Eyebrows and Eyelashes Regrowth Across Different SALT Response Thresholds in Patients with Alopecia Areata: Outcomes from the BRAVE AA Clinical Program

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BACKGROUND

- Alopecia areata (AA) is a clinically heterogenous, immune-mediated, non-scarring hair loss disorder that varies widely in the amount and pattern of hair loss[1]
- Although the scalp is most often affected, AA can develop on any hair-bearing site, including the eyebrows and eyelashes
- Efficacy of baricitinib, an oral selective Janus kinase (JAK)1/JAK2 inhibitor, in the treatment of adult patients with severe AA (defined as Severity of Alopecia Tool [SALT] score ≥50) was demonstrated in the Phase 2/3 trial, BRAVE-AA1, and the Phase 3 trial, BRAVE-AA2, 2 randomized, double-blinded, placebo-controlled trials[2,3]
  - The primary endpoint was the proportion of patients who achieved SALT score ≤20 at Week 36
  - Key secondary endpoints included the proportion of patients with no or minimal gaps on eyebrows and eyelashes at Week 36
- However, the clinical response for the scalp, eyebrows, and eyelashes may vary between patients and over time

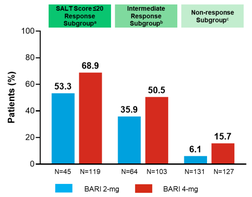
OBJECTIVE

- To evaluate whether patients with AA treated with baricitinib who had not achieved SALT score ≤20 at Week 52 achieved clinically meaningful improvements in eyebrow or eyelash loss

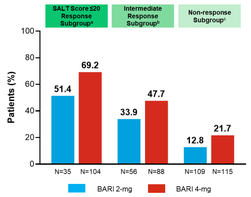
KEY RESULTS

At Week 52, Achievement of Meaningful Improvement in Eyebrow and Eyelash Regrowth Was Observed Across All Response Subgroups, With Greater Response Rates in the SALT Score ≤20 Response Subgroup

ClinRO EB (0,1) With ≥2-Point Improvement



ClinRO EL (0,1) With ≥2-Point Improvement



Note: Analysis population included patients with baseline ClinRO EB and/or EL scores ≥2
[a] Patients who achieved SALT score ≤20 (no more than 20% scalp hair loss) at Week 52;
[b] Patients who failed to reach SALT score ≤20 but achieved SALT30 at ≥1 post-baseline visit;
[c] Patients who never achieved SALT score ≤20 or SALT30 by Week 52

CONCLUSIONS

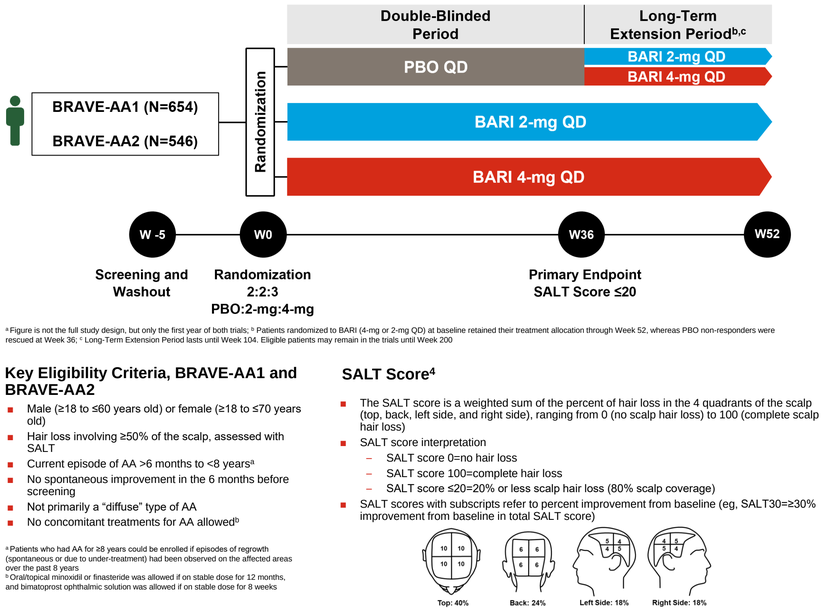
- The data show an impact of baseline severity and duration of hair loss (disease and current episode) on SALT score response rates for scalp, eyebrow, and eyelash hair loss
- Not surprisingly, the highest response rates for eyebrow and eyelash regrowth were observed in patients who had also experienced scalp hair regrowth
- However, about half of the patients with partial scalp response and 15-20% of those with no scalp response experienced meaningful improvement in eyebrow and eyelash regrowth with baricitinib 4-mg, which has been identified as a highly important treatment goal for patients
- Further analyses may be required to clarify if these observations represent different patterns of clinical responses or are linked to different kinetics of hair regrowth between the scalp, eyebrows, and eyelashes
- Longer studies may be required to observe complete benefit

