Outcomes of Down-Titration in Patients With Severe Scalp Alopecia Areata Treated With Baricitinib: An Update Through Week 152 From BRAVE-AA2

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OBJECTIVE

- To report the Week 152 efficacy results, from the BRAVE-AA2 randomized down-titration sub-study, including recapture data after re-treatment

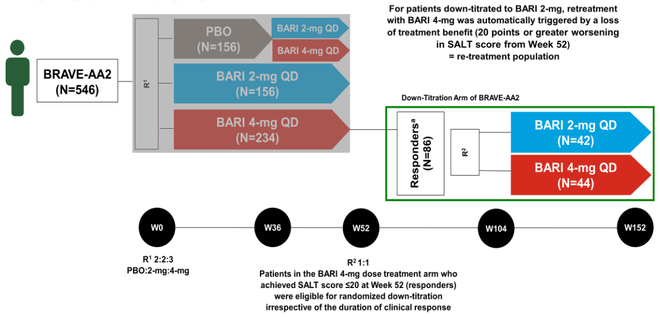
BACKGROUND

- AA is a common autoimmune disorder marked by non-scarring hair loss that may contribute to significant emotional and psychosocial distress[1-3]
- Baricitinib is an oral JAK inhibitor approved for treatment of severe alopecia areata
  - In two randomized, double-blind, placebo-controlled, Phase 3 studies (BRAVE-AA1 [NCT03570749] and BRAVE-AA2 [NCT03899259]), baricitinib 4-mg and 2-mg demonstrated superiority over placebo in hair regrowth after 36 weeks of treatment in adult patients with severe AA[4]
  - BRAVE-AA2 included a randomized down-titration sub-study starting at Week 52 for baricitinib 4-mg responders

AA=alopecia areata; JAK=Janus kinase

Disclosures: B. King has served on advisory boards and/or is a consultant and/or clinical trial investigator for: AbbVie, Almirall, AltruBio, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol Myers Squibb, Concert Pharmaceuticals, Eli Lilly and Company, Horizon Therapeutics, Incyte Corporation, LEO Pharma, Otsuka/Visterra, Pfizer, Regeneron, Sanofi Genzyme, TWi Biotechnology, and Viela Bio; and is on speaker's bureaus for: AbbVie, Incyte Corporation, LEO Pharma, Pfizer, Regeneron, and Sanofi Genzyme; **M. Ohyama** has received lecture and advisory fees from: Eli Lilly Japan K.K., Pfizer Japan, Bristol Myers Squibb Japan, AbbVie GK., Rohto Pharmaceutical, and Taisho Pharmaceutical; and has received research grants from: Maruho, Shiseido, Advantest Corp. and Sun Pharma Japan; **M. Senna** has served on advisory boards and/or has been a consultant for: Arena Pharmaceuticals, Concert Pharmaceuticals, Eli Lilly and Company, and Pfizer; and is a clinical trial investigator for: Concert Pharmaceuticals and Eli Lilly and Company; **J. Shapiro** is a consultant or clinical trial investigator for: Pfizer; and is a consultant for: Eli Lilly and Company; **Y. Dutronc**, **J. Kolodsick**, **G. Yu**, **C. Liu**, and **C. Chiasserini** are employees and shareholders of: Eli Lilly and Company; **B. M. Piraccini** has received honoraria from or been a consultant for: Almirall, Eli Lilly and Company, ISDIN, Pfizer, and Vichy Laboratories. Medical writing assistance was provided by Carren Jepchumba, PharmD of Eli Lilly and Company.

