Chronic inducible urticaria: diagnosis, new strategies and management

Torsten Zuberbier

Disclosure

Presenter's Name: Prof.. Torsten Zuberbier

I have the Relationships with commercial interests as Advisory Board/Speakers Bureau, Research/Clinical Trials, Speaker/Consulting Fees :

Industry consulting, research grants and/or honoraria:

Amgen, AstraZeneca, AbbVie, ALK, Almirall, Astellas, Bayer Health Care, Bencard, Berlin Chemie, Blueprint, FAES, HAL, Henkel, IMEDIC, Kryolan, Leti, L'Oreal, Meda, Menarini, Merck, MSD, Novartis, Nuocor, Pfizer, Sanofi, Stallergenes, Takeda, Teva, UCB, Blueprint Medicine

Organizational Affiliations:

Committee member, "Allergic Rhinitis and its Impact on Asthma" (ARIA)
Member of the Board, German Society for Allergy and Clinical Immunology (DGAKI)
Head, European Centre for Allergy Research Foundation (ECARF)
President , Global Allergy and Asthma European Network (GA²LEN)
Member, Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organisation (WAO)

Who is GA²LEN?
The Network of Excellence

- Created in 2004 under FP6 – an EU Star Project
- A unique model project in the history of medicine

and the Network continues to grow ..

Urticaria guideline 2020

GA²LEN
Global Allergy and Asthma Excellence Network
Network of Excellence

URTICARIA 2020

6th CONSENSUS CONFERENCE ON THE UPDATE AND REVISION OF THE INTERNATIONAL EAACI/GA²LEN/EUROGUIDERM/APAAACI GUIDELINE FOR URTICARIA

BERLIN, 3 DECEMBER 2020

And already looking forward to Dec 2024!

The current uricaria guidelines:

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DOI: 10.1111/all.15090

Allergy WILEY

GUIDELINES

The international EAACI/GA²LEN/EuroGuiDerm/APAACI guideline for the definition, classification, diagnosis, and management of urticaria

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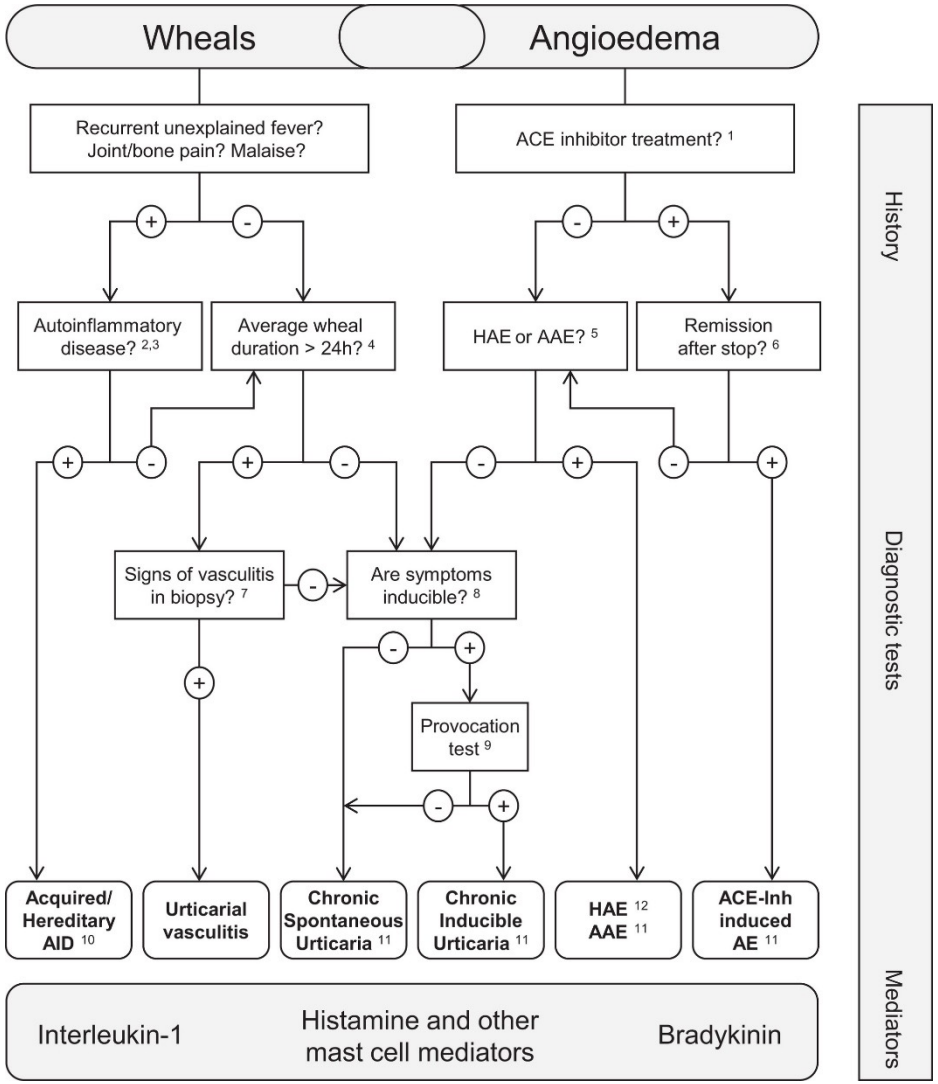
Urticaria Guidelines: Classification

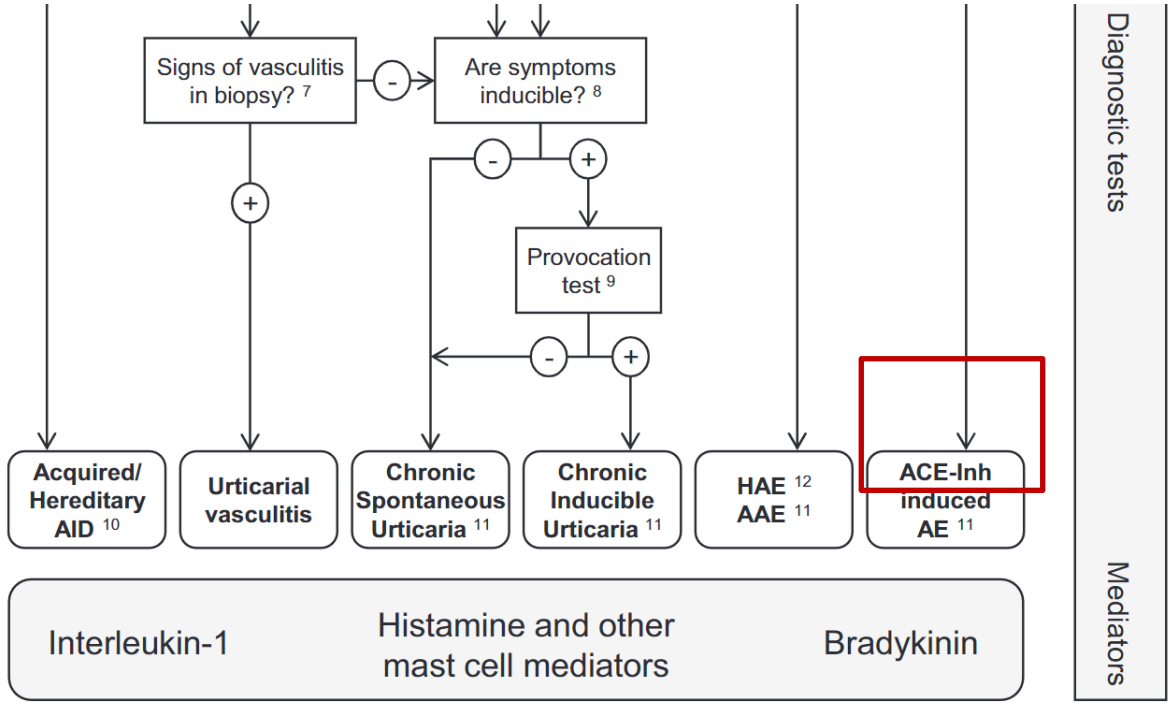
Chronic Urticaria Subtypes	
Chronic Spontaneous Urticaria (CSU)	**Inducible Urticaria**
Spontaneous appearance of wheals, angioedema, or both for >6 weeks due to known[a] or unknown causes.	Symptomatic dermographism[b] Cold urticaria[c] Delayed pressure urticaria[d] Solar urticaria Heat urticaria[e] Vibratory angioedema[f] Cholinergic urticaria Contact urticaria Aquagenic urticaria

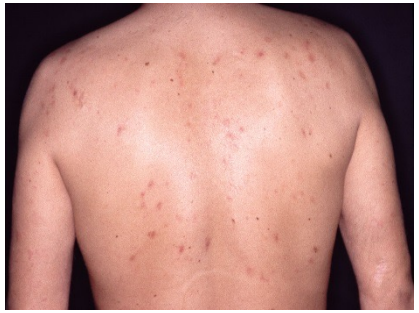
Zuberbier, T. et al. Allergy. 2021

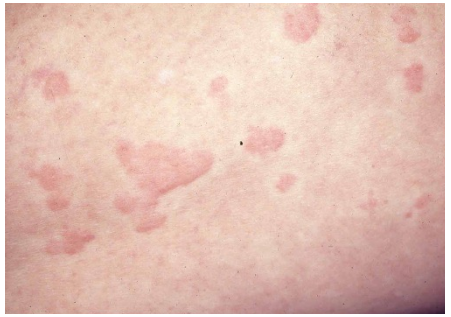
Diagnostics in CINDU

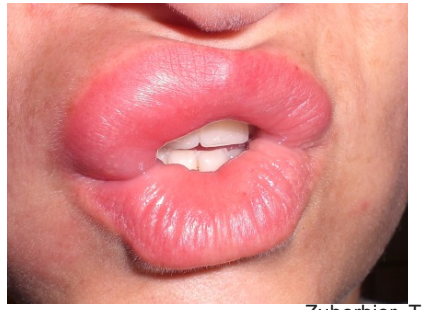


Zuberbier, T. et al. Allergy. 2021



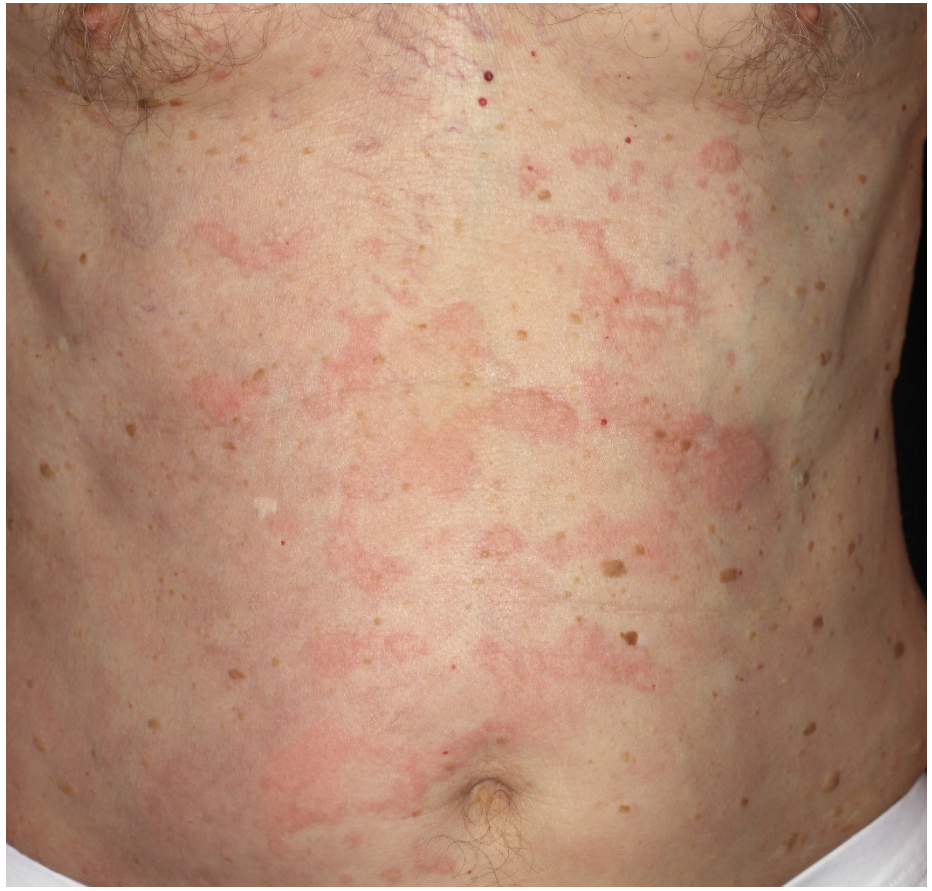


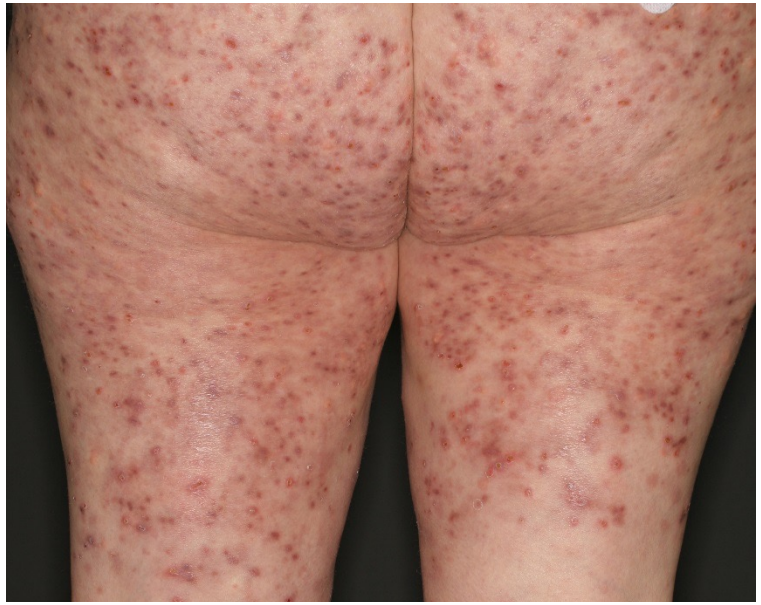




Zuberbier, T. et al. Allergy. 2021

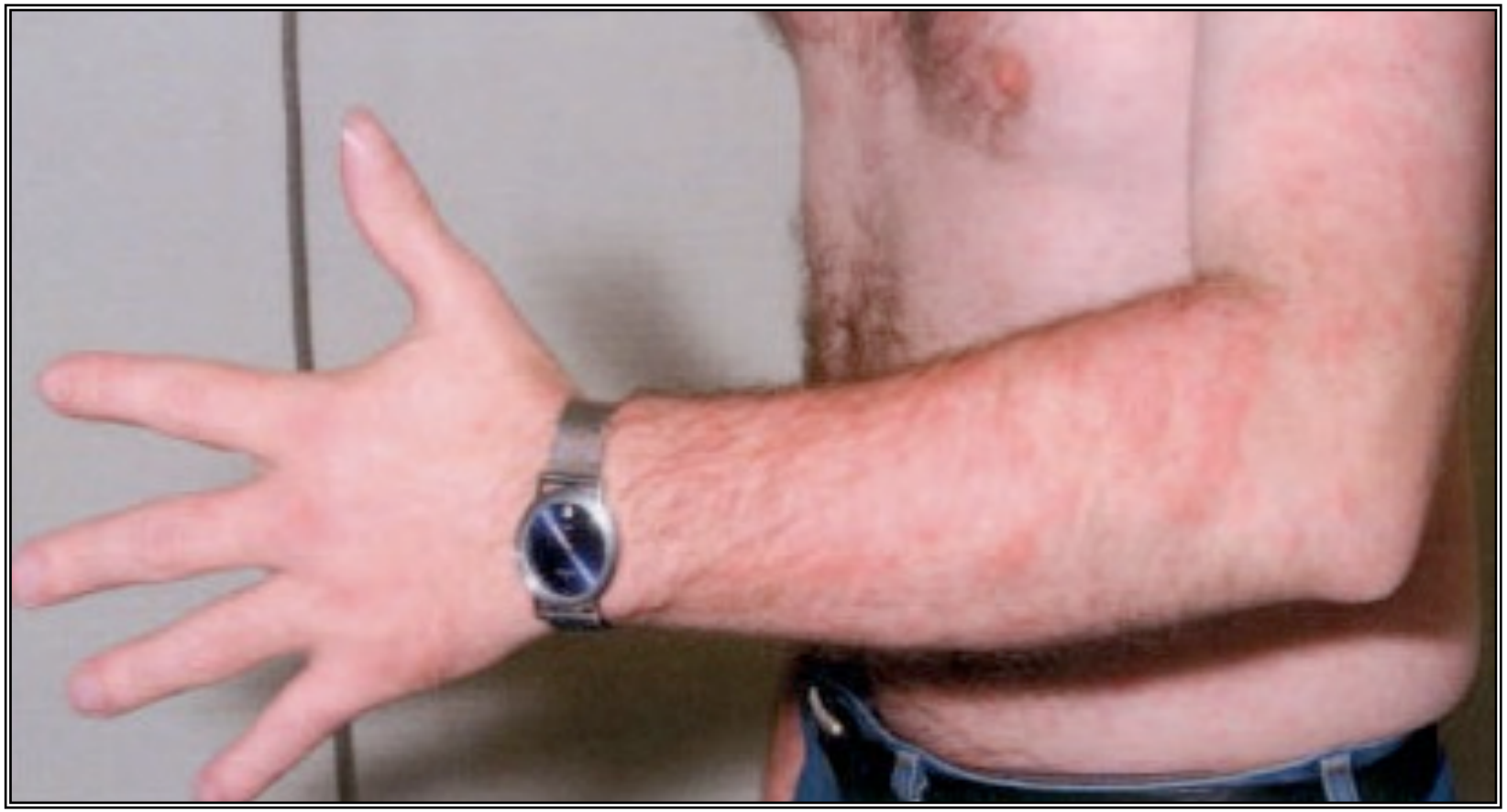
Schnitzler‘s syndrome





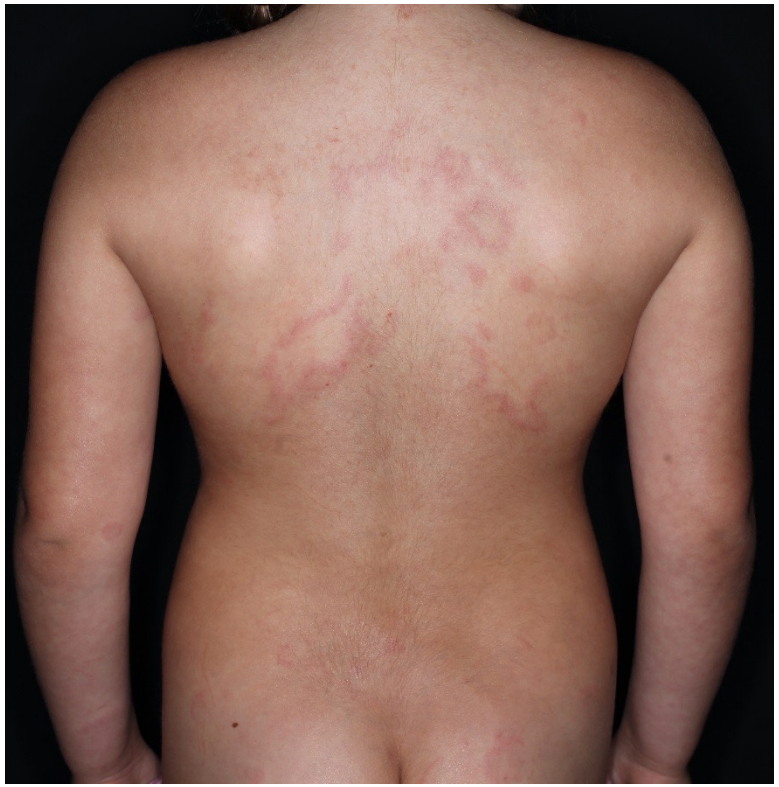
Courtesy of Charité, Dpt. of Dermatology and Allergy

