

**Abstract N°: 65**
**Remibrutinib (LOU064) showed good stability of response in patients with chronic spontaneous urticaria: A novel exploratory analysis of data from the Phase 2b study**

Marcus Maurer<sup>\*1, 2</sup>, Ana Giménez-Arnau<sup>3</sup>, Vipul Jain<sup>4</sup>, Adam Reich<sup>5</sup>, Christine-Elke Ortmann<sup>6</sup>, Pauline Walsh<sup>7</sup>, Sibylle Haemmerle<sup>6</sup>

<sup>1</sup>Urticaria Center of Reference and Excellence (UCARE), Institute of Allergology, Charité–Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt–Universität zu Berlin, Berlin, Germany, <sup>2</sup>Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Allergology and Immunology, Berlin, Germany, <sup>3</sup>Department of Dermatology, Hospital del Mar - IMIM, Universitat Pompeu Fabra, Barcelona, Spain, <sup>4</sup>Division of Clinical Immunology and Allergy, Department of Medicine, McMaster University, Hamilton, Ontario, Canada, <sup>5</sup>Department of Dermatology, Institute of Medical Sciences, Medical College of Rzeszów University, Rzeszów, Poland, <sup>6</sup>Novartis Pharma AG, Basel, Switzerland, <sup>7</sup>Novartis Ireland Limited, Dublin, Ireland

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is characterised by recurrent wheals (hives) and/or angio-oedema for more than 6 weeks. Intermittent worsening of CSU can have a major impact on patients' well-being. Remibrutinib (LOU064) is an oral, highly selective Bruton's tyrosine kinase (BTK) inhibitor that offers fast disease control in patients with CSU who remain symptomatic despite treatment with second-generation H1-antihistamines. It has shown clinical efficacy and a favourable safety profile for up to 12 weeks in a Phase 2b dose-finding study in patients with CSU. Here, we explore the stability of response to remibrutinib during the 12-week treatment period in this Phase 2b study.

**Materials & Methods:**

In the remibrutinib Phase 2b study (NCT03926611), 311 patients with CSU were equally randomised to remibrutinib 10 mg once daily (q.d.)/35 mg q.d./100 mg q.d./10 mg twice daily (b.i.d.)/25 mg b.i.d./100 mg b.i.d. or placebo for 12 weeks. The rates of patients experiencing worsening episodes, the duration of worsening episode, the time to first worsening episode, and the intensity of worsening episode during the treatment period were assessed. A worsening episode was defined as a temporary increase of rolling weekly Urticaria Activity Score (rUAS7)  $\geq 10$  (based on minimal clinically important difference for UAS7) from the lowest rUAS7 achieved before the episode. The end of the worsening episode was defined as the day when rUAS7 dropped back to  $< 10$  points above the initial lowest rUAS7 before the episode. The rUAS7 was calculated as the UAS7 for every possible set of 7 consecutive days across the study treatment period. Patients captured their daily UAS in an e-diary. The number of days, including the first day, spent with a worsening episode was calculated as the duration of the worsening episode. Overall intensity was calculated based on the Area Under the Curve (AUC) for rUAS7 when a patient experienced worsening episode; and peak intensity was defined as maximum rUAS7 when a patient experienced a worsening episode.

**Results:**

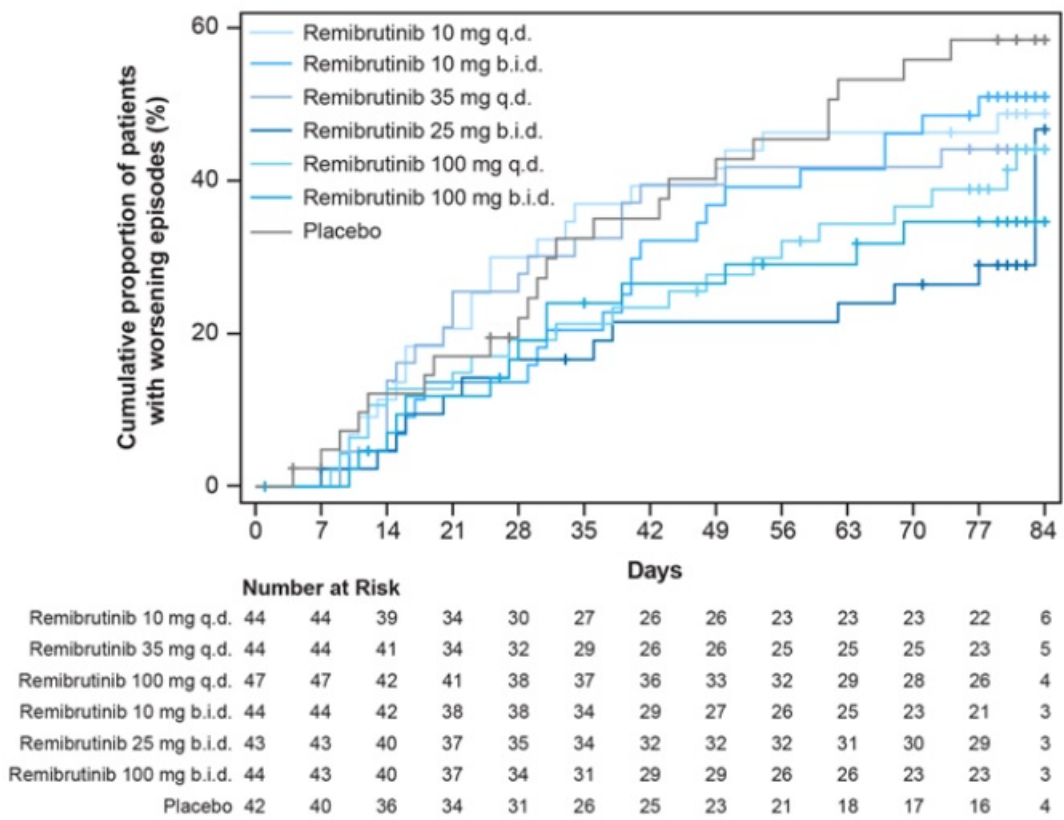
During the treatment period, a higher proportion of patients were free of worsening episodes across remibrutinib doses (range: 50.0% to 69.8% vs placebo [45.2%]). The cumulative proportion of patients with time to first worsening episodes over 12 weeks is presented in **Figure 1**. The mean (SD) duration of worsening episode across remibrutinib doses ranged from 8.9 (6.9) to 21.5 (19.3) days (placebo: 22.0 [19.8] days). The median (95% confidence interval) time to first worsening episode was not reached across remibrutinib arms (except 10 mg b.i.d.

77.0 days [47.0, not applicable {NA}] vs placebo (61.0 days [36.0, NA]). The mean (SD) intensity of worsening episode during the treatment period was lower across remibrutinib doses (range: 164.8 [170.4] to 435.7 [575.4]) versus placebo (708.5 [774.7]). The mean (SD) peak intensity of worsening episode during the treatment period was lower across remibrutinib doses (range: 22.0 [8.3] to 27.4 [8.2]) versus placebo (34.1 [7.5]).

**Conclusion:**

In this exploratory analysis, more patients were free of urticaria worsening in all remibrutinib treatment arms compared with placebo; duration, intensity, and peak intensity of worsening episode were lower with remibrutinib. The treatment response remained stable during the study indicating better disease control for patients on remibrutinib, which may have a favourable impact on patients’ lives.

**Figure 1.** Time to first worsening episode based on rUAS7 in the treatment period (full analysis set)



b.i.d., twice daily; q.d., once daily; rUAS7, rolling weekly Urticaria Activity Score.

**Abstract N°: 70****study of anxiety and depression among chronic urticaria patients**Kiran Vasant Godse\*<sup>1</sup><sup>1</sup>shree skin centre, skin, Navi Mumbai, India**Introduction & Objectives:**

A frequent condition known as chronic urticaria (CU) is characterized by the appearance of wheals, angioedema, or both. CU lowers the quality of life and may also result in psychological discomfort. The literature survey revealed that there aren't many studies dealing with depression and anxiety in these patients. Hence, Hamilton scores for depression and anxiety were used in this study to evaluate the incidence of depression and anxiety in chronic urticaria patients.

**Materials & Methods:**

To evaluate CU patients' levels of depression and anxiety, the Hamilton Rating Scale for Depression (HDRS) and the Hamilton Anxiety Rating Scale (HAMA) were applied. Moreover, in a control group consisting of thirty healthy volunteers, we included thirty CU patients in the study. It was important to observe the patients' urticaria activity score, medications, age, gender, comorbidities, employment status, and income. When it came to levels of depression and anxiety, a comparison was made between the case group and the healthy group.

**Results:**

In the CU patients' group, the mean age was 26.9 years. The questionnaires showed that 14 (46%) subjects in the patient group had moderate to severe signs of anxiety and 21 (70%) had moderate to severe signs of depression. Besides, in the control group, 7 (23.3%) had moderate to severe signs of anxiety and 8 (26.7%) had severe depression.

**Conclusion:** According to the conclusion of the study, individuals with CU exhibit depression and anxiety symptoms more frequently than the control group. Therefore, when treating individuals with CU, we should be aware of the possibility of mental comorbidities.



**Abstract N°: 346****A Case with Angioedema Developed After Mesotherapy with NCTF® 135 HA: Evaluation and Management**Cemre Turk<sup>\*1, 2</sup>, Gonca Gökdemir<sup>3</sup><sup>1</sup>Massachusetts General Hospital, Wellman Center for Photomedicine, Boston, United States, <sup>2</sup>Harvard Medical School, Department of Dermatology, Boston, United States, <sup>3</sup>Prof. Dr. Gonca Gökdemir, Türkiye**Introduction & Objectives:**

Mesotherapy is a non-surgical, minimally invasive, and popular aesthetic procedure. It involves multiple intradermal injections of various pharmacological substances (1). NCTF® 135 HA (New Cellular Treatment Factor) is the quintessential example of a mesotherapy product with a poly-component formulation. It includes vitamins, minerals, amino acids, nucleotides, coenzymes, antioxidants, and hyaluronic acid (2). Although mesotherapy is a common and safe method, it may be rarely related to some serious adverse events (3). We aimed to present a case with angioedema as an acute adverse event of mesotherapy with NCTF® 135 HA, to share our experiences in the management of an angioedema case after mesotherapy, and to discuss what is the best approach for a patient with angioedema after cosmetic procedures.

**Case:**

A 46-year-old woman was presented with crow's feet and periocular skin laxity. There were no known diseases or medications in her history. We intradermally applied 0,4 ml NCTF® 135 HA for each PA side. After 6 hours, she developed bilateral non-pitting, non-pruritic, non-painful periocular edema with mild erythema. She had not any other symptoms. The diagnosis was angioedema. We gave methylprednisolone 40 mg/day and cetirizine 10 mg/day for one week. Her symptoms improved in 5 days.

**Conclusion:**

Although angioedema is an infrequent complication of mesotherapy procedures, HA fillers may cause it more frequently (4). NCTF® 135 HA is the most requested product by patients. Despite its everyday use and thought to be safe, injectors should be aware of the risk of angioedema after application of the NCTF® 135 HA as other HA products.

**Abstract N°: 555**
**Omalizumab-induced paradoxical urticaria, responsive to dupilumab**

 Anne-Claire Fougousse\*<sup>1, 2</sup>, Antoine Badaoui<sup>1, 2</sup>
<sup>1</sup>GEM, Reso, Paris, France, <sup>2</sup>Military Teaching Hospital Begin, Dermatology, Saint Mandé, France

**Introduction & Objectives:**

Omalizumab is an add on treatment for chronic spontaneous urticaria. We report here an original case of omalizumab induced chronic urticaria.

**Materials & Methods:**

Case report.

**Results:**

A 47-year-old woman with history of severe asthma since childhood, allergic conjunctivitis, epilepsy, depression and cardiac arrhythmia consulted for the occurrence of urticaria lesions for 3 months. Her treatment included omalizumab 600mg every 4 weeks for 12 months, montelukast, fluticasone-salmeterol, tiotropium, salbutamol, carbamazepine, topiramate, perampanel, bisoprolol, salicylic acid, agomelatine, mirtazapine and pantoprazole without recent changes. She had no recent history of infection or vaccination, did not recently received oral corticosteroids. She had no personal history of urticaria

She reported urticaria and angioedema lesions for 3 months, without inducible urticaria or extracutaneous signs. Injections of omalizumab did not influence the course of urticaria. Treatment with H1 antihistamines (ebastine up to 4 tabs/day for 1 month, bilastine up to 3 tabs/day for 1 month) associated with hydroxyzine 25 mg/day did not lead to improvement. The urticaria control test (UCT) score was rated 5, indicating an uncontrolled urticaria.

Blood count, renal and hepatic tests were normal, CRP dosage was 15.2mg/L, total IgE level was 389 UI/L. Search for anti-thyroid and antinuclear antibodies was negative. Skin biopsy was compatible with urticaria without evidence for vasculitis or neutrophilic dermatosis. Direct immunofluorescence was negative.

The management of this chronic urticaria included the maintenance of bilastine at 3 tab/day, the discontinuation of omalizumab relayed by dupilumab (600 mg, then 300 mg every other week). The patient reported an improvement in urticarial symptoms after the first injection of dupilumab..After 3 months, the UCT score was rated 15, indicating a complete control of urticaria. She reported minor reactions at the dupilumab injections sites. Chronic urticaria remained well controlled with dupilumab and bilastine, secondarily decreased to 2 tab/day, with a 15 months follow-up. Asthma was well controlled despite some exacerbations with favorable evolution with symptomatic treatment.

**Conclusion:**

We report to our knowledge the first case of chronic urticaria occurring under omalizumab treatment. A case of acute urticaria during the first two injections of omalizumab for asthma, without recurrence during subsequent injections had been reported. Paradoxical omalizumab-induced urticaria has been reported as anaphylaxis reactions, mainly related to polysorbate allergy. To explain this paradoxical urticaria, one could hypothesize that omalizumab would have activated mast cells immunologically by binding to FcR receptors on their surface. Chronic spontaneous urticaria could also have been a comorbidity of her atopy and resist to omalizumab.

Dupilumab was rapidly effective for our patient, as it has been reported for patients with chronic urticaria failing omalizumab. However, we cannot exclude a spontaneous resolution of chronic spontaneous urticaria.

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**Abstract N°: 650****Clinical response to low-dose omalizumab treatment in chronic spontaneous urticaria: A retrospective study of 179 patients**

Min Jae Kim<sup>\*1</sup>, Sae Hoon Kim<sup>2</sup>, Yoon Seok Chang<sup>2</sup>, Sang Woong Youn<sup>1</sup>, Bo Ri Kim<sup>1</sup>

<sup>1</sup>Seoul National University Bundang Hospital, Dermatology, Seongnam-si, Korea, Rep. of South, <sup>2</sup>Seoul National University Bundang Hospital, Internal Medicine, Seongnam-si, Korea, Rep. of South

**Introduction & Objectives:** Omalizumab is effective in patients with chronic spontaneous urticaria who do not respond to antihistamines. Of the licensed dosing schedules (150 or 300 mg/month), Korean patients prefer to receive 150 mg/month for financial reasons. However, real-world experiences of low-dose omalizumab consumption have not been reported. The objective of this study was to assess the long-term treatment outcomes and clinical course of patients with chronic spontaneous urticaria treated with low-dose omalizumab. We also evaluated the clinical factors predictive of early and final complete responses to omalizumab in a real-world setting.

**Materials & Methods:** Records of adult patients with chronic spontaneous urticaria who were treated with omalizumab 150 mg/month for  $\geq 12$  weeks were collected. Baseline disease activity was categorized according to the Urticaria Activity Score 7, and the treatment response to omalizumab was evaluated according to the physician's global assessment. A linear regression model and a Cox proportional hazard regression model were used to identify the clinical factors associated with early and final complete responses.

**Results:** The study included 179 patients, and the mean follow-up duration was  $22.18 \pm 21.1$  months. Baseline disease activity was mild, moderate, and severe in 54.7%, 35.2%, and 10.1% of patients, respectively. A complete response was observed in 133 patients at 12 weeks, among whom 88 patients showed early responses within 4 weeks. Overall, 88.3% of patients achieved final complete responses. During drug discontinuation after clinical remission, 25.6% of patients sustained the responses for 18.31 weeks and in 74.4% relapses were observed after 23.94 weeks. Multivariate analyses revealed that baseline disease activity is more likely to be mild in patients who experienced either early (odds ratio [OR], 0.500; 95% confidence interval [CI], 0.253-0.970;  $P = 0.042$ ) or final complete response (hazard ratio [HR], 0.641; 95% CI, 0.414-0.990;  $P = 0.045$ ). The absence of allergic comorbidities correlated only with early response to omalizumab (OR, 0.354; 95% CI, 0.176-0.692;  $P = 0.003$ ). Smoking was associated with final complete response to omalizumab (HR, 1.570; 95% CI, 1.024-2.408;  $P = 0.039$ ).

**Conclusion:** This study confirms that low-dose omalizumab shows favorable treatment outcomes in patients with antihistamine-refractory chronic spontaneous urticaria. Disease severity, allergic comorbidity, and smoking may be predictive factors for studying the response to omalizumab.



## Abstract N°: 1823

**Patients With Chronic Spontaneous Urticaria Experience Improvement in Quality of Life When Treated With Barzolvolimab**

Marcus Maurer<sup>1, 2</sup>, Martin Metz<sup>1, 2</sup>, John Anderson<sup>3</sup>, Neetu Talreja<sup>4</sup>, Diego Alvarado<sup>5</sup>, Elizabeth Crowley<sup>5</sup>, Diane Young<sup>5</sup>, Kunal Merchant<sup>5</sup>, Elsa Paradise<sup>5</sup>, Margo Heath-Chiozzi<sup>5</sup>, Jonathan Bernstein<sup>6</sup>

<sup>1</sup>Institute of Allergology, Charité – Universitätsmedizin Berlin, Berlin, Germany, <sup>2</sup>Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Allergology and Immunology, Berlin, Berlin, Germany, <sup>3</sup>University of Alabama, Birmingham and VA Medical Center, Clinical Research Center of Alabama, Allervie Health, Birmingham, United States, <sup>4</sup>The Allergy Group and Treasure Valley Medical Research, Boise, United States, <sup>5</sup>Celldex Therapeutics, Inc., Hampton, United States, <sup>6</sup>University of Cincinnati College of Medicine and Bernstein Allergy Group/Clinical Research Center, Cincinnati, United States

**Introduction & Objectives:** Chronic Spontaneous Urticaria (CSU) is a mast cell (MC) driven disease with a large impact on patients' Quality of Life (QoL).\*\* Barzolvolimab (CDX-0159), a monoclonal anti-KIT antibody, is known to reduce disease activity and circulating tryptase, and deplete skin MCs in chronic inducible urticaria. We previously reported that multiple doses of barzolvolimab were well tolerated and demonstrated rapid and durable improvement in symptoms and reduction in serum tryptase at intravenous doses  $\geq 1.5$  mg/kg in patients with antihistamine-refractory CSU. Here we report the impact of barzolvolimab treatment on patients' QoL.

**Materials & Methods:** This is a Phase 1 double-blind placebo-controlled multiple ascending dose trial (NCT04538794). Adult patients with moderate to severe (urticaria activity score over 7 days [UAS7]  $\geq 16$ ) antihistamine-refractory CSU treated with intravenous barzolvolimab in 4 sequentially enrolled ascending dose cohorts (randomized 4:1 barzolvolimab:placebo) 0.5 mg/kg, Q4W (n=12); 1.5 mg/kg, Q4W (n=10); 3 mg/kg, Q8W (n=12); and 4.5 mg/kg, Q8W (n=11) for 12 weeks with a 12-week follow up. Assessments included: safety, urticaria activity score (UAS7), urticaria control test (UCT), Dermatology Life Quality Index (DLQI), physician global assessment (PhyGA), and serum tryptase.

**Results:** Forty-five patients with moderate to severe disease activity and a mean (range) UAS7 = 31.0 (16.3-42.0), UCT = 3.1 (0-12), PhyGA 2.2 (1-3) and a very large impact on QoL, DLQI 11.8 (1-26) pre-treatment, were enrolled. A rapid decrease in the DLQI was noted within 4 weeks in all barzolvolimab treated patients (n=35) 3.5 (0-16) vs placebo (n=10) 9.3(1-25), which was sustained for doses  $\geq 1.5$  mg/kg to week 24. Similarly, the PhyGA for the treated cohorts decreased to 0.6 (0-3) by week 1 vs placebo 2.0 (0-3) and sustained through Week 24. Both parameters trended closely with the dose-dependent improvement in UAS7 and UCT, and tryptase suppression. Barzolvolimab was well-tolerated; adverse events were similar to those reported earlier. Hematology parameters were similar to prior single dose barzolvolimab studies.

**Conclusion:** Treatment with multiple doses of barzolvolimab at  $\geq 1.5$  mg/kg provide rapid and sustained reduction in disease activity that greatly decreases the impact of urticaria on QoL in patients with antihistamine-refractory CSU.



**Abstract N°: 1891**
**Drug survival of omalizumab and antihistamines and related factors in chronic urticaria patients**

 Hande Ermis Akkus<sup>\*1</sup>, Deniz Aksu Arica<sup>1</sup>, Leyla Baykal Selçuk<sup>1</sup>, Etem Arica<sup>1</sup>, Ümmügülsüm Özel<sup>2</sup>
<sup>1</sup>Karadeniz Technical University Faculty of Medicine, Department of Dermatology and Venereology, Trabzon, Türkiye, <sup>2</sup>Karadeniz Technical University Faculty of Medicine, Department of Public Health, Trabzon, Türkiye

**Introduction & Objectives:**

Antihistamines, omalizumab (OMA), and ciclosporin are the approved options for chronic urticaria (CU) treatment. However, there is lacking evidence regarding drug survival. We aimed to define the drug survival of omalizumab, antihistamines, and ciclosporin in CU patients and determine the factors associated with disease duration (DD) and drug survival.

**Materials & Methods:**

We conducted a single-centre, observational, descriptive study in our department among the adult patients diagnosed with chronic spontaneous urticaria (CSU) or chronic inducible urticaria (CindU) who visited our outpatient clinic between 01.03.2022 – 01.03.2023. Age, gender, and BMI of the patients, family history of atopy, personal comorbidities, CU and CindU subtypes, DD, time under antihistamines, omalizumab, reasons for OMA discontinuation, need for emergency care admission (ECA) and hospitalization, the maximum needed dose of antihistamines and omalizumab, baseline and follow-up laboratory tests were recorded.

**Results:**

The study consisted of 93 patients: 70 (75,3%) female and 23(24,7%) male patients with a mean age of 41,53 ( $\pm$ 13,87). CSU, CindU, and CSU with concomitant CindU were observed in 85 (91,3%), 8 (8,6%), and 68 (73,11%) patients, respectively. At the endpoint of the study, 42 patients were still receiving OMA while 15 patients stopped OMA therapy. Of these 15 patients, 10 (66,7%) gave up OMA due to recovery, 2(13,3%) were lost to follow-up, 1 (6,7%) had pregnancy wish, 1 (%6,7) gave up due to ineffectiveness and in 1 patient (6,7%) OMA was initiated too early and therefore ceased by our group. The median omalizumab drug survival (discontinuation owing to any cause) for the first round of 56 patients was 9 (95% CI: 7,69 – 10,31) months.

