Dermatol Ther (Heidelb) (2023) 13:2621–2634
https://doi.org/10.1007/s13555-023-00997-x

ORIGINAL RESEARCH

Hair Loss Profiles and Ritlecitinib Efficacy in Patients with Alopecia Areata: Post Hoc Analysis of the ALLEGRO Phase 2b/3 Study

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Received: June 6, 2023 / Accepted: August 1, 2023 / Published online: September 14, 2023

ABSTRACT

Introduction: Ritlecitinib demonstrated efficacy in patients with alopecia areata (AA) in the ALLEGRO phase 2b/3 study (NCT03732807). However, hair loss presentation may vary based on location (e.g., scalp, eyebrow/eyelash, body). Here, we sought to identify distinct hair loss profiles at baseline and evaluate whether they affected the efficacy of ritlecitinib.

Methods: Patients with AA aged ≥ 12 years with ≥ 50% scalp hair loss were randomized to daily ritlecitinib 10 mg (assessed for dose ranging only), 30 or 50 mg (± 4-week, 200-mg loading dose), or placebo for 24 weeks. Latent class analysis (LCA) identified hair loss profiles based on four baseline measurements: clinician-reported extent of scalp (Severity of Alopecia Tool score), eyebrow hair loss, eyelash hair loss, and patient-reported body hair loss. Logistic regression evaluated ritlecitinib (50 and 30 mg) efficacy vs placebo using Patient Global Impression of Change (PGI-C) and Patient Satisfaction with Hair Growth (P-Sat; amount, quality, and overall satisfaction) responses at

Prior Presentation: This manuscript is based on work that was presented as a poster at the World Congress of Hair Research 2022, Melbourne, VIC, Australia, November 18–21, 2022.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s13555-023-00997-x.

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Week 24, adjusting for key covariates, including latent class membership.

Results: LCA identified five latent classes: (1) primarily non–alopecia totalis (AT; complete loss of scalp hair); (2) non-AT with moderate non-scalp involvement; (3) extensive scalp, eyebrow, and eyelash involvement; (4) AT with moderate non-scalp involvement; and (5) primarily alopecia universalis (complete scalp, face, and body hair loss). Adjusting for latent class membership, patients receiving ritlecitinib 30 or 50 mg were significantly more likely to achieve PGI-C response (30 mg: odds ratio, 8.62 [95% confidence interval, 4.42–18.08]; 50 mg: 12.29 [6.29–25.85]) and P-Sat quality of hair regrowth (30 mg: 6.71 [3.53–13.51]; 50 mg: 8.17 [4.30–16.46]) vs placebo at Week 24. Results were similar for P-Sat overall satisfaction and amount of hair regrowth.

Conclusion: Distinct and clinically relevant hair loss profiles were identified in ALLEGRO-2b/3 participants. Ritlecitinib was efficacious compared with placebo, independent of hair loss profile at baseline.

Trial registration: ClinicalTrials.gov identifier, NCT03732807.