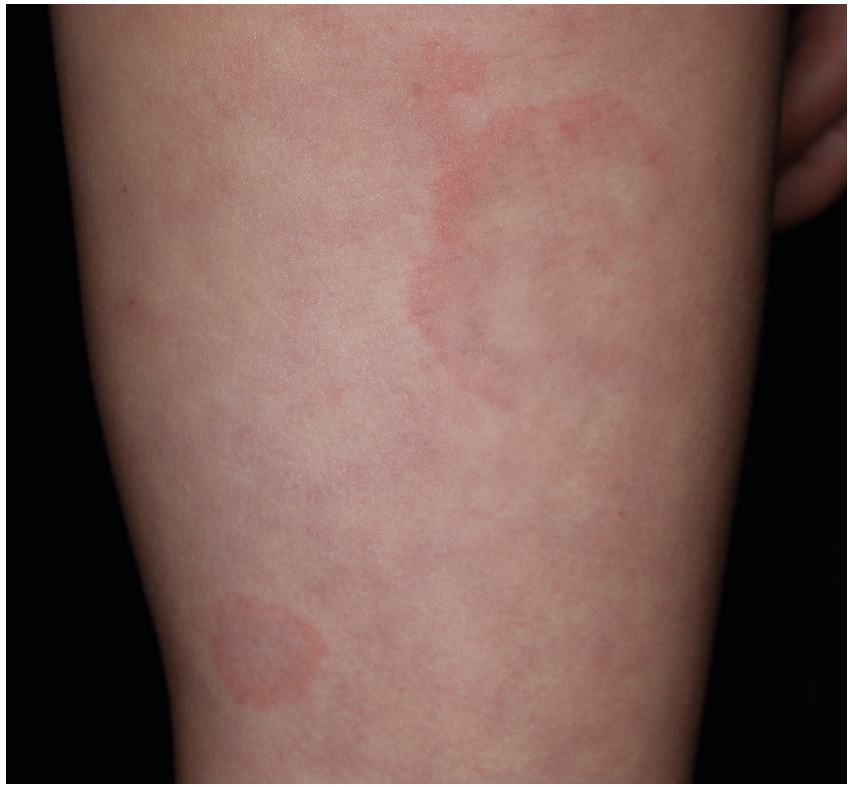
FCAS – familial cold autoinflammatory syndrome



Goldbach-Mansky R et al. Arthritis Rheum 2008;58(8):2432-2442.

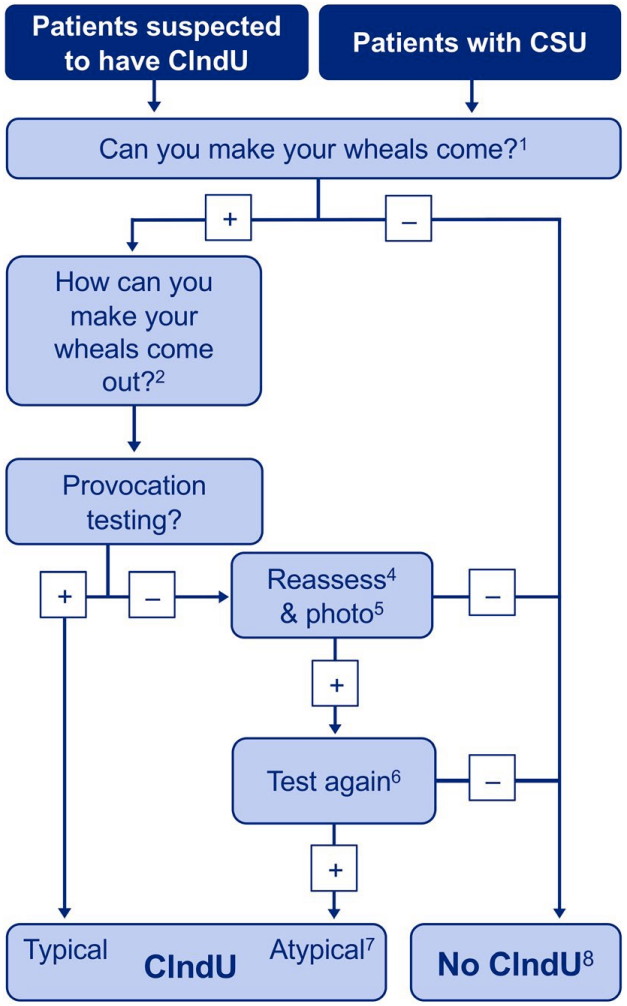
Muckle-Wells Syndrome





Courtesy of Charité, Dpt. of Dermatology and Allergy

CIndU: Diagnostic algorithm



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NEWS & VIEWS: ALGORITHMS IN ALLERGY AND CLINICAL IMMUNOLOGY

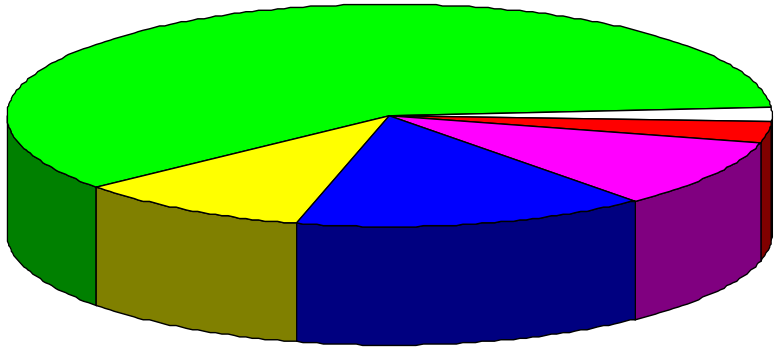
Allergy WILEY

Diagnosis and treatment of chronic inducible urticaria

Maurer et al. *Allergy* 2019; 74:2550–2553

Physical Urticaria – Estimated Distribution

- Symptomatic Dermographism
- Delayed pressure urticaria
- Vibratory urticaria
- Cold contact urticaria
- Heat contact urticaria
- Solar urticaria



Inducible Urticaria – Tests Threshold is Relevant

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Patient information

Name:

Date of birth:

Instructions:

Perform testing as indicated and document presence (+) or absence (-) of weal (W), erythema (E), pruritus (P) and/or angioedema (A) as well as date / time of testing and who performed the test.

1. Symptomatic Dermographism (Urticaria factitia)

Testsite: Upper back / Volar forearm
Test: Moderate stroking of the skin with a blunt smooth object (e. g. closed ballpoint pen tip, wooden spatula) /dermographometer (36 g/mm²)
Reading time: 10 minutes after testing

W	P

Date / Time _____ Test done by _____

If weal and pruritus: Test threshold with dermographometer →

2. Cold contact urticaria

Testsite: Volar forearm / abdomen
Test: Melting ice cube in thin plastic bag/Temp*Test* (4°C) for 5 minutes
Reading times: 10 minutes after testing

W	P

Date / Time _____ Test done by _____

If weal: Test cold stimulation time or temperature threshold →

3. Heat contact urticaria

Testsite: Volar forearm
Test: Heat source/Temp*Test* (45°C) for 5 minutes
Reading times: 10 minutes after testing

W	P

Date / Time _____ Test done by _____

If weal: Test cold stimulation time or temperature threshold →

4. Delayed pressure urticaria

Testsite: Shoulder/Upper Back/Thighs/Volar forearm
Test: Suspension of weights over shoulder (7 kg, shoulder strap width: 3 cm) for 15 min or weighted rods (1.5 cm diameter: 2.5 kg; or 6.5 cm diameter: 5 kg) for 15 min. Dermographometer at 100 g/mm² for 70 sec
Reading times: ≈6 hours after testing

A	E

Date / Time _____ Test done by _____

If angioedema: Test threshold →

5. Solar urticaria

Testsite: Buttocks
Test: UVA 6 J/cm² & UVB 60 mJ/cm²irradition (e. g. Saalmann Multitester SBC LT 400) Visible light (projector)
Reading times: 10 minutes after testing

	W	P
UVA		
UVB		
Visible light		

Date / Time _____ Test done by _____

If weal: Test threshold →

6. Vibratory urticaria/angioedema

Testsite: Volar forearm
Test: Vortex vibrator for 10 minutes, 1000 rpm
Reading times: 10 minutes after testing

A	P

Date / Time _____ Test done by _____

7. Cholinergic Urticaria

Test 1: Exercise using a machine, e. g. bicycle trainer or treadmill, to the point of sweating, then continue for 15 minutes,

if positive test reaction:

Test 2: 42 °C bath, monitor body temperature. Continue bath for 15 min after body temperature has increased by ≥ 1°C over baseline

Reading times: Immediately and 10 minutes after end of test

1. Exercise	W	P

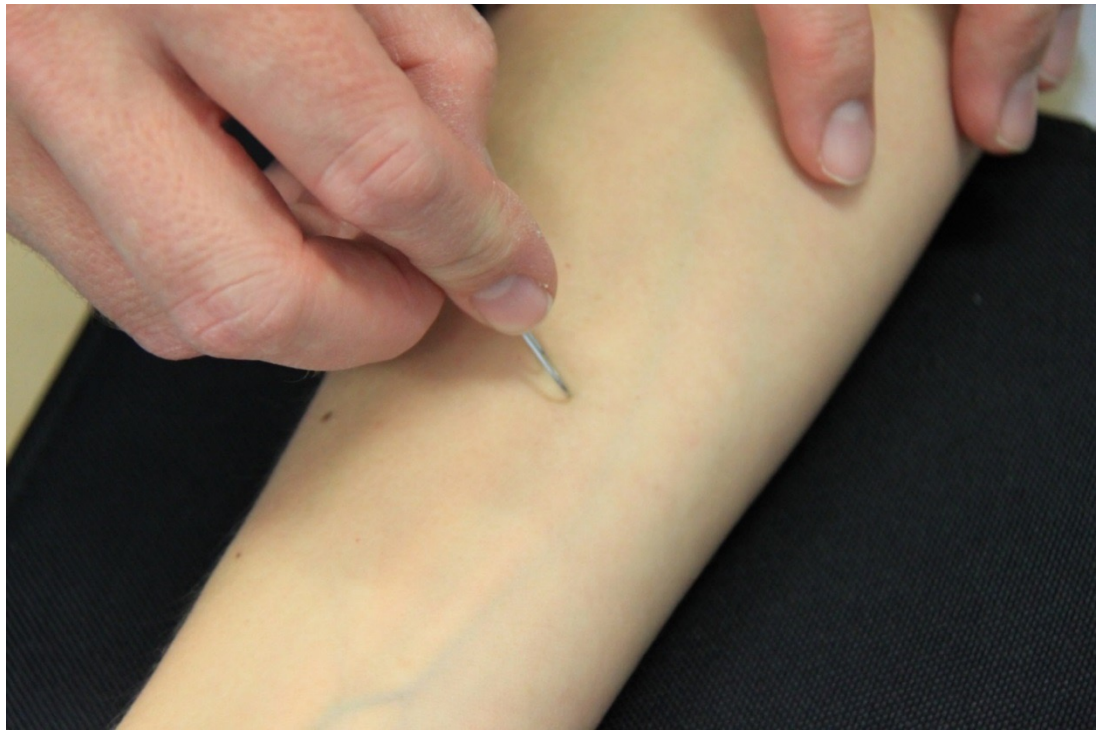
If positive reaction →

2. Hot bath	W	P

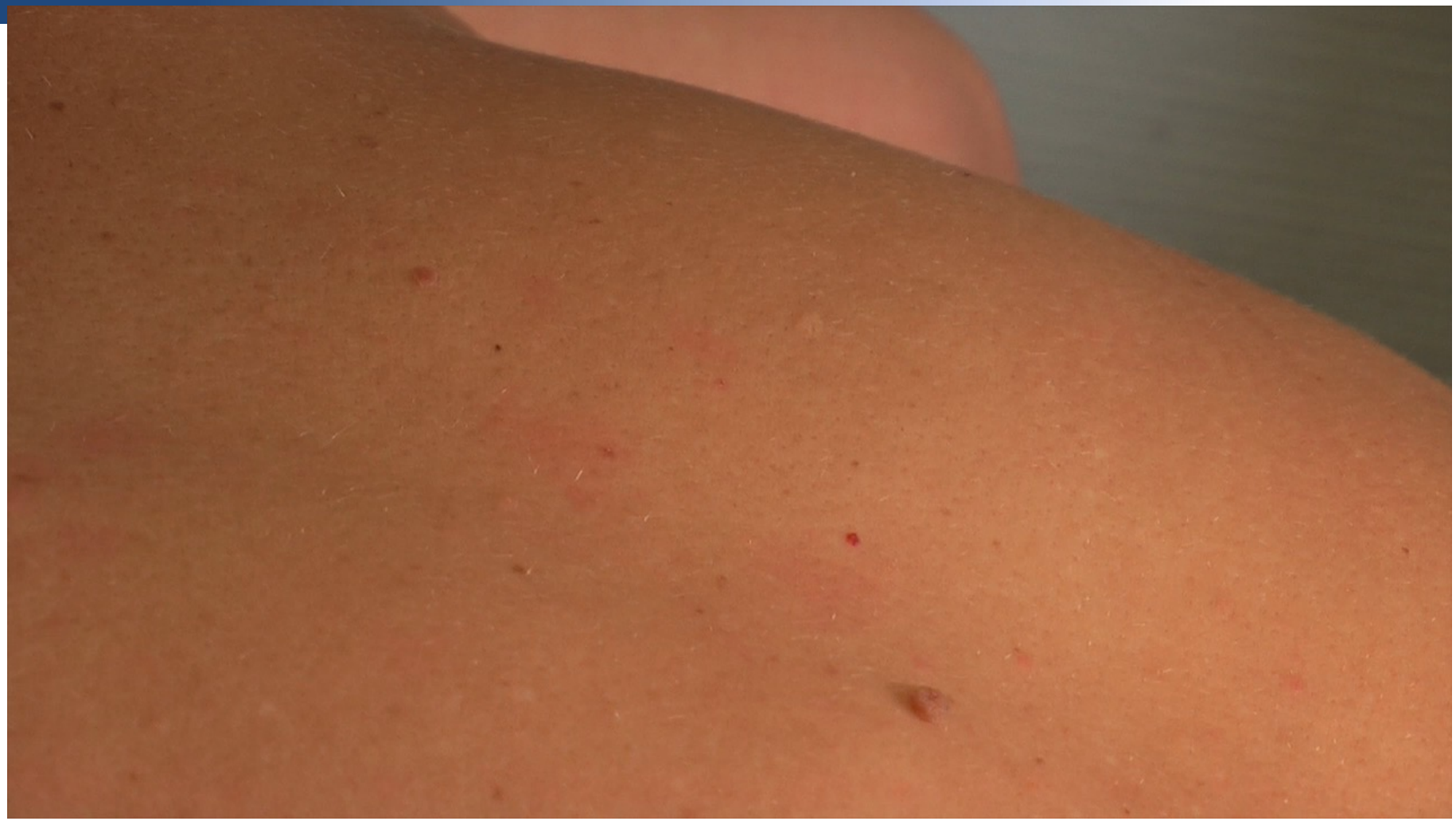
ECARF European Centre for Allergy Research Foundation