The median overall time under OMA (from the beginning to the cessation of OMA, including interruption periods) is 21 (min:1, max:95) months. The patients who required a fourfold (x4) dose of antihistamine, who were admitted to emergency care under OMA stayed statistically significantly longer under OMA overall with a median overall time of 23,5 (min:2, max:95), 52 (min:5, max:95) months, respectively. Plasma fibrinogen values were found strongly positively correlated with the time under OMA ( $r$ :0,92,  $p$ =0,008). Among 55 patients mean OMA administration is 19.12 (SD 18,54).

Of 88 patients, 34 (38,6%) discontinued antihistamines owing to any cause. The median antihistamine survival time was 67 (95% CI: 24,14 – 109,85) months for all CU patients. Mean DD was 45,28 (SD 40,65), 36,62 (SD 29,51), and 47,48 (SD 42,78) in patients for CSU, CindU, and CSU with concomitant CindU, respectively. Median DD was found significantly longer in patients with asthma ( $p$ =0,046), food hypersensitivity (HS) ( $p$ =0,023), dust mite HS ( $p$ =0,041), who needed x4 dose of antihistamines ( $p$ =0,009), who needed ECA due to CU symptoms ( $p$ =0,023) and who needed intermittent glucocorticoids for disease control ( $p$ =0,002). A statistically significant ( $r$ :-0,25,  $p$ =0,03) negative correlation was found between baseline basophil level and DD.

**Conclusion:**

The need for fourfold standard dosed H1-antihistamines, ECA under OMA, the need for intermittent glucocorticoid treatment, accompanying asthma, food, and dust mite hypersensitivity in personal history are associated with prolonged disease duration. High baseline plasma fibrinogen levels and low baseline blood basophil levels may indicate a prolonged treatment course under OMA and longer DD, respectively.

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**Abstract N°: 1925**
**Remibrutinib provides fast and clinically important improvement of CSU disease activity: Post-hoc analysis from the Phase 2b study**

Marcus Maurer<sup>1, 2</sup>, Ana Giménez-Arnau<sup>3</sup>, Joshua Jacobs<sup>4</sup>, Sinisa Savic<sup>5</sup>, Christine-Elke Ortmann<sup>6</sup>, Bharat Suryawanshi<sup>7</sup>, Ivan Nikolaev Ivanov<sup>6</sup>, Michael Wells<sup>8</sup>, Sibylle Haemmerle<sup>6</sup>

<sup>1</sup>Urticaria Center of Reference and Excellence (UCARE), Institute of Allergology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany,

<sup>2</sup>Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Allergology and Immunology, Berlin, Germany, <sup>3</sup>Hospital del Mar -IMIM, Universitat Pompeu Fabra, Barcelona, Spain, <sup>4</sup>Allergy and Asthma Clinical Research, Walnut Creek, California, United States, <sup>5</sup>Department of Clinical Immunology and Allergy, Leeds Teaching Hospital NHS Trust, Leeds, United Kingdom, <sup>6</sup>Novartis Pharma AG, Basel, Switzerland, <sup>7</sup>IQVIA India Ltd, Mumbai, India, <sup>8</sup>Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, United States

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is characterised by the occurrence of itchy wheals (hives) and/or angioedema for >6 weeks and has a substantial impact on patients' quality of life.<sup>1, 2</sup> Remibrutinib (LOU064) is an oral, highly selective Bruton's tyrosine kinase (BTK) inhibitor that offers fast disease control in patients with CSU who remain symptomatic despite treatment with second-generation H1-antihistamines. It has shown clinical efficacy and a favourable safety profile in patients with CSU for up to 12 weeks in a Phase 2b dose-finding study<sup>3</sup> and up to 52 weeks in the follow-on open label extension study.<sup>4</sup> The weekly Urticaria Activity Score (UAS7 range 0–42) is frequently used to evaluate treatment response in clinical studies and clinical practice, with higher scores reflecting higher disease activity.<sup>5</sup> A decrease in UAS7 of 9.5–10.5 points is considered the minimum important difference to (MID) to indicate a meaningful clinical response to therapy. The present analysis explored the onset of action of remibrutinib in terms of early achievement of MID-UAS7 of 10.5 points.

**Materials & Methods:**

This post-hoc analysis evaluated data of 309 CSU patients from the full analysis set (out of 311 CSU patients) who were equally randomised in a 1:1:1:1:1:1 ratio to receive remibrutinib 10 mg once daily (q.d.)/35 mg q.d./100 mg q.d./10 mg twice daily (b.i.d.)/25 mg b.i.d./100 mg b.i.d. or placebo for 12 weeks in the Phase 2b study and a 4-week post-treatment follow-up period (NCT03926611). The proportion of patients achieving MID-UAS7 at any time (between Weeks 0–12) and early (between Weeks 0–2), and the median time to achieve complete response (UAS7=0), and well-controlled disease (UAS7≤6) in patients who had achieved MID-UAS7 early were analysed.

**Results:**

Overall, a higher proportion of patients\*\* achieved MID-UAS7 between Weeks 0–12 across remibrutinib doses versus placebo (77.8–93.2% vs 59.5%). A higher proportion of patients achieved MID-UAS7 early (Weeks 0–2) across all doses of remibrutinib versus placebo (64.4–83.7% vs 23.8%). Of the patients who achieved MID-UAS7 early, the median time to achieve UAS7=0 was shorter for all remibrutinib arms versus placebo: 2–4 weeks versus 5 weeks, respectively, and median time to UAS7≤6 was 2 weeks versus 4 weeks, respectively.

**Conclusion:**

In this post-hoc analysis, the majority of patients achieved MID-UAS7 during the first two weeks of remibrutinib

treatment, thus indicating a fast onset of action for remibrutinib.

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**Abstract N°: 2076****Eating increases and exercise decreases disease activity in patients with symptomatic dermographism**

Ragıp Ertas<sup>1</sup>, Murat Türk<sup>2</sup>, Muhammed Burak Yücel<sup>\*1</sup>, Melba Menoz Roldan<sup>3</sup>, Şule Ketenci Ertaş<sup>4</sup>, Mustafa Atasoy<sup>5</sup>, Marcus Maurer<sup>3</sup>

<sup>1</sup>Urticaria Center of Reference and Excellence (UCARE), Chronic Skin Diseases Unit, Department of Dermatology, University of Health Sciences, Kayseri City Education and Research Hospital, Dermatology, Kayseri, Türkiye,

<sup>2</sup>Erciyes University, Faculty of Medicine, Department of Allergy and Immunology, Kayseri, Türkiye, <sup>3</sup>Charité Campus Benjamin Franklin, Institute of Allergology, Berlin, Germany, <sup>4</sup>Acıbadem Kayseri Hospital, Department of Internal Medicine, Division of Rheumatology, Kayseri, Türkiye, <sup>5</sup>Memorial Ataşehir Hospital, Dermatology and Venereology, İstanbul, Türkiye

**Introduction & Objectives:** Eating can increase disease activity in patients with symptomatic dermographism (SD), the most common subtype of chronic inducible urticaria, but it is unclear how common this is. The effects of exercising on SD disease activity have also not yet been determined. We aimed to evaluate with this study the effect of exercise and nonspecific carbohydrate-rich food intake on the severity and intensity of SD following exercise and non-specific carbohydrate-rich food intake.

**Materials & Methods:** We assessed disease activity by FricTest® provocation testing in 75 SD patients before and after eating, exercising, or both. We determined the rates of food-dependent SD (FD-SD) and food-exacerbated SD (FE-SD). By comparing post- and pre-exercise FricTest® scores, we identified complete responders, i.e. patients with a negative FricTest® response after exercising (ExCR-SD) and partial responders (ExPR-SD). Finally, we evaluated whether exercise protects patients with FD-SD or FE-SD from eating-induced worsening of their SD.

**Results:** Of 64 SD patients, 8 (13%) had FD-SD, 42 (66%) had FE-SD, and 14 (21%) patients showed no negative impact of eating on their disease activity. Physical exercise reduced FricTest® skin provocation test responses in 83% of 58 patients. Of note, exercising protected patients with FD/FE-SD from worsening of their SD due to eating, in half of cases, with higher rates for exercise after eating (67%) than exercise before eating (35%).

**Conclusion:** Our study shows that eating often worsen SD symptoms, and exercise often improves it. Our findings might aid patients to better control their symptoms.

**Abstract N°: 2129****Digital services in Chronic Urticaria care (DiaL-CU) - Preliminary results**

Felix Mühlensiepen<sup>\*1</sup>, Susann May<sup>1</sup>, Michael Hindelang<sup>2, 3</sup>, Johannes Knitza<sup>4</sup>, Alexander Zink<sup>5</sup>, Martin Welcker<sup>6</sup>

<sup>1</sup>Center for Health Services Research, Center for Health Services Research, Rüdersdorf bei Berlin, Germany,

<sup>2</sup>Technical University of Munich, Department of Dermatology and Allergy, School of Medicine, Munich, Germany,

<sup>3</sup>LMU Munich, Pettenkofer School of Public Health, Institute for Medical Information Processing, Biometry and Epidemiology (IBE), Faculty of Medicine, Munich, Germany, <sup>4</sup>Friedrich-Alexander-University Erlangen-Nürnberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3, Erlangen, Germany, <sup>5</sup>Technische Universität München, Klinikum rechts der Isar, München, Germany, <sup>6</sup>Medizinisches Versorgungszentrum für Rheumatologie Dr M Welcker GmbH, Planegg

**Introduction & Objectives:**

Chronic urticaria (CU) is an unpredictable condition with a high burden of disease. It has a significant negative impact on the quality of life of those affected. Despite specialized centers and diverse participation options in the diagnosis and treatment process, the path to diagnosis as well as optimal symptom control proves difficult. Digital health services could support diagnosis and therapy of CU.

-How high is the acceptance of patients and health care professionals (HCP) towards digital health services?

-What opportunities and barriers do patients and HCP experience when using digital health services?

**Materials & Methods:**

The study consists of two questionnaire surveys with patients and physicians in CU care. Both surveys can be completed either paper-pencil based or as an online survey. The questionnaires will be distributed in outpatient and inpatient institutions of CU care (UCARE centers, specialist and primary care practices) as well as patient organisations. The study was approved by data protection officer and the ethics committee of the Brandenburg Medical School Theodor Fontane, Reference ID: E-02-20220224.

**Results:**

At present (09/05/2023), 51 patients and 42 physicians were included in the surveys. Approximately 86% (44/51) of patients and 93% (39/42) of physicians reported that they consider digital health services in urticaria to be useful (strongly agree / agree). Nearly 69% (35/51) of patients reported that digital health services either had no impact at all (39%, 20/51) or positive and negative impact (29%, 15/51) on the doctor-patient relationship. Two-thirds (28/42) of physicians indicated that digital health has a rather positive impact on the physician-patient relationship. Patients most frequently mentioned (multiple answers possible) location-independent use (84%, 43/51), cost savings (76%, 39/51), and flexibility (71%, 36/51) as benefits of digital health services. Similarly, physicians most frequently cited location-independent use (88%, 37/42), accessibility (73%, 31/42), and flexibility (71%, 30/42) as benefits of digital health services in CU care. Main barriers from the patients' perspective were poor quality of current services (39%, 20/51), gaps in data privacy (35%, 18/51), little information about services (29%, 15/51). Physicians cited lack of technical equipment (62%, 26/42), gaps in data privacy (45%, 19/42), little information about services (38%, 16/42) as main barriers.

**Conclusion:**



Early results of our survey study indicate high levels of acceptance among patients and HCP towards digital health services in CU care.

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## Abstract N°: 2239

**Down-dosing and discontinuation of Omalizumab in patients with Chronic Spontaneous Urticaria. A descriptive and analytic unicentric study.**

Joan Ceravalls<sup>1</sup>, Gemma Melé-Ninot<sup>1</sup>, Montserrat Salleras-Redonnet<sup>1</sup>

<sup>1</sup>Hospital Universitari Sagrat Cor, Dermatology, Barcelona, Spain

**Introduction:** Omalizumab is the preferred treatment in Chronic Spontaneous Urticaria (CSU) unresponsive to antihistamines. Given its self-limited nature, various groups have proposed algorithms of interval prolongation prior to discontinuation of the treatment in well-controlled patients, defined by an Urticaria Activity Score 7 (UAS7)  $\leq 6$  and/or Urticaria Control Test (UCT)  $\geq 12$ . However, their utility has been evaluated only in a few studies, while data on which patients may benefit from them is not well-defined.

**Objectives:** to evaluate the process of down-dosing and discontinuation of omalizumab as well as the phenotype of the candidates.

**Materials & Methods:** a retrospective, descriptive and analytic study collected the data of patients diagnosed with CSU treated with standard doses of omalizumab in the Dermatology Department of our center from 2015 to 2022.

**Results:** a total of 57 patients were screened, 44 of which were treated with a de-intensified regimen. Of them, 7 were excluded resulting in 37 patients (71%) who gradually lengthened dosing intervals after 8.1 [2-39] months (m) of treatment at standard dose. Before down-dosing, 62% presented a complete response (CR, UAS7 0 and/or UCT  $\geq 16$ ) while 38% showed a partial response (PR, UAS7 1 - 6 and/or UCT 12-15). The initial dose was 150mg/4 weeks (w), extending to 150mg/6 or 8w according to the clinical response. The mean de-intensification duration was 14.77m [2-55]. While 38% maintained a PR or CR, 62% lost control (UAS7  $> 6$  and/or UCT  $< 12$ ) at 4.9m [1-11] while doing 150mg/4w most frequently. A dosing step-up was performed in 82% of patients, whereas 18% maintained the same dose, achieving PR or CR in all cases. Later, 73% of previously poor-controlled patients during dose reduction, successfully tolerated lengthened interval dosing. Thus, 84% of patients benefited from treatment tapering. No statistically significant (SS) differences were found between patients that did and did not tolerate the first dose reduction, although the latter had higher body mass index, basal total IgE and UAS7.

Omalizumab was discontinued in 51% of patients after 21.79m [5-43], of whom 95% have a follow-up at 12m. The last dose before stopping was mostly 150mg/8w. Sustained remission was observed in 33% of patients, while 67% relapsed but only 66% of them reintroduced omalizumab. Patients that did not require to restart omalizumab at 12m had a ss shorter duration of the disease and a greater proportion of CR before de-intensifying.

Reintroduction of the previous lowest effective dose (LED) was successful in 87% of patients, regaining control of the disease.

**Conclusion:** an extended interval dosing regimen of omalizumab was beneficial for 84% of patients without requiring a previous CR. However, early treatment with omalizumab and achieving CR before de-intensifying seems to favor successful discontinuation at 12m. Patients who relapsed after discontinuation were able to restart at the LED and regain control again.

**Abstract N°: 2264****Neutrophilic urticarial dermatosis: a case report and literature review.**

María López-Pardo Rico<sup>1</sup>, Cecilia Buján Bonino<sup>1</sup>, Carmen Canovas Seva<sup>1</sup>, José Sáez Padilla<sup>1</sup>, Carlos Aliste Santos<sup>2</sup>, Maria Dolores Sanchez-Aguilar Rojas<sup>1</sup>, Hugo Alberto Vazquez Veiga<sup>1</sup>

<sup>1</sup>Complejo Hospitalario Universitario de Santiago de Compostela, Dermatology Department, Santiago de Compostela, <sup>2</sup>Complejo Hospitalario Universitario de Santiago de Compostela, Pathology Department, Santiago de Compostela

**Introduction & Objectives:**

Neutrophilic urticarial dermatosis (NUD) is a chronic entity which consists of outbreaks of slightly elevated pink plaques or macules. Elementary lesions are evanescent, and disappear without scarring in 24-48 hours. It is often accompanied by extracutaneous manifestations such as fever and joint pain and it is strongly associated with systemic inflammatory diseases.

**Materials & Methods:**

A 68-year-old man presented to our department with outbreaks of evanescent and recurrent wheals on the trunk and extremities for 5 years. He had been treated with antihistamines and oral corticosteroids without improvement. He also reported recurrent fever and joint pain. Physical examination revealed erythematous plaques on the trunk and extremities. He did not have any dermatographism. There was no evidence of lymphadenopathy or signs of arthritis.

**Results:**

Laboratory investigations revealed a monoclonal IgM peak and elevated acute phase reactants (C-reactive protein 22 mg/dl). Histopathology evidenced a dense neutrophilic dermal infiltrate of interstitial and perivascular localisation. There was no evidence of vasculitis. A gammagraphy was also requested which confirmed increased bone remodelling. Our patient fulfilled all the Strasbourg criteria for Schnitzler's syndrome. Therefore, treatment with anakinra (interleukin (IL)-1 receptor antagonist, 100 mg/day) was started. He has remained in remission under continued treatment for 1 year.

**Conclusion:**

NUD presents clinically as an urticarial rash and histologically as a neutrophilic dermatosis. Given this diagnosis, screening for inflammatory diseases is warranted. The most frequently associated entities are lupus erythematosus, Schnitzler's syndrome, adult-onset Still's disease and cryopyrin-associated periodic syndromes. Treatment of NUD depends on the clinical context: colchicine, dapsone and anakinra are valid therapeutic alternatives.

**Abstract N°: 2344**
**Depression is underdiagnosed in Chronic Spontaneous Urticaria, UAS-7 may not correlate with quality of life in a predictable way**

 Céline Ueda<sup>1</sup>, Jonathan White<sup>2</sup>
<sup>1</sup>Université Libre De Bruxelles / Campus Érasme, Faculty of Medicine, Anderlecht, Belgium, <sup>2</sup>Erasmus Hospital, Dermatology and Allergology

**Introduction & Objectives:**

Chronic Spontaneous Urticaria (CSU) has a significant burden and impact on quality of life comparable to that of coronary artery disease. Psychiatric comorbidities have been reported in CSU patients and may negatively influence the patient's quality of life. Our objective was to compare the frequency of comorbid depression in CSU patients and the relationship with measures of disease severity and quality of life especially in patients on long-term omalizumab treatment.

**Materials & Methods:**

We recruited adult patients diagnosed with CSU under active treatment. They completed a questionnaire about various disease parameters including treatments and comorbidities. To refine the diagnosis of depression, Patient Health Questionnaire -9 (PHQ-9) data were collected for the whole cohort. CSU quality of life was measured by Chronic Urticaria Quality of Life (CU-QoL) questionnaires. Patients were considered in 3 different treatment groups: a non-omalizumab group, omalizumab <18 months, omalizumab ≥ 18 months (thereafter non-OMA, short-OMA, long-OMA). Additional analysis was undertaken dividing the cohort in depressed and non-affected groups.\*

**Results:**

76 patients were included (45 under Long-OMA; 17 under Short-OMA; 14 under Non-OMA). Comorbid depression was significantly higher among patients under Long-OMA ( $p=0.013$ ) with an Odds Ratio: 12.2 against Non-OMA treated patients and 5.3 against short OMA. The reported depression comorbidity accounted to 21.1% of our whole cohort, 2/3 of them were Long-OMA patients.

PHQ-9 screening result showed 28.9% of our cohort had symptoms compatible with depressive disorder (3 times higher than the general population using PHQ-9), with similar rates in all three treatment groups. Some patients with symptoms compatible with a depressive disorder were only identified by the questionnaire, and were not aware themselves of a possible diagnosis of depressive disorder. Only 1/7 of patients who knew they had depression had psychiatric follow-up in place. 1/3 were unaware of their depressive state (depressive disorder *de novo*). CSU disease activity based on Urticaria disease activity 7 score (UAS-7) was not significantly different in those with no depressive symptoms and depressive disorder *de novo* compared with patients who had already reported comorbid depression. Nevertheless CU-QoL showed a marked reduction in quality of life in those depressive disorder only identified by our questionnaire. A positive correlation between UAS-7 and CU-QoL was verified for patients showing no depressive symptoms.

**Conclusions:**

1. Symptoms suggestive of a depressive disorder are common in CSU patients, even in those with well-controlled physical symptoms.

2. Many patients with depressive symptoms are not aware of them, so screening for depression with the short questionnaire PHQ-9 should be offered for all CSU patients.
3. Measures of CSU disease severity such as UAS-7 do not necessarily correlate with quality of life in a predictable way. Clinicians should assess quality of life separately and not assume that low UAS-7 scores mean good quality of life.
4. We recommend combining UAS-7 scores with CU-QoL to assess the patient's well-being in a holistic way.

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**Abstract N°: 2696**
**Severe cholinergic urticarial: patients' clinical characteristics and therapeutic approach**

Julie Castagna<sup>\*1</sup>, Tetart Florence<sup>2</sup>, Badaoui Antoine<sup>3</sup>, Amsler Emmanuelle<sup>1</sup>, Pralong Pauline<sup>4</sup>, Castelain Florence<sup>5</sup>, Delaunay Juliette<sup>6</sup>, Angèle Soria<sup>1</sup>

<sup>1</sup>Tenon Hospital, Dermatology and Allergy Department, PARIS, France, <sup>2</sup>Rouen university hospital, Dermatology and Allergy Department, ROUEN, France, <sup>3</sup>Private Practice, PARIS, France, <sup>4</sup>Grenoble university hospital, Dermatology and Allergy Department, GRENOBLE, France, <sup>5</sup>Besancon university hospital, Dermatology and Allergy Department, BESANCON, France, <sup>6</sup>Angers university hospital, Dermatology and Allergy Department, ANGERS, France

**Introduction & Objectives:**

Cholinergic urticarial (CholU) is a form of nonphysical chronic inducible urticaria (CIndU). It concerns about 4 to 11.2% of the population. Patients present with itchy wheals after active or passive warming of the body temperature. In severe CholU cases, treatments are nonsedating H1 antihistamines, up dosing in nonresponders and there are some reports of omalizumab efficacy. In this retrospective study of the French Urticaria group (GUS), we report the epidemiological and clinical characteristics of severe cholinergic urticaria patients and describe therapeutic approach.

**Materials & Methods:**

Severity of cholinergic urticarial was defined as a nonresponse to four-fold dose of second generation H1 antihistamines with UAS7 score  $\geq 27$ , or UCT  $\leq 8$ , or more than 10 flare-up per day.

**Results:**

Forty-seven patients were included, 33 men (sex ratio 2.4), with a median age of 17 years (8-55) at the beginning of CholU. The mean disease duration was 8.2 years. Twenty-four patients (51%) had only CholU, while 15 (31.9%) had associated chronic spontaneous urticaria (CSU) and 14 (32.6%) another CIndU associated. Associated CIndU were principally dermatographism and cold urticarial (6 and 5 patients respectively). Majority of patients presented with the classical morphology of CholU: pinhead-sized papular wheal with surrounding erythematous halo (n=32, 68.1%). Four patients had isolated cholinergic pruritus (8.5%). For 24 patients the number of flare-ups per day was known, and the majority was between 1 and 5.

