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A description of alopecia areata in European patients based on real-world survey data: physician-reported characterization of severity and associated treatment utilization

Background: Alopecia areata (AA), an autoimmune disease affecting the hair of the scalp, face, and/or body, can entail substantial psychological and physical burden for patients. There is currently no international agreement on how to treat AA and the approach may vary across countries. *Objectives*: This study investigated the management of AA in clinical practice. *Materials & Methods*: Data from a point-in-time survey conducted in France, Germany, Italy, Spain, and the United Kingdom, between October 2021-June 2022, were analysed for adults with mild, moderate, and severe AA, based on physician assessment. Dermatologists were surveyed about factors used to assess disease severity, physician-reported treatment goals, and treatment patterns for AA, including the use of wigs. *Results*: In total, 239 dermatologists reported on 2,083 patients. Physicians' severity assessment and treatment goals were predominantly driven by scalp hair loss. Topical and intralesional corticosteroids were the most prescribed treatments for mild and moderate AA. Conventional immunosuppressants, oral Janus kinase inhibitors, and topical immunotherapy use generally increased with AA severity and therapy line. Wig use was greatest for severe AA. The primary reasons for the last treatment change in the moderate and severe groups were worsening of condition, lack of initial efficacy, and loss of response, and for mild group were improvement in condition, lack of initial efficacy, and worsening of condition. Findings were generally similar across countries. *Conclusion*: This analysis provides insights into the management of AA in five European countries and confirms the need for more effective therapies, especially for patients with severe AA.

Key words: alopecia areata, real world data, treatment patterns, treatment goals

Alopecia areata (AA) is a chronic autoimmune disease that can result in extensive and even complete hair loss of the scalp, face, and/or body [1]. The prevalence of AA is estimated in the range of 0.1–0.58% [2-5], with about 40% of patients developing symptoms before the age of 20 years [6].

The onset of AA is often sudden, and the evolution is unpredictable [7]. Spontaneous regrowth is frequently observed during the early stages of the disease, however, relapses are common, and hair loss tends to become persistent when it is extensive [8, 9]. AA is often associated with psychological comorbidities such as anxiety and/or depression [10], as well as dermatological and autoimmune diseases, such as atopic dermatitis and autoimmune thyroid diseases [11].

The distortion of appearance characterizing AA hair loss, as well as the unpredictable nature of the disease, often result in a substantial emotional and psychological burden [12]. AA can have a profound impact on patients and affect all aspects of life, including work, leisure, family, relationships, and daily activities [13, 14].

Until the approval of baricitinib in 2022, there was no therapy approved by the European Medicines Agency (EMA; approved in 2022) [15] or the United States Food and Drug Administration (FDA; approved in 2022) [16] for the treatment of AA. Physicians have traditionally prescribed off-label treatments, many of which have not been tested or proven effective in a robust clinical trial setting [17]. With only a few country-specific treatment guidelines available, mostly based on expert opinion, there is currently no international agreement on how to best manage AA in clinical practice [18]. As a result, the therapeutic approach may vary across countries.

With the emergence of effective therapies, there is a need to better understand the current management of AA. The objective of this study was to describe treatment

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approaches in patients with AA in routine clinical practice in five European countries: France, Germany, Italy, Spain, and the United Kingdom (UK). Using real-world data, we investigated factors used to assess disease severity, physician-reported treatment goals, and treatment patterns, including the use of wigs.

Materials and methods

Study design, participants, and data collected

This study used survey data from the Adelphi AA Disease Specific Programme™ (DSP) conducted in France, Germany, Italy, Spain, and the UK. DSPs are large point-in-time studies based on physician and patient surveys that collect real-world data and aim to describe current clinical practice, symptom prevalence, and patients' perception of their health state and quality of life across a range of chronic conditions [19].

For the AA DSP, dermatologists were identified from public lists of healthcare professionals. Physicians were invited to participate in the study if they were involved in treatment decisions for AA and had a minimum of seven consultations with adult AA patients each month. The participating physicians were requested to recruit at least seven patients consulting with mild (n=1), moderate (n=3), and severe (n=3) AA, consecutively, until the severity quota had been reached. Physicians were compensated for their participation according to fair market research rates. For each patient, physicians completed a patient record form (PRF). The patients were adults (aged ≥18 years) with current physician-diagnosed AA, who were not part of a clinical trial at the time of the survey. Disease severity was determined by the dermatologists according to their own definition of the terms "mild," "moderate," and "severe," thus reflecting how physicians assess AA severity in clinical practice.