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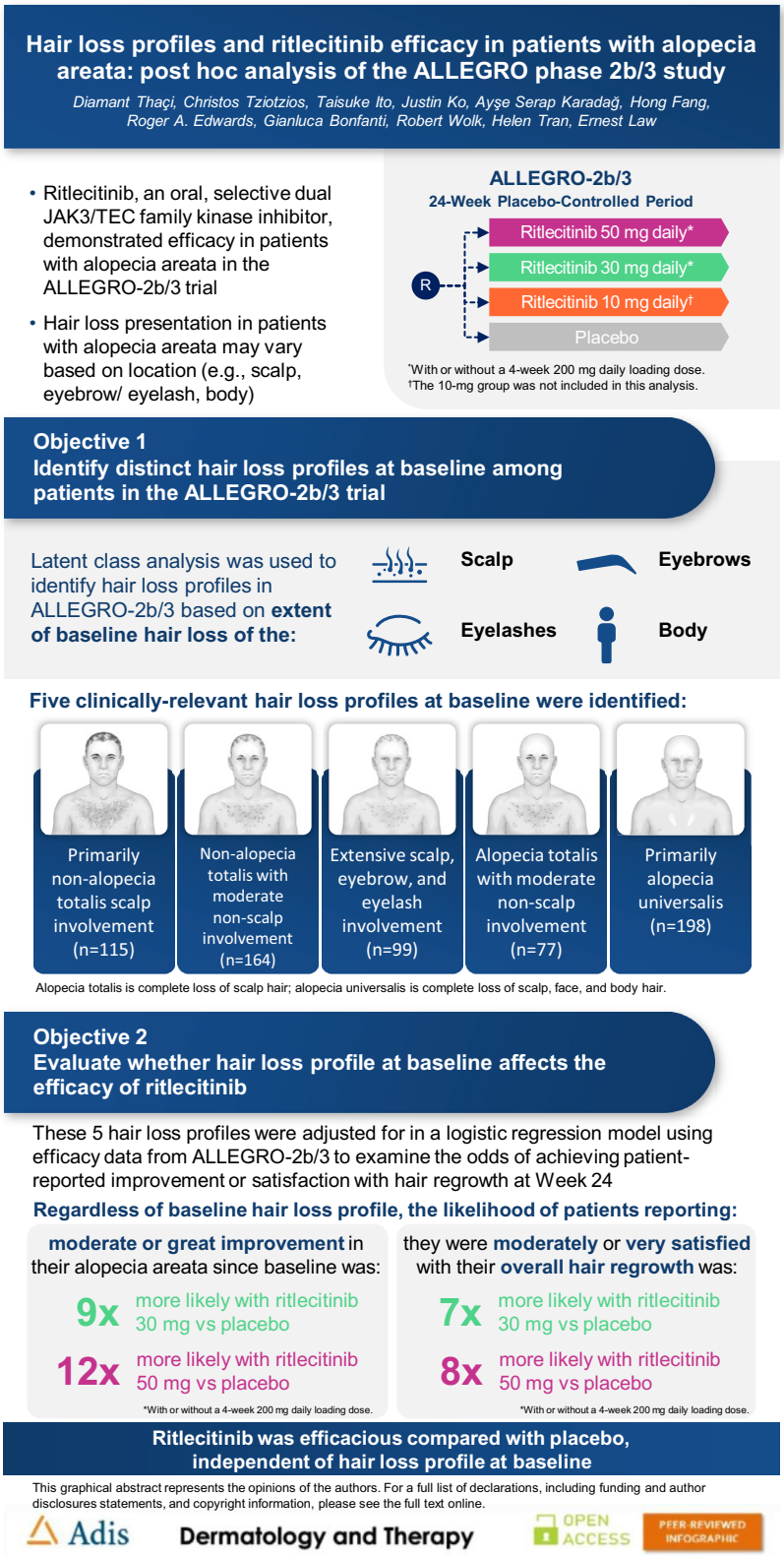
Graphical abstract:



Keywords: Alopecia areata; Hair loss; Latent class analysis; Ritlecitinib

Key Summary Points

Why carry out this study?

Ritlecitinib, an oral inhibitor of Janus kinase (JAK) 3 and the tyrosine kinase expressed in hepatocellular carcinoma (TEC) family kinases, demonstrated efficacy in patients with alopecia areata in the ALLEGRO phase 2b/3 study

In patients with alopecia areata, hair loss presentation may vary based on location of hair loss (such as the scalp, eyebrows, eyelashes, and body)

This post hoc analysis of the ALLEGRO-2b/3 study sought to identify distinct hair loss profiles at baseline and evaluate whether they affected the efficacy of ritlecitinib

What was learned from the study?

Five distinct and clinically relevant hair loss profiles were identified, expanding on the knowledge of heterogeneous alopecia areata profiles based on the extent and location of hair loss

At week 24, ritlecitinib was efficacious compared with placebo, independent of hair loss profile at baseline

DIGITAL FEATURES

This article is published with digital features, including a graphical abstract to facilitate understanding of the article. To view digital features for this article, go to https://doi.org/10.6084/m9.figshare.23703066.

INTRODUCTION

Alopecia areata (AA) is an autoimmune disease that has an underlying immuno-inflammatory pathogenesis and is characterized by nonscarring hair loss of the scalp, face, and/or body [1]. AA affects both children and adults, with an estimated prevalence of 2% in the global population. Extensive AA subtypes include alopecia totalis (AT; complete loss of scalp hair) and alopecia universalis (AU; complete loss of scalp, face, and body hair), which have an estimated prevalence of 0.08% and 0.03%, respectively [2]. Patients with AA may experience psychological and psychosocial effects, including anxiety and depression, that can have a substantial negative impact on quality of life [3–6].

AA typically presents as round patches of hair loss, but clinical presentation can vary based on extent and location of hair loss (e.g., scalp, eyebrow/eyelash, body) [7–9]. AA has an unpredictable disease course and may relapse and remit [10], with approximately 14% to 25% of patients progressing to AT or AU [7]. Extensive forms of AA are reported to be more likely to worsen over time, and patients with AT or AU are less likely to fully recover, more likely to have hair loss that does not improve, and often reported to be dissatisfied with treatment outcomes [11–13].

The pathogenesis of AA involves the loss of immune privilege at the hair follicle and subsequent recognition of exposed hair follicle autoantigens by T cell receptors (TCRs) on autoreactive CD8 + T cells [14–16]. Interferon-γ and interleukin-15, which are reported to be important drivers of AA, transduce signals through the Janus kinase-signal transducer and activator of transcription (JAK-STAT) signaling pathway and are involved in the activation and proliferation of autoreactive T cells [17–19]. Signaling downstream of the TCR involves the tyrosine kinase expressed in hepatocellular carcinoma (TEC) family of kinases, which have also been shown to play a role in the pathogenesis of AA [19–22].

