Electronic Supplementary Material

Article title: Efficacy and safety of baricitinib in patients with severe alopecia areata over 52 weeks of continuous therapy in two phase 3 trials (BRAVE-AA1 and BRAVE-AA2)

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Fig. S1 Disposition of patients randomized to baricitinib in a) BRAVE-AA1 and b) BRAVE-AA2 through 52 weeks

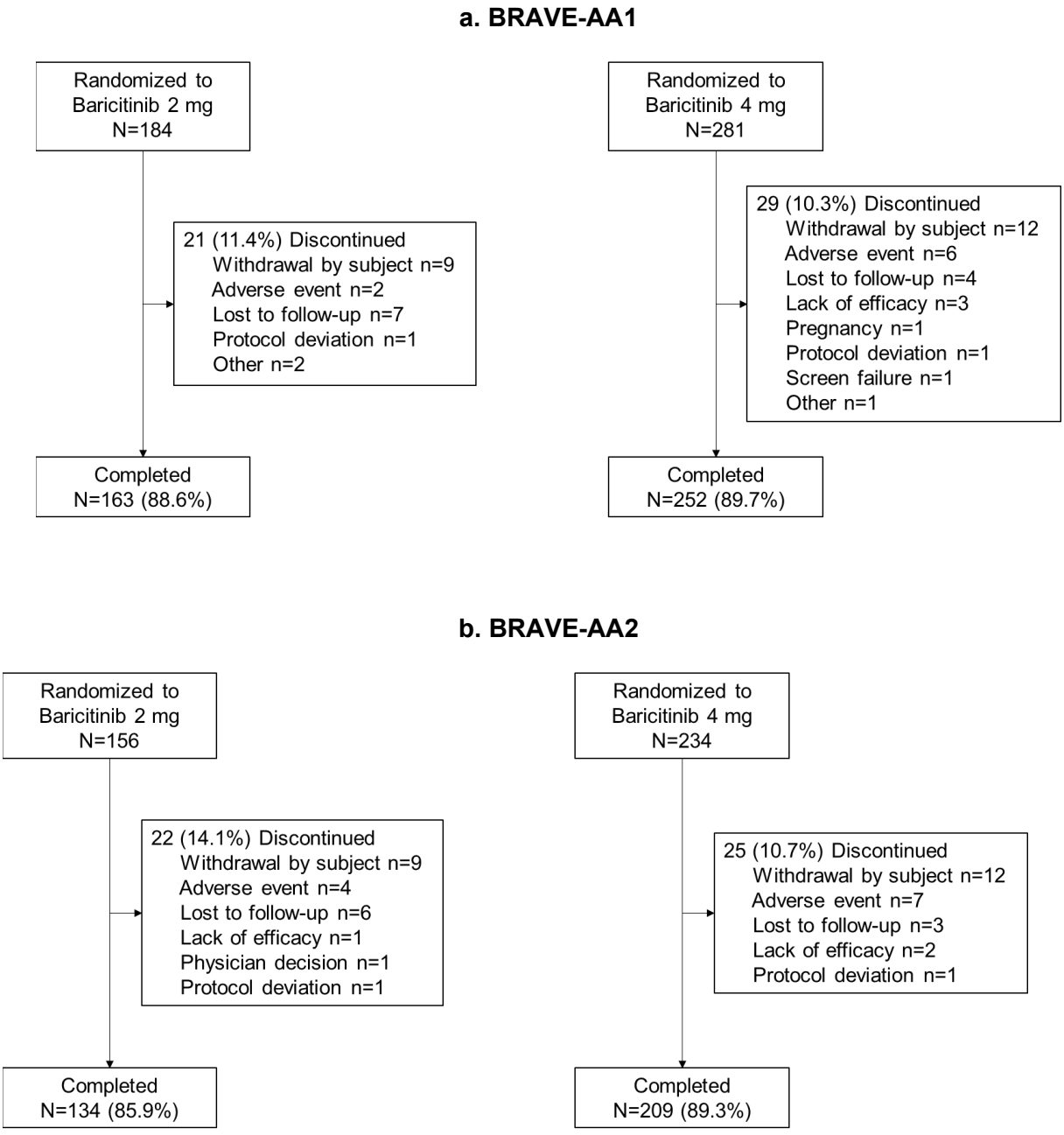
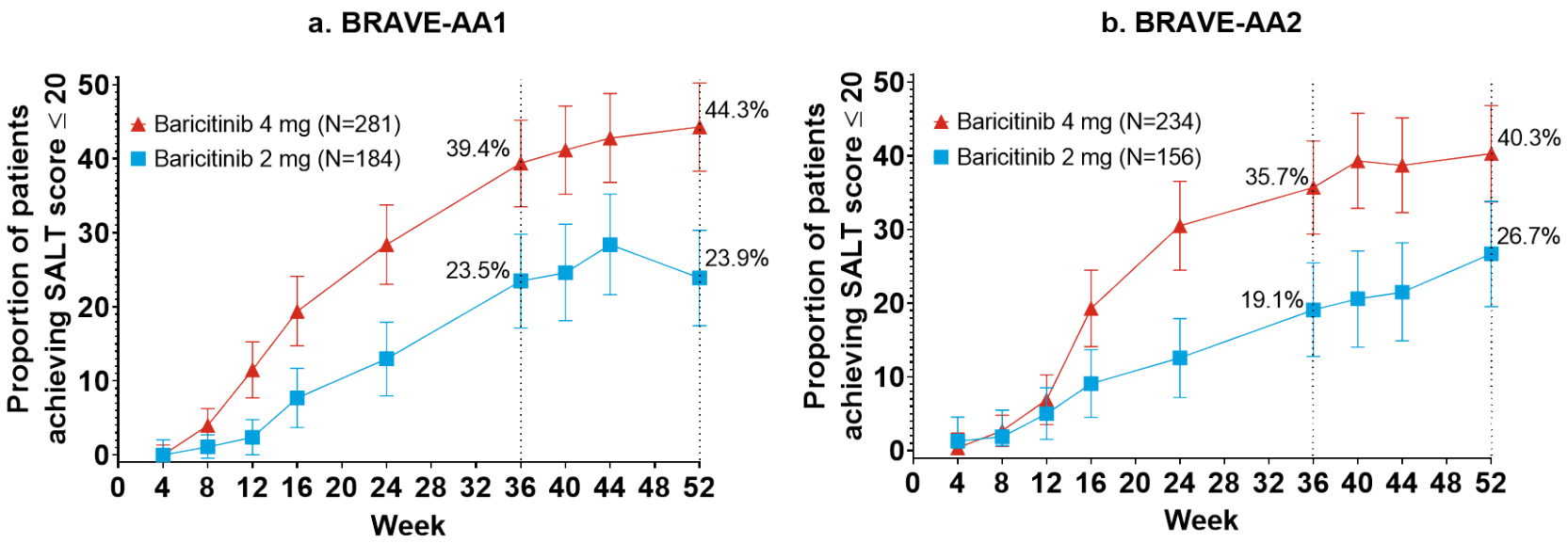


