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RECEIVED 27 November 2023 ACCEPTED 30 January 2024 PUBLISHED 14 February 2024

#### CITATION

Kaneko S, Nakahara T, Sumikawa Y, Fukunaga A, Masuda K and Kakamu T (2024), Disease perception in patients with atopic dermatitis and chronic spontaneous urticaria: a cross-sectional survey in Japan. J. Cutan. Immunol. Allergy 7:12476.

doi: 10.3389/jcia.2024.12476

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# Disease perception in patients with atopic dermatitis and chronic spontaneous urticaria: a cross-sectional survey in Japan

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The opinions of patients with allergic skin diseases often determine their attitudes to treatment. However, little is known about the viewpoints of patients and their concerns regarding their conditions. This novel study is the first to compare relationships between the opinions of patients and their concerns regarding the severity of atopic dermatitis or chronic spontaneous urticaria and the presence or absence of biologics. We also compared and clarified the characteristics of these diseases using a questionnaire that was completed by 359 patients treated at university and city hospitals, as well as dermatology clinics. Covariance analysis was performed to compare both diseases with different backgrounds. Patients with adult atopic dermatitis were more likely than those with chronic idiopathic urticaria to believe that treatment must be continued and that the disease will not spontaneously improve. Patients with severe or poorly controlled atopic dermatitis or chronic spontaneous urticaria often had psychosomatic symptoms and also believed that the disease required continued treatment. Social factors related to wait times and medication were not associated with disease severity. Patients receiving treatment had significantly less anxiety associated with biologics than those who did not receive treatment. Patients with atopic dermatitis had higher physical and mental burden than those with chronic spontaneous urticaria. Therefore, effective treatments must be prescribed. Consideration of these disease-specific characteristics regarding the opinions and concerns of patients can improve patient satisfaction and compliance with treatment, which results in favorable outcomes.

#### KEYWORDS

patient perspective, atopic dermatitis, chronic spontaneous urticaria, cross-sectional survey, Japan

# Introduction

The views that patients have of an illness is a phenomenon consisting of multiple dimensions that overlap but are independent of each other [1]. Atopic dermatitis (AD) is a skin allergy with a high disease burden that decreases the quality of life of patients. In addition, doctors and patients differently rate treatment goals and satisfaction with treatment [2, 3]. Urticaria is a common skin disorder. It mostly comprises acute and chronic spontaneous types that cause wheals to develop over the course of a day or for  $\geq 6$  weeks, respectively [4]. Compliance with treatment of chronic spontaneous urticaria (CSU) is poor when symptoms improve [4], which might be owing to the attitudes of patients [4]. If patients are not eager to treat the disease, they might not be optimistic about or compliant with treatment. In addition, how AD and CSU are perceived by doctors and patients differ. Previous interview viewpoints have shown that patients believe the disease "is like the bad guy in a movie that refuses to die" [5].

This report describes the results of a survey of patients with AD and CSU regarding medication compliance using the Physician Global Assessment (PGA), itch numerical rating scale (NRS), and opinions and concerns that patients have about the disease. The effects of patient-reported outcomes, treatment methods, and other factors on patient perceptions of the disease were analyzed. Insights and concerns regarding each disease were also compared.

## Methods

## Patients

This study included 359 patients who were diagnosed with AD or CSU according to the respective guidelines for these diseases [6, 7]. All patients were treated at the Department of Dermatology of Shimane University Hospital, Masuda Red-Cross Hospital, Kyushu University Hospital, Sapporo Medical University Hospital, Sumikawa Dermatology and Allergy Clinic, Kobe University Hospital, and Kyoto Prefectural University of Medicine University Hospital between May 2020 and February 2022. Patient data were anonymized before analysis.

## Inclusion and exclusion criteria

The inclusion criteria comprised age  $\geq$ 15 years, diagnosis of AD or CSU, and ability to respond to the questionnaire. The exclusion criteria comprised age <15 years and unable to respond to the questionnaire.