The mean number of therapeutic lines per patient was 3, among them omalizumab was prescribed in 43 cases, propranolol in 4 cases and dupilumab in 4 cases. A complete or partial response had been observed with omalizumab in respectively 21/43 (48.8%) and 12/43 (27.9%) patients. Among them, omalizumab dosage had been optimized in 15 patients. Ten patients (23.3%) were non-responder to omalizumab, despite optimization in 7. Response to propranolol was variable and there was no responder to dupilumab.

**Conclusion:**

Despite omalizumab efficacy in almost half of the patients, there is still an unmet need of new therapeutics to treat severe CholU. A clear definition of severe patients is also necessary to better identify these patients. For this purpose, the CholU severity index has been developed but is not currently validated in French. We found that the number of flare-ups per day is an interesting question, while we sometimes have some surprises with the answers.



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**Abstract N°: 2786****5-Year Follow-up Data in Patients with Chronic Spontaneous Urticaria**

Hatice Kübra Çakır<sup>\*1</sup>, Filiz Cebeci Kahraman<sup>2</sup>, Mehmet Salih Gürel<sup>1</sup>, Necmettin Akdeniz<sup>3</sup>

<sup>1</sup>Istanbul Medeniyet Üniversitesi Göztepe Süleyman Yalçın Şehir Hastanesi, İstanbul, Türkiye, <sup>2</sup>Health Sciences University Sultan Abdülhamid Han Training and Research Hospital, dermatology, İstanbul, Türkiye, <sup>3</sup>Memorial Şişli Hospital, Dermatology, İstanbul, Türkiye

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is defined as urticaria, angioedema or both that persists for 6 weeks without a specific identifiable trigger. Chronic urticaria lasts on average 5 years and in severe cases can last longer than 5 years. Since many factors play a role in its etiology, it can sometimes be difficult to control CSU. CSU can resolve spontaneously after approximately 5 years and remission can occur independently of treatment. However, in some cases it is resistant to treatment and may persist for many years. In this study, we investigated the remission status of our patients with CSU who received antihistamine and omalizumab treatment at the end of 5-year follow-up and the factors that may affect remission.

**Materials & Methods:**

We conducted a single-center, retrospective, observational study. Ethical approval for this study was obtained from the ethics committee of Istanbul Medeniyet University (IMU) Faculty of Medicine. The study group included 78 patients between the ages of 18 and 80 who were diagnosed with chronic spontaneous urticaria between April 2016 and April 2017 by our Dermatoallergy Clinic at IMU, Göztepe Prof. Dr. Süleyman Yalçın City Hospital and followed up for 5 years. Patients younger than 18 years of age, patients who did not complete the 5-year follow-up period and patients with inducible urticaria were excluded. The date of diagnosis of urticaria, the treatments used and their duration, the date of the last urticaria-related complaints and thyroid diseases were recorded. Disease duration, used treatments, responses to treatment, remission status and duration, history of thyroid disease were recorded. Only antihistamine users, only omalizumab users, omalizumab and antihistamine users were recorded as the treatment status. Complete remission was defined as the absence of urticarial lesions and angioedema attacks for at least 6 months without treatment and minimal pruritus without the need for medical treatment.

**Results:**

The mean age of the 78 patients was 34.9 years. Of the patients, 60 (76.9%) were female and 18 (23.1%) were male. Of the patients, 30 (38.4%) used only antihistamines, 8 (10.2%) used only omalizumab, and 40 (51.2%) used both antihistamines and omalizumab.

Of the 14 patients (46.6%) who used only antihistamine drugs were still complaining and their treatment was ongoing while 16 (53.3%) were in remission for 39 months. While 7 patients (87.5%) who received only omalizumab treatment still had ongoing treatment and continued symptoms, 1 patient (12.5%) had been in remission for 48 months. Of the 24 patients (60%) who used antihistamine and omalizumab both were suffer from symptoms and ongoing treatment, while 16 (40%) were in remission for 31.4 months.

A history of thyroid disease was present in 6 (42.8%) of 14 patients who received only antihistamines and did not go into remission, 1 (14.2%) of 7 patients who received only omalizumab and did not go into remission, and 8 (33%) of 24 patients who received antihistamines and omalizumab and did not go into remission.

33 of 78 patients (%42,3) had no complaints for at least 6 months and the mean duration of remission was 35.7 months.

**Conclusion:**

Our study highlights that a significant proportion of patients are resistant to omalizumab and combined omalizumab and omalizumab antihistamine treatment and that unknowns in the pathogenesis of CSU should be investigated and new treatment agents should be developed.

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**Abstract N°: 2907****Launch of the ACARE Chronic Angioedema Registry (CARE)**

Thomas Buttgereit<sup>\*1</sup>, Pavel Kolkhir<sup>2</sup>, Annika Gutsche<sup>2</sup>, Felix Aulenbacher<sup>2</sup>, Karsten Weller<sup>2</sup>, Markus Magerl<sup>2</sup>, Henriette Farkas<sup>3</sup>, Anete Grumach<sup>4</sup>, Marcus Maurer<sup>2</sup>

<sup>1</sup>Charité – Universitätsmedizin Berlin, Institute of Allergology IFA, Dermatology, Berlin, Germany, <sup>2</sup>Charité – Universitätsmedizin Berlin Institute of Allergology IFA, Dermatology, Berlin, Germany, <sup>3</sup>Hungarian Angioedema Center of Reference and Excellence, Department of Internal Medicine and Haematology, Semmelweis University, Budapest, Hungary, <sup>4</sup>Clinical Immunology, University Center Faculdade de Medicina do ABC, Santo Andre, Brazil

**Introduction & Objectives:**

Angioedema is a paroxysmal, localized and self-limiting swelling of the subcutaneous and/or submucosal tissue, due to a temporary increase in vascular permeability. Angioedema can be heterogeneous, can occur only once or be chronic (recurrent), with or without wheals, hereditary or acquired, due to mast cell mediators or bradykinin or unknown mechanisms. Despite the high frequency of chronic angioedema and the availability of some retrospectively assessed data on the epidemiology, comorbidities, duration of disease, course of disease, underlying causes, treatment response and medical expenses, many types of angioedema are still insufficiently investigated. A disease registry is an appropriate tool to assess these features in a real-life setting. For this reason, the Chronic Angioedema REgistry (CARE) was initiated in 2023 by the global network of Angioedema Centers of Excellence and Reference (ACARE) as the first medical registry for recurrent angioedema.

The objective of this global registry is to improve the knowledge of angioedema by collecting and analyzing data of patients with different forms of recurrent angioedema in the areas mentioned above and, therefore, to improve the understanding of the disease and its types and subtypes.

**Materials & Methods:**

CARE is a web-based international investigator-initiated, open-ended registry, driven by the academic and scientific interests of its participants. CARE is observational (non-interventional) and collects real life data on all types of chronic angioedema, i.e. mast cell-mediated angioedema with and without wheals, bradykinin-mediated angioedema, hereditary angioedema, drug-induced angioedema, and angioedema of unknown origin. Any physician treating patients with angioedema, regardless of location, medical specialty, or type of practice setting is invited to participate in CARE. CARE aims to collect data on all patients with different types of angioedema, with no intentional selection or exclusion criteria.

Core variables of this registry, assessed at baseline and every 6 months, include: Demographic data, duration of disease, course of the disease, frequency of angioedema, underlying causes, comorbidities, triggering factors, treatment response, disease activity, disease control, quality of life impairment, direct health care costs, and absence from work/school. Furthermore, angioedema related biomarker samples shall be collected in selected ACAREs. CARE core variable data are analyzed twice yearly, and specific analyses are done for investigator-proposed research questions.

It is planned to enroll at least 1000 patients in the first 3 years in CARE to generate a data basis that is comprehensive enough for several types of sub analyses.



**Abstract N°: 2947****Remission and relapse profiles in chronic urticaria using real-world data**

Maria Magdalena Balp<sup>\*1</sup>, Irina Pivneva<sup>2</sup>, Andrii Danyliv<sup>1</sup>, Kathleen Chen<sup>2</sup>, Tom Cornwall<sup>2</sup>, James Signorovitch<sup>3</sup>, Dhaval Patil<sup>4</sup>, Ravneet Kohli<sup>5</sup>, Thomas Severin<sup>6</sup>, Weily Soong<sup>7</sup>, Alexander M. Marsland<sup>8</sup>

<sup>1</sup>Novartis Pharma AG, Basel, Switzerland, Launch HEOR, Basel, Switzerland, <sup>2</sup>Analysis Group, Inc., Montréal, Canada, <sup>3</sup>Analysis Group, Inc., Boston, United States, <sup>4</sup>Novartis Pharmaceuticals Corporation, HEOR INRO, United States, <sup>5</sup>Novartis Healthcare Pvt Ltd., Hyderabad, India, Patient Access Services, Hyderabad, India, <sup>6</sup>Novartis Pharma AG, Basel, Switzerland, IHD DU GDD, Basel, Switzerland, <sup>7</sup>AllerVie Health-Alabama Allergy & Asthma Center, Clinical Research Center of Alabama, Birmingham, AL, United States, Birmingham, Alabama, United States, <sup>8</sup>University of Manchester, Manchester, United Kingdom

**Introduction & Objectives:**

Patients with chronic urticaria (CU) may have heterogeneous remission and relapse patterns and it is unclear which combination of remission/relapse patterns are the most pertinent to differentiate patients in distinct clinical and burden clusters (profiles). The objective of this study was to describe representative patient profiles for different remission/relapse patterns.

**Materials & Methods:**

The Optum Life Science electronic health records (Q1 2007 - Q2 2019) in the United States (US) were used to identify patients diagnosed with CU based on  $\geq 2$  relevant ICD 9/10 codes  $\geq 6$  weeks apart. Clinical remission was defined as  $\geq 12$  months free of CU diagnosis and/or related treatment. Relapse was defined as a CU diagnosis and/or CU-related treatment observed after a period of clinical remission of  $\geq 12$  months. A data-driven clustering algorithm was used to group patients based on remission and relapse characteristics. Different cluster configurations were tested through modelling to maximize intra-cluster similarity and inter-cluster dissimilarity on variables related to key disease characteristics (Figure 1). Clinical characteristics, such as comorbidities and treatments, were assessed by cluster.

**Results:**

A total of 112,443 patients were included in this study with a mean (SD) age of 47.7 (17.3); 77.0% were female (Table 1).

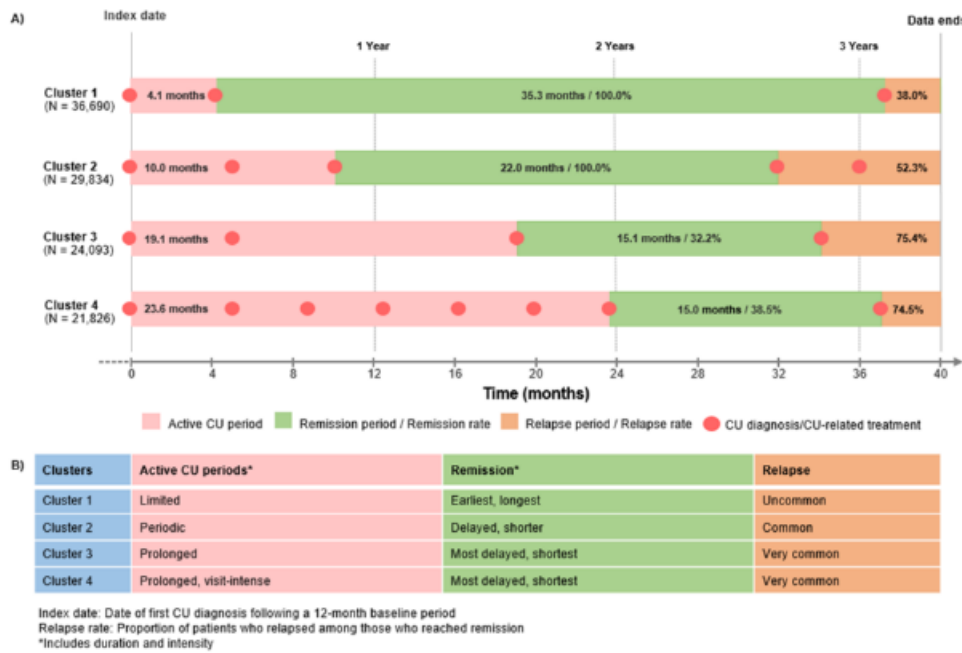
Using CU activity, remission, and relapse characteristics, patients were grouped into 4 clusters. For patients in Cluster 1, the median first active CU disease period lasted 4.1 months (mo) with 100% reaching remission, and a median remission period of 35.3 mo; 38.0% who reached remission had a relapse. For Cluster 2, the median first active CU period was longer (10.0 mo), with 100% reaching remission, had shorter median remission period (22.0 mo), and 52.3% of the patients who reached remission had a relapse. For Clusters 3 and 4, the median first active CU period was much longer (19.1 mo and 23.6 mo) with a lower proportion of patients achieving remission (32.2% and 38.5%), a shorter median remission period (15 mo), and 75% relapsing. In sum, patients in Clusters 3 and 4 had a longer time to remission and a lower proportion achieved remission compared to patients Clusters 1 and 2. In addition, a higher proportion of patients had comorbidities, polypharmacy, higher resource use involving specialist visits and CU-related treatments in Clusters 3 and 4 compared to Clusters 1 and 2. The full profile of the entire CSU cohort and each cluster are presented in Table 1.



Conclusion:

Four distinct clusters of disease activity, remission, and relapse patterns were identified. Patients in Clusters 3 and 4 had much longer active disease periods, a lower remission rate, and more relapses. They also had a higher use of medical resources, more comorbidities and polypharmacy. The cluster definitions reported in this study could be used to develop a prognostic model to predict which patients are at a higher risk of experiencing the relapsing and remitting patterns associated with a higher burden of the disease. Such models may help clinicians better understand the course of disease and support personalized disease management decisions for specific patient profiles.

Figure 1: A) Graphical representation of a patient-persona illustrating median remission and relapse characteristics of each cluster profile B) Cluster characterization



**Table 1: Sociodemographic and clinical characteristics (overall cohort and by cluster)**

	Overall cohort (N=112,443)	Cluster 1 (N=36,690)	Cluster 2 (N=28,834)	Cluster 3 (N=24,093)	Cluster 4 (N=21,826)
<b>Sociodemographic characteristics</b>					
<b>Age (years), mean (SD)</b>					
At diagnosis	47.7 (17.3)	46.3 (17.3)	47.0 (17.4)	48.4 (17.5)	50.0 (16.8)
At first relapse	50.5 (17.3)	50.1 (17.4)	50.0 (17.5)	52.3 (16.9)	52.4 (16.5)
<b>Female, N (%)</b>	86,531 (77.0)	27,284 (74.4)	23,159 (77.6)	18,763 (77.9)	17,325 (79.4)
<b>Ethnicity, N (%)</b>					
African American	14,211 (12.6)	4,262 (11.6)	3,839 (12.9)	3,207 (13.3)	2,903 (13.3)
Asian	2,914 (2.6)	1,079 (2.9)	768 (2.6)	627 (2.6)	440 (2.0)
Caucasian	86,111 (78.4)	26,949 (78.9)	23,334 (78.2)	18,664 (77.5)	17,164 (78.6)
Other/Unknown	7,207 (6.4)	2,400 (6.5)	1,883 (6.3)	1,565 (6.6)	1,319 (6.0)
<b>Clinical characteristics post-CU diagnosis<sup>1</sup></b>					
<b>CCI score, mean (SD)</b>	0.9 (1.6)	0.6 (1.3)	0.9 (1.5)	1.0 (1.7)	1.4 (1.9)
<b>Newly diagnosed comorbidities<sup>2</sup>, N (%)</b>					
Chronic pulmonary disease	14,636 (13.0)	3,946 (10.8)	3,990 (13.4)	3,272 (13.6)	3,428 (15.7)
Depression	11,767 (10.5)	3,207 (8.7)	3,110 (10.4)	2,577 (10.7)	2,873 (13.2)
Asthma	10,566 (9.4)	2,709 (7.4)	2,749 (9.2)	2,416 (10.0)	2,694 (12.3)
<b>Treatments, N (%)</b>					
Oral corticosteroids	68,805 (61.2)	20,294 (55.3)	18,332 (61.4)	15,087 (62.6)	15,092 (69.1)
H1-antihistamines (first or second generation)	85,541 (76.1)	25,240 (68.8)	23,160 (77.6)	18,543 (77.0)	18,596 (85.2)
NSAID agents	36,400 (32.4)	9,509 (25.9)	9,954 (33.4)	8,221 (34.1)	8,716 (39.9)
Narcotic agonist analgesics	34,329 (30.5)	8,819 (24.0)	9,371 (31.4)	7,482 (31.1)	8,657 (39.7)
<b>Number of prescriptions (PPPY), mean (SD)</b>					
Systemic glucocorticoids	1.3 (3.0)	0.7 (1.3)	1.1 (1.8)	1.4 (2.6)	2.7 (5.4)
Proton pump inhibitors	1.0 (3.3)	0.4 (1.4)	0.8 (2.3)	1.0 (2.7)	2.3 (5.8)
Antihistamines (sedating)	0.9 (3.1)	0.3 (0.8)	0.6 (1.4)	0.8 (1.4)	2.5 (6.3)
Antihistamines (non-sedating)	0.6 (1.9)	0.2 (0.5)	0.4 (0.8)	0.5 (1.0)	1.6 (3.9)
H2 antagonists	0.6 (1.9)	0.2 (0.7)	0.4 (1.2)	0.6 (1.5)	1.5 (3.6)
<b>Number of specialist visits (PPPY), mean (SD)</b>					
Family medicine	6.8 (10.3)	4.6 (7.0)	6.1 (8.7)	7.8 (10.6)	10.7 (14.3)
Internal medicine	4.8 (9.3)	3.3 (6.7)	4.2 (8.0)	5.0 (9.6)	7.6 (13.2)
Mid-level provider	4.2 (6.8)	2.5 (4.3)	3.7 (5.4)	4.8 (7.0)	7.1 (10.1)
Emergency medicine	1.2 (2.7)	0.7 (1.6)	1.0 (1.9)	1.3 (2.6)	2.2 (4.5)
Allergy and immunology	0.8 (3.1)	0.3 (1.4)	0.6 (2.3)	0.7 (2.9)	2.0 (5.1)
Dermatology	0.5 (2.0)	0.4 (1.4)	0.4 (1.8)	0.5 (1.9)	0.8 (3.0)
<b>Patients reaching remission, N (%)</b>	82,880 (73.5)	36,690 (100.0)	29,834 (100.0)	7,746 (32.2)	8,410 (38.5)
<b>Patients relapsing, N (%)</b>	41,675 (37.1)	13,953 (38.0)	15,616 (52.3)	5,843 (24.2)	6,263 (28.5)

CCI: Charlson Comorbidity Index; NSAID: nonsteroidal anti-inflammatory drug; PPPY: per-patient-per-year; SD: standard deviation

<sup>1</sup>The prevalence of comorbidities and treatments was assessed during the first 12 months post-CU diagnosis. The number of prescriptions and specialist visits was assessed over the entire follow-up period

<sup>2</sup>Not present pre-CU diagnosis

32<sup>ND</sup> EADV Congress 2023  
11 OCTOBER - 14 OCTOBER 2023  
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**Abstract N°: 3225****Extending omalizumab treatment intervals in patients with chronic spontaneous urticaria (EXTEND trial): Protocol for a multicenter, randomized, open-label, non-inferiority trial.**

Ditte Zhang<sup>\*1</sup>, Jennifer Astrup Sørensen<sup>1</sup>, Christian Vestergaard<sup>2</sup>, Misbah Noshela Ghazanfar<sup>1</sup>, Zarqa Ali<sup>1</sup>, Jacob Thyssen<sup>1</sup>, Alexander Egeberg<sup>1</sup>, Simon Francis Thomsen<sup>1, 3</sup>

<sup>1</sup>Bispebjerg Hospital, Department of Dermatology, Copenhagen, Denmark, <sup>2</sup>Aarhus University Hospital, Department of Dermatology, Aarhus N, Denmark, <sup>3</sup>University of Copenhagen, Department of Biomedical Sciences, Copenhagen N, Denmark

**Introduction & Objectives:**

Omalizumab, an anti-IgE monoclonal antibody, has proven effective in treating chronic spontaneous urticaria (CSU) refractory to antihistamines. However, tapering strategies for omalizumab are currently not well studied. Here we present the rationale and design of the EXTEND trial, a multicenter, randomized, open-label, non-inferiority clinical trial.

The objective of this trial is to investigate if patients with well controlled CSU achieved by standard treatment of 300 mg omalizumab administered subcutaneously every four weeks, can extend treatment intervals to every six weeks, and maintain disease control.

**Materials & Methods:**

Eligible subjects, who achieve an Urticaria Control Test (UCT) score  $\geq 12$  after 12 weeks on omalizumab, will be randomized to continue standard treatment with omalizumab every four weeks (Q4W) or receive treatment in an extended treatment interval every six weeks (Q6W). Both treatment arms will be followed for a total of 36 weeks. Primary endpoint: Absolute difference in average UCT score between treatment arms at week 36. Blood samples, Weekly Urticaria Activity Score (UAS7), Chronic Urticaria Quality of Life Questionnaire (CU2QoL), Dermatology Life Quality Index (DLQI), and records of side effects and flares will be obtained at various times points in the study. Eligible subjects that do not achieve disease control after 12 weeks of standard treatment with omalizumab will be followed in an explorative arm for up to 36 weeks.

**Ethics and dissemination:**

Prior to commencing the study, approvals will be acquired from the national Scientific Ethical Committee, the local Data Protection Agency, and the national Medicines Agency. All study participants are required to provide written informed consent. The study will be conducted according to the Helsinki Declaration and Good Clinical Practice, and findings will be disseminated through publication in international peer-reviewed journals and presented at international conferences.

