Urticaria Voices: Real-world experience of patients living with chronic spontaneous urticaria

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Study design

This study is part of a larger non-interventional cross-sectional research initiative with primary data collection using two independent questionnaires: one for patients diagnosed with chronic urticaria (CU) and one for physicians treating CU. Patients and physicians were recruited independently and physicians did not refer nor recruit their own patients to the study.

The full primary data collection phase involved two separate, self-completed online surveys:

- a 40-minute online survey of patients with CU from the United States of America (USA), Canada, United Kingdom (UK), Germany, France, Italy, and Japan completed a 40-minute online survey between February 22, 2022 and September 15, 2022.
- a 30-minute online survey with CU treating physicians (allergists, dermatologists or immunologists) in the same markets (USA, Canada, UK, Germany, France, Italy, and Japan) between February 16, 2022 and August 24, 2022.

Both patient and physician surveys included a variety of single-choice and multiple-choice questions, rating and ranking questions, open-ended questions as well as validated patient-reported outcome measures (PROMs): the Urticaria Control Test (UCT), the Patient Global Impression of Severity (PGI-S), and the Patient Activation Measure 13 (PAM-13). Questions outside the PROMs were reviewed by the steering committee for appropriateness and were slightly adjusted following the pilot interviews. To be able to directly compare answers from patients and physicians, the corresponding survey sections included complementary wording and identical choice options.

The online questionnaire had been developed by Ipsos SA with input from Novartis and an external steering committee of patient organizations and medical experts in the field ofCU.

Compliance with Novartis and regulatory standards provided assurance that the rights, safety, and well-being of patients participating in non-interventional studies are protected (consistent with the principles that have their origin in the Declaration of Helsinki) and that the study data are credible and responsibly reported.

This study was conducted in accordance with legal and regulatory requirements and fulfilled the criteria of a “European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) study” and followed the “ENCePP Code of Conduct.” This study was designed and was implemented and reported in accordance with the Guidelines for Good Pharmacoepidemiology Practices (GPP) of the International Society for Pharmacoepidemiology (ISPE 2016), the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines, and with the ethical principles laid down in the Declaration of Helsinki.

Institutional Review Board (IRB)/ethical approval was sought for this study based on the rationale that while the study includes “living people” who will complete the self-administered quantitative internet-based survey, there will be no articles or substances tested; hence Ipsos and the sponsor do not believe that these “living people” would be classified as “human subjects”. An exemption from ongoing oversight was sought after and obtained from an IRB, who reviewed and granted international approval. The process required submission of the study protocol and study materials (screener, informed consent, quantitative questionnaire) to the IRB for review.

Sample size calculation

The sample size was calculated using the standard formula for sample size estimation:

Sample size = $Z^2 \times (P \times [1-P]/M^2)$

where

Z represents the Z statistic for the desired confidence level (i.e., 1.96 for a 95% confidence interval)

P is the prevalence of the target population, (the conservative estimate of 0.5 is used for infinite populations [1, 2]).

M is the margin of error or confidence interval

To account for up to 5% of the data loss due to quality checks and cleaning, a total of 1040 participants were recruited across multiple countries (USA, Canada, UK, Germany, France, Italy, and Japan). The final sample size exceeded the calculated minimum and ensured sufficient power for robust statistical analysis while accounting for variability in population estimates.

Country-level data

Table S1 Canada - Patient characteristics and demographics

	All CSU (N=73)	**Only CSU (N=52)**	**Concomitant (N=21)**
Age (years), mean (SD)	45.0 (11.6)	45.5 (11.9)	43.5 (10.9)
[95% CI]	[42.3-47.7]	[42.3-48.7]	[38.8-48.2]
Gender, N (%)			
Female	60 (82%)	42 (81%)	18 (86%)
Male	13 (18%)	10 (19%)	3 (14%)
Years since onset, mean (SD)	10.2 (9.4)	10.4 (9.9)	9.6 (8.5)
Years since CU diagnosis, mean (SD)	7.2 (7.7)	7.5 (7.7)	6.4 (7.8)
No. years between onset and diagnosis, mean (SD)	3.0 (5.8)	2.9 (6.1)	3.2 (5.0)
Number of comorbidities, mean (SD)	2.8 (2.4)	3.5 (2.4)	3.6 (2.4)
Adequate control (UCT 12-16), N (%)	26 (36%)	20 (38%)	6 (29%)
Inadequate control (UCT <11), N (%)	47 (64%)	32 (62%)	15 (71%)
Number of current treatments, mean (SD)	2.0 (1.3)	2.0 (1.3)	2.1 (1.3)
Antihistamines, N (%)	54 (74%)	35 (67%)	19 (90%)
Steroids, N (%)	19 (26%)	15 (29%)	4 (19%)
Biologic, N (%)	29 (40%)	21 (40%)	8 (38%)

CI confidence interval; *CSU* chronic spontaneous urticaria*; CU* chronic urticaria; *SD* standard deviation; *UCT* Urticaria Control Test

Table S2 Canada - Physical symptoms of CSU patients other than itching and hives before, during, and after an exacerbation

