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COMMENTARY

A Patient Charter for Chronic Urticaria

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ABSTRACT

Chronic urticaria (CU) is the recurring development of wheals (aka "hives" or "welts"), angioedema, or both for more than 6 weeks. Wheals and angioedema occur with no definite triggers in chronic spontaneous urticaria, and in response to known and definite physical triggers in chronic inducible urticaria. Approximately 1.4% of individuals globally will have CU during their lifetime. The itching and physical discomfort associated with CU have a profound impact on daily activities, sexual function, work or school performance, and sleep, causing significant impairment in a patient's physical and mental quality of life. CU also places a financial burden on patients and

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healthcare systems. Patients should feel empowered to self-advocate to receive the best care. The voice of the patient in navigating the journey of CU diagnosis and management may improve patient–provider communication, thereby improving diagnosis and outcomes. A collaboration of patients, providers, advocacy organizations, and pharmaceutical representatives have created a patient charter to define the realistic and achievable principles of care that patients with CU should expect to receive. Principle (1): I deserve an accurate and timely diagnosis of my CU; Principle (2): I deserve access to specialty care for my CU; Principle (3): I deserve access to innovative treatments that reduce the burden of CU on my daily life; Principle (4): I deserve to be free of unnecessary treatment-related side-effects during the management of my CU; and Principle (5): I expect a holistic treatment approach to address all the components of my life impacted by CU. The stated principles may serve as a guide for healthcare providers who care for patients with CU and translate into better patient–physician communication. In addition, we urge policymakers and authors of CU treatment guidelines to consider these principles in their decision-making to ensure the goals of the patient are achievable.

Keywords: Angioedema; Chronic urticaria; Health care; Hives; Patient advocacy; Wheals

Key Summary Points

Chronic urticaria (CU) has a substantial negative impact on a patient's physical, mental, and psychosocial quality of life.

The voice of the patient in navigating the journey of CU diagnosis and management may improve patient–provider communication, thereby improving diagnosis and outcomes.

The principles stated in this patient charter may serve as a guide for healthcare providers who care for patients with CU.

We encourage CU patients to speak with their healthcare provider and share how CU is impacting their daily life and understand they have a role in treatment discussions.

We urge policymakers and authors of CU treatment guidelines to consider these principles in their decision-making to ensure the goals of the patient are achievable.

INTRODUCTION

Chronic urticaria (CU) is the recurring development of wheals (aka "hives" or "welts"), angioedema (swelling under the skin or mucus membranes), or both for more than 6 weeks [1]. The wheals or angioedema can appear either spontaneously in chronic spontaneous urticaria (CSU) or be induced by a specific trigger in chronic inducible urticaria (CIndU). Typically, the signs and symptoms of CSU occur every day or almost every day. Many cases of CSU are caused by an autoimmune process (an immune response against a body's own healthy cells or tissues), and some CSU patients have other autoimmune diseases including rheumatoid arthritis and thyroid disease [2]. In CIndU, wheals and angioedema occur after exposure to specific triggers such as heat, cold, sunlight,

increased body temperature, or water (Table 1) [1, 3]. Patients tend to attribute CU to an environmental factor (e.g., allergic response to food); however, CU is not an allergic disease. Contact with allergens such as foods, pollens, molds, or animal dander can sometimes cause acute urticaria, not CU.

Approximately 1.4% of individuals around the world will have CU during their lifetime, with the highest prevalence estimates occurring in Latin America and Asia and the lowest estimates occurring in North America and Europe [4]. CSU is more common than CIndU, as CIndU accounts for approximately 15% of CU; many patients can have both [5]. CU can develop at any age, but most often manifests between the ages of 20 and 40 years [6]. Approximately twice as many women than men are affected by CU [4, 7]. People with CU have an increased risk of autoimmune diseases, psychiatric disorders, and allergic diseases [5]. Among patients with CIndU, dermographism is by far the most common type, whereas CIndU in response to heat, sunlight, vibrations, and water is rare (Table 1) [8]. Both CSU and CIndU can last for years in many patients [7, 9].

Wheals associated with CU are pink, red, or white raised areas of the skin of any shape or size, often surrounded by an area of red skin (aka "flare") (Fig. 1). The skin will not appear red on skin of color. Rather, the wheals may be the same color as the surrounding skin. The wheals

Table 1 Types and triggers of CIndU, their descriptions, and prevalence [1, 3, 8]

Type of CIndU	Trigger	Description	Prevalence in Patients with CIndU
Heat urticaria	Heat	Local itching and swelling of the skin after exposure to heat (e.g., 40°C hot water bottle)	Rare
Cold urticaria	Cold	Local itching and swelling of the skin within 10 min of exposure to cold (i.e., ice cube or cold air); can also cause a systemic reaction such as fainting if the exposure is systemic (e.g., swimming in cold water)	Adults 8–37%, children 9–14%
Solar urticaria	Sunlight	Wheals or angioedema within a few minutes of skin exposure to sunlight (UVA, UVB or visible light)	Rare
Vibratory angioedema	Vibrations	Local itching and swelling after exposure to vibrations (e.g., jackhammer)	Rare
Symptomatic dermographism	Scratching, rubbing	Linear wheal and flare[a] within 10 min after stroking or scratching the skin	Adults 50–78%, children 38%
Delayed pressure urticaria	Delayed pressure	Swelling of the skin within 4–6 h after exposure to pressure (e.g., sitting on a bench, tight clothing)	Adults 3–20%, children 3–9%
Aquagenic urticaria	Water	Small wheals (1–3 mm) in response to contact with water of any temperature, from any source	Rare
Cholinergic urticaria	Exercise, passive warming	Small wheals (1–3 mm) surrounded by large flares[a] in response to increased body temperature induced by exercise, emotional upset, and hot baths or showers	Adults 6–13%, children 19%

CIndU chronic inducible urticaria; *UVA* ultraviolet A; *UVB* ultraviolet B
[a]A flare is an area of red skin surrounding a wheal

