ORIGINAL RESEARCH

Quantifying Physician Preferences for Systemic Atopic Dermatitis Treatments Using a Discrete-Choice Experiment

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ABSTRACT

Introduction: As research continues, new drugs will no doubt be added to the current pool of treatments for moderate-to-severe atopic dermatitis (AD). This raises the need for studies to determine prescriber preferences for different pharmacological options and the factors that influence their choice of treatment. Here we aim to explore physician preferences in the systemic treatment of moderate-to-severe AD, identify the sociodemographic characteristics that can influence physician preferences, and evaluate their satisfaction with current AD therapies.

Methods: A discrete-choice experiment (DCE) survey was administered to physicians treating patients with AD in Spain. Results were analyzed using a conditional logit model to estimate the relative importance of each attribute and the maximum risk accepted to achieve therapeutic benefit.

Results: A total of 28 respondents completed the DCE survey (67.9% female, mean age 45.9 years). Participants identified objective clinical efficacy and risk of severe adverse events (AEs) as the most important attributes, followed by improvement in sleep and pruritus and faster onset of action from the start of the treatment. Respondents gave less importance to mode of administration and therapeutic benefit in other atopic conditions. Respondents were willing to accept an increased risk of severe AEs and mild-to-moderate AEs leading to treatment discon-

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tinuation due to intolerance in order to obtain improvements in efficacy, sleep, and pruritus, and long-term clinical benefit.

Conclusion: Our findings can help prescribers choose the most appropriate systemic AD therapy.

Keywords: Atopic dermatitis; Discrete-choice experiment; Maximum acceptable risk; Physician preference

Key Summary Points
Why carry out this study?
The pool of treatments for moderate-to-severe atopic dermatitis (AD) is increasing
Physician preferences and factors influencing them need to be explored
Discrete-choice experiments allow one to identify physician preferences in patient treatment
What was learned from the study?
Treatment efficacy and safety, and symptom relief, were the most important features, while the route and frequency of administration were considered less relevant
These observations can guide therapeutic choices in AD both now and in the future and will also help other decision-makers involved in the treatment of this highly disabling disease

INTRODUCTION

Atopic dermatitis (AD) is a chronic, relapsing inflammatory disease that is characterized by eczematous lesions [1]. Onset usually occurs in childhood, even though it can present at any age, and has a prevalence of 10–20% [2, 3].

Adult AD has a prevalence of 5–10% [4, 5]. AD diagnosis is based on clinical criteria that include the presence of pruritus and dermatitis [6]. It is also associated with multiple comorbidities that compromise functionality and productivity and affect the patient's health-related quality of life (HRQoL) [1, 6–10]. Moreover, AD negatively impacts mental and psychological health, HRQoL, sleep, work productivity, and activity in adults [11]. Children with AD experience a significant burden with deep impact on HRQoL as well as bullying at school and concerning the domains of daily activities, school, leisure, and personal relationships [12].

According to a study carried out in three areas of Spain, the prevalence of severe AD in adults was 0.08% (95% CI, 0.07–0.09%) [13], representing approximately 10% of patients with AD [14]. As disease symptoms in moderate-to-severe AD are usually not properly controlled with only topical treatment, systemic drugs are usually prescribed [14].

Cyclosporin A and oral corticosteroids are currently the only conventional systemic immunomodulators approved for the treatment of adults with moderate-to-severe AD [15]. Other immunosuppressants, such as methotrexate, azathioprine, and mycophenolate, are used off-label [14].

Biological treatments have recently become available for the treatment of patients with AD. Of these, dupilumab was the first to be licensed for use in moderate-to-severe forms of the disease in children, adolescents, and adults, and marked a paradigm shift in AD management. The use of this human monoclonal antibody (mAb) directed against the IL-4 α-chain receptor gives rapid and sustained improvement in the signs and symptoms of moderate-to-severe AD and in the patient's HRQoL [16, 17]. Since its introduction, evidence of its long-term safety at all ages has been collected [18, 19], even during the COVID-19 pandemic [12]. Recently, the anti-IL-13 mAb tralokinumab has shown a positive benefit/risk profile and has also been approved for use in adults with AD in Europe

[20]. Moreover, several phase 2/3 trials evaluating the efficacy and safety profile of other therapeutic alternatives, such as the mAbs lebrikizumab and nemolizumab, are currently ongoing [21, 22].

Following these advances in the treatment of AD, Janus kinase inhibitors (JAKi) have also been suggested as promising treatments for this disease [23–25]. Among them, upadacitinib and baricitinib, which were originally conceived and marketed for the treatment of rheumatic conditions and were already used off-label in AD, have recently been approved by the European Medicines Agency for their use in AD [26, 27]. Upadacitinib can be used for patients aged 12 years and older, while baricitinib is approved only in adults. Abrocitinib, another JAKi that has shown efficacy and a good safety profile in patients with AD [28, 29], has recently been approved by the UK's Medicines and Healthcare products Regulatory Agency (MHRA) and Japan's Ministry of Health, Labour and Welfare (MHLW) for use in adolescents and adults with moderate-to-severe AD. JAKis offer a different mechanism and onset of action, efficacy, safety profile, and response over time compared with previous treatments, and are thus a valid therapeutic alternative to biologics [30, 31].