**Trial registration number:** The registration of this study at ClinicalTrials.gov is pending.

**Abstract N°: 3229**
**Burden of angioedema in patients with chronic spontaneous urticaria in EU5 and US**

Maria Magdalena Balp<sup>\*1</sup>, Kathryn Krupsky<sup>2</sup>, Bridget L. Balkaran<sup>2</sup>, Shaloo Gupta<sup>2</sup>, Clementine Lienhard<sup>3</sup>, Dhaval Patil<sup>4</sup>, Ravneet Kohli<sup>5</sup>, Florence Tetart<sup>6</sup>, Tariq El-Shanawany<sup>7</sup>, John Reed<sup>8</sup>

<sup>1</sup>Novartis Pharma AG, Basel, Switzerland, Launch HEOR, Basel, Switzerland, <sup>2</sup>Cerner Enviza, an Oracle Company, Kansas City, MO, United States, <sup>3</sup>Novartis Pharmaceuticals France, France, <sup>4</sup>Novartis Pharmaceuticals Corporation, United States, <sup>5</sup>Novartis Healthcare Pvt Ltd., Hyderabad, India, patient Access Services, Hyderabad, India, <sup>6</sup>CHU De Rouen, Department of Dermatology, Rouen, France, <sup>7</sup>University Hospital of Wales, Immunodeficiency Centre for Wales, Cardiff, United Kingdom, <sup>8</sup>Oxford University Hospitals NHS Foundation Trust, Department of Dermatology, Oxford, United Kingdom

**Introduction & Objectives:**

Angioedema in chronic spontaneous urticaria (CSU) has a substantial impact on patient's health-related quality of life (HRQoL) and remains underdiagnosed. The objective of this study was to assess the burden of angioedema associated with CSU among patients in EU5 (France, Germany, Italy, Spain, and United Kingdom) and the US.

**Materials & Methods:**

This cross-sectional study analyzed data from 2020 EU5 and the 2019 US National Health and Wellness Survey, which are nationally representative surveys of patient-reported outcomes. Adult respondents with a physician diagnosis of CSU reported if they experienced angioedema in the past 3 months and patients were categorized into YES-ANGIO and NO-ANGIO groups. Burden associated with angioedema was assessed using SF-12v2 (EU5) and SF-36v2 (US) (Mental [MCS] and Physical Component [PCS] Summary scores), health utility scores (SF6D, EQ-5D), General Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9), and Dermatology Life Quality Index (DLQI). Healthcare resource utilization was reported in terms of % of patients with any healthcare professional (HCP) visits, emergency room (ER) visits, and hospitalizations in the past 6 months. Disease control was assessed using Urticaria Control Test (UCT). Bivariate analyses were conducted to compare the outcomes between YES-ANGIO and NO-ANGIO groups.

**Results:**

Among 379 respondents with CSU in EU5 and 371 in the US, YES-ANGIO represented 24.0% and 38.3% of each cohort while NO-ANGIO represented 76.0% in EU5 and 61.7% in the US. Less than 8.0% of the YES-ANGIO patients had well controlled CSU (UCT  $\geq$  12) compared to >40.0% of patients with NO-ANGIO (EU5: 5.5% vs 41.3% and the US: 7.7% vs 48.9%;  $p < 0.001$  for both). Mean [SD] PCS score was significantly lower (worse) among YES-ANGIO compared to NO-ANGIO (EU5: 42.3 [6.4] vs 48.0 [10.1]; US: 37.7 [7.9] vs 46.1 [10.9];  $p < 0.001$ ). YES-ANGIO patients compared to NO-ANGIO patients had non-significant lower MCS score in EU5 (38.9 [6.0] vs 41.0 [10.2];  $p = 0.068$ ) and significantly lower (worse) score in the US (33.1 [7.1] vs 42.0 [12.3],  $p < 0.001$ ). Mean [SD] health utility scores were significantly lower (worse) among YES-ANGIO patients compared to NO-ANGIO (EU5: SF-6D: 0.55 [0.08] vs 0.64 [0.11]; EQ-5D: 0.49 [0.35] vs 0.75 [0.23]) and the US: SF-6D: 0.49 [0.11] vs 0.64 [0.14]; EQ-5D: 0.59 [0.33] vs 0.74 [0.20];  $p < 0.001$  for all). The % of respondents reporting mild/moderate/severe anxiety (GAD-7  $\geq$  5) and depression (PHQ-9  $\geq$  5) were significantly higher among the YES-ANGIO group compared to NO-ANGIO (EU5: GAD-7: 95.6% vs 63.2%, & PHQ-9: 94.5% vs 66.7%; and the US: GAD-7: 89.4% vs 53.3%; PHQ-9: 93.7% vs 58.1%; (Table 1).

The mean [SD] DLQI score was significantly higher (worse HRQoL) for YES-ANGIO patients versus NO-ANGIO (EU5: 17.6 [7.4] vs 4.2 [5.9] and the US: 19.5 [9.3] vs 4.9 [7.0] all  $p < 0.001$ ). YES-ANGIO patients compared to NO-ANGIO reported a significantly higher ER visits (EU5: 75.8% vs 22.2% and the US: 79.6% vs 28.8%;  $p < 0.001$ ) and hospitalizations (EU5: 72.5% vs 11.8% and the US: 77.5% vs 18.8%;  $p < 0.001$ ) in past six months.

## Conclusion:

This real-world study shows that angioedema among CSU patients is associated with high humanistic and economic burden. CSU patients with angioedema reported significantly worse physical and mental status, lower utility scores, higher % with anxiety, and depression along with significantly higher healthcare resource utilization compared to patients without angioedema.

**Table 1: Humanistic and economic outcomes among CSU patients by angioedema status**

	EU5 (N=379)		US (N=371)	
	YES-ANGIO (N=91)	NO-ANGIO (N=288)	YES-ANGIO (N=142)	NO-ANGIO (N=229)
<b>Poorly controlled (Urticaria Control Test &lt;12), N (%)</b>	86 (94.5) *	169 (58.7)	131 (92.3) *	117 (51.1)
<b>Health related quality of life, mean (SD)</b>				
Mental component summary score (MCS) <sup>1</sup>	38.9 (6.0)	41.0 (10.2)	33.1 (7.1) *	42.0 (12.3)
Physical component summary score (PCS) <sup>1</sup>	42.3 (6.4) *	48.0 (10.1)	37.7 (7.9) *	46.1 (10.9)
SF6D: Health state utility score	0.55 (0.08) *	0.64 (0.11)	0.49 (0.11) *	0.64 (0.14)
EQ-5D utility score	0.49 (0.35) *	0.75 (0.23)	0.59 (0.33) *	0.74 (0.20)
EQ-5D VAS score	59.7 (31.4)	65.9 (25.4)	64.0 (30.3)	68.3 (23.8)
Dermatology Life Quality Index (DLQI)	17.6 (7.4) *	4.2 (5.9)	19.5 (9.3) *	4.9 (7.0)
<b>Mental health, N (%)</b>				
General anxiety disorder - 7, (score ≥5)	87 (95.6) *	182 (63.2)	127 (89.4) *	122 (53.3)
Patient health questionnaire - 9, (score ≥5)	86 (94.5) *	192 (66.7)	133 (93.7) *	133 (58.1)
<b>Healthcare resource utilization, N (%)</b>				
Any HCP visits	88 (96.7)	276 (95.8)	136 (95.8)	219 (95.6)
Emergency room visits	69 (75.8) *	64 (22.2)	113 (79.6) *	66 (28.8)
Hospitalizations	66 (72.5) *	34 (11.8)	110 (77.5) *	43 (18.8)

CSU: chronic spontaneous urticaria; HCP: healthcare professional

<sup>1</sup>Assessed using SF-12v2 and SF-36v2 among EU5 and the US respondents respectively

\* Significance level  $p < 0.001$  (Bivariate analyses: YES-ANGIO vs NO-ANGIO groups)

32<sup>ND</sup> EADV Congress 2023  
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**Abstract N°: 3245**
**Burden of chronic spontaneous urticaria relative to psoriasis and atopic dermatitis in Japan**

Maria Magdalena Balp<sup>\*1</sup>, Michihiro Hide<sup>2</sup>, Akihito Uda<sup>3</sup>, Fuyuko Maki<sup>3</sup>, Ravneet Kohli<sup>4</sup>, Shaloo Gupta<sup>5</sup>, Kathryn Krupsky<sup>5</sup>, Bridget L. Balkaran<sup>5</sup>

<sup>1</sup>Novartis Pharma AG, Basel, Switzerland, Launch HEOR, Basel, Switzerland, <sup>2</sup>Department of Dermatology, Hiroshima City Hiroshima, Citizens Hospital, Hiroshima, Japan, Hiroshima, Japan, <sup>3</sup>Novartis Pharma K.K., Tokyo, Japan, <sup>4</sup>Novartis Healthcare Pvt Ltd., Patient Access Services, Hyderabad, India, <sup>5</sup>Cerner Enviza, an Oracle Company, Kansas City, MO, United States

**Introduction & Objectives:**

Dermatological diseases have an enormous impact on patients in Japan and published evidence on comparative burden of disease is limited. The objective of this study was to assess the burden of chronic spontaneous urticaria (CSU) relative to psoriasis (PSO) and atopic dermatitis (AD) in Japan.

**Materials & Methods:**

Data from adult respondents with a physician diagnosis of CSU, PSO and AD were collected from 2019 Japan National Health and Wellness Survey. Burden was evaluated using SF-12v2 [Mental (MCS) and Physical Component (PCS) Summary scores], health utility scores (SF-6D, EQ-5D-5L), EQ-5D visual analogue scale (VAS), General Anxiety Disorder-7 (GAD-7), Patient Health Questionnaire-9 (PHQ-9), healthcare resource utilization (HRU) in past 6 months and Work Productivity and Activity Impairment (WPAI) questionnaire. A multivariable analysis was conducted to compare outcomes, and the results are presented as adjusted mean/percentage with standard error [SE] and p-values reported for each comparison (CSU as the reference group).

**Results:**

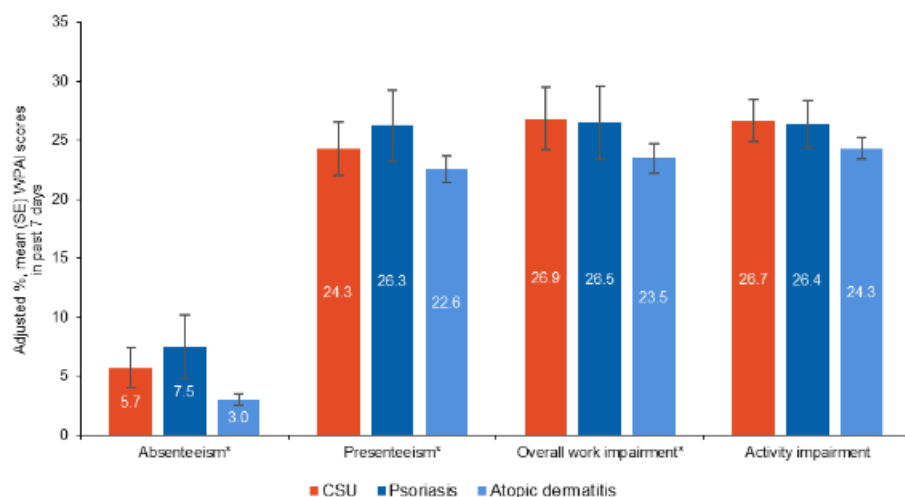
Among 30,006 respondents, 275 had diagnosed CSU, 226 had PSO, and 869 had AD. Mean (SD) age at data collection was 52.7 (14.5), 59.5 (14.8) and 41.2 (14.8); female 60.7%, 27.9% and 52.5% for CSU, PSO and AD, respectively. Patients with CSU had comparable mental and physical status to PSO and AD (MCS: 44.7 [0.6] vs 45.6 [0.7] vs 45.6 [0.3]; PCS: 50.8 [0.4] vs 50.6 [0.5] vs 51.6 [0.2] as well as SF-6D utility scores: 0.72 [0.008] vs 0.72 [0.009] vs 0.73 [0.004] and EQ-5D VAS: 68.2 [1.4] vs 69.6 [1.5] vs 70.9 [0.8];  $p > 0.05$  for all). EQ-5D utility scores in CSU were comparable to PSO (0.80 [0.009] vs 0.82 [0.011];  $p = 0.295$ ) but significantly lower (worse) than AD 0.80 [0.009] vs 0.83 [0.005];  $p = 0.008$ ). Percentage of CSU respondents reporting mild/moderate/severe anxiety (GAD-7  $\geq 5$ ) and depression (PHQ-9  $\geq 5$ ) were comparable to PSO but significantly higher than AD: (GAD-7: 42.3% [3.3] vs 38.4% [3.9];  $p = 0.447$  vs 31.8% [1.8];  $p = 0.006$  and PHQ-9: 45.0% [3.3] vs 43.5% [3.9];  $p = 0.779$  vs 34.4% [1.8];  $p = 0.006$ ). There were no significant differences in HRUs over the past six months between CSU and PSO patients (all  $p$  values  $> 0.05$ ). However, HRUs were significantly higher in CSU compared to AD (any HCP visits: 89.6% [1.9] vs 84.4% [1.4],  $p = 0.039$ ; ER visits: 4.2% [1.3] vs 1.4% [0.4],  $p = 0.006$ ; hospitalizations: 50.0% [3.3] vs 39.2% [1.8],  $p = 0.005$ ). No difference was seen in employment status, absenteeism, presenteeism, overall work impairment and activity impairment between respondents with CSU, PSO and AD ( $p$  values all  $> 0.05$ ) (Figure 1).

**Conclusion:**

After adjusting for confounders, this study demonstrated that patients with CSU, PSO and AD experience similar disease burden on most outcomes assessed. Anxiety, depression, and HRU were significantly higher, and EQ-5D utility scores lower (worse) among CSU compared to AD.



**Figure 1:** Comparative WPAI scores among CSU, psoriasis, and atopic dermatitis cohorts



CSU: Chronic Spontaneous Urticaria; WPAI: Work Productivity And Activity Impairment

\*Assessed only among employed respondents

Note: Models were adjusted for gender, age, university education, employment status (only activity impairment), health insurance type, smoking status, alcohol use, body mass index, Charlson comorbidity index (CCI), and prescription use

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**Abstract N°: 3252**
**Characterization of chronic spontaneous urticaria among patients in EU5, US and Japan**

Maria Magdalena Balp<sup>\*1</sup>, Kathryn Krupsky<sup>2</sup>, Bridget L. Balkaran<sup>2</sup>, Shaloo Gupta<sup>2</sup>, Clementine Lienhard<sup>3</sup>, Dhaval Patil<sup>4</sup>, Ravneet Kohli<sup>5</sup>, Akihito Uda<sup>6</sup>, Fuyuko Maki<sup>6</sup>, Florence Tetart<sup>7</sup>, Tariq El-Shanawany<sup>8</sup>, John Reed<sup>9</sup>, Michihiro Hide<sup>10</sup>

<sup>1</sup>Novartis Pharma AG, Basel, Switzerland, Launch HEOR, Basel, Switzerland, <sup>2</sup>Cerner Enviza, an Oracle Company, Kansas City, MO, United States, <sup>3</sup>Novartis Pharmaceuticals, France, France, <sup>4</sup>Novartis Pharmaceuticals Corporation, USA, United States, <sup>5</sup>Novartis Healthcare Pvt Ltd., Patient Access Services, Hyderabad, India, <sup>6</sup>Novartis Pharma K.K., Tokyo, Japan, <sup>7</sup>Department of Dermatology, CHU De Rouen, France, France, <sup>8</sup>Immunodeficiency Centre for Wales, University Hospital of Wales, Cardiff, United Kingdom, <sup>9</sup>Department of Dermatology, Oxford University Hospitals NHS Foundation Trust, Oxford, United Kingdom, <sup>10</sup>Department of Dermatology, Hiroshima city Hiroshima, Citizens Hospital, Hiroshima, Japan

**Introduction & Objectives:**

The burden of chronic spontaneous urticaria (CSU) varies across different regions and there is a need to further characterize it. The objective of the study was to estimate the prevalence and overall disease burden among patients with CSU in EU5 (France, Germany, Italy, Spain, United Kingdom), the US, and Japan.

**Materials & Methods:**

Data from adult respondents with a physician diagnosis of CSU were collected from EU5 (2020), US (2019), and Japan (2019) National Health and Wellness Survey, a nationally representative survey of patient-reported outcomes. Demographics, clinical characteristics, comorbidities (allowing for Charlson Comorbidity Index (CCI) calculation), Urticaria Control Test (UCT), Dermatology Life Quality Index (DLQI), SF-12/36v2 (mental (MCS) and physical (PCS) component summary scores), Patient Health Questionnaire-9 (PHQ-9), General Anxiety Disorder-7 (GAD-7), and healthcare resource utilization (HRU) (% of patients reporting healthcare professionals (HCP) visits, emergency room (ER) visits, and hospitalisations) in previous 6 months were collected and analysed using descriptive statistics. The 12-month prevalence of diagnosed CSU was weighted by age and gender distributions using the international census projections (2019 for EU5 and 2018 for Japan) and US Census Bureau (2018 for the US).

**Results:**

Among 62,319 in EU5, 74,994 in US and 30,006 respondents in Japan, 539 in EU5, 635 in the US, and 334 in Japan were diagnosed with CSU. The estimated weighted prevalence of CSU was 0.92% in EU5, 0.78% in the US, and 1.1% in Japan. Mean age at data collection and diagnosis ranged from 39.6 to 50.8 years and 37.0 to 39.2 years; mean duration of disease ranged from 9.2 to 11.0 years across the three geographical regions. Most frequently diagnosed comorbidities included allergies, anxiety, depression, asthma, and sleep difficulties. Higher % of respondents had a CCI  $\geq 2$  in EU5 (20.0%) and the US (39.2%) compared to Japan (5.1%). Angioedema occurrence in the past 3 months was reported by 27.1% of patients in EU5, 49.1% in the US, and 3.3% in Japan. More than half of the respondents did not receive treatment (prescription and/or over the counter) and  $\geq 60.0\%$  had poorly controlled disease (UCT score  $< 12$ ) (Table 1). In EU5 and the US, diagnosis of CSU was established first by a general practitioner (35.1 – 36.3%) while in Japan, by a dermatologist (71.8%).

The mean (SD) DLQI score in EU5, the US and Japan was 8.8 (9.3), 13.8 (11.2), and 3.8 (6.0), respectively. The

mean MCS and PCS scores were  $\leq 50$  indicating impairment. More than 70.0% of respondents in EU5 and the US and >40.0% in Japan had mild/moderate/severe anxiety (GAD-7  $\geq 5$ ) and depression (PHQ-9  $\geq 5$ ) (Table 1). The HRU was higher in EU5, and US compared to Japan; any HCP visits: EU5 96.8%, US 96.5%, and Japan 89.8%, ER visits: EU5 40.3%, US 60.2%, and Japan 6.9%, and hospitalizations: EU5 32.1%, US 55.9%, and Japan 9.9%.

## Conclusion:

This real-world study among respondents with diagnosed CSU shows some similarities and differences of the disease profile in the three geographical regions. The diagnosed prevalence of CSU was slightly higher in Japan. CSU was associated with allergic and mental comorbidities, impaired health-related quality of life. A high HRU was reported in EU5 and the US, with higher % of US respondents reporting ER and hospitalizations. The burden of mental health, HRU and angioedema was lower in Japan, which may be attributed to differences in culture and healthcare system.

**Table 1: Characterization of CSU patients**

	EU5 (N=539)	US (N=635)	Japan (N=334)
<b>Patient demographics, and clinical profile</b>			
<b>Age, mean (SD) years</b>			
At data collection	42.4 (14.8)	39.6 (12.6)	50.8 (15.3)
At diagnosis	37.8 (16.8)	37.0 (17.1)	39.2 (14.9)
<b>Gender, %</b>			
Female	58.1	51.7	60.3
<b>Duration of disease, mean (SD) years</b>	9.2 (10.4)	11.0 (12.6)	10.5 (12.4)
<b>CCI score, %</b>			
0	66.8	51.5	88.0
1	13.2	9.3	6.9
$\geq 2$	20.0	39.2	5.1
<b>Most frequent Comorbidities, %</b>			
Allergies	38.4	30.9	39.2
Anxiety	24.1	17.6	3.0
Depression	23.0	20.0	13.5
Headache	23.2	14.0	13.5
Migraine	19.5	15.4	11.1
Obesity	17.8	21.4	2.7
Hypertension	16.9	18.4	13.8
Thyroid condition	15.2	11.5	4.2
Asthma	13.4	12.4	7.8
Sleep difficulties	11.5	8.2	3.6
<b>First CSU Diagnosed by, %</b>			
General practitioner	35.1	36.3	20.0
Dermatologist	34.7	16.4	71.8
Allergist	26.7	39.8	7.7
Others	3.5	7.5	0.5
<b>Urticaria Control Test (UCT), %</b>			
Poorly controlled (UCT<12)	71.6	77.0	61.1
<b>Currently treated, n (%)</b>	261 (48.4)	338 (53.2)	123 (36.8)
Prescription medication only	54 (10.0)	26 (4.1)	NA
Over the counter medication only	175 (32.5)	277 (43.6)	NA
Prescription + over the counter medication	32 (5.9)	35 (5.5)	NA
<b>Disease Burden</b>			
<b>Health related quality of life, mean (SD)</b>			
Mental component summary score (MCS)	40.6 (9.1)	36.3 (10.5)	45.1 (10.0)
Physical component summary score (PCS)	45.6 (9.8)	40.1 (10.0)	50.3 (7.0)
<b>Mental health, % of patients</b>			
General Anxiety Disorder-7 (score $\geq 5$ )	72.4	74.3	41.3
Patient Health Questionnaire-9 (score $\geq 5$ )	75.7	77.6	44.0
<b>Healthcare resource utilization (HRU), % of patients</b>			
All Healthcare professional visits	96.8	96.5	89.8
Emergency room visits	40.3	60.2	6.9
Hospitalizations	32.1	55.9	9.9

CCI: Charlson comorbidity Index; SD: Standard deviation; NA: Not available



**Abstract N°: 3272****Kronik İdiyopatik Ürtikerli Hastalarda Serum Zonulin Düzeyi ve Bağırsak Geçirgenliğinin Değerlendirilmesi ve Serum Zonulin Düzeyi ile Hastalık Şiddeti Arasındaki İlişki**

Ahmet Özsoy<sup>1, 2</sup>, Selda Pelin Karta<sup>2</sup>, Simge Ünal<sup>\*2, 3</sup>, Fevzi Aydın<sup>2</sup>

<sup>1</sup>Türkiye, <sup>2</sup>dışkapı yıldırım beyazıt training and reserch hospital, <sup>3</sup>Usak

**Introduction & Objectives:**

There may be an association between increased intestinal permeability and the progression of Chronic Spontaneous Urticaria (AA).\*\*

It was aimed to evaluate the role of intestinal permeability in the etiopathogenesis of CSU and the relationship between disease severity and zonulin levels by measuring at the zonulin levels, which is an indicator of the increase in intestinal permeability, in the sera of CSU and control groups.

**Materials & Methods:**

61 CSU patients and 59 healthy controls were included. Demographic characteristics, personal and family histories, urticaria activity score, age of onset, duration of last attack, antihistamine dose used, and concomitant diseases of CSU patients were recorded.

**Results:**

A statistically significant difference was found between the patient and control groups in terms of zonulin levels ( $p=0.000$ ). The zonulin levels of patients with angioedema were significantly higher than those without angioedema and a statistically significant difference was found in zonulin levels according to the presence of angioedema ( $p=0.023$ ).