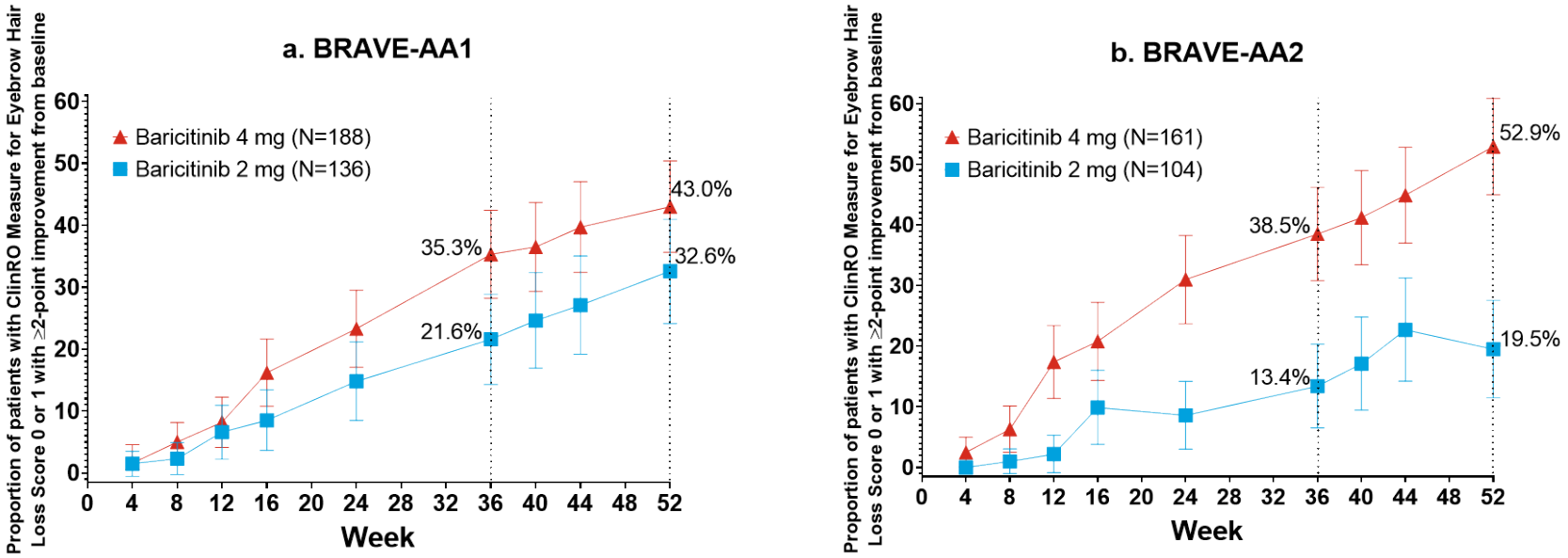
Fig. S2 Proportions of patients achieving SALT score ≤20 through Week 52 in a) BRAVE-AA1 and b) BRAVE-AA2 with multiple imputation applied to missing data