	CSU patients (N=73) N (%)			**Adequately controlled CSU patients (N=26)** N (%)			**Inadequately controlled CSU patients (N=47)** N (%)		
	Before	During	After	Before	During	After	Before	During	After
Sleeping problems	14 (19%)	48 (66%)	17 (23%)	3 (12%)	18 (69%)	3 (12%)	11 (23%)	30 (64%)	14 (30%)
Pain	11 (15%)	37 (51%)	15 (21%)	3 (12%)	17 (65%)	6 (23%)	8 (17%)	20 (43%)	9 (19%)
Fatigue	17 (23%)	40 (55%)	29 (40%)	6 (23%)	12 (46%)	10 (38%)	11 (23%)	28 (60%)	19 (40%)
Reduced concentration	11 (15%)	44 (60%)	14 (19%)	3 (12%)	10 (38%)	6 (23%)	8 (17%)	34 (72%)	8 (17%)
Flushing	21 (29%)	35 (48%)	10 (14%)	5 (19%)	13 (50%)	0 (0%)	16 (34%)	22 (47%)	10 (21%)
Headaches	12 (16%)	19 (26%)	15 (21%)	5 (19%)	6 (23%)	2 (8%)	7 (15%)	13 (28%)	13 (28%)
Gastrointestinal symptoms	18 (25%)	23 (32%)	18 (25%)	6 (23%)	3 (12%)	5 (19%)	12 (26%)	20 (43%)	13 (28%)
Fever	4 (5%)	14 (19%)	4 (5%)	2 (8%)	4 (15%)	2 (8%)	2 (4%)	10 (21%)	2 (4%)
Palpitations	5 (7%)	16 (22%)	8 (11%)	2 (8%)	6 (23%)	3 (12%)	3 (6%)	10 (21%)	5 (11%)
Migraines	12 (16%)	10 (14%)	8 (11%)	3 (12%)	0 (0%)	1 (4%)	9 (19%)	10 (21%)	7 (15%)
Wheezing	6 (8%)	15 (21%)	7 (10%)	2 (8%)	5 (19%)	1 (4%)	4 (9%)	10 (21%)	6 (13%)
Memory problems	9 (12%)	19 (26%)	16 (22%)	3 (12%)	4 (15%)	5 (19%)	6 (13%)	15 (32%)	11 (23%)

CSU chronic spontaneous urticaria; *UCT* Urticaria Control Test

Note: The question in the patient survey used the patient-friendly word “outbreak.” Disease control was measured by UCT, representing patient control in the past 4 weeks - adequate control (UCT12-16), inadequate control (UCT <12).

Table S3 Canada - Emotional, cognitive, and social burden of CSU

	CSU patients (N=73)
Overall negative impact, mean (SD)	6.3 (2.4)
Mental and emotional well-being, mean (SD)	6.2 (3.0)
Social life and intimate relationships, mean (SD)	5.6 (3.3)
Activities of daily living, mean (SD)	5.2 (3.1)
Family life and fulfilling responsibilities to others, mean (SD)	4.8 (3.1)
Professional and academic life, mean (SD)	4.6 (3.2)
Financial life, mean (SD)	3.9 (2.8)

CSU chronic spontaneous urticaria; *SD* standard deviation

Note. Measures of negative impact were collected on a scale from 1 – not at all impacted to 10 – very impacted.

Table S4 Canada - Stigma associated with CSU among patients

	CSU patients (N=73) N (%)
Being asked if I'm contagious	25 (34%)
Being stared at in public	24 (33%)
People refusing to shake my hand or touch me	6 (8%)
Being made the center of jokes	8 (11%)
Bullying	8 (11%)
Humiliation in public	7 (10%)
Public discrimination	7 (10%)
None of the above	30 (41%)

CSU chronic spontaneous urticaria

Table S5 France - Patient characteristics and demographics

	All CSU (N=86)	**Only CSU (N=53)**	**Concomitant (N=33)**
Age (years), mean (SD)	44.2 (14.6)	44.3 (15.2)	44.2 (13.8)
[95% CI]	[41.1-47.3]	[40.2-48.4]	[39.5-48.9]
Gender, N (%)			
Female	57 (66%)	32 (60%)	25 (76%)
Male	29 (34%)	21 (40%)	8 (24%)
Years since onset, mean (SD)	10.4 (11.7)	9.7 (12.1)	11.4 (11.3)
Years since CU diagnosis, mean (SD)	7.8 (10.0)	7.1 (9.6)	9.0 (10.7)
No. years between onset and diagnosis, mean (SD)	2.4 (5.5)	2.5 (6.0)	2.3 (4.5)
Number of comorbidities, mean (SD)	2.0 (1.8)	1.7 (1.7)	2.5 (1.9)
Adequate control (UCT 12-16), N (%)	18 (21%)	17 (32%)	1 (3%)
Inadequate control (UCT <11), N (%)	68 (79%)	36 (68%)	32 (97%)
Number of current treatments, mean (SD)	1.9 (1.7)	1.7 (1.6)	2.2 (1.8)
Antihistamines, N (%)	63 (73%)	37 (70%)	26 (79%)
Steroids, N (%)	29 (34%)	15 (28%)	14 (42%)
Biologic, N (%)	25 (29%)	16 (30%)	9 (27%)

CI confidence interval; *CSU chronic spontaneous urticaria; CU* chronic urticaria; *SD* standard deviation; *UCT* Urticaria Control Test

Table S6 France - Physical symptoms of CSU patients other than itching and hives before, during, and after an exacerbation