Safe and efficacious treatment options for AA are limited. Off-label treatments, such as topical, systemic, or intralesional corticosteroids,

and other immunosuppressants have variable efficacy and/or limited safety. The Janus kinase (JAK) 1/2 inhibitor baricitinib is approved to treat adults with severe AA in some countries, including the United States, European Union, and Japan [23]. Ritlecitinib is an oral, selective dual inhibitor of JAK3 and all five members of the TEC family kinases and is approved for the treatment of severe AA in patients ≥ 12 years old in the US and Japan [24]. In the ALLEGRO phase 2b/3 study, ritlecitinib demonstrated clinical and patient-reported efficacy and an acceptable safety profile in patients aged ≥ 12 years with AA [25].

Despite the known subtypes of AA and heterogeneity in disease presentation, data are lacking on the effectiveness of AA therapies on different clinical presentations. Latent class analysis (LCA) is a patient-centered, data-driven statistical approach to evaluating heterogeneity by identifying different profiles (or classes) of patients within a population who share phenotypic characteristics, based on specific indicators [26]. In AA, LCA may be applied to identify hair loss presentations of trial participants by extent and location of hair loss, which may be important for evaluating the expected efficacy of therapies studied for AA. This post hoc analysis of the ALLEGRO phase 2b/3 study of ritlecitinib in patients with AA used LCA to identify distinct and clinically relevant hair loss profiles at baseline and to evaluate whether they affected the efficacy of ritlecitinib on patient-reported outcomes.

METHODS

Study Design

The design and primary results of the international, randomized, double-blind, placebo-controlled, combined dose-ranging pivotal ALLEGRO phase 2b/3 trial (NCT03732807) have been previously described in detail [25]. Briefly, patients were randomized to receive ritlecitinib 50 mg or 30 mg once daily (QD) with or without a 200-mg QD loading dose for the initial 4 weeks, 10 mg QD, or placebo for 24 weeks. Randomization was stratified by severity (target: ≈ 40% of patients with AT/AU) and age (target: ≈ 15% of adolescents aged 12–17 years in each group).

The protocols were reviewed and approved by the institutional review boards or ethics committees of the participating institutions (**Supplementary Table 1**). The study was conducted in accordance with the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), ICH Guideline for Good Clinical Practice, and the Declaration of Helsinki. Written informed consent was obtained from each patient, parent, or the patient's legal representative.

Patients

Patients in ALLEGRO-2b/3 were aged ≥ 12 years with a diagnosis of AA and ≥ 50% scalp hair loss, including patients with AT or AU, and a current AA episode duration of 6 months to 10 years. Patients with other causes of alopecia, previous use of any JAK inhibitor, or clinically significant depression were excluded. This post hoc analysis included patients who received ritlecitinib 200/50, 200/30, 50, or 30 mg or placebo. The 10-mg dose group was included in the study for pharmacokinetic and safety dose-ranging purposes and was thus excluded from this analysis.

Baseline Categorical Measures

Baseline categorial variables, which were used as indicators for the LCA analysis described next, were based on extent of scalp, eyebrow, eyelash, and body hair loss and included extent of scalp hair loss as measured by Severity of Alopecia Tool (SALT) score (clinician reported); extent of eyebrow hair loss as measured through the Eyebrow Assessment (EBA) score (clinician reported); extent of eyelash hair loss as measured through the Eyelash Assessment (ELA) score (clinician reported); and extent of body hair loss as measured through the Alopecia Areata Patient Priorities Outcome (AAPPO) body assessment (patient reported). SALT

assesses the amount of scalp hair loss with scores ranging from 0 (no scalp hair) to 100 (complete scalp hair loss) (**Supplementary Table 2**), and patients were categorized by baseline SALT score of < 80, ≥ 80 to < 100, or 100. EBA and ELA have 4-point scales ranging from 0 (none or no eyebrows/eyelashes) to 3 (normal eyebrows/eyelashes) (**Supplementary Table 2**), and patients were categorized by EBA or ELA score of 0 (none), 1–2 (minimal/moderate), or 3 (normal). The AAPPO assesses AA-related hair loss, emotional symptoms, and activity limitations. The AAPPO hair loss item subscale score is reported here. Patients describe the current amount of hair loss in different body areas (scalp, eyebrows, eyelashes, and body) using a 5-point response scale ranging from 0 ("no hair loss") to 4 ("complete" hair loss), and improvements with a score of ≥ 2 from baseline are reported (**Supplementary Table 2**); patients were categorized by their responses for body hair loss: 0–1 (no or a little hair loss), 2–3 (moderate or a great deal of hair loss), or 4 (complete hair loss).