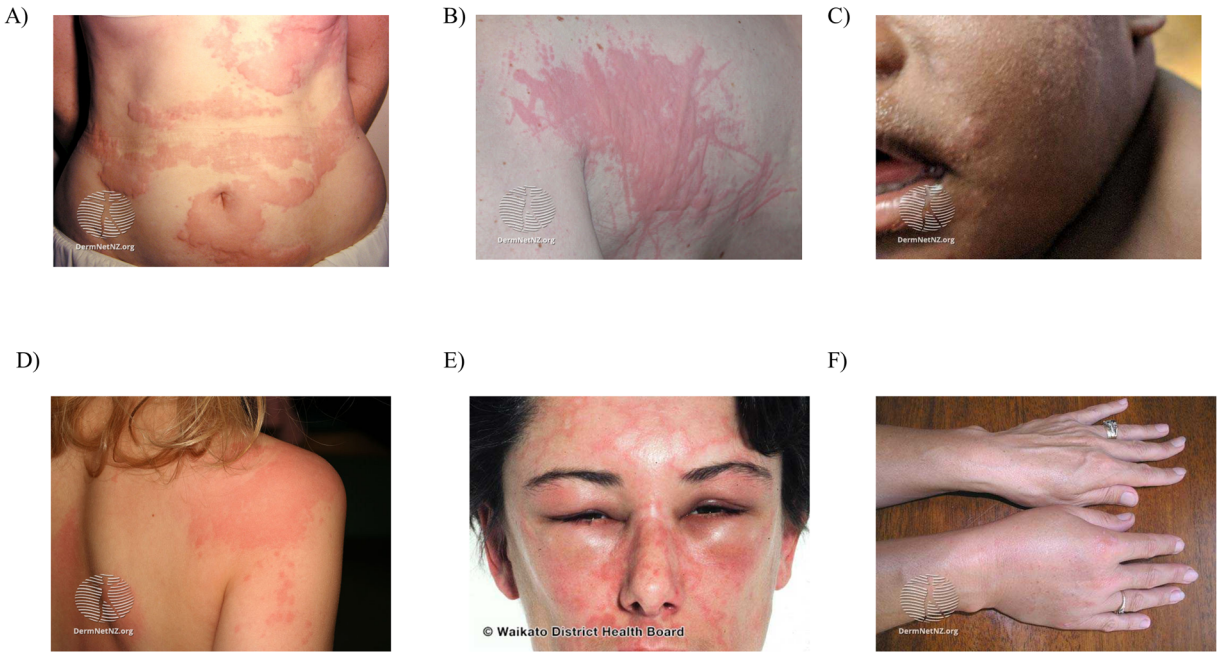

Fig. 1 **A** Wheals associated with CSU. **B** Wheals associated with CIndU (symptomatic dermographism). **C** Urticaria on dark skin. **D** Urticaria in a child. **F** Angioedema and facial urticaria. **G** Angioedema of the right hand. Images reproduced from https://dermnetnz.org/topics/urticaria-images under *Creative Commons Attribution-NonCommercial-NoDerivs 3.0 (New Zealand)*. *CIndU* chronic inducible urticaria, *CSU* chronic spontaneous urticaria

can appear anywhere on the body and are generally itchy, sometimes with a burning sensation, and can be painful [1, 3]. The wheals may disappear within 30 min or last as long as 24 h and sometimes longer. Once the wheal disappears, there is no residual mark or scar. Angioedema is a red or skin-colored deep swelling of the skin commonly on the face, hands, feet, or genitalia (Fig. 1) [1, 3]. The location of the swelling is not generally itchy, but may tingle, burn, or be painful, and take up to 72 h to resolve.

The itching and physical discomfort associated with CU have a profound impact on daily activities, sexual function, and work or school performance, often disturbing a patient's sleep [10–12]. In addition, patients with CU are 3–4 times more likely to experience anxiety and depression than individuals without CU [13]. This emotional distress may be because of the physical discomfort from the wheals or angioedema, anticipation of the next episode, or feelings of social stigmatization because of the physical appearance of the wheals [14]. In turn, the emotional distress associated with CSU may actually induce or exacerbate an episode [15]. The symptom discomfort, emotional distress, impact on work or school, interference with daily activities, and disrupted sleep culminate to significantly impair a patient's physical and mental health-related quality of life (HRQoL) [6, 10, 11]. In addition to the physical and emotional burden, CSU can also place a financial burden on patients or healthcare systems, mainly related to treatment costs and physician visits [10]. Patients with CSU have significantly more physician visits, emergency department visits, and hospitalizations than individuals without CSU [11, 16].

Several clinical organizations have developed and published guidelines for the diagnosis and management of CU [3, 17–21], and the international urticaria guideline was updated in 2022 [1]. While these guidelines provide necessary and high-quality clinical guidance, the voice of the patient in navigating the journey of CU diagnosis and management may improve patient–provider communication, thereby improving diagnosis and outcomes. The purpose of this patient charter was to define the realistic and achievable principles of care that patients with CU should expect to receive. The charter was developed from a collaboration of patients, providers, advocacy organizations, and pharmaceutical representatives.

DEVELOPING THE PATIENT CHARTER

Members of the Global Allergy and Asthma Excellence Network's (GA^2LEN) Urticaria Centers of Reference and Excellence (UCARE) program and representatives of organizations within the Global Allergy & Airways Patient Platform recommended patients, providers, patient advocates, and an industry representative to be involved in developing the CU patient charter. Recommended individuals were extended an invitation to co-author the CU patient charter, and a meeting was held to discuss the patient charter content. The charter was then developed through a series of drafts, author reviews, and revisions.

This article is based on previously conducted studies and does not contain any new studies with human participants or animals performed by any of the authors.

PRINCIPLE 1: I DESERVE AN ACCURATE AND TIMELY DIAGNOSIS OF MY CU

Diagnosis of CU can be a long and frustrating process. In real-world settings, the average time to diagnosis is variable but can take years [10, 14, 22]. Patients experience frustration and anxiety as they desperately seek the cause of their symptoms from healthcare providers, self-analysis of personal routines, and the Internet [14, 23]. Patients often try to treat the disease themselves before they seek professional medical care [14]. Diagnosis may be hindered by a perception among patients and healthcare providers that the disease will be controlled by itself and will disappear spontaneously. Another reason for a delay in CSU diagnosis is that symptoms may not be occurring when the patient visits a healthcare provider, while symptoms may not appear every day in the early stages of the disease. It is helpful for the patient to keep a journal of details of symptoms and to show the healthcare provider photos of the wheals and angioedema. The recently developed UCARE app ChRonic Urticaria Self Evaluation (CRUSE®) for CSU self-evaluation can help patients with documenting their disease and sharing important information with their physicians [24]. Another aspect of CSU that can be confusing and delay diagnosis is that some factors or conditions, like the use of non-steroidal anti-inflammatory medications, opioids, stress, infection, or even food (e.g., pseudoallergic reactions to tomatoes, spices, alcohol), can sometimes, but not predictably, aggravate CSU [1, 25–27].

