



## RESEARCH ARTICLE

# Current status of the satisfaction levels of adult patients receiving drugs for atopic dermatitis and chronic urticaria

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## Abstract

**Objectives:** The satisfaction level of adult patients receiving drugs for atopic dermatitis and chronic urticaria is unclear. The objective of this multicenter study was to assess the satisfaction level of adult patients receiving treatment for allergic skin diseases, primarily atopic dermatitis and chronic urticaria.

**Methods:** We developed a self-administered questionnaire with multiple-choice questions on patient characteristics, quality of life (QOL), and Abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9). We surveyed 302 patients receiving dermatological treatment.

**Results:** The global satisfaction of patients (TSQM-9) was lower for atopic dermatitis treatment compared with that for chronic urticaria. For atopic dermatitis, dupilumab had higher scores for effectiveness and global satisfaction, whereas topical tacrolimus and moisturizers had higher scores for convenience. For chronic urticaria, omalizumab had higher scores for effectiveness and global satisfaction, while antihistamines had a higher score for convenience. The Dermatology Life Quality Index was significantly associated with treatment effectiveness and global satisfaction, and patient satisfaction improved with the corresponding improvement in the QOL. For atopic dermatitis, satisfaction with dupilumab was higher than that with conventional standard therapy, after the confounding factors were eliminated. However, the same trend was not observed for chronic spontaneous urticaria.

**Conclusions:** The satisfaction of the effectiveness for the biologic agents was higher, compared to that with conventional standard therapy. Treatment with biologics is worth exploring for patients who are not satisfied with their existing treatments.

## KEYWORDS

atopic dermatitis, quality of life, treatment effectiveness, treatment satisfaction, urticaria

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## 1 | INTRODUCTION

During the 21<sup>st</sup> century, there has been a paradigm shift toward biologic therapies, represented by tumor necrosis factor inhibitors, for inflammatory bowel diseases and rheumatoid arthritis,<sup>1</sup> since their first use for psoriasis in 2010.<sup>2</sup> This trend has expanded to diseases that are mainly treated with corticosteroids and allergic skin diseases, such as chronic urticaria and atopic dermatitis (AD). Biologic therapies include omalizumab for chronic urticaria and dupilumab for AD.<sup>3,4</sup> Effective treatment strategies are helpful in achieving optimal therapeutic efficacy. However, while biologics are extremely effective, they are also expensive. Therefore, it is important to examine and compare patient satisfaction between the conventional treatments and the new therapies. Patient satisfaction with a treatment is an important indicator for continuing or changing the treatment; however, it is difficult to evaluate and incorporate it into regular clinical practice. Moreover, when patients and their doctors are questioned about treatment satisfaction, they tend to avoid negative feedback. Therefore, there is a gap between the opinions of patients and doctors. To overcome these problems, in this study, we used the Abbreviated Treatment Satisfaction Questionnaire for Medication (TSQM-9), an internationally standardized tool,<sup>5,6</sup> to assess treatment satisfaction of patients with AD and chronic urticaria, in Japan. Specifically, we analyzed whether the satisfaction levels of patients for biologics and standard therapies are different.

## 2 | METHODS

### 2.1 | Patients

We surveyed 302 patients who were treated at the Department of Dermatology in Shimane University Hospital, Kyushu University Hospital, Sapporo Medical University Hospital, Kobe University Hospital, and Kyoto Prefectural University of Medicine University Hospital between May 2018 and January 2019. These patients met the diagnostic criteria for AD and urticaria proposed by the respective guidelines.<sup>7,8</sup> The data of patients were anonymized before analysis.

### 2.2 | Selection criteria

The subjects were patients who met all the following eligibility criteria and did not meet any of the exclusion criteria.

Eligibility criteria were as follows:

1. Diagnosis of AD or chronic urticaria
2. Able to respond to the survey
3. At least 15 years old

Exclusion criteria were as follows:

1. Unable to respond to the survey
2. Younger than 15 years of age

### 2.3 | Questionnaire (Supplementary Methods)

We developed a self-administered questionnaire with multiple-choice questions on age, gender, blood type, smoking history, drinking history, occupation, annual income, educational background, lifestyle, and disease duration. In order to evaluate the quality of life, we used the Dermatology Life Quality Index (DLQI).<sup>9,10</sup> The questionnaire was administered to patients treated with the same drug for at least several months to assess their satisfaction with the drug. The patients were asked to evaluate the drug they considered as their main drug. We used the TSQM-9<sup>5</sup> to assess the satisfaction of patients with the drugs. Permission to use the TSQM-9 was obtained from IQVIA. There are nine questions in the TSQM-9, and each question is answered on a scale of 5–7. The evaluation is divided into three domains, effectiveness domain, convenience domain, and global satisfaction domain, and the points are calculated so that the highest satisfaction level in each domain is 100% (see Supplementary Methods). The physicians used the Investigator Global Assessment (IGA) to evaluate disease severity (overall assessment: remission, 1 point; mild, 2 points; moderate, 3 points; and severe, 4 points) and recorded the corresponding treatments (antihistamines, topical steroids, and biologics) (see Supplementary Methods).

