Urticaria/ Angioedema: Management and Treatment

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Disclosures

- Speakers' Bureau/Advisory Board:
  - Arcutis (psoriasis/atopic dermatitis), Organon (psoriasis/atopic dermatitis), Galderma (acne), Incyte (atopic dermatitis), Pfizer (atopic dermatitis), Sanofi/Regeneron (atopic dermatitis).
  - All relevant financial relationships have been mitigated.

Objectives

- Differentiate between forms of urticaria
- Describe key pathophysiological mechanisms
- Summarize current guideline recommendations
- Discuss patient counseling around the use of current and emerging therapies

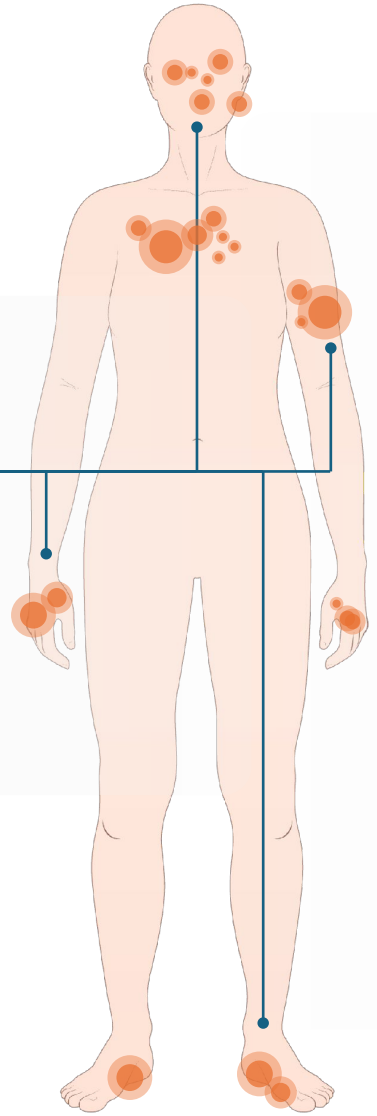
Definition of Urticaria

- Hives or wheals
  - Evanescent, pink edematous papules or plaques that typically have a peripheral pallor
  - Round, annular or serpiginous
    - Associated with itch or burning sensation
    - May affect any part of the face or body
  - Lesions last 30 min to <24 hours
    - If > 24 hours, consider other urticarial dermatoses or vasculitis

Wheals (hives)

May affect **any area** of the body[1,2]

Individual hives are fleeting, and usually resolve within **30 minutes to 24 hours**[3]



May look different on different skin tones

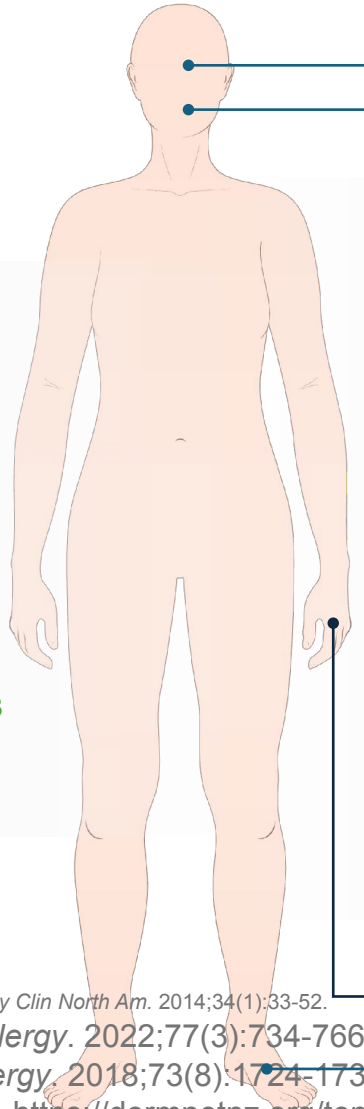
1. Saini SS. *Immunol Allergy Clin North Am*. 2014;34(1):33-52.
2. Kanani A et al. *Allergy Asthma Clin Immunol*. 2018;14(suppl 2):5.
3. Zuberbier T et al. *Allergy*. 2022;77(3):734-766.

