Quantifying patient preferences for treatments for refractory chronic spontaneous urticaria

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Background: In recent years, it has become increasingly common to incorporate the patient perspective into drug development and regulatory decision making.

Objective: This study aimed to measure and quantify patient preferences (priorities and trade-offs) for attributes that characterize current and emerging refractory chronic spontaneous urticaria (rCSU) treatments.

Methods: Adult patients with self-reported rCSU symptoms completed an online discrete choice experiment survey. The survey included 10 questions that asked respondents to choose between 2 hypothetical rCSU treatment profiles having similar attributes with varying levels. The attributes included the following: chance of control of symptoms, time to symptom control, return of symptoms after discontinuation of therapy (complete remission), allergic reaction, risk of kidney dysfunction (usually reversible), and mode and frequency of administration. Relative attribute importance and maximum acceptable risks were calculated.

Results: A total of 213 subjects with a mean age of 51 years completed the survey. Efficacy (symptom control) and mode of administration were the 2 most important attributes to treatment choice, followed by risk of kidney dysfunction and time to achieve symptom control. Complete remission of symptoms and risk of allergic reaction were identified as least important. With regard to mode of administration, topical treatment was the most preferred option and infusion therapy was least preferred. Respondents who were presented with a scenario of refractory and severe chronic spontaneous urticaria were willing to accept increased risk of reversible kidney dysfunction in exchange for improvement in symptom control or complete remission. Respondents were willing to accept infusion over topical treatment if there was significant increase in treatment efficacy.

Conclusion: These study results can be used to inform development and evaluation of future rCSU therapies by product developers and regulatory authorities, respectively. (J Allergy Clin Immunol Global 2025;4:100468.)

Key words: *Patient preference, discrete choice experiment, refractory chronic urticaria, benefit-risk, trade-off, product development, regulatory decision making*

Chronic spontaneous urticaria (CSU), characterized by hives and/or angioedema for at least 6 weeks without an exogenous trigger, affects up to 1% of the US population.[1-5] First-line treatment for CSU involves administration of oral antihistamines that can be escalated to high doses if needed. In approximately 40% of individuals, hives do not respond to maximal antihistamine therapy; these individuals are defined as having antihistamine-refractory CSU (rCSU). The economic, emotional, and quality of life burden of rCSU is significant, and CSU has been found to negatively affect work and school productivity, sleep quality, and social interactions.[2,6-9]

Omalizumab is the only US Food and Drug Administration (FDA)-approved therapy for rCSU. It is a biologic medication that is administered under the skin by injection every 4 weeks in a clinical setting, with a low risk of serious adverse effects. Studies have demonstrated that is has 65% efficacy; however, it has not resulted in long-term remission in randomized controlled studies.[6] Cyclosporine is an oral medication that is not FDA approved for rCSU, but it has been shown to have good efficacy, rapid onset of action, and potential for long-term remission.[10] However, cyclosporine also has potential serious adverse effects, including hypertension and kidney injury.[6] For antihistamine-refractory CSU, international guidelines recommend use of omalizumab and then cyclosporine if needed, whereas the US guidelines allow the use of various other agents, including omalizumab and cyclosporine.[1,3] Several novel therapies with various molecular targets are being developed or studied for treatment of rCSU, with various forms of administration, including topical, oral, and parenteral infusion.[11,12]

Competing treatment options for rCSU present with varying risks, benefits, modes of administration, and other treatment attributes. Patients, who carry the burden of the disease and its associated treatments, have a unique perspective on the attributes and features associated with various treatment options. It has been shown that patients' benefit-risk preferences may be different from those of the providers and regulators who are responsible for prescribing and approving treatment options.[13-17] In recent years, it has become increasingly common to incorporate the patient perspective into health care and regulatory decision making. Patient-centered decision making involves understanding which treatment characteristics are most important to patients, and it can lead to improved adherence and outcomes, reduced costs, and increased satisfaction and quality of life.[13,18-21] In particular, the US FDA has requested the use of quantitative patient

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Abbreviations used
CSU: Chronic spontaneous urticaria
DCE: Discrete choice experiment
FDA: US Food and Drug Administration
MAB: Minimum acceptable benefit
MAR: Maximum acceptable risk
PPI: Patient preference information
rCSU: Refractory chronic spontaneous urticaria
RPL: Random parameters logit
UCT: Urticaria Control Test

preference information (PPI) across the total life cycle of the product (drugs, medical devices, and biologics), which includes the development phase, evaluation phase, and postmarket surveillance.[16,21-25] Discrete choice experiment (DCE) is the most commonly used method to elicit and measure patient preferences and generate quantitative PPI.[24]

To the best of our knowledge, there is no existing study that quantitatively explores patient preferences for outcomes (attributes) associated with treatments for rCSU. The objective of this study was to use the DCE methodology to measure and quantify patients' preferences for these outcomes.