The 2022 international urticaria guideline provides an algorithm for the diagnosis of CU (Fig. 2) [1]. The steps in the algorithm are designed to rule out other diseases that can cause wheals and angioedema, to look for indicators of CSU, and to identify potential triggers of CIndU [1]. Patient history and physical examination are the first steps in the diagnostic process. Certain patient histories such as recurrent fever, use of angiotensin-converting enzyme inhibitors, and the presence of only angioedema can be indicators that symptoms are not caused by CU [1]. The duration of the wheals is also a clue, since a single wheal duration of more than 24 h indicates that the wheals may be due to other conditions, such as urticaria vasculitis, which should be investigated. The next step is basic laboratory tests to look at markers in the blood that may point to an underlying autoimmune disease or inflammation, and the patterns of these test results can sometimes be indicative of the expected course

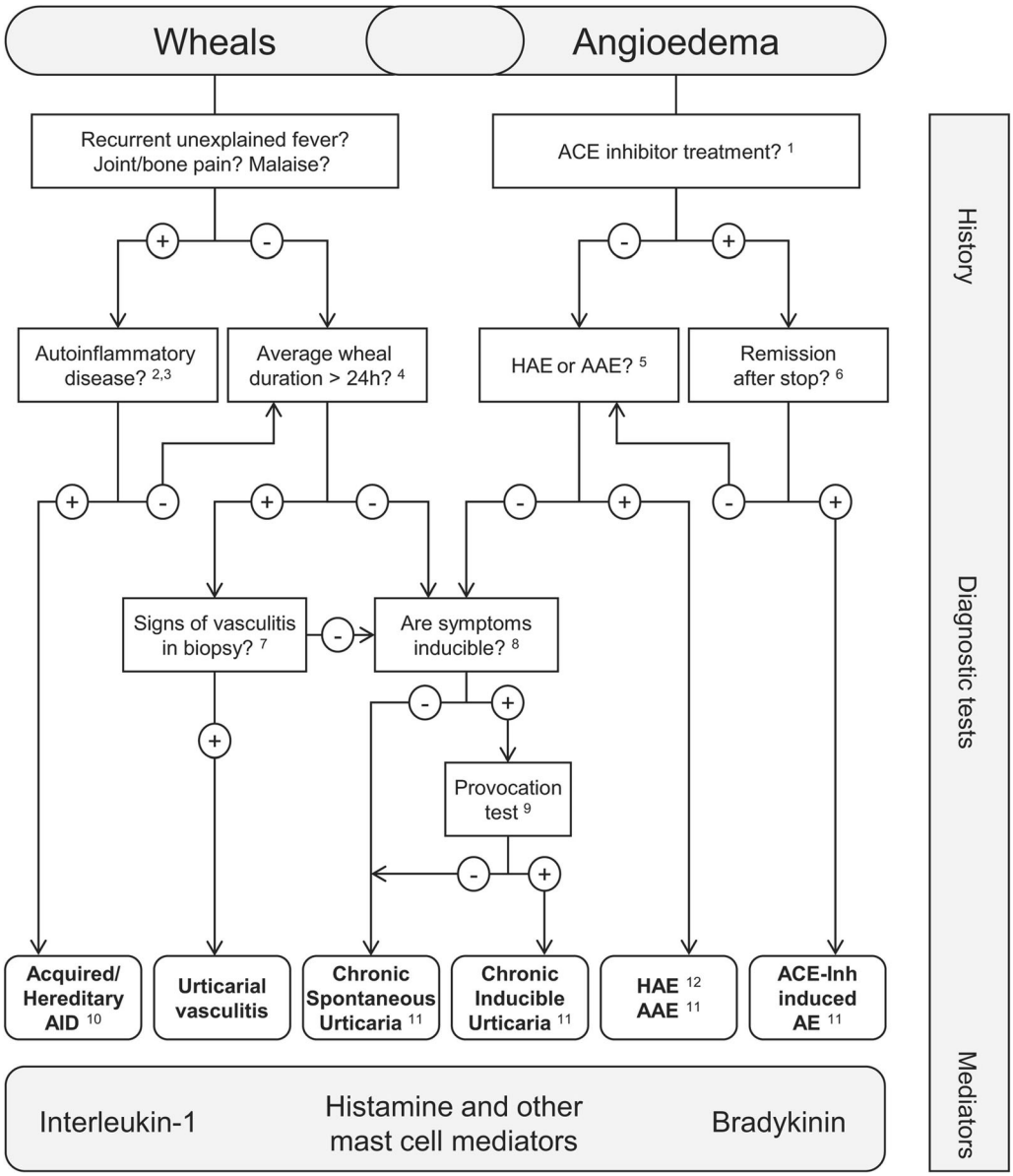

Fig. 2 Diagnostic algorithm for CU. Reproduced from Zuberbier et al., 2022 under Creative Commons Attribution-NonCommercial License [1]. *AAE* acquired angioedema due to C1-inhibitor deficiency, *ACE-Inh* angiotensin-converting enzyme inhibitor, *AE* angioedema, *AID* autoinflammatory disease, *HAE* hereditary angioedema

and response to treatment of CSU [1]. CIndU can be diagnosed by exposing the patient to the suspected trigger and provoking symptoms with standardized provocation tests, although this is not routinely done [28].

Beyond the diagnostic basic laboratory testing recommended by the guideline, extensive additional testing, such as allergy skin testing, does not particularly improve outcomes and is not cost-effective [29]. Therefore, some experts suggest that extensive laboratory testing for CSU should not be performed and should be limited to tests prompted by the patient history [30]. Non-specialists and specialists alike may be driven to keep searching for a cause to try and meet the expectations of patients, despite the

fact the search would likely be unsuccessful [14].

The patient history and limited laboratory tests should be sufficient to differentiate CU from other diseases that cause chronic wheals or angioedema, such as urticarial vasculitis, flushing syndromes, non-mast cell-mediated angioedema, or autoinflammatory diseases. These differential diseases are found at a much lower frequency than CU and usually exhibit only wheals or only angioedema, and often have other associated symptoms such as fever or joint pain [31].

Patients should be able to expect an accurate and timely diagnosis without the burden of unnecessary diagnostic tests. Achieving these expectations will help in relieving a patient's frustration and anxiety induced by diagnostic delays.

PRINCIPLE 2: I DESERVE ACCESS TO SPECIALTY CARE FOR MY CU

Primary healthcare providers including emergency department physicians or pharmacists are often the first point of care for patients experiencing wheals or angioedema. Primary healthcare providers and emergency physicians should be able to perform the patient history and order the basic laboratory tests required for the diagnosis of CU. The international CU guideline has been helpfully modified specifically for use by primary healthcare providers, along with guidance on when to refer to a specialist (i.e., a dermatologist or allergist/immunologist) [32]. In general, primary healthcare providers should refer a patient to specialty care if the diagnosis is in question or they do not have experience managing the CU, and they should do so in a timely manner to avoid the delays that patients experience in diagnosis and receiving care [6].