SALT, Severity of Alopecia Tool.

A SALT score ≤20 indicates ≤20% scalp hair loss. Bars represent 95% confidence intervals. Multiple imputation utilized 100 imputed data sets. If there is no missing data or no variation across the multiple imputed data sets, the results will be based on a single (imputed) data set. The percent response rate and confidence interval are synthetic results from PROC MIANALYZE procedure. Week-36 data points reflect results from the placebo-controlled period.

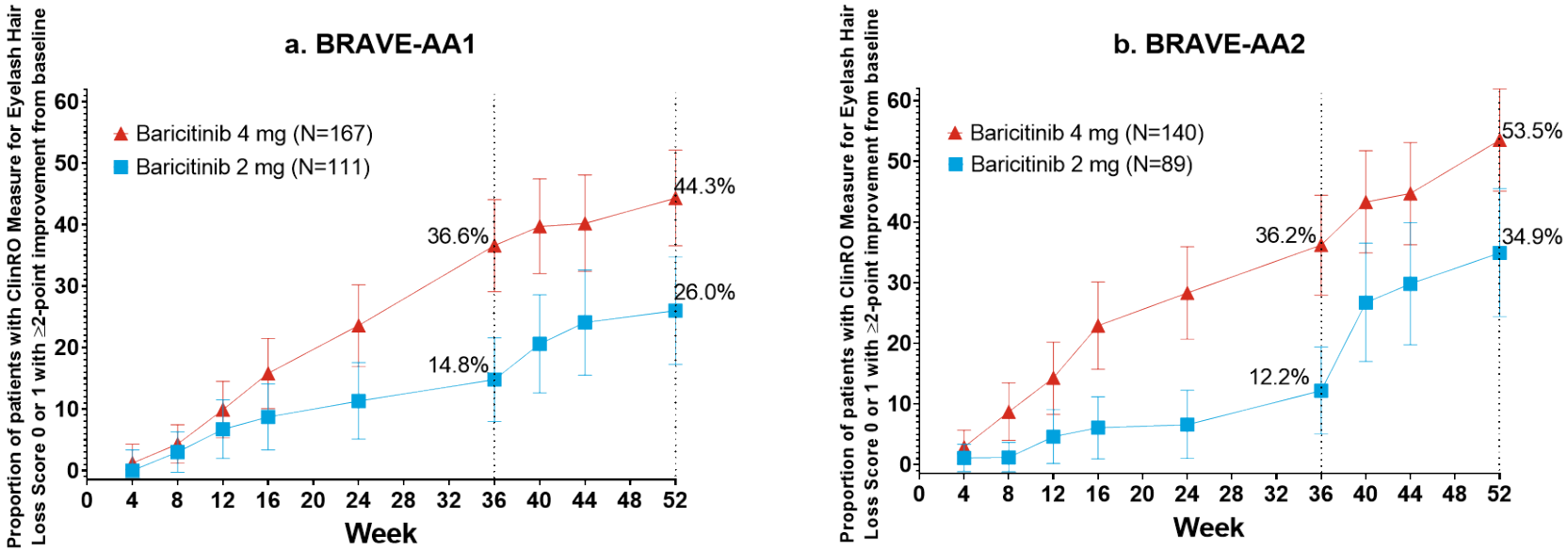
Fig. S3 Proportion of patients achieving ClinRO Measure for Eyebrow Hair Loss™ 0 or 1 with ≥2-point improvement from baseline through Week 52 among patients with a score of ≥2 at baseline in a) BRAVE-AA1 and b) BRAVE-AA2 with multiple imputation applied to missing data



