

The Role of Patients in Alopecia Areata Endpoint Development: Understanding Physical Signs and Symptoms



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Meaningful patient input to understand disease experience and patient expectations for improvement with treatment is essential for the selection and development of outcome measures for alopecia areata (AA) clinical trials. This study explored the physical signs and symptoms of AA through 30 semistructured interviews with adult (n = 25) and adolescent (n = 5) patients experienced with severe or very severe AA. Scalp hair loss was overwhelmingly the most important sign and symptom of AA. Nearly all patients (90%) considered scalp hair loss in their top three most bothersome physical signs and symptoms of AA, with 77% (n = 23) naming scalp hair loss as the most bothersome symptom. Other identified signs and symptoms in the top three most bothersome included eyebrow, eyelash, nose, body, and facial hair loss, as well as eye irritation and nail damage and/or appearance. Eyebrow (16%, n = 4), eyelash (4%, n = 1), nasal (4%, n = 1), and body (4%, n = 1) hair loss were identified by seven adult patients as the most bothersome signs and symptoms of AA. Conceptual saturation confirmed that a comprehensive understanding of this patient population's physical AA-related signs and symptoms was obtained. These findings indicate that the primary objective for new AA treatments for this patient population should be meaningful improvement in scalp hair growth to address the most troubling unmet need.

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INTRODUCTION

Alopecia areata (AA) is a chronic autoimmune disease characterized by patches of nonscarring hair loss that can affect the scalp and body (Islam et al., 2015). AA can affect children, adolescents, and adults, and there is no preventative or currently approved therapy that sustains remission (Hordinsky and Donati, 2014). To demonstrate that a potential treatment is efficacious, there is a need to obtain meaningful patient input for the selection and/or development of clinical trial outcomes that measure what matters most to patients and reflect patients' expectations for improvement with treatment (U.S. Food and Drug Administration, 2018a).

To better understand and document the needs, perspectives, expectations, and priorities of patients with severe or very severe AA ($\geq 50\%$ scalp hair loss), this study explored the patient experience of AA through qualitative, open-ended exploration in one-on-one semistructured patient interviews. Although others have recently conducted and

reported on AA qualitative studies (Davey et al., 2019; Wolf and Baker, 2019), none of the known previous research has aimed to understand the comparative significance of the many AA physical signs and symptoms that patients experience to inform clinical trial outcomes. The purpose of this paper is to document the physical signs and symptoms of AA and their relative importance to patients as reported during these interviews.

RESULTS

Sample characteristics

A total of 30 patients participated in the interview study. Table 1 shows the patients' clinical information summarized by oral JAK inhibitor (JAKi) treatment status and adult and adolescent subgroups, as reported on the case report forms by the recruiting clinicians. A total of 25 patients (83%) were adults, and five patients (17%) were adolescents. A total of 18 patients (60%) were currently treated (n = 15) or had previously been treated (n = 3) successfully with an oral JAKi (defined as patient had started to grow scalp hair). The mean Severity of Alopecia Tool (SALT) score for members of the JAKi-treated group (36.2 [SD = 36.09; range = 0.0–100.0]) was lower than the mean SALT score in the JAKi-treatment-naïve group (90.5 [SD = 18.54; range = 50.2–100.0]). Just under half (n = 13, 43%) of the sample was receiving no treatment for AA at the time of their interviews.

On average, patients in the interview sample received a diagnosis of AA 12 years before the interview. A total of 24 patients (80%) had experienced full or partial eyebrow and/or eyelash loss at some point during their experience of AA.

