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Concordance between clinician-reported and patient-reported outcomes of eyebrow and eyelash hair loss in patients with severe alopecia areata: Results from BRAVE-AA1 and BRAVE-AA2 studies

To the Editor: Eyebrow and eyelash hair loss in alopecia areata (AA) has a profound psychosocial and emotional impact on patients' quality of life.[1] Incorporating patients' perspective is critical for clinical outcomes assessment.[2] Clinician-reported outcome (ClinRO) and patient-reported outcome (PRO) measures, along with photo guides, have been developed to assess clinically meaningful improvements in eyebrow and eyelash hair loss.[3] Based on these measures, we evaluated the concordance between clinician and patient assessment of the extent of eyebrow and eyelash hair loss in adult patients with severe AA using 52-week pooled data from BRAVE-AA1[4] and BRAVE-AA2[4] phase 3 studies.

Patients with complete ClinRO and PRO data for eyebrows/eyelashes at baseline ($N = 1191$), Week (W) 36 ($N = 1055$), and W52 ($N = 1023$), were included. The Spearman's rank correlation coefficient (r_s) was used to assess the monotonic relationships between ordinal scaled i) ClinRO Measure for Eyebrow Hair Loss and PRO Measure for Eyebrows (response scale: 0−3 for both), and ii) ClinRO Measure for Eyelash Hair Loss and PRO Measure for Eyelashes (response scale: 0−3 for both).[3] An r_s of ≥0.5 indicated a strong positive correlation.[5] Proportion of patients with same (concordance) and different (discordance) assessments as those of the clinicians are reported. ClinRO−PRO concordance rates for each score (0, 1, 2, and 3) for eyebrow and eyelash hair loss were evaluated at baseline, W36, and W52. ClinRO−PRO concordance and discordance rates for ≥1- and ≥2-point improvement from baseline in eyebrows and eyelashes were assessed at W36 and W52. All analyses were performed using the observed data.

Strong positive correlations were observed between eyebrow ClinRO and PRO measures at baseline ($r_s = 0.85$), W36 ($r_s = 0.86$), and W52 ($r_s = 0.85$). Similarly, ClinRO and PRO measures for eyelashes were strongly correlated at baseline ($r_s = 0.87$), W36 ($r_s = 0.86$), and W52 ($r_s = 0.83$). ClinRO−PRO concordance rates for eyebrow hair loss were highest for scores of 3 (no notable eyebrow hair: 94.2% to 96.6%) and 0 (full eyebrows: 70.6% to 71.4%) up to W52 (Fig 1). For eyelashes, ClinRO−PRO concordance rates were highest for scores of 3 (no notable eyelashes: 92.3% to 96.2%) and 0 (full eyelashes on each eyelid: 77.0% to 80.2%) up to W52 (Fig 1). For both the eyebrow and eyelash assessments, ClinRO−PRO concordance rates for scores 1 and 2 ranged between 38.9% and 56.2% up to W52 (Fig 1). The discordance for scores 1 and 2 may be due to clinicians' unfamiliarity with the patients' normative appearance. Nonetheless, ClinRO−PRO concordance rates for ≥1-point improvement from baseline in eyebrows and eyelashes were >75% at W36 and W52. (Table I). Similarly, approximately 89% (W36) and 87% (W52) of patients agreed on ≥2-point