As research continues, new drugs will no doubt be added to the current pool of treatments for moderate-to-severe AD [32]. All this raises the need for studies to determine prescriber preferences for different pharmacological options and the factors that influence their choice of treatment.

We performed a discrete-choice experiment (DCE) to elicit and analyze physician preferences with respect to moderate-to-severe AD treatment. The main aim of this study was to explore physician preferences for systemic treatment of moderate-to-severe AD. Secondary objectives were to identify the sociodemographic characteristics that influence physician preferences and to determine their degree of satisfaction with current AD therapies and with others that will become available soon.

METHODS

Statement of Ethics Compliance

In Spain, studies not involving patients are not required to be reviewed by a research ethics committee. Therefore, a research ethics committee approval was not applicable in this study.

Study Development

The study workflow is shown in Fig. 1.

DCE Design

Choice of treatment attributes and levels. We conducted a review of articles published in PubMed over the last 10 years to identify the specific treatment attributes and attribute levels of AD systemic therapies. A focus group consisting of dermatologists and allergists ($n = 6$) was formed and asked to rank a list of attributes extracted from the literature on the basis of their importance in the clinical decision-making process. The group was also asked to suggest other attributes to be included in the DCE that had not been identified in the literature review, and to list the attribute levels according to their relevance in their experience in clinical practice in Spain.
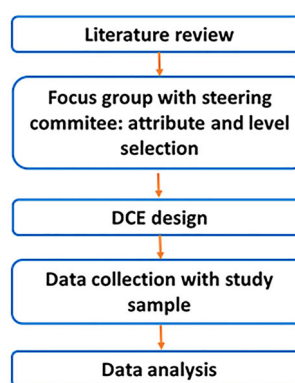

Fig. 1 Workflow of the study

Scenario design and participant selection. Once the attributes and their levels in systemic AD treatments had been defined, the systemic treatment scenarios to be included in the DCE were constructed and selected using a balanced orthogonal design (each attribute level is an independent variant, and each level appears the same number of times). We used fractional factorial analysis to minimize as far as possible the different scenario combinations in order to avoid fatigue when completing the survey and the resulting risk of bias in the answers [33]. The final survey included 12 different scenarios and nine attributes, and participants were asked to choose between two treatment alternatives or neither. The final list of attributes and their levels is presented in Table 1, and Fig. 2 shows an example of a choice task from the DCE. All applicable good practices for the design of DCEs [33–35] were followed.

Ad hoc questionnaire. Participant sociodemographic variables, including sex, age, years of experience with AD, hospital seniority, and region where they work, were collected in an online questionnaire. Physician satisfaction with current drugs used in the systemic treatment of moderate-to-severe AD was also assessed using a series of 5-point Likert-scale questions graded from "strongly disagree" to "strongly agree."

Participants and sample size. A minimum sample size of 28 participants was estimated on the basis of the recommendations of Orme with regard to DCE methodology for attributes with two levels [36]. A total of 58 dermatologists and allergists with wide experience in treating AD were invited to participate.

Survey. The survey was administered online; participants received an email invitation containing the link to the survey portal, where they were then asked to register by entering their email and setting a new password. The survey was available between May and June 2021.

Statistical Analyses

An initial descriptive analysis of participant characteristics was performed using the statistic software IBM SPSS Statistics v25.

Table 1 Attributes and levels included in the discrete-choice experiment questions

Attribute	Levels
Objective clinical efficacy (improvement of dermatitis)	50%
	100%
Onset of action from the start of treatment	< 2 weeks
	≥ 2 weeks
Improvement in sleep and pruritus	VAS < 7
	VAS ≥ 7
Long-term clinical efficacy	1 year
	> 1 year
Risk of severe AEs	< 1%
	≥ 1%
Risk of mild-to-moderate undesirable AEs leading to treatment discontinuation due to intolerance	< 10%
	≥ 10%
Route and frequency of administration	Oral, daily
	SC, every 2 weeks
Therapeutic benefit in other atopic manifestations	Yes
	No
Possible dose modification (individualized treatment)	Yes
	No

AE, adverse events; SC, subcutaneous; VAS, visual analog scale

A conditional logit (clogit) model was used to analyze the DCE, following the good practices in Conjoint Analysis recommended by the International Society for Pharmacoeconomics and Outcomes Research [34]. Clogit is a mathematical regression model in which the physician's choice is the dependent variable (V) and the levels of each attribute are the independent variables ($\beta 1$–βi):

$$V = \beta 0 + \beta 1 \text{ attribute1} \\ + \beta 2 \text{ attribute2} \\ + \beta 3 \text{ attribute3} + \beta 4 \text{ attribute4} \\ + \beta 5 \text{ attribute5}$$

