



NEWSLETTER 1 OCTOBER 2021

The Physician Education and Communication Program

Dear urticaria treating physician,

it is our pleasure to officially launch our 1st UCARE *LevelUp* newsletter.

LevelUp is an interactive physician information and education platform and program. The aims of UCARE LevelUp are to educate physicians on:

- · Guideline recommendations
- Diagnostic workups
- The burden of CU
- Differential diagnosis, comorbidities and consequences of CU
- · The causes and pathogenesis of CU
- How to build strategic therapeutic plans for their patients
- How to effectively communicating with patients
- Improving the use of patient-reported outcome measures (PROMs)
- The work of the UCARE network and how to get in touch if needed

Over the next 16 months, the UCARE *LevelUp* program's 1st phase will achieve its educational goals by utilising the following 10 online formats and activities: webinars, quizzes, a physician education and resources website, newsletters, podcasts, fireside chats, videos, an online journal club, virtual grand rounds and poster sessions.

With all these activities spreading information and advice from the best urticariologists from around the world, the best news is that it is all free of charge and available to all physicians.

With over 126 member Centers in 39 countries, GA²LEN's network of urticaria Centers of reference and excellence (UCARE) is the biggest and most active global consortium of urticariologists and urticaria centers.

The UCARES around the world



Audited 126
Applicant 19
Interest 9

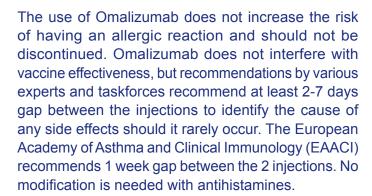


HOT TOPICS

COVID-19 Vaccination in Chronic Spontaneous Urticaria (CSU)

Some studies suggest that COVID-19 infection can worsen CSU in more than a third of patients. Since more variants are emerging being fast spreading and causing severe symptoms such as the Delta variant, vaccination has been strongly recommended especially that studies showed that it continues to be effective at preventing hospitalization and death. Vaccinated individuals appear to be infectious for a shorter period. Neither CSU nor chronic inducible urticaria increases the risk of having an allergic reaction to the COVID-19 Vaccine. Physicians must be aware that vaccination may cause a flare of CSU, which may be confused with vaccine allergy. However, flare up of CSU should not be regarded as a contraindication for COVID-19 vaccination.

Bermingham WH, Ardern-Jones MR, Huissoon AP, Krishna MT. Forewarned is forearmed: chronic spontaneous urticaria as a potentialrisk to effective SARS-CoV-2 vaccine uptake and global public health. Br J Dermatol. 2021 May



The European Taskforce for atopic dermatitis (ETFAD) recommends holding immunosuppressants if possible during vaccination. Clinicians may, therefore, consider pausing immuno-suppressants during vaccination, typically from the vaccination day until 1 week after for JAK-inhibitors and cyclosporine, or until 2 weeks after for methotrex-ate and azathioprine. This can possibly improve chances of appropriate vaccination response. Alternatively, the lowest dose possible may be used, for example 2.5 mg/kg/day cyclosporine, 1 mg/kg/day azathioprine and 7.5 mg/week methotrexate.

Thyssen JP, Vestergaard C, Barbarot S, de Bruin-Weller MS, Bieber T, Taieb A, Seneschal J, Cork MJ, Paul C, Flohr C, Weidinger S, Trzeciak M, Werfel T, Heratizadeh A, Darsow U, Simon D, Torrelo A, Chernyshov PV, Stalder JF, Gelmetti C, Szalai Z, Svensson Å, von Kobyletzki LB, De Raeve L, Fölster-Holst R, Christen-Zaech S, Hijnen DJ, Gieler U, Gutermuth J, Bangert C, Spuls PI, Kunz B, Ring J, Wollenberg A, Deleuran M. European Task Force on Atopic Dermatitis: position on vaccination of adult patients with atopic dermatitis against COVID-19 (SARS-CoV-2) being treated with systemic medication and biologics. J Eur Acad Dermatol Venereol. 2021 May;35(5):e308-e311.

If rescue oral corticosteroids cannot be stopped, the vaccine could be given if the dose is <20 mg/day according to the European Union League Against Rheumatism (EULAR) recommendation on immunosuppressants and COVID-19 vaccination. However, flare up of CSU should not be regarded as a contraindication for COVID-19 vaccination



STUDY RESULTS

CU treatment in older ages-recurrences

In a study from Texas, USA, recurrence rate for chronic urticaria was reported 13% among 341 patients. The remarkable finding regarding the recurrence group is that alternative treatment frequency is significantly higher. Patients with a history of treatment with anti-inflammatory agents, immunosuppressants and omalizumab had a slightly higher recurrence rate than the ones who only received first-line treatment.