Magerl et al. *Allergy* 2009; 64: 1715-21

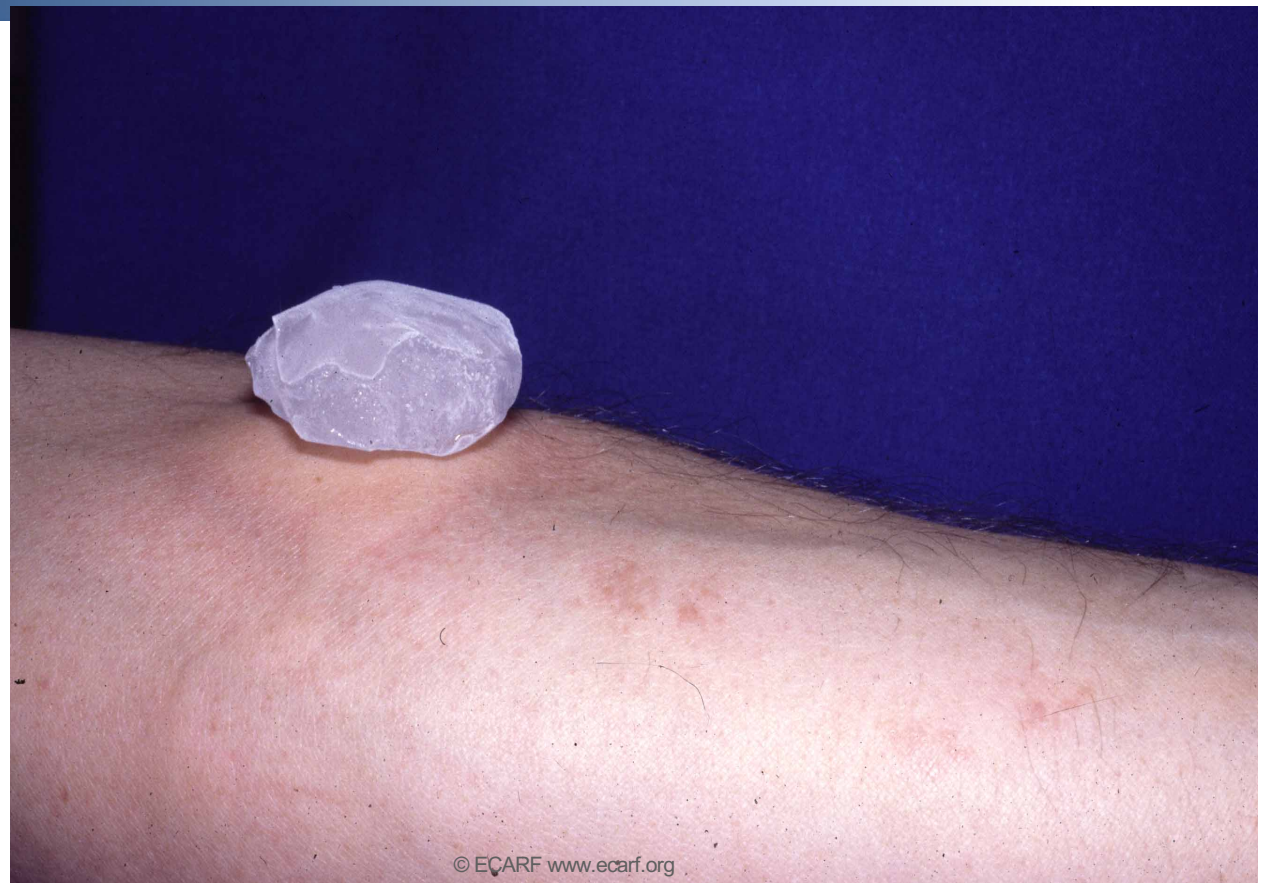
Symptomatic Dermographism



Symptomatic Dermographism



Cold contact urticaria



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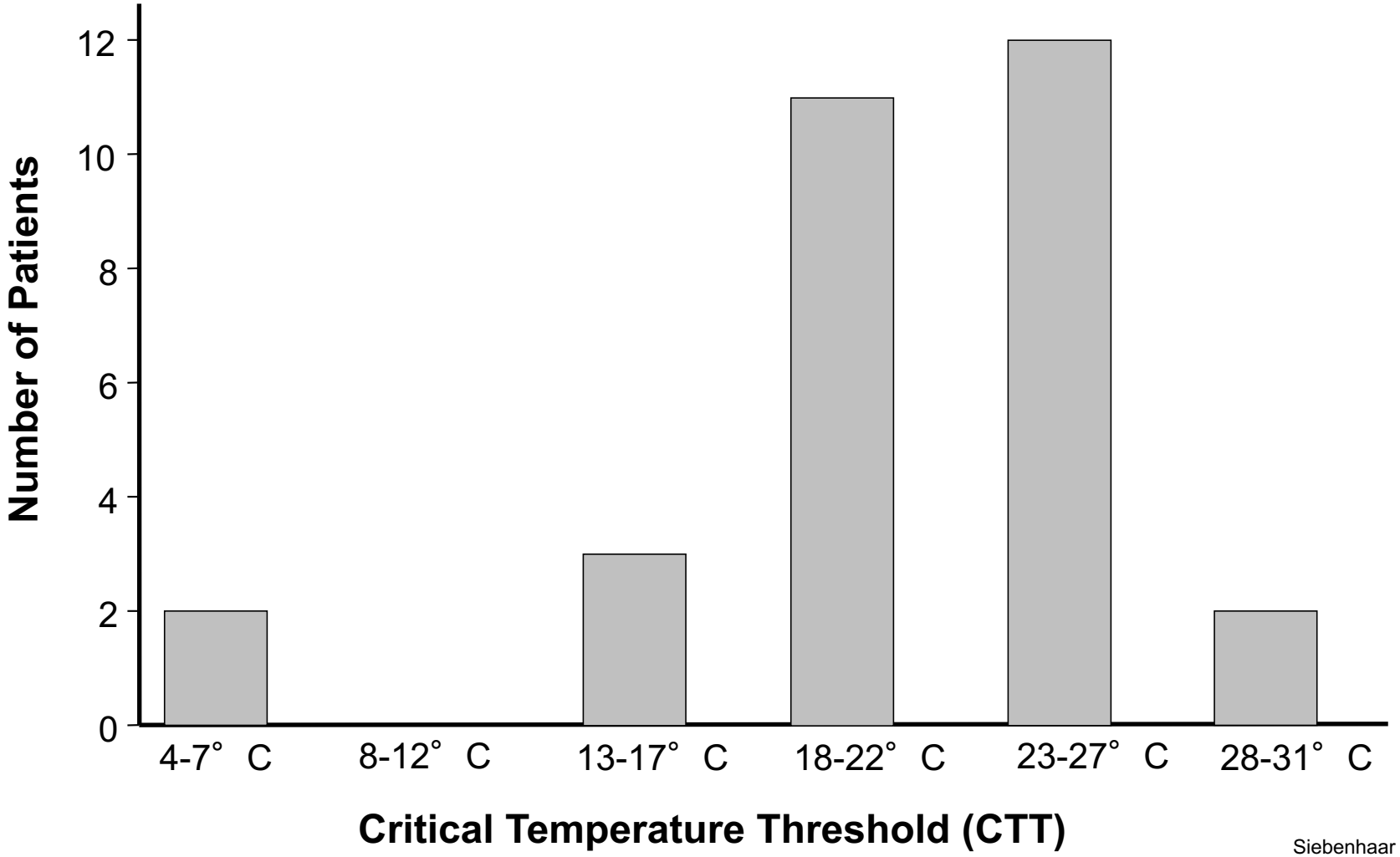
Ice cube in see-through plastic bag, 4°C, 5 min

Cold contact urticaria

TempTest®

Critical temperature thresholds (CTT) at baseline



Siebenhaar et al. *JACI* 2009;123: 672-9

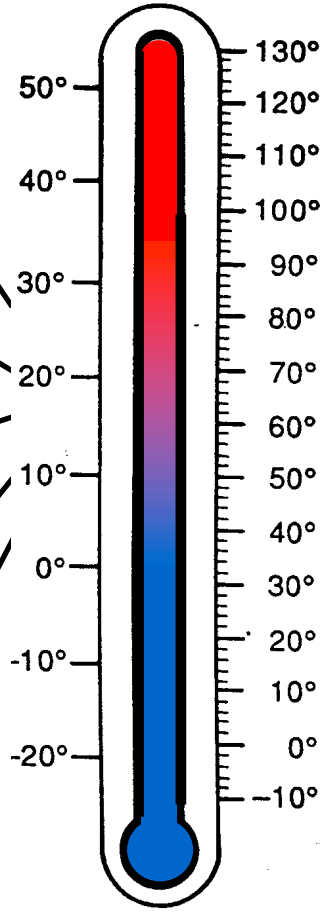
28° C: Swimming in indoor pool

20° C: Using normal toilet seat

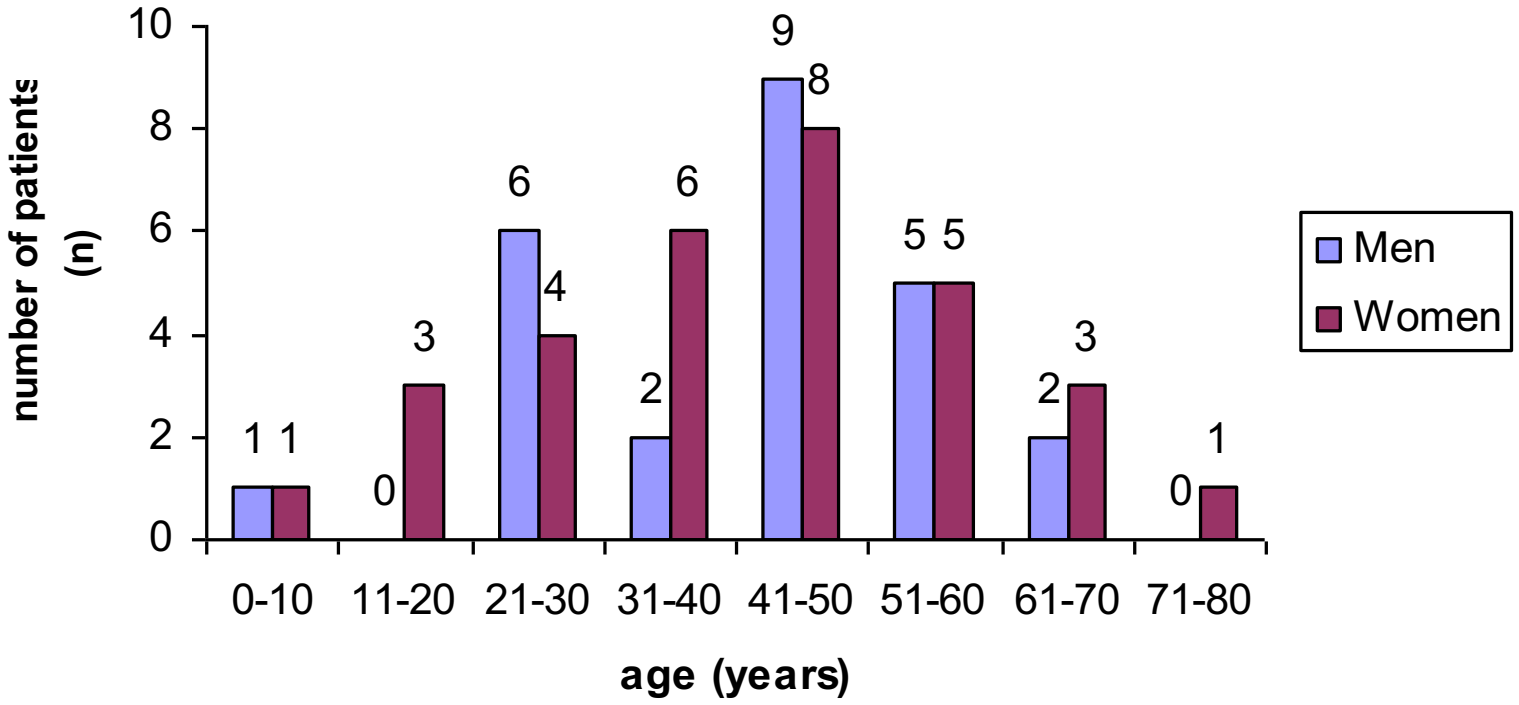
16° C: Swimming in lake

10° C: Preparing food, skiing

4° C: snowball fight, cold drink



Epidemiology



Möller et al 1996 *Hautarzt* 47:510-514

Classification

I. Reactions to cold with positive local tests

1. Immediate cold urticaria
2. Delayed cold urticaria
3. Cold dependent dermographic urticaria
4. Localized cold urticaria
5. Localized reflex cold urticaria
6. Perifollicular cold urticaria
7. Familial delayed cold urticaria

Classification

II. Cold urticaria with generalized responses

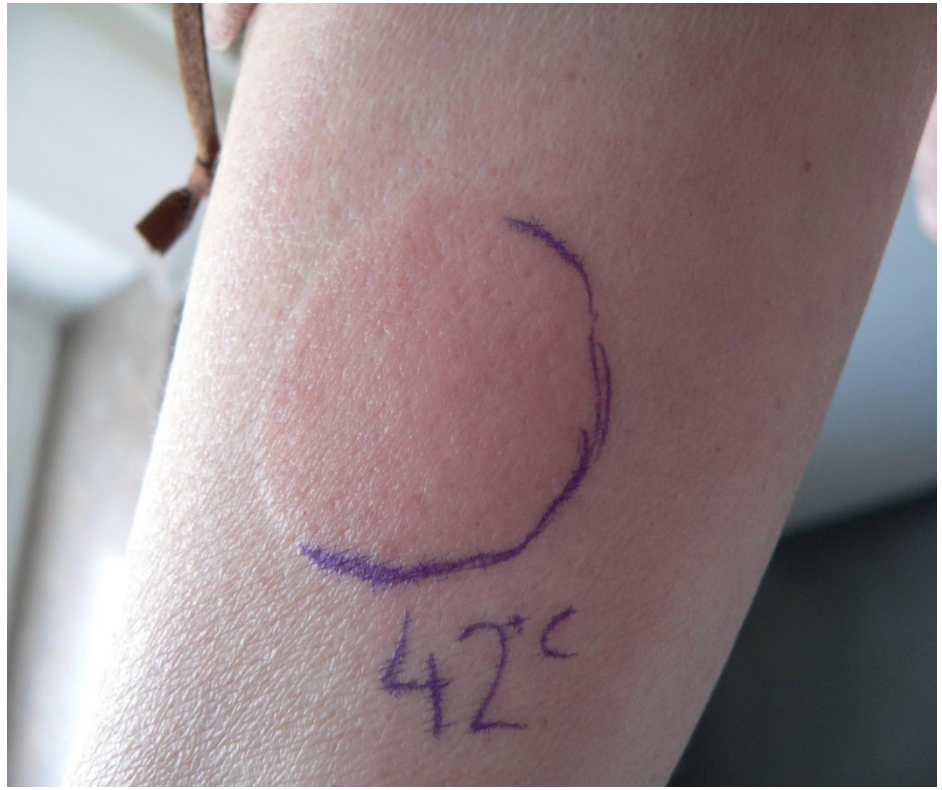
1. Cold wind and air urticaria
2. Cholinergic cold urticaria

Classification

III. Diseases with abnormal serum proteins

1. Cryoglobulinemia
2. Cryofibrinogenemia
3. Cold hemolysins
4. C2- and C4-defects

Heat urticaria



Picture copyright private

Delayed Pressure Urticaria

Testsite:

Shoulder/Upper Back/Thighs/Volar forearm

Test:

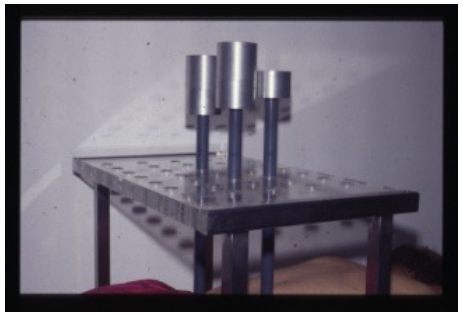
Weight over shoulder (7 kg, strap width 3 cm,15 min)

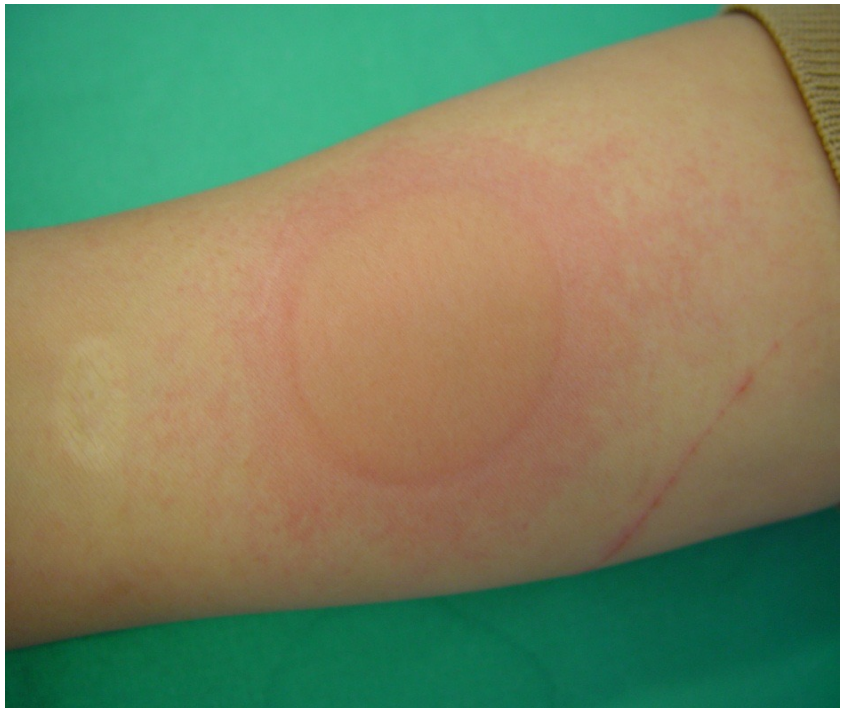
Weighted rod (1.5 cm □, 2.5 kg, 15 min)

Weighted rod (6.5 cm □, 5 kg, 15 min)

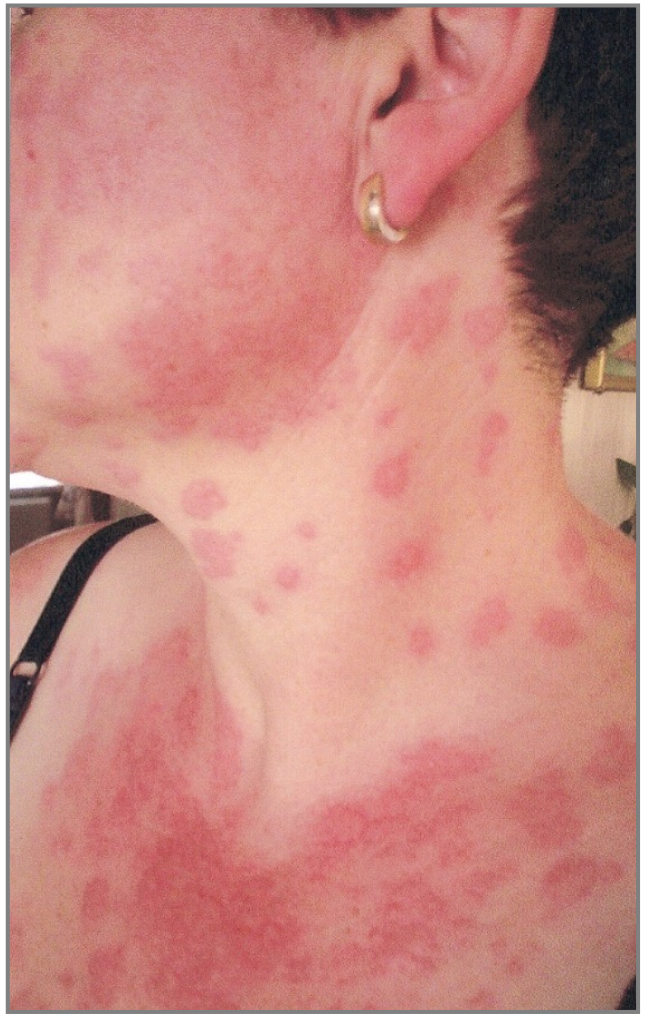
Reading:

6 hours after testing





Solar Urticaria



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Network of Excellence

ECARF European Centre for Allergy Research Foundation

Solar Urticaria

Testsite:	Buttocks
Test:	UVA up to 6 J/cm^2
	UVB up to 60 mJ/cm^2
	Visible light (projector)
Reading:	10 minutes after testing

Magerl et al. *Allergy* 2009;64:1715-21

Solar Urticaria

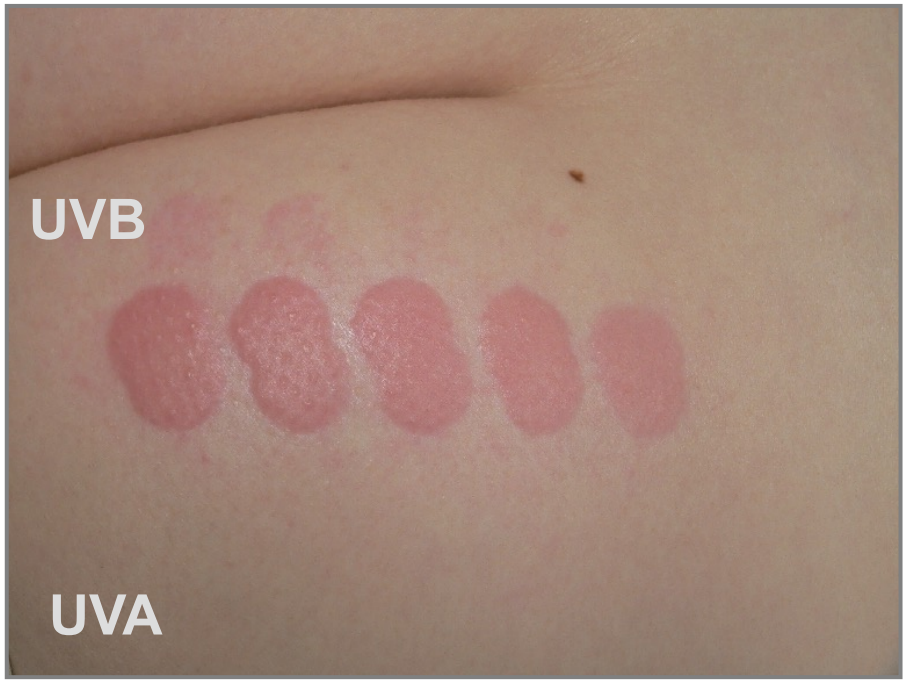
Test site: Buttocks

Test: UVA up to 6 J/cm^2

UVB up to 60 mJ/cm^2

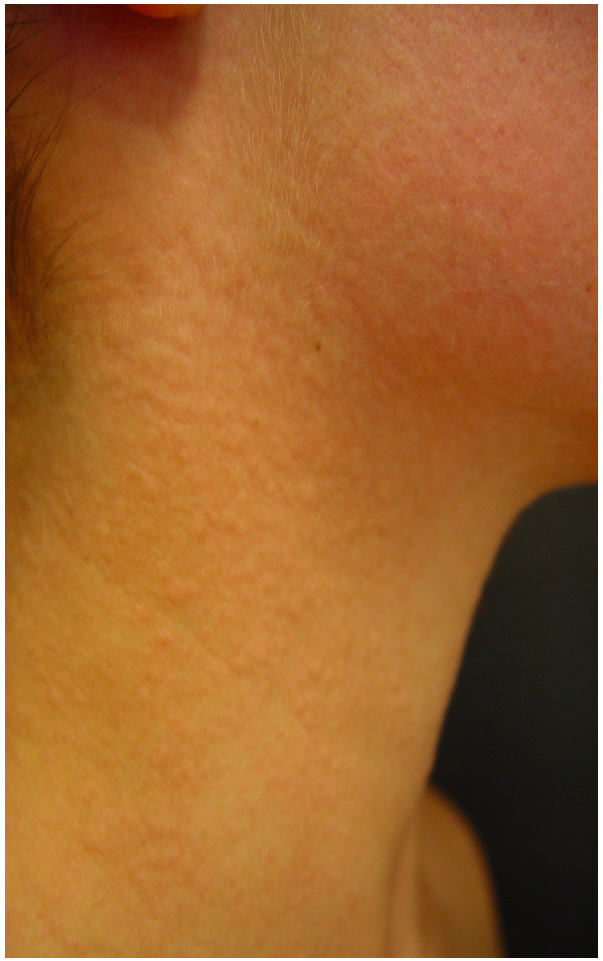
Visible light (projector)