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Abbreviations: AA, alopecia areata; JAKi, JAK inhibitor; SALT, Severity of Alopecia Tool

Table 1. Clinical Characteristics of the Interviewed Patients (n = 30)

Clinical Characteristic	JAKi-Experienced Patients (N = 18)			JAKi-Naive Patients (N = 12)	All Patients (N = 30)		
	Adult Patients, n (%) (N = 13)	Adolescent Patients, n (%) (N = 5)	Total, n (%) (N = 18)	Adult Patients, n (%) (N = 12)	Adult Patients, n (%) (N = 25)	Adolescent Patients, n (%) (N = 5)	Total, n (%) (N = 30)
Clinical description							
AA with ≥50% scalp hair loss experience	2 (15)	2 (40)	4 (22)	2 (17)	4 (16)	2 (40)	6 (20)
AA with ≥50% scalp hair loss experience with partial and/or full eyebrow and/or eyelash loss	11 (85)	3 (60)	14 (78)	10 (83)	21 (84)	3 (60)	24 (80)
Time since diagnosis, years							
Mean (Range)	12.9 (1–47)	3.2 (2–6)	10.2 (1–47)	13.9 (1–42)	13.4 (1–47)	3.2 (2–6)	11.7 (1–47)
Time since commencement of JAKi treatment, months ¹							
Mean (Range)	17.3 (1–34)	5.6 (1–10)	13.4 (1–34)	NA	NA	NA	NA
Current treatment ²							
Oral JAKi	10 (77)	5 (100)	15 (83)	0 (0)	10 (40)	5 (100)	15 (50)
Biotin Forte with zinc	0 (0)	0 (0)	0 (0)	1 (8)	1 (4)	0 (0)	1 (3)
Clobetasol ointment	0 (0)	0 (0)	0 (0)	1 (8)	1 (4)	0 (0)	1 (3)
Diphenylcyclopropenone	2 (15)	0 (0)	2 (11)	0 (0)	2 (8)	0 (0)	2 (7)
Excimer	1 (8)	0 (0)	1 (6)	0 (0)	1 (4)	0 (0)	1 (3)
Intralesional kenalog	1 (8)	0 (0)	1 (6)	1 (8)	2 (8)	0 (0)	2 (7)
Rogaine	0 (0)	0 (0)	0 (0)	1 (8)	1 (4)	0 (0)	1 (3)
Slow-release iron	0 (0)	0 (0)	0 (0)	1 (8)	1 (4)	0 (0)	1 (3)
Vitamin E	0 (0)	0 (0)	0 (0)	1 (8)	1 (4)	0 (0)	1 (3)
No treatment	2 (15)	0 (0)	2 (11)	11 (92)	13 (52)	0 (0)	13 (43)

Abbreviations: AA, alopecia areata; JAKi, JAK inhibitor; NA, not applicable.

¹For n = 15 patients who were currently receiving JAKi at the time of interview.

²Categories not mutually exclusive.

Table 2. Demographic Characteristics of the Interviewed Patients (N = 30)

Demographic Characteristic	Adult Patients, n (%) (N = 25)	Adolescent Patients, n (%) (N = 5)	Total, n (%) (N = 30)
Sex			
Male	11 (44)	2 (40)	13 (43)
Female	14 (56)	3 (60)	17 (57)
Age, y			
Mean (Range)	39.0 (18–72)	16.4 (15–17)	35.2 (15–72)
Ethnicity and/or race			
Caucasian or White	18 (72)	3 (60)	21 (70)
Asian	4 (16)	1 (20)	5 (17)
Black or African American	0 (0)	1 (20)	1 (3)
Other	3 (12)	0 (0)	3 (10)
Education, highest level completed			
High school, no diploma or currently enrolled	1 (4)	5 (100)	6 (20)
High school diploma or equivalent	8 (32)	NA	8 (27)
Some college or associate degree	2 (8)	NA	2 (7)
Bachelor's degree	11 (44)	NA	11 (37)
Master's degree	2 (8)	NA	2 (7)
Doctoral degree	1 (4)	NA	1 (3)
Work status ¹			
Full-time or part-time paid work	17 (68)	1 (20)	18 (60)
Full-time homemaker	3 (12)	0 (0)	3 (10)
Student	5 (20)	5 (100)	10 (33)

Abbreviation: NA, not applicable.

¹Categories not mutually exclusive for adolescent patients.

Concomitant conditions primarily included atopic dermatitis (n = 7, 28%) and thyroid disease (n = 5, 20%) among adults, with no concomitant conditions reported among adolescent patients.