Attribute	Alternative 1	Alternative 2
Objective clinical efficacy (improvement of dermatitis)	10 people out of 10 (100%)	5 people out of 10 (50%)
Onset of action from start of treatment	≥2 weeks	<2 weeks
Improvement in sleep and pruritus	Visual analogue scale <7	Visual analogue scale ≥7
Long-term clinical efficacy	1 year	>1 year
Risk of severe AEs	≥1%	≥1%
Risk of mild/moderate, undesirable AEs leading to treatment discontinuation due to intolerance	<10%	<10%
Route and frequency of administration	SC, every 2 weeks	SC, every 2 weeks
Therapeutic benefit in other atopic manifestations	No	No
Possible dose modification (individualised treatment)	No	Yes

AEs = adverse events, SC = subcutaneous.

Fig. 2 Example choice task. AEs, adverse events; SC, subcutaneous

The utility, that is, the eligibility of a particular alternative was estimated by considering the sum of the attribute importance score of each of the attributes included in the DCE.

The relative importance of each attribute was estimated as the ratio between the range of importance scores of each attribute (maximum to minimum) and the sum of the utility ranges of all attributes.

We performed multiple regression analysis to identify the extent to which physician characteristics influence their preference for each attribute. In this model, the dependent variable was the importance score of each attribute, and the independent variables were the sociodemographic characteristics. The independent variables considered were, in no particular order: (1) age, (2) sex, (3) Autonomous Community in Spain, (4) hospital seniority, (5) years of experience as a specialist, (6) patients with

AD treated per month, and (7) degree of satisfaction with available systemic AD treatments.

As a secondary objective of the study, the maximum acceptable risk (MAR) was calculated to show the extent to which physicians were willing to trade a determined risk or a less desirable characteristic for a clinical benefit.

RESULTS

Focus Group Results

According to the physicians, the most important attributes when prescribing a systemic AD treatment and therefore the ones finally selected were, in no particular order: (1) objective clinical efficacy, (2) onset of action, (3) improvement of sleep and pruritus, (4) long-term efficacy, (5) risk of severe adverse events (AEs), (6) risk of mild-to-moderate undesirable

AEs leading to treatment discontinuation due to intolerance, (7) mode of administration, (8) therapeutic benefit in other atopic manifestations, and (9) possible dose modification to individualize therapies.

Respondent Characteristics

A total of 58 dermatologists and allergists were invited to take part in the survey, of whom 35 accepted the invitation and 28, corresponding to the minimum estimated sample size, finally completed the DCE survey. Most were women (67.9%), and the mean age (SD) was 45.9 (8.9) years. Their sociodemographic characteristics are summarized in Table 2.

Preference Weighting

Results from the clogit model are summarized in Table 3 and plotted in Fig. 3. Physicians participating in the DCE preferred, on average, an objective clinical efficacy of 100%, a ≥ 7 improvement in sleep and pruritus on the visual analog scale (VAS), and long-term efficacy lasting > 1 year ($p < 0.001$, $p < 0.001$, and $p = 0.039$, respectively). Respondents showed their preference for a $< 1\%$ risk rate for severe AEs and for $< 10\%$ mild-to-moderate undesirable AEs leading to treatment discontinuation due to intolerance ($p < 0.001$ in both cases). Respondents were indifferent with regard to the remaining attributes, such as onset of action from the start of treatment, mode of administration, the therapeutic benefit in other atopic manifestations, and the possibility of individualizing treatment, as no statistically significant differences were observed between the levels of these attributes in the DCE.

Objective clinical efficacy was the most important attribute, given the range of attribute levels included in the DCE design, and showed the greatest difference (sixfold) between the lowest (50%) and the highest (100%) utility. The second most important attribute was the risk of severe AEs [nearly fourfold difference in utility from the highest ($\geq 1\%$) to the lowest ($< 1\%$) risk]. These were followed by improvement in sleep and pruritus, onset of action from

Table 2 Sociodemographic characteristics of the sample

Total sample, n	28
Age, years	
Mean (SD)	45.9 (8.9)
31–40, n (%)	9 (32.1)
41–50, n (%)	8 (28.6)
51–60, n (%)	11 (39.3)
Sex	
Female, n (%)	19 (67.9)
Autonomous Community in Spain	
Andalucía; Aragón; Asturias; Comunidad Valenciana; Islas Baleares, n (%)	1 (3.6)
Cataluña, n (%)	10 (35.7)
Comunidad de Madrid, n (%)	13 (46.4)
Hospital level	
Primary, n (%)	5 (17.9)
Secondary, n (%)	3 (10.7)
Tertiary, n (%)	20 (71.4)
Experience as specialist, years	
Mean (SD)	17.0 (9.0)
0–9, n (%)	7 (25.0)
10–19, n (%)	10 (35.7)
20–29, n (%)	7 (25.0)
≥ 30, n (%)	4 (14.3)
Patients with AD treated per month	
Mean (SD)	25.8 (28.6)
0–50, n (%)	27 (96.4)
51–100, n (%)	0 (0)
101–150, n (%)	1 (3.6)