METHODS

We designed and administered a web-enabled DCE survey to elicit preferences of patients in the United States for outcomes (attributes) of rCSU treatments. DCEs offer a systematic way to quantify the relative importance that respondents place on various treatment attributes. DCEs are based on the assumptions that goods or services (eg, treatments) are made up of a set of attribute or features (eg, efficacy and side effects) and that individuals choose the option from which they expect to derive the highest level of utility.[26-29] This study was approved by the Thomas Jefferson University institutional review board for human subject research.

The design and development of the survey instrument and subsequent study conduct followed best research practices and guidelines for PPI studies.[26,30-32] The survey instrument included 7 sections: (1) screener questions that determined participant eligibility; (2) electronic informed consent; (3) an introductory section that provided information (with comprehension checks) about CSU and CSU treatments; (4) a section that provided information (with comprehension checks) about rCSU treatment attributes and levels used in the DCE choice questions; (5) a tutorial on the DCE (with comprehension checks); (6) the DCE choice tasks; and (7) questions that captured respondents' self-reported clinical history, sociodemographic information, and CSU disease severity via the validated Urticaria Control Test (UCT). The UCT is an instrument that evaluates disease control by assigning a score ranging from 0 (no control) to 16 (complete control). Scores less than 12 indicate poorly controlled CSU symptoms.[33-35]

The DCE portion of the survey asked respondents to choose between pairs of hypothetical treatments for rCSU with a common set of attributes. Specifically, respondents were asked to state which treatment they would rather try first to treat their CSU (Fig 1). Choice questions were designed by systematically varying the performance of treatments under each attribute (attribute levels). Table I defines attributes and attribute levels that characterize current and emerging therapies for rCSU. The survey content, including relevant treatment attributes (features, efficacy, and risks) and levels of these attributes, was developed on the basis of a review of the literature on rCSU treatments, publicly available clinical trial data, existing national and global clinical guidelines, and input from the authors with PPI and clinical expertise.[6,11,12,36-40]

The draft survey instrument was pretested during 9 one-to-one semistructured cognitive pretest interviews with people who had a physician-confirmed diagnosis of CSU. We followed a think-aloud protocol to explore the relevance of the DCE attributes to patients, the patient's comprehension and understanding of the survey content, the appropriate number of choice tasks, and the overall burden of the survey. Participants responded to bidding game questions to evaluate their willingness to make trade-offs among attributes and attribute levels.

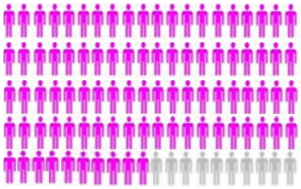
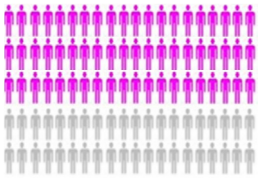
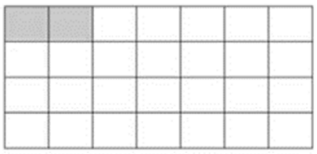
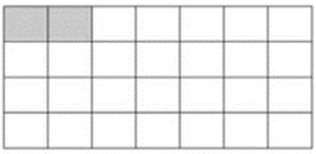
After pretesting, an experimental design was constructed to prepare the different combinations of attribute levels that defined the hypothetical rCSU treatments in each choice task in the DCE.[31] The adopted experimental design included 30 unique DCE choice questions, which were divided into 6 blocks of 5 questions each. Respondents were randomly assigned to 2 nonrepeated blocks and asked to answer a total of 10 DCE questions (ie, 5 questions from each block) to minimize the impact of potential block effects.

A dominated DCE choice question, in which 1 treatment profile was designed to be better than the other (superior to the other), was included as an internal validity check of participant responses. In addition, to account for ordering effects, the presentation of choice questions was randomized across respondents. Respondents who always picked the same treatment option were excluded from the analysis. An additional data quality check involved conducting a scope test (Table I) to evaluate whether respondents were reacting to the actual risk levels presented. Respondents were randomized to 1 of 2 maximum risk levels (20% or 10%). This randomization allows the evaluation of choice patterns with the 2 levels across respondents. We implemented the scope test by examining whether the preference weight for the 20% risk was different from that for the lower risk level (10%).[41]

A priori power calculations to determine a specific sample size for a DCE requires information that is usually unknown at the study-development phase.[42,43] However, we adopted the rule of thumb for minimum sample size determination proposed by Orme (in 2014) and Yang et al (in 2015) for statistical significance (95% CI) of preferential effects in a main effects DCE model.[44,45] Our target sample size of 210 respondents was consistent with other samples in the published health care choice experiments literature.[30,42,43] See the Supplementary Appendix for more information about sample size (available in the Online Repository at www.jaci-global.org).

