46%	

Improvement (defined as 30% improvement from baseline in SALT score) indicates that treatment is working and predicts that continued treatment will lead to a meaningful response (SALT score ≤20) by 1 year

[a]Among those who achieve $SALT_{30}$ at each time point (Weeks 24, 36, 52).

Methods

Key Eligibility Criteria: BRAVE-AA1 and BRAVE-AA2

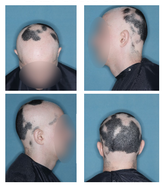
- Male (≥18 to ≤60 years) or female (≥18 to ≤70 years)[a]
- Hair loss involving ≥50% of the scalp, assessed with SALT score
- Current episode of AA >6 months to <8 years[b]
- No spontaneous improvement in the 6 months before screening
- Not primarily a "diffuse" type of AA
- No concomitant treatments for AA allowed[c]

[a]Different upper age limits were included for male and female patients based on differences in the prevalence of concomitant androgenetic alopecia; [b]Patients who had AA for ≥8 years could be enrolled if episodes of regrowth, spontaneous or under treatment, had been observed on the affected areas over the past 8 years; [c]Oral/topical minoxidil or finasteride was allowed if on stable dose for ≥12 months and bimatoprost ophthalmic solution was allowed if on stable dose for ≥8 weeks.

SALT Score[4]

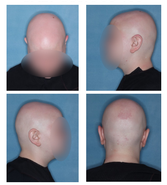
- SALT score interpretation
  - SALT score 0=no hair loss
  - SALT score 100=complete hair loss
  - SALT score ≤20=20% or less hair loss (≥80% scalp coverage)
- SALT subscript interpretation
  - Subscripts refer to percent improvement from baseline (eg, $SALT_{30}$=≥30% improvement from baseline in total SALT score)

Example of Severe AA: SALT Score 50-94



SALT score 62

Example of Very Severe AA: SALT Score 95-100



SALT score 100

Results

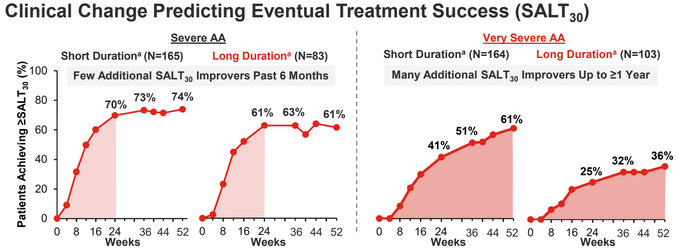
Baseline Demographics and Patient Characteristics

- Very severe subgroups were more likely to have atopic backgrounds and had higher prevalence of significant or total loss of eyebrows and/or eyelashes

Characteristic	Severe AA Short Duration[a] (N=165)	Severe AA Long Duration[a] (N=83)	Very Severe AA Short Duration[a] (N=164)	Very Severe AA Long Duration[a] (N=103)
Age, y, mean (SD)	38.1 (13.3)	39.6 (13.0)	35.1 (12.1)	36.7 (13.7)
Female, %	61.2	72.3	53.7	58.3
Race, %				
White	53.7	53.0	46.3	57.3
Asian	31.7	28.9	42.7	34.0
Black or African American	9.8	14.5	8.5	3.9
Other	2.4	1.2	1.2	1.9
BMI, kg/m², mean (SD)	26.9 (5.5)	26.1 (5.2)	26.0 (5.0)	26.4 (5.1)
Duration of AA since onset, y, mean (SD)	9.1 (10.7)	15.1 (10.9)	10.2 (10.1)	16.3 (11.5)
Patients with atopic background,[b] %	32.1	31.3	40.2	38.8
SALT score, mean (SD)	69.7 (15.0)	69.2 (14.0)	99.4 (1.3)	99.6 (1.2)
ClinRO eyebrow score ≥2, %	48.5	49.4	82.2	93.1
ClinRO eyelash score ≥2, %	35.6	39.8	80.4	83.3

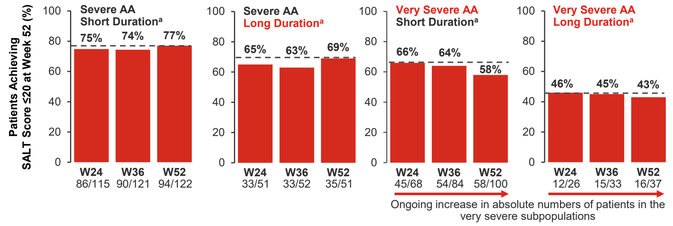
[a]Severe AA/Short duration=baseline SALT score 50-94 and current AA episode duration <4 y; Severe AA/Long duration=baseline SALT score 50-94 and current AA episode duration ≥4 y; Very severe AA/Short duration=baseline SALT score 95-100 and current AA episode duration <4 y; Very severe AA/Long duration=baseline SALT score 95-100 and current AA episode duration ≥4 y; [b]Atopic background is defined as medical history or current atopic dermatitis, allergic rhinitis, allergic conjunctivitis, or allergic asthma.
Note: Percentages are based on the number of patients with non-missing data.

Clinical Change Predicting Eventual Treatment Success ($SALT_{30}$)



Note: Shading indicates time over which response rates notably continue to increase.

Patients Achieving Treatment Success (SALT Score ≤20 at Week 52) Among Those Reaching $SALT_{30}$ at Weeks 24, 36, and 52



Ongoing increase in absolute numbers of patients in the very severe subpopulations

[a]Severe AA/Short duration=baseline SALT score 50-94 and current AA episode duration <4 y; Severe AA/Long duration=baseline SALT score 50-94 and current AA episode duration ≥4 y; Very severe AA/Short duration=baseline SALT score 95-100 and current AA episode duration <4 y; Very severe AA/Long duration=baseline SALT score 95-100 and current AA episode duration ≥4 y.

References: 1. King B, et al. *J Am Acad Dermatol.* 2021;85:847-853. 2. King B, et al. *N Engl J Med.* 2022;386:1687-1699. 3. King B, et al. *Br J Dermatol.* 2023;189:668-673. 4. Olsen EA, et al. *J Am Acad Dermatol.* 2004;51:440-447.

Abbreviations: *AA=alopecia areata; BARI=baricitinib; BMI=body mass index; ClinRO=Clinician-Reported Outcome; JAK=Janus kinase; QD=once daily; SALT=Severity of Alopecia Tool; SALT score ≤20=20% or less hair loss; $SALT_{30}$=≥30% improvement from baseline in SALT score; SD=standard deviation; W=Week; y=year*

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