SD, standard deviation

Table 3 Random parameters logit model estimates: preference weighting ($n = 28$)

Attribute	Level	Mean PW				Significant SE
		Coefficient estimate	OR	SE	p value from previous level	
Objective clinical efficacy (improvement of dermatitis)	50%	0	1	–	< 0.001	Yes
	100%	1.854	6.382	0.248		
Onset of action from the start of treatment	< 2 weeks	0	1	–	0.096	No
	≥ 2 weeks	−0.362	0.696	0.218		
Improvement of sleep and pruritus	VAS < 7	0	1	–	< 0.001	Yes
	VAS ≥ 7	0.880	2.411	0.203		
Long-term clinical efficacy	1 year	0	1	–	0.039	Yes
	> 1 year	0.524	1.688	0.254		
Risk of severe AEs	< 1%	0	1	–	< 0.001	Yes
	≥ 1%	−1.281	0.278	0.203		
Risk of mild-to-moderate undesirable AEs leading to treatment discontinuation due to intolerance	< 10%	0	1	–	< 0.001	Yes
	≥ 10%	−1.173	0.309	0.253		
Mode of administration (route, frequency)	Oral, daily	0	1	–	0.660	No
	SC, every 2 weeks	0.118	1.125	0.268		
Therapeutic benefit in other atopic manifestations	Yes	0	1	–	0.097	No
	No	−0.404	0.668	0.243		
Possible dose modification (individualized treatment)	Yes	0	1		0.887	No
	No	−0.044	0.957	0.307		

The table includes a summary of the preference weights associated with each of the attributes included in the DCE. The column "Level" defines the different values associated with each attribute included in the combinations between which participants had to choose. To obtain attribute importance scores expressed as OR for each of the attribute levels, β logit coefficients were exponentiated. "–" denotes that a 95% confidence interval could not be estimated. The column labeled "p value from previous level" shows the results of a single-sample t-test of the statistical significance of differences between each level and the level immediately preceding it in the table. SEs are based on the normal distribution of each attribute level in the random parameters' logit model, confirmed by the Kolmogorov–Smirnov normality test. All levels within each attribute were statistically different ($p < 0.05$)

AE, adverse events; OR, odds ratio; SC, subcutaneous; SE, standard error; VAS, visual analog scale
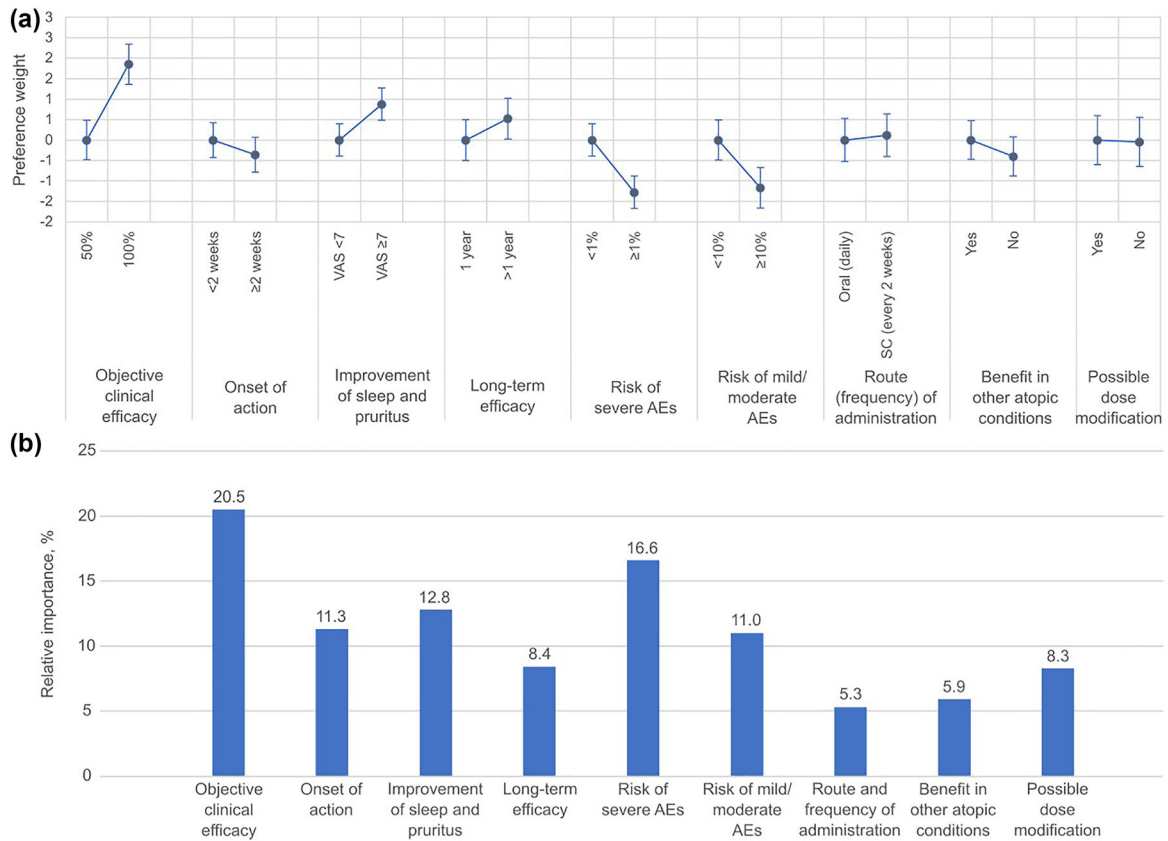
Fig. 3 a Random parameters logit model estimates: preference weights ($n = 28$). **b** Relative importance of the attributes included in the discrete-choice experiment questionnaire. Note: Attributes are presented in the order in which they appear in the discrete-choice experiment questionnaire. The vertical bars on each mean preference weight (PW) represent the 95% confidence interval. Within each attribute, a higher PW indicates that a level is preferred. For example, on average, respondents preferred long-term clinical efficacy > 1 year (OR 1.688, $p < 0.001$) over efficacy lasting 1 year. The change in utility associated with a change in the level of each attribute is shown by the vertical distance between the PWs of any two levels of that attribute. For example, obtaining an objective clinical efficacy rate of 100% is preferable to an efficacy of 50%, as this has nearly six times (OR 6.382; $p = 0.001$) more impact on utility, all else being constant. OR, odds ratio; SC, subcutaneous; VAS, visual analog scale