A European survey of primary healthcare providers found that 65% perceived their knowledge of urticaria and angioedema as inadequate and 75% indicated they had a "great" educational need on these topics [33]. It is therefore not surprising that patients often require frequent physician visits and multiple healthcare providers, sometimes with the feeling of not being taken seriously, before they are diagnosed [14]. Once they are diagnosed, some patients report feeling that their healthcare provider lacks awareness of CSU, and that the approach to treatment is trial and error [14]. Patient surveys indicate that the main reason patients switch physicians is because they are not satisfied with the efficacy of their treatment [34]. Surveys of healthcare providers in different countries demonstrate that the knowledge of CU guidelines among non-specialists is often lacking [35, 36], and that non-specialists tend to treat CU as an acute allergic disease [32]. Furthermore, access to biologics and advanced therapies sometimes used to treat CU may be limited to specialists. Therefore, patient access to specialty care when needed is important to ensure appropriate and adequate treatment.

The GA^{2}LEN/UCARE network is a group of specialty practices that serve as referral centers for CU [37]. Practices in the network have met a number of requirements set by GA^{2}LEN [37], and primary care providers or other specialists can refer their patients to these practices with confidence the patient will receive appropriate treatment (https://ga2len-ucare.com/centers/). However, access to specialty care can differ among countries and can be particularly challenging in low- and middle-income countries. Access can also be challenging in high-income countries, depending on the country's health system organization.

Even when adequate specialty access is available, many times patients do not seek it because they have given up on finding help or believe the disease will resolve on its own [34, 38]. In the case of CIndU, they think they can just avoid the trigger. Such misperceptions highlight the need for physicians to communicate with their patients about the nature of CU and the benefits of treatment. There is also a need for accurate CU information on social media and other online platforms where patients search for information that will hopefully encourage them to seek specialty care [39, 40].

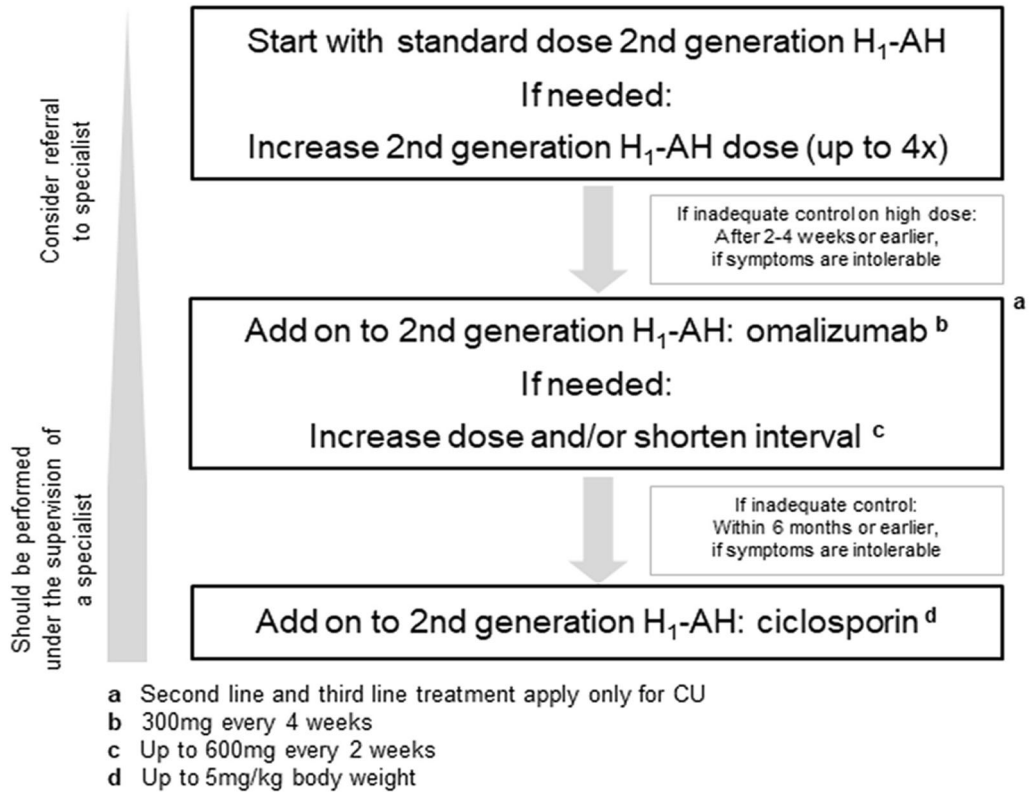

Fig. 3 Recommended treatment algorithm for urticaria. Reproduced from Zuberbier et al., 2022 under Creative Commons Attribution-NonCommercial License [1]. *H1-AH* H1-antihistamines

PRINCIPLE 3: I DESERVE ACCESS TO INNOVATIVE TREATMENTS THAT REDUCE THE BURDEN OF CU ON MY DAILY LIFE

Treatments for CU do not cure the disease, but they can minimize or eliminate symptoms during the duration of the disease. Thus, the goal of treatment in CU from a clinical perspective is to eliminate signs and symptoms until the disease spontaneously resolves ("Treat the disease until it's gone") [1]. From a patient perspective, the main goals of treatment are to be free of itch and wheals, have complete control over CU symptoms, have improved HRQoL, and stay in long-term remission. First-line treatment for CU is an oral antihistamine, which works by inhibiting the actions of one of the substances in the body (histamine) that induces wheals and angioedema [1]. The modern (e.g., 2nd generation) antihistamines are recommended at the standard dose when beginning treatment, but if that is not effective, a dose of up to 4 times higher than the standard approved dose is the next step (Fig. 3) [1]. Such high doses of an antihistamine may be cost-prohibitive for some patients.

