Agreement Between Patient and Physician Assessment of Eyebrow and Eyelash Hair Loss in Two Phase 3 Trials Evaluating Baricitinib in Patients With Severe Alopecia Areata

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OBJECTIVE

- To determine the level of agreement between the PRO and ClinRO measures for the assessment of eyebrow and eyelash hair loss over 52 weeks

CONCLUSIONS

- These analyses showed strong positive correlation between the ClinRO and PRO measures for the assessment of eyebrow/eyelash hair loss
- This indicates high levels of agreement between clinicians and patients on assessments of hair loss and perception of regrowth during treatment when using these instruments

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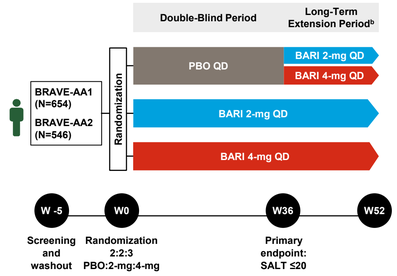
BACKGROUND

- AA is an autoimmune disease characterized by unpredictable hair loss that can range from ≥1 bald patches to total scalp hair loss or total body hair loss[1]
- Baricitinib, an oral selective JAK inhibitor, has demonstrated efficacy in patients with severe AA in 2 Phase 2/3, randomized, double-blind, placebo-controlled trials, BRAVE-AA1 (NCT03570749[2]) and BRAVE-AA2 (NCT03899259[3]), and is approved for the treatment of severe AA in the USA, Europe, and Japan
- Eyebrow and eyelash hair loss is an important manifestation of AA
- To allow proper assessment of eyebrow and eyelash involvement in clinical trials, ClinRO and PRO measures were developed and included in the baricitinib Phase 3 program[4]

STUDY DESIGN[a]



[a] Figure is not the full study design; only the first year of both trials is shown; [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

Key Eligibility Criteria: BRAVE-AA1 and BRAVE-AA2

Inclusion

- Age ≥18 years to ≤60 years (males) or ≤70 years (females)[a]
- Severe or very severe AA
  - Hair loss involving ≥50% of the scalp, as measured by SALT score
- Current episode of AA lasting >6 months to <8 years[b]
- No spontaneous improvement in the 6 months before screening

Exclusion

- Primarily "diffuse" type of AA
- Concomitant treatments for AA[c]

[a] Different upper age limits have been included for male and female patients based on the difference in 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] Not permitted: Topical corticosteroids within 1 week prior to randomization; topical JAK inhibitor, diphenylcyclopropenone, or other topical immunotherapies within 4 weeks prior to randomization; systemic corticosteroids, immunosuppressants, intra-lesional or intra-articular corticosteroid injections, or oral JAK inhibitor within 8 weeks prior to randomization; monoclonal antibody <5 half-lives prior to randomization; probenecid at the time of randomization. Oral/topical minoxidil or finasteride was permitted if on stable dose for 12 months, and bimatoprost ophthalmic solution was allowed if on stable dose for 8 weeks

SUMMARY OF KEY FINDINGS

Spearman's Correlation Score Between ClinRO and PRO Evaluations at Baseline, Week 36, and Week 52

ClinRO EB vs. PRO EB	ClinRO EL vs. PRO EL
0.85-0.86	0.83-0.87

Improvement From Baseline	Agreement Between ClinRO and PRO Evaluations at Week 36 and Week 52	
	EB	EL
≥2 points	87%-89%	87%-90%
≥1 point	~77%	76%-78%

Note: Spearman's correlation can range in score between +1 to -1. A score close to +1 indicates a strong positive correlation

At Weeks 36 and 52:

- Physician and patient perspectives on assessment of eyebrow and eyelash hair loss are strongly correlated when using these instruments
- The agreement between ClinRO and PRO evaluations of a ≥2-point improvement from baseline for eyebrow and eyelash was ~90%
- The agreement between ClinRO and PRO evaluations of a ≥1-point improvement from baseline for eyebrow and eyelash was ~80%