Table 2 details the patients' demographic characteristics summarized by adult and adolescent subgroups. The mean age of adults in the sample was 39.0 years (range = 18–72); on average, adolescent patients were 16.4 years old (range = 15–17). Just under half of the sample was male (43%), and almost a third (30%) of the sample was non-Caucasian. Over half of the adults had been educated to bachelor's degree level or higher (56%); however, adult patients with only a high school diploma or less education (36%) were also represented in the patient sample.

Summary of the patients' physical signs and symptoms of AA

All 30 patients discussed the physical signs and symptoms of AA at the beginning of the interviews. Figure 1 lists the 26 spontaneously reported signs and symptoms of AA noted by interviewees; in addition, other known signs and symptoms were probed by the interviewer. Scalp hair loss was overwhelmingly the most important sign and symptom of AA, with approximately three quarters (77%; n = 23) of the sample listing scalp hair loss as the most bothersome symptom of AA (Table 3).

Adult patients. All (100%, n = 25) adult patients named scalp hair loss as an AA sign and symptom; 88% (n = 22) considered it among their top three most bothersome signs and symptoms, with 72% (n = 18) naming it the most bothersome sign and symptom of AA. The three patients who did not name it in the top three most bothersome signs and symptoms were male and had become used to

living without scalp hair, which they felt was socially acceptable.

Other signs and symptoms identified in the top three most bothersome included eyebrow, eyelash, nose, body, and facial hair loss, as well as eye irritation and nail damage and/or appearance. Eyebrow (16%, n = 4), eyelash (4%, n = 1), nasal (4%, n = 1), and body (4%, n = 1) hair loss were identified by seven patients as the most bothersome signs and symptoms.

A total of 22 adult patients had self-reported eyelash and/or eyebrow involvement. Of these patients, 19 (86%) named eyebrow and/or eyelash hair loss, or eye irritation secondary to eyebrow and/or eyelash hair loss, among the three most bothersome sign and symptoms. Nearly all of these patients (21 of 22; 95%) reported that they would be interested in a treatment for AA scalp hair loss even if it did not address eyebrow and/or eyelash hair loss. However, when 19 of these patients were further queried, nine patients (47%) expressed they might not consider a treatment fully successful if it did not also address eyebrow and/or eyelash hair loss. One patient was not interested or willing to take a treatment for scalp hair loss that did not grow her eyelashes because her eye irritation was so severe.

Adolescent patients. All adolescent patients (100%, n = 5) named scalp hair loss as the most bothersome sign and symptom of AA. Only two other signs and symptoms were named in the top three most bothersome: eyebrow and eyelash hair loss. The three patients with eyebrow and/or eyelash hair loss noted that they would be interested in a treatment for AA scalp hair loss alone, although would be most satisfied with a treatment that addressed eyelashes and eyebrows hair loss as well.

First mention	Domain	Concept	Set 1			Set 2						Set 3				Set 4				Set 5											
			01-M-A-100-N	02-F-A-50.2-N	03-M-A-100-N	04-M-A-100-N	05-F-A-100-N	06-F-A-100-N	07-M-A-100-JAK	08-M-A-40.2-JAK	09-F-A-50-JAK	10-F-A-10-JAK	11-M-A-85-JAK	12-M-A-100-JAK	13-F-A-81.3-N	14-M-P-5-JAK	15-F-A-40-JAK	16-M-A-30-JAK	17-M-A-86.6-JAK	18-F-A-55-N	19-F-A-100-N	20-F-P-60-JAK	21-F-P-2-JAK	22-M-P-20-JAK	23-F-P-0-JAK	24-F-A-1-JAK	25-F-A-10-JAK	26-M-A-100-N	27-F-A-100-N	28-M-A-100-N	29-F-A-1-JAK
Set 1	Hair loss	Scalp	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Eyebrows	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Full body	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Eye irritation	Gritt/sweat in eyes	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Nasal irritation	Inhalation of debris	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Scalp skin sign/symptom	Itching/Numbing/Tingling	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Nose	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Eyelashes	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Legs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Arms	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Armpits	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Nail sign/symptom	Pitting/Splitting/Peeling	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Nasal irritation	Sneezing	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Pubic hair	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Scalp skin sign/symptom	Dry skin/ Dandruff	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Knuckles	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Set 2	Scalp skin sign/symptom	Oily	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
		Hair loss	Facial hair	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Scalp skin sign/symptom		Burning/Inflammation	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Set 3	Hair loss	Chest	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Body hair	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Set 4	Nasal irritation	Nasal dripping	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Ears	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Nail symptom	Nail pain	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
	Hair loss	Abdomen	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Hair loss	Back	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	