Analyses

Selected physician reported data from the AA DSP are presented by severity category (*i.e.*, mild, moderate, and severe AA), overall and by country, using an interim sample with data collected from October 2021 to June 2022. Factors considered important to assess AA severity and physician-reported treatment goals were collected from dermatologists. Patient demographics, clinical characteristics (including comorbidities), as well as information related to AA therapies and wig use were extracted from the PRFs.

This analysis focused on the following six AA treatment groups: topical, intralesional, and systemic corticosteroids (*i.e.*, oral and intravenous regimen); conventional immunosuppressants (azathioprine, cyclosporine A, and methotrexate); oral Janus kinase (JAK) inhibitors (baricitinib, ruxolitinib, tofacitinib, and other oral JAK inhibitor); and topical immunotherapy (1-chloro,2,4,dinitrobenzene [DNCB], squaric acid dibutylester [SADBE], 2,3-diphenylcyclopropenone [DPCP], and others).

Continuous variables were described using mean and standard deviation (SD). Categorical variables were reported as the frequency and percentage within each category. No imputation of missing data was conducted. Analyses were performed using IBM SPSS Data Collection Survey Reporter Version 7.

Compliance with ethics guidelines

The DSP fulfils the definition of a market research survey under the European Pharmaceutical Market Research Association (EphRMA) Code of Conduct [20] and is therefore conducted to market research, rather than clinical, guidelines. Market research surveys are exempt from requiring Institutional Review Board (IRB) approval, however, the Western IRB (WIRB) conducted a methodological review of the AA DSP and provided an exemption.

The DSP was conducted in compliance with the International Council for Harmonisation (ICH) Declaration of Helsinki [21]. Freely given, specific and informed consent was obtained from each respondent to take part in the DSP and for the processing of their personal data. All data provided by physicians and patients were anonymized.

Results

In total, 239 dermatologists (France, n=26; Germany, n=60; Italy, n=59; Spain, n=60; and UK, n=34) provided data for 2,083 patients with mild (n=299), moderate (n=936), and severe AA (n=848) (*supplementary table 1*).

Patient demographics and clinical characteristics

Patient demographics and clinical characteristics across the five countries at the time of data collection are summarized in *table 1*. Overall, the mean (SD) age was 35.7 (11.5) years, and 48% of patients were female. The mean time since AA diagnosis was longer for patients with severe AA (3.7 years) than for patients with moderate (2.6 years) or mild AA (2.4 years). The disease progression was judged uncontrolled (*i.e.*, stable or worsening) in 65% and 76% of patients with moderate and severe AA, respectively, compared with 40% of patients with mild AA. Scalp hair loss was the primary sign reported across all severity groups (mild=72%, moderate=88%, severe=90%). In comparison with mild and moderate AA, a higher percentage of patients with severe AA were currently experiencing hair loss in other areas, the most common locations being eyebrows (44%), eyelashes (33%), and the body (23%). The physician-reported current severity of scalp hair loss increased with AA severity; patients with mild AA did not have severe scalp hair loss, while 85% of patients with severe AA were experiencing severe scalp hair loss (*supplementary figure 2*). Similar patterns were observed for the current severity of other AA signs and symptoms beyond scalp hair loss (*supplementary figure 2*). Concomitant conditions were more frequently reported for patients with severe AA (*table 1*). The three most prevalent concomitant conditions were anxiety, atopic dermatitis, and depression. Similar patterns were seen across countries for patient demographics and clinical characteristics (*supplementary table 2*).

Table 1. Patient demographics and clinical characteristics by physician-reported AA severity.