ClinRO, Clinician-Reported Outcome

A ClinRO score of 0 indicates full coverage, and a score of 1 indicates minimal gaps in eyebrows or eyelashes. Bars represent 95% confidence intervals. Multiple imputation utilized 100 imputed data sets. If there is no missing data or no variation across the multiple imputed data sets, the results will be based on a single (imputed) data set. The percent response rate and confidence interval are synthetic results from PROC MIANALYZE procedure. Week-36 data points reflect results from the placebo-controlled period.

Fig. S4 Proportion of patients achieving ClinRO Measure for Eyelash Hair LossTM 0 or 1 with ≥2-point improvement from baseline through Week 52 among patients with a score of ≥2 at baseline in a) BRAVE-AA1 and b) BRAVE-AA2 with multiple imputation applied to missing data



ClinRO, Clinician-Reported Outcome

A ClinRO score of 0 indicates full coverage, and a score of 1 indicates minimal gaps in eyebrows or eyelashes. Bars represent 95% confidence intervals. Multiple imputation utilized 100 imputed data sets. If there is no missing data or no variation across the multiple imputed data sets, the results will be based on a single (imputed) data set. The percent response rate and confidence interval are synthetic results from PROC MIANALYZE procedure. Week-36 data points reflect results from the placebo-controlled period.

Table S1. Summary of efficacy outcomes at Weeks 36 and 52 with non-responder imputation or modified last observation carried forward applied to missing data (pre-specified analysis).

Outcome	BRAVE-AA1			BRAVE-AA2		
	Placebo (N=189)	Baricitinib 2 mg (N=184)	Baricitinib 4 mg (N=281)	Placebo (N=156)	Baricitinib 2 mg (N=156)	Baricitinib 4 mg (N=234)
Proportion achieving SALT score[a] ≤20, n (%); (95 % CI)						
At Week 36	10 (5.3) (2.9, 9.5)	40 (21.7) (16.4, 28.2)	99 (35.2) (29.9, 41.0)	4 (2.6) (1.0, 6.4)	27 (17.3) (12.2, 24.0)	76 (32.5) (26.8, 38.7)
At Week 52	-	39 (21.2) (15.9, 27.7)	115 (40.9) (35.3, 46.8)	-	38 (24.4) (18.3, 31.7)	86 (36.8) (30.8, 43.1)
Proportion achieving SALT score ≤10, n (%); (95 % CI)						
At Week 36	7 (3.7) (1.8, 7.4)	23 (12.5) (8.5, 18.1)	73 (26.0) (21.2, 31.4)	1 (0.6) (0.1, 3.5)	17 (10.9) (6.9, 16.8)	55 (23.5) (18.5, 29.3)
At Week 52	-	26 (14.1) (9.8, 19.9)	84 (29.9) (24.8, 35.5)	-	26 (16.7) (11.6, 23.3)	65 (27.8) (22.4, 33.8)
Percent change from baseline in SALT score, mean (SD)						
At Week 36	-8.1% (3.1)	-31.2% (37.9)	-46.7% (41.2)	-3.0 (2.7)	-30.0% (36.1)	-48.5% (39.1)
At Week 52	-	-34.1% (38.5)	-52.5% (41.0)	-	-38.0% (38.2)	-54.2% (38.2)
Proportion achieving $SALT_{50}$, n (%); (95 % CI)						
At Week 36	-	56 (30.4) (24.2, 37.4)	130 (46.3) (40.5, 52.1)	-	44 (28.2) (21.7, 35.7)	110 (47.0 (40.7, 53.4)