### 2.4 | Statistical analysis

We used R 3.6.3 to perform all statistical analysis. We recorded the characteristics of the 302 patients and compared these with respect to each disease (AD, chronic spontaneous urticaria, and chronic inducible urticaria). The results are presented as mean  $\pm$ SD, median (25<sup>th</sup>–75<sup>th</sup> percentile), and *n* (%). We used one-way analysis of variance (ANOVA) and Tukey's test or Kruskal–Wallis test and Steel–Dwass test in the NSM3 package for multiple comparisons. We also performed Spearman's rank correlation coefficients to compare the relationship of IGA with DLQI and TSQM-9 (global satisfaction, effectiveness, convenient), and of DLQI with TSQM-9 (global satisfaction, effectiveness, convenient). Results with a probability value of <5% were considered significant.

To determine the satisfaction levels of patients receiving different types of drugs, we conducted a multivariate-adjusted regression analysis using the TSQM-9. For the multivariate-adjusted regression analysis, we selected age, gender, smoking status, disease duration, IGA, and DLQI as the confounding factors. Forty-one patients with AD and 26 patients with chronic spontaneous urticaria were excluded from the analysis, because of missing data or low number (*n* < 10) of drugs used. For AD, the drugs used (topical steroid, cyclosporine,

topical tacrolimus, moisturizer, and biologics) were the explanatory variables, while age, gender, smoking status, disease duration, severity, and DLQI total score were the confounding factors. For urticaria, the drugs used (antihistamines and biologics) were the explanatory variables, and age, gender, smoking status, disease duration, severity, and DLQI total score were the confounding factors. Partial regression coefficient and its 95% confidence interval were calculated. Results with a probability value of less than 5% were considered significant.

### 3 | RESULTS

#### 3.1 | Analysis of patients

Among the 302 patients, 201 patients had AD (111 men, 89 women, 1 unknown; mean age,  $37.7 \pm 12.9$  years) (Table 1), 90 patients had chronic spontaneous urticaria (32 men, 56 women, two unknown; mean age,  $52.0 \pm 15.4$  years), and 11 patients had chronic inducible urticaria (two men, nine women; mean age,  $34.5 \pm 11.2$  years) (Table 1).

The severity of disease in the 296 patients who were surveyed is shown in Figure 1 (missing values for six patients). Moderate disease severity was recorded in 45% of patients with AD, 34% of patients with chronic spontaneous urticaria, and 55% of patients with chronic inducible urticaria.

The drugs that were evaluated for satisfaction were mainly those that were used by the patients for each disease (Figure 2). The patients were asked to evaluate the drug they considered as their main drug. Topical steroids were the most used drugs for AD (used by 56% of patients); antihistamines, for chronic spontaneous urticaria (used by 63% of patients); and antihistamines, the only drugs used for chronic inducible urticaria (100% of patients) (Figure 2). The biologic agent used for AD was dupilumab, and that for chronic spontaneous urticaria was omalizumab. These drugs were used according to the insurance adaptation in real-world settings. Only one drug was evaluated per patient, and although dupilumab was administered in combination

with other drugs, the drug was considered the main drug, according to the patients. Patients with AD had a higher tendency to be male, while those with chronic urticaria had a higher tendency to be female. The disease duration was longer for AD than for chronic urticaria (Table 1).

#### 3.2 | Quality of life, disease severity, and treatment satisfaction by disease

The DLQI and TSQM-9 results by disease are shown in Table 2. The DLQI value of patients with AD was significantly higher than that of patients with chronic spontaneous urticaria (Table 2,  $p < 0.001$ ). With respect to treatment satisfaction, ANOVA revealed significant differences in the TSQM-9 convenience domain between AD and chronic inducible urticaria (Table 2,  $p = 0.028$ ).