	Overall	Mild	Moderate	Severe
	(*n*=2083)	(*n*=299)	(*n*=936)	(*n*=848)
Patient demographics				
Age in years, mean (SD)[1]	35.7 (11.5)	32.0 (10.5)	35.4 (11.2)	37.3 (11.9)
Female, *n* (%)	997 (48)	130 (43)	442 (47)	425 (50)
BMI in kg/m², mean (SD)	24.3 (3.2)	23.9 (2.9)	24.3 (3.1)	24.4 (3.4)
Ethnicity (White/Caucasian), *n* (%)	1885 (90)	283 (95)	838 (90)	764 (90)
Clinical characteristics of AA				
Years since AA diagnosis, mean (SD)	3.0 (5.1)	2.4 (4.1)	2.6 (4.2)	3.7 (6.3)
Disease progression, *n* (%)[2]				
Improving	715 (34)	178 (60)	330 (35)	207 (24)
Stable	890 (43)	95 (32)	392 (42)	403 (48)
Worsening (rapidly and slowly)	477 (23)	26 (9)	213 (22)	238 (28)
Uncontrolled (stable or worsening)	1367 (66)	121 (40)	605 (65)	641 (76)
Current signs and symptoms related to AA, *n* (%)				
Scalp hair loss	1802 (87)	216 (72)	825 (88)	761 (90)
Eyebrow hair loss	566 (27)	11 (4)	178 (19)	377 (44)
Eyelash hair loss	363 (17)	5 (2)	82 (9)	276 (33)
Body hair loss	247 (12)	5 (2)	49 (5)	193 (23)
Eye irritation	64 (3)	5 (2)	22 (2)	37 (4)
Nail damage	208 (10)	10 (3)	80 (9)	118 (14)
Facial hair loss (moustache or beard)	210 (10)	25 (8)	87 (9)	98 (12)
Scalp itching	324 (16)	40 (13)	156 (17)	128 (15)
Scalp burning or stinging	204 (10)	19 (6)	84 (9)	101 (12)
Scalp pain	176 (8)	11 (4)	65 (7)	100 (12)
Scalp irritation	206 (10)	19 (6)	92 (10)	95 (11)
Other	5 (<1)	4 (1)	1 (<1)	0 (0)
Don't know	12 (1)	1 (<1)	7 (1)	4 (<1)
None of the above	133 (6)	49 (16)	46 (5)	38 (4)
Comorbidities, *n* (%)[3]				
No concomitant conditions	1117 (54)	191 (64)	506 (54)	420 (50)
Anxiety	158 (8)	13 (4)	60 (6)	85 (10)
Atopic dermatitis	101 (5)	8 (3)	41 (4)	52 (6)
Depression	97 (5)	5 (2)	30 (3)	62 (7)
Thyroid disease	88 (4)	6 (2)	39 (4)	43 (5)
Atopy	75 (4)	3 (1)	31 (3)	41 (5)
Hypertension	75 (4)	10 (3)	25 (3)	40 (5)

AA: alopecia areata; BMI: body mass index; SD: standard deviation.
[1]Patients <90 years only; *n*=2 (<1%) patients ≥90 years old.
[2]*"How would you describe this patient's disease?".*
[3]*"Please indicate any diagnosed concomitant conditions for this patient". Only comorbidities experienced by 1% or more of patients are reported here.*

In the physician survey, the degree of scalp involvement (36%), the extent of hair loss (26%), and the impact that AA has on the patient's quality of life (9%) were identified as the three most important factors to assess AA severity in clinical practice (*figure 1*).

Physician-reported treatment goals

Reducing scalp hair loss (mild=89%, moderate=92%, severe=84%), improving quality-of-life (mild=42%, moderate=45%, severe=52%), and reducing AA psychological impact (mild=34%, moderate=34%, severe=42%) were the most common treatment goals reported across severity categories by the dermatologists (*figure 2*). Reducing eyebrow or eyelash hair loss was rated as important goals for patients with severe AA, while prevention of relapses or rebound effects was considered an important treatment goal for patients with mild AA.

Treatment patterns

Of the 2,083 patients enrolled in the study, only 152 (7%) were not currently receiving any treatment (mild=9%, moderate=3%, and severe=10%). On average, patients were currently receiving two therapies for AA (mild=1.6, moderate=2.1, and severe=2.0). A similar pattern was seen across countries.

Topical and intralesional corticosteroids (*figure 3*) were the most common treatments for patients with mild (53% and 31%, respectively) and moderate AA (35% and 27%, respectively), while their use was more limited in patients with severe AA. Current use of systemic corticosteroids

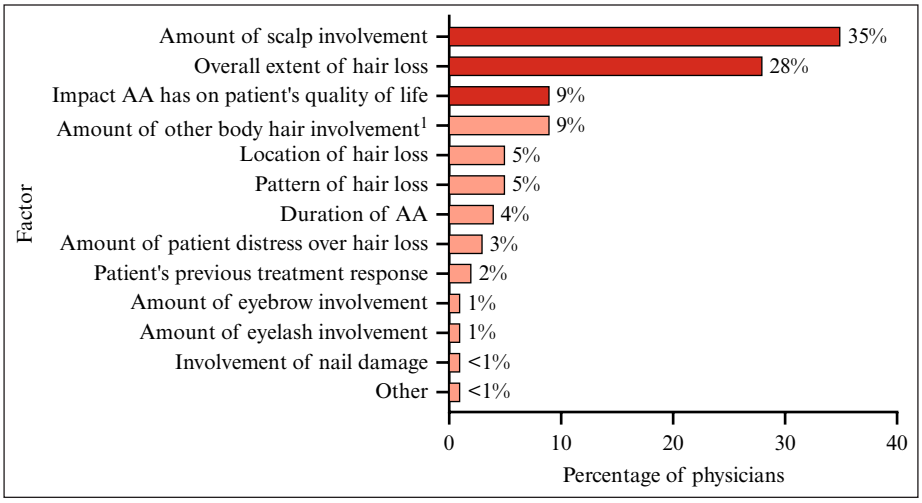

Figure 1. Factors driving physician assessment of disease severity.