Definition of Angioedema

- Sudden, pronounced erythematous or skin-colored deep swelling in superficial tissues (lips, eyelids, genitals, joints)
  - Associated with tingling, burning, tightness, pain, less itch
  - Laryngeal edema is not typical of urticaria
- Resolved over 48 to 72 hours (slower than wheals)

Angioedema

- Can affect the **lips, eyes, cheeks, and extremities**[1]
- Takes up to **72 hours** to resolve[2]
- Associated with greater **disease activity**[3]



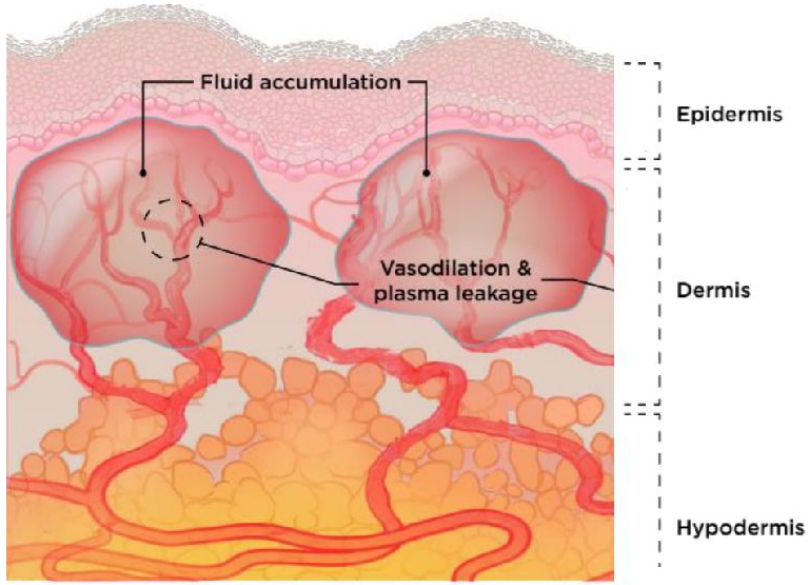
Typical locations of angioedema

Images reproduced with permission of Dermnet NZ.[4]

1. Saini SS. *Immunol Allergy Clin North Am.* 2014;34(1):33-52.
2. Zuberbier T et al. *Allergy*. 2022;77(3):734-766.
3. Sussman G et al. *Allergy*. 2018;73(8):1724-1734.
4. Dermnet NZ. Accessed March 6, 2025. https://dermnetnz.org/topics/urticaria-images

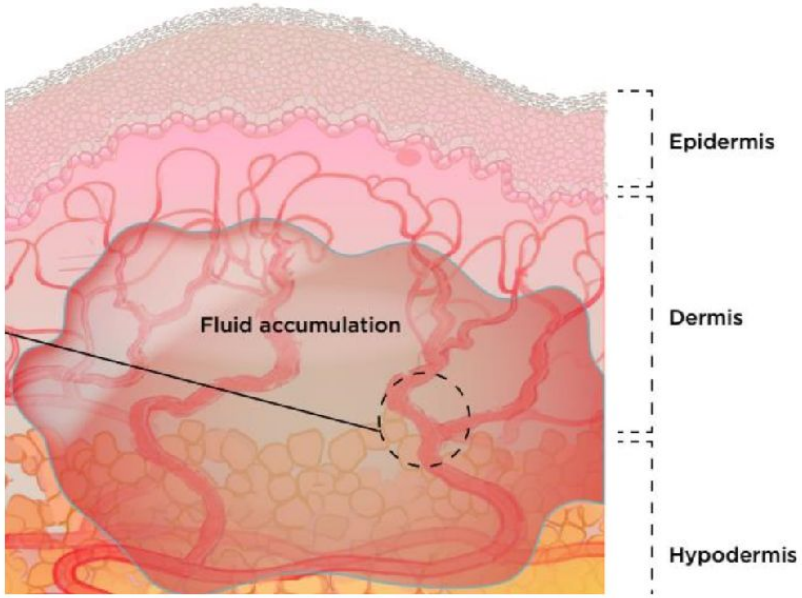
Wheals and Angioedema

Wheals[1,2]



Wheals can occur anywhere, but favor the **arms** and **legs**[3]

Angioedema[1,2]



Angioedema appears most commonly on the **face** (lips, eyelids), **hands**, or **feet**[3,4]

Angioedema in CSU is **not** bradykinin-mediated[4]

CSU, chronic spontaneous urticaria.

