Scalp Hair Regrowth Is Associated With Improvements in Health-Related Quality of Life and Psychological Symptoms in Patients With Severe Alopecia Areata: Results From Two Randomized Controlled Trials

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BACKGROUND

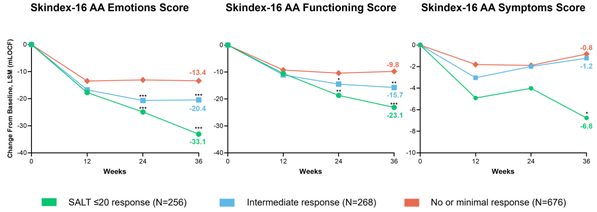
- Alopecia areata (AA) is a common autoimmune disorder that results in hair loss[1]
  - Hair loss can range in severity, from loss of hair in small localized patches on the scalp, to complete loss of hair on the scalp (alopecia totalis) and/or body (alopecia universalis)[1]
- Severe AA is frequently associated with health-related quality of life (HRQoL) impairment and psychological burden[2]
- However, the impact of hair regrowth on HRQoL and psychosocial burden has not been sufficiently investigated

OBJECTIVE

- To evaluate the association between scalp hair regrowth and improvement of HRQoL and psychological burden in patients with severe AA using pooled data from the Phase 3, randomized, placebo-controlled trials, BRAVE-AA1 (NCT03570749) and BRAVE-AA2 (NCT03899259)

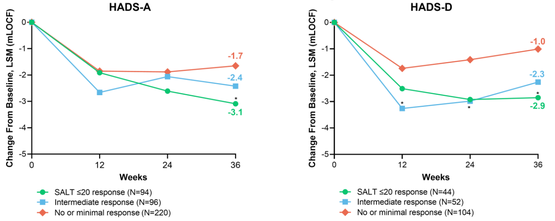
KEY RESULTS

Greater Improvement (Decrease) in All Skindex-16 AA Domain Scores Was Observed in Patients With a SALT ≤20 Response at Week 36



* p<0.05; ** p<0.01; *** p<0.001 vs. no or minimal response

Greater Improvement (Decrease) in Anxiety and Depression Scores Was Observed in Patients With a SALT ≤20 Response at Week 36



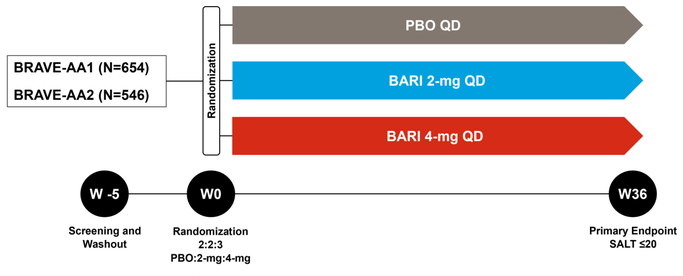
* p<0.05; vs. no or minimal response in patients with borderline or abnormal severity scores at baseline (HADS-A ≥8 or HADS-D ≥8)

CONCLUSIONS

- Patients with severe AA who achieved scalp hair regrowth at Week 36 experienced improvements in HRQoL and symptoms of anxiety and depression when compared with those who had no or minimal regrowth
  - Higher benefit was observed in patients achieving a SALT ≤20 response
  - Improvements were also observed in the intermediate response group, but generally to a lesser extent than those in the SALT ≤20 response group
- These results support the clinical relevance of SALT ≤20, the primary endpoint for the baricitinib clinical program in severe AA
- Longer treatment duration may be needed to assess the full impact on scalp hair regrowth, HRQoL, and symptoms of anxiety and depression

METHODS

Study Design, BRAVE-AA1 and BRAVE-AA2



Note: Figure is not the full study design, but only the PBO-Controlled Period of both trials