**Conclusion:**

These findings suggest that intestinal permeability may play an important role in the pathogenesis of CSU and angioedema.

**Abstract N°: 3318**
**Patient-Reported Symptom Burden in Chronic Inducible Urticaria: Post Hoc Analysis of Baseline Data from a Phase 3 Clinical Trial**

 Diane Whalley<sup>1</sup>, Maria Magdalena Balp<sup>\*2</sup>, Stuart Yarr<sup>3</sup>, Avantika Barve<sup>4</sup>, Miriam Porter<sup>5</sup>
<sup>1</sup>RTI Health Solutions, Manchester, United Kingdom, <sup>2</sup>Novartis Pharma AG, Basel, Switzerland, Launch HEOR, Basel, Switzerland, <sup>3</sup>RTI Health Solutions, United Kingdom, <sup>4</sup>Novartis Pharmaceuticals Corporation, USA, New Jersey, United States, <sup>5</sup>Novartis Pharma AG, Basel, Switzerland, Basel, Switzerland

**Introduction & Objectives:**

Chronic urticaria is associated with recurrent episodes of itchy hives. Studies often focus on chronic spontaneous urticaria, whereas little is known about the patient experience of chronic inducible urticaria (CIndU). The aim of this analysis was to explore patient-reported symptom burden and trigger avoidance associated with CIndU using baseline data from a phase 3 clinical trial.

**Materials & Methods:**

Exploratory analysis was conducted using baseline data from 39 patients diagnosed with CIndU (symptomatic dermographism [SDerm], cholinergic urticaria [CholU], cold urticaria [ColdU]). Patients completed the newly developed Urticaria Symptom Daily Diary (USDD) over 7 days prior to baseline, as well as the Dermatology Life Quality Index (DLQI/Children's DLQI [CDLQI]) and a Patient Global Impression of Severity item (PGIS) at baseline. The USDD collects information on trigger exposure and avoidance, and severity of symptoms (itch, burning, pain, hives) on 0-10 scales. On day 1 of completion, patients indicated whether itch, burning or pain was their most bothersome symptom (MBS). A 7-day score for each symptom (ISS7, BSS7, PSS7, HSS7) was computed as the average of daily scores on trigger-exposure days. The most severe symptom (MSS) was defined as the highest of ISS7, BSS7 and PSS7. Analyses included descriptive statistics, analysis of variance and correlations.

**Results:**

The sample comprised 39 patients: 17 SDerm, 12 CholU, 10 ColdU (mean age 31.8 [SD 13.5, range 12-63]; 51% male). Patients reported trying to avoid triggers on an average of 3.9 days over the 7 days; however, out of 153 attempted trigger-avoidance days across the sample, 71% still resulted in trigger exposure. Patients were exposed to triggers on an average of 3.9 days over the 7 days and experienced symptoms on 86% of trigger-exposure days. Itch was most often the MBS (69%), followed by burning (15%) and pain (5%); patients with CholU were more likely to select burning or pain. Of the 30 patients who reported an MBS and had 7-day scores available, the MBS was also the MSS for 70% of them. Patients with CholU and ColdU were more likely to have different MBS and MSS than those with SDerm. 7-day scores were highest for itch (ISS7) and lowest for pain (PSS7); all scores worsened with increased PGIS (Table 1). Correlations between DLQI/CDLQI and 7-day symptom scores ranged from 0.54 (PSS7) to 0.66 (ISS7).

**Conclusion:**

This analysis shows that while patients in this sample often tried to avoid triggers, complete avoidance was not possible. Within this small sample, itch was frequently the most severe and the most bothersome symptom. Nonetheless, burning was an important symptom for some patients, particularly those with CholU and ColdU. Consideration needs to be given to trigger avoidance and wider symptom experience when assessing patient-centered outcomes in CIndU. Approaches such as the most bothersome symptom have the potential to further

enhance the patient relevance of outcome assessments.

**Table 1. USDD 7-Day Symptom Scores by CIndU Type and PGIS (N = 39)**

Cohort/result	USDD 7-day score: Mean (SD)					
	ISS7	PSS7	BSS7	HSS7	MBSS7	MSSS7
<b>Overall (n = 30-33)</b>	3.10 (2.52)	1.70 (2.42)	2.15 (2.48)	2.55 (2.17)	2.90 (2.61)	3.22 (2.50)
<b>By CIndU type</b>						
SDerm (n = 12-14)	3.10 (2.29)	1.18 (1.54)	1.50 (2.05)	2.32 (1.87)	2.83 (2.31)	3.15 (2.27)
CholU (n = 11)	2.98 (2.13)	1.82 (2.50)	2.37 (2.43)	2.60 (2.01)	2.97 (2.26)	3.19 (2.19)
ColdU (n = 7-8)	3.28 (3.57)	2.47 (3.50)	2.98 (3.18)	2.87 (3.02)	2.91 (3.81)	3.38 (3.48)
<b>By PGIS categories</b>						
Mild (n = 9)	0.91 (0.90)	0.23 (0.50)	0.49 (0.63)	0.87 (0.81)	0.79 (0.85)	1.00 (0.84)
Moderate (n = 12-14)	3.03 (1.97)	1.17 (1.42)	1.54 (1.85)	2.29 (1.46)	2.73 (1.89)	3.13 (1.88)
Severe (n = 8-9)	5.75 (1.93)	4.19 (3.10)	4.99 (2.27)	4.90 (2.11)	5.89 (2.13)	5.93 (1.85)
ANOVA P value	<0.0001	0.0007	<0.0001	<0.0001	<0.0001	<0.0001

ANOVA = analysis of variance; BSS7 = 7-day burning severity score; CholU = cholinergic urticaria; CIndU = chronic inducible urticaria; ColdU = cold urticaria; HSS7 = 7-day hives severity score; ISS7 = 7-day Itch severity score; MBSS7 = 7-day most bothersome symptom score; MSSS7 = 7-day most severe symptom score; PGIS = Patient Global Impression of Severity; PSS7 = 7-day pain severity score; SD = standard deviation; SDerm = symptomatic dermographism; USDD = Urticaria Symptom Daily Diary.

Notes: 7-day symptom scores were computed as the average daily score on trigger-exposure days during the 7 days at baseline; at least 4 diary-completion days were required for the computation of 7-day scores. PGIS categories "No symptoms" (n = 1) and "Very severe" (n = 0) are excluded from the table.



**Abstract N°: 3333**
**Remibrutinib Treatment Improves Itch, Sleep and Activity in Chronic Spontaneous Urticaria Patients: Phase 2b Study Results**

Ana Giménez-Arnau<sup>\*1</sup>, Connie Hsu<sup>2</sup>, Robert Snyder<sup>3</sup>, Lee Clore<sup>4</sup>, Vipul Jain<sup>5</sup>, Karine Lheritier<sup>6</sup>, Pauline Walsh<sup>7</sup>, Sibylle Haemmerle<sup>6</sup>, Michael Wells<sup>8</sup>, Ivan Nikolaev Ivanov<sup>6</sup>, Marcus Maurer<sup>9, 10</sup>

<sup>1</sup>Department of Dermatology, Hospital del Mar - IMIM, Universitat Pompeu Fabra, Barcelona Spain, <sup>2</sup>Research Solutions of Arizona, Litchfield Park, Arizona, USA, <sup>3</sup>Riverchase Dermatology, Pembroke Pines, Florida, USA, <sup>4</sup>Allergy and Asthma Specialists, PSC, Owensboro, Kentucky, USA, <sup>5</sup>Division of Clinical Immunology and Allergy, Department of Medicine, McMaster University, Hamilton, Ontario, Canada, <sup>6</sup>Novartis Pharma AG, Basel, Switzerland, <sup>7</sup>Novartis Ireland Limited, Dublin, Ireland, <sup>8</sup>Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, USA, <sup>9</sup>Urticaria Center of Reference and Excellence (UCARE), Institute of Allergology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, <sup>10</sup>Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Allergology and Immunology, Berlin, Germany

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is characterised by wheals (hives) and/or angio-oedema (>6 weeks) and has a major impact on patients' wellbeing. Remibrutinib (LOU064) is an oral, highly selective Bruton's tyrosine kinase (BTK) inhibitor that offers fast disease control in patients with CSU who remain symptomatic despite treatment with second-generation H1-antihistamines. We explored the effect of remibrutinib on itch severity, sleep and activity interference in patients with CSU.

**Materials & Methods:**

In this Phase 2b study (NCT03926611), 311 patients with CSU were equally randomised to remibrutinib

10 mg once daily (q.d.)/35 mg q.d./100 mg q.d./10 mg twice daily (b.i.d.)/25 mg b.i.d./100 mg b.i.d. or placebo for 12 weeks. Outcomes presented include change from baseline in weekly Itch Severity Score (ISS7), weekly Sleep Interference Score (SIS7), and weekly Activity Interference Score (AIS7), and the proportion of patients with ISS7=0 (no itch), SIS7=0 (no sleep interference) and AIS7=0 (no activity interference) at Weeks 2, 4, and 12.

**Results:**

The mean baseline ISS7, SIS7, and AIS7 were 12.6 to 14.6, 10.2 to 12.2 and 10.5 to 13.1 (any remibrutinib dose) versus 11.8, 10.3 and 10.8 (placebo), respectively. The change from baseline in ISS7, SIS7 and AIS7 was greater with remibrutinib versus placebo at Week 2 (ISS7: -9.5 to -6.3 vs -1.1; SIS7: -8.6 to -5.2 vs

-1.3; AIS7: -9.1 to -5.2 vs -1.8), Week 4 (ISS7: -9.6 to -6.4 vs -2.0; SIS7: -8.9 to -5.3 vs -2.6; AIS7: -9.2 to -6.3 vs -2.3) and Week 12 (ISS7: -9.4 to -6.9 vs -3.1; SIS7: -8.7 to -6.3 vs -2.9; AIS7: -9.1 to -6.3 vs -3.0), respectively. A higher proportion of patients achieved ISS7=0 with remibrutinib versus placebo at Week 2 (17.0% to 32.6% vs 0%), Week 4 (19.1% to 41.9% vs 2.4%), and Week 12 (26.7% to 46.5% vs 19.0%). Similarly, a higher proportion of patients achieved SIS7=0 with remibrutinib versus placebo at Week 2 (34.9% to 44.2% vs 12.5%), Week 4 (31.9% to 58.1% vs 15.0%) and Week 12 (48.9% to 64.1% vs 33.3%), and AIS7=0 at Week 2 (34.9% to 52.5% vs 15.0%), Week 4 (37.0% to 55.0% vs 15.0%) and Week 12 (51.1% to 60.0% vs 24.3%).

**Conclusion:**

Remibrutinib demonstrated rapid (as early as Week 2) and sustained improvements, up to complete absence of itch, and no sleep and activity interference versus placebo.

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**Abstract N°: 3549**
**Remibrutinib (LOU064) treatment decreases disease activity in patients with chronic spontaneous urticaria: Post hoc analysis from the Phase 2b study**

Ana Giménez-Arnau<sup>\*1</sup>, Marcus Maurer<sup>2, 3</sup>, Robert Snyder<sup>4</sup>, Christine-Elke Ortmann<sup>5</sup>, Bharat Suryawanshi<sup>6</sup>, Ivan Nikolaev Ivanov<sup>5</sup>, Merin Kuruvilla<sup>7</sup>, Sibylle Haemmerle<sup>5</sup>

<sup>1</sup>Department of Dermatology, Hospital del Mar -IMIM, Universitat Pompeu Fabra, Barcelona, Spain, <sup>2</sup>Urticaria Center of Reference and Excellence (UCARE), Institute of Allergology, Charité-Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, <sup>3</sup>Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Allergology and Immunology, Berlin, Germany, <sup>4</sup>Riverchase Dermatology, Pembroke Pines, Florida, USA, <sup>5</sup>Novartis Pharma AG, Basel, Switzerland, <sup>6</sup>IQVIA India Ltd, Mumbai, India, <sup>7</sup>Novartis Pharmaceuticals, East Hanover, New Jersey, USA

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is characterised by recurrent wheals (hives) and/or angioedema for more than 6 weeks that can have a major impact on patients' well-being. Remibrutinib (LOU064) is an oral, highly selective Bruton's tyrosine kinase (BTK) inhibitor that offers fast disease control in patients with CSU who remain symptomatic despite treatment with second-generation H1-antihistamines. It has shown clinical efficacy and a favourable safety profile for up to 12 weeks in a Phase 2b dose-finding study in patients with CSU. This analysis explores the shift of weekly Urticaria Activity Score (UAS7) severity bands with remibrutinib treatment in patients with CSU inadequately controlled with H1-antihistamines.

**Materials & Methods:**

In the remibrutinib Phase 2b study (NCT03926611), 311 patients with CSU were randomised equally to remibrutinib 10 mg once daily (q.d.)/35 mg q.d./100 mg q.d./10 mg twice daily (b.i.d.)/25 mg b.i.d./100 mg b.i.d., or placebo for 12 weeks. The CSU disease activity band shift was defined based on 5 standard UAS7 bands: UAS7=28–42 (severe), UAS7=16–27 (moderate), UAS7=7–15 (mild), UAS7=1–6 (well-controlled) and UAS7=0 (complete response). The proportion of patients with a shift in CSU disease activity at Weeks 2, 4, and 12 in the subgroup of patients with moderate and severe CSU disease activity band at baseline was analysed.

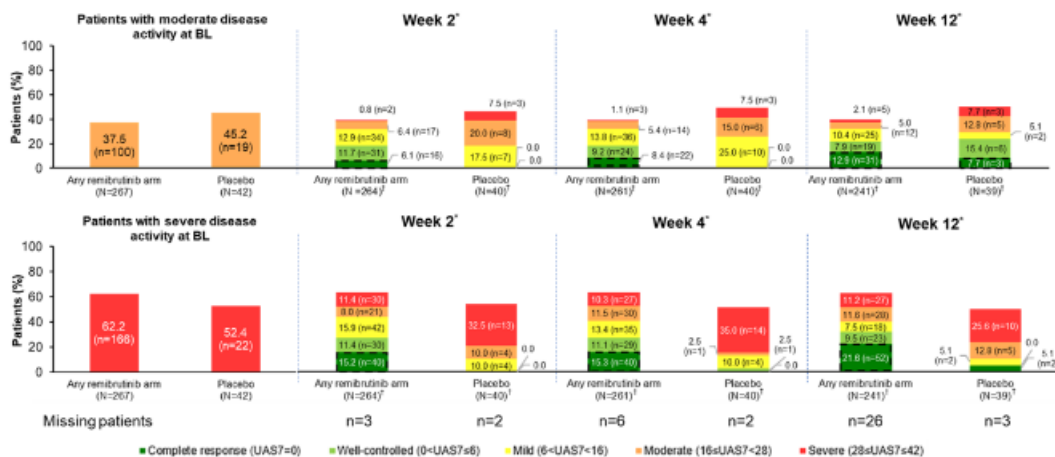
**Results:**

At baseline, 37.5% of patients in any remibrutinib arm and 45.2% of patients in the placebo arm had moderate CSU disease activity and 62.2% and 52.4%, respectively, had severe CSU disease activity. The proportion of patients with shift in CSU disease activity band at Weeks 2, 4, and 12 in subgroup of patients with moderate and severe CSU disease activity at baseline is presented in the **Figure 1**. At Week 2, 81.0% (81/100) and 81.6% (133/163) of the patients with moderate and severe disease activity at baseline, respectively, improved their disease activity and moved to a lower disease activity band. The response was maintained at Week 4 and Week 12 in moderate disease activity (82.8% [82/99] and 81.5% [75/92], respectively) and severe disease activity (83.2% [134/161] and 81.8% [121/148], respectively), with majority of the patients in moderate and severe disease activity at baseline, remained with lower disease activity during the study. At Week 2, a higher proportion of patients with moderate and severe CSU disease activity in any remibrutinib arm (vs the placebo arm) shifted to well-controlled and complete response bands. The improvement was further sustained at Week 4 and Week 12, with a higher proportion of patients both in moderate and severe CSU disease activity bands in any remibrutinib arm (vs the placebo arm) shifted to well-controlled and complete response bands.

## Conclusion:

This post hoc analysis shows that remibrutinib treatment decreases CSU disease activity within 2 weeks in more than 80% of patients who had moderate or severe CSU disease activity at baseline, and the response was sustained during 12 weeks of study. More patients treated with remibrutinib were free of disease activity at all timepoints measured.

**Figure 1. CSU disease activity at Weeks 2, 4 and 12 in patients with moderate or severe disease at baseline¶**



\*Patients with both baseline and treatment epoch post-baseline values were included and the percentages are based on baseline total number of patients; †Number patients with available baseline data.¶

BL, baseline; CSU, chronic spontaneous urticaria; N, total number of patients randomised at the baseline; n, number of patients in each CSU disease activity band; UAS7, weekly Urticaria Activity Score.¶



**Abstract N°: 3707**
**Normocomplementemic Urticarial Vasculitis in a Pediatric Patient**

 João Teixeira<sup>\*1</sup>, Ana Matos<sup>1</sup>, João Nascimento<sup>2</sup>, Jose Carlos Cardoso<sup>1</sup>, Leonor Castendo Ramos<sup>1</sup>
<sup>1</sup>Coimbra University Hospital Center, Dermatology and Venereology, <sup>2</sup>Coimbra University Hospital Center, Pediatrics

**Introduction & Objectives:**

Urticarial vasculitis is a rare clinical entity consisting of two essential findings: clinical manifestations of urticaria and histopathologic evidence of leukocytoclastic vasculitis of the small vessels. Peak incidence is in the fourth decade of life with female predominance and reported pediatric cases have been sparse to date. Clinical suspicion of this entity should be raised in the setting of persisting urticarial lesions for >24 hours, bruising-like associated changes or systemic symptoms such as arthralgias, abdominal pain, eye symptoms or fever. Skin biopsy is essential to confirm the diagnosis and laboratory work-up should include complement levels and autoimmunity to further characterize the disease. Pediatric cases remain a challenge, both in diagnostic and therapeutic grounds, in part due to its rarity. This case highlights the need for interdisciplinary evaluation of challenging cases, particularly, stressing the role of Dermatology in the evaluation of patients with urticarial lesions with atypical features and systemic symptoms.

**Materials & Methods:**

We report a case of an 8-year-old Caucasian girl presenting with pruriginous and migratory erythematous plaques associated with episodic fever and arthritis with 2 years duration.

**Results:**

An 8-year-old Caucasian girl was referred to our Dermatology department complaining of pruriginous, and migratory erythematous and oedematous plaques associated with episodic fever and arthritis with 2 years duration. There was a history of chickenpox 2 months before the first episode and serum sickness-like reaction was initially presumed as the most likely diagnosis. Treatment was initiated with oral prednisone with complete resolution of the lesions and articular findings; however, subsequent episodes were noted with increasing poor response to oral steroid and antihistamine therapy. After 6 months of follow-up, chronic spontaneous urticaria emerged as an alternative diagnosis. Physical examination at that time revealed urticarial plaques and symptomatic dermographism. Laboratory work-up demonstrated positive ANA titers 1:160, positive anti-TPO, elevated IgE and ESR. Complement C3, C4 and C1q levels were normal and anti-Ds-DNA antibodies were negative. Dermatology consultation was requested at this point. Detailed clinical history revealed urticarial plaques persisting for more than 24 hours with residual bruising after resolution of the urticarial lesions, raising the clinical suspicion of urticarial vasculitis. Skin biopsy showed papillary dermal oedema and moderate inflammatory infiltrate with predominance of neutrophils and occasional eosinophils. Karyorrhexis, capillary vessel wall damage, and red blood cell extravasation were also present. After careful clinicopathological correlation, the diagnosis of normocomplementemic urticarial vasculitis was established. The patient was started on colchicine in association with oral prednisone and antihistamines with poor response after 6-months. Hydroxychloroquine was added but with no benefit. To the date of writing, oral dapsone is being considered as the next therapeutic step.

**Conclusion:**

Urticarial vasculitis is a rare and yet poorly understood clinical entity with very few pediatric cases reported to

date. Diagnostic and treatment challenges are significant in this age group, stressing the role of the Dermatologist and the need for interdisciplinary consultation in such patients.

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**Abstract N°: 4026****Chronic spontaneous urticaria following anti-SARS-CoV-2 vaccination**

Billel Merrouche<sup>1</sup>, Lydia Iberraken<sup>1</sup>, Hind Medjitena<sup>2</sup>, Houria Sahel<sup>1</sup>

<sup>1</sup>University Hospital Center Lamine Debaghine, Department of Dermatology, Bab El Oued, Algiers, Algeria,

<sup>2</sup>National Pharmacovigilance Centre,, Algiers, Algeria

**Introduction:**

Chronic spontaneous urticaria (CSU) is a common dermatological pathology defined by the non-reproducible occurrence by provocation tests and without exposure to external stimuli, of urticarial papules and/or angioedema over for more than 6 weeks or longer. We report a case of CSU following anti-COVID-19 vaccination with the Sinovac-CoronoVac vaccine.

**Case presentation:**

A 58-year-old woman with a history of insulin-requiring type 2 diabetes and hypertension treated with nicardipine for several years; presented with pruritic superficial and deep generalized urticarial lesions evolving in flare-ups for more than 1 year. These lesions had started 24 hours after the first injection of Sinovac-CoronoVac vaccine.

The extracutaneous clinical examination was normal. No abnormalities were found in biological, immunological and histopathological investigations (histology of a skin biopsy, direct immunofluorescence). Antihistamine treatment with 4 tablets/day controlled the urticarial flares. The case was reported to pharmacovigilance services. The second vaccine dose was not administered.

**Discussion:**

CSU is rarely observed after vaccination. The main cause is influenza and hepatitis B vaccines . A few cases following vaccination against SARS-CoV-2 have been described in the literature: Especially with mRNA vaccines (Pfizer-BioNTech/Comirnaty® and Moderna/Spikevax®), more rarely with other vaccines. They appear after the first and/or second dose, within 1 to 15 days after the injection, with superficial and/or deep involvement. Quadruple-dose antihistamines yield a favorable response, as observed in our case. However, in some instances, this treatment was not sufficient (resistance and relapse), and required the introduction of omalizumab, resulting in clinical remission.

The exact pathophysiological mechanism of this CSU is still not fully understood, but may involve vaccine-induced her T cell-mediated immune responses. Cases of exacerbation of CSU after administration of the COVID-19 vaccine have also been reported. Considering the delayed onset and negative etiological explorations in our patient raise questions about the critical role of vaccination.

**Conclusion:**

We describe an exceptional case of CSU after Sinovac's COVID-19 vaccination. Thus, it is necessary to recognize vaccination as a potential trigger of chronic urticaria.