METHODS

Study Design,[a] BRAVE-AA1 and BRAVE-AA2

- This analysis included Weeks 0-52 of both studies
- The analysis included only patients enrolled in the active treatment arms (baricitinib 4-mg and baricitinib 2-mg; patients in the placebo arm were not included)

Study Design,[a] BRAVE-AA1 and BRAVE-AA2



[a] Figure is not the full study design, but only the first year of both trials; [b] Patients randomized to BARI (4-mg or 2-mg QD) at baseline retained their treatment allocation through Week 52, whereas PBO non-responders were rescued at Week 36; [c] Long-Term Extension Period lasts until Week 104. Eligible patients may remain in the trials until Week 200

Key Eligibility Criteria, BRAVE-AA1 and BRAVE-AA2

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

[a] Patients who had AA for ≥8 years could be enrolled if episodes of regrowth (spontaneous or due to under-treatment) had been observed on the affected areas over the past 8 years
[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

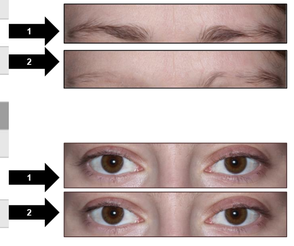
SALT Score[4]

- The SALT score is a weighted sum of the percent of hair loss in the 4 quadrants of the scalp (top, back, left side, and right side), ranging from 0 (no scalp hair loss) to 100 (complete scalp hair loss)
- SALT score interpretation
  - SALT score 0=no hair loss
  - SALT score 100=complete hair loss
  - SALT score ≤20=20% or less scalp hair loss (80% scalp coverage)
- SALT scores with subscripts refer to percent improvement from baseline (eg, SALT30=≥30% improvement from baseline in total SALT score)

ClinRO Measures for Eyebrow and Eyelash Hair Loss™,5

ClinRO Measure for Eyebrow Hair Loss™	
0	Full coverage and no areas of hair loss
1	Minimal gaps **and** even distribution
2	Significant gaps **or** uneven distribution
3	No notable eyebrow hair
ClinRO Measure for Eyelash Hair Loss™	
0	Continuous line along the eyelids on both eyes
1	Minimal gaps **and** even distribution along the eyelids on both eyes
2	Significant gaps **or** uneven distribution along the eyelids
3	No notable eyelashes

Example Photo Guides



Response Subgroups

- Baricitinib 4-mg and 2-mg subgroups were defined by the degree of scalp hair regrowth (SALT score) at Week 52
  - **SALT score ≤20 Response:** Patients who achieved SALT score ≤20 (no more than 20% scalp hair loss) at Week 52
  - **Intermediate Response:** Patients who failed to reach SALT score ≤20 at Week 52 but achieved $SALT_{30}$ at ≥1 post-baseline visit
  - **Non-response:** Patients who never achieved SALT score ≤20 or $SALT_{30}$ by Week 52

Statistical Analyses

- This analysis only included patients enrolled in the baricitinib 4-mg and 2-mg treatment arms at baseline (N=855, 71.3% of all enrolled patients)
- Data were pooled from BRAVE-AA1 and BRAVE-AA2 and summarized by response subgroup using descriptive statistics
- Proportion of patients achieving clinically meaningful improvement in eyebrow or eyelash regrowth at Week 52, respectively, was assessed as:
  - ClinRO EB (0,1), with ≥2-point improvement from baseline (among patients with baseline scores ≥2)
  - ClinRO EL (0,1), with ≥2-point improvement from baseline (among patients with baseline scores ≥2)
- Non-responder imputation was used for data censored after permanent study drug discontinuation or data collected remotely due to the COVID-19 pandemic