### Questionnaire

Patients completed a questionnaire developed for this study (Table 1) and described their diagnosis and disease severity using the PGA, which provides a composite score on a scale of 0-4. The questionnaire was self-administered and included multiple-choice items regarding age, sex, occupation, annual income, educational level, lifestyle, and disease duration. A section based on the Patient-Oriented Eczema Measure (POEM) was also included [6, 8]. Mild, moderate, and severe AD was defined by POEM scores of <7, 8-16, and >16, respectively. Symptom control was assessed using the self-administered urticaria control test (UCT) [7, 9]. Patients with CSU who had UCT scores of <12 and  $\ge 12$  were, respectively, classified as having poorly and well-controlled disease. Patients described their current medications, willingness to undergo treatment, and satisfaction with the treatment plan using an 11point scale. Their opinions and concerns regarding their disease were described using a 5-point scale.

### Statistical analysis

All data were statistically analyzed using R 4.0.3 software [10]. Statistical significance was set at p < 0.05. The characteristics of patients with AD and CSU were compared. Continuous variables are presented as means and standard deviations or as medians and interquartile ranges. Categorical variables are presented as numbers and ratios (%).

The basic characteristics of each disease were compared using Mann–Whitney U tests. The responses of the patients to POEM were compared using Kruskal–Wallis tests. The UCT results and differences between biologic treatments were compared using Wilcoxon rank sum tests.

As disease severity significantly impacts the opinions and concerns of patients, we adjusted the data for severity, age, and sex and used analyses of covariance (ANCOVA) for comparisons.

## Results

## Analysis of patients

This study included 359 patients, of which 202 had AD (113 men and 89 women; mean age:  $39.3 \pm 13.6$  years) and 157 had CSU (51 men and 106 women; mean age:  $48.5 \pm 17.0$  years) (Table 2). The PGA scores were higher in patients with AD than with CSU (p < 0.001, Mann–Whitney U test) and significantly correlated with POEM (p < 0.001, Kruskal–Wallis test) and UCT (p < 0.001, Wilcoxon rank sum test) scores (Tables 2, 3). The motivation to undergo treatment and ratio of patients who believed that the disease would be cured was higher among those with CSU than with AD (p < 0.001 Mann–Whitney U test).

### TABLE 1 Questionnaire items.

No.	Sub no.	Item	Possible responses
1ª	1	Disease name	1. Atopic dermatitis
			2. Chronic spontaneous urticaria
	2	Severity (Physician Global Assessment)	1. Clear or almost clear
		Assessment)	2. Mild
			3. Moderate
			4. Severe
2		Age	Years
3		Sex	Male or Female
4		Current salary	Yen
5		How long have you had your current disease?	Years
6		What is your level of schooling?	Graduate school, college, community college,
7		List your current medications (Multiple answers allowed)	vocational school, high school, middle school cyclosporine oral steroids topical steroids antihistamine topical tacrolimus moisturizer biologics (Xolair, Dupixent) others
8	1	If you have atopic dermatitis, please answer the POEM questionnaire	Score
	2	If you have chronic idiopathic urticaria, please answer the UCT questionnaire	Score
9	1	Itch numerical rating scale	Score
		Please select one number that best describes your itchiness in the last 24 h	
		11-point evaluation	
		0 1 2 3 4 5 6 7 8 9 10	-
		No itchiness Highest possible itchiness	
10		What is your viewpoint of your disease?	
	1	Requires continued treatment	1 Strongly disagree
	2	Cannot be healed	2 Disagree
	3	It is like the bad guy in a movie who does not die	3 Neither agree nor disagree
	4	Related to mental state	4 Agree
	5	Difficult disease	5 Strongly agree