Reading: 10 minutes after testing



Cholinergic Urticaria

- 89 % with mild to moderate symptoms
- typically, pinpoint-sized wheals of a short duration (ca. 15-30 min)
- invariably associated with pruritus



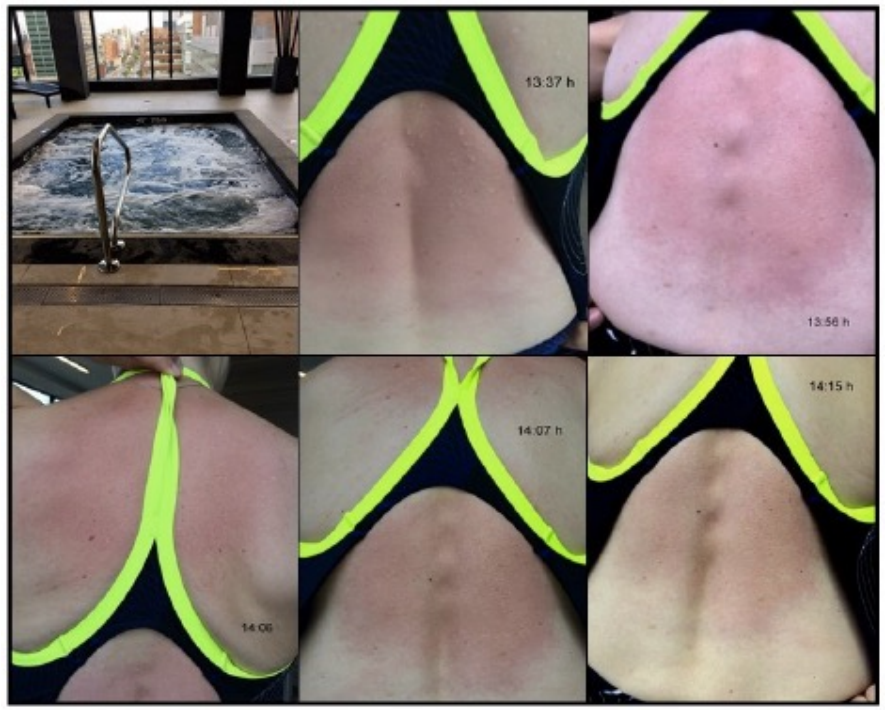
Zuberbier et al. *J Am Acad Dermatol* 1994;31:978-81

Cholinergic Urticaria

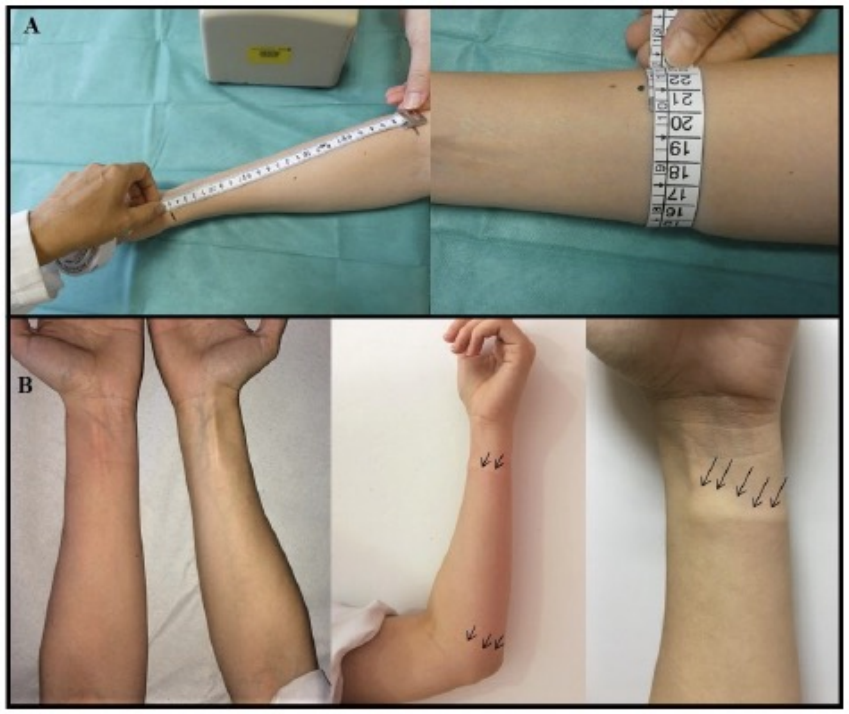
Eliciting factor	Wheal (%)	Pruritus (%)
Hot Shower	69	71
Sweating	56	62
Sports	47	49
Emotional Disstress	20	24
Fever	9	9
Very warm food (e.g.soups)	9	9
Alcohol	9	9
Mild Exercise	5	13
Spicy food	2	2

Zuberbier et al. J Am Acad Dermatol 1994; 31:978-81

Vibratory urticaria-angioedema



Circumscribed “peau d´orange-like” erythemato-edematous plaques after exposure jacuzzi jets (cholinergic and heat urticaria were ruled out)

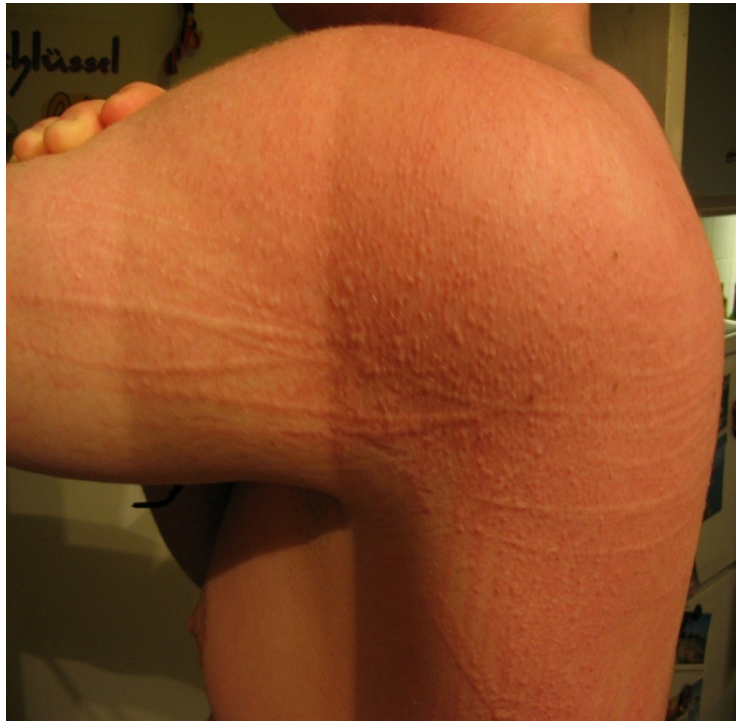


Reaction after provocation with vortex mixer for 5 minutes

Vergara de la Campa et al. *J Eur Acad Dermatol Venereol* 2020
doi: 10.1111/jdv.16396. Online ahead of print.

Management

Look at the real life, patients´ needs and comorbidities



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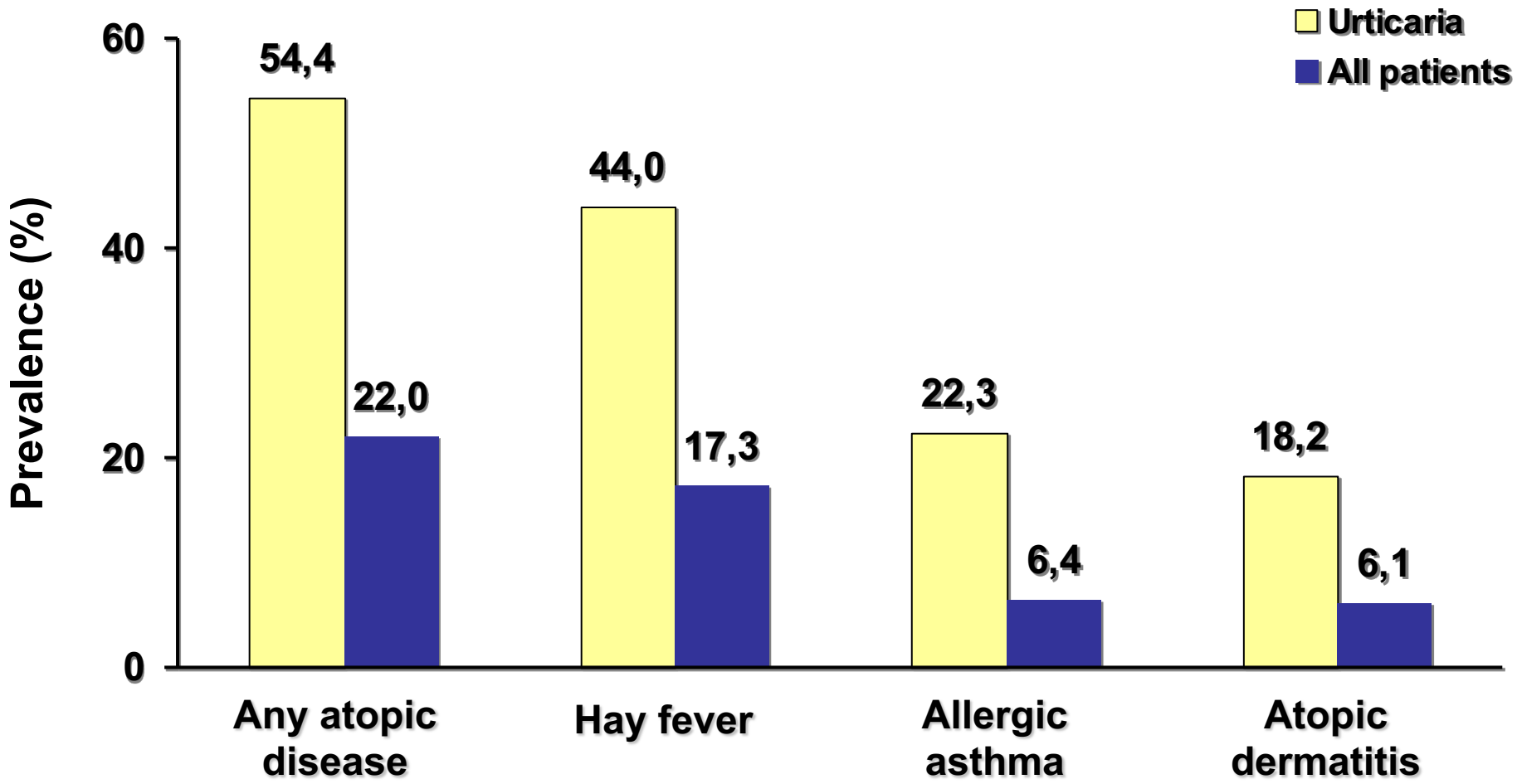
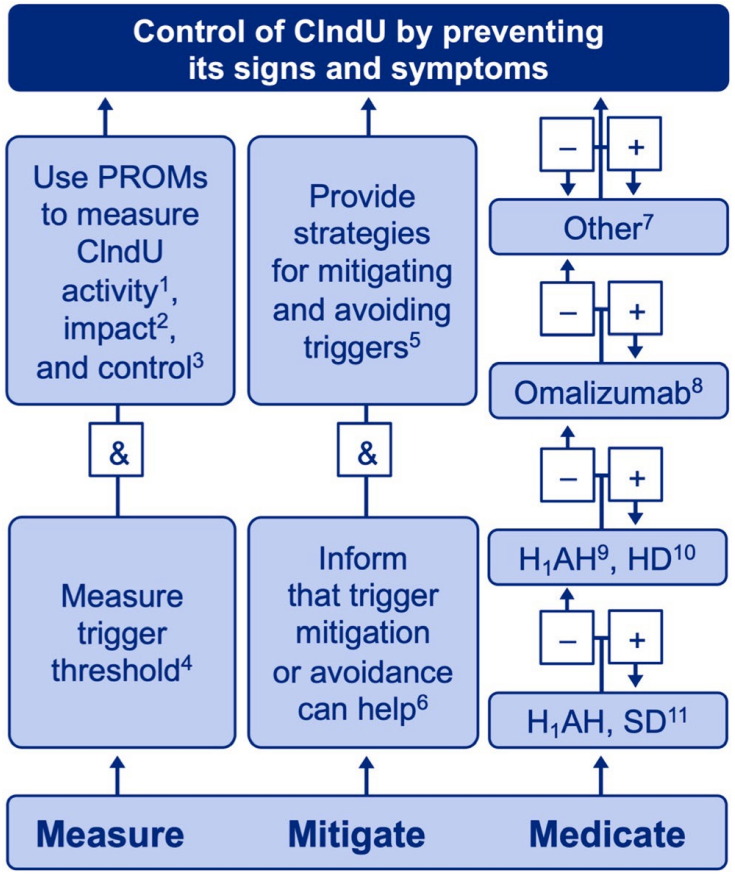
Prevalence of Atopic Comorbidities in Patients With Urticaria

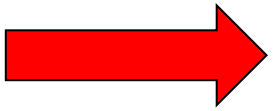


The three M's of managing CIndU: Measure, Mitigate, and Medicate.



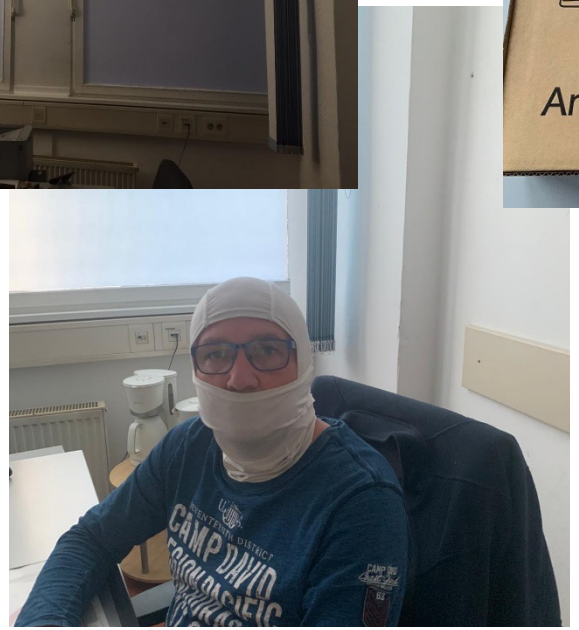
Maurer et al. *Allergy* 2019; 74:2550–2553