1. Navinés-Ferrer A, et al. *J Immunol Res.* 2016;2016:8163803. 2. Bernstein JA, Moellman J. *Int J Emerg Med.* 2012;5(1):39. 3. Kolkhir P, et al. *Nat Rev Dis Primers.* 2022;8(1):61. 4. Maurer, M, Magerl, M. *Clinic Rev Allerg Immunol.* 2021;61(1):40-49.

Angioedema vs Anaphylaxis

Anaphylaxis is highly likely when one of the following occurs[1]:

1. Acute onset of an illness with involvement of the **skin** and/or **mucosal tissue**
2. Acute onset of **hypotension** or **bronchospasm** or **laryngeal involvement** after exposure to a known or highly probably allergen, even in the absence of typical skin involvement

	Angioedema[2,4]	Anaphylaxis[1]
Definition	Localized swelling	Systemic allergic reaction
Speed of onset	Rapid to gradual depending on subtype	Rapid - within minutes to hours
Symptoms	Rapid swelling, tingling, tightness	Respiratory compromise, hypotension, severe gastrointestinal symptoms
Severity	Rarely life-threatening (**Mortality rate:** 0.24-0.34 PMPY)[5]	Potentially life-threatening (**Mortality rate:** 0.63-0.76 PMPY)[6]
First-line treatment	H_1-antihistamines*	Epinephrine

PMPY, per million person-years.
*Mast cell-mediated angioedema.

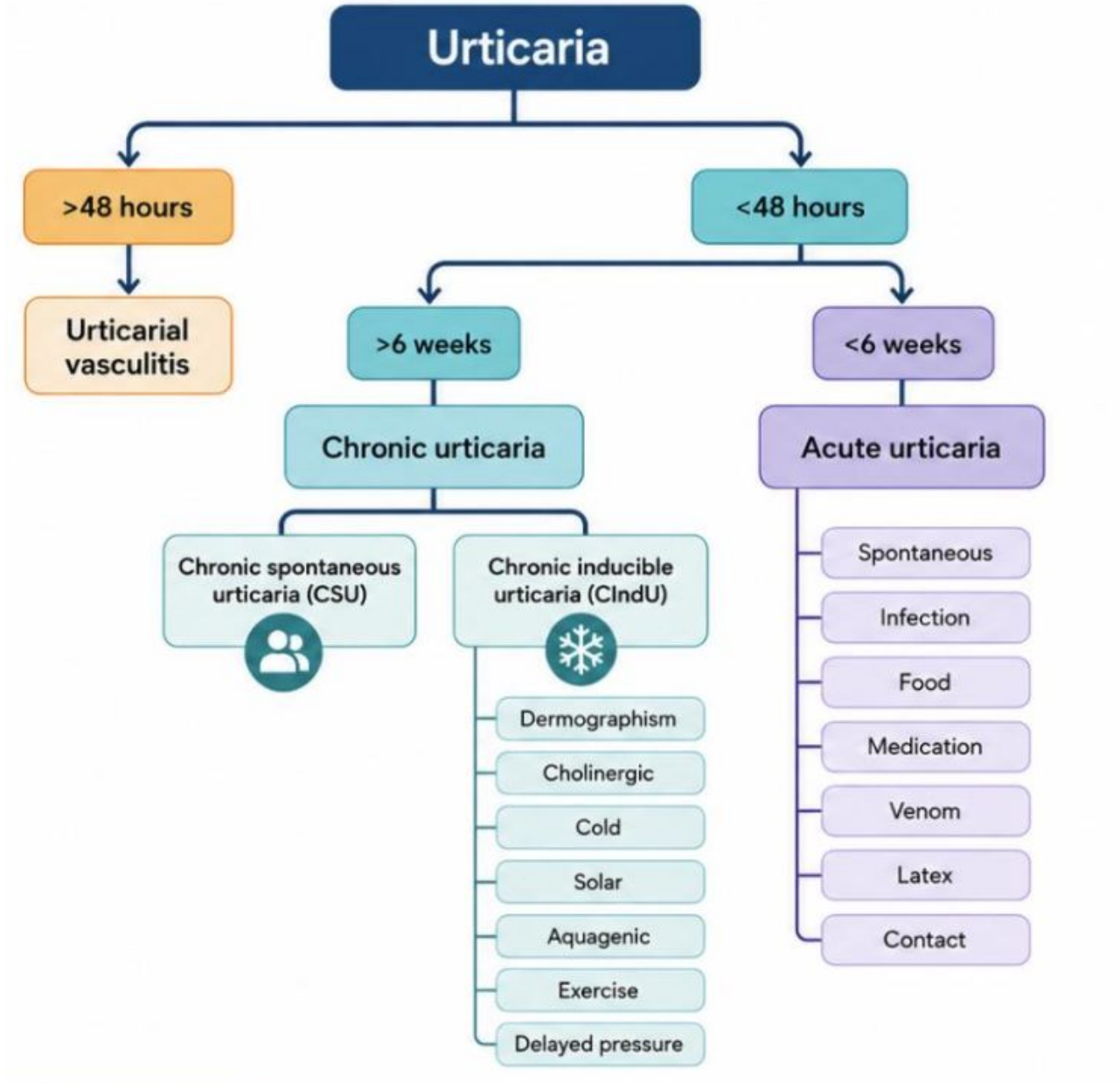
1. Cardona V et al. *World Allergy Organ J*. 2020;13(10):100472. **2.** Nedelea I, Deleanu D. *Exp Ther Med.* 2019;17(2):1068-1072. **3.** Spickett GP, Stroud C. *Clin Med (Lond)*. 2011;11:390-396. **4.** Lacuesta G et al. *Allergy Asthma Clin Immunol.* 2024;20(suppl 3):65. **5.** Kim SJ et al. *Ann Allergy Asthma Immunol.* 2014;113(6):630-634. **6.** Ma L et al. *J Allergy Clin Immunol.* 2014;133(4):1075-1083.