the start of the treatment, and the risk of mild-to-moderate AEs.

Maximum Acceptable Increase in Risk

Clogit analyses were also used to determine the MAR of AEs in return for an improvement in any of the efficacy-related attributes [37]. Resulting MAR values are presented in Table 4. Respondents were willing to trade a noticeably high MAR (nearly 150%) of mild-to-severe AEs for a 50–100% increase in objective clinical efficacy. Respondents were also willing to accept increases of nearly 70% in the risk of AEs for an improvement of < 7 to ≥ 7 on the VAS in sleep and pruritus, and an increase of nearly 40% in the risk of AEs to achieve a long-term efficacy of > 1 year.

In contrast, respondents were not willing to trade an increase in the risk of AEs for improvements in any of the other attributes included in the DCE survey.

Table 4 Maximum acceptable risk of severe AEs and of mild-to-moderate undesirable AEs leading to treatment discontinuation due to intolerance (n = 28)

Attribute	From level	To level	Mean, %	95% CI, %
Risk of severe AEs				
Objective clinical efficacy (improvement of dermatitis)	50%	100%	144.73	106.79–182.68
Improvement of sleep and pruritus	VAS < 7	VAS ≥ 7	68.70	37.64–99.79
Long-term clinical efficacy	1 year	> 1 year	40.91	2.04–79.77
Risk of mild-to-moderate undesirable AEs leading to treatment discontinuation due to intolerance				
Objective clinical efficacy (improvement of dermatitis)	50%	100%	158.06	116.62–199.50
Improvement of sleep and pruritus	VAS < 7	VAS ≥ 7	75.02	41.10–108.94
Long-term clinical efficacy	1 year	> 1 year	44.67	2.23–87.11

By estimating the maximum acceptable risk (MAR), it is possible to evaluate the maximum risk that respondents are willing to accept to obtain a therapeutic benefit in the systemic treatment of AD from one level to the other level included in the table. The MAR was estimated as the ratio between two utility differences, one associated with an improvement and the other associated with a less desirable attribute. For example, respondents were willing to accept up to 150% increase in the risk of severe AEs in order to improve the objective clinical efficacy rate from the 50% level to the 100% level, all else being constant

AE, adverse events; CI, confidence interval; VAS, visual analog scale

Subgroup Analyses

We analyzed whether the respondents' sociodemographic characteristics influenced their preferences for a particular attribute (Supplementary Material, Table S1). According to our analysis, women are more likely to prefer 100% efficacy than men (p = 0.031), in other words, women attach more importance to objective treatment efficacy than men. Women also showed a stronger preference for minimizing the risk of mild-to-severe AEs than men (p = 0.015). None of the other factors included in the analysis showed a significant impact on clinician preferences.