	TABLE 1 (Continued) Questionnaire items.					
No.	Sub no.	Item	Possible responses			
	6	Improves naturally				
	7	Improves with treatment				
11		How much do each of the following things bother you in relation to your illness?				
	1	Itchiness	Five-level evaluation			
	2	Pain	1 Not at all troublesome			
	3	Multiple symptoms	2 Not troublesome			
	4	Willingness to seek treatment	3 Neutral			
	5	Not improving	4 Troublesome			
	6	Chronic exacerbation/ remission cycle	5 Very troublesome			
	7	Few patients have the same disease				
	8	Long waiting time required to see a doctor				
	9	Expensive to treat				
	10	Unknown exacerbating factors				
	11	Understanding my symptoms				
	12	Mental illness				
	13	Restriction of daily life due to illness				
	14	Not knowing how long the treatment will last				
	15	Physician fails to indicate treatment goals				
	16	Not knowing the treatment goals				
	17	Concerns regarding my appearance				
	18	Not being able to confide in my doctor				
	19	Not knowing how to apply ointments				
	20	Concerns regarding the use of topical steroids				
	21	Concerns regarding the use of antihistamines (itch relievers)				
	22	Anxiety regarding the use of oral cyclosporine				
	23	Anxiety regarding the use of biologics (Xolair or Dupixent)				

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No.	Sub no.	Item	Possible responses
	24	Continuing treatment without forgetting	
12		How motivated are you to seek treatment for your illness?	Scale number 10 is good
		11-point evaluation	
		0 1 2 3 4 5 6 7 8 9 10	
		Not at all Very motivated	
13		Do you think your illness will be cured?	Scale number 10 is good
		11-point evaluation	
		0 1 2 3 4 5 6 7 8 9 10	
		No Yes	
14		Please provide us with any feedback you may have about this questionnaire (free response)	Free response

<sup>a</sup>This item was completed by a physician.

## Opinions and concerns of patients regarding AD and CSU based on their reported outcomes

Patient age, sex, disease duration, income, willingness to undergo treatment, and ratio of those who believed that they would be cured were not related to the POEM scores. The itch NRS was associated with the POEM score (p < 0.001). Significantly more patients with low POEM scores were treated with biologics than in the other groups (p < 0.001). Patients with high POEM scores were more likely to report psychological problems (p = 0.012), difficulty with their disease (p < 0.001), and that continued treatment was necessary (p < 0.001; Table 4). Patients with high POEM scores were significantly more concerned about physical symptoms, such as itching and pain, and psychological symptoms, such as long waits for medical treatment, being unable to confide in a doctor, and concerns regarding medications were not related to the POEM scores (Table 5).

Patients with well-controlled CSU were older (p < 0.001), had lower itch NRS scores (p < 0.001), and were more likely to believe that the disease would be cured (p < 0.001) than those with poorly controlled CSU. Sex, disease duration, income, and willingness to undergo treatment were not associated with the UCT scores. The rate of biologic treatment was significantly higher among patients with well-than poorly controlled CSU (p < 0.023). Patients in the latter group more often reported that continued treatment of CSU is necessary and that the disease was "like a movie villain who does not die easily" than those with well-controlled CSU (Table 4). Physical symptoms, such as itching and pain, and psychological symptoms, such as mental distress, were significantly more frequent in the poorly than in the wellcontrolled group. However, no social factors were associated with the UCT scores (Table 5).

# Patients' opinions and concerns regarding AD and CSU based on the use of biologics

Dupilumab was prescribed to 41 patients with mild AD. Patients who were treated were significantly older (p = 0.005) and had a longer disease duration (p < 0.001) and lower itch NRS scores (p < 0.001) than those who were not treated with this biologic. Opinions of AD did not significantly different between patients treated with biologics and those who were not (Table 6). Patients who were treated with biologics were less likely to report concerns regarding itching (p = 0.02), various symptoms (p = 0.008), symptoms that did not improve (p < 0.001), repeated exacerbation/remission cycles (p = 0.002), mental stress (p = 0.032), discomfort with their appearance (p =0.006), and anxiety regarding their treatment (p < 0.001). However, the belief that few patients had the same disease and concerns regarding the cost of treatment were significantly more frequent among patients treated with biologics than those who were not (Table 7).