	CSU patients (N=86)			**Adequately controlled CSU patients (N=18)**			**Inadequately controlled CSU patients (N=68)**		
	N (%)			N (%)			N (%)		
	Before	During	After	Before	During	After	Before	During	After
Sleeping problems	28 (33%)	46 (53%)	32 (37%)	7 (39%)	7 (39%)	9 (50%)	21 (31%)	39 (57%)	23 (34%)
Pain	21 (24%)	42 (49%)	32 (37%)	5 (28%)	7 (39%)	4 (22%)	16 (24%)	35 (51%)	28 (41%)
Fatigue	26 (30%)	42 (49%)	30 (35%)	7 (39%)	6 (33%)	8 (44%)	19 (28%)	36 (53%)	22 (32%)
Reduced concentration	19 (22%)	33 (38%)	20 (23%)	2 (11%)	6 (33%)	6 (33%)	17 (25%)	27 (40%)	14 (21%)
Flushing	11 (13%)	19 (22%)	7 (8%)	1 (6%)	1 (6%)	0 (0%)	10 (15%)	18 (26%)	7 (10%)
Headaches	20 (23%)	22 (26%)	15 (17%)	2 (11%)	2 (11%)	2 (11%)	18 (26%)	20 (29%)	13 (19%)
Gastrointestinal symptoms	20 (23%)	31 (36%)	15 (17%)	5 (28%)	8 (44%)	3 (17%)	15 (22%)	23 (34%)	12 (18%)
Fever	13 (15%)	19 (22%)	3 (3%)	1 (6%)	1 (6%)	0 (0%)	12 (18%)	18 (26%)	3 (4%)
Palpitations	14 (16%)	23 (27%)	12 (14%)	2 (11%)	3 (17%)	2 (11%)	12 (18%)	20 (29%)	10 (15%)
Migraines	15 (17%)	17 (20%)	11 (13%)	1 (6%)	0 (0%)	0 (0%)	14 (21%)	17 (25%)	11 (16%)
Wheezing	12 (14%)	15 (17%)	14 (16%)	0 (0%)	2 (11%)	0 (0%)	12 (18%)	13 (19%)	14 (21%)
Memory problems	14 (16%)	21 (24%)	17 (20%)	2 (11%)	2 (11%)	3 (17%)	12 (18%)	19 (28%)	14 (21%)

CSU chronic spontaneous urticaria; *UCT* Urticaria Control Test

Note. The question in the patient survey used the patient-friendly word “outbreak”. Disease control was measured by UCT, representing patient control in the past 4 weeks - adequate control (UCT = 12-16), inadequate control (UCT <12).

Table S7 France - Emotional, cognitive, and social burden of CSU

	CSU patients (N=86)
Overall negative impact, mean (SD)	6.3 (2.2)
Mental and emotional well-being, mean (SD)	6.0 (2.7)
Social life and intimate relationships, mean (SD)	5.4 (3.0)
Activities of daily living, mean (SD)	5.3 (3.0)
Family life and fulfilling responsibilities to others, mean (SD)	4.8 (2.9)
Professional and academic life, mean (SD)	4.6 (3.2)
Financial life, mean (SD)	3.7 (2.7)

CSU chronic spontaneous urticaria; *SD* standard deviation

Note. Measures of negative impact were collected on a scale from 1 – Not at all impacted to 10 – Very impacted.

Table S8 France - Stigma associated with CSU among patients

	CSU patients (N=86) N (%)
Being asked if I'm contagious	18 (21%)
Being stared at in public	22 (26%)
People refusing to shake my hand or touch me	9 (10%)
Being made the center of jokes	19 (22%)
Bullying	5 (6%)
Humiliation in public	7 (8%)
Public discrimination	2 (2%)
None of the above	41 (48%)

CSU chronic spontaneous urticaria

Table S9 Germany - Patient characteristics and demographics

	All CSU (N=79)	**Only CSU (N=44)**	**Concomitant (N=35)**
Age (years), mean (SD)	37.7 (11.8)	42.4 (11.1)	31.7 (10.0)
[95% CI]	[35.1-40.3]	[39.1-45.7]	[28.4-35.0]
Gender, N (%)			
Female	34 (43%)	9 (20%)	25 (71%)
Male	45 (57%)	35 (80%)	10 (29%)
Years since onset, mean (SD)	9.2 (8.4)	8.5 (9.7)	10.0 (6.3)
Years since CU diagnosis, mean (SD)	7.9 (7.9)	7.5 (9.2)	8.4 (5.9)
No. years between onset and diagnosis, mean (SD)	1.2 (1.4)	0.8 (1.5)	1.6 (1.1)
Number of comorbidities, mean (SD)	2.8 (2.3)	2.2 (2.4)	3.6 (1.9)
Adequate control (UCT 12-16), N (%)	10 (13%)	8 (18%)	2 (6%)
Inadequate control (UCT <11), N (%)	69 (87%)	36 (82%)	33 (94%)
Number of current treatments, mean (SD)	5.0 (4.6)	3.3 (3.8)	7.1 (4.8)
Antihistamines, N (%)	65 (82%)	32 (73%)	33 (94%)
Steroids, N (%)	52 (66%)	26 (59%)	26 (74%)
Biologic, N (%)	35 (44%)	12 (27%)	23 (66%)