In another study from Canada, median duration of CSU was less than 2 years in 30% of the patients. Duration expanded to 10 years or more in 16% of the patients. The first group had a relatively older age of onset (48 \pm 17 years) when the other ones had a younger age of onset (22 \pm 16 years).

Patients with co-existing autoimmune/thyroid disease (19%) trended towards a shorter median duration of CSU. Symptomatic relief was higher with guidelines based therapy versus various alternative medicines, such as acupuncture, traditional Chinese medicine and naturopathic medicine.

Kim JK, Har D, Brown LS, Khan DA. Recurrence of Chronic Urticaria: Incidence and Associated Factors. J Allergy Clin Immunol Pract. 2018 Mar-Apr;6(2):582-585. doi: 10.1016/j.jaip.2017.07.012. Epub 2017 Sep 6. PMID: 28888844.

Stepaniuk P, Kan M, Kanani A. Natural history, prognostic factors and patient perceived response to treatment in chronic spontaneous urticaria. Allergy Asthma Clin Immunol. 2020 Jul 15;16:63. doi: 10.1186/s13223-020-00459-5. PMID: 32834828; PMCID: PMC7371813.

TREATMENT ADVICE

Treatment advice: H1 antihistamines

As histamine plays a key role in the wealing reaction typical of urticaria, the symptomatic therapy option of choice, recommended by the guidelines, is the use of H1 antihistamines. First-generation H1-antihistamines (e.g. hydroxyzine) are no longer recommended for use in chronic urticaria, as they are more sedating than the second-generation of antihistamines [SGAH] (e.g. cetirizine) and carry a higher risk of side effects such as dry mouth, blurred vision, headache, glaucoma, and urinary retention.

The use of a standard-dose modern 2nd generation H1-antihistamines is recommended as the first-line symptomatic treatment for urticaria. However, no recommendation can be made on which to choose because there is no head-to-head evidence for every possible treatment comparison. Their use should be continuously over two to four weeks before going to the next step. In case of pregnancy, antihistamines of choice are cetirizine and loratadine.

If the use of standard doses of SGAH doesn't lead to an adequate disease control (UAS7 \leq 6 and/or UCT \geq 12) current guidelines recommend a higher dosage, up to four times of standard dose, of the same SGAH. It was shown that the rate of response to standard dosages of antihistamines in patients with CSU was 38.6% and there is 60% likelihood of response to increased doses of antihistamines.

Regarding the safety of up-dosing antihistamines, most SGAH have an excellent safety profile with no evidence of cardiotoxicity even when updosed up to four times their standard licensed dose.

PROJECTS

Project CURICT, chronic urticaria – patient use of information and communication technologies



We interviewed Dr. Ivan Cherrez about the CURICT project he chaired and would like to share his replies with you, to get a better idea of this UCARE project and the impact it can have on your patients and urticaria patients in general.

Dr. Cherrez, could you briefly explain what CURICT stands for? The CURICT project is about the usage, quality and relevance of information and communications technologies in patients with chronic urticaria.

Why did you decide to do a study among patients with urticaria and social networks? This study was done because we know that patients with chronic diseases are interested in being informed about self-management of their disease and that a good patient-physician relationship improves adherence to treatment.

Thanks to the rise of Information and Communication Technologies, patients have access to information about their diseases. According to our previous study, email and SMS (short message service) were the most popular ICT methods for patients looking for and receiving information about chronic respiratory diseases.

It is extremely important for patients with CU to understand their disease, the potential trigger factors, clinical treatments, and prognosis. Using information and communications technology, physicians can provide social support, provide social interaction, and improve relationships with their patients. For instance, we designed a study to explore what are the frequency and preferences of using ICT in CU.

Was it a study only in the center of it in Guayaquil, Ecuador, or did more centers participate? How did you manage to do a study with so many centers?

Our previous studies on ICT and chronic diseases gave us experience; we decided to modify our survey and apply it to CU patients. We met with Dr. Marcus Maurer at a meeting, and he invited us to conduct the study as part of UCARE (Urticaria Centers of Reference and Excellence). We were able to collect 1841 surveys from 17 countries around the world due to the enthusiasm and cooperation of all UCARE members.