The relationship between disease severity and satisfaction showed that IGA was weakly correlated with the DLQI ( $r_s = 0.252$ ,  $p < 0.001$ ), TSQM-9 effectiveness domain ( $r_s = -0.209$ ,  $p < 0.001$ ), and TSQM-9 global satisfaction domain ( $r_s = -0.184$ ,  $p = 0.001$ ) in all examined patients. Moreover, we found that the DLQI was moderately correlated with the TSQM-9 effectiveness domain ( $r_s = -0.364$ ,  $p < 0.001$ ) and TSQM-9 global satisfaction domain ( $r_s = -0.406$ ,  $p < 0.001$ ) (Spearman's rank correlation coefficients) in all examined patients.

The satisfaction level of patients for each AD drug is presented in Table 3. We have presented the satisfaction levels of multiple patients for one drug ( $n = 199$ ). Patients with AD expressed higher levels of satisfaction for dupilumab with respect to effectiveness and global satisfaction, and for topical tacrolimus and moisturizers with respect to convenience.

The satisfaction levels of patients for drugs for chronic spontaneous urticaria ( $n = 90$ ) are presented in Table 4. Patients with chronic spontaneous urticaria expressed higher satisfaction levels for omalizumab with respect to effectiveness and global satisfaction, and for antihistamines with respect to convenience.

TABLE 1 Basic characteristic in this study

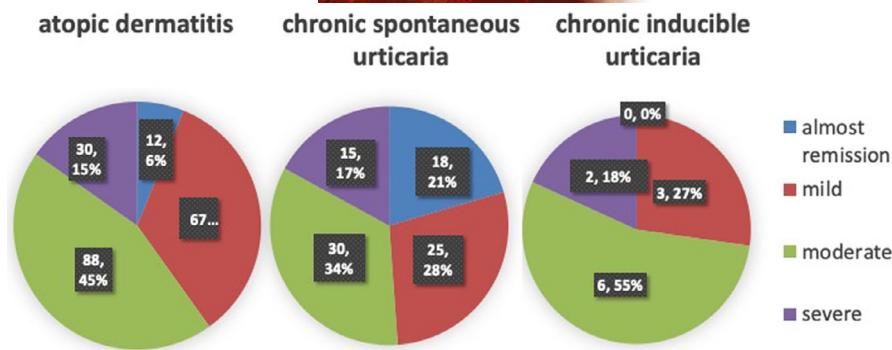
	Number (female, male, unknown)	Age Mean $\pm$ SD years	Disease duration Median years (25–75 percentile)
Atopic dermatitis	201 (89, 111, 1)	$37.7 \pm 12.9$	30 (20–40)
Chronic spontaneous urticaria	90 (56, 32, 2)	$52.0 \pm 15.4$	5 (3–11)
Chronic inducible urticaria	11 (9, 2)	$34.5 \pm 11.2$	8 (7–13)
Total	302	$41.8 \pm 11.2$	21 (7–33)
<i>p</i> -value		$<0.001^a$	$<0.001^b$

Abbreviation: SD, standard deviation.

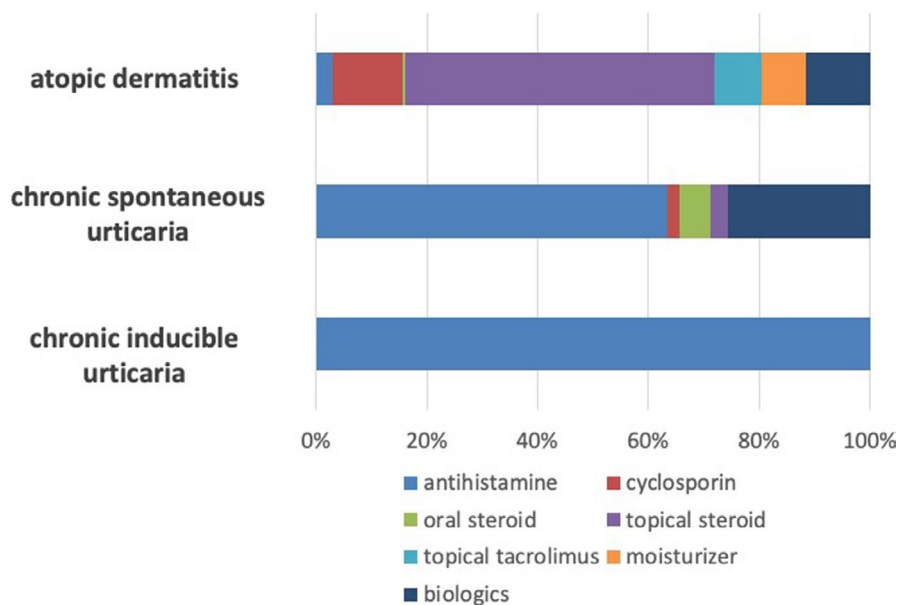
<sup>a</sup>Since a normal distribution was confirmed for ages, the description was the mean  $\pm$  standard deviation, and the comparison was a one-way analysis of variance (ANOVA) and the multiple comparison by the Turkey method. Atopic dermatitis and chronic inducible urticaria were significantly younger than those in chronic spontaneous urticaria. Atopic dermatitis vs. Chronic spontaneous urticaria  $p < 0.001$ . Atopic dermatitis vs. Chronic inducible urticaria  $p = 0.717$ . Chronic spontaneous urticaria vs. chronic inducible urticaria  $p < 0.001$ .