Survey respondents were identified through Dynata, an online consumer panel of the US population. Interested participants were directed to the secure online DCE survey to confirm eligibility (see the Supplementary Appendix for screener questions). After confirmation of eligibility, an electronic informed consent form was also administered before respondents could proceed to complete the survey. Eligible respondents were residents of the United States with a self-reported diagnosis of CSU symptoms who were currently taking antihistamines and had not received any treatments for rCSU, were older than 18 years at the time of the study,

Suppose you have hives, itching and/or swelling symptoms that are not controlled by your current antihistamine medicine. Suppose your doctor recommends that you take an additional medicine to help control these symptoms. Your doctor recommends that you consider two new medicines, Medicine A and Medicine B. To help you think through these options, your doctor put together the following table describing how these medicines work.

Feature	Medicine A	Medicine B
Chance of controlling CSU symptoms (hives, itching and/or swelling) with medicine	 90 people out of 100 (90%)	 60 people out of 100 (60%)
How long it takes to control CSU symptoms after starting medicine	 2 days	 2 days
CSU symptoms return after stopping medicine	 Yes	 Yes
Chance of severe allergic reaction with medicine that requires carrying an epi pen	No	 Yes
Chance of reduced kidney function with the medicine (usually restored after stopping medicine)	 0 people out of 100 (0%)	 6 people out of 100 (6%)
How you take the medicine	 Topical cream twice daily	 Topical cream twice daily

Based on the information in the table above, which medicine would you **choose first**?

☐ Medicine A

☐ Medicine B

FIG 1. Sample DCE question.

TABLE I. Final attributes and levels adopted for the DCE

Respondent facing attribute	Attribute levels
Chance of controlling CSU symptoms (hives, itching and/or swelling) with medicine	• 40% • 60% • 90% • 100%
CSU symptoms return after medicine is no longer being taken	• Yes • No
Chance of severe allergic reaction with the medicine	• Yes • No
Time required to control CSU symptoms after patient has started taking the medicine	• 2 d • 2 wk • 3 mo • 6 mo
Chance of reduced kidney function with the medicine (function is usually restored after the patient has stopped taking the medicine)	• 0% • 6% • 10% or 20%*
How the medicine is taken	• Topical cream applied to the affected area twice daily • 2 injections in the arm administered in clinic by a nurse every 4 wk • 2 injections under the skin of the belly self-administered at home every 4 wk • Oral (1 pill) taken daily • Infusion (that lasts about 8 h) given at an infusion center once per month

*Respondents were randomly assigned to either 10% or 20% for the highest level for risk of kidney dysfunction.

were able to provide informed consent, and were able to read and answer the online survey in English.

All analyses were conducted using Stata (Stata Corp LLC, College Station, Tex), and all statistical tests were 2 sided with a significance level of .05. Analysis of demographic and other patient characteristics, including age, sex, education, and race/ethnicity were evaluated by using summary statistics, including mean and frequencies (percentages). Choices from the DCE questions were analyzed by using random-parameters logit (RPL) regression models following good research practices. All attribute levels were specified as effects-coded (instead of dummy-coded) categoric variables for identification purposes for all attribute levels during estimation. This implies that the preference weight for a level in each attribute was constrained to be the negative sum of the preference weights for the other levels of the attribute. The RPL model yielded a set of relative preference weights (log odds coefficients) for the attribute levels included in the DCE. The preference weights indicate how preferences for rCSU treatment change with changes in the study attribute levels. The absolute value of the preference weights is meaningless; however, higher preference weights can be interpreted as having a greater impact on treatment choice (utility) than that of the lower preference weights for different levels of the same attribute. The estimated preference weights were used to derive the relative importance of DCE attributes by calculating the greatest difference in preference weights that can be induced with changes in each attribute, as well as to compute equivalences (trade-offs) between attributes, including maximum acceptable risk (MAR) and minimum acceptable benefit (MAB). Specifically, we computed the MAR of kidney dysfunction that respondents are willing to accept for a given increase in treatment effectiveness or benefit (improved symptom control or complete remission). We computed the MAB of rCSU symptom control required by respondents to accept a less desirable mode of administration (see the Supplementary Appendix).[16,32]

RESULTS

The online survey was fielded from May 5, 2023, to May 23, 2023. A total of 8253 people from Dynata's panel who were expected to meet the study inclusion criteria responded to the invitation by clicking on the survey link. Of those who responded, 1820 were eligible and consented to participate, with 217 respondents completing the survey. Four respondents always chose the same answer (medicine A or B), indicating nonattendance, and they were excluded from subsequent analysis.