STUDY DESIGN



[a] SALT score ≤20

BARI=baricitinib; PBO=placebo; QD=once daily; R=randomization; SALT=Severity of Alopecia Tool; W=Week

KEY ELIGIBILITY CRITERIA

BRAVE-AA2

- Age ≥18 years to ≤60 years (males) or ≤70 years (females)
- Severe or very severe AA, fulfilling the following criteria:
  - Current episode of AA lasting >6 months to <8 years[a]
  - Hair loss involving ≥50% of the scalp, as measured by SALT score
  - No spontaneous improvement in the 6 months before screening
- Not primarily "diffuse" type of AA
- No concomitant treatments for AA allowed[b]

Down-titration sub-study

- At Week 52, patients treated with baricitinib 4-mg since baseline, who had a SALT score ≤20 (responders) were randomized in a 1:1 ratio to either stay on baricitinib 4-mg or transition to baricitinib 2-mg (randomized down-titration)

[a] Patients who had AA for ≥8 years could be enrolled if episodes of regrowth, spontaneous or due to undertreatment, had been observed on the affected areas and were anticipated to continue on a stable dose up to Week 36; [b] 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. *AA=alopecia areata; SALT=Severity of Alopecia Tool*

KEY RESULT

Clinical Response (SALT score≤20) was maintained in patients through Week 152:

SALT=Severity of Alopecia Tool

RESULTS

Down-Titration Population: Demographics and Baseline Characteristics

	Down-Titration Population	
	BARI 4-mg/ BARI 4-mg (N=44)	BARI 4-mg/ BARI 2-mg (N=42)
Age, years	35.6 (10.9)	36.5 (13.6)
Female, n (%)	23 (52.3)	33 (78.6)
Race, n (%)		
White	30 (68.2)	25 (59.5)
Asian	11 (25.0)	14 (33.3)
Black or African American	1 (2.3)	2 (4.8)
BMI, kg/m²	25.7 (4.9)	27.2 (5.6)
Duration of AA since onset, years	11.1 (10.3)	9.6 (10.0)
Duration of current AA episode, n (%)		
<4 years	33 (75.0)	30 (71.4)
≥4 years	11 (25.0)	12 (28.6)
SALT score	78.5 (20.4)	83.7 (17.0)
Severity, n (%)		
Severe (SALT score 50-94)	26 (59.1)	27 (64.3)
Very severe (SALT score 95-100)	18 (40.9)	15 (35.7)

Notes: Data are mean (SD) unless stated otherwise. The denominator may vary based on the actual total N in each category; percentages are manually generated AA=alopecia areata; BARI=baricitinib; BMI=body mass index; SALT=Severity of Alopecia Tool; SD=standard deviation

CONCLUSIONS

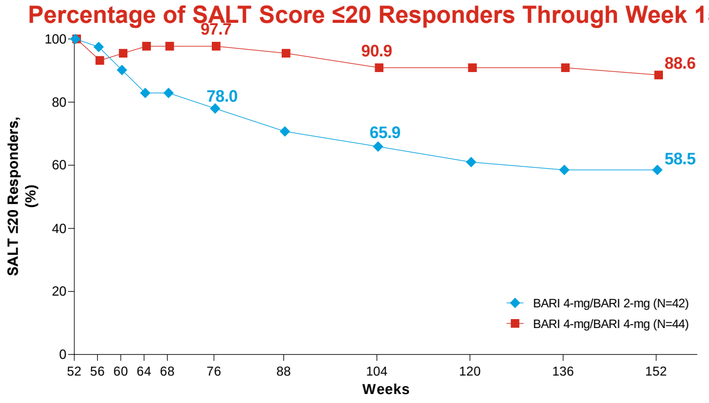
- At Week 152, SALT score ≤20 was maintained by 89% of responders who remained on baricitinib 4-mg
- Among patients who were down-titrated, 59% maintained response through Week 152
- Overall, 36.6% of patients down-titrated to baricitinib 2-mg met criteria for retreatment with 4mg (20 points or greater worsening in SALT score from Week 52)
- Successful down-titration was observed more frequently in patients who achieved a *stable response* from week 36 to 52 and/or those who achieved a *depth of response* of SALT<=5 before they were down-titrated
- Successful dose modulation of baricitinib is possible, although more work is needed to optimize the process of down-titration. The timing of down-titration that was prespecified in BRAVE-AA2 may not reflect optimal clinical parameters. Data suggest that stability and depth of response are important variables to consider

