Trajectories For Scalp Hair Regrowth In Patients With Severe Alopecia Areata Treated With Baricitinib

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BACKGROUND

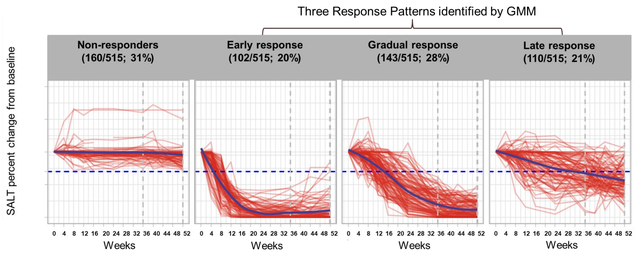
- Alopecia areata (AA) is a chronic autoimmune disorder characterized by unpredictable hair loss, that can affect any hair-bearing area.[1]
- The oral Janus kinase (JAK)1/JAK2 inhibitor baricitinib has demonstrated efficacy for patients with severe AA,[2,3] and has been approved for the treatment of severe AA in various regions including the USA, EU, and Japan.
- Little is known about the overall pattern of clinical response to treatment of patients with severe AA. Such information will be important to guide health care providers and patients seeking treatment.

OBJECTIVE

- This post hoc analysis of integrated data from two Phase 3 trials (BRAVE-AA1 [NCT03570749] and BRAVE-AA2 [NCT03899259]) describes trajectories of clinical response in patients with severe AA treated with baricitinib 2mg or 4mg over 52 weeks.

KEY RESULTS

Identification of response patterns based on SALT score percent change from baseline among 4mg-treated patients



The red lines indicate individual patients, the thick purple lines are the smoothing lines using local polynomial regression fitting, and the blue dotted lines indicate a 30% improvement from baseline in SALT score ($SALT_{30}$). Data were censored after permanent study drug discontinuation or data collected at remote visits due to the COVID-19 pandemic.

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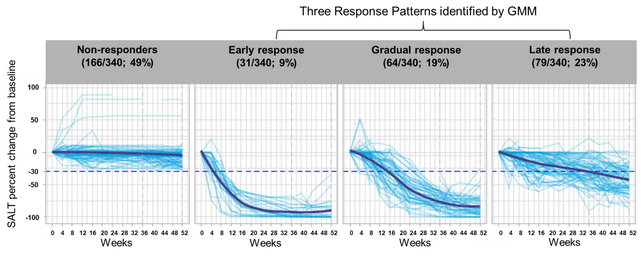

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CONCLUSIONS

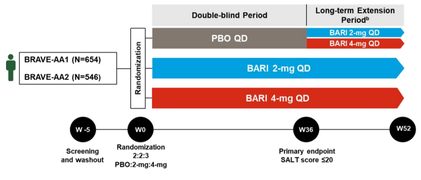
- These analyses revealed three response patterns among patients with severe AA who achieved $SALT_{30}$ on baricitinib at any point within 52 weeks: early, gradual and late.
- These findings can help to inform the treatment expectations for scalp hair regrowth as they suggest that baseline disease characteristics (severity and duration of current episode) may factor into a patient's trajectory of response.
- Longer treatment duration may be needed for some patients to assess the full impact of treatment on scalp hair regrowth.

REFERENCES

1. Pratt C, et al. *Nat Rev Dis Primers*. 2017;3:17011.
2. King B, et al. *N Engl J Med* 2022; 386:1687-1699.
3. King B, et al. *J Am Acad Dermatol*. 2021;85:847-853.

