Chronic Urticaria:
What I Wish my Patients Knew

Dr. Marcus Maurer

Marcus Maurer
Charité - Universitätsmedizin Berlin, Institute of Allergology,
Berlin, Germany
The mission of
ALLERGY & ASTHMA
NETWORK
Is to end the needless death
and suffering due to asthma,
allergies and related
conditions through outreach,
education, advocacy and
research.

Disclosure of Significant Relationships with
Commercial Companies and Organizations

Marcus Maurer is or was a Speaker and/or advisor for Allakos, Almirall
Hermal, Amgen, ArgenX, Bayer, BioCryst, CellDex, Dyax, FAES,
Genentech, Leo, Lilly, Merckle Recordati, Kyowa Kirin, Moxie, MSD,
Novartis, Pharvaris, Riemser, Sanofi Aventis, Shire, Takeda, Tribute
Pharmaceuticals, UCB, and Uriach.
Doctor,

What is this?

Severe pruritus
Several hours

Burning, painful
Several days
What is Urticaria?
**What is a wheal?**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Elevated</strong></td>
<td>You can feel it when you touch it</td>
</tr>
<tr>
<td><strong>Red</strong></td>
<td>But can be white at the beginning</td>
</tr>
<tr>
<td><strong>Short-lived</strong></td>
<td>Stays for a couple of hours</td>
</tr>
<tr>
<td><strong>Itchy</strong></td>
<td>You want to rub it</td>
</tr>
</tbody>
</table>

**More examples**

![Images of various skin conditions](image-url)
What is angioedema?

**Short-lived**
Hours to a few days

**Swelling**
Feels and looks bigger

**Not dangerous**
Lips/Eyes > Hands/Feet > Tongue

**Feel and look vary**
Itchy, painful or not; red or not

More examples
Chronic Urticaria

Wheals, angioedema, or both for > 6 weeks

Itchy Wheals and/or Angioedema
10 types of Chronic Urticaria

Spontaneous Urticaria
- Due to known cause
- Due to unknown cause

Physical Urticaria
Symptomatic dermographism
Cold Urticaria
Delayed pressure urticaria
Solar urticaria
Heat urticaria
Vibratory urticaria
Cholinergic urticaria
Contact urticaria
Aquagenic Urticaria

Zuberbier et al., *Allergy* 2014: 69; 868-887

CSU > ClndU

24% CSU
76% ClndU

www.urticaria-registry.com
Angioedema in CSU

Maurer et al., *Allergy* 2017: 72; 2005-2016

Angioedema in CSU

Maurer et al., *Clin. Exp. Allergy* 2017: 47; 684-692
Doctor,
When you test me, does it cause this?

CSU – The Diagnostic Workup

- **Confirm** (differential diagnosis)
- **Cause** (e.g. TlaiCSU, TIlbaiCSU)
- **Comorbidities** (e.g. ClndU, autoimmunity, depression/anxiety)
- **Consequences** (e.g. sleep, distress, sexual health)
- **Cofactors** (e.g. triggers, aggravators)
- **Components** (e.g. biomarkers, predictors)
- **Course** (activity, impact and control)

Zuberbier et al., *Allergy* 2022; 77: 734-766
CSU – The Diagnostic Workup

- ESR and/or CRP
- Differential blood count
- IgE, IgG-anti-TPO

Zuberbier et al., *Allergy* 2022; 77: 734-766

CSU – The Diagnostic Workup

Question

Answer

Test

No test

Zuberbier et al., *Allergy* 2022; 77: 734-766
## CSU – The Diagnostic Workup

<table>
<thead>
<tr>
<th>Component</th>
<th>Description</th>
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<td>Confirm</td>
<td>(differential diagnosis)</td>
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</table>

Zuberbier et al., Allergy 2022; 77: 734-766
CSU is a mast cell driven disease


Mast cell degranulation

Mast cell degranulation


What degranulates mast cells in CSU?