CI confidence interval; *CU* chronic urticaria; *SD* standard deviation; *UCT* Urticaria Control Test

Table S10 Germany - Physical symptoms of CSU patients other than itching and hives before, during, and after an exacerbation

	CSU patients (N=79)			**Adequately controlled CSU patients (N=10)**			**Inadequately controlled CSU patients (N=69)**		
	N (%)			N (%)			N (%)		
	Before	During	After	Before	During	After	Before	During	After
Sleeping problems	36 (46%)	39 (49%)	18 (23%)	2 (20%)	5 (50%)	3 (30%)	34 (49%)	34 (29%)	15 (22%)
Pain	25 (32%)	36 (46%)	12 (25%)	0 (0%)	9 (90%)	2 (20%)	25 (36%)	27 (39%)	10 (14%)
Fatigue	31 (39%)	32 (41%)	13 (16%)	1 (10%)	3 (30%)	1 (10%)	30 (43%)	29 (42%)	12 (17%)
Reduced concentration	26 (33%)	25 (32%)	9 (11%)	2 (20%)	6 (60%)	3 (30%)	24 (35%)	19 (28%)	6 (9%)
Flushing	28 (35%)	26 (33%)	13 (16%)	3 (30%)	3 (30%)	0 (0%)	25 (36%)	23 (33%)	13 (19%)
Headaches	33 (42%)	27 (34%)	7 (9%)	2 (20%)	2 (20%)	0 (0%)	31 (45%)	25 (36%)	7 (10%)
Gastrointestinal symptoms	26 (33%)	16 (20%)	5 (6%)	1 (10%)	1 (10%)	1 (10%)	25 (36%)	15 (22%)	4 (6%)
Fever	25 (32%)	18 (23%)	7 (9%)	1 (10%)	4 (40%)	0 (0%)	24 (35%)	14 (20%)	7 (10%)
Palpitations	20 (25%)	12 (15%)	6 (8%)	0 (0%)	1 (10%)	0 (0%)	20 (29%)	11 (16%)	6 (9%)
Migraines	29 (37%)	18 (23%)	9 (11%)	1 (10%)	1 (10%)	0 (0%)	28 (41%)	17 (25%)	9 (13%)
Wheezing	24 (30%)	12 (15%)	2 (3%)	1 (10%)	1 (10%)	0 (0%)	23 (33%)	11 (16%)	2 (3%)
Memory problems	23 (29%)	9 (11%)	1 (1%)	1 (10%)	0 (0%)	0 (0%)	22 (32%)	9 (13%)	1 (1%)

CSU chronic spontaneous urticaria

Note. The question in the patient survey used the patient-friendly word “outbreak”. Disease control was measured by UCT, representing patient control in the past 4 weeks - Adequate control (UCT = 12-16), Inadequate control (UCT <12).

Table S11 Germany - Emotional, cognitive, and social burden of CSU

	CSU patients (N=79)
Overall negative impact, mean (SD)	7.5 (2.3)
Mental and emotional well-being, mean (SD)	4.8 (2.9)
Social life and intimate relationships, mean (SD)	4.2 (2.7)
Activities of daily living, mean (SD)	4.2 (2.7)
Family life and fulfilling responsibilities to others, mean (SD)	3.5 (2.5)
Professional and academic life, mean (SD)	4.0 (2.7)
Financial life, mean (SD)	3.7 (2.8)

CSU chronic spontaneous urticaria; *SD* standard deviation

Note. Measures of negative impact were collected on a scale from 1 – Not at all impacted to 10 – Very impacted.

Table S12 Germany - Stigma associated with CSU among patients

	CSU patients (N=79) N (%)
Being asked if I'm contagious	32 (41%)
Being stared at in public	34 (43%)
People refusing to shake my hand or touch me	21 (27%)
Being made the center of jokes	13 (16%)
Bullying	15 (19%)
Humiliation in public	17 (22%)
Public discrimination	14 (18%)
None of the above	18 (23%)

CSU chronic spontaneous urticaria

Table S13 Italy - Patient characteristics and demographics

	All CSU (N=64)	**Only CSU (N=41)**	**Concomitant (N=23)**
Age (years), mean (SD)	42.4 (10.9)	43.9 (11.6)	39.8 (9.3)
[95% CI]	[39.7-45.1]	[40.3-47.5]	[36.0-43.6]
Gender, N (%)			
Female	45 (70%)	30 (73%)	15 (65%)
Male	19 (30%)	11 (27%)	8 (35%)
Years since onset, mean (SD)	9.6 (11.1)	8.8 (11.5)	11.1 (10.5)
Years since CU diagnosis, mean (SD)	7.8 (8.3)	6.6 (7.1)	10.1 (9.9)
No. years between onset and diagnosis, mean (SD)	1.7 (6.8)	2.2 (8.4)	0.9 (1.4)
Number of comorbidities, mean (SD)	1.9 (1.5)	1.6 (1.4)	2.3 (1.6)
Adequate control (UCT 12-16), N (%)	10 (16%)	7 (17%)	3 (13%)
Inadequate control (UCT <11), N (%)	54 (84%)	34 (83%)	20 (87%)
Number of current treatments, mean (SD)	2.1 (1.3)	2.1 (1.4)	2.0 (1.2)
Antihistamines, N (%)	53 (83%)	35 (85%)	18 (78%)
Steroids, N (%)	34 (53%)	22 (54%)	12 (52%)
Biologic, N (%)	5 (8%)	3 (7%)	2 (9%)