"What are the three most important factors you use to determine the severity of alopecia areata?"

AA: Alopecia areata.
[1]Outside of the scalp, eyebrows, and eyelashes.
Physicians had to complete at least one patient record form to be included. Physicians listed three factors. Percentages do not sum to 100%.

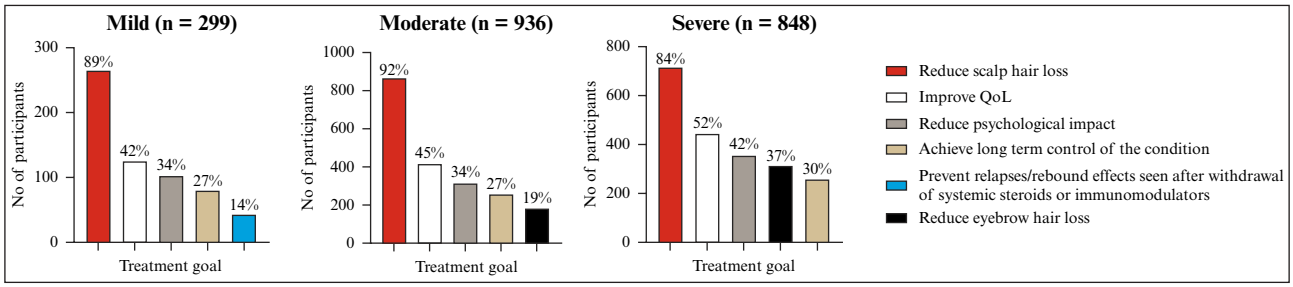

Figure 2. Five main treatment goals by disease severity.

"What are your main treatment goals for this patient?"

QoL: Quality of life.
Physicians could list more than one main treatment goal for each patient.
Other less commonly-reported treatment goals not presented here were: reduce eyelash hair loss, prevent relapses/rebound effects seen after withdrawal of systemic steroids or immunomodulators, reduce scalp itching / irritation, reduce impact on patient's ability to do what they enjoy, minimize adverse events, reduce impact on patient's ability to work/study, reduce scalp pain / burning or stinging, reduce facial hair loss, reduce body hair loss, reduce nail damage, reduce eye irritation, and others.

was higher in moderate (27%) and severe AA (26%) than in mild AA (8%). Conventional immunosuppressants, oral JAK inhibitors, and topical immunotherapy were more commonly used in patients with severe AA (26%, 17%, and 15%, respectively). The current treatments were generally similar across individual countries (*supplementary figure 1*). Of note, a higher proportion of patients with severe AA in France were prescribed conventional immunosuppressants (43%) and oral JAK inhibitors (39%) compared to those in the other countries. On the other hand, patients with mild and moderate AA in Germany were prescribed intralesional corticosteroids (4% and 8%, respectively) much less frequently than in other countries.

Only 31 patients (1%) had never received any treatment for AA across severity groups. The proportion of patients who had received at least two lines of treatment for AA increased with disease severity (mild=33%, moderate=47%, severe=62%). Across all severity groups, topical corticosteroids were the most frequently prescribed first-line treatment (mild=60%, moderate=52%, severe=43%), and their use was less frequent as second- and third-line treatments (*figure 4*). The use of intralesional corticosteroids was more common for mild AA and increased with subsequent lines of therapy, at up to 57% of patients as third-line treatments. Systemic corticosteroids were frequently prescribed for patients with moderate or severe AA. In patients with severe AA, their