At Week 52	-	57 (31.0) (24.7, 38.0)	146 (52.0) (46.1, 57.7)	-	58 (37.2) (30.0, 45.0)	123 (52.6) (46.2, 58.9)
Proportion achieving $SALT_{90}$, n (%); (95 % CI)						
At Week 36	6 (3.2) (1.5, 6.8)	21 (11.4) (7.6, 16.8)	63 (22.4) (17.9, 27.6)	1 (0.6) (0.1, 3.5)	13 (8.3) (4.9, 13.7)	50 (21.4) (16.6, 27.1)
At Week 52	-	21 (11.4) (7.6, 16.8)	80 (28.5) (23.5, 34.0)	-	22 (14.1) (9.5, 20.4)	61 (26.1) (20.9, 32.0)
Proportion achieving ClinRO Measure for Eyebrow Hair Loss™ 0 or 1[b] with ≥2-point improvement from baseline[c], n (%); (95 % CI)						
At Week 36	4 (3.2) (1.3, 8.0)	26 (19.1) (13.4, 26.5)	59 (31.4) (25.2, 38.3)	5 (4.5) (1.9, 10.0)	12 (11.5) (6.7, 19.1)	56 (34.8) (27.9, 42.4)
At Week 52	-	38 (27.9) (21.1, 36.0)	74 (39.4) (32.7, 46.5)	-	17 (16.3) (10.5, 24.6)	80 (49.7) (42.1, 57.3)
Proportion achieving ClinRO Measure for Eyelash Hair Loss™ 0 or 1[b] with ≥2-point improvement from baseline[d], n (%); (95 % CI)						
At Week 36	3 (3.1) (1.1, 8.8)	15 (13.5) (8.4, 21.1)	56 (33.5) (26.8, 41.0)	5 (5.6) (2.4, 12.4)	9 (10.1) (5.4, 18.1)	47 (33.6) (26.3, 41.7)

At Week 52	-	24 (21.6) (15.0, 30.2)	68 (40.7) (33.6, 48.3)	-	27 (30.3) (21.8, 40.5)	71 (50.7) (42.5, 58.9)

CI, confidence interval; ClinRO, clinician-reported outcome; n, number of patients in the specified category; N, total population size; SALT, Severity of Alopecia Tool; $SALT_{50}$, ≥50% improvement from baseline in SALT score; $SALT_{90}$, ≥90% improvement from baseline in SALT score; SD, standard deviation

Data is non-responder imputation or missing data imputed with modified last observation carried forward (pre-specified analysis).

[a]The SALT score indicates the percentage of scalp hair loss. Subscripts of SALT indicate the percentage of improvement in score from baseline.

[b]A ClinRO score of 0 indicates full coverage, and a score of 1 indicates minimal gaps in eyebrows or eyelashes.

[c]Analysis was restricted to patients with baseline scores ≥2 (BRAVE-AA1: N=136 [baricitinib 2 mg] and N=188 [baricitinib 4 mg]; BRAVE-AA2: N=104 [baricitinib 2 mg] and N=161 [baricitinib 4 mg]).

[d]Analysis was restricted to patients with baseline scores ≥2 (BRAVE-AA1: N=111 [baricitinib 2 mg] and N=167 [baricitinib 4 mg]; BRAVE-AA2: N=89 [baricitinib 2 mg] and N=140 [baricitinib 4 mg]).

Table S2. Summary of efficacy outcomes at Weeks 36 and 52 with multiple imputation applied to missing data.

Outcome	BRAVE-AA1			BRAVE-AA2		
	Placebo (N=189)	**Baricitinib 2 mg (N=184)**	**Baricitinib 4 mg (N=281)**	**Placebo (N=156)**	**Baricitinib 2 mg (N=156)**	**Baricitinib 4 mg (N=234)**
Proportion achieving SALT score[a] ≤20, % of patients (95 % CI)						
At Week 36	6.2 (2.6, 9.9)	23.5 (17.17, 29.82)	39.4 (33.52, 45.18)	3.3 (0.3, 6.3)	19.1 (12.77, 25.45)	35.7 (29.39, 42.00)
At Week 52	-	23.9 (17.45, 30.33)	44.3 (38.31, 50.23)	-	26.7 (19.54, 33.82)	40.3 (33.76, 46.81)
Proportion achieving SALT score ≤10, % of patients (95 % CI)						
At Week 36	4.1 (1.1, 7.0)	13.3 (8.26, 18.36)	28.2 (22.80, 33.58)	1.0 (-0.8, 2.8)	11.8 (6.62, 17.07)	25.3 (19.59, 31.03)
At Week 52		15.4 (10.03, 20.82)	31.7 (26.05, 37.26)	-	17.8 (11.64, 24.01)	29.6 (23.53, 35.61)
Proportion achieving $SALT_{50}$, % of patients (95 % CI)						
At Week 36	-	33.7 (26.63, 40.85)	52.4 (46.40, 58.43)	-	32.0 (24.45, 39.63)	51.8 (45.17, 58.39)
At Week 52	-	36.7 (29.32, 44.07)	57.5 (51.51, 63.54)	-	41.8 (33.72, 49.93)	58.1 (51.49, 64.69)
Proportion achieving $SALT_{90}$, % of patients (95 % CI)						