Outcome Measures

Patient-reported outcomes were assessed using the Patient Global Impression of Change (PGI-C) and Patient Satisfaction with Hair Growth (P-Sat) at Week 24. PGI-C is a single-item scale on which patients rate the improvement or worsening of AA compared with the start of the study, using a scale of 7 responses ranging from "greatly improved" to "greatly worsened" (**Supplementary Table 2**). PGI-C response was defined as "moderately improved" or "greatly improved." P-Sat assesses patient satisfaction with hair regrowth since the start of the study in 3 domains: amount, quality, and overall (**Supplementary Table 2**). P-Sat response was defined as "moderately" or "very" satisfied for each domain.

Statistical Analysis

LCA was used to identify hair loss profiles based on aforementioned scalp, eyebrow, eyelash, and body hair loss indicators at baseline. Latent class models with varying numbers of classes were estimated, and model selection was based on consideration of several criteria, including clinical interpretability; model fitness (log-likelihood, Akaike information criterion [AIC], Bayesian information criterion [BIC]), in which consistent AIC and the sample size–adjusted BIC were derived from AIC and BIC, respectively, by modifying the penalizing part of the metric (smaller values of AIC, BIC, consistent AIC, and sample size–adjusted BIC indicate better fit in the model); classification diagnostics (relative entropy); and smallest average latent class posterior probability, which assessed the average probability of each class model accurately predicting class membership for individuals.

After selection of the final LCA model, LCA class was assigned to each patient and included as a key covariate for the logistic regression analysis. Two logistic regression models evaluated the likelihood of achieving PGI-C score and P-Sat response for ritlecitinib (50 and 30 mg, with or without a 4-week 200-mg QD loading dose) vs placebo. An all-variable model considered all covariates listed above to adjust for the variables of interest. A stepwise model was used as a sensitivity analysis, in which nonsignificant covariates were excluded to increase precision for the independent variables of interest. Covariates included age (continuous), sex (male vs female), body mass index (continuous), prior pharmacological treatment for AA (yes or no), active hair shedding (yes or no), treatment arm (ritlecitinib 30 mg or 50 mg vs placebo), ritlecitinib 200-mg daily loading dose for 4 weeks (yes or no), and LCA class membership. Odds ratios were calculated for PGI-C response and P-Sat response for ritlecitinib 30 mg and 50 mg vs placebo. All analyses were implemented using R software: "glm" function of the "stats" package for logistic regressions and "poLCA" function of the "poLCA" package for LCA.

RESULTS

Patients

A total of 655 patients were randomized to and 653 were treated with ritlecitinib 200/50 mg, 200/30 mg, 50 mg, 30 mg, or placebo. Of the 655 randomized patients, mean age ranged from 32.4 to 34.5 years, 54.6% to 65.6% of patients were women, and 60.8% to 71.8% were white (Table 1). Of the 653 treated patients, 13.7% to 23.1% had baseline SALT scores of 50 to < 80, 30.8% to 40.5% had baseline SALT scores of ≥ 80 to < 100, and 45.8% to 46.5% had baseline SALT score of 100. Across the treatment groups at baseline, 44.3% to 50.4% of patients had no eyebrow hair and 15.2% to 18.5% had normal eyebrow hair, 37.2% to 43.1% had no eyelash hair and 22.1% to 26.9% had normal eyelash hair, and 13.0% to 16.2% reported no body hair loss, while 34.6% to 40.5% reported complete body hair loss.

Latent Class Analysis

A summary of the performance results (goodness-of-fit statistics and diagnostic statistics) for two- to nine-class latent class models is shown in **Supplementary Table 3**, showing that the three-, four-, and five-class models had the lowest BIC values. The distribution of variables used as indicators (extent of baseline scalp, eyebrow, eyelash, and body hair loss) within the classes identified by LCA for the three-, four-, and five-class models are shown in **Supplementary Fig. 1**. The five-class model identified distinct classes of patients with AT and AU (based on a baseline SALT score of 100) and was selected as the optimal model. In "class 4" of the five-class model, 100% of patients had a SALT score of 100 (complete scalp hair loss) and varying degrees of eyebrow, eyelash, and body hair loss, indicating that most of these patients had AT. In "class 5" of the five-class model, 91.9% of patients had a SALT score of 100 (complete scalp hair loss), 96.5% had no eyebrow hair, 89.4% had no eyelash hair, and 99.5% had no body hair, indicating that most of these patients had AU.

Based on baseline scalp, eyebrow, eyelash, and body hair loss categories, the classes from the five-class LCA model can be further described as (Fig. 1):

- Class 1, primarily non-AT scalp involvement (n = 115): most of these patients had normal eyebrow, eyelash, and body hair, and very few had complete scalp hair loss.
- Class 2, non-AT with moderate non-scalp involvement (n = 164): most of these patients had minimal to moderate eyebrow and eyelash hair loss, and none had complete scalp hair loss.
- Class 3, extensive scalp, eyebrow, and eyelash involvement (n = 99): most of these patients had complete eyebrow and/or eyelash hair loss, some body hair loss, and ≥ 80% scalp hair loss.
- Class 4, AT with moderate non-scalp involvement (n = 77): most of these patients had some eyebrow, eyelash, and body hair loss, and all had complete scalp hair loss.
- Class 5, primarily AU (n = 198): most of these patients had complete loss of eyebrow, eyelash, body, and scalp hair.