At least 40% of patients do not respond adequately to antihistamines, even at the higher doses [8]. These patients tend to have more severe symptoms and more sleep problems compared with patients who respond to antihistamine treatment [12]. For patients who do not respond to antihistamine treatment, the next step is to add omalizumab (Fig. 3) [1]. Omalizumab is a monoclonal antibody (aka, "biologic") that binds to immunoglobulin E (IgE) in the blood, preventing some of the biological mechanisms that lead to the development of wheals and angioedema [8]. Many patients who do not benefit from antihistamine treatment respond well to omalizumab [41, 42]. The dose of omalizumab may be increased or it

Table 2 Patient-reported outcome measures in CSU and areas of use

	UAS	CU-Q_2oL	UCT	AAS	AE-QoL	AECT
Applicable in patients with:						
Wheals and no angioedema	+	+	+	–	–	–
Wheals and angioedema	+	+	+	+	+	+
No wheals and angioedema	–	–	+	+	+	+
Number of items	2	23	4	5	17	4
Retrospective assessment	–	+	+	–	+	+
(recall period)		2 weeks	4 weeks 7 days		4 weeks	4 weeks 3 months
Prospective assessment	+	–	–	+	–	–
(frequency)	1× or 2×/day			1×/day		
MCID	11	3–15[a]	3	8	6	3
Cost-free for:						
Patient management	+	+	+	+	+	+
Academic research	+	+	+	+	+	+
Industry studies	+	–	–	–	–	–
Language/country versions available[b]	+[c]	Italian, German, Greek, Hebrew, Korean, Persian, Polish, Portuguese, Spanish, Thai, Turkish	> 90 language versions available	> 80 language versions available	> 50 language versions available	> 40 language versions available

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AAS Angioedema Activity Score, *AECT* Angioedema Control Test, *AE-QoL* Angioedema Quality of Life Questionnaire, *CSU* chronic spontaneous urticaria, *CU-Q_2oL* Chronic Urticaria Quality of Life Questionnaire, *MCID* minimal clinically important difference, *UAS* Urticaria Activity Score, *UCT* Urticaria Control Test

[a]The MCID of the CU-Q_2oL has been assessed in two independent studies performed in different patient collectives in Europe and Asia. While one study found an MCID of 3 points [46], the MCID identified in the other study was higher with 15 points [47]

[b]Additional language/country versions may be or are in preparation

[c]The UAS is available in several languages. The original source is the EAACI/GA^{2}LEN/EDF/WAO urticaria guideline [1]. Due to its easy structure, the UAS is usually translated but not formally linguistically validated

may be given more often to optimize disease control (Fig. 3) [1]. Non-responders to omalizumab should be reevaluated for alternative diagnoses, such as autoimmune diseases. For patients who do not respond to antihistamines or omalizumab, nowadays the immunosuppressant ciclosporin is the recommended third-line medication [8]. A large number of biologics (e.g., dupilumab, rituximab, TNF α inhibitors, secukinumab) and other novel therapies (e.g., bruton tyrosine kinase inhibitors, anti-IL-5 monoclonal antibodies, tezepelumab, lirentelimab, etc.) are under investigation for the treatment of CSU [43]. Should these treatments prove effective, patients will need access to these new options.

Determining the response or non-response to CSU treatment in real-world settings is necessary when navigating the different treatment steps. Response to treatment is best measured using patient-reported outcome measures (Table 2) [44]. Use of patient-reported outcomes is encouraged to determine if any changes in treatment are needed [45]. A minimal clinically important difference, which is the minimum score change from before treatment to after treatment that signals a clinically important treatment response, has been determined for many of the patient-reported outcomes used for CSU (Table 2) [44, 46, 47]. Importantly, the patient-reported outcomes tools for CSU have been translated into many languages (Table 2); however, few of the patient-reported outcomes have been specifically validated for use by children [44, 48]. The GA^{2}LEN taskforce recommends the Urticaria Activity Score to measure symptoms and the Chronic Urticaria Questionnaire on Quality of Life to measure HRQoL [49]. The Urticaria Control Test is a simple 4-question measure of disease control that can easily be used in daily clinical practice [45]. The Angioedema Activity Score, Angioedema Control Test, and Angioedema Quality of Life Questionnaire can also be used when angioedema is present [44, 50]. The only tools specifically for measuring disease activity in the subtypes of CIndU are the Cold Urticaria Activity Score, the Symptomatic Dermographism Activity Score, and the Cholinergic Urticaria Activity Score [51–53], although disease control in patients with CIndU in general can be measured with the Urticaria Control Test [44]. In addition, the GA^{2}LEN/UCARE network has developed the CRUSE® app (https://cruse-control.com) that allows patients to fill out a patient-reported outcome questionnaire daily on their smart device and send the results to their physician [24]. CRUSE enables individual patients to monitor and document their CSU disease activity, and the data collected from the app by UCARE provide insights at a population level into how different medications affect HRQoL and how treatments can be improved [24]. Patient-reported outcomes should be interpreted with the caveat that a patient can develop a tolerance to the pain and burden of CU over time. Therefore, a lack of change or improvement in outcomes during follow-up visits may be a reflection of adaption of the patient to the disease.

Levels of certain proteins found in the blood (aka "biomarkers") can sometimes indicate the likelihood of a patient with CSU to respond to treatment. For example, high levels of C-reactive protein may indicate the patient will not respond well to antihistamines, and low total IgE and low FcepsilonRI in blood basophils may indicate the patient will not respond well to omalizumab but may respond to ciclosporin (Fig. 4) [54–56]. Certain clinical characteristics, such as severe activity of the disease, concomitant CIndU, previous steroid treatment, and poor disease control or HRQoL, may also be indicators of potential non-response to antihistamines (Fig. 4) [54, 57]. Sex and age do not appear to be associated with the likelihood of response to any current CSU treatment [54]. Use of biomarkers and clinical characteristics can potentially eliminate the trial and error approach to CSU treatment, improving the patient treatment journey. However, more research into biomarkers of response is still needed, and guidance of treatment decisions should still be driven by treatment response indicated by patient-reported outcomes.

Given that nearly half of patients with CU do not improve with antihistamines, patients should be made aware of innovative treatments and have access to such treatments to improve symptoms and reduce their burden of disease.