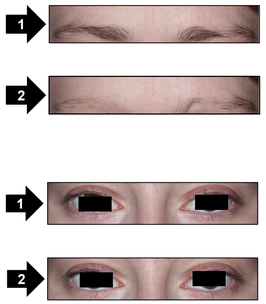
Methods

ClinRO Measures for Eyebrow and Eyelash Hair Loss™ and PRO Measures for Eyebrows and Eyelashes™[4]

	ClinRO Measure for Eyebrow Hair Loss[a]		PRO Measure for Eyebrows[b]
0	The eyebrows have full coverage and no areas of hair loss	0	I have full eyebrows on each eye
1	There are minimal gaps in eyebrow hair and distribution is even	1	I have a minimal gap(s) **or** a minimal amount of thinning in at least one of my eyebrows
2	There are significant gaps in eyebrow hair or distribution is not even	2	I have a large gap(s) **or** a large amount of thinning in at least one of my eyebrows
3	No notable eyebrow hair	3	I have no or barely any eyebrow hairs

	ClinRO Measure for Eyelash Hair Loss[a]		PRO Measure for Eyelashes[b]
0	The eyelashes form a continuous line along the eyelids on both eyes	0	I have full eyelashes on each eyelid
1	There are minimal gaps and the eyelashes are evenly spaced along the eyelids on both eyes	1	I have a minimal gap **or** minimal gaps along the eyelids
2	There are significant gaps along the eyelids or the eyelashes are not evenly spaced along the eyelids	2	I have a large gap or large gaps along the eyelids
3	No notable eyelashes	3	I have no or barely any eyelash hair

Example Photo Guides



[a] Should examine both eyebrows from 2 feet away; [b] Should examine the upper and lower eyelashes of both eyes

Statistical Analyses

- Eyebrow and eyelash hair loss was assessed by patients and physicians, at every visit, using the PRO and ClinRO measures, with supporting photoguides
- Analyses were conducted among patients who had all scores available
- Spearman's correlations of absolute PRO measures with each respective ClinRO measure for eyebrow/eyelash were calculated for baseline, Week 36, and Week 52 assessments
- Agreement on the ≥2-point and ≥1-point improvements from baseline assessments between PRO and ClinRO measures at Weeks 36 and 52 was evaluated
- Observed data from across 3 arms for each time point from the Intent-to-Treat population were used

Results

Demographics and Baseline Characteristics

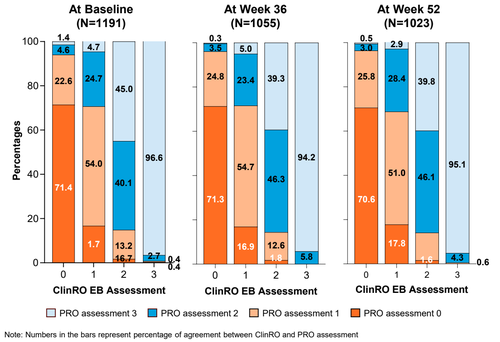
	BARI (N=1200)
Age,[a] years	37.5 (12.9)
Female, n (%)	728 (60.7)
Race,[b] n (%)	
White	620 (51.8)
Asian	435 (36.3)
Black	98 (8.2)
Duration of AA since onset, years	12.2 (10.9)
Duration of current AA episode, years, n (%)	
<4	787 (65.6)
≥4	413 (34.4)
SALT score	85.3 (18.0)
SALT score category,[c] n (%)	
Severe - SALT score 50-94 (non-AT)	561 (46.8)
Very severe - SALT score 95-100 (consistent with AT)	638 (53.2)
ClinRO EB 3,[d] n (%)	523 (43.9)
ClinRO EL 3,[d] n (%)	446 (37.4)