Urticaria Classification: Duration

- Acute <6 weeks
  - Acute, intermittent urticaria, episodes for hours or days, but recur over months to years
- Chronic >6 weeks, most days of the week
  - Episodic: recurrent but <2 days per week

Chronic Urticaria Classification: Triggers

- Spontaneous (CSU)
  - Arise spontaneously with no reproducible stimuli
  - Urticaria may also be elicited by specific stimuli (CIndU), but symptoms occur with or without triggers
  - Known (autoimmunity) or unknown cause
- Inducible (CIndU)
  - Triggered consistently and reproducibly by definite, subtype-specific stimuli
  - **Always** occur when trigger is present
  - **Never** occur the trigger is absent
  - Subtype specific trigger is not relevant in other forms of inducible urticaria, other than the rare overlap (cold cholinergic urticaria)


Urticaria
>48 hours
<48 hours
Urticarial vasculitis
>6 weeks
<6 weeks
Chronic urticaria
Acute urticaria
Chronic spontaneous urticaria (CSU)
Chronic inducible urticaria (CIndU)
Dermographism
Cholinergic
Cold
Solar
Aquagenic
Exercise
Delayed pressure
Spontaneous
Infection
Food
Medication
Venom
Latex
Contact

Subtypes of chronic inducible urticaria

The **estimated prevalence** of **CIndU** is **0.5%**[1]

	Symptomatic dermographism	Cold urticaria	Cholinergic urticaria	Delayed pressure urticaria	Heat urticaria	Solar urticaria	Aquagenic urticaria	Contact urticaria
								
TRIGGER	Sheer force on the skin[1]	Cold exposure[1]	Active or passive body warming[1]	Sustained pressure on the skin[1]	Heat[1]	UV and/or visible light exposure[1]	Contact with water[1]	Contact with eliciting agent[1]
PREVALENCE	50% to 78%[1,2]	8% to 37%[1,2]	6% to 13%[1,2]	3% to 20%[1,2]	Very rare[1,2]	Very rare[1,2]	Very rare[1,2]	Very rare[1]

Images reproduced with permission of Dermnet NZ.[3]

CIndU, chronic inducible urticaria; UV, ultraviolet.