Ritlecitinib Treatment Effect

Among patients receiving ritlecitinib 30 mg and higher, 52.0% to 68.2%, 45.2% to 64.3%, 28.6% to 72.7%, 37.5% to 50.0%, and 15.8% to 37.8% of patients in classes 1, 2, 3, 4, and 5 achieved PGI-C response at Week 24, respectively, compared with 20.0%, 13.9%, 9.1%, 0.0%, and 2.2% receiving placebo (Table 2).

Adjusting for latent class membership, patients receiving ritlecitinib 30 or 50 mg (with or without a 200-mg daily loading dose for 4 weeks) were significantly more likely to achieve PGI-C response at Week 24 compared with those receiving placebo (Fig. 2). Adjusting for latent class membership, patients receiving ritlecitinib 30 or 50 mg were also significantly more likely to be satisfied with amount of, quality of, and overall hair regrowth based on P-Sat response at Week 24 compared with those receiving placebo (Fig. 3).

Table 1 Baseline characteristics

	All randomized patients (N = 655)				
	Placebo (n = 131)	**Ritlecitinib 30 mg (n = 132)**	**Ritlecitinib 50 mg (n = 130)**	**Ritlecitinib 200/30 mg (n = 130)**	**Ritlecitinib 200/50 mg (n = 132)**
Age, mean (SD), years	34.0 (15.0)	33.7 (14.8)	32.4 (13.4)	33.7 (13.8)	34.5 (15.0)
Female, n (%)	86 (65.6)	80 (60.6)	71 (54.6)	85 (65.4)	81 (61.4)
White, n (%)	94 (71.8)	91 (68.9)	79 (60.8)	90 (69.2)	92 (69.7)
Patients with AT or AU, n(%)	60 (45.8)	61 (46.2)	60 (46.2)	60 (46.2)	60 (45.5)
	Patients who received treatment (N = 653)				
	Placebo (n = 131)	**Ritlecitinib 30 mg (n = 132)**	**Ritlecitinib 50 mg (n = 130)**	**Ritlecitinib 200/30 mg n = 129)**	**Ritlecitinib 200/50 mg (n = 131)**
SALT score					
50 to < 80, n (%)	18 (13.7)	29 (22.0)	30 (23.1)	28 (21.7)	25 (19.1)
≥ 80 to < 100, n (%)	53 (40.5)	42 (31.8)	40 (30.8)	41 (31.8)	46 (35.1)
100, n (%)	60 (45.8)	61 (46.2)	60 (46.2)	60 (46.5)	60 (45.8)
EBA score					
0 (no eyebrow)	58 (44.3)	59 (44.7)	59 (45.4)	59 (45.7)	66 (50.4)
1 (minimal eyebrow)	33 (25.2)	38 (28.8)	31 (23.8)	31 (24.0)	32 (24.4)
2 (moderate eyebrow)	16 (12.2)	15 (11.4)	16 (12.3)	18 (14.0)	12 (9.2)
3 (normal eyebrow)	24 (18.3)	20 (15.2)	24 (18.5)	21 (16.3)	21 (16.0)
ELA score					
0 (no eyelash)	52 (39.7)	51 (38.6)	56 (43.1)	48 (37.2)	55 (42.0)
1 (minimal eyelash)	24 (18.3)	37 (28.0)	25 (19.2)	30 (23.3)	36 (27.5)
2 (moderate eyelash)	21 (16.0)	14 (10.6)	14 (10.8)	17 (13.2)	11 (8.4)
3 (normal eyelash)	34 (26.0)	30 (22.7)	35 (26.9)	34 (26.4)	29 (22.1)
AAPPO-body*					
0 (no hair loss)	17 (13.0)	21 (15.9)	21 (16.2)	17 (13.2)	19 (14.5)
1 (little hair loss)	21 (16.0)	13 (9.8)	10 (7.7)	12 (9.3)	14 (10.7)
2 (moderate hair loss)	13 (9.9)	14 (10.6)	18 (13.8)	13 (10.1)	15 (11.4)
3 (great deal of hair loss)	27 (20.6)	36 (27.3)	35 (26.9)	39 (30.2)	36 (27.5)
4 (complete hair loss)	53 (40.5)	48 (36.4)	45 (34.6)	48 (37.2)	47 (35.9)

AAPPO, Alopecia Areata Patient Priorities Outcome; EBA, Eyebrow Assessment; ELA, Eyelash Assessment; SALT, Severity of Alopecia Tool