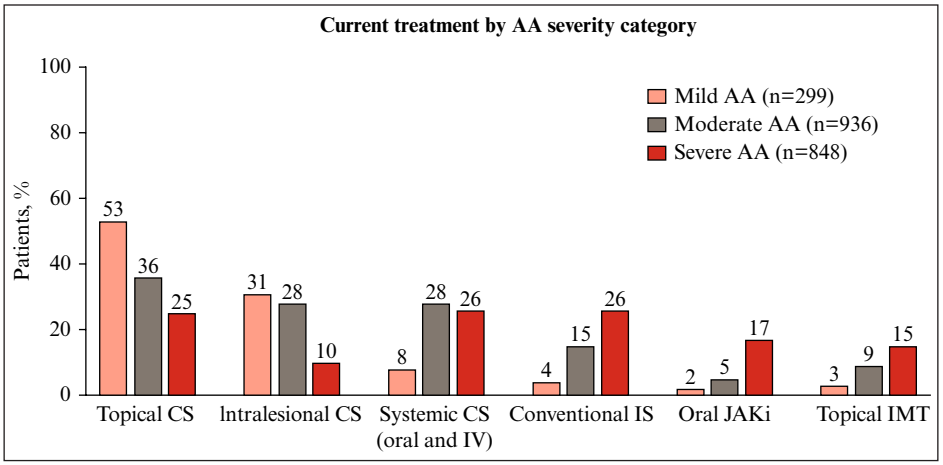

Figure 3. Current treatment by disease severity.

AA: alopecia areata; CS: corticosteroid; IMT: immunotherapy; IS: systemic immunosuppressant; IV: intravenous; JAKi: Janus kinase inhibitor; SADBE: squaric acid dibutylester.
Conventional systemic immunosuppressants included: azathioprine, cyclosporine, or methotrexate.
Oral JAKi included: baricitinib, ruxolitinib, tofacitinib, and other JAKis.
Topical immunotherapy included: DPCP, SADBE, DNCB, and others.
Physicians could list more than one treatment.

use decreased from 40% as first-line to 25% as third-line treatment. No clear trend could be seen for moderate AA. The use of conventional immunosuppressants increased with severity and regimen line. Oral JAK inhibitors were mostly prescribed as a third-line therapy for severe patients (21%). Topical immunotherapy was more frequently used for severe AA as a second- or third-line treatment (15% for both versus 9.3% as first line) and for moderate AA as a third-line option (18%). Similar patterns were seen across countries in the proportion of patients that were never treated for AA, the number of treatment lines, and the use of each treatment group by line and severity.

The reasons for changing from previous to current treatment are presented in *figure 5*. In patients with moderate or severe AA, the three main reasons reported by physicians were worsening of the condition (moderate=46% and severe=47%), lack of initial efficacy (moderate=23% and severe=28%), and loss of response over time (moderate=21% and severe=26%). The three main reasons for the most recent treatment change in patients with mild AA were improvement of the condition (28%), lack of initial efficacy (19%), and worsening of the condition (27%).

The use of wigs

Wig use at any time increased with disease severity (mild=2%, moderate=9%, severe=39%) (*figure 6*). The majority of those who had ever used a wig were female (78%). Similar patterns were seen across countries.

Discussion

This study investigated the management of AA in adults using dermatologist-reported real-world data collected in five European countries (France, Germany, Italy, Spain, and the UK).

Across all countries, the physician assessment of AA severity was primarily driven by the extent of scalp hair loss. This is consistent with previous reports [22, 23] and with the clinical characteristics, as 85% of patients with severe AA had severe scalp hair loss versus none with mild AA. While there is no unique definition of disease severity for AA, experts generally agree that the driver for the definition of AA severity should be the extent of scalp hair loss [24]. It has also been suggested to incorporate additional features in AA disease severity assessment, such as quality of life or psychological burden [25]. In our study, physicians judged the impact on quality of life to be an important factor to consider when assessing AA severity but to a lesser extent than the degree of hair loss.

When surveyed about the treatment goals for each patient enrolled, dermatologists reported reduction of scalp hair loss to be the main goal across severity groups. Improving quality of life and reducing psychological burden were considered second and third goals across severity, respectively. There is no universal agreement on what the treatment goals should be in patients with AA, however, arresting the progression of hair loss, inducing hair regrowth and improving quality of life are among those generally put forward by experts [26, 27].

Only 7% of all patients were not receiving any treatment at the time of the survey. Reasons for leaving AA untreated were not collected and could include spontaneous regrowth, a "wait and see" approach, or the absence of a suitable option, especially for severe AA [7].