CI confidence interval; *CSU* chronic spontaneous urticaria; *SD* standard deviation; *UCT* Urticaria Control Test

Table S14 Italy - Physical symptoms of CSU patients other than itching and hives before, during, and after an exacerbation

	CSU patients (N=64)			**Adequately controlled CSU patients (N=10)**			**Inadequately controlled CSU patients (N=54)**		
	N (%)			N (%)			N (%)		
	Before	During	After	Before	During	After	Before	During	After
Sleeping problems	15 (23%)	37 (58%)	16 (25%)	1 (10%)	2 (20%)	2 (20%)	14 (26%)	35 (65%)	14 (26%)
Pain	16 (25%)	42 (66%)	15 (23%)	2 (20%)	4 (40%)	2 (20%)	14 (26%)	38 (70%)	13 (24%)
Fatigue	24 (38%)	32 (50%)	25 (39%)	6 (60%)	3 (30%)	3 (30%)	18 (33%)	29 (54%)	22 (41%)
Reduced concentration	12 (19%)	29 (45%)	9 (14%)	0 (0%)	2 (20%)	1 (10%)	12 (22%)	27 (50%)	8 (15%)
Flushing	14 (22%)	25 (39%)	8 (13%)	2 (20%)	2 (20%)	1 (10%)	12 (22%)	23 (43%)	7 (13%)
Headaches	18 (28%)	22 (34%)	8 (13%)	2 (20%)	2 (20%)	0 (0%)	16 (30%)	20 (37%)	8 (15%)
Gastrointestinal symptoms	10 (16%)	21 (33%)	9 (14%)	0 (0%)	2 (20%)	2 (20%)	10 (19%)	19 (35%)	7 (13%)
Fever	9 (14%)	12 (19%)	3 (5%)	0 (0%)	1 (10%)	1 (10%)	9 (17%)	11 (20%)	2 (4%)
Palpitations	8 (13%)	14 (22%)	5 (8%)	0 (0%)	1 (10%)	0 (0%)	8 (15%)	13 (24%)	5 (9%)
Migraines	21 (33%)	22 (34%)	6 (9%)	1 (10%)	2 (20%)	0 (0%)	20 (37%)	20 (37%)	6 (11%)
Wheezing	8 (13%)	11 (17%)	5 (8%)	0 (0%)	0 (0%)	1 (10%)	8 (15%)	11 (20%)	4 (7%)
Memory problems	9 (14%)	8 (13%)	2 (3%)	1 (10%)	1 (10%)	0 (0%)	8 (15%)	7 (13%)	2 (4%)

CSU chronic spontaneous urticaria; *UCT* Urticaria Control Test

Note. The question in the patient survey used the patient-friendly word “outbreak”. Disease control was measured by UCT, representing patient control in the past 4 weeks - Adequate control (UCT = 12-16), Inadequate control (UCT <12).

Table S15 Emotional, cognitive, and social burden of CSU

	CSU patients (N=64)
Overall negative impact, mean (SD)	6.3 (1.6)
Mental and emotional well-being, mean (SD)	6.2 (2.3)
Social life and intimate relationships, mean (SD)	6.2 (2.1)
Activities of daily living, mean (SD)	5.6 (2.2)
Family life and fulfilling responsibilities to others, mean (SD)	5.3 (2.3)
Professional and academic life, mean (SD)	5.3 (2.6)
Financial life, mean (SD)	5.7 (2.5)

CSU chronic spontaneous urticaria; *SD* standard deviation

Note. Measures of negative impact were collected on a scale from 1 – Not at all impacted to 10 – Very impacted.

Table S16 Italy - Stigma associated with CSU among patients

	CSU patients (N=64) N (%)
Being asked if I'm contagious	19 (30%)
Being stared at in public	22 (34%)
People refusing to shake my hand or touch me	9 (14%)
Being made the center of jokes	4 (6%)
Bullying	3 (5%)
Humiliation in public	6 (9%)
Public discrimination	4 (6%)
None of the above	25 (39%)

CSU chronic spontaneous urticaria

Table S17 Japan - Patient characteristics and demographics

	All CSU (N=41)	**Only CSU (N=30)**	**Concomitant (N=11)**
Age (years), mean (SD)	49.1 (8.3)	50.0 (8.4)	46.8 (8.2)
[95% CI]	[46.6-51.6]	[47.0-53.0]	[42.0-51.6]
Gender, N (%)			
Female	21 (51%)	12 (40%)	9 (82%)
Male	20 (49%)	18 (60%)	2 (18%)
Years since onset, mean (SD)	12.9 (13.8)	11.4 (12.7)	17.3 (16.3)
Years since CU diagnosis, mean (SD)	10.6 (12.1)	9.3 (11.7)	13.9 (13.1)
No. years between onset and diagnosis, mean (SD)	2.3 (7.1)	2.0 (5.8)	3.3 (10.2)
Number of comorbidities, mean (SD)	1.3 (1.5)	1.2 (1.5)	1.5 (1.6)
Adequate control (UCT 12-16), N (%)	13 (32%)	9 (30%)	4 (36%)
Inadequate control (UCT <11), N (%)	28 (68%)	21 (70%)	7 (64%)
Number of current treatments, mean (SD)	1.6 (1.1)	1.7 (1.2)	1.5 (0.8)
Antihistamines, N (%)	33 (80%)	22 (73%)	11 (100%)
Steroids, N (%)	12 (29%)	9 (30%)	3 (27%)
Biologic, N (%)	3 (7%)	3 (10%)	0 (0%)