METHODS

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



[a] Figure is not the full study design, but only the first 52 weeks of both trials; [b] Patients randomized to BARI (4-mg or 2-mg QD) at baseline retained their treatment allocation through W52, whereas PBO non-responders were rescued at W36; [c] 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; [d] 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

Methods

- Non-responders were defined as having never reached at least a 30% improvement in SALT score from baseline ($SALT_{30}$)* within 52 weeks of treatment with 2mg or 4mg baricitinib.
- For patients who achieved $SALT_{30}$ at any point within 52 weeks, a machine-learning growth mixture model (GMM) was applied to cluster patients into response pattern subgroups based on SALT score percent change from baseline.
- For each response pattern, the following outcomes were analyzed:
  - Proportion of patients achieving the BRAVE-AA1/2 primary endpoint of SALT score ≤20 (≤20% scalp hair loss), and
  - Proportion of patients achieving ≥50% improvement from baseline in SALT score ($SALT_{50}$).

*SALT30 threshold was used during the Phase II dose-decision process[3]

Key Eligibility Criteria

- Male or female ≥18 years old; ≤60 years for males and ≤70 years for females
- Hair loss involving ≥50% of the scalp, as measured by the SALT score
- Current episode of AA >6 months to <8 years[c]
- No spontaneous improvement in the 6 months prior to screening
- No concomitant treatments for AA[d]

Statistical Analyses

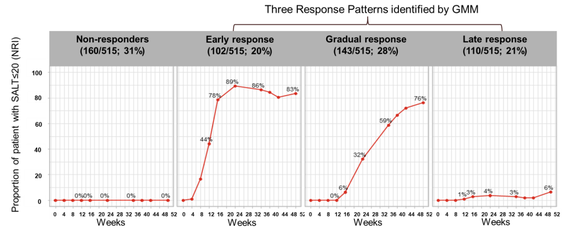
- The full analysis set for patients randomized to 2mg or 4mg baricitinib was considered in these analyses.
- Data were censored after permanent study drug discontinuation or if collected remotely due to the COVID-19 pandemic.
- Non-responder imputation was applied to binary endpoints (i.e., SALT score ≤20, $SALT_{50}$) for missing data.

RESULTS

Baseline AA severity and duration of current episode influence the pattern of clinical response

	2mg (N=340)				4mg (N=515)			
Parameter	Non-responders 166/340 (49%)	Early response 31/340 (9%)	Gradual response 64/340 (19%)	Late response 79/340 (23%)	Non-responders 160/515 (31%)	Early response 102/515 (20%)	Gradual response 143/515 (28%)	Late response 110/515 (21%)
Age								
Mean (SD)	38.9 (13.0)	36.7 (10.8)	40.4 (12.1)	36.4 (13.8)	37.1 (13.2)	37.6 (13.1)	36.9 (12.4)	36.8 (13.6)
Gender								
Female (%)	106 (63.9%)	20 (64.5%)	42 (65.6%)	44 (55.7%)	89 (55.6%)	68 (66.7%)	91 (63.6%)	61 (55.5%)
Race								
White (%)	87 (52.4%)	15 (48.4%)	35 (54.7%)	48 (60.8%)	77 (48.1%)	57 (55.9%)	79 (55.2%)	54 (49.1%)
Asian (%)	60 (36.1%)	16 (51.6%)	26 (40.6%)	23 (29.1%)	50 (31.3%)	37 (36.3%)	49 (34.3%)	45 (40.9%)
Black or African American (%)	14 (8.4%)	0 (0%)	1 (1.6%)	4 (5.1%)	23 (14.4%)	4 (3.9%)	11 (7.7%)	8 (7.3%)
Other (%)	5 (3.0%)	0 (0%)	2 (3.1%)	3 (3.8%)	10 (6.3%)	4 (3.9%)	4 (2.8%)	2 (1.8%)
Duration Current AA Episode (years)								
Mean (SD)	4.87 (6.24)	2.48 (2.51)	2.93 (4.30)	4.08 (4.74)	4.63 (3.91)	3.33 (3.21)	2.97 (2.72)	3.54 (3.13)
Duration Current AA Episode								
<4 years (%)	98 (59.0%)	26 (83.9%)	54 (84.4%)	52 (65.8%)	76 (47.5%)	72 (70.6%)	107 (74.8%)	74 (67.3%)
>=4 years (%)	68 (41.0%)	5 (16.1%)	10 (15.6%)	27 (34.2%)	84 (52.5%)	30 (29.4%)	36 (25.2%)	36 (32.7%)
Duration since AA Onset (years)								
Mean (SD)	14.1 (11.0)	7.99 (8.63)	11.3 (10.2)	12.1 (10.9)	14.8 (11.8)	10.2 (10.5)	9.60 (9.79)	11.9 (11.3)
AA Severity Categories								
Severe (SALT score 50-94) (%)	49 (29.5%)	28 (90.3%)	31 (48.4%)	39 (49.4%)	44 (27.5%)	76 (74.5%)	79 (55.2%)	49 (44.5%)
Very Severe (SALT score 95-100) (%)	117 (70.5%)	3 (9.7%)	33 (51.6%)	40 (50.6%)	116 (72.5%)	26 (25.5%)	64 (44.8%)	61 (55.5%)
SALT Score								
Mean (SD)	91.7 (14.7)	72.2 (15.1)	81.9 (20.5)	83.9 (19.1)	91.4 (15.7)	76.9 (18.3)	83.2 (18.4)	86.0 (17.7)
Classified as Universalis								
Yes (%)	77 (46.4%)	13 (41.9%)	34 (53.1%)	29 (36.7%)	86 (53.8%)	31 (30.4%)	64 (44.8%)	57 (51.8%)