Topical and intralesional corticosteroids were the most prescribed treatments among patients with mild and moderate AA. Current use of systemic corticosteroids was higher in patients with moderate and severe AA than in mild forms. Our results are generally aligned with data

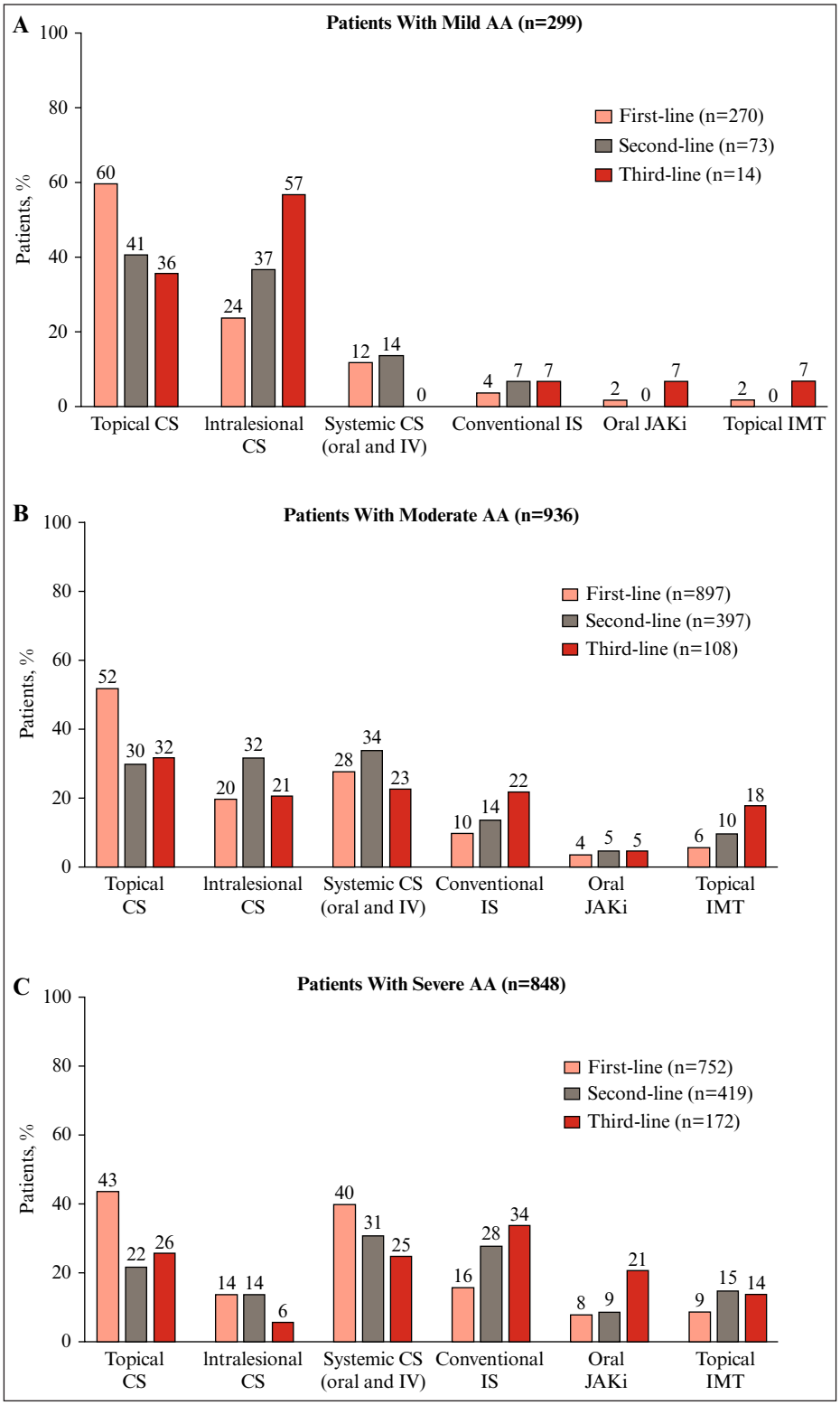

Figure 4. Treatment lines for mild (**A**), moderate (**B**), and severe (**C**) AA.

AA: alopecia areata; CS: corticosteroid; DNCB: 1-chloro,2,4,dinitrobenzene; DPCP: 2,3-diphenylcyclopropenone; IMT: immunotherapy; IS: systemic immunosuppressant; IV: intravenous; JAKi: Janus kinase inhibitor; SADBE: squaric acid dibutylester.
Conventional systemic immunosuppressants included: azathioprine, cyclosporine, or methotrexate.
Oral JAKi included: baricitinib, ruxolitinib, tofacitinib, and other JAKis.
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Physicians could list more than one treatment.