CI confidence interval; *CSU* chronic spontaneous urticaria; *SD* standard deviation; *UCT* Urticaria Control Test

Table S18 Japan - Physical symptoms of CSU patients other than itching and hives before, during, and after an exacerbation

	CSU patients (N=41)			**Adequately controlled CSU patients (N=13)**			**Inadequately controlled CSU patients (N=28)**		
	N (%)			N (%)			N (%)		
	Before	During	After	Before	During	After	Before	During	After
Sleeping problems	3 (7%)	15 (37%)	6 (15%)	1 (8%)	4 (31%)	1 (8%)	2 (7%)	11 (39%)	5 (18%)
Pain	3 (7%)	6 (15%)	5 (12%)	0 (0%)	0 (0%)	0 (0%)	3 (11%)	6 (21%)	5 (18%)
Fatigue	9 (22%)	14 (34%)	10 (24%)	2 (15%)	3 (20%)	2 (15%)	7 (25%)	11 (39%)	8 (29%)
Reduced concentration	1 (2%)	15 (37%)	6 (15%)	0 (0%)	4 (31%)	0 (0%)	1 (4%)	11 (39%)	6 (21%)
Flushing	3 (7%)	10 (24%)	4 (10%)	0 (0%)	1 (8%)	0 (0%)	3 (11%)	9 (32%)	4 (14%)
Headaches	2 (5%)	1 (2%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	2 (7%)	1 (4%)	1 (4%)
Gastrointestinal symptoms	2 (5%)	2 (5%)	2 (5%)	1 (8%)	1 (8%)	1 (8%)	1 (4%)	1 (4%)	1 (4%)
Fever	1 (2%)	5 (12%)	2 (5%)	0 (0%)	1 (8%)	0 (0%)	1 (4%)	4 (14%)	2 (7%)
Palpitations	3 (7%)	3 (7%)	4 (10%)	1 (8%)	1 (8%)	1 (8%)	2 (7%)	2 (7%)	3 (11%)
Migraines	3 (7%)	1 (2%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	3 (11%)	1 (4%)	1 (4%)
Wheezing	1 (2%)	3 (7%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)	3 (11%)	1 (4%)
Memory problems	0 (0%)	3 (7%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)	0 (0%)	2 (7%)	0 (0%)

CSU chronic spontaneous urticaria; *UCT* Urticaria Control Test

Note. The question in the patient survey used the patient-friendly word “outbreak”. Disease control was measured by UCT, representing patient control in the past 4 weeks - Adequate control (UCT 12-16), Inadequate control (UCT <12).

Table S19 Japan - Emotional, cognitive, and social burden of CSU

	CSU patients (N=41)
Overall negative impact, mean (SD)	6.8 (2.1)
Mental and emotional well-being, mean (SD)	5.5 (3.0)
Social life and intimate relationships, mean (SD)	4.4 (3.2)
Activities of daily living, mean (SD)	4.0 (2.7)
Family life and fulfilling responsibilities to others, mean (SD)	3.7 (2.8)
Professional and academic life, mean (SD)	3.5 (2.8)
Financial life, mean (SD)	4.8 (2.8)

CSU chronic spontaneous urticaria; *SD* standard deviation

Note. Measures of negative impact were collected on a scale from 1 – Not at all impacted to 10 – Very impacted.

Table S20 Japan - Stigma associated with CSU among patients

	CSU patients (N=41) N (%)
Being asked if I'm contagious	6 (15%)
Being stared at in public	4 (10%)
People refusing to shake my hand or touch me	4 (10%)
Being made the center of jokes	1 (2%)
Bullying	1 (2%)
Humiliation in public	0 (0%)
Public discrimination	0 (0%)
None of the above	31 (76%)

CSU chronic spontaneous urticaria

Table S21 UK - Patient characteristics and demographics

	All CSU (N=87)	**Only CSU (N=45)**	**Concomitant (N=42)**
Age (years), mean (SD)	43.2 (11.3)	42.6 (12.6)	43.8 (9.9)
[95% CI]	[40.8-45.6]	[38.9-46.3]	[40.8-46.8]
Gender, N (%)			
Female	51 (59%)	31 (69%)	20 (48%)
Male	36 (41%)	14 (31%)	22 (52%)
Years since onset, mean (SD)	8.9 (9.2)	6.9 (6.1)	11.0 (11.3)
Years since CU diagnosis, mean (SD)	6.8 (7.8)	5.7 (5.6)	7.9 (9.5)
No. years between onset and diagnosis, mean (SD)	2.1 (5.5)	1.2 (2.1)	3.1 (7.5)
Number of comorbidities, mean (SD)	3.1 (4.4)	1.8 (1.9)	4.5 (5.7)
Adequate control (UCT 12-16), N (%)	14 (16%)	9 (20%)	5 (12%)
Inadequate control (UCT <11), N (%)	73 (84%)	36 (80%)	37 (88%)
Number of current treatments, mean (SD)	3.8 (2.5)	3.4 (2.5)	4.3 (2.5)
Antihistamines, N (%)	77 (89%)	38 (84%)	39 (93%)
Steroids, N (%)	56 (64%)	28 (62%)	28 (67%)
Biologic, N (%)	44 (51%)	19 (42%)	25 (60%)