1. Maurer M et al. *Allergy Clin Immunol Pract.* 2018;6(4):1119-1130. **2.** Pozderac I et al. *Acta Dermatovenerol Alp Pannonica Adriat.* 2020;29(3):141-148.
3. Dermnet NZ. Accessed April 25, 2025. https://dermnetnz.org/topics

Distinguishing CSU From Other Diseases

CSU[1]

- Wheals with or without angioedema
- Lasts >6 weeks
- No known trigger

Urticarial vasculitis[2]

- Average wheal duration >24 hours
- Signs of vasculitis in biopsy

Bullous pemphigoid[3]

- Prodromal phase: pruritic urticarial lesions
- Typically affects patients >60 years old
- Additional testing may confirm diagnosis

Pityriasis (tinea) versicolor[4]

- Discolored or light pink scaly patches, usually affecting the trunk and arms
- Chronic superficial fungal skin infection

Misdiagnosis may complicate CSU patient's journey[5]

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CSU, chronic spontaneous urticaria.

1. Zuberbier T, et al. *Allergy.* 2022;77(3):734-766. 2. Davis M, van der Hilst J. *The Journal of Allergy and Clinical Immunology: In Practice.* 2018;6(4):1162-1170. 3. Baigrie D, Nookala V. Bullous Pemphigoid. [Updated 2023 Mar 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. 4. Łabędź, N. et al. *Life.* 2023;13(10):2097. 5. Sanchez J, et al. *J Allergy Clin Immunol Pract.* 2017;5(2):464-470.

The Clinical Presentation of CSU is Heterogeneous

~95% of patients have itchy wheals

fleeting nature, usually lasting 30 minutes to 24 hours and resolving without residual marks[1-4]

~35% -45% of patients may have accompanying angioedema

typically resolving slower than wheals (up to 72 hours)[2-6]

Symptoms are often relapsing and remitting[7]

Images reprinted with permission from: DermNet New Zealand. Original images located at: https://dermnetnz.org/imagedetail/8123-urticaria (top left, first image); https://dermnetnz.org/imagedetail/5207-urticaria-in-dark-skin bottom (left, first image); https://dermnetnz.org/imagedetail/15206-urticaria-in-a-child (bottom left, second image); from Kolkhir P, et al. *Nat Rev Dis Primers*. 2022;8(1):61 (top left, second image); from Shutterstock. https://www.shutterstock.com/image-photo/young-woman-allergic-reaction-angioedema-643990609 (right side, first image); from Shutterstock, https://www.shutterstock.com/image-photo/comparison-normal-right-hand-left-swollen-1395702005 (top right corner image); and from Batista M, Alves F, and Gonçalo M. *Journal of the Portuguese Society of Dermatology and Venereology*. 2019;77(2):119-127. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/) (bottom right corner image).

CSU, chronic spontaneous urticaria.

1. DermNet. Angioedema. Accessed December 18, 2024. https://dermnetnz.org/topics/angioedema 2. Kolkhir P, et al. *Nat Rev Dis Primers*. 2022;8(1):61. 3. Saini SS, Kaplan AP, *J Allergy Clin Immunol Pract*. 2018;6(4):1097-1106.

CSU affects up to 1% of the United States population[1-4]

Estimated incidence is **0.2% to 0.8%** in the **United States**[1-4]

Global estimated prevalence has been increasing in recent years[5]

Women are affected 2x as often as men[3]

Onset of symptoms is typically between **20 and 40 years of age**[6]

CSU, chronic spontaneous urticaria.

1. Patil D et al. Poster presented at: AAD Annual Meeting, March 25-29, 2022; Boston, MA, USA. Poster 33826. **2.** Riedl MA et al. *Ann Allergy Asthma Immunol.* 2025;134(3):324-332.e4.
3. Wertenteil S et al. *J Am Acad Dermatol.* 2019;81(1):152-156. **4.** Vietri J et al. *Ann Allergy Asthma Immunol.* 2015;115(4):306-311. **5.** Fricke J et al. *Allergy*. 2020;75(2):423-432.
6. Maurer M et al. *Allergy.* 2011;66(3):317-330.