RESULTS

Demographics and Patient Characteristics by SALT Score Response Subgroup

	Pooled BARI 2-mg (N=340) and BARI 4-mg (N=515) Population From BRAVE-AA1 and -AA2					
	SALT Score ≤20 Response Subgroup[a]		Intermediate Response Subgroup[b]		Non-response Subgroup[c]	
	BARI 2-mg (N=77)	BARI 4-mg (N=201)	BARI 2-mg (N=97[d])	BARI 4-mg (N=154[e])	BARI 2-mg (N=166)	BARI 4-mg (N=160)
Proportion of patients in subgroups, n/N (%)	77/340 (22.6)	201/515 (39.0)	97/340 (28.5)	154/515 (29.9)	166/340 (48.8)	160/515 (31.1)
Age, years	37.6 (11.4)	36.7 (12.9)	38.2 (13.8)	37.6 (13.0)	38.9 (13.0)	37.1 (13.2)
Female, n (%)	54 (70.1)	132 (65.7)	52 (53.6)	88 (57.1)	106 (63.9)	89 (55.6)
Race, n (%)						
American Indian or Alaska Native	1 (1.3)	3 (1.5)	3 (3.1)	1 (0.7)	1 (0.6)	4 (2.5)
Asian	34 (44.2)	71 (35.3)	31 (32.3)	60 (39.2)	60 (36.1)	50 (31.3)
Black	1 (1.3)	12 (6.0)	4 (4.2)	11 (7.2)	14 (8.4)	23 (14.4)
Native Hawaiian or other Pacific Islander	0	0	1 (1.0)	1 (0.7)	1 (0.6)	0
White	41 (53.2)	111 (55.2)	57 (59.4)	79 (51.6)	87 (52.4)	77 (48.1)
Multiple	0	4 (2.0)	0	1 (0.7)	3 (1.8)	6 (3.8)
BMI, kg/m²	25.4 (4.8)	26.0 (5.1)	26.2 (4.8)	26.8 (5.6)	26.4 (5.8)	26.5 (4.9)
Duration of AA since onset, years	10.6 (9.4)	10.2 (10.5)	11.4 (11.0)	11.0 (10.5)	14.1 (11.0)	14.8 (11.8)
Duration of current AA episode, n (%)						
<4 years	65 (84.4)	151 (75.1)	67 (69.1)	102 (66.2)	98 (59.0)	76 (47.5)
≥4 years	12 (15.6)	50 (24.9)	30 (30.9)	52 (33.8)	68 (41.0)	84 (52.5)

Data are mean (standard deviation) unless stated otherwise
[a] Patients who achieved SALT score ≤20 (no more than 20% scalp hair loss) at Week 52; [b] Patients who failed to reach SALT score ≤20 but achieved $SALT_{30}$ at ≥1 post-baseline visit;
[c] Patients who never achieved SALT score ≤20 or $SALT_{30}$ by Week 52; [d] N=96 for race; [e] N=153