Omalizumab was prescribed to 46 patients with CSU. Patients treated with this biologic were significantly older (p < 0.001) than those who were not. Significantly more females with CSU were prescribed omalizumab than no biologic (p = 0.035). The itch NRS score was lower (p = 0.028) among patients treated with omalizumab than among those who were not. In addition, patients treated with omalizumab were more willing to undergo treatment (p < 0.001) and more likely to believe that the disease would be cured (p = 0.001) than those who were not treated with this biologic. Patients who were treated with omalizumab were highly likely to describe CSU as "a movie villain who does not die easily" and express difficulty with the disease (Table 6). Fewer patients treated with omalizumab reported anxiety regarding the use of biologics, although more reported believing that few patients had the same disease and that they had concerns about mental distress and the cost of treatment (Table 7).

# Comparison of disease effects on opinions and concerns of patients

The ANCOVA results showed that patients with CSU were significantly more willing to seek medical treatment (p = 0.035) and more likely to believe that their illness would be cured (p = 0.003) than those with AD. More patients with CSU expressed

### TABLE 2 Patients' characteristics.

	Atopic dermatitis	Chronic spontaneous urticaria
Total patients, n (male, female)	202 (m 113, f, 89)	157 (m, 51, f, 106)
Age (y; means ± SD)	39.3 ± 13.6	48.5 ± 17.0
Median disease duration, y (IQR)	26.5 (13-37)	4 (1-10)
Median patient-reported outcomes y (IQR)	POEM 9 (4–17)	UCT 12 (9–16)
PGA*		
0 clear or almost clear	11 (6%)	52 (33%)
1: Mild	70 (35%)	54 (34%)
2: Moderate	67 (33%)	29 (19%)
3: Severe	23 (11%)	10 (6%)
No response	31 (15%)	12 (8%)
Highest education level, <i>n</i> (%)		
Graduate school	3 (1.5%)	6 (3.8%)
University	84 (41.6%)	42 (26.9%)
Junior college	10 (5.1%)	15 (9.6%)
Vocational school	18 (8.7%)	16 (10.3%)
High school	50 (25.5%)	50 (31.4%)
Junior high school	11 (5.1%)	8 (5.1%)
No response	26 (13.3%)	20 (12.8%)

\*p < 0.001 (Mann–Whitney U test). IQR, interquartile range; n, number; POEM, Patient-oriented Eczema Measure; SD, standard deviation; UCT, urticaria control test.

TABLE 3 Physician global assessment and patient-reported outcomes.

	Atopic dermatitis			Chronic spontaneous urticaria		
PGA	$POEM \le 7$	POEM 8-16	$POEM \ge 17$	UCT < 12	$UCT \ge 12$	
Clear or almost clear n (%)	7 (9.5)*	3 (5.1)	0 (0.0)*	8 (12.1)†	43 (51.8) <sup>†</sup>	
Mild <i>n</i> (%)	38 (51.4)*	16 (27.1)	10 (20.0)*	17 (25.8)	34 (41.0) <sup>†</sup>	
Moderate n (%)	14 (18.9)*	28 (47.5)*	18 (36.0)	27 (40.9)*	2 (2.4)†	
Severe n (%)	4 (5.4)*	3 (5.1)*	15 (30.0)*	8 (12.1) <sup>†</sup>	$0 (0.0)^{\dagger}$	
No answer n (%)	11 (14.9)	9 (15.3)	7 (14.0)	6 (9.1)	4 (4.8)	

\*p < 0.001 (Kruskal–Wallis test). \*p < 0.001 Wilcoxon rank sum test. PGA, physician global assessment; POEM, Patient-oriented Eczema Measure; UCT, urticaria control test.

TABLE 4 Opinions of AD and CSU based on patient-reported outcomes.