Epidemiology

- Acute urticaria affects up to 20-20% of the overall population
- Chronic urticaria has a lifetime prevalence of 1.8% and will affect up to 1% of the population at any given time
- 40% CU associated with angioedema
- 20% are inducible or physical urticarias
- 80% spontaneous or idiopathic urticaria (prevalence 1% in US, similar in other countries)
- 2:1 predominance in women
- Affects all ages, peaks between 3rd to 5th decades

Patients with CSU experience a prolonged disease journey

01 Symptom onset

Average physicians consulted before diagnosis[1]: **4.6**

02 Diagnosis

Time to diagnosis[1]: **1.6 years**

Average disease duration[2]: **2 to 5 years**

03 Management

Main-treating physicians switched after diagnosis an average of[1]: **2.8 times**

Over **50%** of patients remain symptomatic with first-line H_1-AH therapy[3]

Only **45%** may achieve remission by 5 years[4]

CSU, chronic spontaneous urticaria; H_1-AH, H_1-antihistamine.

1. Bernstein JA et al. Poster presented at: AAAAI/WAO Joint Congress; February 28-March 3, 2025; San Diego, CA, USA. **2.** Saini SS, Kaplan AP. *J Allergy Clin Immunol Pract.* 2018;6(4):1097-1106.
3. Maurer M et al. *Allergy.* 2011;66(3):317-330. **4.** Balp MM et al. *Dermatol Ther (Heidelb)* 2022;12(1):15-27.

CSU can persist for several years

Estimated median disease duration of[1]

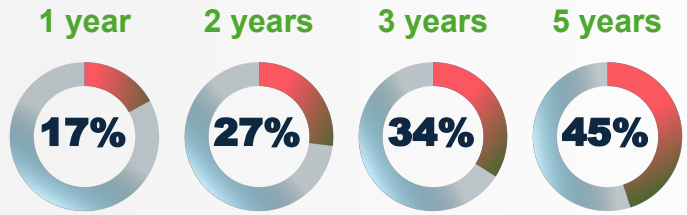
2 to 5 years

Some patients can be affected for **>20 years**[2]

Disease duration is **highly variable**[2]

Symptoms can be **daily** or **almost daily,** or **intermittent/ recurrent**[3]

Spontaneous remission rates[2,*]



Recurrence may occur months or years after full remission in[3,4]

Up to 31%

CSU, chronic spontaneous urticaria.
*Cumulative weighted average estimates.

1. Saini SS, Kaplan AP. *J Allergy Clin Immunol Pract*. 2018;6(4):1097-1106. **2.** Balp MM et al. *Dermatol Ther (Heidelb)* 2022;12(1):15-27. **3.** Zuberbier T et al. *Allergy*. 2022;77(3):734-766.
4. Kolkhir P et al. *Nat Rev Dis Primers*. 2022;8(1):61.

Psychiatric comorbidities are prevalent in patients with CSU[1]

Sleep wake disorders[1-6]

Up to 56%

of patients with CSU experience sleep-wake disorders

Impairments in sleep quality is related to higher rates of anxiety and depression[7]

Mental health

Up to 67%

of patients with CSU experience

ANXIETY[1-6,8-10]

Up to 70%

patients with CSU experience

MOOD DISORDERS[1-6,8-10]

(including depression)

Patients with CSU observed

~3x increased risk

of mortality due to

SUICIDAL IDEATION[11,*]

Frequency of deaths due to suicidal ideations or suicide attempts

CSU: 3.89% (190,713/272,190)

Controls: 1.25% (210,012/12,728,913)

CI, confidence interval; CSU, chronic spontaneous urticaria; HR, hazard ratio.

*Limitations of the study include the retrospective design potentially resulting in underdiagnosis, overdiagnosis, misdiagnosis, uncontrolled confounders such as comorbidities, self-selection, and reverse causality.[11]

1. Konstantinou GN, Konstantinou GN. *Clin Transl Allergy.* 2019;9:42. **2.** Riedl MA et al. *Ann Allergy Asthma Immunol.* 2025;134(3):324-332.e4.
3. Mosnaim G et al. *Ann Allergy Asthma Immunol.* 2025;134(3):315-323.e3. **4.** Balp MM et al. *J Eur Acad Dermatol Venereol.* 2018;32(2):282-290.
5. Mendelson MH et al. *J Dermatolog Treat.* 2017;28(3):229-236. **6.** Vietri J et al. *Ann Allergy Asthma Immunol.* 2015;115(4):306-311. **7.** Sánchez-Díaz M et al. *Int J Environ Res Public Health.* 2023;20(4):3508.
8. Buttgereit T et al. *J Allergy Clin Immunol Pract.* 2023;11(11):3515-3525.e4. **9.** Bitan DT et al. *Arch Dermatol Res.* 2021;313(1):33-39. **10.** Balp MM et al. *JEADV Clin Pract.* 2024;3(2):508-520.
11. Kolkhir P et al. *J Allergy Clin Immunol.* 2025;155(4):1290-1298.