Table II presents the characteristics of the final sample of respondents (N = 213). The average age was 51 years, and 57% self-identified as female, with White individuals comprising 80% of the sample. A majority of the sample (57%) reported having a mixture of hives that may itch and swelling, 38% reported mainly having hives, and 6% reported mainly swelling. Almost 92% of the sample reported a UCT score suggesting that they were experiencing poor control of their hives, itching, and/or swelling. Most of the sample (61%) had a history of experiencing a severe allergic reaction in the past. A majority of the sample (87%) reported not having kidney disease. All but 1 respondent had at least a college or technical school education.

Most of the respondents (n = 197 [92.3%]) selected the superior profile in the DCE-dominated choice question. This suggests that most respondents paid attention to the attribute levels when answering the DCE choice question. In addition, the results of the scope test (Table III and Fig 2) confirmed that respondents were sensitive to the actual risk levels presented for the kidney dysfunction attributes presented in the experiment. The higher level of risk for kidney dysfunction (20%) presented with a greater disutility relative to the lower risk level (10%).

The results of the final RPL model are summarized in Table III and Fig 2. The RPL model results are divided into 2 groups of parameters, mean preference weights and SD parameters (Table III). The mean preference weights indicate the relative preferences for the average patient with CSU, whereas the SD estimates capture expected population-level heterogeneity in the preference weights. Both mean preference weight and SD estimates include SEs that capture the error around the estimates.

Fig 2 presents the mean preference weights (and 95% CIs). Among the respondents, preferences for symptom control, time required to control symptoms, complete remission of symptoms (return of symptoms after discontinuation of therapy), allergic reaction and risk of kidney dysfunction (which is usually reversible) were ordered as expected, with better clinical levels associated with higher preference weights. On average, respondents preferred higher levels of symptom control, lower rates of time to achieve control, lower rates of kidney dysfunction, no allergic reaction, and no return of symptoms. Regarding the attribute mode of administration (how the medicine is taken), topical cream twice daily was the most preferred option and infusion for about 8 hours at an infusion clinic was the least preferred option.

TABLE II. Sample characteristics

Characteristic	Overall (N = 213)
Age (y)	
Mean	50.7
Median	50
Minimum-maximum	20-88
Age category, no. (%)	
≤41	74 (35.8)
41<Age≤61	70 (30.9)
Age>61	69 (32.4)
How the patient's CSU symptoms present, no. (%)	
Mainly as hives that may itch	80 (37.6)
As a mixture of hives that may itch and swelling	121 (56.8)
Mainly as swelling	12 (5.6)
Whether the patient sometimes experiences hives that may itch and or swelling on the face including eyes, nose, and lips, no. (%)	
Yes	144 (67.6)
No	69 (32.4)
Whether the patient has ever experienced a severe allergic reaction (anaphylaxis), no. (%)	
Yes	61 (28.6)
No	146 (68.5)
Does not know/is not sure	6 (2.8)
Whether the patient has ever been told by a doctor or other medical providers that he or she has a kidney disease, no. (%)	
Yes	25 (11.7)
No	186 (87.3)
Does not know/is not sure	2 (0.9)
UCT score	
Mean	7.8
Median	8
UCT score category, no. (%)	
<12 (poorly controlled symptoms)	195 (91.6)
≥12 (well-controlled symptoms)	18 (8.5)
Sex, no. (%)	
Female	121 (56.8)
Male	91 (42.7)
Other	1 (0.5)
Prefer not to answer	
Racial designation, no. (%)	
American Indian or Alaska Native	5 (2.4)
Asian	9 (4.2)
Black or African American	23 (10.8)
Native Hawaiian	0
White	171 (80.3)
Other	5 (2.4)
Highest level of education completed, no. (%)	
Less than high school	1 (0.5)
High school graduate or equivalent (eg, GED certificate)	1 (0.5)
Some college but no degree	29 (13.6)
Technical school	48 (22.5)
2-Year college degree (associate's degree)	9 (4.2)
4-Year college degree (eg, BA or BS)	25 (11.7)
Some graduate school but no degree	55 (25.8)
Graduate or professional degree (eg, MBA, MS, MD, PhD)	9 (4.2)
Prefer not to answer	36 (16.9)

UCT is the patient-reported outcome measurement used to assess disease activity and control.