Respondents' Degree of Satisfaction with Available Systemic AD Treatments

Respondents were also asked to rate their degree of satisfaction with the available systemic AD treatments in terms of the attributes included in the DCE survey. The majority were satisfied with current systemic AD therapies in terms of their clinical efficacy (75.00%, n = 21), onset of action (67.86%, n = 19), improvement in sleep and pruritus (67.86%, n = 19), risk of severe AEs (60.72%, n = 17), and mode of administration (67.86%, n = 19). The degree of satisfaction with the other aspects included in the analysis was around 40%. Thus, 57.14% (n = 16) of respondents were generally satisfied with current treatments.

The results of these questionnaires were also used to perform an analysis to determine the extent to which the respondents' degree of satisfaction influences their preferences. Only three of the comparisons between respondent preferences and degree of satisfaction were statistically significant. Respondents who were fairly dissatisfied with the risk of mild-to-moderate or severe AEs associated with current systemic AD therapies showed preference for a ≥ 7 improvement in sleep and pruritus (p = 0.041 and p = 0.005 for mild-to-moderate and severe AEs, respectively). Also, as expected, respondents who were dissatisfied with the long-term efficacy of current systemic AD therapies preferred a long-term efficacy of > 1 year (p = 0.005).

DISCUSSION

In the context of a new era in the treatment of AD following the approval of several new active principles and the wide range of AD drugs already available, we analyzed prescriber preferences for the different attributes of systemic treatments for moderate-to-severe AD in Spain. Our results show that the main attributes that experts in Spain take into consideration when choosing an AD drug are, in this order, objective efficacy, the risk of severe AEs, improvement in sleep and pruritus, onset of action from start of the treatment, and the risk of mild-to-moderate AEs. MAR analysis showed that experts were willing to trade an increased risk of severe and mild-to-moderate AEs for increased benefit in terms of objective efficacy and improvement in sleep and pruritus.

This is in line with the results of a similar study performed in Japan, in which physicians were more likely to value the efficacy of biological therapies in the treatment of AD [38]. In terms of AEs, another study in the USA comparing physician and patient preferences reported that the former are more concerned with the possibility of long-term AEs than the latter [39].

As in the aforementioned studies [38, 39], two recently published DCEs performed in patients with moderate-to-severe AD [40] and in adults, adolescents, and caregivers of children with mild-to-severe AD [41] showed that respondents gave similar importance to efficacy and safety of systemic AD treatments. In Boeri et al. [40], adult patients valued the probability of skin clearance at 16 weeks as the most important efficacy attribute, while patients participating in the recent study by Ervin et al. [41] valued the speed and duration of symptom relief as the most important attribute included in the DCE. Systemic short-term and long-term AD drug-related AEs, particularly malignancy, serious infection, and venous thromboembolism [40], were of equal importance for respondents in both studies [40, 41]. Prescriber and patient opinions differed in the case of other attributes. As previously seen in other preference studies, clinicians in our study rated the mode of administration as not very important, while patients with AD tend to give it considerable importance [38, 39, 41] and prefer oral drugs over injectables [40].

The differences in physician preferences were not significantly influenced by any of the respondents' sociodemographic characteristics except for sex, with women showing a slightly greater preference for high efficacy and less risk of mild-to-moderate AEs compared with men. However, men represented less than 30% of the sample, and these differences in opinions may be influenced by sample composition. Further research is needed to confirm this trend.

The results of our study can also be used to infer physician preference for a particular drug over another when treating moderate-to-severe AD. Compounds such as mAb and JAKis that reduce AD symptoms and improve the likelihood of skin clearance [27, 42] might be preferred by physicians prescribing systemic AD treatments, since our respondents rated improvement of dermatitis as the most important attribute. Similarly, dupilumab, which does not increase the risk of long-term AEs, might also be preferred over other systemic immunosuppressants, such as methotrexate or azathioprine, which increase the risk of malignancy [43]. Safety issues with JAKis have also been reported [44], although this aspect in the context of AD remains unclear.

Most respondents were generally satisfied with current systemic AD treatments, although the overall satisfaction rate was less than 60%. Satisfaction was lower for some attributes, including long-term maintenance of clinical efficacy, risk of mild-to-moderate AEs, possibility of dose adjustment, and benefit in other atopic conditions. This suggests that opinions differ considerably among physicians, and the drugs currently available do not meet all their needs. This, however, did not greatly influence the treatment preferences of our respondents. Our correlation analysis shows that low satisfaction with mild-to-moderate AE risk correlated with a preference for greater improvement in sleep and pruritus, and low satisfaction with the duration of efficacy of current treatments correlated with a greater preference for long-term clinical efficacy.

Although the utility of DCEs in determining patient and physician preferences has been demonstrated [33–35], this study has limitations inherent to its specific design. The definition of attributes and levels, a critical step in this method, inevitably depends on the group of experts that prioritized them from evidence available in the literature. However, we were careful to include both dermatologists and allergists in the focus group in order to collect both points of view and minimize bias. However, as the sample of this study was not stratified by specialty, we are not able to compare preferences according to this factor. Our decision to limit the number of levels to two per attribute for the sake of simplifying the choice task might also have oversimplified the complexity of AD treatment. The scenarios included in the DCE survey are hypothetical; thus, the combinations of attributes that are rated in the DCE may not exist in clinical practice. However, the purpose of the study is to determine which characteristics are most highly valued by clinicians, and this may help in decision-making.