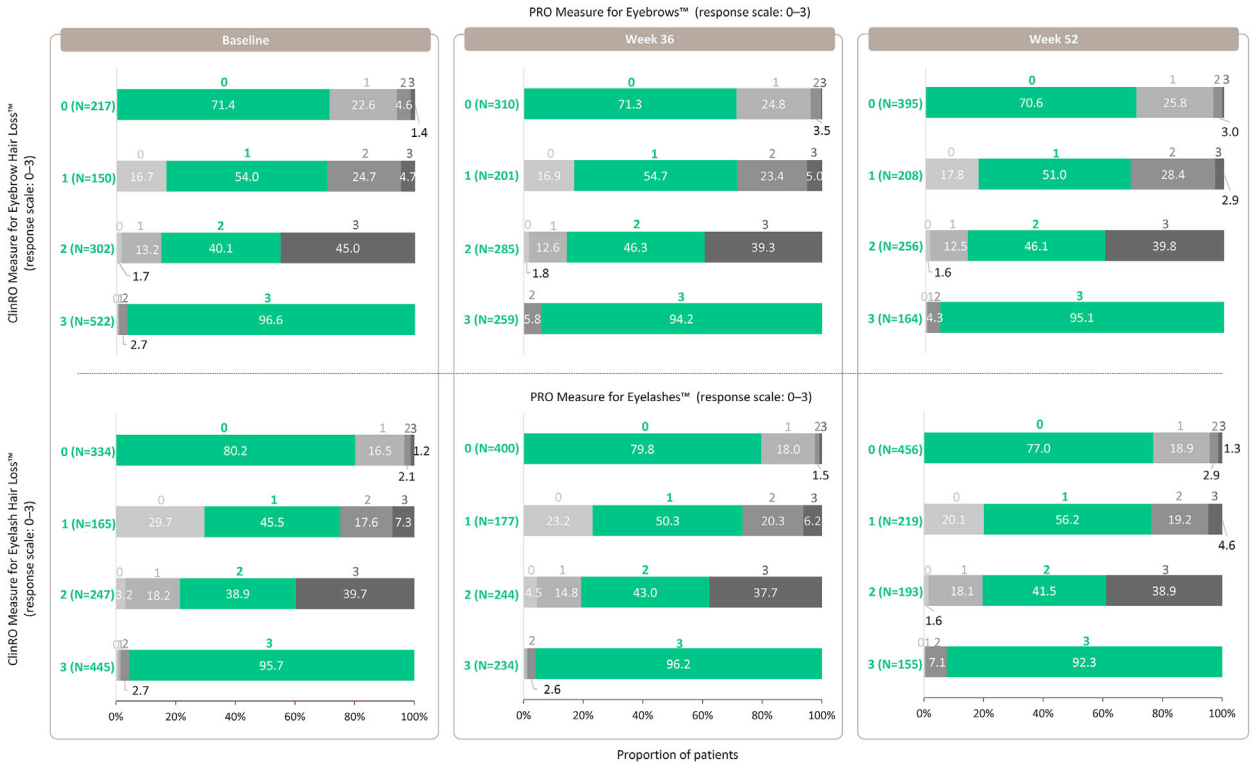

Fig 1. Alopecia areata: concordance rates for observed ClinRO and PRO scores for eyebrow and eyelash assessment at baseline, Week 36, and Week 52. The figure shows agreement between the individual item scores of the ClinRO (Y axis) and PRO (X axis) measures of eyebrow and eyelash hair loss. Agreement on each item score is shown by *green color*: 0 = full coverage, 1 = minimal loss, 2 = significant gaps/loss, and 3 = no notable hair. *Gray* represents discordance between the ClinRO and PRO measures. Data labels are not added if proportion of patients was <1%. *ClinRO*, Clinician-reported outcome; *PRO*, patient-reported outcome.

Table I. ClinRO—PRO concordance and discordance rates for ≥1- and ≥2-point improvement from baseline in eyebrows and eyelashes at weeks 36 and 52

Measurement	Week		*N* (%)
Improvement in eyebrows			
≥1 point improvement from baseline	36	Agree	810 (77.22)
		Disagree	239 (22.78)
	52	Agree	784 (77.09)
		Disagree	233 (22.91)
≥2 point improvement from baseline	36	Agree	938 (89.42)
		Disagree	111 (10.58)
	52	Agree	887 (87.22)
		Disagree	130 (12.78)
Improvement in eyelashes			
≥1 point improvement from baseline	36	Agree	817 (77.88)
		Disagree	232 (22.12)
	52	Agree	777 (76.40)
		Disagree	240 (23.60)
≥2 point improvement from baseline	36	Agree	941 (89.70)
		Disagree	108 (10.30)
	52	Agree	889 (87.41)
		Disagree	128 (12.59)

ClinRO, Clinician-reported outcome; *PRO*, patient-reported outcome.

improvement from baseline in eyebrows and eyelashes (Table I).