STATISTICAL ANALYSES

- Assessment of scalp hair loss relied on the Severity of Alopecia Tool (SALT)
- This analysis included a subset of patients (N=86) initially randomized to baricitinib 4-mg who were responders (SALT score ≤20) at Week 52
- Data collected after the treatment discontinuation or retreatment with BARI 4mg after loss of treatment benefit were censored for evaluation of efficacy during the down-titration period. Data collected after the treatment discontinuation were censored for the summary of response recapture following the retreatment
- Last observation carried forward (LOCF) was used to impute missing or censored data*

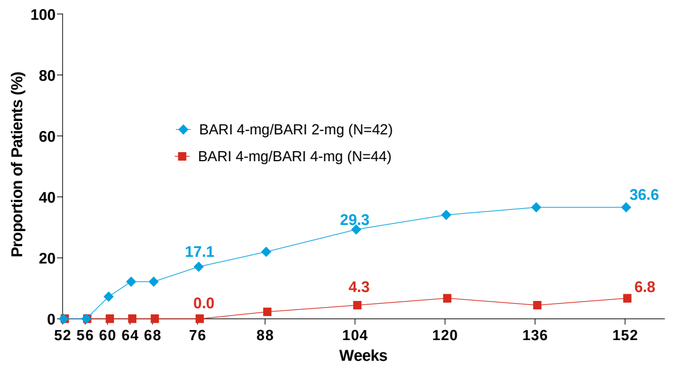
**In previous disclosures descriptive statistics were summarized using hybrid imputation of NRI and MI. For summary statistics, data after re-treatment or treatment discontinuation were censored and handled with NRI while data collected at remote visits were censored and handled with MI. SALT=Severity of Alopecia Tool*

Percentage of SALT Score ≤20 Responders Through Week 152



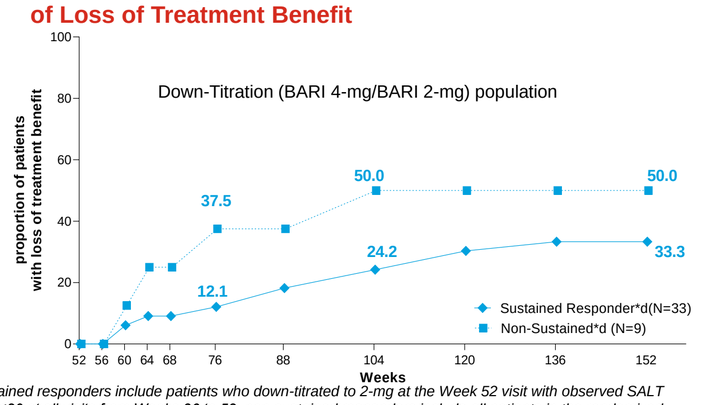
BARI=baricitinib; LOCF= last observation carried forward; SALT=Severity of Alopecia Tool

Percentage of Patients With Loss of Treatment Benefit (20 points or greater worsening in SALT score from Week 52) Through Week 152



BARI=baricitinib; LOCF= last observation carried forward; SALT=Severity of Alopecia Tool

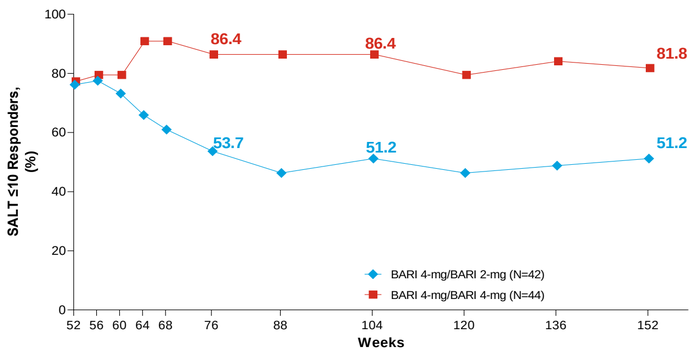
Sustained Response[a] Was Associated With Lower Incidence of Loss of Treatment Benefit