*AAPPO body data were not available for 1 patient in the 50-mg group

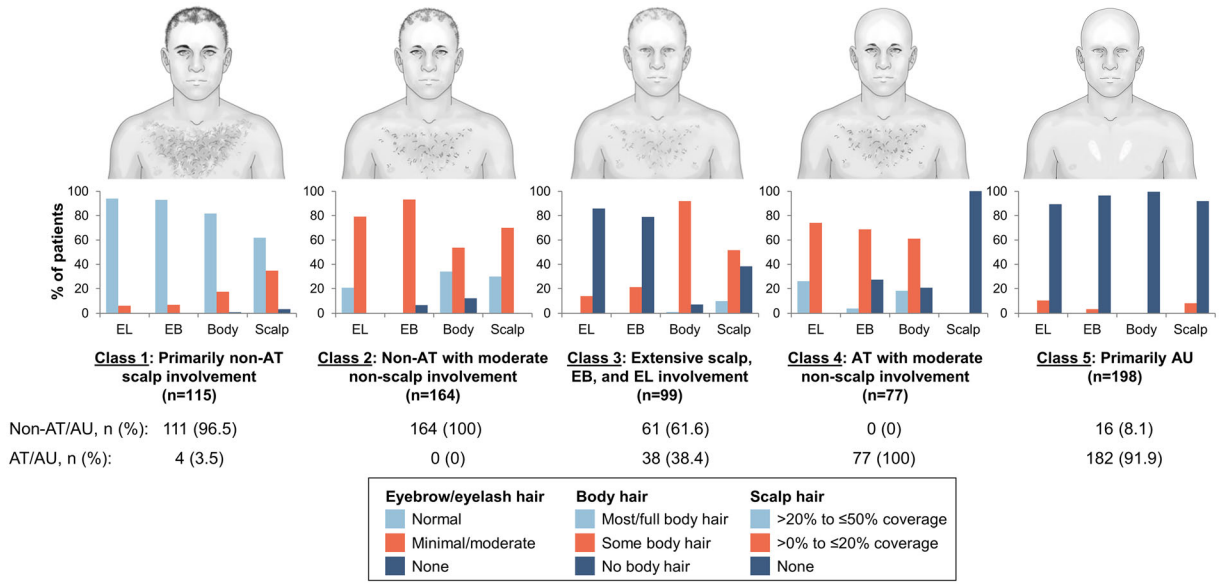


Fig. 1 Hair loss profiles identified from latent class analysis. AT, alopecia areata; AU, alopecia universalis; EB, eyebrow; EL, eyelash

DISCUSSION

In this post hoc analysis of the ALLEGRO phase 2b/3 trial population of patients with AA, LCA identified five distinct and clinically relevant hair loss profiles and demonstrated favorable patient-reported efficacy for ritlecitinib vs placebo after 24 weeks of treatment regardless of baseline hair loss profile. These data expand the knowledge of heterogeneous AA profiles based on the extent and location of hair loss. While the identification of two distinct classes of patients with AT or AU in the five-class model is consistent with known clinical subtypes [2], the other three classes in the five-class model were primarily distinguished by the varying extent of eyebrow and eyelash involvement.

The pattern of hair loss at presentation and how it may affect response to treatment could be an important consideration for patients and physicians when making treatment decisions for AA. The LCA performed using baseline patient characteristics to identify different profiles of patients with AA demonstrated that the ALLEGRO phase 2b/3 trial had a diverse population of patients regarding the extent and location of hair loss. The range in extent of eyebrow, eyelash, and body hair loss was well distributed throughout the population and across treatment groups.

Across each of the five hair loss profiles identified from the LCA, higher proportions of patients receiving ritlecitinib achieved PGI-C responses at Week 24 compared with placebo. The proportions of patients with PGI-C response tended to be lower in the classes of patients with more extensive hair loss, consistent with previous analyses demonstrating lower SALT response rates in patients with AT/AU [27]. Patients with AA have abnormal hair cycling, which may lead to variability in the time it takes to regrow hair [8, 9]. Given the duration of time it can take for hair to regrow, it is likely that patients with more extensive hair loss at baseline need longer treatment times to achieve response and experience the full impact of therapy.

Logistic regression demonstrated that patients receiving ritlecitinib 50 mg or 30 mg QD were significantly more likely to report moderate or great improvement from baseline (based on PGI-C) and report satisfaction with amount, quality, and overall hair regrowth (based on P-Sat) compared with patients receiving placebo, independent of their hair loss profile at baseline. These results were