IL-3R, IL-4R, IL-6R, IL-10R, IL-15R  
C3aR, C5aR, CR1/2, CR3, CR4  
CXCR1, 2, 4, CCR3, 5  
PAR2, OTRs, AβR  
TrkA, MC-1/MC-5  
PIR-A/PIR-B  
CD40L, OX40  
TSLP, IL-25, IL-33

FcsRI, FcsRIIb, FcsRIII  
TLR1, 2, 3, 4, 6, 7, 8, 9  
c-kit, CD48, LTβR  
ETα/ETβ, uPAR  
CB1/CB2, VR  
GITR, B7-1, -2  
MRGPX2, NK1R

**FcεRI degranulates mast cells in CSU!**

![Diagram showing FcεRI and its associated molecules]

*Church et al., Immunol. Rev. 2018: 282; 232-247*

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**How does FcεRI degranulate mast cells in CSU?**

The role of FcεRI in CSU

Maurer et al., *Front. Immunol.* 2018: 9; 689
The role of FcεRI in CSU

Maurer et al., *Front. Immunol.* 2018: 9; 689
The role of FcεRI in CSU

Maurer et al., *Front. Immunol.* 2018: 9; 689

The role of FcεRI in CSU

Maurer et al., *Front. Immunol.* 2018: 9; 689
The role of FcεRI in CSU

Autoimmunity Type I

Maurer et al., Front. Immunol. 2018: 9; 689

Autoimmunity Type IIb

IgG-anti-FcεRI


Autoimmunity Type I

IgG-anti-IgE
High responder rates in omilizumab-treated patients with Type I autoimmune CSU

Maurer et al., J Allergy Clin Immunol 2011; 128: 202-209

Sánchez et al., Allergy Asthma Immunol Res 2019; 11: 29-42
The role of FcεRI in CSU

Only 1 in 12 CSU patients has “true” TIIb autoimmune CSU

N = 182

n=107, 59%
n=105, 58%
n=46, 25%

Schoepke et al., Allergy 2019; 2427-2436

The endotypes of CSU

Autoimmune CSU (aiCSU)

Autoallergic CSU (aaCSU)

Kolkhir et al., J. Allergy Clin. Immunol. 2017; 139; 1772
Type IIb aiCSU
“True“ autoimmunity

- Rate of autoimmune comorbidity: High
- Rate or allergy comorbidity: Unknown
- Rate of ANA-positivity: Elevated
- Rate of eosinopenia: Elevated
- Rate of basopenia: Elevated
- Disease duration: Long
- Disease activity: High
- CRP: Elevated
- Total IgE: Low
- Antihistamines: Poor response
- Omalizumab: Lower response rate
- Speed of omalizumab response: Slow
- Cyclosporine: Higher rates of responders
- Fenebrutinib: Fast, good & sustained response

Type I aiCSU
Autoallergy

- Unknown rate of autoimmune comorbidity
- Higher rate or allergy comorbidity
- Unknown rate of ANA-positivity
- Unknown rate of eosinopenia
- Unknown rate of basopenia
- Unknown disease duration
- Unknown disease activity
- Unknown CRP levels
- High or normal total IgE
- Unknown antihistamine response
- High omalizumab response rates
- Fast onset of omalizumab effects
- Unknown response to cyclosporine
- Unknown response to fenebrutinib


Doctor,
I think its what I eat
Possible Triggers (NOT CAUSES!!!) of CSU

- NSAIDs (Ibu, Diclo, ASS)
- Viral Infections
- Stress

Doctor, How long will I have this?
Chronic urticaria is of long duration

5 - 7 years on average

CSU in children: severe = long lasting!

Yilmaz et al., Allergy Asthma Proc. 2017;38:136-142
Doctor,
I need something that helps!

What is the goal of treating patients with chronic urticaria?

Treat the disease until it’s gone

Zuberbier et al., Allergy 2022; 77: 734-766
International Urticaria Guideline

2nd generation H₁-Antihistamine (1x daily)

If needed:
Updose (up to 4x daily)

Add on Omalizumab (300mg, every 4 weeks)

If needed:
Updose (increase dose und/oder shorten interval)

Ciclosporin

After 2-4 weeks, if inadequate control or earlier, if symptoms are intolerable

Under specialist supervision

Consider referral to specialist

Management of urticaria

UCT score

UCT <12

Control level
Uncontrolled

Action
Step up

After 6 months, if inadequate control or earlier, if symptoms are intolerable

Zuberbier et al., Allergy 2022; 77: 734-766
Management of urticaria

- **UCT score**
  - UCT <12
  - UCT 12 – 15

- **Control level**
  - Uncontrolled
  - Well controlled
  - Complete Control

- **Action**
  - Step up
  - Optimize
  - Step down

Zuberbier et al., Allergy 2022; 77: 734-766
Doctor,
I think it's a little better…

Be a Pro. Use PROMS!