**Abstract N°: 4100****Chronic spontaneous urticaria and the role of autoreactivity**

Vesna Trajkova<sup>1</sup>, Hristina Breshkovska<sup>2</sup>, Irena Dimitrovska<sup>1</sup>, Daniela Buklioska Iliovska<sup>3</sup>

<sup>1</sup>General City Hospital "8mi Septemvri", Dermatology department, skopje, North Macedonia, <sup>2</sup>State Dermatology Clinic, Dermatology department, skopje, North Macedonia, <sup>3</sup>General City Hospital "8mi Septemvri", Pulmonary Department, skopje, North Macedonia

**Introduction & Objectives:** Autologous serum skin test (ASST) is mostly used in chronic spontaneous urticaria (CSU) to show autoreactivity. Autoreactive reactions take place in antibody-mediated autoimmune and cell-mediated processes counting auto-allergic reaction, which is autoimmunity specifically mediated by immunoglobulin E autoantibodies to self-antigens. Direct (skin, ASST) and indirect (presence of auto-antibodies, prevalence of autoimmune diseases) evidence of autoimmune disease in CSU are found.

**Materials & Methods:** This prospective study was conducted from December 2021- November 2022 in the department of Dermatology in City General Hospital "8mi Septemvri", Skopje, North Macedonia. 230 patients 18-70 years old with CSU were included. ASST was performed by the intradermal injection of the patient's own serum into the volar part of the forearm and classified as having a positive or a negative ASST. Medical history, including history of personal or familial atopy (asthma, atopic dermatitis and allergic rhinitis), autoimmune and non-autoimmune diseases were recorded. For assessing disease activity was UAS7 was recorded. Autoimmunity was defined in the case of a personal history of autoimmune disease or in the presence of at least one type of autoimmune antibodies: anti-TPO, anti-nuclear antibodies (ANA) and rheumatoid factor (RF). Additional blood analysis were made: CBC, IgE, D-dimer

**Results:** This study included 230 patients with CSU and 130 healthy subjects- control group (CG), mean age was 41.8 years.\*\*\* 60,87% of CSU patients were ASST positive, 63.04% had positive autoimmune status. We did not found statistical differences between positive and negative ASST in concomitant non-autoimmune diseases in CSU patients ( $p=0.71$ ) and in disease activity in CSU ( $p=0.29$ ). Positive\*\* ASST was presented in 86.9% patients with positive autoimmune status. Patients with positive ASST had personal and familial history of autoimmune disease ( $p<0.0001$  and  $p=0.0003$  accordingly), concomitant autoimmune diseases 73.57%, personal history of asthma 60.71%, familial history of asthma 53.57%, increased D-dimer levels ( $p=0.048$ ), increased platelet counts ( $p<0.0001$ ), decreased IgE levels ( $p<0.0001$ ) and increased Anti-TPO levels ( $p<0.0001$ ), compared to patients with negative ASST.

**Conclusion:** Since nearly 30 years, several lines of evidence argue for an auto-immune basis of CSU, or at least in a subgroup of them. In this study, we focused on associations of concomitant autoimmune disease and/or presence auto-antibodies and positivity of ASST. The latest publications suggest that autoimmunity and autoallergy are seen as major CSU endotypes: auto-allergic CSU -linked to IgE autoantibodies and autoimmune CSU due to autoantibodies that directly activate mast cells. In latest studies ASST as autoreactivity test in CSU is often connected with autoimmunity in CSU.



**Abstract N°: 4199**
**Remibrutinib, an oral, highly selective BTKi in development for CSU: Analysis of safety data from the completed Phase 2 studies in inflammatory immune-mediated diseases**

Ana Giménez-Arnau<sup>\*1</sup>, Tanuja Chitnis<sup>2</sup>, Mitzi Williams<sup>3</sup>, Laura Airas<sup>4</sup>, Sarbjit Saini<sup>5</sup>, Michihiro Hide<sup>6</sup>, Gordon Sussman<sup>7</sup>, Jin Nakahara<sup>8</sup>, Robert Bermei<sup>9</sup>, Thomas Dörner<sup>10</sup>, Brett Loop<sup>11</sup>, Virginia De Las Heras<sup>12</sup>, Roman Willi<sup>12</sup>, Bernd Kieseier<sup>12, 13</sup>, Sibylle Haemmerle<sup>12</sup>, Richard Siegel<sup>14</sup>, Bruno Cenni<sup>14</sup>, Heinz Wiendl<sup>15</sup>, Marcus Maurer<sup>16, 17</sup>, Xavier Montalban<sup>18</sup>, Artem Zharkov<sup>12</sup>

<sup>1</sup>Hospital del Mar - IMIM, Universitat Pompeu Fabra, Department of Dermatology, Barcelona, Spain, <sup>2</sup>Brigham and Women's Hospital, Department of Neurology, Boston, United States, <sup>3</sup>Joi Life Wellness Group, Atlanta, United States, <sup>4</sup>Turku University Hospital and University of Turku, Turku, Finland, <sup>5</sup>Johns Hopkins Asthma and Allergy Center, Baltimore, United States, <sup>6</sup>Hiroshima City Hiroshima Citizens Hospital, Hiroshima, Japan, <sup>7</sup>University of Toronto, Toronto, Canada, <sup>8</sup>Keio University School of Medicine, Department of Neurology, , Tokyo, Japan, <sup>9</sup>Mellen Center for MS, Cleveland Clinic, Cleveland, United States, <sup>10</sup>Charite Universitätsmedizin Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany, <sup>11</sup>Novartis Pharmaceutical Corporation, Cambridge, United States, <sup>12</sup>Novartis Pharma AG, Basel, Switzerland, <sup>13</sup>Heinrich-Heine University, Department of Neurology , Duesseldorf, Germany, <sup>14</sup>Novartis Institutes for Biomedical Research, Basel, Switzerland, <sup>15</sup>Institute of Translational Neurology, University of Münster, Department of Neurology , Münster, Germany, <sup>16</sup>Urticaria Center of Reference and Excellence (UCARE), Institute of Allergology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, <sup>17</sup>Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Allergology and Immunology, Berlin, Germany, <sup>18</sup>Department of Neurology-Neuroimmunology, Centre d'Esclerosi Múltiple de Catalunya (Cemcat), Hospital Universitari Vall d'Hebron, Barcelona, Spain

**Introduction & Objectives:**

Remibrutinib (LOU064) is an oral, highly selective BTK inhibitor that offers fast disease control in CSU patients who remain symptomatic despite H1-antihistamines. Remibrutinib showed high selectivity and potency in vitro, with the potential to minimise off-target toxicity and associated adverse events (AEs). Here, we report the safety profile seen in the completed Phase 2 clinical trials of remibrutinib in chronic spontaneous urticaria (CSU), Sjögren syndrome (SjS) and asthma, including participants with long-term treatment.

**Materials & Methods:**

This analysis of safety data from completed Phase 2 studies will supplement the current evidence on safety and tolerability of remibrutinib across immune-mediated conditions (CSU, SjS and asthma). It will include the analysis of the recently completed Phase 2 open-label extension in CSU. Safety assessments comprised AEs, including serious and AEs of special interest (AESI), vital signs, electrocardiograms (ECG), and laboratory parameters.

**Results:**

Previous analysis of safety data from Phase 2 clinical trials in CSU, SjS and asthma showed that AEs reported with remibrutinib were comparable to placebo in core studies; infections (primarily upper respiratory tract infections) were most common AEs. AESI observed with remibrutinib including bleeding, infections and cytopenia did not increase with longer-term exposure. To date, no new safety concerns were noted in clinical data and lab parameters (blood cell counts and blood biochemistry, liver enzymes included). The safety analysis of



remibrutinib across immune-mediated inflammatory conditions will be presented at the congress.

**Conclusion:**

This analysis will provide further information regarding the safety and tolerability profile of remibrutinib in the completed Phase 2 studies in other inflammatory immune-mediated diseases, in addition to CSU and will supplement the current evidence on safety and tolerability of remibrutinib in CSU.

**32<sup>ND</sup> EADV Congress 2023**  
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**Abstract N°: 4212**
**Dupilumab: a new frontier for chronic urticaria. A case series and a review of the literature**

Luca Valtellini<sup>1, 2</sup>, Eleonora Quattri<sup>1, 2</sup>, Francesca Barei<sup>1, 2</sup>, Gabriele Perego<sup>1, 2</sup>, Martina Zussino<sup>1</sup>, Angelo Marzano<sup>1, 2</sup>, Silvia Ferrucci<sup>\*1</sup>

<sup>1</sup>Policlinico of Milan, Dermatology, Milano, Italy, <sup>2</sup>University of Milan, Department of Physiopathology and Transplantation, Milano, Italy

**Dupilumab: a new frontier for chronic urticaria. A case series and a review of the literature**
**Introduction & Objectives:**

Chronic urticaria (CU) is a mast cell-driven disease featured by recurrent, fugacious and itchy wheals and/or angioedema lasting for more than 6 weeks. The disease is divided into two forms: chronic spontaneous urticaria (CSU), without defined eliciting factors involved, and chronic inducible urticaria (CindU), associated with a specific triggering factor. It is a disabling condition that affects substantially patients' quality of life. No curative treatment exists and all available therapies aim to control and prevent the symptoms. Current management guidelines recommend second-generation histamine1-antihistamines (sgH1-AH) as first line therapy. If symptoms are incompletely controlled with high dose sgH1-AH, add-on therapy with omalizumab (monoclonal antibody against IgE) is recommended. Finally, cyclosporine is considered as last line option when previous therapies fail to achieve clinical response. However, there are some patients with refractory CU or who develop secondary failure to therapy. Thereby, additional efficacious alternative treatment options are needed. One of these therapies is Dupilumab, a fully human anti-interleukin (IL)-4 receptor  $\alpha$  monoclonal antibody that blocks both IL-4 and IL-13 signaling. There are several case reports and case series in the literature describing improvement in CU symptoms during treatment with Dupilumab. Furthermore, 5 clinical trials are registered for evaluation of this drug in CU.

In this report, we want to assess the overall efficacy of Dupilumab treatment in CU.

**Materials & Methods:**

We report a case series of 7 patients suffering from both AD and CU who were treated with Dupilumab at standard doses for AD (600 mg s.c. followed by 300 mg every other week). Among the patients, 3 suffered from cholinergic urticaria (of which 1 with overlapping cold urticaria), 3 from CSU (of which 1 with associated angioedema and 1 with overlapping cold urticaria), 1 from aquagenic urticaria. Clinical outcome was assessed using UCT (Urticarial Control Test) score, EASI (Eczema Area and Severity Index), DLQI (Dermatology Life Quality Index), pruritus NRS (Numerical Rating Scale) and sleep NRS scores at baseline, after 4 and 12 weeks of treatment and then every 16 weeks to date.

The UCT cut-off value for well-controlled CU is 12 out of 16 points. An improvement of  $\geq 6$  points is considered a marked response.

To contextualise the report, a literature review was subsequently undertaken. The PubMed database was searched by using "dupilumab" AND "urticaria" as keywords. We only considered cases of adult patients.

**Results:**

In our cohort of patients, median UCT score at baseline was 4 (2,5-4,5) while at the end of the follow-up has increased to 13 (10,5-15,5). Simultaneously with the improvement in CU, all patients had a reduction in DA, achieving EASI-50 after 4 weeks of treatment and EASI-75 after 12 weeks. DLQI had also improved.

As for the results of the review, a total of eleven articles were included, two case series and nine case reports for a total of 17 patients (8 with CSU and 5 with CindU [2 with cholinergic urticaria, 2 with cold urticaria and 1 with adrenergic urticaria]). A positive outcome was reached in all patients, without report of side effects (Table 1).

## Conclusion:

Dupilumab could be a promising treatment option for both spontaneous and inducible chronic urticaria.

Larger controlled studies are needed to validate it.

Table 1.

Reference	N° patients	CSU/CINDU	Atopy	Onset of improvement	Previous treatments
Lee et al	6	CSU	Yes	3 mo	Antihistamines, gabapentin, montelukast, ranitidine, omalizumab
Erricchetti et al	2	CSU	Yes (1 patient)	8 wk	Antihistamines, ciclosporin, omalizumab montelukast (1 patient), methotrexate (1patient)
Zhu et al	1	CSU	No	3 wk	Antihistamines, omalizumab
Sun et al	1	CSU	No	1 wk	Antihistamines, omalizumab, ciclosporin, phototherapy
Puxkandal et al	1	CSU	No	2 mo	Antihistamines, prednisone, omalizumab
Sirufo et al	1	Cholinergic urticaria/CSU	No	2 wk	Antihistamines, prednisone, montelukast, omalizumab
Marchal et al	1	Cold urticaria	No	Not specified, but early	Antihistamines, omalizumab
Ferrucci et al	1	Cold urticaria	Yes	1 mo	Antihistamines, prednisone, omalizumab
Goodman et al	1	Adrenergic urticaria	No	2 wk	Antihistamines, dapsone montelukast, omalizumab, propranolol
Holm et al	1	CSU	Yes	3 mo	Antihistamines, topical and oral CS, omalizumab
Fohr et al	1	Cholinergic urticaria/CSU	Yes	2 mo	Antihistamines, prednisone, omalizumab

Abbreviations: CSU, chronic spontaneous urticaria; CINDU, chronic inducible urticaria; CS, corticosteroids; mo, months; wk, weeks



**Abstract N°: 4221****Smartphone photographs of chronic urticaria taken by patients are of good quality and useful in the clinic**

Jennifer Astrup Soerensen<sup>\*1</sup>, Zarqa Ali<sup>1</sup>, Ditte Zhang<sup>1</sup>, Misbah Ghazanfar<sup>1</sup>, Johan Allerup<sup>1</sup>, Marcus Maurer<sup>2, 3</sup>, Emek Kocatürk<sup>2, 3, 4</sup>, Christian Vestergaard<sup>5</sup>, Simon Francis Thomsen<sup>1, 6</sup>

<sup>1</sup>Copenhagen University Hospital Bispebjerg, Department of Dermato-Venereology and Wound Healing Centre, København NV, Denmark, <sup>2</sup>Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Institute of Allergology, Berlin, Germany, <sup>3</sup>Fraunhofer Institute for Translational Medicine and Pharmacology ITMP, Allergology and Immunology, Berlin, Germany, <sup>4</sup>Koç University School of Medicine, Department of Dermatology, Istanbul, Türkiye, <sup>5</sup>Aarhus University Hospital, Department of Dermatology and Venereology, Aarhus, Denmark, <sup>6</sup>University of Copenhagen, Department of Biomedical Sciences, Denmark

**Introduction & Objectives:**

Chronic urticaria (CU) is a severely itching skin disease characterized by transient wheals and/or angioedema for more than six weeks. Given the nature of urticaria, symptoms are often not present when patients see their treating physician - making the clinical diagnosis of urticaria more challenging.

The use of smartphone photographs for clinical photography and consultations in dermatology is growing rapidly. The aim of this study was to evaluate the quality and diagnostic value of smartphone photographs captured by patients prior to their first visit at an urticaria outpatient clinic.

**Materials & Methods:**

A survey regarding the quality and utility of smartphone photographs of urticarial skin lesions in patients with CU attending the outpatient clinic for the first time was conducted. Up to three random patient-selected photographs of skin lesions were evaluated by a physician.

Baseline data including sex, age, disease duration, Urticaria Activity Score (UAS7), Urticaria Control Test (UCT), Dermatology Life Quality Index (DLQI), and CU subtype was collected from all patients at the first visit.

**Results:**

Of 148 patients, 118 (79.7%) had taken photographs of their skin lesions prior to the consultation, and 75% took photographs with the intention of presenting them to their physician. The photographs were of wheals in 90% of the cases, and angioedema in 8%. In total, 72% of the smartphone photographs had the skin lesion in focus, 64% had good resolution, 48% had good lighting. Only 9% of the smartphone photographs were blurred, 10% had bad lighting, 4% had bad resolution, and 8% did not have the lesion in focus. Moreover, 86% of the smartphone photographs were found to be useful for clinical evaluation. At least one photograph of good/very good quality was presented by 86% of the patients, and 97% had at least one photograph that was useful for clinical evaluation.

Significantly more patients with recurrent angioedema had taken smartphone photographs of their skin lesions as compared to patients without angioedema (47.5 vs. 26.7%,  $p=0.04$ ). In contrast, there were no statistically significant differences between patients who had taken photographs of their skin lesions compared to those who had not, regarding sex, age, disease duration, UAS7, UCT, DLQI, or CU subtype.

**Conclusion:**

Patients with CU often take smartphone photographs of their skin lesions on their own initiative prior to the first hospital contact to present the photographs to a physician. These smartphone photographs are very often of good quality and suitable for clinical evaluation. This may allow for remote assessment of urticaria based on smartphone photographs of skin lesions taken by the patients.

**32<sup>ND</sup> EADV Congress 2023**  
**11 OCTOBER - 14 OCTOBER 2023**  
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**Abstract N°: 4268****Female patients with chronic spontaneous urticaria have more systemic symptoms and comorbidities and worse quality of life: Chronic Urticaria Registry (CURE) results**

Emek Kocatürk Göncü<sup>\*1, 2</sup>, Pavel Kolkhir<sup>2</sup>, Pascale Salameh<sup>2</sup>, Yana Hackler<sup>2</sup>, Riccardo Asero<sup>3</sup>, Leonie Herzog<sup>2</sup>, Thomas Buttgereit<sup>2</sup>, Hanna Bonnekoh<sup>2</sup>, Elena Kovalkova<sup>4</sup>, Alicja Kasperska-Zajac<sup>5</sup>, Kanokvalai Kulthanan<sup>6</sup>, Meryem Khoshkhui<sup>7</sup>, Jonny Peter<sup>8</sup>, Aurelie Du Thanh<sup>9</sup>, Raisa Meshkova<sup>10</sup>, Michael Makris<sup>11</sup>, Laurence Bouillet<sup>9</sup>, Simon Francis Thomsen<sup>12</sup>, Joachim Dissemond<sup>13</sup>, Petra Staubach-Renz<sup>13</sup>, Susanne Abraham<sup>13</sup>, Inna Danilycheva<sup>10</sup>, Martijn Van Doorn<sup>14</sup>, Mojca Bizjak<sup>15</sup>, Claudio Parisi<sup>16</sup>, Karsten Weller<sup>13</sup>, Stamatis Gregoriou<sup>11</sup>, Mohamed Abuzakouk<sup>17</sup>, Daria Fomina<sup>11</sup>, Clive Grattan<sup>18</sup>, Ana Giménez-Arnau<sup>19</sup>, Marcus Maurer<sup>13</sup>

<sup>1</sup>Koç University Hospital, Dermatology, Türkiye, <sup>2</sup>Charité Campus Benjamin Franklin, Berlin, Germany, <sup>3</sup>Ambulatorio di Allergologia, Putignano, Italy, <sup>4</sup>Clinical State Hospital 52, Center of Allergy and Immunology, Moscow, Russian Federation, <sup>5</sup>European Center for Diagnosis and Treatment of Urticaria/Angioedema, European Center for Diagnosis and Treatment of Urticaria/Angioedema, Katowice, Poland, <sup>6</sup>Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, Bangkok, Thailand, <sup>7</sup>Iran, <sup>8</sup>South Africa, <sup>9</sup>France, <sup>10</sup>Russian Federation, <sup>11</sup>Greece, <sup>12</sup>Denmark, <sup>13</sup>Germany, <sup>14</sup>Netherlands, <sup>15</sup>Slovenia, <sup>16</sup>Argentina, <sup>17</sup>United Arab Emirates, <sup>18</sup>United Kingdom, <sup>19</sup>Spain

**Female patients with chronic spontaneous urticaria have more systemic symptoms and comorbidities and worse quality of life: Chronic Urticaria Registry (CURE) results**

**Introduction & Objectives:** Chronic spontaneous urticaria (CSU) is a heterogeneous and female predominant skin disease, which is thought to present differently in female than male patients. In this study we aimed to investigate gender differences regarding disease activity, comorbidities, and quality of life in CSU patients.

**Materials & Methods:** We analyzed baseline data from CSU patients in the ongoing, prospective, international, multicenter, observational Chronic Urticaria Registry (CURE; data cut: May 2023).

**Results:** Across 4136 CSU patients, 2994 (72.4%) were female and the female/male ratio was significantly higher in patients >18 y compared to ≤18 y (2.7 vs 1.4; p<0.001). Female patients showed higher rates of angioedema (59.6% vs 51.7%; p<0.001), systemic symptoms (fever [4.1% vs 3.3%; p<0.001], joint/bone/muscle pain [15.7% vs 10.2%; p<0.001], malaise [14.8% vs 11.8%; p<0.001]), positive family history for chronic urticaria (8.6% vs 5.2%; p=0.002), concomitant diseases (obesity, asthma, thyroid disorders, autoimmune diseases, gastrointestinal diseases and depression), elevated ESR (19.1% vs 10.1%; p<0.001) and use of immunosuppressive medications (20.5% vs 16.7%; p=0.006) as well as higher quality of life impairment (total CU2QoL score 32 vs 27.7; p<0.001), while male patients had a higher rate of diabetes mellitus (7.8% vs 5.1%, p=0.004).

**Conclusion:** Female patients appear to have a distinct CSU phenotype, which manifests with more systemic symptoms and comorbidities and worse quality of life highlighting the need for a tailored intervention and treatment approach.

**Abstract N°: 4478****An Open-label, Sequential Dose-Escalation Study to Assess the Safety, Pharmacokinetics and Pharmacodynamic Effects of THB001 in Adult Patients With Chronic Cold Urticaria.**

Brianne Leary<sup>1</sup>, Robert Rissmann<sup>2</sup>, Martin Metz<sup>3</sup>, Marcus Maurer<sup>3</sup>, Heike Rockmann<sup>4</sup>, Martijn Van Doorn<sup>5</sup>, Thomas Rustemeyer<sup>6</sup>, Ismaahan Abdisalaam<sup>2</sup>, Ted Snyder<sup>1</sup>, Steven Sweeney<sup>1</sup>, Edward Conner<sup>\*7</sup>

<sup>1</sup>Third Harmonic Bio, Cambridge, United States, <sup>2</sup>Centre for Human Drug Research, Leiden, Netherlands, <sup>3</sup>Charité, Berlin, Germany, <sup>4</sup>UMC Utrecht, Dermatology, Utrecht, Netherlands, <sup>5</sup>Erasmus MC, Dermatology, Rotterdam, Netherlands, <sup>6</sup>Amsterdam University Medical Center, Department of Dermatology, Amsterdam, Netherlands, <sup>7</sup>Third Harmonic Bio, San Francisco, United States

**Introduction & Objectives:**

Chronic urticaria is a common disease characterized by recurrent wheals and/or angioedema that has considerable impact on patient quality of life. The mast cell is believed to be the major effector cell in most forms of urticaria. While therapies exist, such as antihistamines and the approved anti-IgE antibody omalizumab, many patients have inadequate responses, and there remains a high unmet medical need for more effective therapies.

THB001 is a highly potent and selective oral small molecule inhibitor of wild-type KIT that was in development as a potential therapy for mast cell driven diseases.