Figure 1. Saturation analysis of all spontaneously reported physical signs and symptoms of AA. X indicates that a patient spontaneously reported experiencing this concept; other patients may have experienced a sign and symptom and discussed their experience when probed by the interviewer. Dark blue boxes indicate the first patient report of a specific physical sign and symptom of AA. AA, alopecia areata.

Saturation analysis

A saturation analysis for the physical signs and symptoms of AA details the breadth of the interviewed patients’ physical experiences (Figure 1). All mentioned signs and symptoms of AA were spontaneously reported by patients in the first 24 interviews (Set 1–Set 4). With no new physical sign and symptom concepts emerging in the interviews with the final set of six patients (set 5; gray columns in Figure 1), saturation was achieved, demonstrating that a comprehensive understanding of the patient experience of the physical signs and symptoms of AA was obtained during these interviews.

DISCUSSION

This study provided greater understanding of patients’ physical signs and symptoms of AA through extensive one-on-one concept elicitation interviews. Understanding what is most important to patients is essential to adequately identify and measure meaningful treatment outcomes. Systematically collected patient input can identify key unmet medical needs and important clinical outcomes to be studied in clinical trials (U.S. Food and Drug Administration, 2018b). Moreover, an understanding of these signs and symptoms is necessary in the selection and/or development of key primary and secondary outcome measures and associated endpoints for AA treatment investigations.

Although not surprising, scalp hair loss was confirmed as the most bothersome physical symptom of AA, as noted by 77% of the sample. Despite overenrollment of patients with eyebrow and/or eyelash involvement (80% of the sample), scalp hair loss remained the top-ranked bothersome physical sign and symptom. This finding substantiates that the primary

objective for new AA treatments should meaningfully address this unmet patient need.

The reported bothersome aspects of eyebrow and/or eyelash loss cannot be ignored in these data. Although few patients named either eyebrows or eyelashes as the most bothersome sign and symptom overall, many adult and adolescent patients named eyebrow and eyelash hair loss as one of their three most bothersome symptoms. Although nearly all patients with missing eyebrow or eyelash hairs reported that they would be interested in a treatment for AA scalp hair loss even if it did not address eyebrow and/or eyelash hair loss, nine of these patients may not consider such a treatment to be fully successful. The value of eyebrows and eyelashes was noted by this sample and deserves meaningful assessments in AA treatment investigations as key outcomes important to patients with AA with hair loss in these areas.

Nose hair loss and body hair loss were each reported in great detail by two adult patients as their most bothersome symptom of AA. Nonetheless, neither may warrant current inclusion as key assessments in clinical trials owing to their rarity, as documented in this sample. The systematic concept elicitation process provides confidence that no other key physical aspects of AA are being overlooked owing to our sampling; all 26 spontaneously reported physical signs and symptom concepts emerged before the final six patient interviews as detailed in the saturation grid.

There are limitations in this study. This study focused on patients who had experienced severe or very severe AA (≥50% scalp hair loss), and the generalizability of these findings to patient populations with milder AA has not been

