Characterizing Loss of Response Occurring in a Small Number of Patients During 3 Years of Long-Term Maintenance Therapy With Baricitinib 4-mg: Results From BRAVE-AA1 and -AA2 Trials

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OBJECTIVE

- In this post hoc analysis, we characterize patterns of loss of response during maintenance treatment (Weeks 52-152) among the 10.9% (n=14) of patients who demonstrated loss of response (SALT score >20) at Week 152 and explore differences between patients who lost versus maintained response

CONCLUSIONS

- A small number of patients (12 patients) experienced true loss of response during long-term maintenance therapy with baricitinib 4-mg
  - Two additional patients experienced loss of response due to treatment interruption
- Time to loss of response was variable and showed no obvious patterns
- Half of those who lost response (unrelated to treatment interruption) experienced maximal worsening to no greater than SALT score ≤40
- Definitive identification of risk factors for loss of response is not possible due to small sample size; however, the following were observed:
  - Higher disease severity and chronicity among those who lost response
  - Antecedent COVID-19 infection or vaccine among some patients who lost response
  - A full review of patient narratives to identify other potential antecedent factors was not performed
- Future research is needed to confirm what factors potentially trigger loss of response on baricitinib monotherapy and to determine the potential role of adjunctive therapies in mitigating this risk

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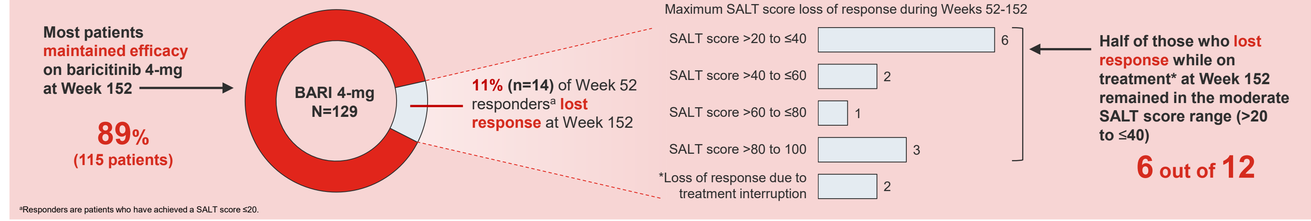
BACKGROUND

- Alopecia areata (AA) can have a waxing and waning course with relapses even while on treatment[1,2]
  - In its most severe presentations, AA can be chronic and difficult to treat[3]
- Baricitinib, an approved systemic therapy for severe AA, demonstrated a high level of sustained efficacy (89.1%) through 152 weeks among patients who achieved a SALT score ≤20 at Week 52 following treatment with once-daily baricitinib 4-mg in the (BRAVE-AA1 and BRAVE-AA2) Phase 3 trials[4]

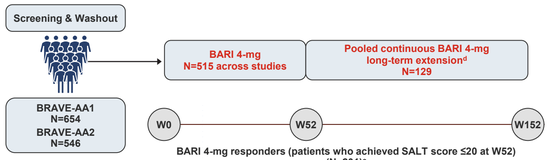
KEY RESULTS



[a]Responders are patients who have achieved a SALT score ≤20.

Methods

BRAVE-AA1 and BRAVE-AA2 Study Design:[a] Characterization of Patterns in Loss of Response During Maintenance Treatment With Continuous Baricitinib 4-mg (Weeks 52-152)[b]



[a]Figure is not the full BRAVE-AA1 and BRAVE-AA2 program; [b]Baricitinib 2-mg dose is not included in this analysis because patients receiving continuous baricitinib 2-mg in BRAVE-AA2 who experienced a 20-point worsening of SALT score post W52 were rescued to baricitinib 4-mg; [c]SALT ≤20 responders in BRAVE-AA1 were randomized 3:1 at W52 to remain on baricitinib 4-mg or transition to placebo; SALT ≤20 responders in BRAVE-AA2 were randomized 1:1 at W52 to remain on baricitinib 4-mg or down-titrate to 2-mg; [d]Patients who achieved SALT score ≤20 at W52 and who subsequently continued on the baricitinib 4-mg dose comprised the long-term extension group.