The results obtained give us a global view of how ICT use is shared throughout the world.

In your opinion, if you must summarize in one sentence: what was the most important thing that was learned from the study? The principal results from our study are as follows: The majority of CU patients have access to ICTs. Patients with CU preferred one-to-one ICTs (SMS, WhatsApp, and email) to ask physicians about urticaria.

Could you tell us a bit more on your findings?

Although the majority of CU patients have access to ICTs, the use of ICT varies by country, age, and educational level. One-to-many ICT (YouTube, web browsers) are most commonly used by CU patients to obtain general health and CU related information. For the one-to-one ICTs (SMS, WhatsApp, and email) to ask a physician about urticaria, Email rated highest for this purpose, while WhatsApp performed best for communicating with other patients.

The majority of patients with CU have a high level of interest in an app to monitor and control diseases.

Patients with co-morbid condition Inducible Chronic Urticaria are more likely to express interest in mobile apps to assess their health.

More female patients and patients with higher education were found to use disease management apps.

App development for disease prevention and control was associated with less interest in people of older ages.

Maurer M, Weller K, Magerl M, Maurer RR, Vanegas E, Felix M, et al. The usage, quality and relevance of information and communications technologies in patients with chronic urticaria: A UCARE study. The World Allergy Organization journal. 2020;13(11):100475.

Cherrez-Ojeda I, Vanegas E, Cherrez A, Felix M, Weller K, Magerl M, et al. How are patients with chronic urticaria interested in using information and communication technologies to guide their healthcare? A UCARE study. The World Allergy Organization journal. 2021;14(6):100542

Cherrez-Ojeda I, et al. Maurer M. Urticaria Patients Are Highly Interested in Apps to Monitor Their Disease Activity and Control: A UCARE CURICT Analysis. JACI-IP submitted.



PROJECTS

SolU-CE (Solar urticaria a Comprehensive Evaluation)

This project has been started by Lea Kiefer recently and the project plan is currently under development and revision. The intent is to perform a analysis of patients with historical or physical evidence of reactions to solar radiation and light in various seasons and geographical regions of the world. Collection of detailed real-life data on many still not well-defined disease characteristics should give new insights and are expected to globally improve the understanding of SolU and consequently optimize evaluation, treatment strategies and improve future care all over the world.

Steering committee members are: Ana Gimenez Arnau (Spain), Kanokvalai Kulthana (Thailand), Lea Kiefer (Germany), Lesley Rhodes (UK), Atsushi Fukunaga (Japan), Margarida Gonçalo (Portugal), Emek Kocatürk Göncü (Turkey), Heike Röckmann (Netherlands).

If you are interested in participating in this project, please e-mail Dr. Lea Alice Kiefre at: lea-alice.kiefer@charite.de

PROJECTS

COVAC-CU (Effects of COVID-19 Vaccination on Chronic Urticaria Patients)

Here is another project that has been started by Emek Kocatürk recently, and is planned to expand. The design of the study is: international, multicenter, observational (non-interventional), cross-sectional.

The main objective is to evaluate the effects of COVID-19 vaccination, analyze the risk factors and prevalence of COVID-19 vaccine associated reactions in patients with chronic urticaria (CU).

Steering committee members of the project are: Marcus Maurer (Germany), Simon Francis Thomsen (Denmark), Emek Kocatürk Göncü (Turkey), Torsten Zuberbier (Germany), Luis Felipe Ensina (Brazil), Ted Popov (Bulgaria), Martijn van Doorn (Netherlands), Ana Gimenez Arnau (Spain), Riccardo Asero (Italy), Paulo Ricardo (Brazil), Romi Saini (USA), Clive Grattan (UK), Niall Conlon (Ireland), Ivan Cherrez (Equador).

If you are interested in participating in this project, please e-mail Dr. Emek Kocatürk at: dremekozgur@gmail.com

PUBLICATIONS

We are very proud to announce that UCARE network studies about the effects of the COVID-19 pandemic on chronic urticaria have been published.

Congratulations to the collaborating centers for the great teamwork!

The global impact of the COVID-19 pandemic on the management and course of chronic urticaria

AIM:

To understand how CU patients are affected by the COVID-19 pandemic; how specialists alter CU patient management; and the course of CU in patients with COVID-19.