Table 3. Most Bothersome Physical Signs and Symptoms of AA

Sign and Symptom	Adults (N = 25)		Adolescents (N = 5)		Total (N = 30)		Example Patient Quotes ²
	In Top Three ¹ Most Bothersome, n (%)	Most Bothersome, n (%)	In Top Three ¹ Most Bothersome, n (%)	Most Bothersome, n (%)	In Top Three ¹ Most Bothersome, n (%)	Most Bothersome, n (%)	
Scalp hair loss	22 (88)	18 (72)	5 (100)	5 (100)	27 (90)	23 (77)	I would say scalp (...). Because it affects how I feel about myself to go out and resume a normal life, to go to a concert or go swimming or go to the beach. (27-F-A-100-N)
Eyebrow hair loss	16 (64)	4 (16)	2 (40)	0 (0)	18 (60)	4 (13)	A lot of people see bald people shave their heads, like it's a normal thing. It's accepted in society. But like the eyebrows, when people see that, they automatically think like there's something wrong there. (07-M-A-100-JAK)
Eyelash hair loss	14 (56)	1 (4)	2 (40)	0 (0)	16 (53)	1 (3)	I'd probably rather have nice eyelashes than nice hair. (17-M-A-86.6-JAK)
Nose hair loss	3 (12)	1 (4)	0 (0)	0 (0)	3 (10)	1 (3)	So number one would be nose hairs (... because the) functional aspect of it. I need it to stop. Every day or every 20 minutes I'm blowing my nose and I can feel my sinuses just expanding exponentially. (26-M-A-100-N)
Body hair loss	2 (8)	1 (4)	0 (0)	0 (0)	2 (7)	1 (3)	The body hair, eyelashes and scalp hair, yeah. (24- F-A-1-JAK)
Facial hair loss	3 (12)	0 (0)	0 (0)	0 (0)	3 (10)	0 (0)	I had a full beard, literally. A full beard and it's all gone. (26-M-A-100-N)
Eye irritation	2 (8)	0 (0)	0 (0)	0 (0)	2 (7)	0 (0)	Dust gets in my eyes. Sweat falls in, and it's more of a nuisance having to clean my eyes out every night. That's my biggest thing. Every night I got to clean my eyes. If I don't, it irritates the hell out of me the next day. (01-M-A-100-N)
Nail damage and/or appearance	1 (4)	0 (0)	0 (0)	0 (0)	1 (3)	0 (0)	Just really ugly. ... Can't put any polish on, because then they start peeling, so — I can't do anything to them. ... I can't use them like I used to, as a tool... they'll just split right away. (05-F-A-100-N)

Abbreviations: AA, alopecia areata; F, female; JAKi, JAK inhibitor; M, male.

¹Three adult and two adolescent patients described only scalp hair loss as a bothersome sign and symptom of AA.

²Patient codes denoted the participant number (1–30), sex (F or M), adult (A) or adolescent (P), Severity of Alopecia Tool score (0–100), and previous JAKi treatment (JAK) or JAKi-naive (N).

investigated. In addition, adolescent patients aged 12–17 years were targeted for inclusion; however, all participating adolescents were in the upper ages of this range (aged 15–17 years), which therefore limits the generalizability of the findings to younger adolescents with AA. In addition, this study was completed in United States patients only and, as a result, may not be generalizable to other countries and cultures without further exploration. Finally, this paper focused on physical signs and symptoms; the patient-reported psychosocial impacts of AA will be reported in a future publication.

The successful development of new treatments includes engaging, listening to, and trusting patients to voice their needs, perspectives, expectations, and priorities throughout the drug development process. In collaboration with other stakeholders, including clinicians, caregivers, regulators, and payers, the valuable input from patients can provide a clear focus to inform the selection and/or development of clinical outcomes. These systematic interviews of patients with AA who had experienced $\geq 50\%$ scalp hair loss indicate that the primary objective for new AA treatments for this patient population is a meaningful improvement in scalp hair growth.

MATERIALS AND METHODS

Sample and eligibility criteria

This study aimed to recruit 30 adult or adolescent patients (aged ≥ 12 years) from the United States with a clinician-confirmed diagnosis of AA and experience with $\geq 50\%$ scalp hair loss.

Purposive sampling was used to recruit patients with eyebrow and/or eyelash involvement in addition to scalp involvement to allow exploration of the comparative importance of these experiences to patients. In addition, some patients who had previously been treated with JAKi were recruited so that this study could explore these patients' experiences and expectations for treatment success. The JAKi-treatment-naïve patients were required to have a current AA episode (stable or worsening) lasting >6 months but <8 years. Patients with androgenic alopecia or other significant dermatologic conditions (e.g., psoriasis and atopic dermatitis) that in the opinion of their clinician may be severe enough to impact the results of this study were excluded.