Question No	Question	AD <sup>a</sup> POEM $\leq 7$ ( <i>n</i> = 73) POEM 8-16 ( <i>n</i> = 57) POEM $\geq 17$ ( <i>n</i> = 47)	CSU <sup>b</sup> UCT <12 ( $n = 65$ ) UCT ≥12 ( $n = 83$ )
10-1	Continued treatment required	<0.001	0.022
10-2	Things that go with us without being healed	0.224	0.386
10-3	It's like the bad guy in a movie who doesn't die	0.286	0.010
10-4	Related to mental state	0.012	0.178
10-5	Difficult disease	<0.001	0.574
10-6	Things that get better naturally	0.024	0.783
10-7	Just like studying, things get better with effort	0.816	0.337

<sup>a</sup>Kruskal–Wallis test.

<sup>b</sup>Wilcoxon rank sum test. AD, atopic dermatitis; CSU, chronic spontaneous urticaria.

Question No	Question	AD <sup>a</sup> POEM $\leq 7$ ( $n = 73$ ) POEM 8–16 ( $n = 57$ ) POEM $\geq 17$ ( $n = 47$ )	CSU <sup>b</sup> UCT <12 $(n = 65)$ UCT $\ge 12 (n = 83)$
11-1	Itchiness	<0.001	<0.001
11-2	Pain	<0.001	0.010
11-3	Having various symptoms	<0.001	0.001
11-4	Unwillingness to seek treatment	0.048	<0.001
11-5	Not getting better	<0.001	<0.001
11-6	Repeated exacerbation and remission of symptoms over a long period of time	<0.001	<0.001
11-7	Few patients with the same disease	0.026	0.337
11-8	Long waiting time to see a doctor	0.447	0.437
11-9	Expensive to treat	0.170	0.388
11-10	Unknown exacerbating factors	<0.001	0.049
11-11	Understanding my symptoms	<0.001	0.009
11-12	Mental illness	<0.001	<0.001
11-13	Restriction of daily life due to illness	<0.001	<0.001
11-14	Not knowing how long the treatment will last	<0.001	0.001
11-15	Physician failure to indicate treatment goals	0.049	0.003
11-16	Not knowing what your treatment goals are	<0.001	0.009
11-17	Concerns about appearance	<0.001	<0.001
11-18	Not being able to tell your doctor what you want to say	0.076	0.079
11-19	Not knowing how to apply ointment	0.052	0.417
11-20	Concern about treatment with topical steroids	0.222	0.932
11-21	Concern about treatment with antihistamines (itch relievers)	0.874	0.152
11-22	Anxiety about oral cyclosporine treatment	0.792	0.553
11-23	Anxiety about treatment with biologics (Xolair, Dupixent, etc.)	0.328	0.646
11-24	Continuing treatment (without forgetting)	0.030	0.422

### TABLE 5 Results of a significant difference test by patient-reported outcomes for each patient problem.

<sup>a</sup>Kruskal–Wallis test.

<sup>b</sup>Wilcoxon rank sum test.

the opinion that their disease could be cured naturally than those with AD (Table 8). Physical symptoms were frequent in patients with AD. Concerns regarding exacerbating factors, ointment application, and anxiety regarding topical steroids were more prevalent among patients with CSU than those with AD (Table 9).

# Discussion

Patients' images of disease are currently being investigated as narrative-based medicine [11]. In addition, since

medication compliance increases with treatment satisfaction, images of a disease might also be associated with compliance [12]. The opinions of patients about diseases have been investigated in the fields of psychiatry [1] and diabetes [13]. By contrast, information about such opinions, particularly about allergic diseases, is scant in the field of dermatology. Therefore, our findings contain valuable information. Medication compliance is essential to effectively treat AD and CSU. Increasing patient satisfaction with treatment and their realization of the beneficial effects of drugs improve their compliance [12, 14], as we showed