[a] N=1198; [b] N=1197; [c] N=1199; [d] N=1191

Notes: Data are mean (SD) unless stated otherwise. Data represent baseline characteristics of the pooled Week 36 efficacy population

Concordance of ClinRO and PRO on Eyebrow Assessment at Baseline, Week 36, and Week 52

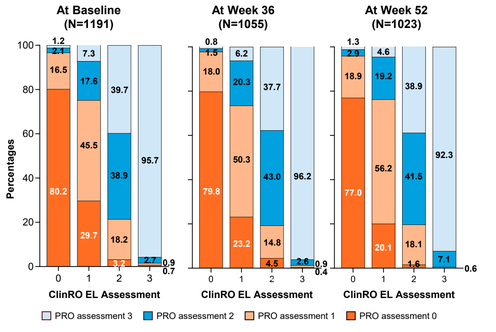
- The highest concordance between ClinRO and PRO on eyebrow assessments was observed for measures of 0 and 3 at baseline, Week 36, and Week 52
- Concordance between ClinRO and PRO on eyebrow assessment was lowest for ClinRO and PRO measures of 2 at baseline, Week 36, and Week 52



Note: Numbers in the bars represent percentage of agreement between ClinRO and PRO assessment

Concordance of ClinRO and PRO on Eyelash Assessment at Baseline, Week 36, and Week 52

- The highest concordance between ClinRO and PRO on eyelash assessments was observed for measures of 0 and 3 at baseline, Week 36, and Week 52
- Concordance between ClinRO and PRO on eyelash assessment was lowest for ClinRO and PRO measures of 2 at baseline, Week 36, and Week 52



Note: Numbers in the bars represent percentage of agreement between ClinRO and PRO assessment

Correlation Analyses of PRO and ClinRO Measurement of Eyebrows and Eyelashes

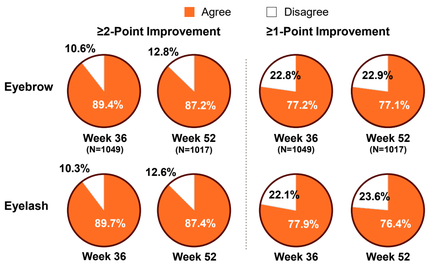
- Spearman's correlation scores between the ClinRO and PRO measures on eyebrow ranged from 0.85 to 0.86
- Spearman's correlation scores between the ClinRO and PRO measures on eyelash ranged from 0.83 to 0.87

Time Point	N	Spearman's Correlation Score	
		ClinRO EB vs. PRO EB	ClinRO EL vs. PRO EL
Baseline	1191	0.85	0.87
Week 36	1055	0.86	0.86
Week 52	1023	0.85	0.83

Note: Spearman's correlation can range in score between +1 to -1. A score close to +1 indicates a strong positive correlation

Summary of Agreement Between ≥2-Point and ≥1-Point Improvement of Eyebrow or Eyelash PRO and ClinRO Assessments at Week 36 and Week 52

- At Week 36, there was an 89% and 90% agreement between ClinRO and PRO evaluations of a ≥2-point improvement from baseline, respectively, for eyebrow and eyelash. At Week 52, these proportions were 87% for both eyebrow and eyelash
- At Week 36, there was 77% and 78% agreement between ClinRO and PRO evaluations of a ≥1-point improvement from baseline, respectively, for eyebrow and eyelash. At Week 52, these proportions were 77% and 76% for eyebrow and eyelash, respectively



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2. King B, et al. *J Am Acad Dermatol.* 2021;85:847-853.
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Abbreviations: *AA=alopecia areata; AT=alopecia totalis;BARI=baricitinib; ClinRO = clinician-reported outcome; EB=eyebrow; EL=eyelash; JAK=Janus kinase; PBO=placebo; PRO=patient-reported outcome; QD=once daily; SALT=Severity of Alopecia Tool; SD=standard deviation; W=Week*

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