MATERIALS AND METHODS:

Our cross-sectional, international, questionnairebased, multicenter UCARE COVID-CU study assessed the impact of the pandemic on patient consultations, remote treatment, changes in medications, and clinical consequences.

RESULTS:

The COVID-19 pandemic severely impairs CU patient care, weekly number of patients decreased by more than 50% and the rate of face-to-face consultations decreased by 62%.

CU does not affect the course of COVID-19 with only 4% of CU patients having a severe course of COVID-19, but COVID-19 results in CU exacerbation in one of three patients, with higher rates in patients with severe COVID-19.

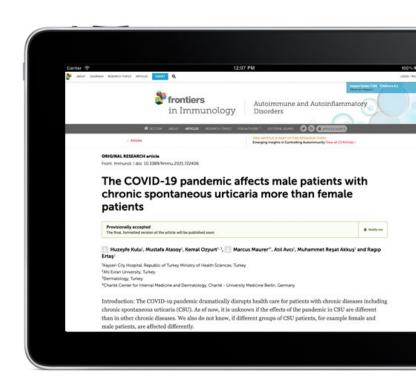
Cyclosporine and systemic corticosteroids, but not antihistamines or omalizumab, are used less during the pandemic.

CONCLUSION:

The COVID-19 pandemic brings major changes and challenges for CU patients and their physicians. The long-term consequences of these changes, especially the increased use of remote consultations, require careful evaluation.

Authors: Emek Kocatürk, Andaç Salman, Ivan Cherrez-Ojeda, Paulo Ricardo Criado, Jonny Peter, Elif Comert-Ozer, Mohamed Abuzakouk, Rosana Câmara Agondi, Mona Al-Ahmad, Sabine Altrichter, Rand Arnaout, Luisa Karla Arruda, Riccardo Asero, Andrea Bauer, Moshe Ben-Shoshan, Jonathan A. Bernstein, Mojca Bizjak, Isabelle Boccon-Gibod, Hanna Bonnekoh, Laurence Bouillet, Zenon Brzoza, Paula Busse, Regis A Campos, Emily Carne, Niall Conlon, Roberta F. Criado, Eduardo M. de Souza Lima, Semra Demir, Joachim Dissemond, Sibel Doğan Günaydın, Irina Dorofeeva, Luis Felipe Ensina, Ragıp Ertaş, Silvia Mariel Ferrucci, Ignasi Figueras-Nart, Daria Fomina, Sylvie M Franken, Atsushi Fukunaga, Ana M. Giménez-Arnau, Kiran Godse, Margarida Gonçalo, Maia Gotua, Clive Grattan, Carole Guillet, Naoko Inomata, Thilo Jakob, Gul Karakaya, Alicja Kasperska-Zając, Constance H Katelaris, Mitja Košnik, Dorota Krasowska, Kanokvalai Kulthanan, M. Sendhil Kumaran, Claudia Lang, José Ignacio Larco-Sousa, Elisavet Lazaridou, Tabi Anika Leslie, Undine Lippert, Oscar Calderón Ilosa, Michael Makris, Alexander Marsland, Iris V. Medina, Raisa Meshkova, Esther Bastos Palitot, Claudio A.S. Parisi, Julia Pickert, German D. Ramon, Mónica Rodríguez-Gonzalez, Nelson Rosario, Michael Rudenko, Krzysztof Rutkowski, Jorge Sánchez, Sibylle Schliemann, Bulent Enis Sekerel, Faradiba S. Serpa, Esther Serra-Baldrich, Zhiqiang Song, Angèle Soria, Maria Staevska, Petra Staubach, Anna Tagka, Shunsuke Takahagi, Simon Francis Thomsen, Regina Treudler, Zahava Vadasz, Solange Oliveira Rodrigues Valle, Martijn B.A. Van Doorn, Christian Vestergaard, Nicola Wagner, Dahu Wang, Liangchun Wang, Bettina Wedi, Paraskevi Xepapadaki, Esra Yücel, Anna Zalewska-Janowska, Zuotao Zhao, Torsten Zuberbier, Marcus Maurer

The COVID-19 pandemic affects male patients with chronic spontaneous urticaria more than female patients



The COVID-19 pandemic dramatically disrupts health care for patients with chronic diseases, including chronic spontaneous urticaria (CSU). Currently it is unknown if the effects of the pandemic in CSU are different than in other chronic diseases. We also do not know, if different groups of CSU patients, for example female and male patients, are affected differently.