Question No	Question	$AD^{a}$	CSU <sup>a</sup>
		Dupilumab+ $(n = 41)$	Omalizumab+ $(n = 46)$
		Dupilumab-( <i>n</i> = 142)	Omalizumab-( <i>n</i> = 103)
10-1	Continued treatment required	0.586	0.924
10-2	Things that go with us without being healed	0.519	0.665
10-3	It is like the bad guy in a movie who does not die	0.888	0.012
10-4	Related to mental state	0.311	0.061
10-5	Difficult disease	0.577	<0.001
10-6	Things that get better naturally	0.052	0.572
10-7	Just like studying, things get better with effort	0.494	0.569

#### TABLE 6 Patient's images of AD and CSU with or without biologics.

<sup>a</sup>Wilcoxon rank sum test. AD, atopic dermatitis; CSU, chronic spontaneous urticaria.

herein. We also found that patients who applied biologics reported fewer symptoms, although the cost of treatment was a concern. These findings suggested that the high cost of biologics forces patients to choose between paying for treatment or experiencing symptoms. In addition, fewer patients described anxiety regarding the application of biologics. The severity of AD and treatment satisfaction correlated in a study that assessed patients using the Treatment Satisfaction Questionnaire for Medication [15]. Reducing disease severity increases patient satisfaction and adherence to treatment regimens, creating a cycle that results in sufficient therapeutic effects.

Psychosocial effects (such as isolation, sociability, stigma, effects of illness on activity, and hopelessness) and noncompliance can be used to identify patients with psoriasis who require additional support to overcome issues with treatment compliance [16]. We did not identify any correlations between the opinions and concerns of patients regarding AD or CSU. Disease severity often correlates with the opinions and concerns of patients, as the present study also found. These findings highlight the importance of relieving symptoms to improve patient opinions of the disease. We evaluated viewpoints and concerns before and after treatment with biologics in a small subset of patients (data not shown). Although the subset was small, the findings suggested that symptomatic relief owing to treatment improved the opinions and reduced the concerns of patients regarding their disease.

That mental illness also correlates with severity is a notable concern (Table 5), and psychosomatic therapy is important in treating allergic diseases. However, not many allergists practice psychosomatic therapy. Allergic diseases associated with psychosomatic disorders are often severe or refractory to treatment with a conventional bio-medical model. A psychosomatic diagnosis and treatment are necessary according to the psycho-socio-eco-medical model of disease understanding [17].

Atopic dermatitis is an inflammatory skin disease that affects over 1 in 10 children in Japan [6]. Although it is believed that AD remits with age, epidemiological studies have found that AD follows a lifelong episodic course when it presents after the age of 12 years [18, 19]. A gradual change in treatment expectations from cure to control is associated with a long-term acceptance of AD and a hope of being cured [5]. By increasing awareness regarding the longterm nature of eczema among adolescents, effective self-care habits can be encouraged [5]. Our patients did not report the belief that AD improves naturally, which might be because adults with AD were included in the study and AD often cannot be cured if it presents in adulthood. By contrast, patients were more likely to report the belief that CSU naturally improves, which corresponded to the median duration of CSU being 4 years.

The viewpoints and concerns of the patients were subjectively evaluated. Therefore, a comparator was included to increase understanding of the significance of our findings. Therefore, we compared the viewpoints and concerns of patients with AD and CSU using a multivariate analysis. More patients with CSU reported that the symptoms naturally improves, as eruptions appear and disappear. Many patients agreed that the image of disease presented in the other questions applied to AD. More patients with AD reported concerns regarding their physical and mental symptoms than those with CSU. Patients with AD reported concerns regarding antihistamines, which lead to less noticeable effects in patients with AD than in those with CSU. In addition, patients with CSU reported concerns regarding topical drugs, which are not recommended in international [9] or Japanese [7] guidelines. These guidelines must be adhered to in clinical practice.