A protocol and semistructured interview guide were developed with input from expert dermatologists. The study protocol was reviewed and approved by Western Institutional Review Board #20171820.

Recruitment procedure

All patients were recruited via clinician referral from two clinical sites in the United States, University of California, Irvine and Yale University. Participants who met the eligibility criteria were invited to participate and provided with a verbal explanation of the study requirements. Adult patients (aged ≥ 18 years) who were interested in participating were then provided with an information and consent form that detailed the requirements of the study. For adolescent patients (aged 12–17 years), the informed consent process required both the adolescent participant and their parent and/or guardian to read and sign the information and consent form.

Interview procedure

In accordance with the Food and Drug Administration's PRO Guidance for Industry (U.S. Department of Health and Human

Services et al., 2009), this study was designed to gather open-ended patient input. The semistructured interview guide included open-ended questions to explore patients' experience of AA, including the physical signs and symptoms they experienced. Interviews were conducted between October 10, 2017 and October 25, 2017 by an experienced qualitative researcher trained in interview techniques and clinical outcome assessment development. Interviews lasted approximately 90 minutes and were conducted face-to-face at the clinical site of the referring dermatologist or a nearby hotel meeting room. All interviews were audio-recorded and transcribed verbatim.

Analysis

Demographic and clinical information was descriptively summarized. Interview transcripts were reviewed in full and all identifying information, such as names and specific locations, was removed. Participants were allocated a code to allow data to be reported anonymously. The codes used denoted the participant number, sex, age group, SALT score, and previous treatment with JAKi. For example, patient 27-F-A-100-N was the 27th patient to be interviewed, a female, an adult, had a SALT score of 100, and was naïve to JAKi treatment. Conversely, patient 22-M-P-20-JAK was the 22nd patient to be interviewed, a male, an adolescent, had a SALT score of 20, and had received successful JAKi treatment.

Transcripts were analyzed using thematic techniques (Braun and Clarke, 2006) aided by ATLAS.ti version 7.5, computer-assisted qualitative data analysis software, which facilitated the coding and organization of data. The analysis took a phenomenological interpretative approach, seeking to understand the multiple realities of participants rather than one true reality and focusing on the perceptions, feelings, and lived experiences of participants (Guest et al., 2012). Three phases of thematic analysis were followed to explore open-ended data: transcripts were reviewed by the lead analysts and overarching ideas identified; descriptive codes were assigned to quotes within the transcripts; and codes were collated into potential themes and compared and contrasted to identify relationships between them. In this way, the key signs and symptoms of AA were identified with supportive quotes.

The first two transcripts were coded by the research team to develop a preliminary codebook for the interview. Using this codebook, the research team coded remaining interview transcripts and identified any new codes that emerged in subsequent interviews. When a new concept emerged, a retrospective review of previous interview transcripts was conducted to ensure that this concept was not overlooked during the initial coding.

Saturation analysis

Conceptual saturation was used as a method to guide sampling and analysis for this qualitative study (U.S. Department of Health and Human Services et al., 2009). Defined as the point at which no new concept-relevant information emerges (Fusch and Ness, 2015), reaching saturation is an indication that comprehensive understanding of the patient experience has been achieved and that no more interviews are required.

After completion of all 30 interviews, conceptual saturation was assessed in line with industry guidelines (Patrick et al., 2011a, 2011b). First, transcripts were divided into five sets of six patients based on the chronological order of interview completion. Next, transcripts in set two were compared with the previous interviews to identify whether any new concepts had arisen. If no new concepts had emerged in set two, saturation was considered to have been

attained. However, if new concept(s) were identified by at least four patients, the third set of interviews were reviewed. This process continued for all sets, and saturation was deemed to have been achieved when no new concepts arose.

Data availability statement

Owing to the sensitive nature of this qualitative data set, the data cannot be shared for ethical reasons to protect patients' identities that may be disclosed in the detailed responses provided during the interviews.