The largest difference in preference weights associated with an attribute defines the full impact of an attribute on the treatment choices made by the average respondent in the DCE. This is a common measure of overall attribute importance based on the levels presented in the DCE questions.[46] Fig 3 shows the relative attribute importance from the DCE. Over the ranges presented in the survey, the most important change among respondents was an increase in control of symptoms from 40% to 100%, followed by change in mode of administration from topical to infusion, and then a reduction in kidney dysfunction from 20% to 0%. The remaining attributes followed in decreasing order of importance: a change in time to achieve control of symptoms from 6 months to 2 days, a change in complete remission of symptoms (CSU symptoms return) from yes to no, and a change in allergic reaction (from yes to no).

Table IV presents the MAR of treatment-related kidney dysfunction that patients with CSU would be expected to accept if accompanied by improvements in symptom control or complete remission. The MAR results show that respondents in the sample were willing to accept increased risk of kidney dysfunction to gain a 1%-point increase in control benefit or complete remission of symptoms. On average, respondents were willing to accept a 0.45%-point increase in the risk of kidney dysfunction for a 1%-point increase in the chance that they can control CSU symptoms. This MAR implies that the average respondent was willing to accept a 4.5%-point increase in kidney dysfunction risk to achieve a 10%-point increase in control of symptoms. On the other hand, the average patient in the sample was willing to accept a 15.4%-point increase in kidney risk provided treatment could lead to complete remission.

Table V presents the treatment MAB or the minimum improvement in treatment effectiveness that respondents would exchange for a more bothersome treatment option. On average, respondents in the sample were willing to accept infusion over topical treatment if treatment efficacy increased by 60%-points.

DISCUSSION

To our knowledge, this study is the first to assess patient preferences for rCSU treatments via a DCE approach. The results show that for the changes in attributes presented in this study, efficacy (symptom control) and mode of administration were the 2 most important attributes to treatment choice. These were followed by the attributes that characterized treatment safety and time to achieve symptom control. Complete remission of symptoms and risk of allergic reaction were identified as the least important attributes. Findings from the MAR analysis showed that respondents in the sample were willing to accept an increased risk of treatment-related side effect (reduced kidney function) in exchange for improvements in control of symptoms or complete remission of symptoms after treatment discontinuation. This MAR result may reflect the treatment scenario of refractory and severe CSU symptoms with which patients were presented. In addition, consistent with clinical guidelines, respondents were made aware that treatment that might cause kidney dysfunction was accompanied by routine laboratory monitoring and treatment discontinuation if kidney dysfunction occurred, and they were also informed that potential kidney dysfunction is usually reversible after treatment discontinuation. With regard to the attribute mode of administration (how the medicine is taken), although a topical treatment was the most preferred option and

TABLE III. RPL preference estimates and SD of preference estimates (N= 213)

Attribute	Level	Coefficient	SE	Test statistic	*P* value*
Mean preference estimates†					
Control of symptoms	40%	–1.064	0.165	–6.46	.000
	60%	–0.304	0.095	–3.190	.001
	90%	0.470	0.111	4.230	.000
	100%	0.898	0.138	6.490	.000
Time to symptom control	2 d	0.518	0.114	4.54	.000
	2 wk	0.417	0.100	4.180	.000
	3 mo	–0.214	0.104	–2.060	.039
	6 mo	–0.720	0.123	–5.85	.000
Return of symptoms	Yes	–0.546	0.074	–7.36	.000
	No	0.546	0.074	7.360	.000
Allergic reaction	Yes	–0.368	0.072	5.13	.000
	No	0.368	0.072	5.130	.000
Reduced kidney function	0%	0.670	0.124	5.38	.000
	6%	0.218	0.086	2.530	.011
	10%	–0.288	0.137	–2.100	.035
	20%	–0.599	0.163	–3.680	.000
How the medicine is taken	Topical	0.561	0.174	3.230	.001
	Injections in the clinic	0.116	0.106	1.090	.276
	Injections at home	0.127	0.130	0.980	.328
	Oral pill	0.325	0.111	2.920	.003
	Infusion	–1.129	0.189	–5.970	.000
SD estimate‡					
Control of symptoms	40%	1.494	0.289	5.180	.000
	60%	0.025	0.160	0.160	.876
	90%	0.667	0.160	4.170	.000
	100%	0.851	0.164	5.180	.000
Time to symptom control	2 d	0.799	0.283	2.830	.005
	2 wk	0.140	0.177	0.800	.426
	3 mo	0.444	0.157	2.830	.005
	6 mo	0.496	0.180	2.760	.006
Return of symptoms	Yes	0.550	0.083	6.600	.000
	No	0.550	0.830	6.600	.000
Allergic reaction	Yes	0.663	0.095	6.950	.000
	No	0.663	0.095	6.950	.000
Reduced kidney function	0%	1.425	0.288	4.950	.000
	6%	0.012	0.118	0.100	.921
	10%	0.513	0.175	2.930	.003
	20%	0.900	0.156	5.760	.000
How the medicine is taken	Topical	2.528	0.554	4.560	.000
	Injections clinic	0.278	0.315	0.880	.378
	Injections home	0.675	0.227	2.980	.003
	Oral pill	0.367	0.291	1.260	.207
	Infusion	1.208	0.195	6.200	.000