Key Eligibility Criteria for BRAVE-AA1 and BRAVE-AA2

Inclusion

- Age ≥18 years to ≤60 years (males) or ≤70 years (females)
- Severe or very severe AA
  - Hair loss encompassing ≥50% of the scalp, as measured by the Severity of Alopecia Tool (SALT)
- Current episode of AA lasting >6 months to <8 years[a]

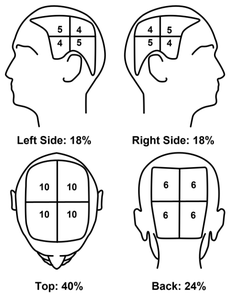
Exclusion

- 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 were allowed if on stable dose for 12 months and bimatoprost ophthalmic solution was allowed if on stable dose for 8 weeks

SALT Score[3]

- Assesses hair loss in each quadrant of the scalp
- The SALT score is a weighted sum of the percent of hair loss in the 4 quadrants of the scalp, ranging from 0 to 100
- Examples:
  - SALT 0=no scalp hair loss
  - SALT 50=50% scalp hair loss
  - SALT 100=complete scalp hair loss



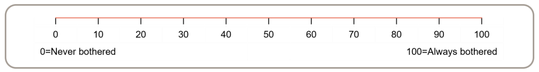
Patient Subgroups

- Patients were categorized into 3 groups according to scalp hair regrowth at Week 36:
  1. **SALT ≤20 Response** (N=256): Met the primary endpoint of SALT ≤20 (ie, ≥80% scalp hair coverage)
  2. **Intermediate Response** (N=268): Did not meet the primary endpoint but achieved ≥30% improvement from baseline in SALT score at any post-baseline visit up to Week 36 ($SALT_{30}$)
  3. **No or Minimal Response** (N=676): Did not achieve $SALT_{30}$ at any post-baseline visit up to Week 36

Assessments

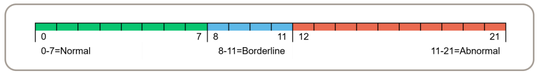
Skindex-16 adapted for AA: Assessed effects of AA on HRQoL over 3 domains:

- Emotions, symptoms, and functioning
- Each domain score ranged from 0 to 100, with higher scores indicating worse HRQoL



Hospital Anxiety and Depression Scale (HADS): Assessed levels of anxiety (HADS-A) and depression (HADS-D)[a]

- Each domain score ranged from 0 to 21, with higher scores indicating greater anxiety or depression
- Used to identify patients with borderline or abnormal severity scores at baseline (HADS-A ≥8 or HADS-D ≥8)



[a] Patients with significant uncontrolled neuropsychiatric disorder were not eligible for the study

Statistical Analyses

- Data were pooled from the 3 arms (placebo, baricitinib 4-mg, and baricitinib 2-mg) of BRAVE-AA1 and BRAVE-AA2 and analyzed independently of treatment allocation
- Change from baseline in Skindex-16 domains, HADS-A, and HADS-D scores were analyzed using analysis of covariance with modified last observation carried forward imputation for missing data
  - Data after permanent study drug discontinuation were censored and not carried forward
- Percentage of patients who shifted from borderline or abnormal to normal HADS-A and HADS-D scores were analyzed using logistic regression with non-responder imputation