Question no.	Question	$\mathrm{AD}^{\mathrm{a}}$	CSU <sup>a</sup>	
		Dupilumab+ $(n = 41)$	Omalizumab+ $(n = 46)$	
		Dupilumab-( <i>n</i> = 142)	Omalizumab (n = 103)	
11-1	Itchiness	0.020	0.575	
11-2	Pain	0.065	0.477	
11-3	Having various symptoms	0.008	0.042	
11-4	Unwillingness to seek treatment	0.852	0.235	
11-5	Not getting better	<0.001	0.297	
11-6	Repeated exacerbation and remission of symptoms over a long period of time	0.002	0.413	
11-7	Few patients with the same disease	0.011	0.002	
11-8	Long waiting time to see a doctor	0.054	0.097	
11-9	Expensive to treat	<0.001	<0.001	
11-10	Unknown exacerbating factors	0.050	0.682	
11-11	Understanding my symptoms	0.198	0.653	
11-12	Mental illness	0.032	0.032	
11-13	Restriction of daily life due to illness	0.433	0.132	
11-14	Not knowing how long the treatment will last	0.911	0.813	
11-15	Physician failure to indicate treatment goals	0.823	0.870	
11-16	Not knowing what your treatment goals are	0.325	0.289	
11-17	Concerns about appearance	0.006	0.159	
11-18	Not being able to tell your doctor what you want to say	0.280	0.295	
11-19	Not knowing how to apply ointment	0.220	0.864	
11-20	Concern about treatment with topical steroids	0.620	0.609	
11-21	Concern about treatment with antihistamines (itch relievers)	0.908	0.909	
11-22	Anxiety about oral cyclosporine treatment	0.254	0.469	
11-23	Anxiety about treatment with biologics (Xolair, Dupixent, etc.)	<0.001	<0.001	
11-24	Continuing treatment (without forgetting)	0.731	0.055	

### TABLE 7 Significant difference tests between patients with and without biologics for each problem.

<sup>a</sup>Wilcoxon rank sum test.

### TABLE 8 Images of AD and CSU diseases compared using ANCOVA.

Question No	Question	Sum of square	Df	Mean square	F	P
10-1	Continued treatment required	2.79	1	2.786	6.726	0.010*
10-2	Things that go with us without being healed	26.50	1	26.453	24.155	<0.001*
10-3	It is like the bad guy in a movie who does not die	8.80	1	8.832	7.097	0.008*
10-4	Related to mental state	10.90	1	10.904	11.736	<0.001*
10-5	Difficult disease	29.66	1	29.665	31.831	<0.001*
10-6	Things that get better naturally	15.71	1	15.708	20.856	< 0.001 <sup>+</sup>
10-7	Just like studying, things get better with effort	56.30	1	56.340	52.663	<0.001*

Significantly higher scores in \*AD, †CSU. ANCOVA, analysis of covariance; AD, atopic dermatitis; CSU, chronic spontaneous urticaria.