Avoiding physical stimuli



Avoiding physical stimuli

Avoiding physical stimuli in severe light urticaria



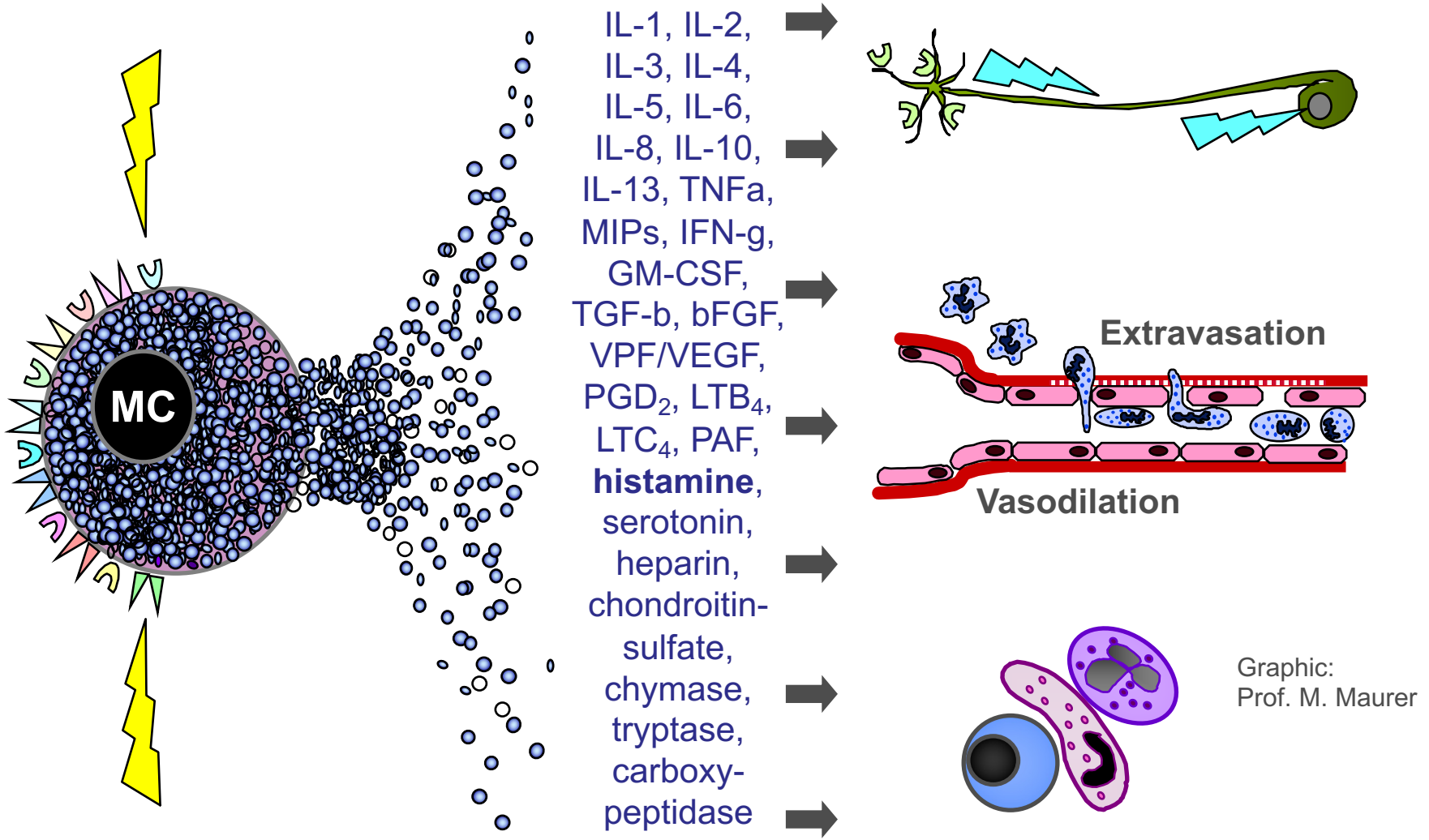
Inducible Urticaria - Management

Histamine is key

but…

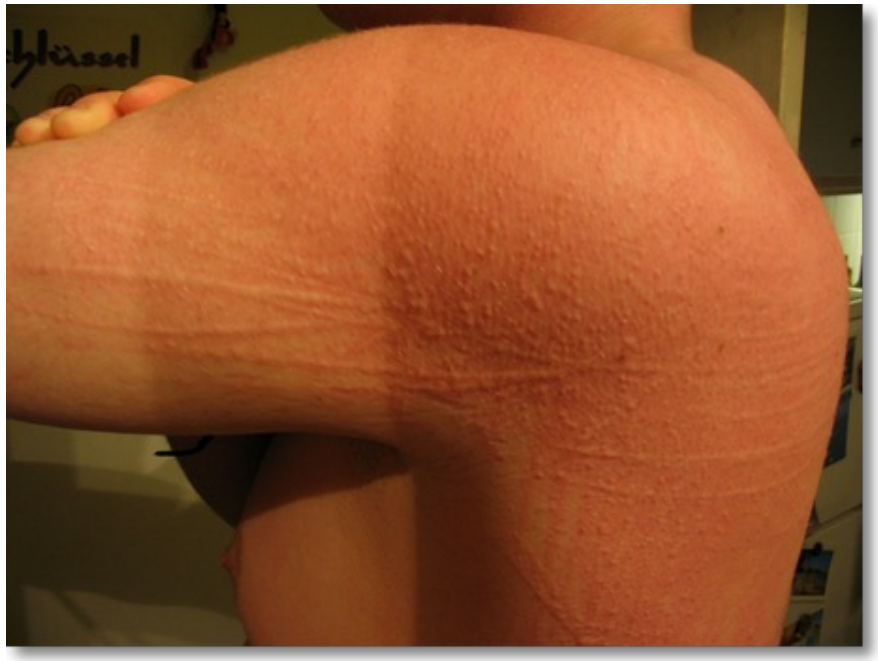
Urticaria – Pathogenesis

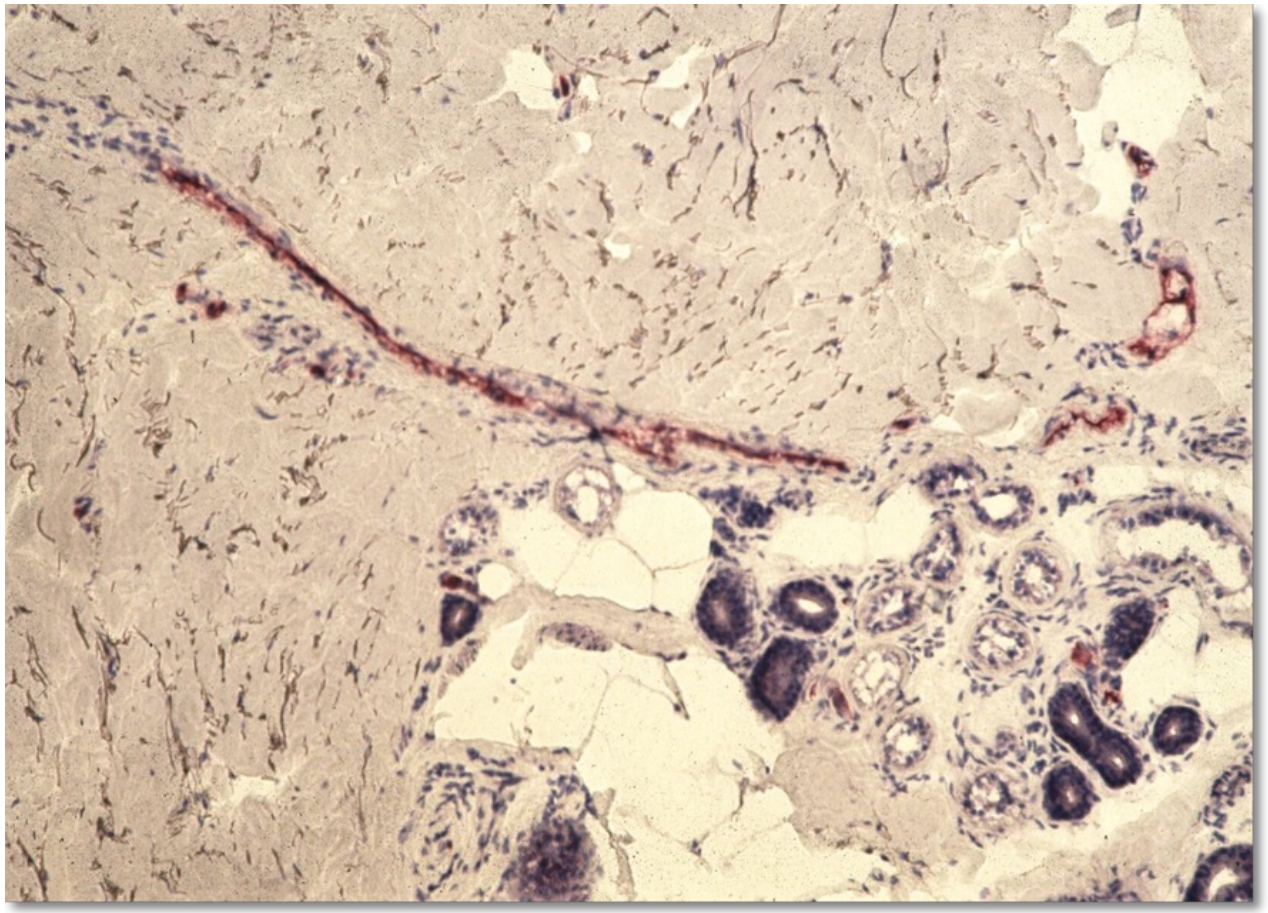
Mast cells are the key effector cells in the induction of urticaria symptoms



Graphic:
Prof. M. Maurer

Urticaria Factitia
(Dermographic Urticaria)





Modern Antihistamines

Control early phase

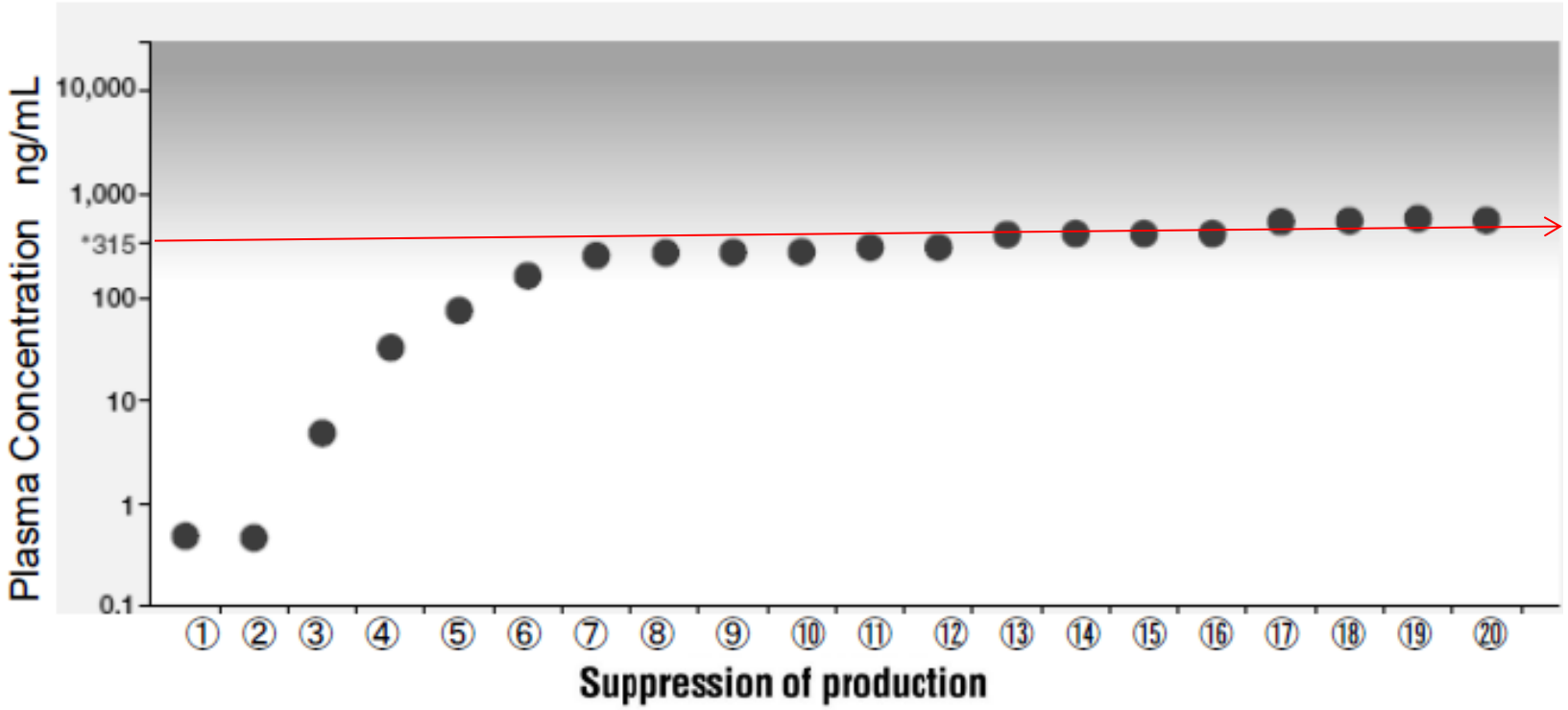
Histamin
Tryptase
LTC4
PGD2

Control late phase

Cytokines
Chemokines
Adhesionsmolecules
Inflammatory cells
(Eosinophils, Neutrophils)

Agrawal et al. *Allergy*. 2000;55:276; Agrawal. *Clin Exp Allergy*. 2004;34:1342; Anthes et al. *Allergy*. 2000;55:277; Genovese et al. *Clin Exp Allergy*. 1997;27:559; Kleine-Tebbe et al. *J Allergy Clin Immunol*. 1994;93:494; Kreutner et al. *Arzneimittelforschung*. 2000;50:345; Lippert et al. *Exp Dermatol*. 1995;4:272; Molet et al. *Clin Exp Allergy*. 1997;27:1167; Schroder et al. *Clin Exp Allergy*. 2001;31:1369; Vignola et al. *Allergy*. 1995;50:200.

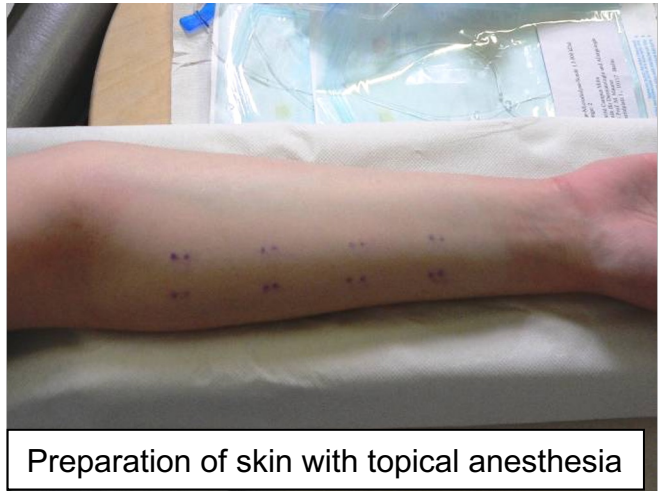
Fexofenadine Plasma (Blood) concentration and Suppression of production



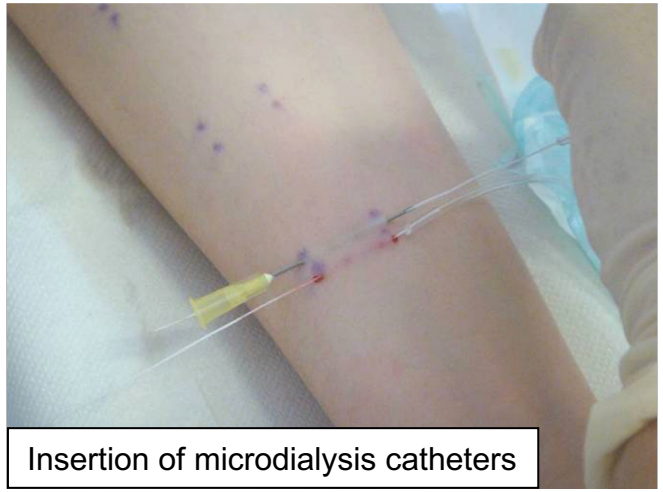
① GM-CSF
② sICAM-1
③ ECP
④ TARC (keratinocyte)
⑤ IL-5
⑥ iNOS
⑦ RANTES
⑧ Eotaxin
⑨ TARC
⑩ IL-4
⑪ MMP-2
⑫ MMP-9
⑬ substance-P
⑭ MDC (keratinocyte)
⑮ NO
⑯ RANTES (keratinocyte)
⑰ basocyte histamine
⑱ LT
⑲ IL-8
⑳ eosinophilic leukocyte

戸倉新樹 皮膚アレルギーフロンティア 4(3);66,2006
Yoshiki Tokura, Dermatology Allergy Frontier 4(3);66,2006

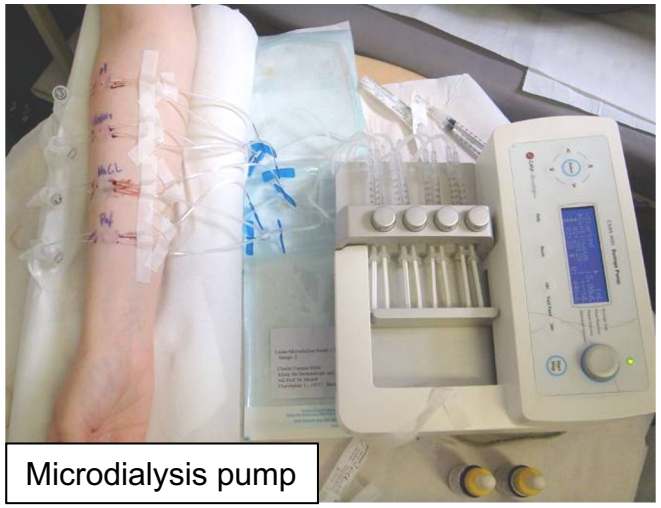
Skin microdialysis



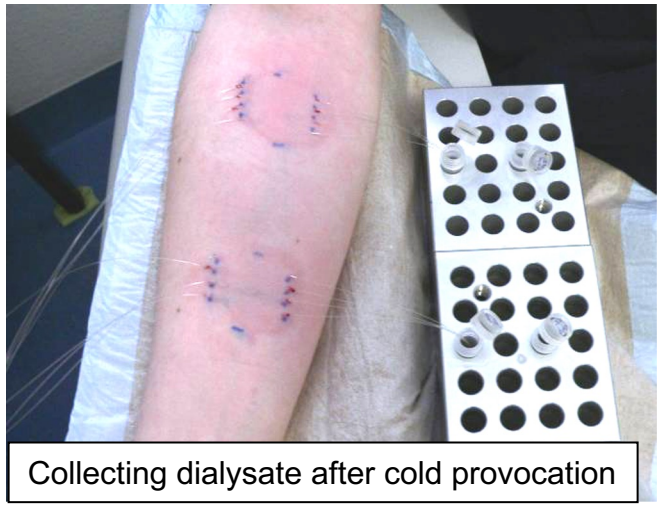
Preparation of skin with topical anesthesia