CONCLUSION

Even considering the study limitations, this is one of the first studies to describe physician preferences in the context of systemic treatment in patients with moderate-to-severe AD, and the only study of its kind in Spain. The definition of the attributes that prescribers consider the most important and the risks they are willing to assume in order to obtain a clinical benefit will, we believe, guide therapeutic choices in AD both now and in the future, and will also help other decision-makers involved in the treatment of this highly disabling disease.

ACKNOWLEDGEMENTS

Compliance with Ethics Guidelines. In Spain, opinion studies not involving patients are not required to be reviewed by a research ethics committee. Therefore, a research ethics committee approval was not applicable in this study.

Data Availability. All data generated or analyzed during this study are included in this published article/as ementary information files.

REFERENCES

1. Boguniewicz M, Fonacier L, Guttman-Yassky E, et al. Atopic dermatitis yardstick: practical recommendations for an evolving therapeutic landscape. Ann Allergy Asthma Immunol. 2018;120(1):10-22.e2.

2. Kowalska-Olędzka E, Czarnecka M, Baran A. Epidemiology of atopic dermatitis in Europe. J Drug Assess. 2019;8(1):126–8.

3. Nutten S. Atopic dermatitis: global epidemiology and risk factors. Ann Nutr Metab. 2015;66(Suppl 1):8–16.

4. Silverberg JI, Gelfand JM, Margolis DJ, et al. Patient burden and quality of life in atopic dermatitis in US adults. Ann Allergy Asthma Immunol. 2018;121(3):340–7.

5. Barbarot S, Auziere S, Gadkari A, et al. Epidemiology of atopic dermatitis in adults: results from an international survey. Allergy. 2018;73(6):1284–93.

6. Siegfried EC, Hebert AA. Diagnosis of atopic dermatitis: mimics, overlaps, and complications. J Clin Med. 2015;4(5):884–917.

7. Chamlin SL. The psychosocial burden of childhood atopic dermatitis. Dermatol Ther. 2006;19(2):104–7.

8. Deckert S, Kopkow C, Schmitt J. Nonallergic comorbidities of atopic eczema: an overview of systematic reviews. Allergy. 2014;69(1):37–45.

9. Napolitano M, Megna M, Patruno C, et al. Adult atopic dermatitis: a review. G Ital Dermatol Venereol. 2016;151(4):403–11.

10. Weidinger S, Novak N. Atopic dermatitis. Lancet. 2016;387(10023):1109–22.

11. Girolomoni G, Luger T, Nosbaum A, et al. The economic and psychosocial comorbidity burden among adults with moderate-to-severe atopic dermatitis in Europe: analysis of a cross-sectional survey. Dermatol Ther. 2021;11(1):117–30.

12. Stingeni L, Belloni Fortina A, Baiardini I, et al. Atopic dermatitis and patient perspectives: insights of bullying at school and career discrimination at work. J Asthma Allergy. 2021;14:919–28.

13. Sicras-Mainar A, Navarro-Artieda R, Sánchez L, et al. Prevalence of severe atopic dermatitis in adults in 3 areas of Spain. J Investig Allergol Clin Immunol. 2018;28(3):195–7.

14. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part II. J Eur Acad Dermatol Venereol. 2018;32(6):850–78.

15. Amber T, Tabassum S. Cyclosporin in dermatology: a practical compendium. Dermatol Ther. 2020;33(6):e13934.

16. Griffiths C, de Bruin-Weller M, Deleuran M, et al. Dupilumab in adults with moderate-to-severe atopic dermatitis and prior use of systemic non-steroidal immunosuppressants: analysis of four phase 3 trials. Dermatol Ther. 2021;11(4):1357–72.

17. Tan XL, Thomas BR, Tan YJ, et al. Effects of systemic therapies on pruritus in adults with atopic dermatitis: a systematic review and meta-analysis. Clin Exp Dermatol. 2021;47:658.

18. Patruno C, Napolitano M, Argenziano G, et al. Dupilumab therapy of atopic dermatitis of the elderly: a multicentre, real-life study. J Eur Acad Dermatol Venereol. 2021;35(4):958–64.

19. Patruno C, Fabbrocini G, Longo G, et al. Effectiveness and safety of long-term dupilumab treatment in elderly patients with atopic dermatitis: a multicenter real-life observational study. Am J Clin Dermatol. 2021;22(4):581–6.

20. Wollenberg A, Howell MD, Guttman-Yassky E, et al. Treatment of atopic dermatitis with tralokinumab, an anti–IL-13 mAb. J Allergy Clin Immunol. 2019;143(1):135–41.