<sup>b</sup>For disease duration for which a normal distribution was not confirmed, multiple comparisons were performed by the Kruskal-Wallis test and Steel-Dwass method. Atopic dermatitis had a significantly longer duration in patients with chronic inducible urticaria and chronic idiopathic urticaria. Atopic dermatitis vs. Chronic spontaneous urticaria  $p < 0.001$ . Atopic dermatitis vs. chronic inducible urticaria  $p < 0.001$ . Chronic spontaneous urticaria vs. Chronic inducible urticaria  $p = 0.283$

**FIGURE 1** Disease severity among target patients. Investigator-scored disease severity in the Investigator Global Assessment (IGA) (IGA: 1–4 points were scored by the clinician's comprehensive evaluation; a score of 1 indicates almost in remission)



**FIGURE 2** List of drugs evaluated for treatment satisfaction. These drugs mainly include those used by patients for each disease. The biologic agent used for atopic dermatitis was dupilumab and that for chronic spontaneous urticaria was omalizumab



### 3.3 | Factors contributing to treatment satisfaction

Owing to the exclusion of patients with missing data, the total number of patients in the multiple regression analysis decreased. Nonetheless, the overall trends such as gender, age, disease duration, DLQI, and TSQM-9 were the same (Tables 1, 2, 5, and 6). A multiple regression analysis was performed using data from 160 patients with AD who used topical steroids ( $n = 95$ ; 59.4%), cyclosporine ( $n = 20$ ; 12.5%), topical tacrolimus ( $n = 14$ ; 8.8%), moisturizers ( $n = 11$ ; 6.9%), and dupilumab ( $n = 20$ ; 12.5%). Multivariate-adjusted regression analysis for AD patients is shown in Table 7. Adjusted  $R^2$  values were 0.314 for TSQM-9 global satisfaction, 0.259 for TSQM-9 effectiveness, and 0.142 for TSQM-9 convenience. Dupilumab was positively related to TSQM-9 global satisfaction (coefficients (95% CI); 5.741 (1.261 to 10.220),  $p = 0.002$ ) and TSQM-9 effectiveness (coefficients (95% CI); 13.856 (6.632 to 21.080),  $p < 0.001$ ). Topical tacrolimus was positively related to TSQM-9 convenience (coefficients (95% CI); 9.818 (1.417–18.220),  $p = 0.023$ ). The DLQI score was negatively related to TSQM-9 global satisfaction domain (coefficients (95% CI);  $-1.345$  ( $-1.261$  to  $-0.924$ ),  $p < 0.001$ ), TSQM-9 effectiveness (coefficients (95% CI);  $-1.235$  ( $-1.690$  to  $-0.780$ ),  $p < 0.001$ ), and TSQM-9 convenience (coefficients (95% CI);  $-0.835$  ( $-1.290$  to  $-0.380$ ),  $p < 0.001$ ) (Table 7). Multivariate-adjusted regression analysis for

chronic spontaneous urticaria patients is shown in Table 8. Adjusted  $R^2$  values were 0.176 for TSQM-9 global satisfaction, 0.183 for TSQM-9 effectiveness, and  $-0.176$  for TSQM-9 convenience. The DLQI score was negatively related to TSQM-9 global satisfaction (coefficients (95% CI);  $-2.751$  ( $-4.018$  to  $-1.483$ ),  $p < 0.001$ ) and TSQM-9 effectiveness (coefficients (95% CI);  $-2.662$  ( $-3.957$  to  $-1.367$ ),  $p < 0.001$ ) (Table 8).

## 4 | DISCUSSION

Here, we investigated the characteristics and satisfaction levels of patients receiving treatment for allergic diseases, such as AD and chronic urticaria, in real-world clinical settings. In addition, the effect of each drug used for AD and chronic spontaneous urticaria on patient satisfaction level was examined. Satisfaction with biologic agents was higher than that with conventional standard therapy in patients with AD, but not in patients with chronic spontaneous urticaria. The DLQI score was negatively related to TSQM-9 in AD and chronic spontaneous urticaria, which means that high satisfaction was positively correlated with a high quality of life (QOL). High treatment satisfaction for chronic diseases is important to achieve better medication adherence.<sup>11</sup> Furue et al.