Insertion of microdialysis catheters

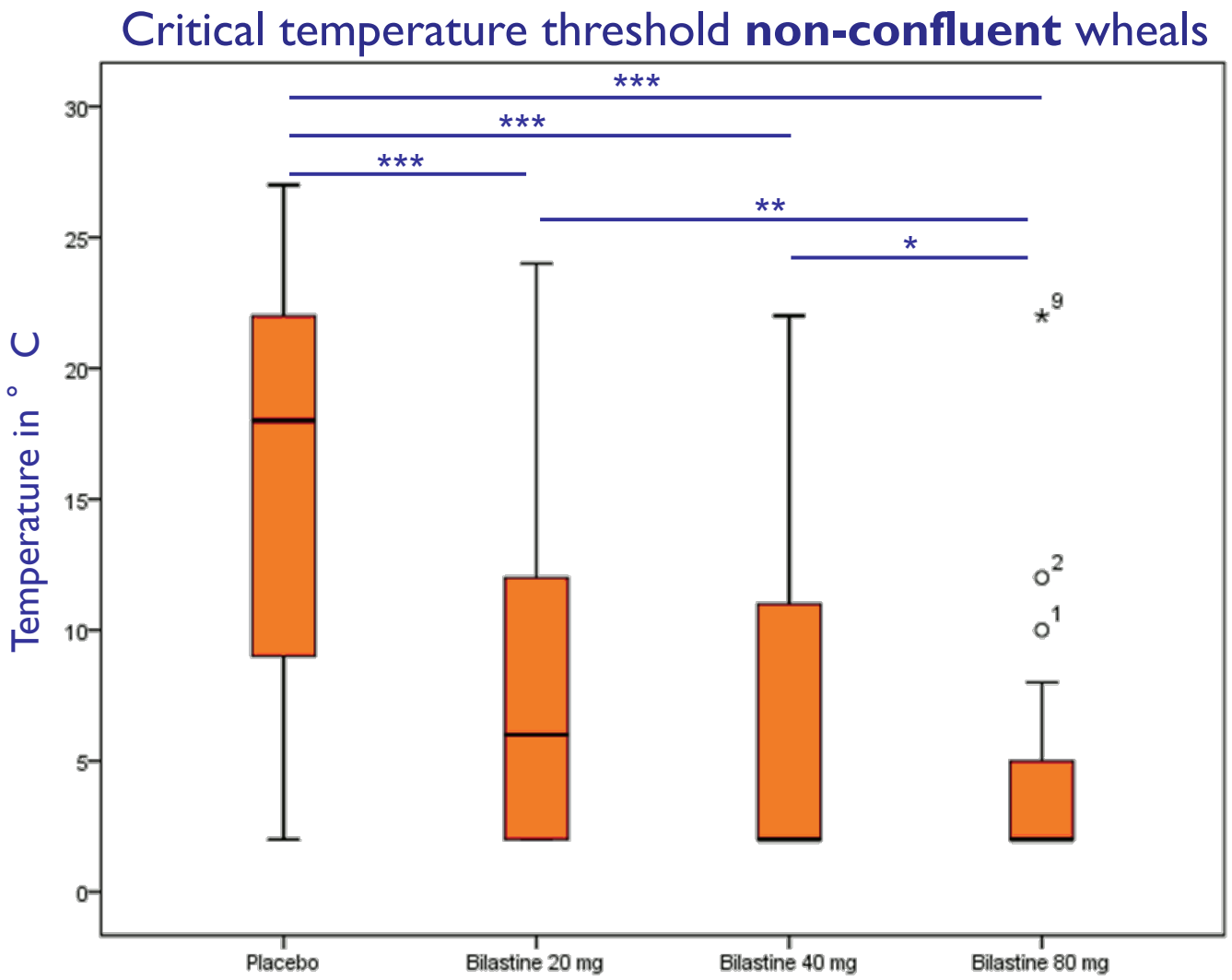


Microdialysis pump



Collecting dialysate after cold provocation

Bilastine reduces temperature thresholds

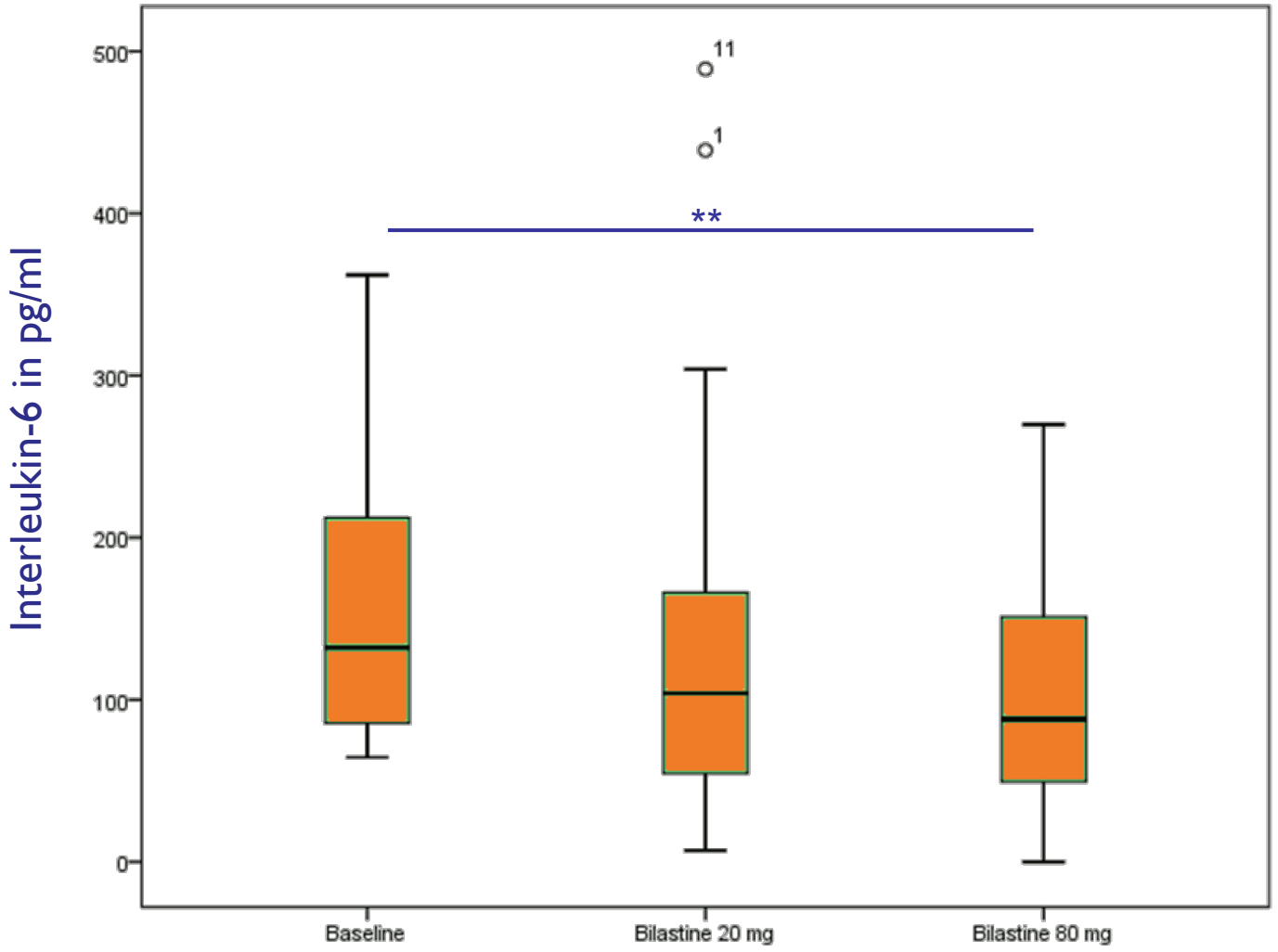


* P ≤ 0.05

** P ≤ 0.005

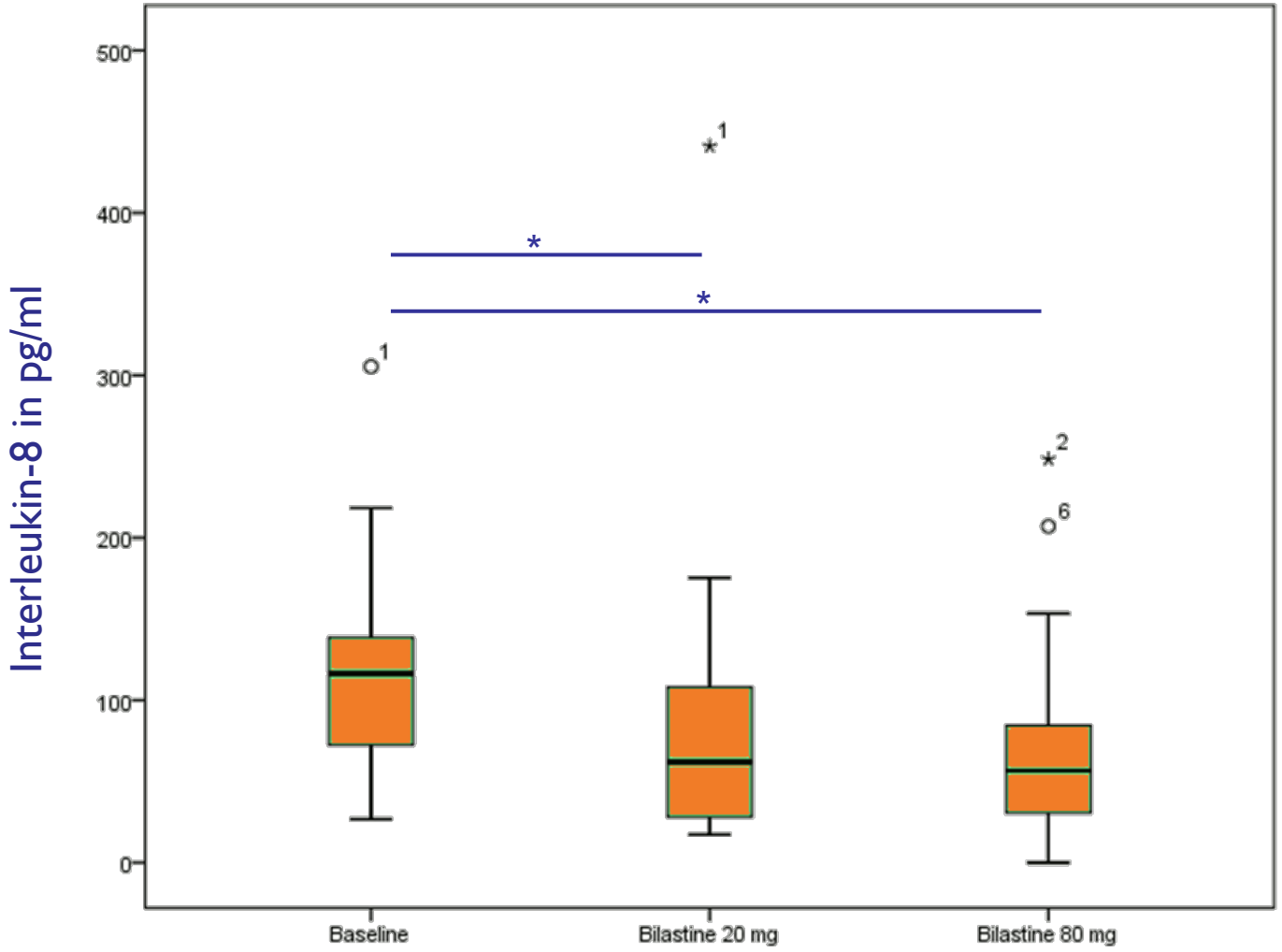
*** P ≤ 0.0001

Bilastine reduces release of IL-6 (3h)



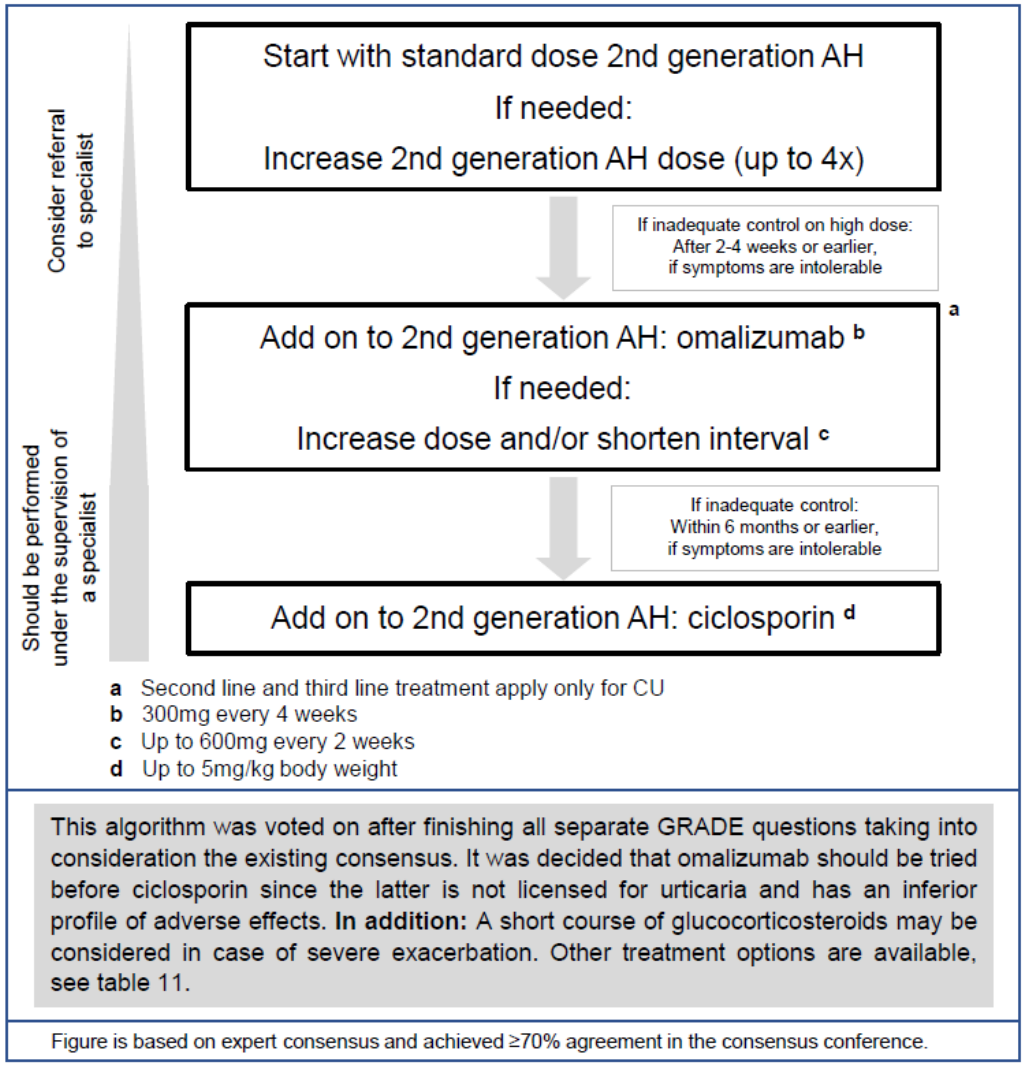
** P ≤ 0.005

Bilastine reduces release of IL-8 (3h)



* P ≤ 0.05

Urticaria treatment algorithm

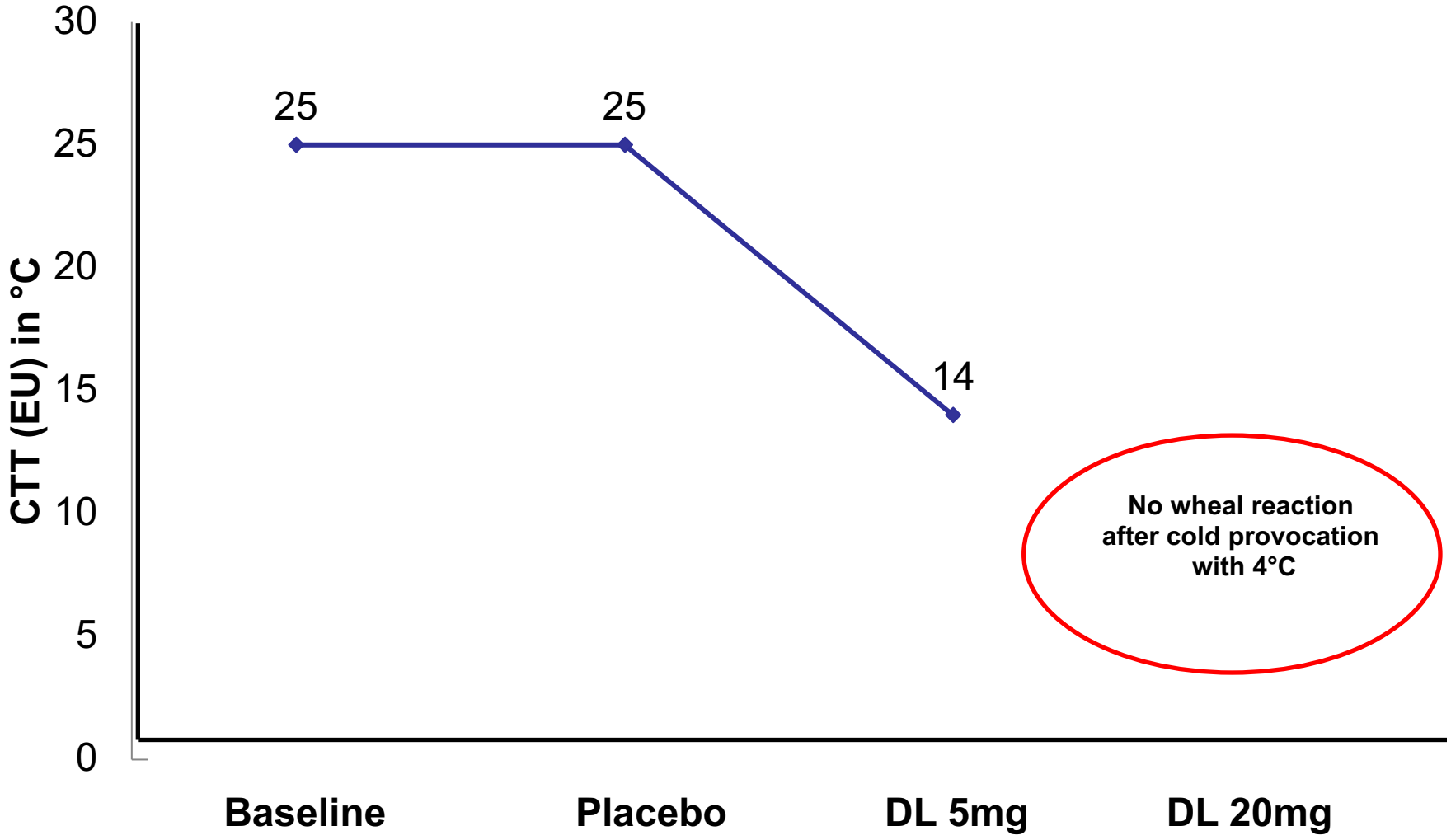


This algorithm was voted on after finishing all separate GRADE questions taking into consideration the existing consensus. It was decided that omalizumab should be tried before ciclosporin since the latter is not licensed for urticaria and has an inferior profile of adverse effects. **In addition:** A short course of glucocorticosteroids may be considered in case of severe exacerbation. Other treatment options are available, see table 11.

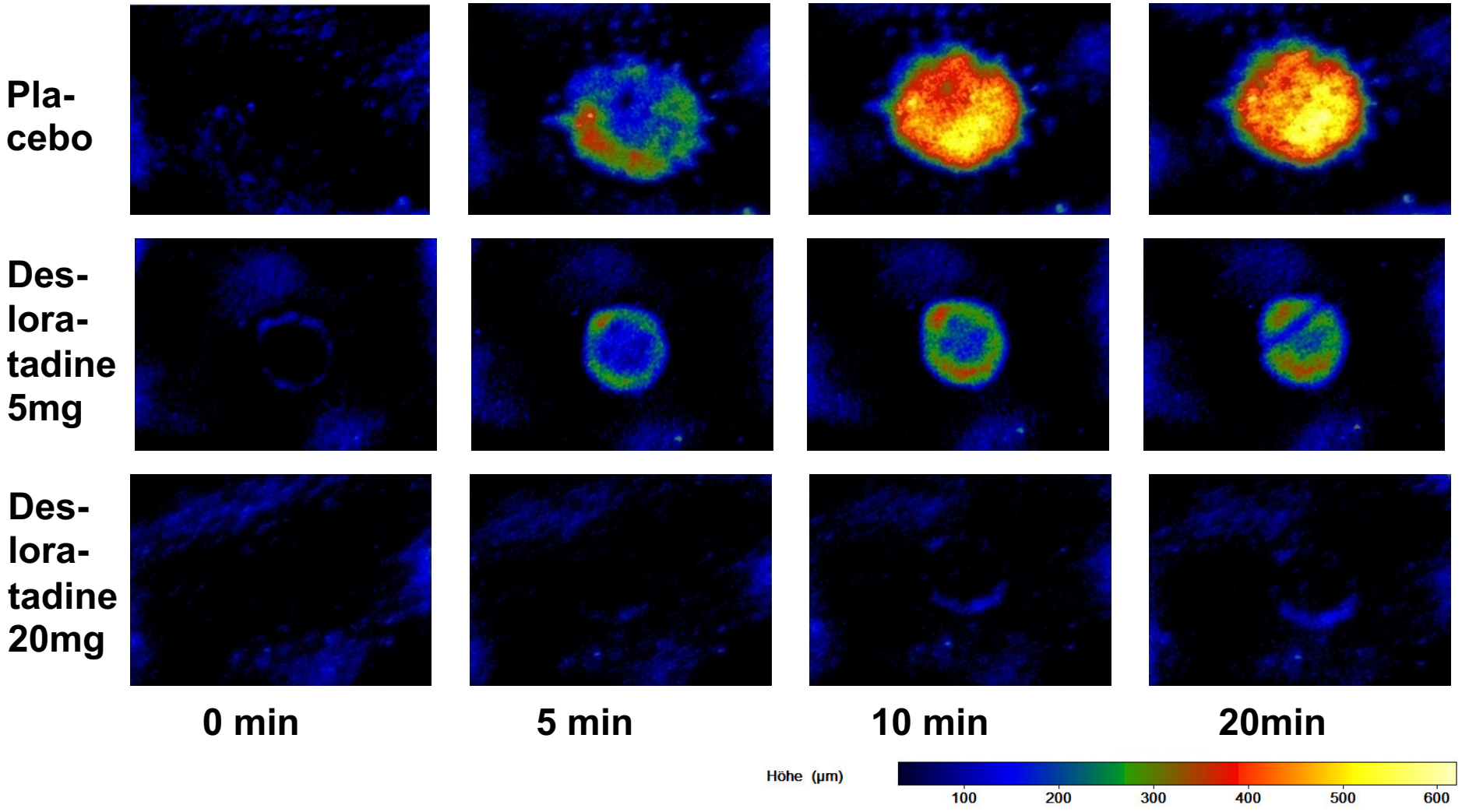
Figure is based on expert consensus and achieved ≥70% agreement in the consensus conference.