21. Chu CY. Treatments for childhood atopic dermatitis: an update on emerging therapies. Clin Rev Allergy Immunol. 2020;61:114–27.

22. Chun PIF, Lehman H. Current and future monoclonal antibodies in the treatment of atopic dermatitis. Clin Rev Allergy Immunol. 2020;59: 208–19.

23. Chang PH, Huang SF, Chang PS, et al. Safety considerations of systemic Janus kinase inhibitors in atopic dermatitis applications. J Dermatol. 2021;48(11):1631–9.

24. Le M, Berman-Rosa M, Ghazawi FM, et al. Systematic review on the efficacy and safety of oral Janus kinase inhibitors for the treatment of atopic dermatitis. Front Med. 2021;8:682547.

25. Traidl S, Freimooser S, Werfel T. Janus kinase inhibitors for the therapy of atopic dermatitis. Allergol Select. 2021;5:293–304.

26. Guttman-Yassky E, Silverberg JI, Nemoto O, et al. Baricitinib in adult patients with moderate-to-severe atopic dermatitis: a phase 2 parallel, double-blinded, randomized placebo-controlled multiple-dose study. J Am Acad Dermatol. 2019;80(4):913-21.e9.

27. Guttman-Yassky E, Thaçi D, Pangan AL, et al. Upadacitinib in adults with moderate to severe atopic dermatitis: 16-week results from a randomized, placebo-controlled trial. J Allergy Clin Immunol. 2020;145(3):877–84.

28. Ferreira S, Guttman-Yassky E, Torres T. Selective JAK1 inhibitors for the treatment of atopic dermatitis: focus on upadacitinib and abrocitinib. Am J Clin Dermatol. 2020;21:783.

29. Simpson EL, Sinclair R, Forman S, et al. Efficacy and safety of abrocitinib in adults and adolescents with moderate-to-severe atopic dermatitis (JADE MONO-1): a multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Lancet. 2020;396(10246):255–66.

30. He H, Guttman-Yassky E. JAK inhibitors for atopic dermatitis: an update. Am J Clin Dermatol. 2019;20(2):181–92.

31. Rodrigues MA, Torres T. JAK/STAT inhibitors for the treatment of atopic dermatitis. J Dermatolog Treat. 2020;31(1):33–40.

32. Puar N, Chovatiya R, Paller AS. New treatments in atopic dermatitis. Ann Allergy Asthma Immunol. 2021;126(1):21–31.

33. Hauber AB, González JM, Groothuis-Oudshoorn CG, et al. Statistical methods for the analysis of discrete choice experiments: a report of the ISPOR Conjoint Analysis Good Research Practices Task Force. Value Health. 2016;19(4):300–15.

34. Bridges JF, Hauber AB, Marshall D, et al. Conjoint analysis applications in health—a checklist: a report of the ISPOR Good Research Practices for Conjoint Analysis Task Force. Value Health. 2011;14(4): 403–13.

35. Reed Johnson F, Lancsar E, Marshall D, et al. Constructing experimental designs for discrete-choice experiments: report of the ISPOR conjoint analysis experimental design good research practices task force. Value Health. 2013;16(1):3–13.

36. Orme BK. Getting started with conjoint analysis: strategies for product design and pricing research: Research Publishers, LLC; 2005. p. 179.

37. Boeri M, McMichael AJ, Kane JPM, et al. Physician-specific maximum acceptable risk in personalized medicine: implications for medical decision making. Med Decis Making. 2018;38(5):593–600.

38. Okubo Y, Ho KA, Fifer S, et al. Patient and physician preferences for atopic dermatitis injection treatments in Japan. J Dermatolog Treat. 2020;31(8): 821–30.

39. McAlister RO, Tofte SJ, Doyle JJ, et al. Patient and physician perspectives vary on atopic dermatitis. Cutis. 2002;69(6):461–6.

40. Boeri M, Sutphin J, Hauber B, et al. Quantifying patient preferences for systemic atopic dermatitis treatments using a discrete-choice experiment. J Dermatol Treat. 2020;2020:1–10.

41. Ervin C, Crawford R, Evans E, et al. Patient and caregiver preferences on treatment attributes for atopic dermatitis. J Dermatol Treat. 2021;2021:1–9.

42. Gooderham MJ, Forman SB, Bissonnette R, et al. Efficacy and safety of oral Janus kinase 1 inhibitor abrocitinib for patients with atopic dermatitis: a phase 2 randomized clinical trial. JAMA Dermatol. 2019;155(12):1371–9.

43. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. J Am Acad Dermatol. 2014;71(2):327–49.

44. Bechman K, Subesinghe S, Norton S, et al. A systematic review and meta-analysis of infection risk with small molecule JAK inhibitors in rheumatoid arthritis. Rheumatology. 2019;58(10):1755–66.