**Materials & Methods:**

THB001-01-002 was a phase 1b, open-label, dose-escalation study designed to evaluate the safety and tolerability of up to 3 doses of THB001 administered twice daily over 12 weeks in patients with cold urticaria (ColdU). Men and women between the ages of 18-75 diagnosed with ColdU for a minimum of 3 months and refractory to antihistamine treatment were eligible for enrollment. Critical temperature threshold was measured using a TempTest<sup>®</sup> device to confirm eligibility and was used for the assessment of pharmacodynamic (PD) effect and clinical response over time. Serum tryptase was analyzed as a marker of mast cell specific PD effect.

**Results:**

A total of five female participants were enrolled into the study in the initial 200 mg twice daily dose cohort. The first participant completed the full 12-week dosing period with no signs or symptoms of liver toxicity. The second and third participants presented with elevations in alanine transaminase (ALT) and aspartate transaminase (AST) at their week 8 study visits. Treatment with THB001 was promptly discontinued following repeat labs confirming the results. There was no exposure to alcohol, concomitant medications, or herbal supplements. An extended liver panel including viral serology, auto-immunity, serum amylase and lipase was performed and was unremarkable. Albumin and coagulation parameters were normal indicating no impact on synthetic function. The adverse events (AEs) were reported as drug-induced liver injury (DILI) and were categorized as moderate in severity and related to study drug. The AEs eventually resolved when the transaminase values returned to normal.

Dosing of the fourth and fifth participants was halted at weeks 4 and 3 of dosing, respectively. Neither had signs or symptoms of liver toxicity.

Other than the DILI AEs noted above, all AEs were mild in severity. No SAEs were reported.

Preliminary results showed promising PD effects including clinical responses as measured by TempTest and serum

tryptase. The full dataset of all enrolled participants including safety, tolerability, PK, PD and clinical response will be presented.

**Conclusion:**

The study was halted early due to transaminase elevations in two participants enrolled in the first dose cohort (200mg BID THB001). The underlying cause is being investigated. These data, along with the PK, PD and clinical data to be presented from this study, will inform our next generation oral kit inhibitor program currently under development.

32<sup>ND</sup> EADV Congress 2023  
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**Abstract N°: 4787**
**IL-6 and IL-17 as Potential Biomarkers in Chronic Spontaneous Urticaria: Associations with Disease Characteristics and Healthy Volunteer Comparisons**

 Abhishek De<sup>\*1</sup>, Sushil Singh<sup>1</sup>, Kiran Vasant Godse<sup>2</sup>
<sup>1</sup>Calcutta National Medical College, Dermatology, Kolkata, India, <sup>2</sup>D.Y. Patil University, Dermatology, Navi Mumbai, India

**Introduction & Objectives:**

The pathogenesis of chronic spontaneous urticaria (CSU) is poorly understood, with limited treatment options. An increase in IL-4, IL-5, and IFN-gamma in the cytokine profile suggests a mixed Th 1/Th2 response in CU. IL-6 trans-signaling and elevated IL-17 of the Th17 pathway are critically involved in the initiation and promotion of inflammatory and autoimmune diseases, including CSU.

**Aims and Objectives**

- To evaluate the levels of IL-6 and IL-17 in the patients of CU and compare them with healthy controls.
- To study the correlation between IL-6 and IL-17 cytokines with the demographic variables and autoimmunity in CU.
- Correlation between IL6 and IL17 with disease activity and durations.

**Materials & Methods:**

This is a single-center cross-sectional study on patients with CSU presenting in the outpatient department of dermatology. We included only patients above 12 years of age who have not taken immunosuppressives or biologics like omalizumab in the last 4 weeks. Patients were subjected to routine blood testing, including tests for autoimmunity using a complete blood count, including absolute basophil and eosinophil counts, CRP, ANA (hep2), Anti-TPO antibodies, RA factor, and IgE. We also subjected them to a test for IL 6 and IL 17. An age-matched health control group was also tested for the same. SPSS version 25 was used to do the statistical calculations.

**Results:**

A total of 46 patients were included in the study group, of which 29 (63.04%) were found to be of auto-allergic types (Type 1 endotype CSU) and 17 (36.96%) were found to be auto-immune type. IL 6 levels were significantly raised (p values less than 0.001 in Mann Whitney Test) in the patients of CSU (Mean  $\pm$  S.D.=4.39  $\pm$  3.98) when compared to the healthy control (Mean  $\pm$  S.D.=2.88  $\pm$  0.76). Similarly, IL17 levels were significantly elevated (p values less than 0.001 in Mann Whitney Test) in the patients of CSU (Mean  $\pm$  S.D.= 5.40 $\pm$ 4.4) when compared to the healthy control (Mean  $\pm$  S.D. = 3.88 $\pm$ 0.33). Both IL6 and IL17 values correlated with CRP values (p values=0.002 in Pearson correlation) and disease severity indicated by UAS7 scores (P<0.001 with ANOVA for severe disease). Also, both IL6 and 17 levels correlated with type 2 B endotypes of the disease {P<0.001(independent samples t-test[F-test])}. However, both cytokines' elevation was not significantly associated with gender distribution (IL6: p value=0.53; IL:17: p value=0.86), duration of the disease IL6: p value=0.48; IL:17: p value=0.37).

**Conclusion:**

Our study showed there is a significantly higher level of IL 6 and IL 17 in the patients with CSU in comparison to healthy controls. The cytokines were significantly high in the severe form of the disease and the autoimmune (type 2B) endotype of the disease. CRP levels correlated with cytokines and might serve as a biomarker of disease activity. Our study also suggests IL-6 and IL-17 blockers might be used as molecular targets in the treatment of severe and recalcitrant type 2B CSU.

**32<sup>ND</sup> EADV Congress 2023**  
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**Abstract N°: 4823**
**Remibrutinib Improves Chronic Spontaneous Urticaria in Patients Irrespective of Previous Anti-IgE Treatment: Results from a Phase 2b Study**

Marcus Maurer<sup>1, 2</sup>, Alexander Greiner<sup>3</sup>, Sridhar Guduri<sup>4</sup>, Jeffrey Leflein<sup>5</sup>, Sibylle Haemmerle<sup>6</sup>, Karine Lheritier<sup>6</sup>, Pauline Walsh<sup>7</sup>, Ivan Nikolaev Ivanov<sup>6</sup>, Ana Giménez-Arnau<sup>8</sup>

<sup>1</sup>Urticaria Center of Reference and Excellence (UCARE), Institute of Allergology, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, <sup>2</sup>Fraunhofer Institute for Translational Medicine and Pharmacology (ITMP), Allergology and Immunology, Berlin, Germany, <sup>3</sup>Allergy and Asthma Medical Group and Research Center, and University of California at San Diego, San Diego, California, United States, <sup>4</sup>Centricity Research Inc., Columbus, Ohio, United States, <sup>5</sup>Respiratory Medicine Research Institute of Michigan, Ann Arbor, Michigan, United States, <sup>6</sup>Novartis Pharma AG, Basel, Switzerland, <sup>7</sup>Novartis Ireland Limited, Dublin, Ireland, <sup>8</sup>Department of Dermatology, Hospital del Mar -IMIM, Universitat Pompeu Fabra, Barcelona, Spain

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is characterised by the occurrence of itchy hives, angioedema or both lasting for longer than 6 weeks. Second-generation H1-antihistamines (H1-AH) are recommended as first-line treatment for CSU with dose escalation up to 4 times the licensed dose if symptoms persist. In patients who are unresponsive to up-dosed H1-AH treatment, the guidelines recommend use of the anti-immunoglobulin E (IgE) monoclonal antibody, omalizumab, as an add-on biologic therapy. Remibrutinib (LOU064) is an oral, highly selective Bruton's tyrosine kinase (BTK) inhibitor that offers fast disease control in patients with CSU who remain symptomatic despite treatment with second-generation H1-AH. Here, we explore the effect of remibrutinib in patient subgroups with or without previous use of anti-IgE treatment for CSU from the phase 2b study.

**Materials & Methods:**

In this multicentre, randomised, double-blind, placebo-controlled, Phase 2b study (NCT03926611), 311 adult CSU patients uncontrolled by H1-AH were stratified by history of anti-IgE treatment and equally randomized to receive remibrutinib 10 mg once daily (q.d.)/35 mg q.d./100 mg q.d./10 mg twice daily (b.i.d.)/25 mg b.i.d./100 mg b.i.d. or placebo for 12 weeks. Outcomes included change from baseline in weekly Urticaria Activity Score (UAS7) and proportion of patients achieving UAS7=0 and UAS7≤6 at Week 12, with or without a history of anti-IgE treatment.

**Results:**

At baseline, 27% (84/311) of patients had a history of anti-IgE treatment. At Week 12, no consistent difference in UAS7 change from baseline was observed between subgroups with or without a history of anti-IgE treatment: remibrutinib 10 mg qd: -21.1 and -20.6; remibrutinib 35 mg qd: -25.2 and -19.0; remibrutinib 100 mg qd: -7.7 and -18.8; remibrutinib 10 mg bid: -14.8 and -20.5; remibrutinib 25 mg bid: -25.8 and -18.7; and remibrutinib 100 mg bid: -26.2 and -18.1; and placebo: -2.8 and -9.7. At Week 12, no consistent difference in UAS7=0 was observed between subgroups with or without a history of anti-IgE treatment: remibrutinib doses (9.1% to 50.0% and 21.2% to 39.4%, respectively) and placebo (8.3% and 16.7%, respectively). Similar observations were reported in proportion of patients achieving UAS7≤6, across remibrutinib doses and placebo, at Week 12.

**Conclusion:**

Remibrutinib (all doses) showed improvement in UAS7 and achievement of UAS7=0 and UAS7≤6 irrespective of previous anti-IgE treatment. Larger studies are required to confirm the findings of this Phase 2b study.

**32<sup>ND</sup> EADV Congress 2023**  
**11 OCTOBER - 14 OCTOBER 2023**  
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**Abstract N°: 4875****In Chronic Spontaneous Urticaria, Complete Response to Antihistamine Treatment Is Linked to Low Disease Activity**

Murat Türk<sup>1</sup>, Ragıp Ertas<sup>\*2</sup>, Ümit Murat Şahiner<sup>3</sup>, Pavel Kolkhir<sup>4</sup>, Bülent Enis Şekere<sup>3</sup>, Özge Soyer<sup>3</sup>, Atil Avcı<sup>2</sup>, Mustafa Atasoy<sup>5</sup>, Kemal Ozyurt<sup>6</sup>, Yekta Türk<sup>7</sup>, Engin Zeydan<sup>8</sup>, Marcus Maurer<sup>4</sup>

<sup>1</sup>Erciyes University, Allergy and Immunology, Kayseri, Türkiye, <sup>2</sup>Health Sciences University, Kayseri City Hospital, Dermatology, Kayseri, Türkiye, <sup>3</sup>Hacettepe University School of Medicine, Pediatric Allergy and Immunology, Ankara, Türkiye, <sup>4</sup>Charité Campus Benjamin Franklin, Berlin, Germany, <sup>5</sup>Memorial Ataşehir Hospital, Dermatology, Türkiye, <sup>6</sup>AEÜ Tıp Fakültesi, Dermatology, Türkiye, <sup>7</sup>ASELSAN Head Office, Ankara, Türkiye, <sup>8</sup>Centre Tecnològic de Telecomunicacions de Catalunya (CTTC), Castelldefels, Spain

**Introduction & Objectives:** The use of predictors of response to a specific treatment in patients with chronic spontaneous urticaria (CSU) can improve disease management, help prevent unnecessary healthcare costs, and save time. In this study, we aimed to identify predictors of complete response to standard-dosed and higher than standard-dosed antihistamine treatments in patients with CSU.

**Materials & Methods:** Medical records of 475 CSU patients, 120 of them <18 years old, from 3 different centers were analyzed. We used 15 machine learning (ML) models as well as traditional statistical methods to predict complete response to standard-dosed and higher than standard-dosed antihistamine treatment based on 17 clinical parameters.

**Results:** CSU disease activity, which was assessed by urticaria activity score (UAS), was the only clinical parameter that predicted complete response to standard-dosed and higher than standard-dosed antihistamine treatment, with ML models and traditional statistics, for all age groups. Based on ROC analyses, optimal cut-off values of disease activity to predict complete response were UAS <3 and UAS <4 for standard-dosed (area under the ROC curve [AUC] = 0.69;  $p = 0.001$ ) and higher than standard-dosed (AUC = 0.79;  $p = 0.001$ ) antihistamine treatments, respectively. Also, ML models identified lower total IgE (<150 IU/mL) as a predictor of complete response to a standard-dosed antihistamine and lower CRP (<3.4 mg/mL) as a predictor of complete response to higher than standard-dose antihistamine treatment.

**Conclusion:** In this study, we showed that patients with UAS <3 are highly likely to have complete response to standard-dosed AH and those with a UAS <4 are highly likely to have complete response to higher than standard-dosed AH treatment. Low CSU disease activity is the only universal predictor of complete response to AH treatment with both ML models and traditional statistics for all age groups.

**Abstract N°: 4896****Efficacy of Oral Tofacitinib in Chronic Spontaneous Urticaria Resistant to Antihistamines: A Six-Month Follow-Up Retrospective Chart analysis**Abhishek De<sup>1</sup>, Kiran Vasant Godse<sup>\*2</sup><sup>1</sup>Calcutta National Medical College, Dermatology, Kolkata, India, <sup>2</sup>D.Y. Patil University, Dermatology, Mumbai, India**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is a distressing skin condition characterized by the recurrent appearance of itchy hives. A subset of CSU patients remains resistant to conventional treatment with high-dose antihistamines. Tofacitinib, a Janus kinase inhibitor, has shown promise in various inflammatory skin diseases. We aimed to evaluate the efficacy of oral tofacitinib in patients with CSU resistant to antihistamines.

**Materials & Methods:**

This study examined data retrospectively of seven patients who were diagnosed with CSU and were treated with tofacitinib for at least six months. These patients initially exhibited resistance to treatment with four-fold up-dosed antihistamines. One of the patients was already tried on omalizumab and another was tried on cyclosporin. The patients were administered oral tofacitinib at a dosage of 5 mg twice daily for a period of six months. Patients were followed up monthly for disease control and side effects. The response to treatment was evaluated using the Urticaria Activity Score over 7 days (UAS7) and Urticaria Control Test (UCT). Paired t-tests were conducted to determine the statistical significance of the results using SPSS version 25 software.

**Results:**

Six out of the seven patients demonstrated a significant improvement in both UAS7 and UCT scores after six months of treatment with oral tofacitinib. The mean UAS7 score decreased from 24.86 at baseline to 3.83 at the study endpoint ( $p < 0.0001$ ). Similarly, the mean UCT score increased from 0.57 at baseline to 14 at the study endpoint ( $p < 0.0001$ ). The standard deviations for both measures were 4.85 and 0.98 at baseline, and 3.1 and 3.1 at the study endpoint for UAS7 and UCT, respectively.

**Conclusion:**

In this six-month follow-up study, oral tofacitinib demonstrated significant efficacy in the treatment of CSU patients resistant to high-dose antihistamines. Most patients experienced a remarkable reduction in urticaria activity and an improvement in disease control. These findings suggest that tofacitinib holds promise as a potential therapeutic option for this challenging subset of CSU patients. However, larger, and randomized controlled trials are warranted to further investigate the long-term safety and effectiveness of tofacitinib in this population.

**Abstract N°: 4957**

**Urticaria Voices: Patients' perspective on the negative impact of chronic spontaneous urticaria on their lives as well as their treatment goals**

Karsten Weller<sup>\*1</sup>, Pedro Laires<sup>2</sup>, Maria Magdalena Balp<sup>3</sup>, Tara Raftery<sup>4</sup>, Pallavi Saraswat<sup>5</sup>, Jessica McCarthy<sup>6</sup>, Mihai Dricu<sup>7</sup>, Tonya Winders<sup>8</sup>, Jonathan A. Bernstein<sup>9, 10</sup>

<sup>1</sup>Department of Dermatology and Allergy, Charité – University Medicine Berlin, Germany, <sup>2</sup>National School of Public Health, Universidade Nova de Lisboa, Lisbon, Portugal, <sup>3</sup>Novartis Pharma AG, Basel, Switzerland, <sup>4</sup>Novartis Ireland Ltd., Dublin, Ireland, <sup>5</sup>Novartis Healthcare Pvt. Ltd, Hyderabad, India, <sup>6</sup>Novartis Pharmaceuticals Corporation, East Hanover, USA, <sup>7</sup>Ipsos SA, Basel, Switzerland, <sup>8</sup>Global Allergy and Airways Patient Platform, Vienna, Austria, <sup>9</sup>Division of Rheumatology, Allergy and Immunology, University of Cincinnati, Cincinnati, Ohio, United States, <sup>10</sup>Bernstein Allergy Group and Clinical Research Center, Cincinnati, Ohio, United States

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is characterized by unpredictable itchy wheals/hives and/or angioedema for more than 6 weeks and can significantly impact health-related quality of life (HRQoL). This study investigated the burden of CSU on HRQoL and patients' personal treatment goals.

**Materials & Methods:**

Urticaria Voices was a global cross-sectional online survey with CSU patients in the US, Canada, UK, Germany, France, Italy, and Japan. Eligible patients had a self-reported clinician-provided diagnosis of CSU and followed a prescribed treatment. Patients were recruited through nationally representative online panels of the general population and patient advocacy groups. The perceived negative impact of CSU on six HRQoL domains and the personal importance of sixteen treatment goals were assessed with a ten-point Likert scale (higher score indicated higher importance). All patients completed the Urticaria Control Test (UCT) to assess symptom control in the past four weeks. Statistical differences between adequately and inadequately controlled patients were assessed for HRQoL with independent sample t-tests assuming unequal variances.

**Results:**

582 CSU patients (62% women, mean [standard deviation (SD)] age 42 [11.9] years) responded to the survey. Most patients (80%) were inadequately controlled (UCT score < 12) and reported a significantly higher negative impact than controlled patients on the HRQoL domains assessed (Table 1). Among inadequately controlled patients, 82% reported currently taking antihistamine (AH) medication for their CSU after their doctor had already switched the types of AH on average 2.4 times and increased their dosage on average 2 times.

**Conclusion:**

Four out of five of the CSU patients in this study were inadequately controlled on their current treatment, with most of them (82%) being on AH medication. These patients reported a significantly higher negative impact across all HRQoL domains compared to adequately controlled patients. The most impacted domains were mental & emotional wellbeing, social life & intimate relationships, and activities of daily living. The results further suggest that treatments that target symptom relief, complete control and improved HRQoL are important for CSU patients and therapies which address these goals effectively are needed.



**Table 1. The negative impact of CSU on HRQoL**

Impacted HRQoL domains	All CSU patients (N=582) Mean [SD]	Inadequately controlled CSU patients <sup>1</sup> (N=468) Mean [SD]	Adequately controlled CSU patients <sup>2</sup> (N=114) Mean [SD]	P Values
Mental and emotional wellbeing	6.0 [2.8]	6.3 [2.6]	4.9 [3.0]	< 0.001*
Social life and intimate relationships	5.5 [2.9]	5.8 [2.7]	4.6 [3.1]	< 0.001*
Activities of daily living]	5.4 [2.9]	5.6 [2.8]	4.2 [3.0]	< 0.001*
Family life	5.0 [2.8]	5.3 [2.7]	3.7 [2.9]	< 0.001*
Professional and academic life	4.8 [3.0]	5.2 [2.9]	3.2 [2.8]	< 0.001*
Finances	4.7 [2.8]	5.0 [2.8]	3.2 [2.7]	< 0.001*

*Note. The negative impact was assessed on a scale from 1 (not at all negatively impacted) to 10 (extremely highly negatively impacted).*

<sup>1</sup> Patients with a UCT score <12 score of 11 or lower on the UCT. <sup>2</sup> Patients with an UCT score ≥ of 12 or higher on the UCT.

\* Statistically significant differences in the perceived negative impact of CSU between adequately and inadequately controlled CSU patients.

Regarding the importance of treatment goals (Table 2), patients rated as extremely important being free of itch and hives, having complete control over symptoms, improved quality of life and staying in remission over the long term.

**Table 2. The importance of treatment goals**

Treatment goals	CSU patients (N=582) Mean [SD]
Be free of itch and hives	7.9 [2.5]
Complete control over chronic urticaria symptoms (itch, hives and/or angioedema)	7.7 [2.7]
Improve overall quality of life	7.6 [2.7]
Staying in remission from symptoms over the long term	7.6 [2.7]
Good (but not complete) control over chronic urticaria symptoms (itch, hives and/or angioedema)	7.4 [2.6]
Improved sleep	7.2 [2.7]
Have no more visible skin defects	7.2 [2.8]
Improve general functioning	7.1 [2.8]
Improve mental and emotional wellbeing	7.1 [2.8]
Use a minimum of medications	7.1 [2.6]
No more burning sensation	7.1 [2.9]
No more pain	7.1 [2.9]
Minimize side effects of treatment	6.8 [2.8]
Be free of angioedema	6.7 [3.2]
Keep the costs of the treatment affordable	6.6 [2.9]
Be less dependent on doctors and clinical visits	6.6 [2.8]

*Note. The importance of treatment goals was assessed on a scale from 1 (not at all important) to 10 (extremely important).*



**Abstract N°: 5005****Urticaria Voices: Opportunity for greater shared treatment decision-making by leveraging the existing high-quality relationship between patients and physicians**

Tonya Winders<sup>\*1</sup>, Pedro Laires<sup>2</sup>, Maria Magdalena Balp<sup>3</sup>, Jessica Mccarthy<sup>4</sup>, Tara Raftery<sup>5</sup>, Pallavi Saraswat<sup>6</sup>, Mihai Dricu<sup>7</sup>, Jonathan A. Bernstein<sup>8, 9</sup>, Karsten Weller<sup>10</sup>

<sup>1</sup>Global Allergy and Airways Patient Platform, Vienna, Austria, <sup>2</sup>National School of Public Health, Universidade Nova de Lisboa, Lisbon, Portugal, <sup>3</sup>Novartis Pharma AG, Basel, Switzerland, <sup>4</sup>Novartis Pharmaceuticals Corporation, East Hanover, USA, <sup>5</sup>Novartis Ireland Ltd., Dublin, Ireland, <sup>6</sup>Novartis Healthcare Pvt. Ltd, Hyderabad, India, <sup>7</sup>Ipsos SA, Basel, Switzerland, <sup>8</sup>Division of Rheumatology, Allergy and Immunology, University of Cincinnati, Cincinnati, Ohio, United States, <sup>9</sup>Bernstein Allergy Group and Clinical Research Center, Cincinnati, Ohio, United States, <sup>10</sup>Department of Dermatology and Allergy, Charité – University Medicine Berlin, Germany

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is characterized by unpredictable itchy wheals/hives and/or angioedema for more than 6 weeks due to known or unknown causes. This study investigated the perceptions and potential gaps between patients and physicians on the quality of their relationship and the treatment decision-making process.