CI confidence interval; *CSU* chronic spontaneous urticaria; *CU* chronic urticaria*; SD* standard deviation; *UCT* Urticaria Control Test; *UK* United Kingdom

Table S22 UK - Physical symptoms of CSU patients other than itching and hives before, during, and after an exacerbation

	CSU patients (N=87)			**Adequately controlled CSU patients (N=14)**			**Inadequately controlled CSU patients (N=73)**		
	N (%)			N (%)			N (%)		
	Before	During	After	Before	During	After	Before	During	After
Sleeping problems	26 (30%)	64 (74%)	28 (32%)	4 (29%)	9 (64%)	3 (21%)	22 (30%)	55 (75%)	25 (34%)
Pain	38 (44%)	49 (56%)	32 (37%)	3 (21%)	6 (43%)	4 (29%)	35 (48%)	43 (59%)	28 (38%)
Fatigue	32 (37%)	49 (56%)	29 (33%)	6 (43%)	7 (50%)	6 (43%)	26 (36%)	42 (58%)	23 (32%)
Reduced concentration	20 (23%)	41 (47%)	14 (16%)	2 (14%)	8 (57%)	5 (36%)	18 (25%)	33 (45%)	9 (12%)
Flushing	28 (32%)	46 (53%)	26 (30%)	3 (21%)	5 (36%)	2 (14%)	25 (34%)	41 (56%)	24 (33%)
Headaches	27 (31%)	41 (47%)	23 (26%)	2 (14%)	2 (14%)	1 (7%)	25 (34%)	39 (53%)	22 (30%)
Gastrointestinal symptoms	16 (18%)	40 (46%)	8 (9%)	2 (14%)	3 (21%)	1 (7%)	14 (19%)	37 (51%)	7 (10%)
Fever	28 (32%)	40 (46%)	19 (22%)	3 (21%)	5 (36%)	1 (7%)	25 (34%)	35 (48%)	18 (25%)
Palpitations	23 (26%)	34 (39%)	20 (23%)	0 (0%)	4 (29%)	2 (14%)	23 (32%)	30 (41%)	18 (25%)
Migraines	16 (18%)	28 (32%)	25 (29%)	5 (36%)	2 (14%)	3 (21%)	11 (15%)	26 (36%)	22 (30%)
Wheezing	15 (17%)	31 (36%)	11 (13%)	2 (14%)	2 (14%)	1 (7%)	13 (18%)	29 (40%)	10 (14%)
Memory problems	10 (11%)	24 (28%)	10 (11%)	1 (7%)	2 (14%)	1 (7%)	9 (12%)	22 (30%)	9 (12%)

CSU chronic spontaneous urticaria; *UCT* Urticaria Control Test; *UK* United Kingdom

Note. The question in the patient survey used the patient-friendly word “outbreak”. Disease control was measured by UCT, representing patient control in the past 4 weeks - Adequate control (UCT 12-16), Inadequate control (UCT <12).

Table S23 UK - Emotional, cognitive and social burden of CSU

	CSU patients (N=87)
Overall negative impact, mean (SD)	6.7 (2.2)
Mental and emotional well-being, mean (SD)	5.8 (2.7)
Social life and intimate relationships, mean (SD)	5.8 (2.5)
Activities of daily living, mean (SD)	5.9 (2.6)
Family life and fulfilling responsibilities to others, mean (SD)	5.5 (2.6)
Professional and academic life, mean (SD)	5.2 (2.8)
Financial life, mean (SD)	4.8 (2.8)

CSU chronic spontaneous urticaria; *SD* standard deviation; *UK* United Kingdom

Note. Measures of negative impact were collected on a scale from 1 – Not at all impacted to 10 – Very impacted.

Table S24 UK - Stigma associated with CSU among patients

	CSU patients (N=87) N (%)
Being asked if I'm contagious	39 (45%)
Being stared at in public	33 (38%)
People refusing to shake my hand or touch me	23 (26%)
Being made the center of jokes	18 (21%)
Bullying	17 (20%)
Humiliation in public	17 (20%)
Public discrimination	20 (23%)
None of the above	20 (23%)