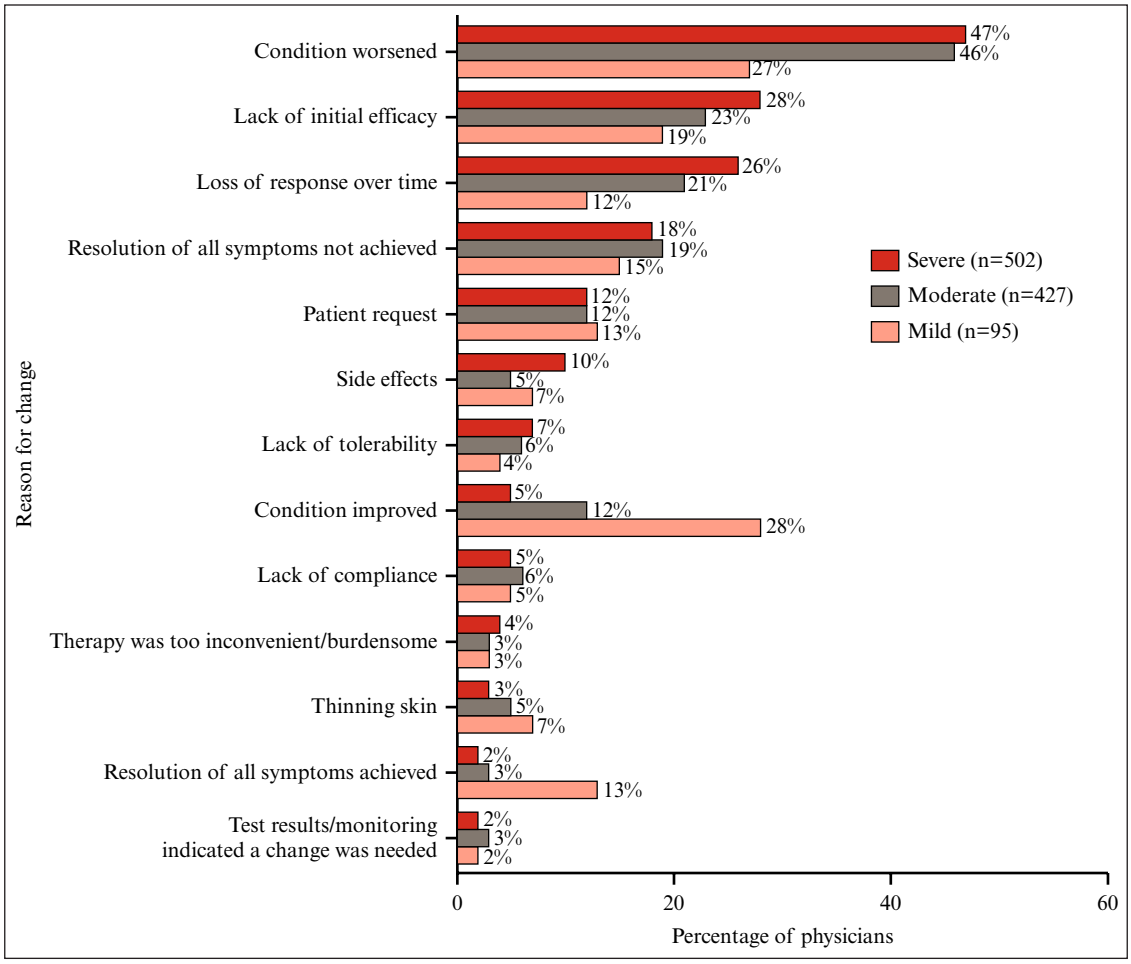

Figure 5. Reasons for most recent treatment change by disease severity.
"Why was the switch from the previous to the current regimen made?"

Physicians could list more than one reason for a change in treatment for each patient. Only changes that were reported for >1% of patients overall are listed.

reported in other countries. In a recent study in Japan, topical corticosteroids were the most frequently prescribed treatment for AA [28]. Several studies have described treatment patterns in the United States and reported similar findings [29-31]. Despite limited evidence, corticosteroids remain the mainstay of AA pharmacological management [7, 26]. In a recent consensus statement, experts considered corticosteroids to be an appropriate first-line treatment for AA, irrespective of disease severity [18].

Use of conventional immunosuppressants increased with disease severity and subsequent lines of therapy. Similar patterns have been observed in the United States [29]. This is consistent with published expert opinions that position conventional immunosuppressants mostly for adult patients with severe AA and generally after corticosteroids or as steroid-sparing agents [18, 26, 27].

Oral JAK inhibitors were mostly prescribed to patients with severe AA, and rates increased with subsequent lines of therapy. Several studies have demonstrated that the JAK-signal transducer and activator of transcription (STAT) pathway plays a central role in AA pathogenesis [1]. The JAK-STAT pathway has been investigated as a treatment target for AA over recent years [32]. As of 2022, baricitinib is the first and only JAK inhibitor approved for the treatment of severe AA in adults.