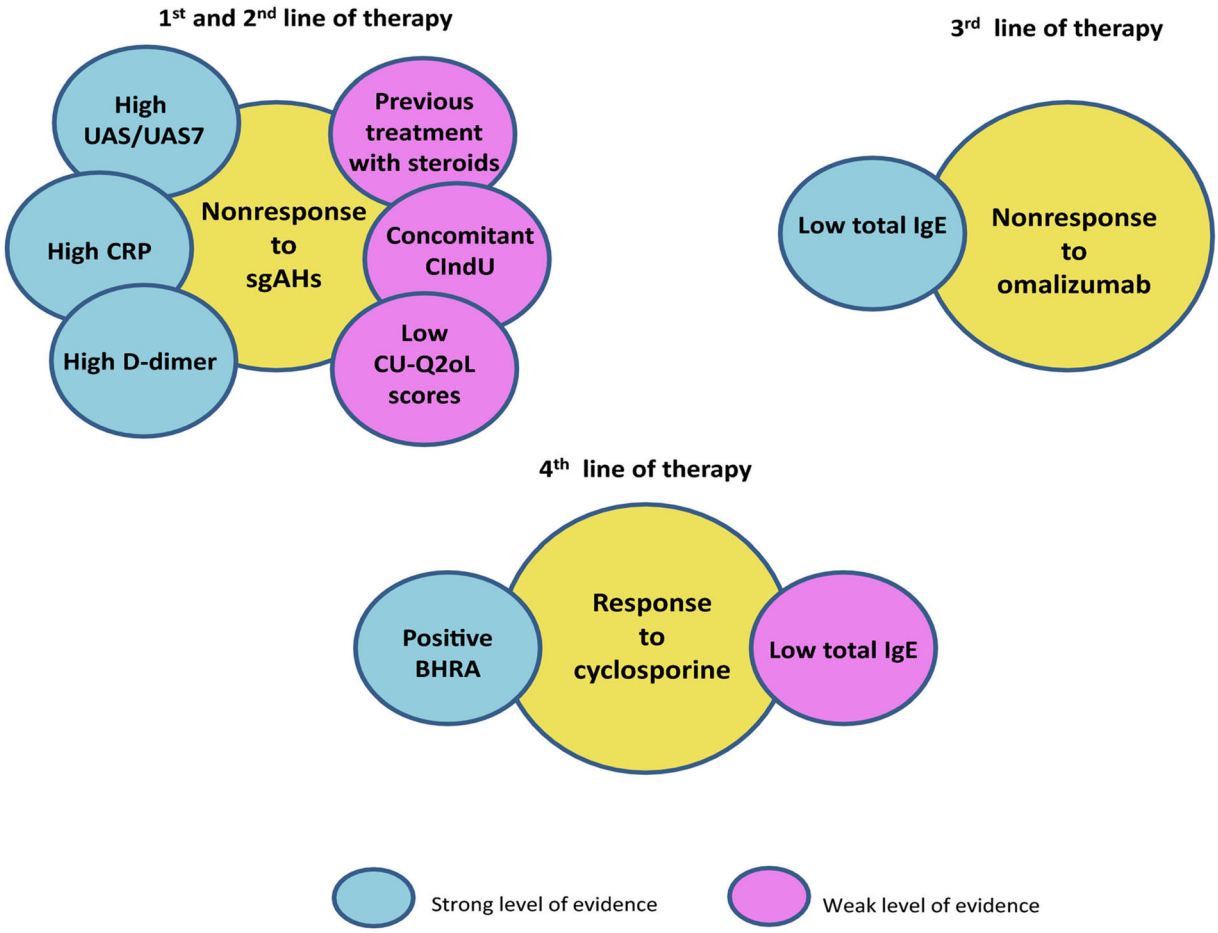

Fig. 4 Predictors of nonresponse to second-generation antihistamines and omalizumab and response to cyclosporine. Reproduced from Fok et al., 2021 under Creative Commons Attribution-NonCommercial License [54]. *BHRA* basophil histamine release assay, *CIndCU* chronic inducible urticaria, *CRP* C-reactive protein, *CU-Q2oL* Chronic Urticaria Quality of Life Questionnaire, *sgAHs* second-generation H1-antihistamines, *UAS* Urticaria Activity Score

The severity of disease should be monitored by patient-reported outcomes to assess if changes in dosing regimen are needed or if treatment should be stopped altogether [45]. Available biomarkers and clinical characteristics may be used to tailor individualized treatment.

PRINCIPLE 4: I DESERVE TO BE FREE OF UNNECESSARY TREATMENT-RELATED SIDE-EFFECTS DURING THE MANAGEMENT OF MY CU

Essentially, all medications carry some risk of side effects. However, patients with CU deserve to receive treatments that will avoid unnecessary side effects, and the potential side effect burden of each CU treatment should be part of the shared decision-making conversations between healthcare providers and patients. Patients generally start treatment for CU with an antihistamine (Fig. 3) [1]. Older, first-generation antihistamines (i.e., diphenhydramine, chlorpheniramine, brompheniramine, hydroxyzine, etc.) have been used over-the-counter for treating allergic diseases and urticaria for decades. The first-generation antihistamines cross the blood–brain barrier inducing central nervous system effects of drowsiness, sedation, fatigue, mental fog, and impaired motor responses [58, 59]. The effects are similar to

alcohol even at the lowest manufacturer-recommended doses, and their use has been implicated in vehicle, airplane, and workplace accidents [58, 60]. Because of their side effects, the use of first-generation antihistamines in the treatment of CU is not recommended [1]. More modern, second-generation antihistamines (e.g., bilastine, rupatadine, ebastine, loratadine, cetirizine, desloratadine, fexofenadine, etc.) that have very limited sedating effects have been available since the 1980s and provide a preferred treatment option [59]. Yet, in a worldwide survey of 1140 physicians, 15% of the respondents who claimed to follow a CU treatment guideline reported prescribing first-generation antihistamines as a first-line treatment for CSU [2].

While second-generation antihistamines at manufacturer-recommended doses have limited or no nervous system effects compared with the first generation [59], their prescribing information still cautions against driving or operating potentially dangerous equipment. Increasing the standard dose of second-generation antihistamines up to 4× for the treatment of CSU has been found to increase the risk of drowsiness more than threefold compared with standard dosing [61]. A survey of patients with CSU treated with either standard doses or up to 4× the standard approved dose of second-generation antihistamines found no significant difference in the number of patients experiencing unwanted effects or sedating effects; however, 74% of patients considered the unwanted effects of up-dosed antihistamines as somewhat or considerably worse compared with standard doses [62]. A side-effect of drowsiness or sedation may limit a patient's ability to drive, severely impacting their work/school attendance and their lifestyle. There may also be a profound negative effect on work/school performance and daily activities. Therefore, although second-generation antihistamines are generally safe and well tolerated, the goal should be to use the lowest dose possible to achieve optimal disease control.

A short burst of oral corticosteroids (OCS) is standard treatment for severe flare-ups of many diseases that involve inflammatory processes, including CSU, despite a lack of randomized controlled trials proving their effectiveness in CSU [1]. In a worldwide survey, 19% of physicians who claim to follow CU guidelines prescribe a short course (less than 10 days) of OCS as first-line treatment for CSU [2]. There appears to be an overreliance on OCS for CSU [63–65], which can have damaging long-term effects. Evidence suggests that even 4 or more bursts of OCS during a patient's lifetime can increase the risk of type 2 diabetes, cardiovascular/cerebrovascular disease, osteoporosis and bone fractures, cataracts, depression/anxiety, kidney impairment, and pneumonia [66]. Because of the long-term effects, maintenance use of OCS is considered the "last resort" for treating severe asthma [67], and one of the principles in the severe asthma patient charter is "I deserve not to be reliant on systemic corticosteroids."[68] Similarly, patients with CSU deserve to avoid the side effects of long-term OCS use through optimizing non-OCS guideline-recommended treatments, when possible.