[a] *Sustained responders include patients who down-titrated to 2-mg at the Week 52 visit with observed SALT score ≤20 at all visits from Weeks 36 to 52; non-sustained responders include all patients in the randomized down-titration population who did not meet the sustained responders criteria*

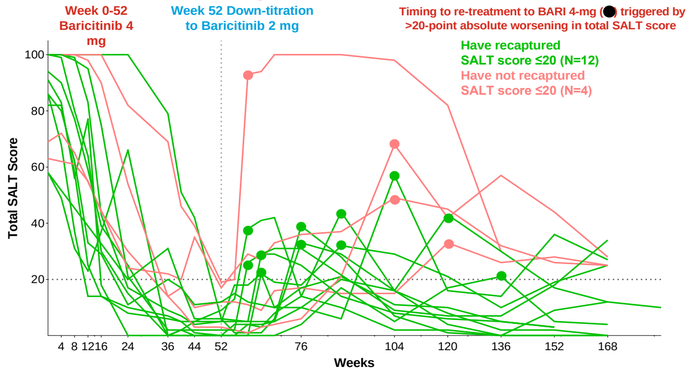
BARI=baricitinib; LOCF= last observation carried forward; SALT=Severity of Alopecia Tool

Percentage of SALT Score ≤10 Responders Through Week 152



BARI=baricitinib; LOCF= last observation carried forward; SALT=Severity of Alopecia Tool

SALT Score Trajectories of Individual Patients in the Down-Titration Re-treatment Population[a]

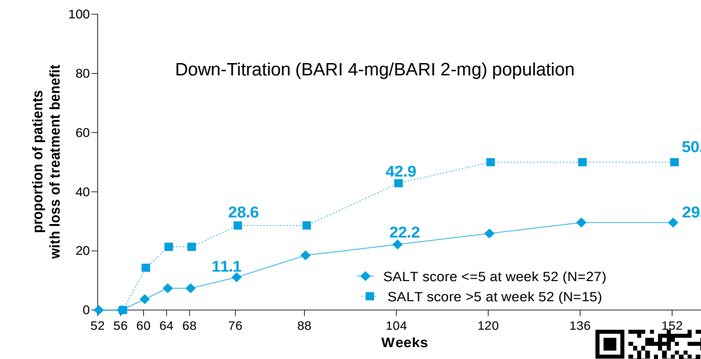


One patient was not included in the trajectory plot as this patient was inadvertently retreated at Week 76 despite not experiencing loss of treatment benefit. At the time of analysis, 12/16 (75%) had already recaptured SALT ≤20.

[a] *Re-treatment from the BARI 2-mg to 4-mg dose after down-titration was automatically triggered by a loss of treatment benefit (>20-point absolute worsening in total SALT score)*

BARI=baricitinib; SALT=Severity of Alopecia Tool

Greater Depth of Response (SALT Score ≤5 at Week 52) Was Associated With Lower Incidence of Loss of Treatment Benefit



BARI=baricitinib; LOCF= last observation carried forward; SALT=Severity of Alopecia Tool

Abbreviations: AA=alopecia areata; BARI=baricitinib; BMI=body mass index; JAK=Janus kinase; Obs=observed; PBO=placebo; QD=once daily; R=randomization; SALT=Severity of Alopecia Tool; SD=standard deviation; W=Week; *LOCF= last observation carried forward.* **References**: 1. Liu LY, et al. *J Am Acad Dermatol*. 2016;75:806-812.e3. 2. Liu LY, et al. *J Am Acad Dermatol*. 2018;79:556-558.e1 3. Aldhouse NVJ, et al. *J Patient Rep Outcomes*. 2020;4:76. 4. King B, et al. *N Engl J Med.* 2022;386:1687-1699. 5. Olsen EA, et al. *J Am Acad Dermatol.* 2004;51:440-447