Proportion of 4mg-treated patients who achieved a SALT score ≤20 response over 52 weeks in different response pattern subgroups



Data were censored after permanent study drug discontinuation or data collected at remote visits due to the COVID-19 pandemic. Non-responder imputation (NRI) was applied to missing and censored data.

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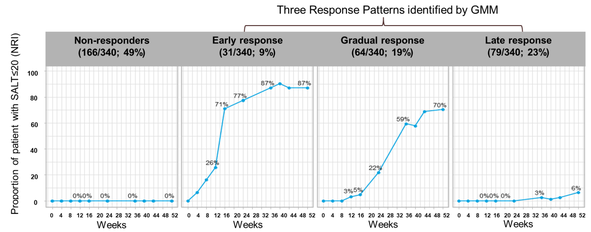

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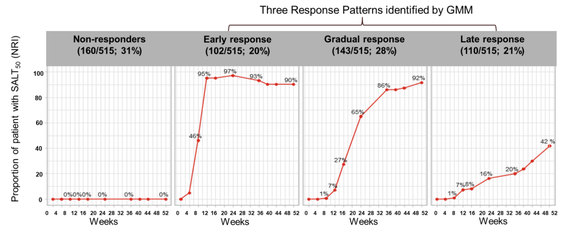
Proportion of 4mg-treated patients who achieved a ≥50% improvement from baseline in SALT score over 52 weeks in different response pattern subgroups



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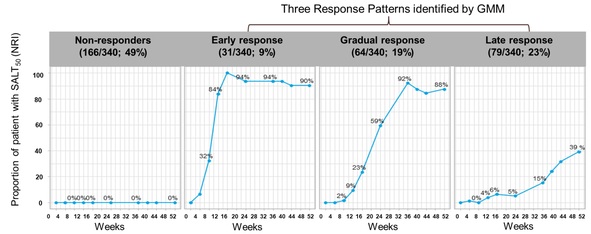

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- Growth mixture modelling revealed that 2mg or 4mg baricitinib-treated patients with severe AA clustered into response pattern groups based on time to onset of a $SALT_{30}$ response:

- As reported previously, overall higher response rate was observed with baricitinib 4mg vs. 2mg, particularly when considering early and gradual responders.
- 48% and 28% of 4 mg and 2 mg-treated patients respectively, were early and gradual responders.
  - Approximately 90% of early and gradual responders achieved $SALT_{50}$ by Week 52, regardless of dose.
- 21% and 23% of 4mg and 2mg-treated patients, respectively, experienced a delayed (late) response (>36 weeks).
  - Approximately 40% of delayed responders achieved $SALT_{50}$ at Week 52, regardless of dose.
- Baseline severity and duration of current episode are associated with response pattern
  - Early response was more frequent among patients with severe AA (SALT score 50-94) compared to those with very severe AA (SALT score 95-100).
  - Longer duration of current AA episode (≥4 years) and very severe AA (SALT score 95-100) were more commonly observed amongst non-responders.