TABLE 2 TSQM-9 domain scores and quality of life by each disease

	DLQI median (25–75 percentile)	TSQM-9 Effectiveness domain % (mean ± SD)	TSQM-9 Convenience domain % (mean ± SD)	TSQM-9 Global Satisfaction domain % (mean ± SD)
Atopic dermatitis N = 201	4 (2–8)	66.2 ± 18.2	68.1 ± 16.4	67.1 ± 17.4
Chronic spontaneous urticaria N = 90	1 (0–3)	68.6 ± 16.6	72.0 ± 17.5	72.2 ± 18.0
Chronic inducible urticaria N = 11	2 (1–6)	72.7 ± 12.8	81.3 ± 16.5	77.3 ± 14.6
total	3 (1–6)	67.2 ± 17.6	69.7 ± 16.9	68.9 ± 17.7
p-value	<0.001 <sup>a</sup>	0.317	0.014 <sup>b</sup>	0.021 <sup>c</sup>

Abbreviations: DLQI: Dermatology Life Quality Index; TSQM-9, Abbreviated Treatment Satisfaction Questionnaire for Medication.

<sup>a</sup>For DLQI for which a normal distribution was not confirmed, multiple comparisons were performed by the Kruskal–Wallis test and Steel–Dwass method. The DLQI of atopic dermatitis was significantly higher than that of chronic spontaneous urticaria. Atopic dermatitis vs. Chronic spontaneous urticaria  $p < 0.001$ . Atopic dermatitis vs. Chronic inducible urticaria  $p = 0.333$ . Chronic spontaneous urticaria vs. Chronic inducible urticaria  $p = 0.245$

<sup>b</sup>Since a normal distribution was confirmed for TSQM-9 Convenience domain, the description was the mean ± standard deviation, and the comparison was a one-way analysis of variance (ANOVA) and the multiple comparison by the Turkey method. Atopic dermatitis had a significantly lower TSQM-9 convenience domain than chronic inducible urticaria. Atopic dermatitis vs. Chronic spontaneous urticaria  $p = 0.157$ . Atopic dermatitis vs. Chronic inducible urticaria  $p = 0.028$ . Chronic spontaneous urticaria vs. Chronic inducible urticaria  $p = 0.176$ .

<sup>c</sup>Since a normal distribution was confirmed for TSQM-9 Global Satisfaction domain, the description was the mean ± standard deviation, and the comparison was a one-way analysis of variance (ANOVA) and the multiple comparison by the Turkey method. Atopic dermatitis was not significant for chronic inducible urticaria, but the score tended to be low. Atopic dermatitis vs. Chronic spontaneous urticaria  $p=0.053$ . Atopic dermatitis vs. Chronic inducible urticaria  $p=0.133$ . Chronic spontaneous urticaria vs. Chronic inducible urticaria  $p=0.614$

TABLE 3 TSQM-9 domain scores, quality of life, and disease severity in atopic dermatitis (n = 199)

	Number	DLQI (mean ± SD)	TSQM-9 Effectiveness domain (mean ± SD)	TSQM-9 Convenience domain (mean ± SD)	TSQM-9 Global Satisfaction domain (mean ± SD)	IGA (mean ± SD)
Antihistamine	6	4.67 ± 4.68	65.7 ± 15.1	62.0 ± 26.4	66.7 ± 21.0	2.60 ± 0.55
Cyclosporin	25	6.48 ± 4.17	60.7 ± 14.9	71.3 ± 13.7	60.9 ± 16.0	3.25 ± 0.44
Topical steroid	112	6.47 ± 6.15	65.3 ± 18.2	66.1 ± 16.1	65.7 ± 17.7	2.68 ± 0.82
Topical tacrolimus	17	4.41 ± 3.71	62.4 ± 18.9	75.5 ± 14.6	69.3 ± 15.7	2.38 ± 0.81
Moisturizer	16	5.13 ± 6.80	69.1 ± 14.5	75.7 ± 15.4	71.4 ± 15.2	2.19 ± 0.65
Dupilumab	23	4.96 ± 4.52	79.7 ± 18.5	66.9 ± 17.0	77.6 ± 15.4	2.77 ± 0.87

Abbreviations: DLQI, Dermatology Life Quality Index; IGA, Investigator Global Assessment; TSQM-9: Abbreviated Treatment Satisfaction Questionnaire for Medication.