Table 2 PGI-C responder status at Week 24

	Placebo	Ritlecitinib 30 mg	Ritlecitinib 50 mg	Ritlecitinib 200/30 mg	Ritlecitinib 200/50 mg
Class 1: Primarily non-AT scalp involvement					
No. of patients	25	22	25	22	21
Response	5 (20.0)	12 (54.5)	13 (52.0)	15 (68.2)	12 (57.1)
No response	16 (64.0)	6 (27.3)	10 (40.0)	5 (22.7)	8 (38.1)
N/A	4 (16.0)	4 (18.2)	2 (8.0)	2 (9.1)	1 (4.8)
Class 2: Non-AT with moderate non-scalp involvement					
No. of patients	36	35	28	31	34
Response	5 (13.9)	21 (60.0)	18 (64.3)	14 (45.2)	20 (58.8)
No response	31 (86.1)	12 (34.3)	9 (32.1)	16 (51.6)	11 (32.4)
N/A	0 (0)	2 (5.7)	1 (3.6)	1 (3.2)	3 (8.8)
Class 3: Extensive scalp, eyebrow, and eyelash involvement					
No. of patients	11	21	24	21	22
Response	1 (9.1)	6 (28.6)	12 (50.0)	7 (33.3)	16 (72.7)
No response	10 (90.9)	14 (66.7)	10 (41.7)	10 (47.6)	5 (22.7)
N/A	0 (0)	1 (4.8)	2 (8.3)	4 (19.0)	1 (4.5)
Class 4: AT with moderate non-scalp involvement					
No. of patients	14	16	13	18	16
Response	0 (0)	6 (37.5)	5 (38.5)	7 (38.9)	8 (50.0)
No response	14 (100.0)	9 (56.3)	7 (53.8)	9 (50.0)	8 (50.0)
N/A	0 (0)	1 (6.3)	1 (7.7)	2 (11.1)	0 (0)
Class 5: Primarily AU					
No. of patients	45	38	40	37	38
Response	1 (2.2)	6 (15.8)	14 (35.0)	14 (37.8)	11 (28.9)
No response	42 (93.3)	24 (63.2)	22 (55.0)	22 (59.5)	21 (55.3)
N/A	2 (4.4)	8 (21.1)	4 (10.0)	1 (2.7)	6 (15.8)

AT, alopecia totalis; AU, alopecia universalis; PGI-C, Patient Global Impression of Change

independent of the baseline covariates of age, sex, body mass index, prior pharmacological treatment for AA, and active hair shedding.

This is the first study to our knowledge to classify patients with AA using LCA. Some previous studies used gene expression profiling to identify distinct groups in AA based on disease duration and disease phenotype [28, 29]. In one study, gene expression profiling of scalp skin biopsies from patients with AA and healthy controls revealed distinct clusters based on presence or absence of disease as well as disease phenotype (patchy compared with AT or AU) [29].

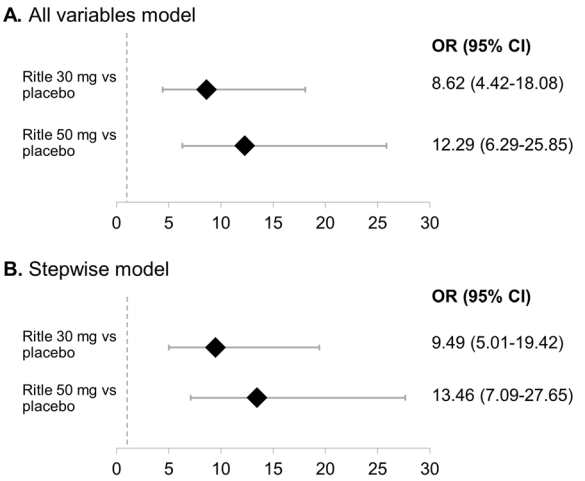


Fig. 2 Odds ratios for PGI-C response* at Week 24. BMI, body mass index; LCA, latent class analysis; OR, odds ratio; PGI-C, Patient Global Impression of Change; ritle, ritlecitinib. *PGI-C response was defined as "moderately improved" or "greatly improved." Covariates included in the all variables model were age, sex, BMI, prior pharmacological treatment for alopecia areata, active shedding, treatment arm, ritlecitinib loading dose, and membership in one of the five LCA classes. Covariates included in the stepwise model were sex, BMI, treatment arm, and membership in one of the five LCA classes