<table>
<thead>
<tr>
<th></th>
<th>CSU</th>
<th>ClndU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease activity</td>
<td>UAS</td>
<td>AAS</td>
</tr>
<tr>
<td>Disease control</td>
<td>UCT</td>
<td>AECT</td>
</tr>
<tr>
<td>Quality of life</td>
<td>CU-Q2oL</td>
<td>AE-QoL</td>
</tr>
</tbody>
</table>

moxie-gmbh.de
Urticaria Control Test (UCT)

1. How much have you suffered from the **physical symptoms of the urticaria (itch, hives (welts) and/or swelling)** in the last four weeks?
   - O very much
   - O much
   - O somewhat
   - O a little
   - O not at all
   - 0 points

2. How much was your **quality of life** affected by the urticaria in the last 4 weeks?
   - O very much
   - O much
   - O somewhat
   - O a little
   - O not at all
   - 0 points

3. How often was the **treatment** for your urticaria in the last 4 weeks **not enough** to control your urticaria symptoms?
   - O very often
   - O often
   - O sometimes
   - O seldom
   - O not at all
   - 0 points

4. **Overall**, how well have you had your urticaria under control in the last 4 weeks?
   - O not at all
   - O a little
   - O somewhat
   - O well
   - O very well
   - 0 points

---

Urticaria Control Test (UCT)

1. How much have you suffered from the physical symptoms of the urticaria (itch, hives (welts) and/or swelling) in the last four weeks?
   - O very much
   - O much
   - O somewhat
   - O a little
   - O not at all

2. How much was your quality of life affected by the urticaria in the last four weeks?
   - O very much
   - O much
   - O somewhat
   - O a little
   - O not at all

3. How often was the treatment for your urticaria symptoms (including avoidance of triggers)?
   - O very often
   - O often
   - O sometimes
   - O seldom
   - O not at all

4. Overall, how well have you had your urticaria under control in the last 4 weeks?
   - O not at all
   - O a little
   - O somewhat
   - O well
   - O very well


≥12 = ✔

16 = 😊

Where do I get help and information?
Providing excellence in urticaria management

Aims:

- Increase the knowledge of urticaria via research, studies and education
- Promote the awareness of urticaria via advocacy activities
- Improve the care/treatment of urticaria patients worldwide

- 135 certified UCAREs in 42 countries (as of July 2022)
- 20 scientific UCARE projects (16 current and upcoming, 4 completed)
- UCARE LevelUp – the education program for physicians
- UCARE 4U – the education program for patients
- Meetings: UDAY (October 1), GUF and UCARE Conference (alternating annually in December)
- CRUSE – The UCARE Chronic Urticaria Self evaluation app
- Website: www.ga2len.ucare.com

UCARE Center Overview

<table>
<thead>
<tr>
<th>Region</th>
<th>Country</th>
<th>UCARE Centers</th>
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</thead>
<tbody>
<tr>
<td>North America</td>
<td>Canada</td>
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<td></td>
<td>Mexico</td>
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<td>South America</td>
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<td></td>
<td>UK</td>
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</tbody>
</table>

Applicant Centers 23

- New UCAREs in 2022: 10
- New UCAREs in 2021: 13
UCARE Programs

UCARE LevelUp: Physician Education Platform

**Aims:**
- Update physicians on recent developments in urticaria,
- Establish a platform for interaction among physicians who treat patients with CU,
- Improve the interaction of general practitioners and specialist
- Build strategic therapeutic plans for patient
- Improve the use of patient-reported outcome measures (PROMs)
- Streamline the CU patient journey to disease control

**Activities:**
- Webinar
- Video
- Newsletter
- Podcast
- Website
- Journal clubs
- Fireside chat
- Poster session
- Grand rounds
UCARE LevelUp: Patient Education Platform Stats