The study showed that ClinRO and PRO scores for eyebrow and eyelash hair loss were strongly correlated up to W52. A majority of patients' assessment of ≥1- and ≥2-point improvement from baseline in eyebrows and eyelashes was consistent with that of the clinicians up to W52. These findings suggest that patients' assessments of eyebrows and eyelashes using these established PROs can provide a similar evaluation as the clinicians' assessments.

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Data availability statement: Lilly provides access to all individual participant data collected during the trial, after anonymization, with the exception of pharmacokinetic or genetic data. Data are available to request 6 months after the indication studied has been approved in the United States and European Union and after primary publication acceptance, whichever is later. No expiration date of data requests is currently set once data are made available. Access is provided after a proposal has been approved by an independent review committee identified for this purpose and after receipt of a signed data sharing agreement. Data and documents, including the study protocol, statistical analysis plan, clinical study report, and blank or annotated case report forms, will be provided in a secure data sharing environment. For details on submitting a request, see the instructions provided at www.vivli.org.

Key words: Alopecia areata; ClinRO; eyebrow; eyelash; PRO.

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Clinical features and diagnostic challenges of genital ulcer biopsies: A retrospective study

To the Editor: Diagnosing genital ulcers based on clinical findings alone is inaccurate in over 50% of cases.[1] Thus, objective studies, including laboratory tests and histopathologic examinations, are commonly employed when attempting to achieve an accurate diagnosis. The differential diagnosis for genital ulcers is extensive,[2,3] with one study highlighting the diagnostic complexity of female genital ulcers, finding that histology was nonspecific in 74% of ulcers.[4] Given this knowledge gap, we performed a multi-institutional retrospective study to evaluate the utility of skin biopsies in the diagnosis of ulcers of the external genitalia.

An IRB-approved retrospective chart review was conducted for biopsies performed of external genital ulcers at 2 tertiary care referral centers from 2010 to 2022. We utilized ICD-10 diagnosis codes pertaining to genital ulceration (Supplementary Table I, available via Mendeley at https://data.mendeley.com/datasets/vnfyht7jff/6). Detailed inclusion and exclusion criteria are provided in Supplementary Methods, available via Mendeley at https://data.mendeley.com/datasets/vnfyht7jff/6.

Table I. Patient demographics with clinical and histologic characteristics of genital ulcers

Measure	Number of lesions (%)
Total number of lesions	98
Age, mean ± standard deviation	56.1 ± 19.0 years old
Sex	
Female	87 (88.8)
Male	11 (11.2)
Biopsy type	
Punch	65 (66.3)
Shave	11 (11.2)
Excision	7 (7.1)
Not specified	15 (15.3)
Biopsy provider	
Obstetrics-gynecology	66 (67.3)
Dermatology	23 (23.5)
Other*	9 (9.2)
Histologic special stain	
Infectious	61 (62.2)
None	29 (29.6)
Neoplastic	22 (22.4)
Conclusive histologic diagnosis	
No	70 (71.4)
Yes	28 (28.6)
Infectious	8 (8.1)
Neoplastic	11 (11.2)
Inflammatory	9 (9.2)
Final clinical diagnosis	
Inflammatory	39 (39.8)
Infectious	12 (12.2)
Neoplastic	14 (14.3)
Other†	6 (6.1)
Diagnosis not specified	27 (27.6)
Healing outcomes	
Healed	60 (61.2)
Not healed‡	12 (12.2)
Not reported	26 (26.5)

*Other biopsy providers included emergency medicine (1), hematology and oncology (1), family medicine (4), and urology (3).
†Other final clinical diagnoses included trauma (2), vulvodynia (1), calciphylaxis (1), granulation tissue (1), and multifactorial (1).
‡Final clinical diagnoses of nonhealed genital ulcers included: inflammatory (4), malignancy (2), infectious (1), other (2), and unspecified (3).

Ninety-eight ulcers were included. Most patients (88%) were female, and the mean age was 56 years old. Fifty-nine (61%) patients presented with a single genital ulcer, while 38 (39%) presented with multiple ulcers. Obstetrician-gynecologists performed most of the biopsies (67%), with punch biopsies being most common (66%). Most biopsies were evaluated with histologic stains to detect infection (62%), including herpes simplex virus (48%),