TABLE 4 TSQM-9 domain scores, quality of life, and disease severity in chronic spontaneous urticaria (n = 90)

	number	DLQI (mean ± SD)	TSQM-9 Effectiveness domain (mean ± SD)	TSQM-9 Convenience domain (mean ± SD)	TSQM-9 Global Satisfaction domain (mean ± SD)	IGA (mean ± SD)
Antihistamine	57	2.30 ± 3.11	68.1 ± 13.9	75.0 ± 15.2	72.2 ± 16.1	2.11 ± 0.85
Cyclosporin	2	11.0 ± 14.1	50.0 ± 23.6	52.8 ± 35.4	57.1 ± 30.3	3.50 ± 0.71
Oral steroid	5	0.80 ± 1.30	63.3 ± 13.9	67.8 ± 16.8	64.3 ± 13.4	3.20 ± 0.84
Topical steroid	3	5.00 ± 6.93	59.3 ± 8.49	61.1 ± 15.7	42.9 ± 10.1	3.20 ± 0.84
Omalizumab	23	1.87 ± 2.65	73.9 ± 22.0	67.8 ± 20.7	77.6 ± 20.1	3.13 ± 0.97

Abbreviations: DLQI, Dermatology Life Quality Index; IGA, Investigator Global Assessment; TSQM-9: Abbreviated Treatment Satisfaction Questionnaire for Medication.

examined factors associated with increased adherence via an on-line survey of Japanese patients with AD, psoriasis, urticaria, and tinea and found that adherence to oral medication was associated

with age, gender, alcohol consumption, examination frequency, drug effects, and treatment satisfaction.<sup>12,13</sup> The adherence to topical medications was associated with age, examination

TABLE 5 Analytic subject with multiple regression analysis.

	Gender Male, Female	Age Mean $\pm$ SD years	Disease duration Median years (25–75 percentile)
Atopic dermatitis	94 (58.8%) 66 (41.2%)	38.2 $\pm$ 12.6	30 (20–40)
Chronic spontaneous urticaria	21 (32.8%) 43 (67.2%)	51.2 $\pm$ 15.2	6 (3–13)

Abbreviation: SD, standard deviation

TABLE 6 Analytic TSQM-9 domain scores and quality of life by each disease with multiple regression analysis

	DLQI median (25–75 percentile)	TSQM-9 Effectiveness domain % (mean $\pm$ SD)	TSQM-9 Convenience domain % (mean $\pm$ SD)	TSQM-9 Global Satisfaction domain % (mean $\pm$ SD)
Atopic dermatitis N = 160	4 (2–8)	67.6 $\pm$ 16.8	68.1 $\pm$ 15.6	67.8 $\pm$ 16.2
Chronic spontaneous urticaria N = 64	1 (0–3)	69.4 $\pm$ 17.6	73.2 $\pm$ 18.5	74.7 $\pm$ 17.1

DLQI: Dermatology Life Quality Index; TSQM-9: Abbreviated Treatment Satisfaction Questionnaire for Medication.

TABLE 7 Multivariate-adjusted regression analysis with TSQM-9 as the objective variable in atopic dermatitis (n = 160)

	TSQM-9 Effectiveness domain (Partial regression coefficient (95% confidence interval)) Adjusted R <sup>2</sup> = 0.259 F statistic = 6.559 (p < 0.001)	TSQM-9 Convenience domain (Partial regression coefficient (95% confidence interval)) Adjusted R <sup>2</sup> = 0.142 F statistic = 3.638 (p < 0.001)	TSQM-9 Global Satisfaction domain (Partial regression coefficient (95% confidence interval)) Adjusted R <sup>2</sup> = 0.314 F statistic = 8.272 (p < 0.001)
Drugs (for topical steroids)			
Cyclosporin	0.208 (–7.308, 7.754)	3.931 (–3.585, 11.448)	–5.835 (–12.792, 1.122)
Topical tacrolimus	–3.818 (–12.220, 4.583)	9.818 (1.417, 18.220)*	1.072 (–6.704, 8.849)
Moisturizer	–3.818 (–12.220, 4.583)	7.810 (–1.573, 17.193)	1.730 (–6.955, 10.414)
Dupilumab	13.856 (6.632, 21.080)*	0.558 (–6.666, 7.782)	10.937 (4.251, 17.624)*
Age	–0.071 (–0.295, 0.153)	–0.030 (–0.255, 0.194)	–0.196 (–0.404, 0.012)
Male	1.886 (–2.954, 6.725)	2.462 (–2.378, 7.302)	5.741 (1.261, 10.220)*
Current smoker	–1.908 (–9.471, 5.656)	–3.842 (–11.406, 3.721)	–1.152 (–8.153, 5.849)
Disease duration	0.019 (–0.190, 0.229)	–0.174 (–0.383, 0.036)	0.014 (–0.180, 0.208)
IGA (3 or 4 point)	–6.078 (–11.209, –0.946)*	1.404 (–3.728, 6.535)	–2.312 (–7.062, 2.438)
DLQI	–1.235 (–1.690, –0.780)*	–0.835 (–1.290, –0.380)*	–1.345 (–1.766, –0.924)*