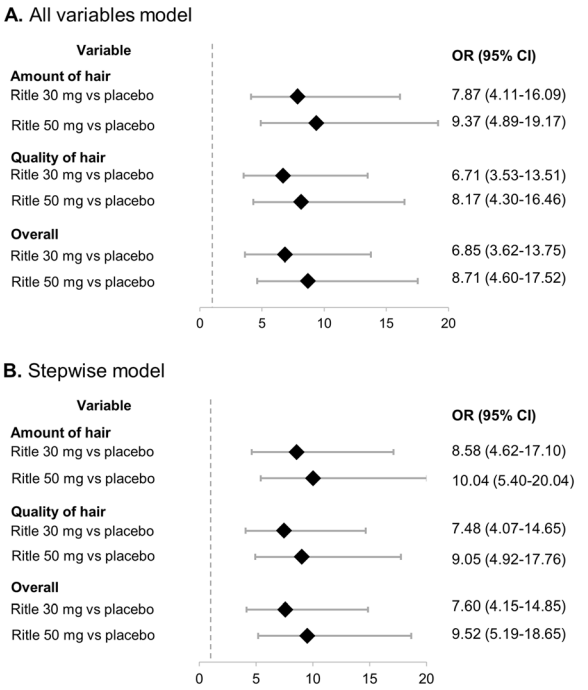


Fig. 3 Odds ratios for P-Sat response* at Week 24. BMI, body mass index; LCA, latent class analysis; OR, odds ratio; P-Sat, Patient Satisfaction with Hair Growth; ritle, ritlecitinib. *P-Sat response was defined as "moderately" or "very" satisfied at Week 24. Covariates included in the all variables models were age, sex, BMI, prior pharmacological treatment for alopecia areata, active shedding, treatment arm, ritlecitinib loading dose, and membership in one of the five LCA classes. Covariates included in the stepwise model for P-Sat (amount of hair) were age, sex, BMI, treatment arm, and membership in one of the five LCA classes. Covariates included in the stepwise models for P-Sat (quality of hair) and for P-Sat (overall) were age, sex, treatment arm, and membership in one of the five LCA classes

This study had some limitations. This is a post hoc analysis of a randomized controlled trial, and inclusion criteria were restricted to patients with severe AA (≥ 50% scalp hair loss) and a current AA episode of < 10 years. The placebo-controlled period of the study was limited to 24 weeks, and more time is likely needed to observe the full effect of ritlecitinib on all hair loss profiles. This study focused on understanding how different hair loss profiles at baseline differentially responded to ritlecitinib; future studies may examine how patient and disease characteristics, such as age of onset, disease or episode duration, nail involvement, presence of comorbidities, and biomarkers could yield other underlying profiles of patients with AA and how they may differentially respond to therapy. For example, nail involvement is often observed in severe cases of AA and may be more refractory to treatment [30].

In conclusion, clinically distinct hair loss profiles in patients with AA were identified from the ALLEGRO phase 2b/3 trial. Ritlecitinib 50 mg and 30 mg QD was efficacious compared with placebo, independent of baseline hair loss profile.

ACKNOWLEDGEMENTS

The authors thank the study participants and their families.

Medical Writing, Editorial, and Other Assistance Third-party medical writing assistance, provided by Ellen Mercado, PhD, of

Health Interactions, Inc, was funded by Pfizer Inc.

Author Contributions. Roger A. Edwards, Gianluca Bonfanti, Robert Wolk, Helen Tran, and Ernest H. Law contributed to study conception and design. Diamant Thaçi, Christos Tziotzios, Taisuke Ito, Ayşe Serap Karadağ, Hong Fang, Roger A. Edwards, Helen Tran, and Ernest H. Law contributed to the acquisition of data. Gianluca Bonfanti, Helen Tran, and Ernest Law contributed to drafting the manuscript. Gianluca Bonfanti and Roger A. Edwards contributed to the statistical analysis. All author revised the manuscript critically for important intellectual content and reviewed and approved the final content of the manuscript.

Funding. This study was sponsored by Pfizer Inc, New York, NY. Funding for the journal's Rapid Service Fee was also provided by Pfizer Inc.

Data Availability. Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions, and exceptions, Pfizer may also provide access to the related individual de-identified participant data. https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.

Declarations

Conflict of Interest. Diamant Thaçi: consultant, investigator, speaker, and participant in scientific advisory boards for AbbVie, Almirall, Amgen, Biogen Idec, BMS, Janssen-Cilag, Galderma, Galapagos, LEO Pharma, Eli Lilly, New Bridge, Novartis, Pfizer, Regeneron, Samsung, Sanofi, Sun Pharma, and UCB; Christos Tziotzios: speaker for LEO Pharma; principal and chief investigator for Pfizer; and consultant for Pfizer; Taisuke Ito: consultant, investigator, speaker, and participant in scientific advisory boards for Pfizer, Eli Lilly, Maruho, Meiji Seika Pharma, and Hisamitsu; Justin Ko: consultant, investigator, speaker, and participant in advisory boards for Eli Lilly, Pfizer, AbbVie, Arena, and Concert; Ayşe Serap Karadağ: consultant, speaker, and/or participant in scientific advisory boards for L'Oréal, Novartis, AbbVie, Pfizer, UCB, and Abdi İbrahim; Hong Fang: nothing to report; Roger A. Edwards: employee/owner of Health Services Consulting Corporation and paid consultant for Pfizer in connection with this study; Gianluca Bonfanti is an employee of Engineering Ingegneria Informatica, a paid subcontractor to Health Services Consulting Corporation in conjunction with this study and development of this manuscript. Robert Wolk, Helen Tran, and Ernest Law are employees of Pfizer and hold stock or stock options in Pfizer.

Ethical Approval. The protocol was reviewed and approved by the institutional review boards or ethics committees of the participating institutions. The study was conducted in accordance with the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), International Council for Harmonisation Guideline for Good Clinical Practice, and the Declaration of Helsinki. All participants provided informed consent.

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