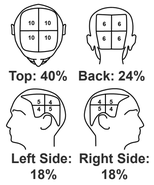
Key Eligibility Criteria: BRAVE-AA1 and BRAVE-AA2

- 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[5]

- The SALT score is a weighted sum of the percentage of hair loss in the 4 quadrants of the scalp (left side, right side, top, and back), ranging from 0 (no hair loss) to 100 (complete hair loss)
- SALT scores with subscripts refer to percent improvement from baseline (eg, $SALT_{30}$=≥30% improvement from baseline in total SALT score)
- 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)



Assessments and Statistical Analyses

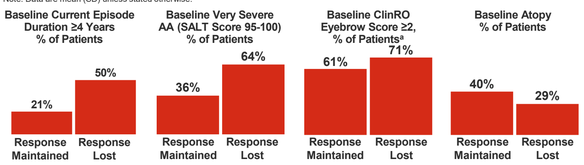
- Patient records were reviewed to identify patients who demonstrated loss of response at Week 152
  - Loss of response was defined as SALT score >20 at Week 152 (ie, loss of SALT score ≤20)
- Descriptive statistics were used to summarize baseline characteristics and the timing and extent of scalp hair loss for these patients
- Occurrence of COVID-19 infections, other serious infections, and treatment interruptions were examined as potential antecedents to the loss of response; baseline demographics and clinical characteristics were also considered

Results

Baseline Demographics and Patient Characteristics of Baricitinib 4-mg Week 52 Responders

	BARI 4-mg Week 52 Responders[a]	
	Response Maintained (N=115)	Response Lost (N=14)
Age, years	37.0 (12.6)	34.1 (8.7)
Female, n (%)	71 (61.7)	9 (64.3)
Race, n (%)		
White	60 (52.2)	11 (78.6)
Asian	45 (39.1)	3 (21.4)
Black or African American	7 (6.1)	0
Other	3 (2.6)	0
BMI, kg/m²	25.4 (4.9)	24.7 (3.1)
Duration of AA since onset, years	10.2 (10.3)	13.6 (10.5)
Duration of current AA episode	2.8 (2.5)	4.4 (3.7)
<4 years, n (%)	91 (79.1)	7 (50.0)
≥4 years, n (%)	24 (20.9)	7 (50.0)
Patients with atopic background[b]	46 (40.0)	4 (28.6)
SALT score	79.3 (18.9)	86.4 (20.9)
SALT score category, n (%)		
Severe – non-AT (SALT score 50-94)	74 (64.3)	5 (35.7)
Very severe – consistent with AT (SALT score 95-100)	41 (35.7)	9 (64.3)
ClinRO Eyebrow score ≥2, n (%)	70 (60.9)	10 (71.4)
ClinRO Eyelash score ≥2, n (%)	61 (53.0)	7 (50.0)

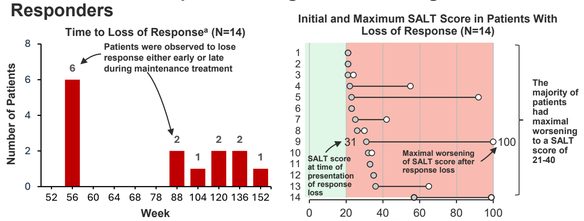
[a]BARI 4-mg–treated patients with SALT score ≤20 at W52; [b]Atopic background is defined as medical history or current atopic dermatitis, allergic rhinitis, allergic conjunctivitis or allergic asthma.
Note: Data are mean (SD) unless stated otherwise.



- Sample size is small, which is a limitation, but shows some numerical differences in baseline disease characteristics between those losing (10.9%, n=14/129) and those maintaining (89.1%, n=115/129) treatment response

[a]A ClinRO or PRO score of 2 indicates significant gaps in eyebrow(s)/eyelashes, and a score of 3 indicates no notable eyebrow(s)/eyelashes.

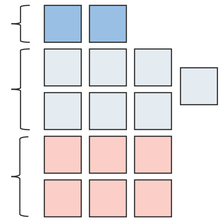
Time to Loss of Response Among Baricitinib 4-mg Week 52 Responders



[a]Loss of response defined as SALT score >20.
Notes: Time to loss of response may not reflect actual time at which SALT score ≤20 was lost because most patients waited until their next clinic visit to be reassessed. Time intervals between clinic visits were extended from every 4 weeks through W68 to every 16 weeks after W88. Data for patients who discontinued the study treatment were set as missing for all subsequent visits. LOCF was used to impute missing data.