**Materials & Methods:**

Urticaria Voices is a global cross-sectional online survey with CSU patients and CSU-treating physicians in the US, Canada, UK, Germany, France, Italy, and Japan. Patients with a self-reported clinician-provided diagnosis of CSU and prescription were recruited through nationally representative online panels of the general population and patient advocacy groups. Dermatologists, allergists, or immunologists treating CSU patients who could make autonomous treatment decisions were invited from specialized online panels. Respondents used ten-point scales to assess various metrics of the patient-physician relationship. Patients rated perceived level of trust, empathy and care, attentiveness, and medical care they receive from their physicians, while physicians rated their perceived ability to establish trust, empathy and care, and a high-quality relationship with their patients. Furthermore, respondents were asked to identify the final treatment decision-maker: the patient, the physician or jointly. Pooled global results of patient-physician relationship are reported in terms of top 3 box scoring, i.e., percentage of respondents selecting the 3 highest ratings on the scale.

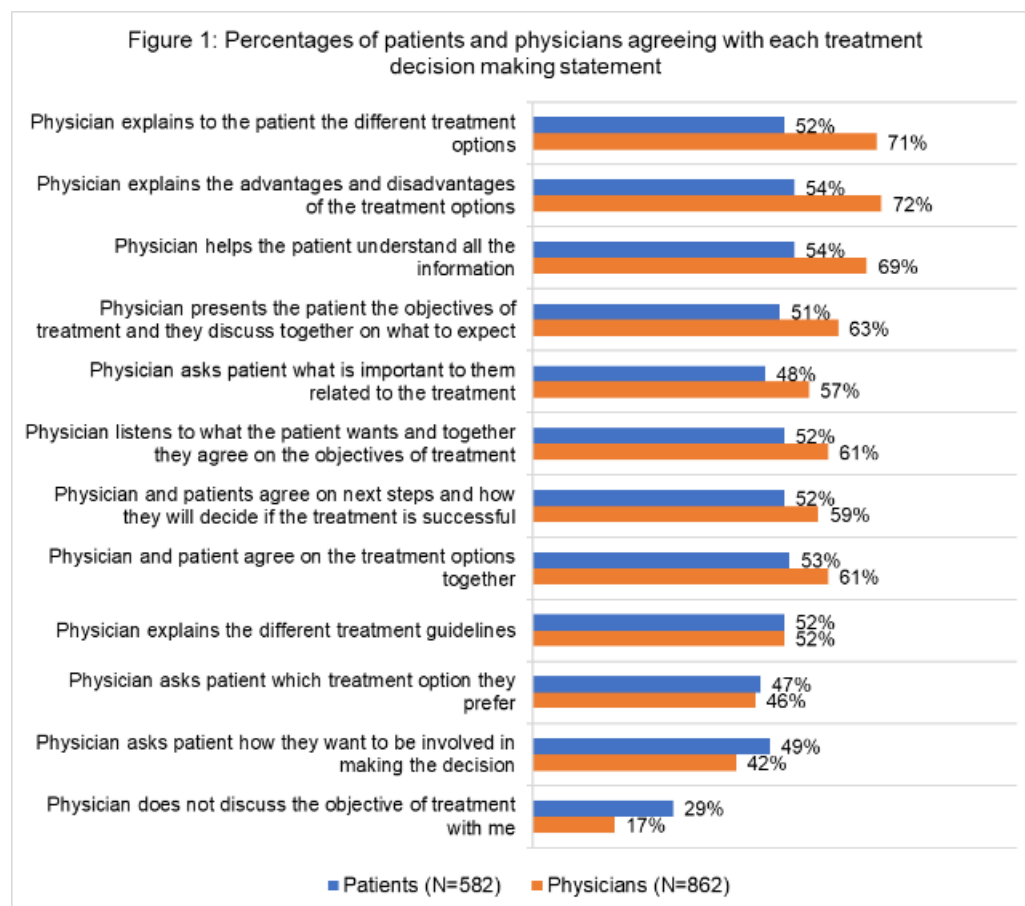
**Results:**

582 CSU patients (62% women, mean age 42 years [SD 11.9]) and 862 CSU-treating physicians were included in the study. Physicians and patients were aligned on high levels of trust (65% and 68%) and empathy and care (64% and 66%). Patients reported further high levels of attentiveness (67%) and medical care (60%) that they receive from their treating physician. Physicians reported an overall high quality of relationship (66%) with their patients. Less than one third of patients (35%) and half of physicians (51%) believed the final treatment decision is made together by the patient with the physician. Only a minority of patients (17%) and physicians (7%) felt that the physician made the final treatment decision.

**Conclusion:**

Respondents largely aligned on perceived quality of the patient-physician relationship, with two thirds reporting very high levels of trust, empathy & care, and medical care. Despite these encouraging findings, there is potential

for improved dialogue between patients and physicians regarding treatment preferences and objectives. Encouraging shared decision-making may help physicians better understand patients' needs and preferences and work towards a tailored treatment plan, thus improving treatment adherence and ultimately better health outcomes.



**Abstract N°: 5038**
**Chronic spontaneous urticaria is linked to systemic microcirculatory changes**

Yora Mostmans<sup>\*1</sup>, Marcus Maurer<sup>2</sup>, Bertrand Richert<sup>3</sup>, Vanessa Smith<sup>4</sup>, Karin Melsens<sup>4</sup>, Viviane De Maertelaere<sup>5</sup>, Ines Saidi<sup>6</sup>, Francis Corazza<sup>7</sup>, Olivier Michel<sup>8</sup>

<sup>1</sup>CHU Brugmann, ULB, Immunology-Allergology, Bruxelles, Belgium, <sup>2</sup>Charité – Universitätsmedizin Berlin, Dermatology, Berlin, Germany, <sup>3</sup>CHU Brugmann, Dermatology, Bruxelles, Belgium, <sup>4</sup>Ghent University Hospital, rheumatology, Gent, Belgium, <sup>5</sup>Université Libre De Bruxelles / Campus Érasme, Statistics, Anderlecht, Belgium, <sup>6</sup>Université Libre De Bruxelles / Campus Érasme, Dermatology, Anderlecht, Belgium, <sup>7</sup>Université Libre De Bruxelles / Campus Érasme, Immunology, Anderlecht, Belgium, <sup>8</sup>Université Libre De Bruxelles / Campus Érasme, Immunology-Allergology, Anderlecht, Belgium

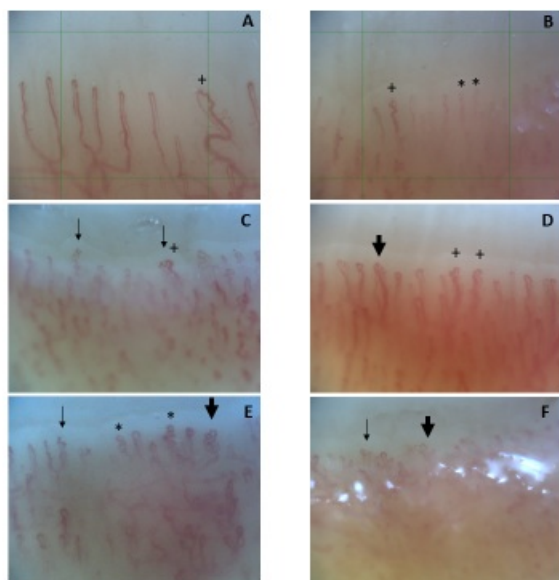
**Chronic spontaneous urticaria is linked to systemic microcirculatory changes**

**Introduction & Objectives:** Chronic spontaneous urticaria (CSU) is a chronic inflammatory skin disease where activation of endothelial cells (ECs) at sites of skin lesions leads to increased blood flow, leakage of fluid into the skin, cellular infiltration, and vascular remodeling. It is unknown if CSU comes with systemic vascular changes. The objective of this study is to assess patients with CSU for systemic vascular changes.

**Materials & Methods:** We investigated CSU patients (n = 49) and healthy controls (HCs, n = 44) for microvascular abnormalities by nailfold videocapillaroscopy (NVC) as well as blood levels of the soluble EC biomarkers vascular endothelial growth factor (VEGF), soluble E-selectin, and stem cell factor (SCF). Patients were also assessed for clinical characteristics, disease activity, and markers of autoimmune CSU (aiCSU).

**Results:** As assessed by NVC, CSU patients had significantly lower capillary density ( $p < 0.001$ ), more capillary malformations and more irregular capillary dilations ( $p < 0.001$  respectively) as compared to HCs. Serum levels of VEGF, soluble E selectin and SCF were similar in CSU patients and HCs. CSU patients with higher VEGF levels had significantly more abnormal capillaries ( $p = 0.019$ ), especially more crossings ( $p = 0.019$ ) (Figure 1). Patients with low IgE or increased anti-TPO levels, markers of aiCSU, had significantly more capillaries and less capillary dilations than patients without these markers.\*\*

**Conclusion:** The results of our study suggest that CSU comes with systemic microcirculatory changes, which be driven, in part, by VEGF. Our findings also suggest that NVC could be a useful clinical tool for the identification of patients with aiCSU patients.



**Figure 1. Microvascular abnormalities on NVC in CSU patients**

**Figure legend:** Nailfold videocapillaroscopy images of six different CSU patients showing (A-B) decreased capillary density, 5 capillaries/1 mm grid and 6 capillaries/1mm grid respectively, (A-D) irregular dilations (>20 $\mu$ m) (+), and (B-F) capillary malformations including abnormally tortuous capillaries (crossings\*), ramified ("bushy") capillaries (bold arrow) and concave tips (regular arrow).



**Abstract N°: 5119****Chronic spontaneous urticaria in Belgium: deciphering the clinical profile and treatment of patients visiting an urban city immunology department**

Yora Mostmans<sup>\*1</sup>, Bertrand Richert<sup>2</sup>, Viviane De Maertelaer<sup>3</sup>, Ines Saidi<sup>4</sup>, Francis Corazza<sup>5</sup>, Olivier Michel<sup>6</sup>

<sup>1</sup>CHU Brugmann, Immunology-Allergology, Bruxelles, Belgium, <sup>2</sup>CHU Brugmann, Dermatology, Bruxelles, Belgium,

<sup>3</sup>Université Libre De Bruxelles / Campus Érasme, Statistics, Anderlecht, Belgium, <sup>4</sup>Université Libre De Bruxelles / Campus Érasme, Dermatology, Anderlecht, Belgium, <sup>5</sup>Université Libre De Bruxelles / Campus Érasme, Immunology, Anderlecht, Belgium, <sup>6</sup>Université Libre De Bruxelles / Campus Érasme, Immunology-Allergology, Anderlecht, Belgium

**Chronic spontaneous urticaria in Belgium: deciphering the clinical profile and treatment of patients visiting an urban city immunology department**

**Introduction & Objectives:** Chronic urticaria (CSU) is a chronic inflammatory mast cell-driven disorder of which reliable clinical data in Belgium are lacking. This study focusses on clinical characteristics of CSU patients presenting at an urban Immunology-Allergology department.

**Materials & Methods:** Outpatients with CSU were included from 2018-2021. Clinical characteristics, Dermatology Life Quality Index (DLQI) and Urticaria activity score (UAS7) were collected by thorough anamnesis and questionnaires. Furthermore, patients underwent provocation testing, an autologous serum skin test (ASST) and a blood analysis.

**Results:** The study included 49 CSU patients and 20 non-CSU subjects. CSU was distributed differently with age and sex, showing higher numbers in female patients below the age of 46 years. 67% of CSU patients had accompanying angioedema of which 9% were reported genital. CSU patients scored a mean 8/30 on their DLQI questionnaire. There was no significant difference in IgE, C reactive protein (CRP) and tryptase levels between CSU patients and controls. Oral glucocorticosteroids were prescribed in 23% of CSU patients during their disease course though only half of these patients had a severity grade 4 CSU. In 82% of the included CSU patients, Urticaria Control Test (UCT) scores were below 12. When we hypothetically considered low IgE levels and high IgG anti-TPO levels as differentiation marker for autoimmune(ai)CSU and non-aiCSU, we found that 4% of all included CSU patients could be considered aiCSU.

**Conclusion:** Generally, the inner-city population displayed the same clinical characteristics, as previous cohorts from Northern Europe. The relatively high rate of CSU patients receiving oral glucocorticosteroid treatment for their disease though not always classified as severe, underlines the need to train doctors of various specialties in the treatment algorithms of CSU. Furthermore, by looking at potential autoimmune characteristics, our findings open perspectives on the identification of new routinely used clinical parameters for the detection of aiCSU, a relatively small immunological subtype of CSU.



**Abstract N°: 5411**
**Urticaria Voices: The use of Patient-Reported Outcome Measures for monitoring chronic spontaneous urticaria in clinical practice**

Jonathan Bernstein<sup>\*1, 2</sup>, Pedro Laires<sup>3</sup>, Maria Magdalena Balp<sup>3</sup>, Pallavi Saraswat<sup>4</sup>, Tara Raftery<sup>5</sup>, Jessica McCarthy<sup>6</sup>, Mihai Dricu<sup>7</sup>, Tonya Winders<sup>8</sup>, Karsten Weller<sup>9</sup>

<sup>1</sup>University of Cincinnati, Division of Rheumatology, Allergy and Immunology, Cincinnati, United States, <sup>2</sup>Bernstein Allergy Group and Clinical Research Center, Cincinnati, Ohio, United States, <sup>3</sup>Novartis Pharma AG, Basel, Switzerland, <sup>4</sup>Novartis Healthcare Pvt. Ltd., Hyderabad, India, <sup>5</sup>Novartis Ireland Ltd., Ireland, <sup>6</sup>Novartis Pharmaceuticals Corp., East Hanover, United States, <sup>7</sup>Ipsos SA, Basel, Switzerland, <sup>8</sup>Global Allergy and Airways Patient Platform, Vienna, Austria, <sup>9</sup>Charité – Universitätsmedizin Berlin, Department of Dermatology and Allergy, Berlin, Germany

**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is characterized by unpredictable itchy wheals/hives and/or angioedema for more than 6 weeks without any identifiable external trigger. The unpredictability of symptoms makes assessment and monitoring of symptoms challenging. Patient-Reported Outcome Measures (PROMs) assess symptoms, health-related quality of life (HRQoL) due to a disease as well as improvement due to treatment. However, the extent of PROMs' use in clinical practice to manage CSU is not well understood. This study investigated the frequency of PROM usage from both patients' and physicians' perspectives.

**Materials & Methods:**

Urticaria Voices is a global cross-sectional online survey with CSU patients and CSU-treating physicians in the US, Canada, UK, Germany, France, Italy, and Japan. Patients with a self-reported clinician-provided diagnosis of CSU and prescription treatment were recruited through nationally representative online panels of the general population and patient advocacy groups. Dermatologists, allergists, or immunologists treating CSU patients who could make autonomous treatment decisions were invited from specialized online panels. Investigated PROMs included four CU-specific PROMs (Urticaria Control Test [UCT], Itch Severity Scale [ISS], Urticaria Activity Score [UAS7], Chronic Urticaria Quality of Life [CU-Q2oL]), three angioedema-specific PROMs (Angioedema Activity Score [AAS], Angioedema Control Test [AECT], Angioedema Quality of Life questionnaire [AE-QoL]) and the Dermatology Quality of Life Index (DLQI). Physicians additionally evaluated the use of the Patient Global Impression of Severity (PGI-S).

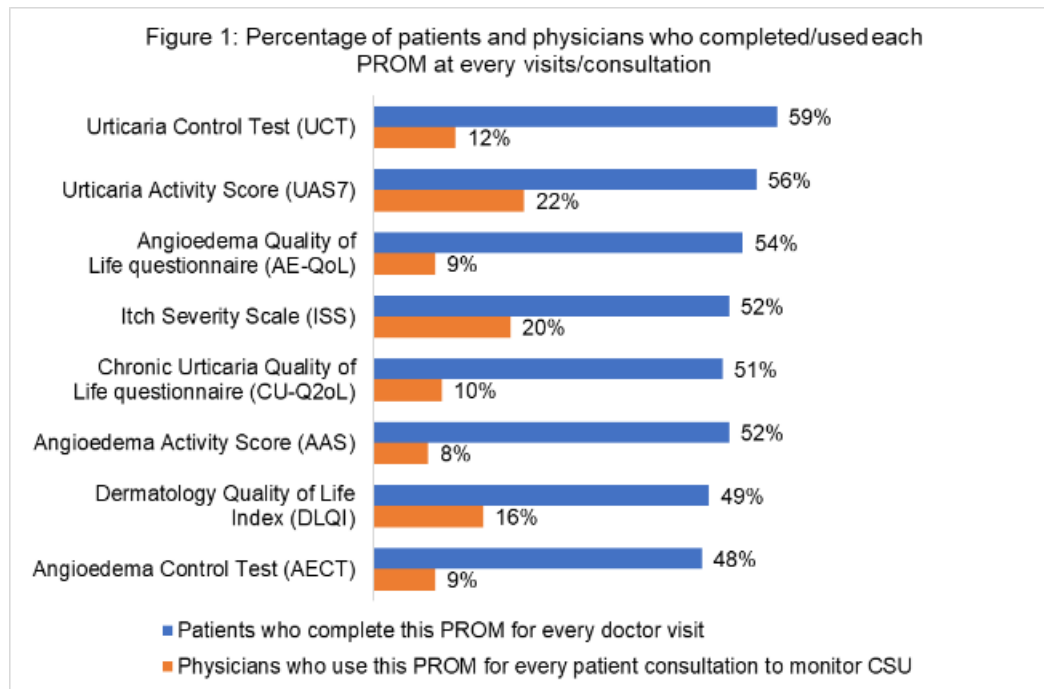
**Results:**

582 CSU patients (62% women, mean age 42 years [SD 11.9]) and 862 CSU-treating physicians were included in this study. 80% of CSU patients recognized at least 1 of the prompted PROMs. Among these, 69% reported completing at least 1 PROM during every doctor's visit, 27% completed at least 1 PROM for some doctor visits (but not every visit) and a minority (4%) didn't recall completing any of the PROMs. Among physicians, 45% reported using at least 1 PROM for every patient consultation, 44% use at least 1 PROM at some consultations and 11% don't use any of the PROMs when seeing patients. In addition to PROMs, most physicians also ask patients general questions about symptoms (84%), HRQoL (77%) and visually inspect the skin (71%) to assess and monitor symptoms and treatment outcomes.

**Conclusion:**



PROMs are not extensively used in clinical practice. Only half of patients reported completing UCT at every visit but only 1 in 8 physicians in the survey reported using it for every patient consultation. Majority of the physicians relied on more subjective and less standardized methods to assess symptoms and monitor treatment outcomes. Increased use of PROMs in clinical practice may facilitate improved monitoring of symptoms, inform treatment decisions and support clinical outcomes.



**Abstract N°: 5634****Correlation of Periostin and Interleukin-13 with Chronic Spontaneous Urticaria- a case control study**Alpana Mohta<sup>1</sup><sup>1</sup>Sardar Patel Medical College, Bikaner, India**Introduction & Objectives:**

Chronic spontaneous urticaria (CSU) is a complex, idiopathic skin disease characterized by various cellular infiltrations. Mast cells and CD4+ T helper 2 cells are known to play key roles in the development and maintenance of CSU. The aim of this study was to investigate the levels of periostin and IL-13 in the sera of patients with CSU and healthy controls, and to determine their relationship to the pathogenesis of CSU.

**Materials and Methods:**

The study recruited 100 patients with CSU and 50 healthy normal controls. Serum levels of periostin and IL-13 were measured and compared between the two groups.

**Results:**

The study found that periostin levels were significantly lower in the CSU group than in healthy controls (p value-0.001). Additionally, periostin levels were lower in patients with severe CSU compared to those with mild CSU (p value-0.02). However, IL-13 levels were significantly higher in patients with CSU than in healthy controls (p value-0.03).

**Conclusion:**

The results suggest that periostin and IL-13 may be independently related to the pathogenesis of CSU. The findings imply that periostin may have a suppressive effect on the development of CSU and IL-13 may have a promoting effect on the development of CSU. Further research is needed to fully understand the relationship between periostin and IL-13 in CSU.



**Abstract N°: 6072****Acquired C1-esterase inhibitor deficiency associated with splenic marginal zone lymphoma.**

Emilia Loewe<sup>1</sup>, Tillmann Schill<sup>1</sup>, Julie Schanz<sup>2</sup>, Michael P. Schoen<sup>1</sup>, Undine Lippert<sup>1</sup>

<sup>1</sup>University Medicine Göttingen, Dermatology, Göttingen, Germany, <sup>2</sup>University Medicine Göttingen, Haematology, Göttingen, Germany

**Introduction & Objectives:**

Acquired C1-esterase inhibitor (C1-INH) deficiency angioedema (C1-INH-AAE) is a rare disorder and a form of bradykinin-mediated angioedema. The increase in vascular permeability of the skin and mucosa causes recurrent episodes of swelling (edema) and induces, albeit less frequently, abdominal pain. In the case of unclear abdominal complaints without additional visible swelling, a diagnosis of angioedema could be overlooked. Laboratory diagnostics with low levels of C1-INH and complement factor 4 are crucial for the diagnosis. In addition, very low levels of C1q and anti-C1-INH inactivating autoantibodies are frequently found. Importantly, C1-INH-AAE may also be associated with hematologic malignancies.

**Materials & Methods:**

We present a 78-year-old female patient with a 10-month history of recurrent abdominal pain, accompanied by nausea and vomiting often following breakfast. Extensive gastroenterological diagnostics revealed no pathological findings apart from a slightly enlarged spleen seen by ultrasound.

Since the results of food allergy testing in our department were unremarkable, we revisited the patient's medical history and conducted additional laboratory tests.

**Results:**

Interestingly, the patient complained of severe attacks of abdominal pain that increased over 12 hours and lasted up to 24 hours or more. Laboratory tests showed reduced C1-INH levels and functional activity, as well as a hyperactivation of complement factors C3c and C4. She denied a family history of angioedema and C1-INH-deficiency. Further diagnostics via CT showed an infiltration of the spleen. Examination of the bone marrow revealed a lymphoproliferative infiltration without lymphadenopathy, suspicious for splenic marginal zone lymphoma.

In summary, due to the bone marrow infiltration, stage IVA splenic marginal zone lymphoma was diagnosed. After initiation of monotherapy with the chimeric monoclonal anti-CD20 antibody rituximab, the abdominal symptoms resolved. During the therapy, laboratory values including the C1-INH functional activity and complement factors normalized.

**Conclusion:**

In contrast to HAE, AAE patients have no family history of angioedema and are characterized by the late onset of symptoms.

In our case, due to the close association of C1-INH-AAE with lymphoproliferative diseases, the marginal zone lymphoma was discovered and treated promptly. The positive effect of successful systemic lymphoma therapy on the abdominal pain attacks indicates a close connection between autoimmunity and lymphoproliferation. Routine screening for an underlying hematological malignancy, especially of the B-cell line, should be performed in

patients with C1-INH-AAE.

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