*Measures the probability that the coefficient is different from zero, where zero is the mean effect.
†Mean preference estimates are log odds coefficients representing the relative benefit and harm of an attribute level relative to the mean effect for that attribute, which was normalized to zero. The SE of the log odds coefficients represents our level of certainty around the mean preferences for the attributes.
‡Characterizes the expected variation in mean preference estimates across respondents in the population based on sample-level variation. The SE on the SD parameters represents our level of certainty about that estimated preference variation.

infusion therapy was the least preferred option, respondents were willing to accept infusion over topical treatment if there were significant increases in treatment efficacy. Notably, the MAB analysis showed that a minimum increase in treatment efficacy of 60% was required for respondents to accept a trade-off between topical and infusion therapy. Future research is needed to further build the understanding of preferences for rCSU treatments by age, sex, location of symptoms, and disease severity.

These findings have potential implications for rCSU drug development, evaluation of attributes (outcomes) of rCSU therapies by regulatory authorities, and rCSU treatment guidelines. Respondents showed a strong preference for topical and oral treatments and were averse to infusion therapy. Currently, however, there is no FDA-approved oral or topical therapy for rCSU. Therefore, this may be an area of unmet need in which the development of additional oral and topical rCSU therapies may be beneficial.

The MAR results that capture treatment risk tolerance, can be used by drug developers, along with other relevant data, to inform end point performance targets within clinical trial design. Additionally, findings from the risk tolerance analysis may aid in benefit-risk evaluation by allowing regulators to determine