Huzeyfe Kulu1, Mustafa Atasoy1, Kemal Ozyurt1, Marcus Maurer2, Atıl Avcı1, M. Reşat Akkuş1, Ragıp Ertaş1

AIM.

To understand how CSU patients and subgroups are affected by the COVID-19 pandemic in their disease activity and control and treatment, using psoriasis as control.

PATIENTS AND METHODS:

We analyzed 399 patients (450 visits) with CSU or psoriasis assessed during August 2019, i.e. before the pandemic, or August 2020, i.e. during the pandemic, for changes in disease activity, disease control, and the treatment they used, and how these changes are linked to age, gender, and disease duration.

RESULTS:

Male but not female patients with CSU had markedly increased disease activity during the pandemic. CSU patients' age or disease duration were not linked to changes. Male and female patients with psoriasis showed similar increases in disease activity and decreases in disease control.

The rate of omalizumab treatment, during the pandemic, was unchanged in male patients and increased in female patients with CSU. The efficacy of omalizumab treatment, during the pandemic, was reduced in male patients but not female patients with CSU.

CONCLUSION:

Male but not female CSU patients, during the COVID-19 pandemic, show loss of disease control linked to loss of omalizumab efficacy. The reasons for this need to be investigated.

RESEARCH AND RESULTS

Very recent highlights from research on chronic spontaneous urticaria

21% of the CSU patients experienced a second episode of CSU

Toubi E et al reported that 21% of the CSU patients experienced a second episode of CSU after a mean of 2.9 years of full remission and the presence of bronchial asthma, increased total IgE, and autoimmunity (mostly anti-TPO antibodies) were found to be significantly higher in the recurrence group. They hypothesized that the persistence of this immune- mediated/ autoimmune milieu in CSU patients may maintain mast cell instability longer, thereby predicting the possibility of CSU recurrence rather than a life-long full remission.

Toubi E, Vadasz Z. Predictive features associated with chronic spontaneous urticaria recurrence. J Dermatol. 2021 Sep 14.



Nagayama K et al reported that severity of sleep-disordered breathing (SDB) is correlated with the severity of CSU independently of the BMI and physicians should consider comorbid SDB when treating patients with CSU (ref).

New marker for autoimmune urticaria

Kolkhir P et al suggested a new marker for the detection of type IIb autoimmunity in patients with CSU which is "aTPO↑IgE↓" aTPO↑IgE↓ was linked to higher age at CSU onset, being female, angioedema, and shorter CSU duration. aTPO↑IgE↓ was associated with markers of aiCSU, BAT, autologous serum skin test positivity, basopenia, eosinopenia and low response rate to antihistamine treatment.

Kolkhir P, Kovalkova E, Chernov A, Danilycheva I, Krause K, Sauer M, Shulzhenko A, Fomina D, Maurer M. Autoimmune Chronic Spontaneous Urticaria Detection with IgG Anti-TPO and Total IgE. J Allergy Clin Immunol Pract. 2021 Aug 4:S2213-2198(21)00884-9.



New Guidelines

The new urticaria guideline that was recently published adopts a patient-oriented approach and guides on how to manage patients once control is achieved and also suggests to consider patients' comorbidities as well as patients' treatment preferences.

EAACI published a new guideline on the use of omalizumab for the treatment of chronic spontaneous urticaria in adults and in the paediatric population 12-17 years old. It sheds light on selection of responders, the definition of response, strategies to enhance the responder rate, the duration of treatment and its regimen (in the clinic or home-based) and its cost-effectiveness following the GRADE approach. It also discusses future therapeutic approaches and perspectives as well as research priorities.

Agache I, Akdis C, Akdis M, Brockow K, Chivato T, Del Giacco S, Eiwegger T, Eyerich K, Giménez-Arnau A, Gutermuth J, Guttman-Yassky E, Maurer M, Ogg G, Ong PY, O'Mahony L, Schwarze J, Warner A, Werfel T, Palomares O, Jutel M. EAACI Biologicals Guidelines-Omalizumab for the treatment of chronic spontaneous urticaria in adults and in the paediatric population 12-17 years old. Allergy. 2021 Jul 29.