Zuberbier, T. et al. Allergy. 2021

AUDACU-Patient #24: Knut, S. 62y



Patient #24: Volumetric changes under treatment



Urticaria treatment algorithm

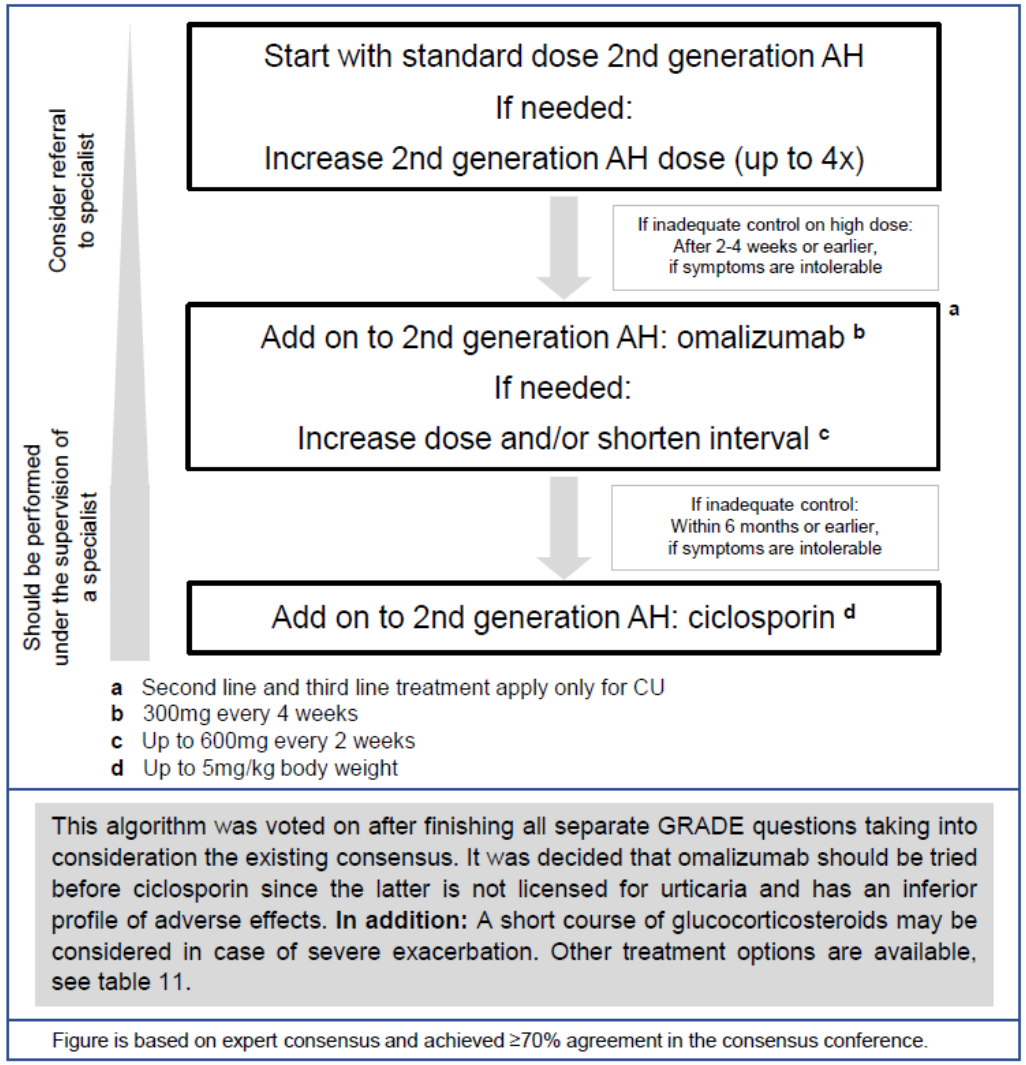


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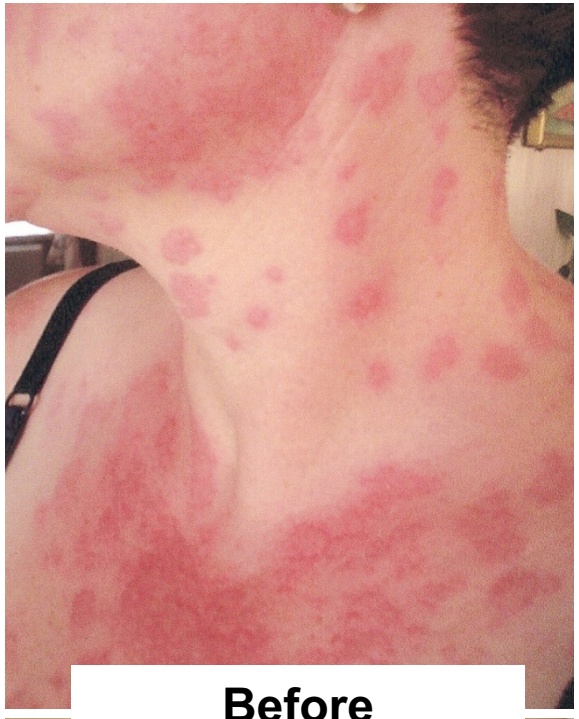
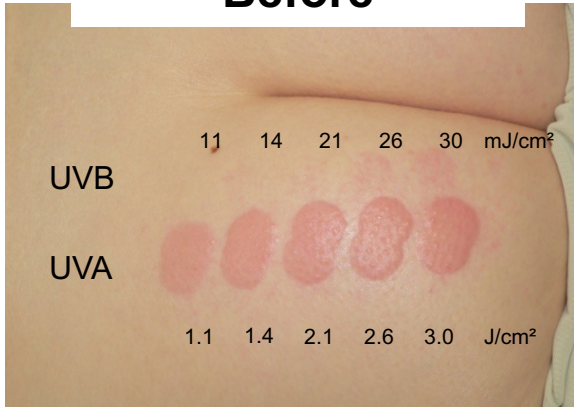
Figure is based on expert consensus and achieved ≥70% agreement in the consensus conference.

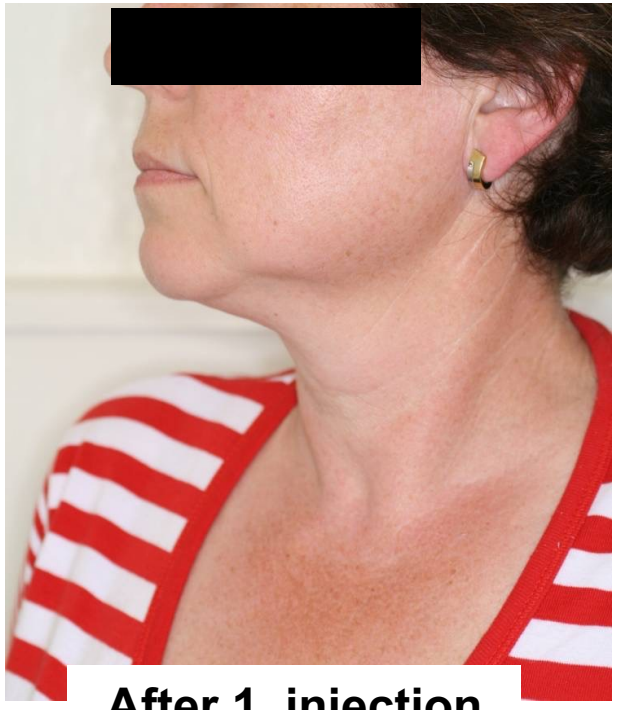
Zuberbier, T. et al. Allergy. 2021

Omalizumab can work in solar urticaria

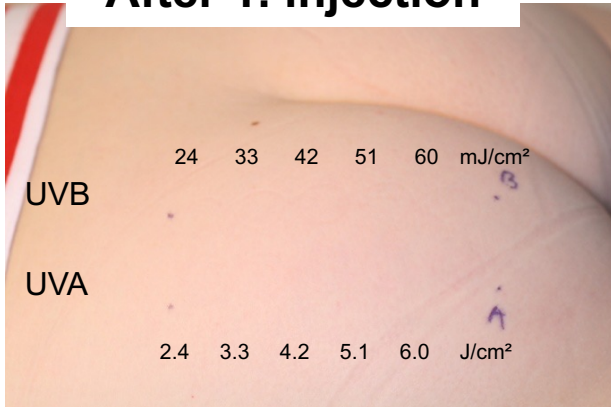


Before



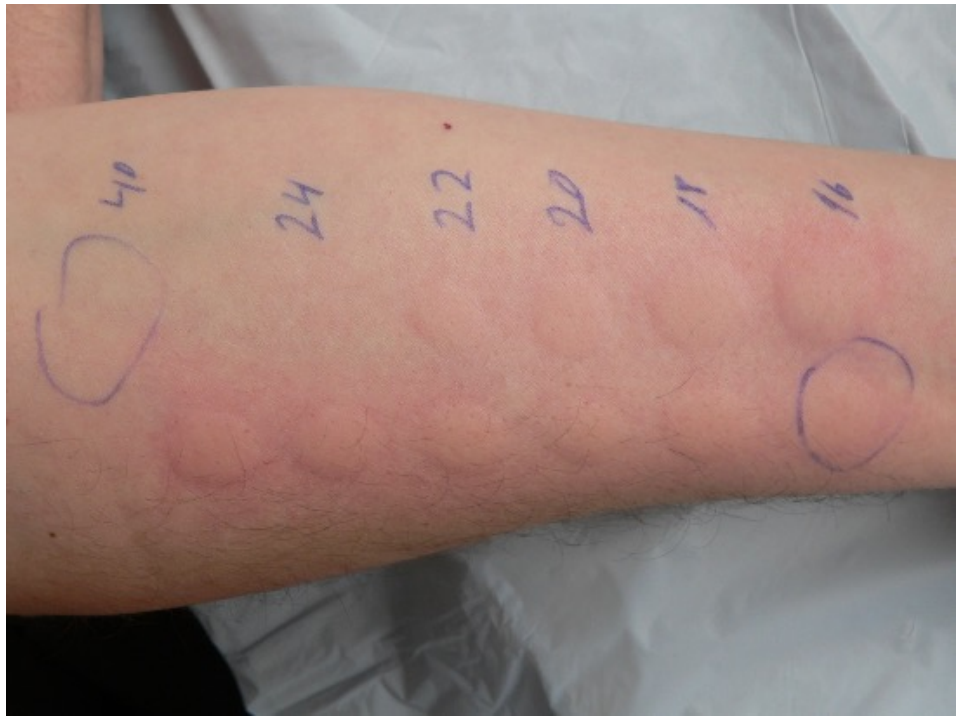


After 1. injection

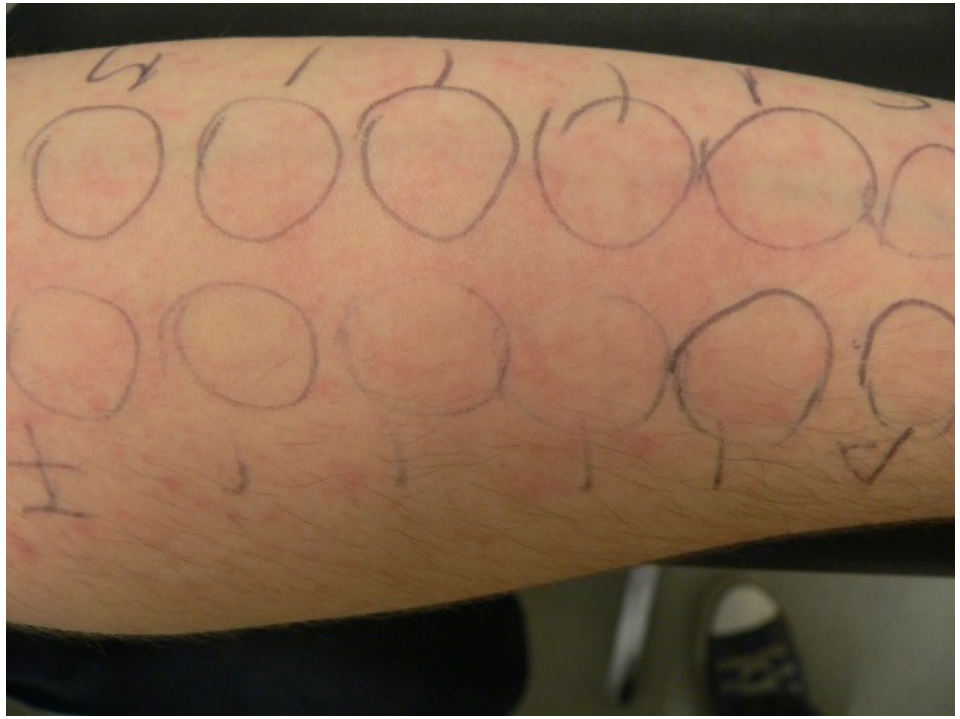


Güzelbey et al. 2008; 63:1563-5

Omalizumab can work in cold urticaria



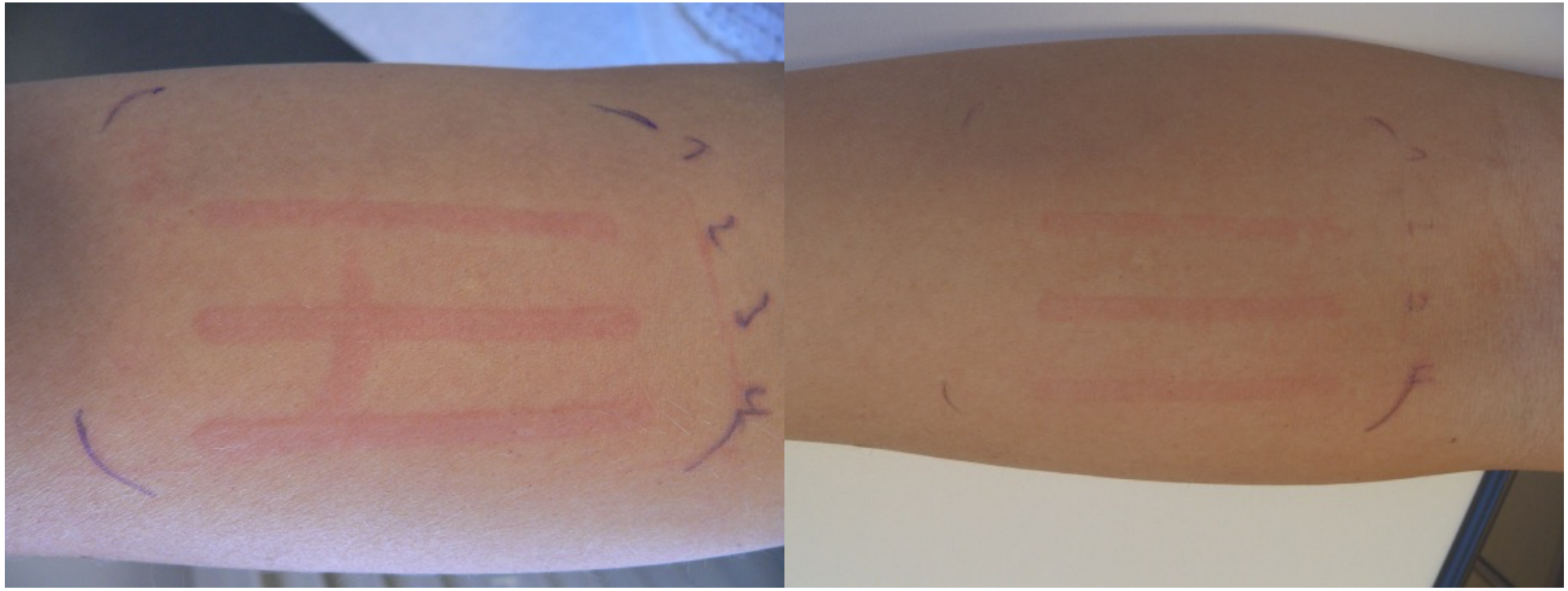
Before



After

Metz M et al 2010, Int Arch Allergy Immunol;154:177–80

Omalizumab can work in symptomatic dermogrpahism / urticaria factitia



Before **After**

Metz M et al 2010, Int Arch Allergy Immunol;154:177–80

Omalizumab in real life

Received: 17 May 2024 | Revised: 25 July 2024 | Accepted: 11 September 2024
DOI: 10.1111/all.16334

Allergy EAACI WILEY

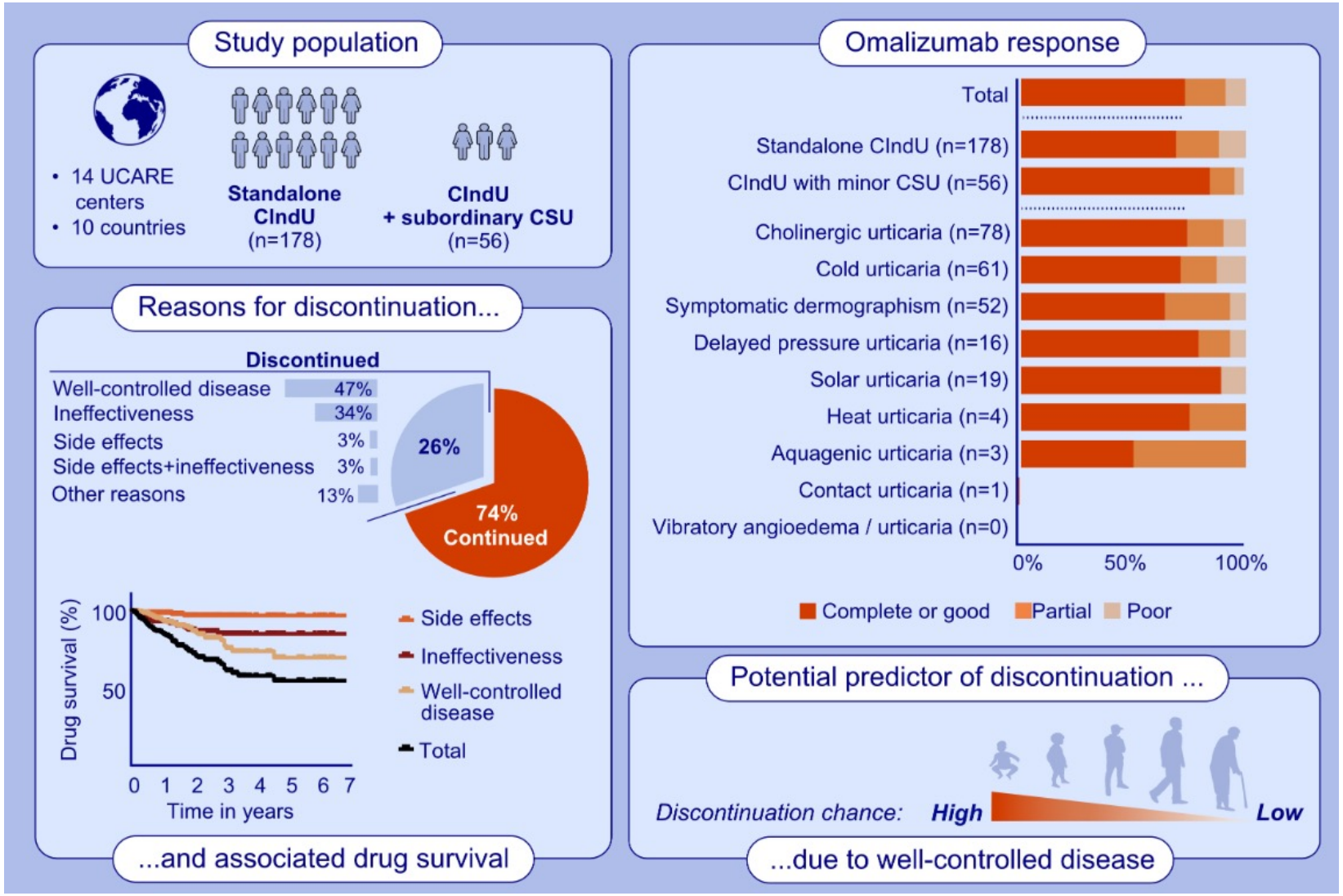
ORIGINAL ARTICLE

Atopic Dermatitis, Urticaria and Skin Disease

Omalizumab is effective and safe in chronic inducible urticaria (CIndU): Real-world data from a large multi-national UCARE study

R. Soegiharto[1] | M. Alizadeh Aghdam[1] | J. A. Sørensen[2] | E. van Lindonk[3] | F. Bulut Demir[4] | N. Mohammad Porras[5] | Y. Matsuo[6] | L. Kiefer[7,8] | A. C. Knulst[1] | M. Maurer[7,8] | C. Ritchie[9] | M. Rudenko[10] | E. Kocatürk[7,11] | R. F. J. Criado[12] | S. Gregoriou[13] | T. Bobylev[14] | A. Kleinheinz[14] | S. Takahagi[6] | M. Hide[6,15] | A. M. Giménez-Arnau[5] | A. Salman[4,16] | R. Oztas Kara[17] | B. S. Dikicier[17] | M. B. A. van Doorn[3,18] | S. F. Thomsen[2] | J. M. P. A. van den Reek[19] | H. Röckmann[1]

- Omalizumab is highly effective and safe in CIndU patients, with long estimated treatment duration mainly reflecting long disease duration.