Question no.	Question	Sum of square	Df	Mean square	F	p
11-1	Itchiness	4.08	1	4.078	4.275	0.040*
11-2	Pain	33.00	1	33.000	24.537	< 0.001*
11-3	Having various symptoms	22.00	1	22.012	17.965	< 0.001*
11-4	Unwillingness to seek t reatment	9.63	1	9.633	12.439	<0.001*
11-5	Not getting better	0.10	1	0.055	0.045	0.833
11-6	Repeated exacerbation and remission of symptoms over a long period	4.22	1	4.216	4.195	0.041*
11-7	Few patients with the same disease	0.56	1	0.564	0.606	0.437
11-8	Long waiting time to see a doctor	0.39	1	0.388	0.387	0.534
11-9	Expensive to treat	3.90	1	3.941	3.441	0.065
11-10	Unknown exacerbating factors	4.96	1	4.959	5.099	0.025 <sup>†</sup>
11-11	Understanding my symptoms	1.27	1	1.271	1.433	0.232
11-12	Mental illness	2.6	1	2.609	2.356	0.126
11-13	Restriction of daily life due to illness	7.7	1	7.708	6.019	0.015*
11-14	Not knowing how long the treatment will last	0.50	1	0.450	0.429	0.513
11-15	Physician failure to indicate treatment goals	1.05	1	1.051	1.262	0.262
11-16	Not knowing what your treatment goals are	0.70	1	0.699	0.605	0.437
11-17	Concerns about appearance	49.4	1	49.390	40.670	< 0.001*
11-18	Not being able to tell your doctor what you want to say	1.55	1	1.554	2.540	0.112
11-19	Not knowing how to apply ointment	9.20	1	9.250	6.556	0.011 <sup>+</sup>
11-20	Concern about treatment with topical steroids	10.40	1	10.365	4.946	$0.027^{+}$
11-21	Concern about treatment with antihistamines (itch relievers)	14.8	1	14.830	8.596	0.004*
11-22	Anxiety about oral cyclosporine treatment	0.50	1	0.470	0.131	0.718
11-23	Anxiety about treatment with biologics (Xolair, Dupixent, etc.)	8.50	1	8.496	2.362	0.125
11-24	Continuing treatment (without forgetting)	13.10	1	13.096	12.526	< 0.001*

<b>TABLE 9 Results</b>	of	multivariate	analysis	comparing	the	difficulties	of	AD	and	CSU.

Significantly higher scores in \*AD and  $^{\dagger}\text{CSU}.$ 

This study is not without limitations. Patients who responded to the questionnaire were seen by dermatologists and allergists at hospitals offering relatively innovative care. This could have affected the range of treatment choices. All our patients were old enough to answer questions, which might have introduced bias. Simple comparisons between AD and CSU were difficult because of differences in mean disease activity, so analysis of covariance (ANCOVA) was performed to compare the two diseases.

In conclusion, patients' opinions and concerns differ based on specific diseases. Patients' opinions are influenced by disease severity and types of treatment. Patients were concerned about ineffective treatment. Understanding these characteristics can be used to improve patient satisfaction and compliance, ultimately resulting in favorable outcomes.

# Data availability statement

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

# **Ethics statement**

This study was approved by the ethics committees and Deans of the Faculty of Medicine of Shimane University (approval no. 4418), Masuda RedCross Hospital (approval no. 80), Kyushu University (approval no. 2020-327), SUMIKAWA Dermatology and Allergy Clinic (approval no. 20200717), Kobe University (approval no. B200149), Kyoto Prefectural University (approval no. ERB-C-1828-1), and Fukushima Medical University School of Medicine (approval no. 2020-101). This study proceeded according to the Declaration of Helsinki (2013 amendment). All patients provided written, informed consent to participate in this study.

## Author contributions

All authors participated in the design, interpretation of the studies and analysis of the data and review of the manuscript; SK, TN, YS, AF and KM conducted the questionnaire, TK analyzed the questionnaire. All authors wrote the manuscript.

# Funding

This study was partially supported by Collaborative Research Grants 2020–2022 from the Japanese Society for Cutaneous Immunology and Allergy.

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## Conflict of interest

SK has received an honorarium as a speaker from Ely-Lilly Japan and Abbvie. TN has received an honorarium as a speaker from Sanofi, Maruho, Ely-Lilly Japan and Abbvie. YS has received fees as a speaker from Sanofi, Maruho, Ely-Lilly Japan and Abbvie. AF has received fees as a speaker from Sanofi, Maruho, Ely-Lilly Japan, Abbvie, Torii, Novartis, Taiho, Tanabe-Mitsubishi and fees for funded research/joint research from Taiho. KM has received honoraria as a speaker for Sanofi and grants as an investigator for Eli Lilly Japan.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Acknowledgments

We thank the clerk in the Masuda RedCross Hospital for assisting with this study. We also thank Editage (www.editage. com) for English language editing.

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