<table>
<thead>
<tr>
<th>Format</th>
<th>Number of events</th>
<th>Live Registrations</th>
<th>Views on demand</th>
<th>Events in preparation</th>
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<tbody>
<tr>
<td>Webinar</td>
<td>3</td>
<td>480 (136 / 43 / 301)</td>
<td>474 (172 / 186 / 116)</td>
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<td>Educational Video</td>
<td>3</td>
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<td>602 (280 / 168 / 154)</td>
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<tr>
<td>Newsletter</td>
<td>3</td>
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<td>Podcast</td>
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<td>Fireside Chat</td>
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<td>228 (62 / 109 / 57)</td>
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<tr>
<td>Journal Club</td>
<td>11</td>
<td>Not applicable</td>
<td>Not applicable</td>
<td>6</td>
</tr>
<tr>
<td>Grand Round</td>
<td>0</td>
<td>Not Available</td>
<td>Not Available</td>
<td>1</td>
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<tr>
<td>Poster Session</td>
<td>1</td>
<td>24</td>
<td>Not applicable</td>
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</tbody>
</table>

UCARE 4U: Patient Education Platform

Aims:
- Bringing extensive information directly to patients affected by urticaria
- Update patients on recent developments in urticaria
- Help patients understand causes of Chronic Urticaria (CU)
- Improve patients’ understanding of trigger
- Educate patients on the simultaneous presence of comorbidities with CU
- Unite patient and physician efforts to improve the treatment of CU
- Expand the knowledge of treatment options for patients with CU

Activities:

- UDAY
- WEBSITE
- WEBiNAR
- Social Media

https://ucare-4u.com/
UCARE 4U: Patient Education Platform Stats

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<tbody>
<tr>
<td>Webinar</td>
<td>3</td>
<td>380 (160 / 121 / 99)</td>
<td>1162 (459 / 200 / 66 / 35 / 98 / 21 / 58 / 25 / 24 / 55 / 77 / 44)</td>
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Social Media

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<tr>
<th>Channel</th>
<th>Number of Hits</th>
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<td>Twitter (LU and 4U)</td>
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<td>YouTube</td>
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<td>Reddit</td>
<td>5,437</td>
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<tr>
<td>Instagram</td>
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</tbody>
</table>

UCARE Tools

- ChRonic
- Urticaria
- Self-Evaluation

UCARE CRUSE Sponsors

- NOVARTIS
- Cellidex therapeutics
- MOXIE
CRUSE® – Chronic Urticaria Self Evaluation App

The CRUSE® advantage for patients and physicians

- CRUSE® enables patients to fill out their Patient Reported Outcome Measure (PROMs) daily on their smart device
- CRUSE® reminds patients to monitor their quality of life through push notification
- CRUSE® allows patients to send a report of their PROM scores to their treating physician via Email, WhatsApp or other communication paths
- CRUSE® promotes continued monitoring and documentation of CSU disease activity, impact and control that is needed for patients to receive optimal treatment

CRUSE® app contributes to the understanding of Urticaria through data collection (all anonymized)

- Giving us a true understanding on how patients live
- Seeing the patients’ experience on how different medication affects their quality of life
- Allowing insight on how treatment can be improved

www.cruse-control.com

CRUSE® – Global Launch and availability

<table>
<thead>
<tr>
<th>Q1 2022</th>
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<th>Q3 2022</th>
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</table>
Global Urticaria Forum

What to expect?
- 2 days to learn and exchange ideas on chronic urticaria and related diseases
- Scientific sessions with oral presentations
- Overview lectures by international experts
- Workshops and poster sessions
- Discussions and scientific interactions with fellow urticaria researchers and physicians
- The newest insights on urticaria pathogenesis, subtypes, biomarkers, comorbidities, diagnostic work up, impact of disease, and treatment
- Many practical tips on how to manage urticaria and other mast cell-driven diseases
- A special focus will be on recurrent angioedema with all of its many subtypes

7-8 December 2022
Berlin, Germany

Website: www.globalurticariaforum.org
Email us: guf@remember-management.de
Call us: +49 30 47 37 25 77

In cooperation with
The Charité UCARE in Berlin

marcus.maurer@charite.de
Do you have Chronic Inducible Cold Urticaria?

Take part in a research interview and earn $185

https://survey.cmix.com/3DD9872D/7E305C4Q/en-US

#Sponsored by IQVIA

QUESTIONS

We’ll get to as many questions as we can!

The webinar recording will be posted to our website along with a printable copy of the slides.
Thank you for listening!
We appreciate you being here.

**NEXT** Advances Webinar:

**Current & Future Treatments for Food Allergy**

September 27, 2022
Dr. Katherine Anagnostou

Please stay online for 2-3 minutes to complete the evaluation survey – we use this information to plan future webinars!