- We recommend the use of the treatment algorithm as described in Figure 1 for the symptomatic treatment of chronic spontaneous urticaria.

- We recommend aiming for complete symptom control in the treatment of urticaria.

New results from clinical studies and case reports

Remibrutinib

NOVARTIS

Search Global | en Menu

Home > Clinical trials > Recruiting Clinical Trials > A Study to Investigate Efficacy, Safety, and Tolerability of Remibrutinib Compared With Placebo in Adults With CINDU

A Study to Investigate Efficacy, Safety, and Tolerability of Remibrutinib Compared With Placebo in Adults With CINDU Inadequately Controlled by H1-antihistamines

Last Update: Oct 08, 2024

A 52-week Multi-center, Randomized, Double-blind, Placebo Controlled, Basket Study With an Open-label Extension to Investigate the Efficacy, Safety, and Tolerability of Remibrutinib (LOU064) in Chronic Inducible Urticaria (CINDU) in Adults Inadequately Controlled by H1-antihistamines

ClinicalTrials.gov Identifier:NCT05976243 Novartis Reference Number:CLOU064M12301

Condition	Chronic Inducible Urticaria
Phase	Phase3
Overall Status	Recruiting
Number of Participants	348
Start Date	Dec 07, 2023
Completion Date	Dec 31, 2028
Gender	All
Age(s)	18 Years - (Adult, Older Adult)

https://www.novartis.com/clinicaltrials/study/nct05976243

Remibrutinib

Received: 1 November 2022 | Revised: 22 January 2023 | Accepted: 7 February 2023

DOI: 10.1002/clt2.12227

ORIGINAL ARTICLE

Remibrutinib inhibits hives effector cells stimulated by serum from chronic urticaria patients independently of FcεR1 expression level and omalizumab clinical response

Ramón Gimeno[1,2,3] | Clara Ribas-Llauradó[2] | David Pesque[4] | Evelyn Andrades[2,4] | Bruno Cenni[5] | Barbara Ambros[6] | Ramon Pujol[2,3,4] | Ana M. Giménez-Arnau[2,3,4]

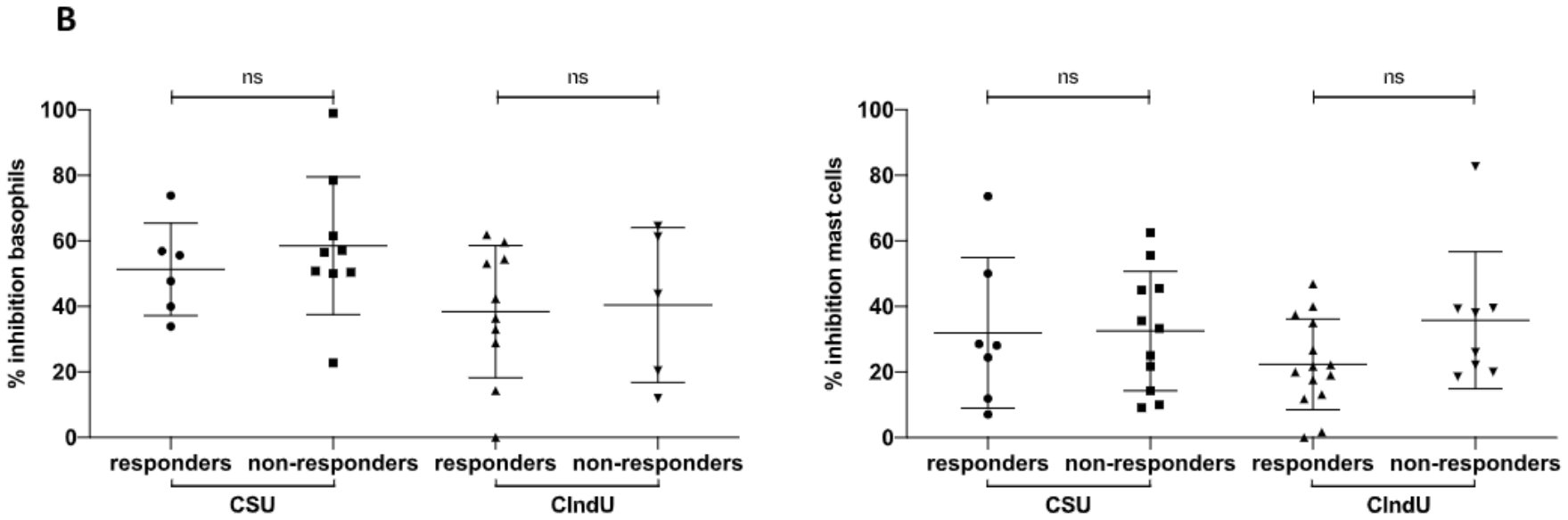
Methods:

- 22 patients with CSU and 22 patients CindU were included in the study together with a sex-matched control group.
- Patients were classified as responders or non-responders to anti-IgE therapy based on their clinical data, FcεR1a expression on blood basophils and total IgE levels.
- Changes on CD63 expression—as an activation marker, were used to evaluate in vitro the response of basophils and mast cells to serum exposure and the inhibitory effects of remibrutinib.

Remibrutinib

Results:

- Remibrutinib inhibits degranulation induced by IgE cross-linking in mast cells and basophils and also the activation triggered by factors present in the sera of CSU and CindU patients.
- Patient's serum induces a greater degranulation of effector cells than controls.
- Activation of mast cells and basophils by patient sera and remibrutinib effects were not related to omalizumab responsiveness.



(B) CSU or CIndU patients are classified in responders or non-responders to omalizumab therapy and the inhibitory effect of remibrutinib in each situation assessed as indicated before.

Gimeno et al 2023, Clin Transl Allergy.

Remibrutinib

Results:

- Remibrutinib inhibits degranulation induced by IgE cross-linking in mast cells and basophils and also the activation triggered by factors present in the sera of CSU and CindU patients.
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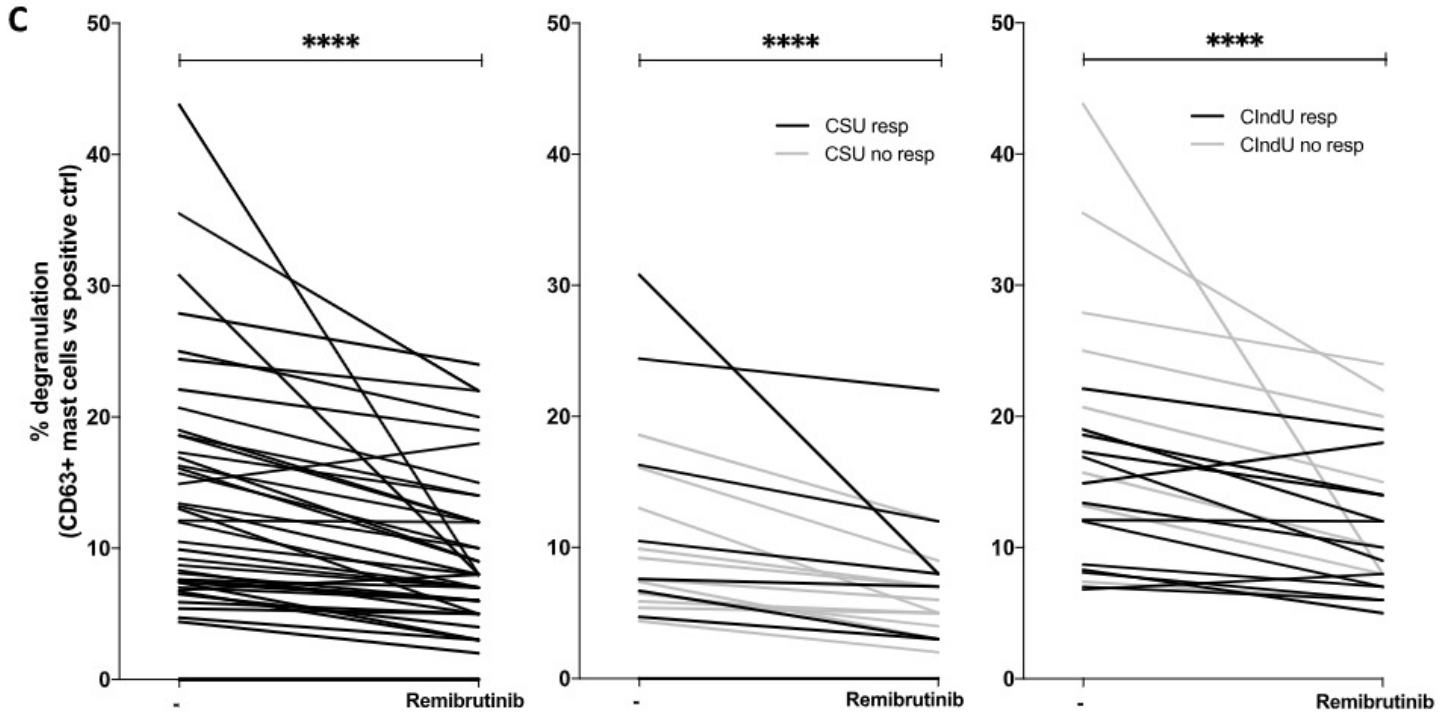

(C) Effect of BTK inhibition by remibrutinib on the activation induced by patient's serum using mast cells

- Left = all CU patients
- Middle = only CSU patients
- Right = CIndU patients

Patients are further characterized as responsive (resp) or not (no resp) to omalizumab.
Percentage of inhibition is referred to the maximum obtained with a positive control

Gimeno et al 2023, Clin Transl Allergy.

Dupilumab

Dupilumab for the Treatment of Chronic Inducible Cold Urticaria in Patients Who Remain Symptomatic Despite the Use of H1-antihistamine (LIBERTY-CINDU CUrIADS)

Not Recruiting | 12-80 years | All | Phase 3 | 82 participants needed

Study Overview

Primary Objective:

To demonstrate the efficacy of dupilumab in adult and adolescent participants with primary acquired chronic inducible cold urticaria (ColdU) who remain symptomatic despite the use of an H1-antihistamine

Secondary Objectives:

To demonstrate the efficacy of dupilumab on primary acquired chronic inducible ColdU disease control To demonstrate the efficacy of dupilumab on primary acquired chronic inducible ColdU local signs and symptoms (hives/wheals, itch, burning sensation and pain) after provocation test To demonstrate the efficacy of dupilumab on primary acquired chronic inducible ColdU disease activity To demonstrate improvement in health-related quality-of-life and overall disease status and severity To evaluate the ability of dupilumab in reducing the proportion of participants who require rescue therapy To evaluate the proportion of participants with cold exposure triggered urticaria To evaluate safety outcome measures To evaluate immunogenicity of dupilumab

Study details

The duration of study for each participant included 2-4 weeks of screening period, 24 weeks of treatment period and 12 weeks of post treatment period.

https://www.sanofistudies.com/us/en/listing/286355/dupilumab-for-the-treatment/

Barzolvolimab

Celldex Announces Barzolvolimab Met All Primary and Secondary Endpoints with High Statistical Significance in Positive Phase 2 Study in Chronic Inducible Urticaria

October 26, 2024

- *First to demonstrate clinical benefit in patients with chronic inducible urticaria (CIndU) in large, randomized, placebo-controlled study*
- *Favorable safety and tolerability*
- *Plan to advance CIndU into Phase 3 development*

- positive results from the Celldex's Phase 2 clinical trial of barzolvolimab incold urticaria (ColdU) and symptomatic dermographism (SD).
- The study includes patients who remain symptomatic despite treatment with antihistamines.
- Barzolvolimab is a humanized monoclonal antibody that specifically binds the receptor tyrosine kinase KIT with high specificity and potently inhibits its activity, which is required for mast cell function and survival.

Summary of Clinical Assessments at Week 12						
	Cold Urticaria			Symptomatic Dermographism		
All measurements at Week 12	150 mg q4w (n=32)	300 mg q8w (n=32)	Placebo (n=32)	150 mg q4w (n=33)	300 mg q8w (n=33)	Placebo (n=31)
Primary endpoint: % of patients with negative provocation test (complete response)	46.9% **p=0.0023**	53.1% **p=0.0011**	12.5%	57.6% **p<0.0001**	42.4% **p=0.0003**	3.2%
% of patients with complete or partial response per provocation test	62.5% **p=0.0118**	75% **p=0.0006**	31.3%	66.6% **p<0.0001**	57.5% **p=0.0002**	12.9%
Improvement in Critical Temperature (CTT) and Critical Friction (CFT) Thresholds	-8.82°C **p<0.0001**	-9.61°C **p<0.0001**	-0.30°C	-2.46 pins **p<0.0001**	-2.27 pins **p=0.0002**	-0.82 pins
% of patients with Urticaria Control Test >12	58.6% **p=0.0048**	68.8% **p<0.0001**	31.0%	54.8% **p=0.0015**	65.5% **p<0.0001**	32.0%

https://ir.celldex.com/news-releases/news-release-details/celldex-announces-barzolvolimab-met-all-primary-and-secondary

EVO756

Evommune enrols first subject in chronic inducible urticaria therapy trial

Patients in the trial will receive EVO756 orally once a day for four weeks.

September 4, 2024

- EVO756 is a selective MRGPRX2 antagonist and could offer a new oral treatment option for mast cell-mediated diseases, with pre-clinical data claimed to indicate its ability to prevent mast cell degranulation across all relevant ligand categories.

- Phase II clinical trial, multicentre study aims to assess the safety and efficacy of EVO756 in approximately 30 patients suffering from symptomatic dermographism or cold urticaria, which are the two most prevalent types of CIndU.

https://www.clinicaltrialsarena.com/news/evommune-urticaria-therapy-trial/?cf-view

Benralizumab

Benefit of benralizumab treatment in a patient with chronic symptomatic dermographism

K.C. Bergmann, S. Altrichter, M. Maurer*
Allergie-Centrum-Charité, Department of Dermatology and Allergy, Charité – Universitätsmedizin Berlin, Berlin, Germany
*Correspondence: M. Maurer. E-mail: marcus.maurer@charite.de

Conclusion:

- the benefit of treatment with benralizumab, experienced by this patient with SD, suggests a role for interleukin-5 and eosinophils in the pathogenesis of this condition.
- Benralizumab and other interleukin-5-targeted treatments may be considered as treatment options in otherwise treatment-resistant patients with SD.

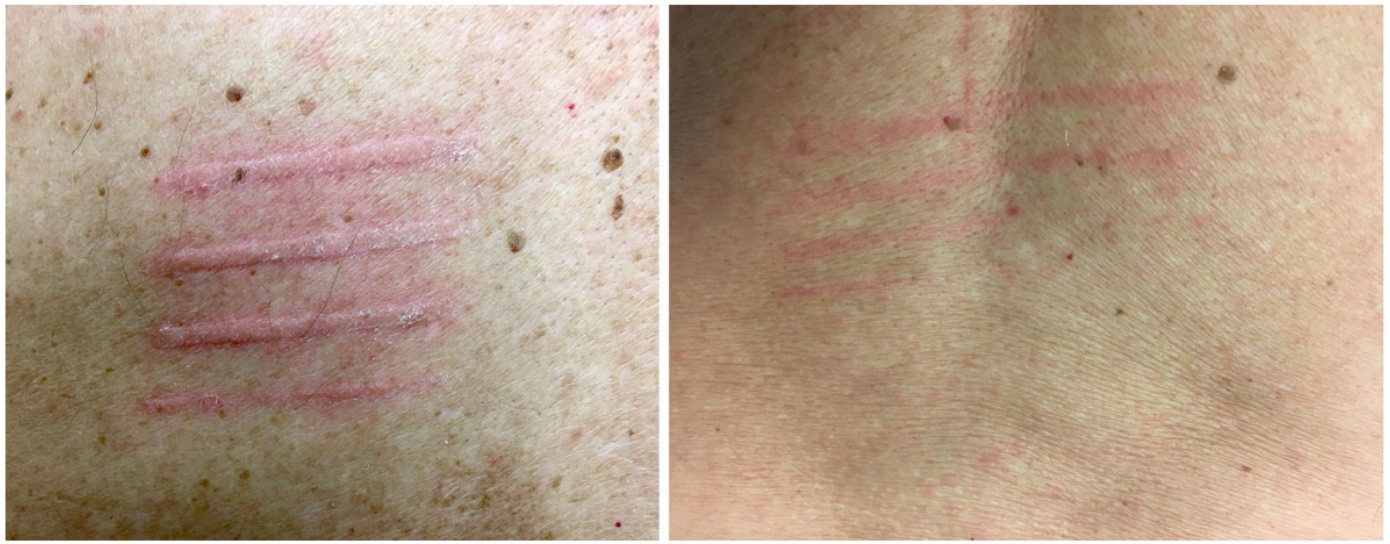

Figure 1 Results of skin provocation testing including trigger threshold measurements before and 3 months after the start of treatment with benralizumab. Left: positive responses, i.e. itchy weals, to scratching with all four pins of FricTest®, before benralizumab treatment. Right: negative responses, i.e. erythema without wealing or itch, to all four pins of FricTest®, 3 months after the initiation of benralizumab treatment.

Bergmann et al (2019). *Journal of the European Academy of Dermatology and Venereology.*

Summary

Most important for a better management:

- A good patient history
- Determine threshold
- Counsel on avoidance and on prophylaxis
- Use step wise treatment
- Adapt to need

For a better life with allergies