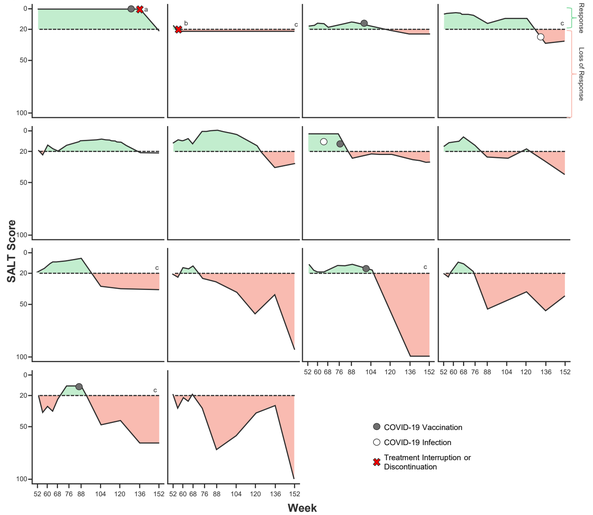
COVID-19 Vaccinations, COVID-19 Infections, and Treatment Interruptions During Maintenance Period Among Patients Who Lost Response Between Week 52 and Week 152

- One patient had interruption in treatment beginning at Week 136[a]
  One patient was discontinued from treatment due to adverse event
- Seven patients had none of the prespecified details regarding loss of response
- Six patients who lost response had received a COVID-19 vaccination and/or experienced a COVID-19 infection during the maintenance period[a,b]



[a]Patient who had treatment interruption at W136 had also received a COVID-19 vaccine; [b]Four patients received a COVID-19 vaccine and no COVID-19 infection; One patient experienced a COVID-19 infection and no COVID-19 vaccine; One patient experienced a COVID-19 infection and subsequently received a COVID-19 vaccine.
Notes: Causation cannot be determined between these events and loss of response. Sample size was small. Analysis of the ITT population for COVID-19 infection or vaccine was not performed. Patient narratives were not reviewed for other potential antecedent events.

Individual Patient Trajectories From Week 52 Through Week 152 (N=14)



[a]Patient's treatment was interrupted from W136 through W152; [b]Patient's treatment was withdrawn after 58 weeks due to adverse event; [c]Patient trajectory shows LOCF data.
Notes: Time to loss of response may not reflect actual time at which SALT score ≤20 was lost because most patients waited until their next clinic visit to be reassessed. Time intervals between clinic visits were extended from every 4 weeks through W68 to every 16 weeks after W88.

References: 1. McKenzie PL, Castelo-Soccio L. *J Am Acad Dermatol*. 2022;86:683-685. 2. Rossi A, et al. *J Cosmet Dermatol*. 2021;20:3753-3757. 3. King B, et al. *J Am Acad Dermatol*. 2021;85:847-853. 4. Senna M, et al. Poster presented at: AAD 2024. Poster 49690. 5. Olsen EA, et al. *J Am Acad Dermatol*. 2004;51:440-447.

Abbreviations: *AA=alopecia areata; ATotal=alopecia totalis; BARI=baricitinib; BMI=body mass index; ClinRO=clinician-reported outcome; COVID-19=coronavirus disease 2019; ITT=intent-to-treat; LOCF=last observation carried forward; PRO=patient-reported outcome; SALT=Severity of Alopecia Tool; SD=standard deviation; W=Week*

Disclosures: **M. M. Senna** has served on advisory boards and/or has been a consultant for: Arena Pharmaceuticals, Concert Pharmaceuticals, Eli Lilly and Company, **S. Taylor** has been an investigator for: Concert Pharmaceuticals, Croma-Pharma, Eli Lilly and Company, Immune Tolerance Network, and Pfizer; has been a consultant, speaker, and/or advisory board member for: AbbVie, Arcutis, Beiersdorf, Biorez, Cantec Pharmaceuticals, Evolus, Galderma Laboratories, Glo Getter Aesthetics, Johnson & Johnson, L'Oreal, LuminDx, Medscape/WebMD, Scientis, and Vichy Laboratoires; and has received book royalties from: McGraw Hill. **B. Piraccini** has received honoraria from or been a consultant for: Almirall, Eli Lilly and Company, ISDIN, Pfizer, and Vichy Laboratoires; **J. Shapiro** is a consultant or clinical trial investigator for: Pfizer; and is a consultant for: Eli Lilly and Company; **N. Somani**, **J. Jedynak**, **S. Ogwu**, and **A. Buchanan** are employees and shareholders of: Eli Lilly and Company; **B. Craiglow** has received fees and/or honoraria from: Concert Pharmaceuticals, Eli Lilly and Company, Incyte Corporation, Pfizer, Regeneron, and Sanofi Genzyme; **M. Ohyama** has received lecture and advisory fees from: AbbVie GK, Bristol Myers Squibb Japan, Eli Lilly Japan K.K., Pfizer Japan, Rohto Pharmaceutical, and Taisho Pharmaceutical; and has received research grants from: Advantest Corporations, Maruho, Shiseido, and Sun Pharma Japan
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