ABBREVIATIONS

AA=alopecia areata; BARI=baricitinib; PBO=placebo; QD=once daily; SALT=Severity of Alopecia Tool; W=Week; GMM=growth mixture modelling; SALT≤20 = Severity of Alopecia Tool score of less than or equal to 20; $SALT_{50}$ = Severity of Alopecia Tool score 50% improvement from baseline; $SALT_{30}$ = Severity of Alopecia Tool score 30% improvement from baseline; $SALT_{50}$ = Severity of Alopecia Tool score 50% improvement from baseline

DISCLOSURES

- BK has served on advisory boards and/or is a consultant and/or is a clinical trial investigator for Abbvie, AltruBio Inc, Almirall, AnaptysBio, Arena Pharmaceuticals, Bioniz Therapeutics, Bristol-Meyers Squibb, Concert Pharmaceuticals Inc, Equillium, Horizon Therapeutics, Eli Lilly and Company, Incyte Corp, Janssen Pharmaceuticals, LEO Pharma, Otsuka/Visterra Inc, Pfizer Inc, Regeneron, Sanofi Genzyme, TWI Biotechnology Inc, and Viela Bio. He is on speaker bureaus for Abbvie, Eli Lilly and Company, Incyte Corp, Pfizer Inc, Regeneron and Sanofi Genzyme. JS has received travel reimbursement and speaking honoraria from Eli Lilly and Company. MO has received lecture fees from Eli Lilly Co. and advisory fees from Eli Lilly Co., Pfizer Inc., Janssen Pharmaceutical KK.(Japan), Taisho Pharmaceutical Co, and ROHTO Pharmaceutical Co. and grants/research funds form Shiseido Co., Maruho Co., and Sun Pharma Japan Ltd. AE has received research funding from Pfizer, Eli Lilly, Novartis, Bristol-Myers Squibb, AbbVie, Janssen Pharmaceuticals, Boehringer Ingelheim, the Danish National Psoriasis Foundation, the Simon Spies Foundation, and the Kgl Hofbundtmager Aage Bang Foundation, and honoraria as consultant and/or speaker from AbbVie, Almirall, Leo Pharma, Zuellig Pharma Ltd., Galápagos NV, Sun Pharmaceuticals, Samsung Bioepis Co., Ltd., Pfizer, Eli Lilly and Company, Novartis, Union Therapeutics, Galderma, Dermavant, UCB, Mylan, Bristol-Myers Squibb, McNeil Consumer Healthcare, Horizon Therapeutics, Boehringer Ingelheim, and Janssen Pharmaceuticals. RS reported serving as a consultant or paid speaker for or participating in clinical trials sponsored by LEO, Pharma, Amgen, Inc, Novartis Pharmaceuticals Corporation, Merck & Co, Celgene Corporation, Coherus BioSciences, Janssen Global Services, LLC, Regeneron Pharmaceutical Inc, Medimmune, LLC, GlaxoSmithKline, Cutanea, Samson Clinical, Boehringer Ingelheim, Pfizer, Inc, Merck Sharpe & Dohme, Oncobiologics, Inc, F. Hoffman–La Roche, Ltd, Eli Lilly and Company, and Bayer AG and is serving as the current President of the Australasian Hair and Wool Research Society. YD, YFC, WSW, YD, and NS are employees and shareholders of Eli Lilly and Company.
- This study previously presented at The World Congress For Hair Research 2022, Melbourne Australia, 18 – 21 November 2022

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