\*p < 0.05.

frequency, drug effects, and treatment satisfaction.<sup>12,13</sup> The adherence to both oral and topical medications was higher when treatment satisfaction was higher, and this confirmed the importance of assessing satisfaction levels. Nakahara et al. examined the relationship between patient-assessed severity and TSQM-9 in AD and found that severe disease was associated with reduced satisfaction.<sup>14</sup> This is supported by the results of our study. The results of the multivariate-adjusted regression analysis, which took into account the effects of confounding factors, indicated that the DLQI contributed to treatment satisfaction (TSQM-9, Tables 7 and 8) in AD, and the drugs associated with increased TSQM-9 scores were dupilumab (for global satisfaction and

effectiveness domains) and topical tacrolimus (for convenience domain). This indicated that after adjusting for disease severity, age, sex, or DLQI, the use of biologics for AD treatment presented a positive effect on satisfaction. We performed a similar analysis for chronic spontaneous urticaria but did not obtain the same findings for omalizumab. This difference between AD and chronic spontaneous urticaria might be attributed to differences in the use of topical steroids in AD (used as a reference) and oral antihistamines in chronic spontaneous urticaria or because of the differences between both the diseases. The best treatment should be chosen depending on severity of the disease and the patient's lifestyle. It may also be helpful to consider that the effectiveness



TABLE 8 Multivariate-adjusted regression analysis with TSQM-9 as the objective variable in chronic spontaneous urticaria ( $n = 64$ )

	TSQM-9 Effectiveness domain (Partial regression coefficient, (95% confidence interval)) Adjusted $R^2 = 0.183$ F statistic = 3.018 ( $p = 0.009$ )	TSQM-9 Convenience domain (Partial regression coefficient, (95% confidence interval)) Adjusted $R^2 = -0.034$ F statistic = 0.707 ( $p = 0.666$ )	TSQM-9 Global Satisfaction domain (Partial regression coefficient, (95% confidence interval)) Adjusted $R^2 = 0.011$ F statistic = 2.923 ( $p = 0.011$ )
Drugs (for oral antihistamine)			
Omalizumab	5.333 (-5.434, 16.100)	-10.617 (-23.339, 2.106)	2.184 (-8.353, 12.721)
Age	-0.051 (-0.318, 0.215)	-0.041 (-0.356, 0.274)	-0.114 (-0.375, 0.147)
Male	-5.144 (-14.062, 3.774)	2.124 (-8.413, 12.662)	1.370 (-7.358, 10.097)
Current smoker	-5.963 (-17.921, 5.995)	0.689 (-13.441, 14.820)	-0.590 (-12.294, 11.113)
Disease duration	-0.084 (-0.471, 0.304)	-0.053 (-0.510, 0.405)	-0.018 (-0.397, 0.361)
IGA (3 or 4 point)	-0.396 (-10.432, 9.640)	2.017 (-9.841, 13.876)	-0.806 (-10.628, 9.016)
DLQI	-2.662 (-3.957, -1.367)*	-1.050 (-2.580, 0.480)	-2.751 (-4.018, -1.483)*

Abbreviations: TSQM-9: Abbreviated Treatment Satisfaction Questionnaire for Medication; IGA: Investigator Global Assessment; DLQI: Dermatology Life Quality Index.

\* $p < 0.05$

of a biologic agent and the convenience of topical agents for AD and antihistamines for chronic spontaneous urticaria have led to increased patient satisfaction.

A study in South Korea investigated why patients with moderate to severe AD were dissatisfied with hospital treatment and sought folk remedies.<sup>15</sup> That study suggested a negative chain of events in which treatment satisfaction decreased, because the condition remained severe, thereby reducing medication adherence.