PRINCIPLE 5: I EXPECT A HOLISTIC TREATMENT APPROACH TO ADDRESS ALL THE COMPONENTS OF MY LIFE IMPACTED BY CU

Many facets of daily life are negatively affected by the physical manifestations of CU, such as the interference with daily activities and sleep because of the physical discomfort of the itching and burning [11]. There is also a tremendous impact on mental health as patients experience anxiety, frustration, depression, fear of life-threatening throat swelling, poor body image, and even suicidal thoughts [11, 14, 69–71]. For some patients, the anxiety of CSU can lead to a CSU episode, particularly in patients who have a psychological condition in which they have difficulty recognizing or expressing emotion (alexithymia) [72]. In these patients, the anxiety actually manifests physically as wheals and angioedema. Socially, patients may feel isolated and alone, stigmatized by others who are afraid the symptoms are contagious [14]. Often patients simply give up on ever controlling their

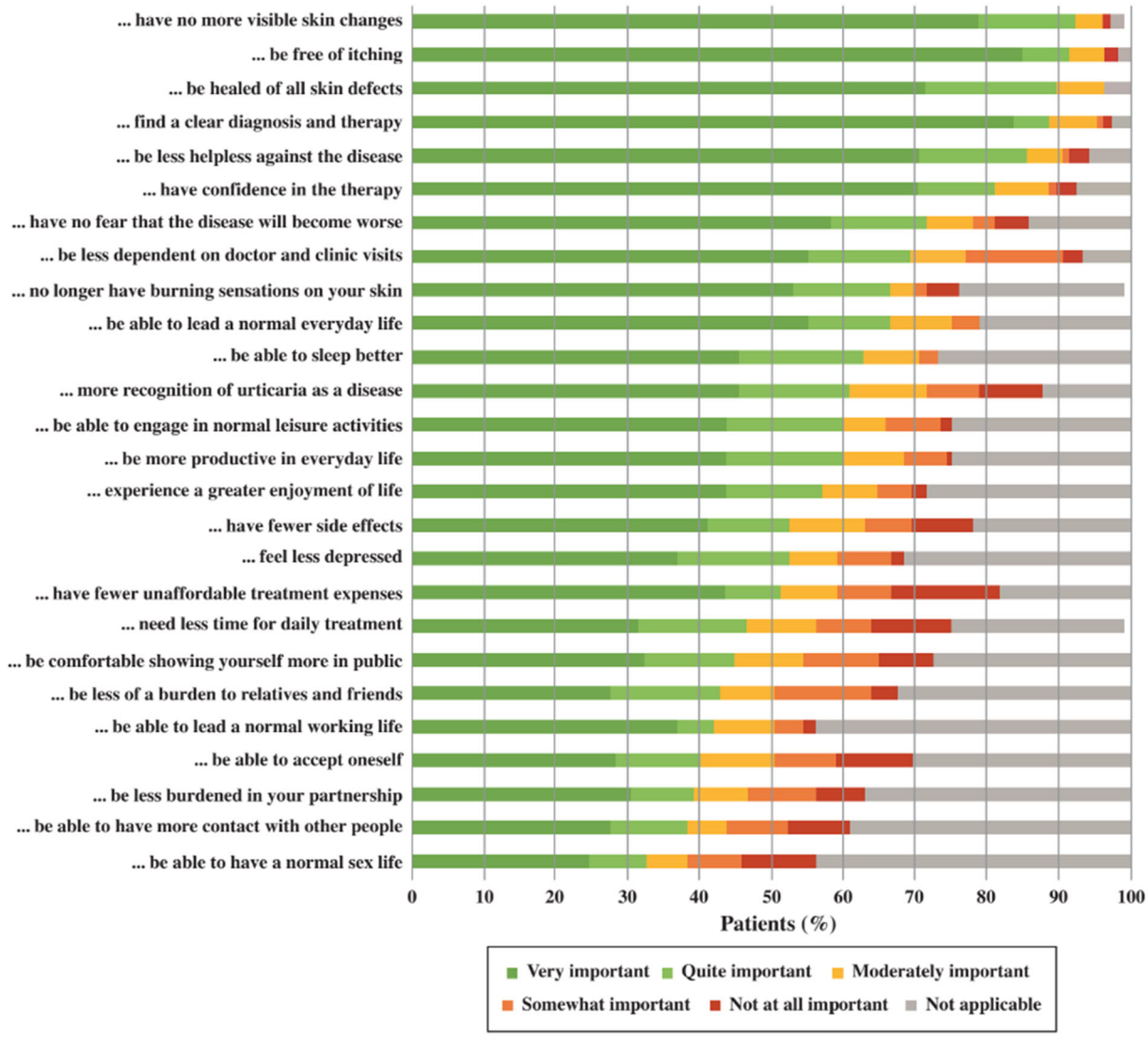

Fig. 5 Patient needs in CSU ($n = 103$). Reproduced with permission from Sommer et al., 2020 [73]. *CSU* chronic spontaneous urticaria

CU [38]. The presence of comorbidities adds to the physical, emotional, and financial burdens. Thus, the goal of therapy for CU should be not only to relieve symptoms but also to improve mental health and quality of life. Identified needs in the management of CSU from a patient perspective include freedom from skin changes, confidence in therapy, freedom from fear of the disease getting worse, improved sleep, better daily productivity, more enjoyment of life, and many others (Fig. 5) [73].

Shared decision-making conversations among patients, their families, and healthcare providers are an opportunity to discuss the patient's goals. These conversations need to include what the patient should expect from the healthcare provider, treatment options, and how the patient needs to be active in their own treatment and management using patient-reported outcomes. Active participation in deciding on treatments may give patients more confidence in their therapy and relieve some of their feelings of powerlessness [14]. A shared