At Week 36	3.3 (0.7, 6.0)	11.9 (7.09, 16.61)	24.1 (18.99, 29.24)	0.8 (-0.7, 2.3)	9.0 (4.35, 13.59)	22.6 (17.16, 28.12)
At Week 52	-	12.3 (7.38, 17.13)	29.7 (24.19, 35.13)	-	14.9 (9.15, 20.60)	27.2 (21.33, 32.99)
Proportion achieving ClinRO Measure for Eyebrow Hair Loss™ 0 or 1[b] with ≥2-point improvement from baseline[c], % of patients (95 % CI)						
At Week 36	4.4 (0.3, 8.5)	21.6 (14.28, 28.83)	35.3 (28.22, 42.44)	5.5 (1.0. 10.1)	13.4 (6.53, 20.35)	38.5 (30.80, 46.21)
At Week 52	-	32.6 (24.14, 40.97)	43.0 (35.62, 50.39)	-	19.5 (11.50, 27.56)	52.9 (44.95, 60.85)
Proportion achieving ClinRO Measure for Eyelash Hair Loss™ 0 or 1[b] with ≥2-point improvement from baseline[d], % of patients (95 % CI)						
At Week 36	4.4 (-0.2, 8.9)	14.8 (7.93, 21.58)	36.6 (29.09, 44.06)	6.9 (1.3, 12.4)	12.2 (5.03, 19.40)	36.2 (27.93, 44.41)
At Week 52	-	26.0 (17.28, 34.72)	44.3 (36.55, 52.11)	-	34.9 (24.39, 45.47)	53.5 (45.08, 61.93)

CI, confidence interval; ClinRO, clinician-reported outcome; N, total population size; SALT, Severity of Alopecia Tool; $SALT_{50}$, ≥50% improvement from baseline in SALT score; $SALT_{90}$, ≥90% improvement from baseline in SALT score

Values represent means of proportions or percentages on the basis of 100 imputed data sets and cannot be presented as numerator and denominator. Multiple imputation reflects variation both within and across imputations.

[a]The SALT score indicates the percentage of scalp hair loss. Subscripts of SALT indicate the percentage of improvement in score from baseline.

[b]A ClinRO score of 0 indicates full coverage, and a score of 1 indicates minimal gaps in eyebrows or eyelashes.

[c]Analysis was restricted to patients with baseline scores ≥2 (BRAVE-AA1: N=136 [baricitinib 2 mg] and N=188 [baricitinib 4 mg]; BRAVE-AA2: N=104 [baricitinib 2 mg] and N=161 [baricitinib 4 mg]).

[d]Analysis was restricted to patients with baseline scores ≥2 (BRAVE-AA1: N=111 [baricitinib 2 mg] and N=167 [baricitinib 4 mg]; BRAVE-AA2: N=89 [baricitinib 2 mg] and N=140 [baricitinib 4 mg]).

Table S3. Summary of serious adverse events.