For psoriasis, the TSQM-9 domain score for treatment satisfaction was significantly correlated with both the Psoriasis Area and Severity Index, which is used to score the severity of psoriasis eruptions, and the Psoriasis Disability Index, which is a QOL scale. Good management of QOL and the status of skin were reported to be associated with high levels of treatment satisfaction.<sup>16</sup> Moreover, satisfaction was higher in patients treated with biologics ( $n = 67$ ) than in those not treated with biologics ( $n = 93$ ).<sup>16</sup> In the present study, we obtained similar results for AD. It was observed that despite the high costs of the biologic drugs, patients had high levels of satisfaction when they experienced the beneficial effects of these drugs. Our data on annual income can only be used for reference, because only a few patients provided this information. However, the average annual income of patients with AD was 2.56 million yen ( $n = 111$ ), which was less than 3.94 million yen ( $n = 47$ ) for patients with chronic spontaneous urticaria and 3.25 million yen ( $n = 6$ ) for patients with chronic inducible urticaria. As the question related to the annual income was directed to the patient, it was unclear whether the patient received support from parents or medical assistance. Furthermore, the average duration of the two diseases was different and therefore, it is possible that the comparison was not accurate. In this study, we questioned patients who were actually using medications in the real-world setting. Therefore, being in an environment where they can use that medication may be a source of bias. This could be due to a desire to not change medications and to maintain the status quo.

This study had the following limitations. This study was restricted to patients with access to expensive drugs, such as biologics, and the satisfaction levels were not assessed after administering all types of medications. Another limitation is that the target patients were being treated at university hospitals. In addition, this study did not consider the duration of therapy. A study conducted in Japan on psoriasis patients found that satisfaction was the highest when monthly costs were 5000 yen or less.<sup>17</sup> However, we were unable to confirm these findings for AD or chronic urticaria in the present study. These aspects warrant further study in the future.

## 5 | CONCLUSIONS

We performed a large survey involving 302 patients with AD or chronic urticaria in five university hospitals. The effectiveness domain and global satisfaction domain of the TSQM-9 improved with an improvement in the QOL. Satisfaction with biologic agents was higher, compared to that with conventional standard therapy, in patients with AD. A similar tendency was observed in patients with chronic spontaneous urticaria, although it was not significant. In all cases, satisfaction with biologics was high, suggesting that treatment with biologics is worth exploring for patients who are not satisfied with their existing treatments.

## ACKNOWLEDGEMENTS

This study was partially supported by Collaborative Research Grants 2017-2019 from the Japanese Society for Cutaneous Immunology and Allergy. We thank the research assistant in the Department of Dermatology of Shimane University for assisting with this study.

## CONFLICT OF INTEREST

SK has received grants as an investigator from Ely-Lilly, Japan. TN has received an honorarium as a speaker in Sanofi Maruho. AF

has received fees as a speaker from Sanofi, Taiho Pharmaceutical Co., and Novartis. AF has received fees for funded research/joint research from Taiho Pharmaceutical Co. KM has received fees as a speaker from Sanofi and Mitsubishi Tanabe Pharma. EM has received honoraria as a speaker from Maruho, Novartis, Tanabe-Mitsubishi, and Taiho and has received grants as an investigator from Eisai, Maruho, Kyowa-Kirin, Taiho, Celgene, Novartis, Parexel, and Integrated Development Associates. The remaining authors have no conflict of interest.

## DECLARATION SECTION

Approval of the research protocol: All investigators involved in this study carried out this study in accordance with the latest edition of the Declaration of Helsinki. This study was approved by the ethics committee of Shimane University and the Dean of the Faculty of Medicine (approval no. 3312), the ethics committee of Kyushu University and Dean of the Faculty of Medicine (approval no. 30-134), the ethics committee of Sapporo Medical University School of Medicine and Dean of the Faculty of Medicine (approval no. 302-45), ethics committee of Kobe University and Dean of the Faculty of Medicine (approval no. 180136), and the ethics committee of Kyoto Prefectural University and Dean of the Faculty of Medicine (approval no. 15476). All patients consented to participate in this study. Dr. Eishin Morita is a member of the Journal of Cutaneous Immunology and Allergy Editorial Board. Management of the peer review process, and all editorial decision making, for this article was undertaken by Editor in Chief.

Informed Consent: All the patients provided informed written consent to participate in this study.

Registry and the Registration No. of the study/trial: N/A.

Animal Studies: N/A.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

**How to cite this article:** Kaneko S, Nakahara T, Sumikawa Y, Fukunaga A, Masuda K, Kakamu T, et al. Current status of the satisfaction levels of adult patients receiving drugs for atopic dermatitis and chronic urticaria. *J Cutan Immunol Allergy.* 2022;5:4–11. <https://doi.org/10.1002/cia.21220>