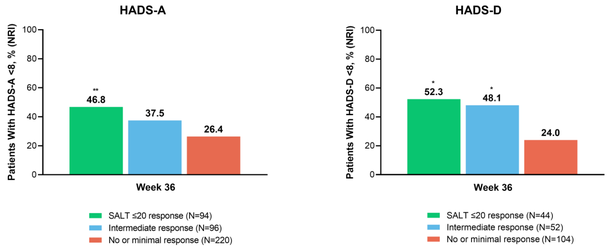
RESULTS

Demographics and Baseline Characteristics, by Hair Regrowth Response Group

	Response Categories According to Scalp Hair Regrowth at Week 36 for Pooled Treatment Arms		
	SALT ≤20 Response (N=256)	Intermediate Response (N=268)	No or Minimal Response (N=676)
Age, years	37.4 (12.5)	37.3 (12.6)	37.7 (13.1)
Female, n (%)	166 (64.8)	149 (55.6)	413 (61.1)
Duration from onset of AA, years	9.0 (9.3)	11.5 (10.7)	13.6 (11.2)
Duration of current AA episode, years	3.0 (3.5)	3.5 (3.0)	4.4 (5.0)
SALT score	77.3 (18.9)	81.8 (18.3)	89.8 (16.1)
SALT category, n (%)			
Severe (SALT 50-94)	179 (69.9)	157 (58.6)	225 (33.3)
Very severe (SALT 95-100)	77 (30.1)	111 (41.4)	450 (66.7)
Skindex-16 AA domain score[a]			
Symptoms	19.4 (20.2)	19.0 (20.9)	17.6 (19.9)
Emotions	70.3 (25.9)	68.3 (27.3)	67.0 (28.7)
Functioning	52.4 (30.9)	50.0 (32.6)	49.5 (32.2)
Patients with B/AB anxiety (HADS-A ≥8), n (%)	94 (36.7)	96 (35.8)	220 (32.5)
Patients with B/AB depression (HADS-D ≥8), n (%)	44 (17.2)	52 (19.4)	104 (15.4)
HADS-A score[b]	10.5 (2.7)	10.3 (2.3)	10.7 (2.8)
HADS-D score[b]	10.0 (1.9)	9.7 (2.0)	9.9 (2.0)

Data are mean (standard deviation) unless stated otherwise
[a] In patients with baseline assessment of Skindex-16 adapted for AA
[b] In patients with baseline HADS-A ≥8 or HADS-D ≥8

Patients With a SALT ≤20 Response at Week 36 Were More Likely to Achieve Normal Anxiety and Depression Scores (HADS <8)



* p<0.05; ** p<0.01 vs. no or minimal response in patients with borderline or abnormal severity scores at baseline (HADS-A ≥8 or HADS-D ≥8)

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1. Pratt C, et al. *Nat Rev Dis Primers*. 2017;3:17011
2. Mostaghimi A, et al. *Dermatol Ther (Heidelb)*. 2021;11:867-883.
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ABBREVIATIONS

AA=alopecia areata; B/AB=borderline/abnormal; BARI=baricitinib; HADS-A=Hospital Anxiety and Depression Scale–Anxiety; HADS-D=Hospital Anxiety and Depression Scale–Depression; HRQoL=health-related quality of life; LSM=least squares mean; mLOCF=modified last observation carried forward; NRI=non-responder imputation; PBO=placebo; QD=once daily; SALT=Severity of Alopecia Tool; W=Week

DISCLOSURES

- **B. M. Piraccini** has been an Investigator for, received honoraria and/or consulting fees from, and/or been a speaker for: Concert Pharmaceuticals, Eli Lilly and Company, ISDIN, and Pfizer; **M. Ohyama** has received advisory and/or lecture fees from: Eli Lilly Japan K.K., Janssen, Pfizer Japan, Rohto Pharmaceutical, and Taisho Pharmaceutical; and has received research grants from: Maruho, Shiseido, and Sun Pharma Japan; **B. Craiglow** has received honoraria and/or fees from: Eli Lilly and Company, Pfizer, Regeneron, and Sanofi Genzyme; **A. Bewley** has received honoraria and/or consulting fees from: AbbVie, Almirall, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Novartis, Sanofi, and UCB Pharma; **Y. Ding, Y.-F. Chen, Y. Dutronc, E. Pierce, and F. Durand** are employees and stockholders of: Eli Lilly and Company; A. Mostaghimi has been a consultant for: AbbVie, Concert Pharmaceuticals, Digital Diagnostics, Eli Lilly and Company, and Pfizer
- Medical writing assistance was provided by Linda Donnini, PhD, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company
- This study is previously presented at European Academy of Dermatology and Venereology - 31st Congress, 2022

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Study was sponsored by Eli Lilly and Company, under license from Incyte Corporation