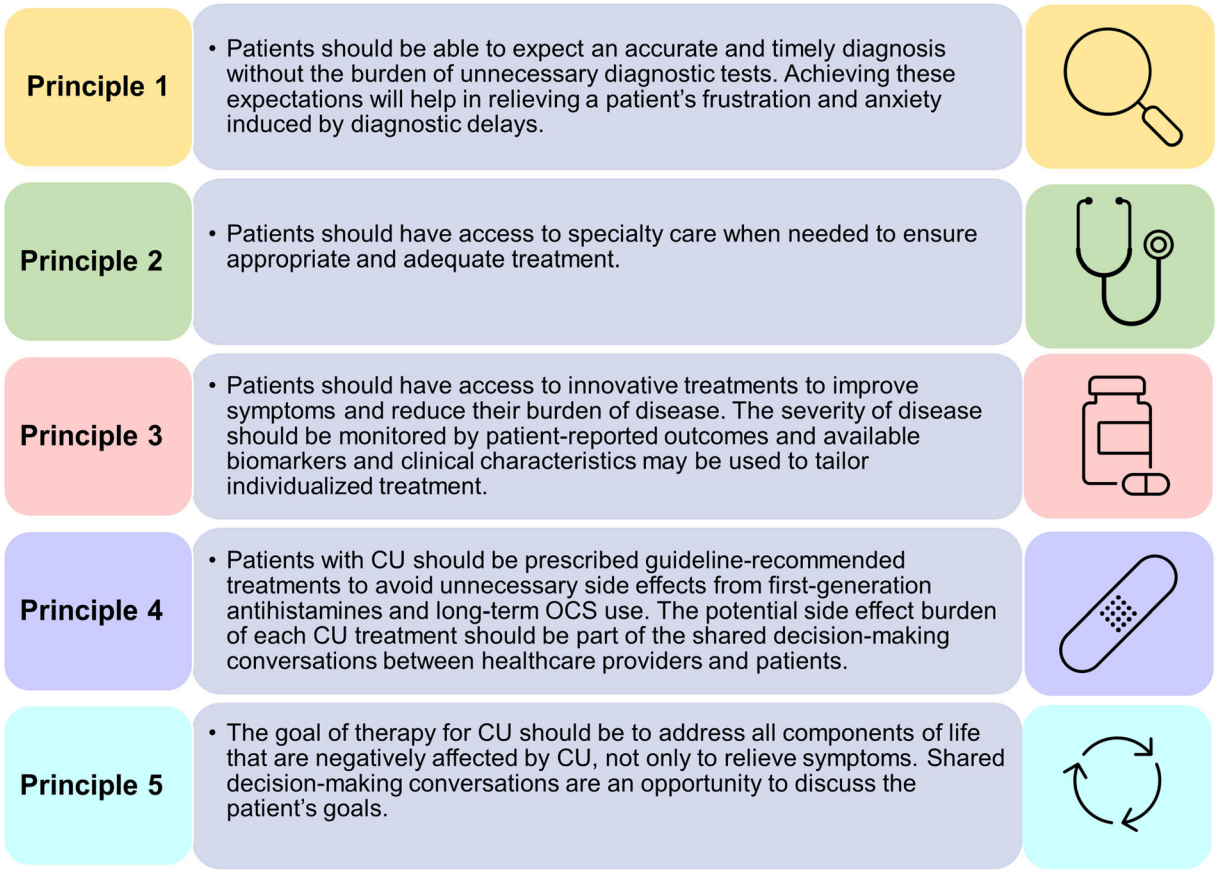

Fig. 6 Key recommendations of the CU patient charter. *CU* chronic urticaria, *OCS* oral corticosteroid

decision-making tool for CSU is available to provide guidance for these conversations [74].

The negative impact of CSU on mental health may be overlooked during the trial and error process of pharmacological treatment. As one patient said "You feel very helpless. You don't feel like anybody understands what you're feeling. You feel like you're going mad/crazy" [14]. One surveyed physician remarked that "I, at times, have thought there needs to be a psychiatrist next to me…"[14]. In theory, professional psychological help may benefit patients with CSU, but it could also add to the financial burden and take away even more time from work or daily obligations. More research is needed regarding the pros and cons of psychological interventions in CSU.

Patients can learn to cope with CU. Two activities that may relieve patient anxiety and frustration are access to good quality information and seeking support from fellow patients. Patients often seek information on the Internet throughout their disease journey, even before seeking a physician visit [23]. The Internet can have misinformation that leads to confusion and further anxiety; on the other hand, it can have helpful, accurate information that may relieve anxiety and frustration [75]. Some helpful resources are patient advocacy groups and professional allergy and dermatology organizations that provide accurate information about CU in patient-friendly language. The groups and organizations also help connect patients with each other, through online groups and events such as Urticaria Day celebrated on October 1 every year and supported by Urticaria Network E.V., UCARE, and others (https://urticariaday.org) [76]. Emotional support from other patients on internet forums, social media, or events such as Urticaria Day can help remind

patients that they are not alone and help them deal with the challenges of living with CU [77].

DISCUSSION

Patients have become increasingly involved in their healthcare decisions in recent years, and patient preferences and goals are a key aspect of shared decision-making. The perspective of the patient can shift the emphasis of treatment from simply efficacy and safety to considering how the treatment affects the overall well-being of the patient. Encouragingly, pharmaceutical companies and patient advocacy groups have begun collaborating to incorporate the voice of the patient into educational tools and studies for CU [78, 79]. This CU patient charter provides principles of care that will hopefully be incorporated into individual patient care, policy decisions, and guidelines to improve the quality of care for patients with CU. Key recommendations of the patient charter are shown in Fig. 6.

We recognize that there are challenges to implementing some of the principles. For example, although patients deserve a timely diagnosis, the fact is that the nature of CSU makes it inherently challenging to diagnose. We encourage knowledgeable sources (i.e., patient advocacy groups, pharmaceutical companies, and professional organizations) to continue to increase awareness of CU to patients and healthcare providers and to provide accurate information on the Internet for patients seeking answers to unexplained wheals and angioedema.

Another challenge is that not all patients will have access to specialists or innovative treatments, because of barriers related to cost, country-specific healthcare systems, location, and other reasons. A workforce development of specialists is needed to provide more options for care, and training of primary healthcare providers, emergency department physicians, and pharmacists in CU awareness and management is needed to fill in the gaps when access to specialists is not possible.

The aim of Principle 4 is to be free of *unnecessary* side effects. This can be achieved by avoiding first-generation antihistamines and using only second-generation antihistamines as recommended by international treatment guidelines. The lowest dose of a second-generation antihistamine necessary to achieve disease control should be used to avoid unnecessary side effects. In addition, healthcare providers should prescribe OCS only in the short term for a severe flare-up, rather than as first-line treatment, as is being practiced by nearly a quarter of surveyed physicians in many countries [2, 36], and by 46% of surveyed physicians in Latin America [35]. We encourage healthcare providers to take advantage of the information and guidance provided by endorsed treatment guidelines, as they are reflective of the most current evidence-based medicine.

The expectation of a holistic approach to address all the aspects of life negatively affected by CU, as stated in Principle 5, should be an achievable expectation for every patient. Patient–provider communication is the key to this Principle, and we encourage shared decision-making conversations to identify patient treatment goals.

CONCLUSION

The principles stated in this patient charter may serve as a guide for healthcare providers who care for patients with CU and translate into better patient–physician communication. We encourage CU patients to speak with their healthcare provider and share how CU is impacting their daily life and understand they have a role in treatment discussions. In addition, we urge policymakers and authors of CU treatment guidelines to consider these principles in their decision-making to ensure the goals of the patient are achievable.

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Declarations

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