CSU chronic spontaneous urticaria; *UK* United Kingdom

Table S25 USA - Patient characteristics and demographics

	All CSU (N=152)	**Only CSU (N=105)**	**Concomitant (N=47)**
Age (years), mean (SD)	39.6 (10.4)	40.0 (11.0)	38.7 (8.9)
[95% CI]	[37.9-41.3]	[37.9-42.1]	[36.2-41.2]
Gender, N (%)			
Female	94 (62%)	69 (66%)	25 (53%)
Male	58 (38%)	36 (34%)	22 (47%)
Years since onset, mean (SD)	6.9 (9.4)	5.3 (7.2)	10.7 (12.4)
Years since CU diagnosis, mean (SD)	5.3 (7.2)	3.9 (5.2)	8.4 (9.7)
No. years between onset and diagnosis, mean (SD)	1.6 (5.3)	1.3 (4.7)	2.3 (6.3)
Number of comorbidities, mean (SD)	2.4 (2.6)	2.1 (2.4)	3.3 (2.8)
Adequate control (UCT 12-16), N (%)	23 (15%)	19 (18%)	4 (9%)
Inadequate control (UCT <11), N (%)	129 (85%)	86 (82%)	43 (91%)
Number of current treatments, mean (SD)	2.8 (1.9)	2.5 (1.7)	3.6 (2.0)
Antihistamines, N (%)	115 (76%)	73 (70%)	42 (89%)
Steroids, N (%)	88 (58%)	58 (55%)	30 (64%)
Biologic, N (%)	52 (34%)	32 (30%)	20 (43%)

CI confidence interval; *CSU* chronic spontaneous urticaria; *CU* chronic urticaria*; SD* standard deviation; *UCT* Urticaria Control Test; *USA* United States of America

Table S26 USA - Physical symptoms of CSU patients other than itching and hives before, during, and after an exacerbation

	CSU patients (N=152)			**Adequately controlled CSU patients (N=23)**			**Inadequately controlled CSU patients (N=129)**		
	N (%)			N (%)			N (%)		
	Before	During	After	Before	During	After	Before	During	After
Sleeping problems	40 (26%)	111 (73%)	46 (30%)	7 (30%)	16 (70%)	4 (17%)	33 (26%)	95 (74%)	42 (33%)
Pain	60 (39%)	106 (70%)	46 (30%)	7 (30%)	16 (70%)	2 (9%)	53 (41%)	90 (70%)	44 (34%)
Fatigue	41 (27%)	76 (50%)	47 (31%)	6 (26%)	14 (61%)	5 (22%)	35 (27%)	62 (48%)	42 (33%)
Reduced concentration	23 (15%)	64 (42%)	31 (20%)	3 (13%)	12 (52%)	4 (17%)	20 (16%)	52 (40%)	27 (21%)
Flushing	27 (18%)	50 (33%)	18 (12%)	5 (22%)	7 (30%)	2 (9%)	22 (17%)	43 (33%)	16 (12%)
Headaches	52 (34%)	74 (49%)	37 (24%)	5 (22%)	4 (17%)	4 (17%)	47 (36%)	70 (54%)	33 (26%)
Gastrointestinal symptoms	30 (20%)	50 (33%)	26 (17%)	4 (17%)	8 (35%)	4 (17%)	26 (20%)	42 (33%)	22 (17%)
Fever	20 (13%)	46 (30%)	18 (12%)	3 (13%)	6 (26%)	1 (4%)	17 (13%)	40 (31%)	17 (13%)
Palpitations	14 (9%)	45 (30%)	13 (9%)	0 (0%)	4 (17%)	0 (0%)	14 (11%)	41 (32%)	13 (10%)
Migraines	26 (17%)	43 (28%)	20 (13%)	4 (17%)	5 (22%)	3 (13%)	22 (17%)	38 (29%)	17 (13%)
Wheezing	8 (5%)	39 (26%)	17 (11%)	1 (4%)	2 (9%)	1 (4%)	7 (5%)	37 (29%)	16 (12%)

Memory problems	14 (9%)	34 (22%)	19 (13%)	2 (9%)	3 (13%)	2 (9%)	12 (9%)	31 (24%)	17 (13%)

CSU chronic spontaneous urticaria; *UCT* Urticaria Control Test; *USA* United States of America
Note. The question in the patient survey used the patient-friendly word “outbreak” Disease control was measured by UCT, representing patient control in the past 4 weeks - Adequate control (UCT=12-16), Inadequate control (UCT <12)

Table S27 USA - Emotional, cognitive, and social burden of CSU

	CSU patients (N=152)
Overall negative impact, mean (SD)	6.6 (2.2)
Mental and emotional well-being, mean (SD)	6.7 (2.6)
Social life and intimate relationships, mean (SD)	6.2 (2.7)
Activities of daily living, mean (SD)	6.0 (2.8)
Family life and fulfilling responsibilities to others, mean (SD)	5.7 (2.8)
Professional and academic life, mean (SD)	5.4 (2.9)
Financial life, mean (SD)	5.5 (2.8)

CSU chronic spontaneous urticaria; *SD* standard deviation; *USA* United States of America

Note. Measures of negative impact were collected on a scale from 1 – Not at all impacted to 10 – Very impacted.

Table S28 USA - Stigma associated with CSU among patients

	CSU patients (N=152) N (%)
Being asked if I'm contagious	53 (35%)
Being stared at in public	53 (35%)
People refusing to shake my hand or touch me	31 (20%)
Being made the center of jokes	25 (16%)
Bullying	17 (20%)
Humiliation in public	19 (13%)
Public discrimination	10 (7%)
None of the above	58 (38%)

CSU chronic spontaneous urticaria; *USA* United States America

References:

1. Bland JM. The tyranny of power: is there a better way to calculate sample size? BMJ. 2009;6;339:b3985.
2. Pourhoseingholi MA, Vahedi M, Rahimzadeh M. Sample size calculation in medical studies. Gastroenterol Hepatol Bed Bench. 2013;6(1):14-7.