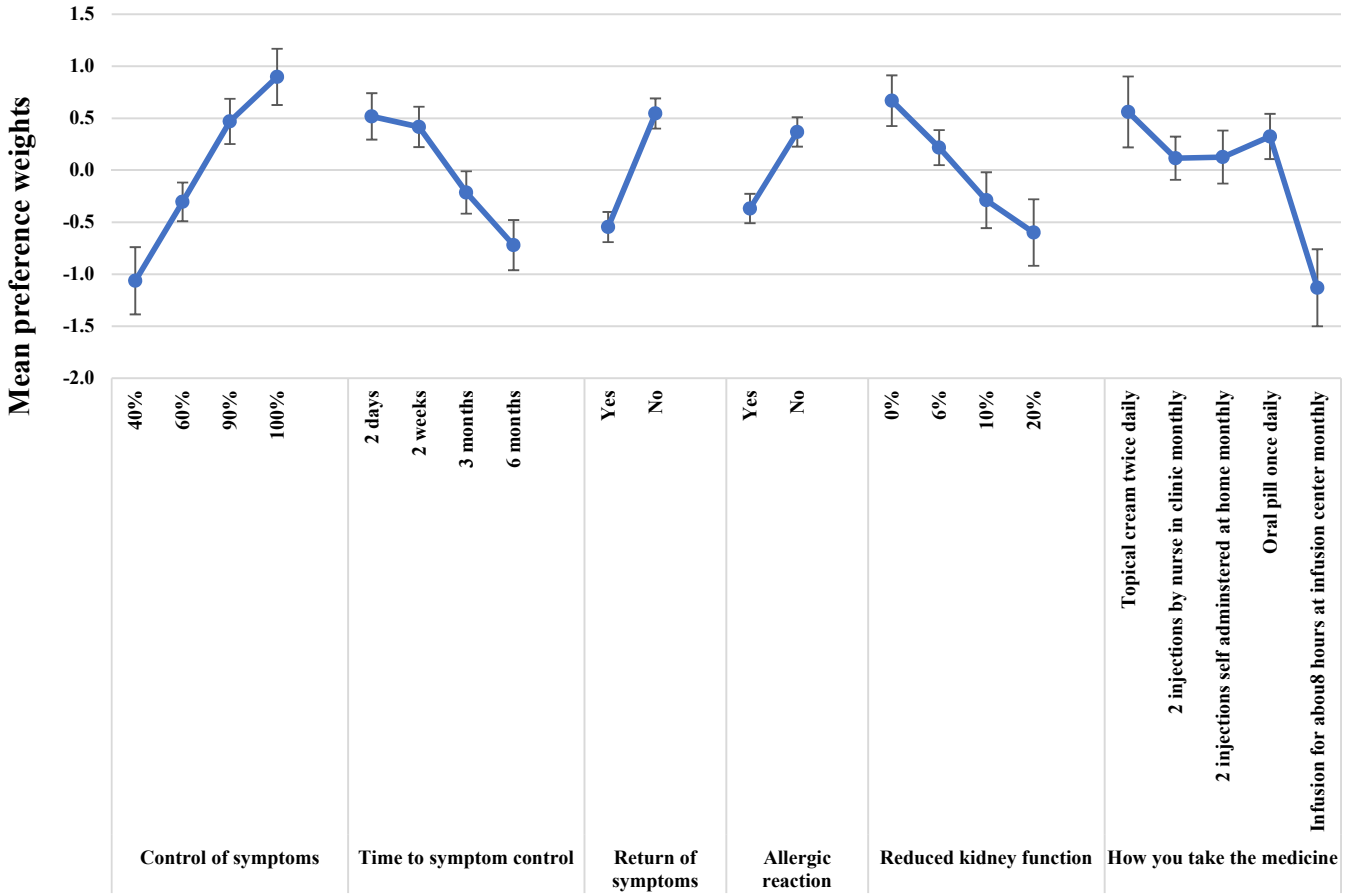


FIG 2. Patient preference weights (N = 213). Mean preference weights (and 95% CIs) for the respondents from the categoric RPL model are presented. Vertical distance between preference weights represents the relative importance (change in utility) of moving from one level of an attribute to another level of the same attribute measured in log odds. Within each attribute, a higher preference weight (PW) shows that the level is more preferred. For example, on average, respondents preferred 2 days to achieve symptom control (PW = 0.518) more than a 2-week time frame (PW = 0.41). It should be remembered that on its own, the value of the point estimate (PW) is meaningless.

whether a new rCSU product is acceptable to patients by comparing its benefit-risk profile to that of an existing predicate rCSU therapy. The results may also be useful in the postmarket setting to inform an expanded use for a medical product (label expansion). Cyclosporine is approved by the FDA for indications such as solid organ transplantation, rheumatoid arthritis, and psoriasis.[47] However, cyclosporine remains an off-label drug for treatment of rCSU, although it is recommended by current clinical guidelines as a treatment option in certain circumstances, at low doses, with close monitoring for adverse effects, and with the shortest duration required to maintain symptom control. Given that respondents in this study were willing to tolerate a degree of risk of kidney dysfunction in exchange for a certain degree of improved symptom control and complete remission, these results demonstrate how PPI may be used to inform a label expansion of a therapy with a profile reflecting these attributes for the appropriate rCSU population. It is important to note that according to the FDA guidance on PPI, data regarding PPI do not change assessment standards for medical products, nor do they replace clinical data evidence requirements. Rather, PPI supplements clinical evidence by providing the patient perspective in a quantitative and structured way. Lastly, whereas current management guidelines for rCSU appropriately focus on safety and efficacy of rCSU treatments, our PPI results reflect other patient-informed priorities, such as mode of treatment administration, which may additionally be considered.

These findings may be understood in the context of studies showing that the burden of rCSU on quality of life is significant. As the DCE study respondents on average had poor symptom control, these findings regarding preference may be specifically applicable to real-life populations with severe and poorly controlled symptoms.