RESEARCH AND RESULTS

Recent highlights from congresses and meetings from European Academy of Dermatology and Venereology (EADV) Virtual Congress 2020:

Results of the PREG-CU study

Treatment patterns and outcomes in patients with chronic urticaria during pregnancy: Results of the PREG-CU study, a UCARE Project. In this presentation, Professor Emek Kocatürk Göncü described the results of the PREG-CU study (a UCARE project) which analysed the impact of chronic spontaneous urticaria and chronic inducible urticaria on pregnancy. The study found that patients with chronic urticaria have similar pregnancy outcomes compared to the general population.

Prevalence and predictors of angioedema in a large sample of hospital outpatients with chronic urticaria

In this ePoster, Dr Jennifer Astrup Sørense described the results of a study to determine the occurrence and predictors of angioedema. She found that almost half of all patients with chronic urticaria have concomitant angioedema. These patients were characterised by a female preponderance, higher levels of chronic spontaneous urticaria only, a lower quality of life, showed signs of autoimmunity and had a greater need of immunosuppressive treatment.

Ligelizumab achieves fast control of symptoms

Ligelizumab achieves fast control of symptoms in more patients with chronic spontaneous urticaria compared with omalizumab: analysis of the first 12 weeks of the Phase 2b study. The results showed that ligelizumab has a faster onset of action, with higher rates of patients achieving well-controlled or completely controlled disease during the first few weeks, and is stable in more patients over the first 12 weeks than omalizumab.



EVENTS

Urticaria Day



News from the event 1 October 2021 urticariaday.org





Follow us and join the conversation







Subscribe to our video channel

youtube.com/urticariaday



Taskforce News:

Journal Clubs

14 / 21 / 28 October 2021 and every two weeks thereafter

Quizzes

Solar Urticaria - planned for end of October 2021

Webinar

Burden of the disease on Chronic Urticaria Patient - planned for November 2021

Poster sessions

A call for posters from junior physicians will be coming soon. Topic: Diagnosis / Deadline: 10 January 2022

Grand Rounds

Open Topic planned for November 2021

Podcast

All things Urticaria has been integrated into the LevelUp program.

Keep an eye out for the *LevelUp* website due to be launched soon.

UPCOMMING EVENTS

GA²LEN UCARE Urticaria Conference

Invitation to the GA²LEN UCARE Urticaria Conference 2021



Michihiro HIDE MD. PhD

It is a pleasure to invite you to the UCARE Urticaria Conference 2021, which will be held from December 9 (Thu.) to 11 (Sat.), 2021, at the Hiroshima Prefectural Medical Association Hall in Hiroshima, Japan. This is a biennial international conference on urticaria held under the supervision of the Global Allergy and Asthma European Network (GA²LEN). The theme of the Conference 2021 is "A new era for urticaria – Advances in its classification and breakthroughs in its treatment."

This UCARE conference in Hiroshima GA²LEN is an international academic organization on allergy, based in Europe, and covered all over the world. It integrates research facilities in various countries to promote research and develop international clinical practice guidelines. The Urticaria Centers of Reference and Excellence (UCARE) network comprises certified UCARE facilities specializing in urticaria and angioedema and has held biennial academic meetings since 2017. The programs of these meetings include presentations on the latest study findings in the pathogenesis, biomarkers, comorbidities, diagnostic work up, impact of disease, and treatment, as well as many practical tips on how to manage urticaria and other mast cell-driven diseases, and meetings of international collaborative research groups.

The UCARE Conference 2021 in Hiroshima will be held in a hybrid format of on-site and online, thereby enabling as many people as possible to participate from various regions, including Europe, the Americas, and Asia. The programs will include special lectures, symposiums, and general presentations, as well as various practical training sessions and case studies. Moreover, you can enjoy special Japanese-style sessions and events. I look forward to many people taking this opportunity to attend this conference.

17 November 2021

Interact Perceptorship

Recurrent angioedema with a special focus on China

29 November 2021

Make A Difference 3

No Attacks, normal life, complete control - The aims of angioedema treatment

09 - 11 December 2021

UCARE Conference 2021-

Hiroshima Japan

A new era for urticaria - Advances in its classification and breakthroughs in its treatment

12 – 13 November 2021

PAAM Digital 2021, Pediatric Allergy and Asthma Meeting

EAACI – Event

27 – 30 January 2022

Winter School on Basic Immunnology Reaserach in Allergy and Clinical Immunology 2022

EAACI – Event

Links to more information:

www.ga2len-ucare.com www.acare-network.com www.globalurticariaforum.org www.allergie-centrum-charite.de www.urtikaria.net

Contact us

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