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CONFLICT OF INTEREST

HK, SK, NVJA, and JM are employees of DRG Abacus, a health economic and outcomes research consultancy that consults with various pharmaceutical companies. FN and YD are employees and stockholders at Eli Lilly and Company. KWW was an employee and stockholder at Eli Lilly and Company at the time this research was conducted; she is now an employee and stockholder at Pfizer Inc. BAK has served on advisory boards and is a consultant and clinical trial investigator for Eli Lilly and Company; he is a consultant for Aclaris Therapeutics, Eli Lilly and Company, Concert Pharmaceuticals, Pfizer Inc, and Dermavant Sciences. Eli Lilly and Company have commissioned DRG Abacus, JMK, and BAK to consult on clinical outcomes assessment strategies for AA.

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AUTHOR CONTRIBUTIONS

Conceptualization: KWW, HK, SK, NVJA, JM, FN, BAK; Data Curation: HK, SK, NVJA, JM, NAM, BAK; Formal Analysis: HK, SK, NVJA, JM; Funding

Acquisition: FN; Investigation: KWW, NVJA, BAK; Methodology: KWW, HK, SK, NVJA, FN, BAK; Project Administration: KWW, HK, SK, NVJA, FN, YD, NAM, BAK; Resources: HK, SK, NVJA; Software: HK, SK, NVJA, JM; Supervision: KWW, HK, SK, NVJA, F, BAK; Validation: KWW, HK, SK, NVJA, JM, YMK, BAK; Visualization: KWW, HK, SK, NVJA, JM, FN, YD, BAK; Writing - Original Draft Preparation: KWW, HK, SK, NVJA, JM, FN, YD, NAM, YMK, BAK; Writing - Review and Editing: KWW, HK, SK, NVJA, JM, FN, YD, NAM, YMK, BAK

REFERENCES

- Braun V, Clarke V. Using thematic analysis in psychology. *Qual Res Psychol* 2006;3:77–101.
- Davey L, Clarke V, Jenkinson E. Living with alopecia areata: an online qualitative survey study. *Br J Dermatol* 2019;180:1377–89.
- Fusch PI, Ness LR. Are we there yet? Data saturation in qualitative research. *Qual Rep* 2015;20:1408–16.
- Guest G, MacQueen KM, Namey EE. *Applied thematic analysis*. Thousand Oaks: SAGE; 2012.
- Hordinsky M, Donati A. Alopecia areata: an evidence-based treatment update. *Am J Clin Dermatol* 2014;15:231–46.
- Islam N, Leung PS, Huntley AC, Gershwin ME. The autoimmune basis of alopecia areata: a comprehensive review. *Autoimmun Rev* 2015;14:81–9.
- Patrick DL, Burke LB, Gwaltney CJ, Leidy NK, Martin ML, Molsen E, et al. Content validity—establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO good research practices task force report: part 1—eliciting concepts for a new PRO instrument. *Value Health* 2011a;14:967–77.
- Patrick DL, Burke LB, Gwaltney CJ, Leidy NK, Martin ML, Molsen E, et al. Content validity—establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO Good Research Practices Task Force report: part 2—assessing respondent understanding. *Value Health* 2011b;14:978–88.
- U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), Center for Biologics Evaluation and Research (CBER), Center for Devices and Radiological Health (CDRH). Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims. <https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf>; 2009. (accessed January 19, 2019).
- U.S. Food and Drug Administration. Discussion document for patient-focused drug development public workshop on guidance 2: methods to identify what is important to patients. <https://www.fda.gov/downloads/Drugs/NewsEvents/UCM620707.pdf>; 2018a. (accessed January 19, 2019).
- U.S. Food and Drug Administration. Discussion document for patient-focused drug development public workshop on guidance 3: select, develop or modify fit-for-purpose clinical outcome assessments. <https://www.fda.gov/downloads/Drugs/NewsEvents/UCM620708.pdf>; 2018b. (accessed January 19, 2019).
- Wolf JJ, Baker PH. Alopecia areata: factors that impact children and adolescents. *J Adolesc Res* 2019;34:282–301.