This study has some limitations. As with all DCEs, preferences elicited from the study are contingent on hypothetical rCSU scenarios, attribute and attribute levels, and other information presented in the survey. Thus, choices do not carry the same consequences as real-world treatment decisions. However, we implemented several strategies to mitigate potential hypothetical bias. We used a question format that is most consistent with the way in which such real-world decisions would be made, arguably providing a way to elicit information that is compatible with preference-revealing choices. The survey included tutorials (with comprehension checks) that provided education about CSU, rCSU, and features that characterize current and emerging

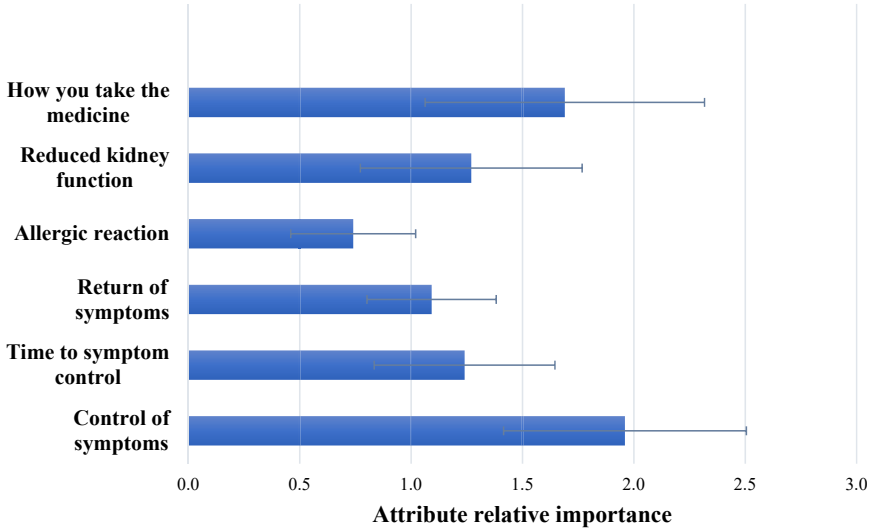


FIG 3. Relative overall attribute importance. Bars show attribute relative importance scores (and 95% CI) of a change in each attribute over the range assessed in the survey.

TABLE IV. MAR of kidney dysfunction for improved control of symptoms and complete remission of symptoms

Attribute	Change in control of symptoms		Mean MAR
Control of symptoms	1%-point increase in control		0.45% (95% CI = 0.29%-0.61%)
	From level	To level	
Complete remission (symptoms return after discontinuation of therapy)	Yes	No	15.40% (95% CI = 9.91%-20.84%)

TABLE V. MAB of control of symptoms associated with change in mode of administration

Attribute	From level	To level	Mean MAB
Mode of administration (how the medicine is taken)	Topical	Infusion	59.60% (95% CI = 36.33%-82.87%)

rCSU therapies, with the goal of closely reflecting information that the patient and clinician utilize to make decisions in the real-world clinical setting. Also, early qualitative pretesting work suggests that the attributes included, as well as the information provided about the attributes, were considered complete by patients with CSU, thus minimizing the risk of leaving out key aspects of treatment choices in this population.

Another potential limitation of the study is the self-reporting of urticaria by members of a panel, which by the nature of recruitment, could not be confirmed via physical examination or diagnosis code. Our respondents' characteristics and preferences may not reflect the characteristics and preferences of the entire population of patients with CSU. However, we included robust screener questions that were used to confirm the eligibility of study participants. For example, respondents were not asked directly whether they had the condition but were instead asked to select symptoms that characterized the condition from a list of other symptoms and conditions. Respondents who selected all conditions were terminated. In addition, the sampling process was not weighted to ensure representativeness of the population of individuals with CSU, and this may have affected the representativeness of our results. Nevertheless, at the very least, the evidence collected through this study provides information on the breadth of perspectives in the population. Survey respondents may have differences in baseline knowledge and information about CSU and rCSU treatment characteristics that may make this study susceptible to information bias. However, by providing consistent information and tutorials on CSU, rCSU treatment attributes, and comprehension questions, we provided a common knowledge or information base for study participants. Respondents were also encouraged to use only information provided in the survey when answering the choice questions.

This study also has important strengths. As far as we know, this is the first study to investigate patient preferences for rCSU treatment attributes via a quantitative DCE approach allowing for a clear understanding of distribution of preferences. In addition, the study was conducted according to best practices in the design and analysis of DCE data. Furthermore, the pretest results and survey data, including validity checks and well-ordered preference estimates, show that the majority of the sample understood the survey content.

Conclusion

There are several current and emerging therapies for treatment of rCSU. These treatment options present varying risks, benefits,

mode of administration, and other treatment attributes. The findings from this study provide insights into how respondents with CSU symptoms prioritize the benefits, risks, and other attributes, as well as their willingness to make trade-offs between these attributes when considering treatment. The results of this study can inform the development of drugs for rCSU and the evaluation of future rCSU therapies by regulatory authorities.

DISCLOSURE STATEMENT

Disclosure of potential conflict of interest: The authors declare that they have no relevant conflicts of interest.

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