n (%) [IR]	BRAVE-AA1		BRAVE-AA2	
	Baricitinib 2 mg (N=183)	Baricitinib 4 mg (N=280)	Baricitinib 2 mg (N=155)	Baricitinib 4 mg (N=233)
Patients with ≥1 serious adverse event	5 (2.7) [2.4]	11 (3.9) [2.8]	4 (2.6) [2.3]	13 (5.6) [4.5]
Cardiac disorders				
Ventricular tachycardia	0	1 (0.4) [0.3]	0	0
Acute myocardial infarction	1 (0.5) [0.5]	0	0	0
Cardiac failure congestive	0	0	1 (0.6) [0.6]	0
Aortic valve incompetence	0	0	0	1 (0.4) [0.3]
Gastrointestinal disorders				
Food poisoning	0	1 (0.4) [0.3]	0	0
Inguinal hernia	0	0	0	1 (0.4) [0.3]
General disorders and administration site conditions				
Chest pain	0	1 (0.4) [0.3]	0	0
Asthenia	1 (0.5) [0.5]	0	0	0
Cyst	0	1 (0.4) [0.3]	0	0
Hepatobiliary disorders				
Cholecystitis acute	0	0	1 (0.6) [0.6]	1 (0.4) [0.3]
Hepatitis acute	0	1 (0.4) [0.3]	0	0
Infections and infestations				
Appendicitis	0	0	0	1 (0.4) [0.3]
Pyelonephritis	0	0	1 (0.6) [0.6]	1 (0.4) [0.3]
COVID-19 pneumonia	0	0	1 (0.6) [0.6]	0
COVID-19	0	0	0	1 (0.4) [0.3]
Herpes zoster	0	0	0	1 (0.4) [0.3]

Injury, poisoning, and procedural complications				
Facial bones fracture	0	2 (0.7) [0.5]	0	0
Ankle fracture	1 (0.5) [0.5]	1 (0.4) [0.3]	1 (0.6) [0.6]	0
Foot fracture	1 (0.5) [0.5]	0	0	0
Clavicle fracture	0	1 (0.4) [0.3]	0	0
Lumbar vertebral fracture	0	0	0	1 (0.4) [0.3]
Hand fracture	1 (0.5) [0.5]	0	0	0
Radius fracture	1 (0.5) [0.5]	0	0	0
Neoplasms benign, malignant and unspecified (including cysts and polyps)				
B-cell lymphoma	0	0	0	1 (0.4) [0.3]
Uterine leiomyoma	0	0	0	1 (0.7) [0.6][a]
Nervous system disorders				
Guillain-Barre syndrome	0	1 (0.4) [0.3]	0	0
Sciatica	0	0	0	1 (0.4) [0.3]
Pregnancy, puerperium and perinatal conditions				
Abortion missed	0	1 (0.6) [0.4][b]	0	0
Product issues				
Device dislocation	0	0	0	1 (0.4) [0.3]
Vascular disorders				
Hypertension	0	0	0	1 (0.4) [0.3]
Eye disorders				
Glaucoma	0	0	0	1 (0.4) [0.3]

IR, incidence rate; n, number of patients in the specified category; N, number of patients in the analysis set.

[a]Denominator and patient years adjusted because the event is specific to females: N=102 (baricitinib 2 mg), N=144 (baricitinib 4 mg)

[b]Denominator and patient years adjusted because the event is specific to females: N=108 (baricitinib 2 mg), N=164 (baricitinib 4 mg).

Table S4. Permanent discontinuation of study drug due to adverse event by system organ class.

n (%) [IR]	BRAVE-AA1		BRAVE-AA2	
	Baricitinib 2 mg (N=183)	Baricitinib 4 mg (N=280)	Baricitinib 2 mg (N=155)	Baricitinib 4 mg (N=233)
Investigations	2 (1.1) [1.0]	1 (0.4) [0.3]	1 (0.6) [0.6]	3 (1.3) [1.0]
Blood and lymphatic system disorders	0	1 (0.4) [0.3]	0	2 (0.9) [0.7]
Neoplasms benign, malignant and unspecified (includes cysts and polyps)	0	1 (0.4) [0.3]	0	1 (0.4) [0.3]
Cardiac disorders	0	1 (0.4) [0.3]	1 (0.6) [0.6]	0
General disorders and administration site conditions	1 (0.5) [0.5]	0	0	1 (0.4) [0.3]
Hepatobiliary disorders	0	1 (0.4) [0.3]	0	1 (0.4) [0.3]
Musculoskeletal and connective tissue disorders	0	1 (0.4) [0.3]	1 (0.6) [0.6]	0
Infections and infestations	0	0	1 (0.6) [0.6]	1 (0.4) [0.3]
Endocrine disorders	0	1 (0.4) [0.3]	0	0
Nervous system disorders	0	1 (0.4) [0.3]	0	0
Psychiatric disorders	1 (0.5) [0.5]	0	0	0
Vascular disorders	0	0	0	1 (0.4) [0.3]

IR, incidence rate; n, number of patients in the specified category; N, number of patients in the analysis set.