Baseline Disease Characteristics by SALT Score Response Subgroup

	Pooled BARI 2-mg (N=340) and BARI 4-mg (N=515) Population From BRAVE-AA1 and -AA2					
	SALT Score ≤20 Response Subgroup[a]		Intermediate Response Subgroup[b]		Non-response Subgroup[c]	
	BARI 2-mg (N=77)	BARI 4-mg (N=201[d])	BARI 2-mg (N=97)	BARI 4-mg (N=154[e])	BARI 2-mg (N=166)	BARI 4-mg (N=160[f])
SALT score	76.9 (19.1)	80.6 (18.8)	84.4 (19.0)	84.4 (17.9)	91.7 (14.7)	91.4 (15.7)
SALT category, n (%)						
Severe (SALT score 50-94)	53 (68.8)	127 (63.2)	45 (46.4)	77 (50.0)	49 (29.5)	44 (27.5)
Very severe (SALT score 95-100)	24 (31.2)	74 (36.8)	52 (53.6)	77 (50.0)	117 (70.5)	116 (72.5)
ClinRO EB, n (%)						
0	23 (29.9)	53 (26.5)	19 (19.6)	29 (19.0)	21 (12.7)	18 (11.4)
1	9 (11.7)	28 (14.0)	14 (14.4)	21 (13.7)	14 (8.4)	13 (8.2)
2	16 (20.8)	49 (24.5)	23 (23.7)	39 (25.5)	42 (25.3)	34 (21.5)
3	29 (37.7)	70 (35.0)	41 (42.3)	64 (41.8)	89 (53.6)	93 (58.9)
ClinRO EL, n (%)						
0	33 (42.9)	72 (36.0)	30 (30.9)	42 (27.5)	34 (20.5)	33 (20.9)
1	9 (11.7)	24 (12.0)	11 (11.3)	23 (15.0)	23 (13.9)	10 (6.3)
2	10 (13.0)	51 (25.5)	21 (21.6)	37 (24.2)	30 (18.1)	29 (18.4)
3	25 (32.5)	53 (26.5)	35 (36.1)	51 (33.3)	79 (47.6)	86 (54.4)

Data are mean (standard deviation) unless stated otherwise
[a] Patients who achieved SALT score ≤20 (no more than 20% scalp hair loss) at Week 52; [b] Patients who failed to reach SALT score ≤20 but achieved SALT30 at ≥1 post-baseline visit;
[c] Patients who never achieved SALT score ≤20 or SALT30 by Week 52; [d] N=200 for ClinRO EB; [e] N=153 for ClinRO EB; [f] N=158 for ClinRO EB

Demographics and Baseline Characteristics by SALT Score Response Subgroup

- The higher proportion of female patients in the responder subgroup compared with intermediate responders and compared with the overall population suggests a potential contribution of undiagnosed androgenetic alopecia to overall hair loss in male patients
- Responders and intermediate responders tended to have shorter duration of disease and current AA episode at baseline compared with non-responders
- Baseline severity of scalp, eyebrow, and eyelash hair loss was higher in the non-response subgroup

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ABBREVIATIONS

AA=alopecia areata; BARI=baricitinib; BMI=body mass index; CI=confidence interval; ClinRO=clinician-reported outcome; ClinRO EB=ClinRO Measure for Eyebrow Hair Loss; ClinRO EL=ClinRO Measure for Eyelash Hair Loss; COVID-19=coronavirus disease 2019; PBO=placebo; QD=once daily; SALT=Severity of Alopecia Tool; SALT30=≥30% improvement from baseline in total SALT score; 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, and Pfizer; and is a clinical trial investigator for: Concert Pharmaceuticals and Eli Lilly and Company; **O. Kwon** has been a consultant for: Eli Lilly and Company; and has received clinical study funds from: Addpharma, Eli Lilly and Company, and Pfizer; **B. M. Piraccini** has received honoraria from or been a consultant for: Almirall, Eli Lilly and Company, ISDIN, Pfizer, and Vichy Laboratoires; **R. Sinclair** has been an investigator for and/or provided professional services to: AbbVie, Aerotek Scientific, Akeso Biopharma, Amgen, Arcutis, Arena Pharmaceuticals, Ascend Laboratories, AstraZeneca, Bayer Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Coherus BioSciences, Connect Biopharma, Cutanea, Dermira, Eli Lilly and Company, Galderma, GlaxoSmithKline, Janssen, LEO Pharma, MedImmune, Merck Sharp & Dohme, Novartis, Oncobiologics, Pfizer, Regeneron, Reistone Biopharma, Roche, Samson Medical Technologies, Sanofi, Sun Pharma, and UCB Pharma; **S. Ball, Y. Ding, Y.-F. Chen, and Y. Dutronc** are employees and shareholders of: Eli Lilly and Company; **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 bureaus for: AbbVie, Incyte Corporation, LEO Pharma, Pfizer, Regeneron, and Sanofi Genzyme

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