The use of topical immunotherapy was mostly reported in patients with severe AA as a second- or third-line treatment. Topical immunotherapy involves the use of potent allergens that produce a contact dermatitis, which, through an unknown mechanism, allows hair to regrow [1]. Topical immunotherapy is not widely available and must be applied by trained personnel as it can induce a contact dermatitis in patients, relatives, and staff [7]. Our results are aligned with published guidelines, which generally position topical immunotherapy for extensive and chronic scalp hair loss.

Dermatologists reported that a high proportion of patients had switched therapies due to the condition becoming worsened, a lack of initial efficacy, or a loss of response over time. The main reasons for treatment change were consistent with the disease progression, which was judged uncontrolled in 40%, 65%, and 76% of patients with mild, moderate, and severe AA,

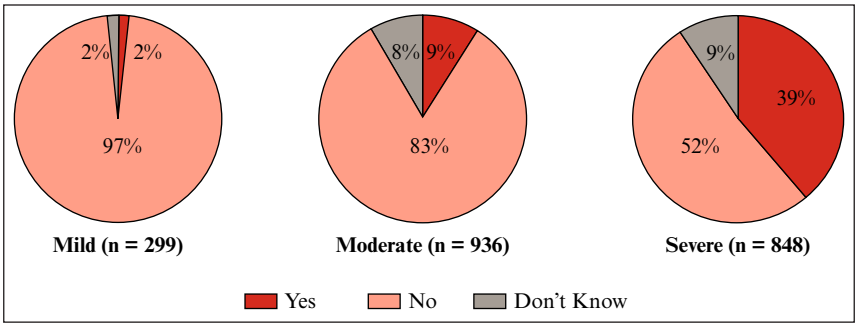

Figure 6. Use of wigs by disease severity.
"Has this patient ever used a wig for their alopecia areata?"

Percentages do not sum to 100% due to rounding.

respectively. Traditional therapeutic options for the treatment of AA have not been well evaluated in clinical trials and their efficacy seem to be limited, especially for patients with severe AA [7, 17].
A small proportion of patients with mild (2%) or moderate (9%) AA had used a wig at some point due to their AA. Conversely, use of wig was reported by 39% of patients with severe AA. Wig use was notably more common among females compared to males. Concealment strategies, such as wigs, are encouraged in some guidelines and may improve patients' quality of life [7, 10, 33].
Apart from a few exceptions, data were similar across the five European countries, especially with regards to treatment patterns. This might reflect that despite universal agreement on how to best manage patients with AA, published guidelines and expert consensus are generally aligned on a set of principles that include the use of corticosteroids as first-line options and a step-up approach for patients with increasing severity and regimen line [7, 18, 26].
This study provides real-world data collected from dermatologists selected using minimal exclusion criteria on a large sample of adult patients with AA in five European countries. Moreover, information on AA management and treatment patterns was provided along with patient clinical characteristics. Another strength of the study is the use of standardized data collection tools, which facilitate between-country comparisons. There are also limitations to this study. Firstly, real-world studies have the potential for sampling, selection, and recall bias. Additionally, the definition of AA severity was based on clinical judgement, which may vary between physicians. However, as there is no unique definition of disease severity for AA, this approach should reflect how physicians assess severity in clinical practice. Reducing scalp hair loss was selected among the main treatment goals in the highest number of patients. However, the wording of this treatment goal and of the other goals related to hair loss did not allow us to distinguish between arresting the progression of hair loss and inducing hair regrowth. Future studies should examine the relative importance of these two goals for the management of AA. Furthermore, the description of AA therapies was not exhaustive but rather focused on a limited number of mutually exclusive groups of treatments. This choice was made to focus on treatments recommended for adults with AA in existing guidelines and consensus statements [7, 26, 27]. Treatment options not recommended or only recommended as adjunctive therapies were not considered in this analysis. Information on the different protocols used for each treatment group (*e.g.*, pulse versus continuous corticosteroid regimen) was also not captured. Finally, due to enrolment challenges there were fewer dermatologists from France and the UK relative to the other countries. However, patients' clinical characteristics were consistent across the five countries, and the few differences observed between countries in terms of treatment patterns were not exclusively limited to these two countries. ■

Conclusions

Treatment of patients with AA mostly relied on corticosteroids as the main first-line regimen across AA severity categories. Use of conventional immunosuppressants, oral JAK inhibitors, and topical immunotherapy was more common in patients with severe AA, especially after failure of first-line treatments. Treatment patterns by severity were generally similar across the five European countries, although variations were observed.

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