Your next patient…

- 42 year-old woman presents with daily itchy wheals for 5 months
- Individual lesions disappear within 12 hours
- New lesions develop daily
- Lip swelling twice a month
- ANA ordered by PCP

What is your next step?

Most Visits Can Be Organized Around 4 Questions

- Is this urticaria or a mimicker?
- What kind of urticaria?
- Do I need additional workup?
- How do I treat?

Kanani et al. Allergy Asthma Clin Immunology 2018

Questions to ask in the history

- How long does each wheal last?
- Is it itchy, painful or burning?
- Any swelling or angioedema (lips, tongue, GI symptoms)?
- Any triggers, such as pressure, cold, heat or exercise?
- Taking any medications (NSAIDs, ACE inhibitors, opioids?)
- Any joint symptoms, weight loss or fever?
- Personal or family history of thyroid or autoimmune disease?

Classification of Urticaria

Rule out vasculitis first

- Fixed lesions or lesions >48 hours raise concern for urticarial vasculitis

Classify by timing

- Chronic urticaria symptoms last longer than 6 weeks

Look for Definite Triggers

- Determine if symptoms occur spontaneously or are reproducibly trigger-induced

If angioedema predominates

- Consider other forms of angioedema, especially when wheals are absent

What to look for in the physical exam

- Migratory, blanchable, edematous wheals
- Brown macules with Darier sign (consider Mastocytosis)
- Dermographism present
- Angioedema without wheals (consider HAE)

RED FLAG

- Any lesion lasting more than 24 hours
- Bruising, purpura or residual discoloration

Urticaria Mimickers

- Urticarial vasculitis
- Bullous pemphigoid (prebullous stage)
- Adult-onset Still's disease (AOSD)
- Eosinophilic Dermatosis of Hematologic Malignancy (EDIHM)
- Hypereosinophilic Syndrome (HES)
- Mast cell activation syndrome (MCAS)
- Bradykinin-mediated angioedema (HAE)
- Exercise-induced anaphylaxis
- Cryopyrin-associated periodic syndrome (CAPS)
- Schnitzler's syndrome (recurrent urticarial rash and monoclonal gammopathy, recurrent fever attacks, bone and muscle pain, arthralgia, or arthritis and lymphadenopathy)
- Gleich's syndrome (episodic angioedema with eosinophilia)
- Well's syndrome (granulomatous dermatitis with eosinophilia/eosinophilic cellulitis)

Laboratory testing has limited benefits in CSU

The number of performed laboratory tests did not correlate with the number of identified diagnoses in a systemic review of 6462 patients with chronic urticaria[1]

There is limited value to laboratory testing beyond the guideline recommendations unless prompted by patient history and/or physical examination[2]

<1%

of laboratory tests improve clinical outcomes[3-5]

- Screening tests are not cost-effective

~$570

Average cost per patient[3,4]

CSU, chronic spontaneous urticaria.

1. Kozel MMA et al. *J Am Acad Dermatol.* 2003;48(3):409-416. **2.** Maurer M et al. *Adv Ther.* 2024;41(1):14-33. **3.** Shaker M et al. *J Allergy Clin Immunol.* 2020:8(7):2360-2369. **4.** Carrillo-Martin I et al. *J Allergy Clin Immunol Pract.* 2019;7(8):2823-2832. **5.** Tarbox JA et al. *Ann Allergy Asthma Immunol.* 2011;107:239-243.

Workup (uncomplicated CSU)

- CBC with differential (screens for eosinophilia, infection, marrow disease)
- CRP or ESR (if elevated raise concern for vasculitis or autoinflammation)
- Total IgE (Low IgE predicts poor omalizumab response; very high may suggest atopy and guide treatment)
- TSH +/- anti TPO (screens for autoimmune thyroid disease with is common in CSU)

Workup (only when red flags are present)

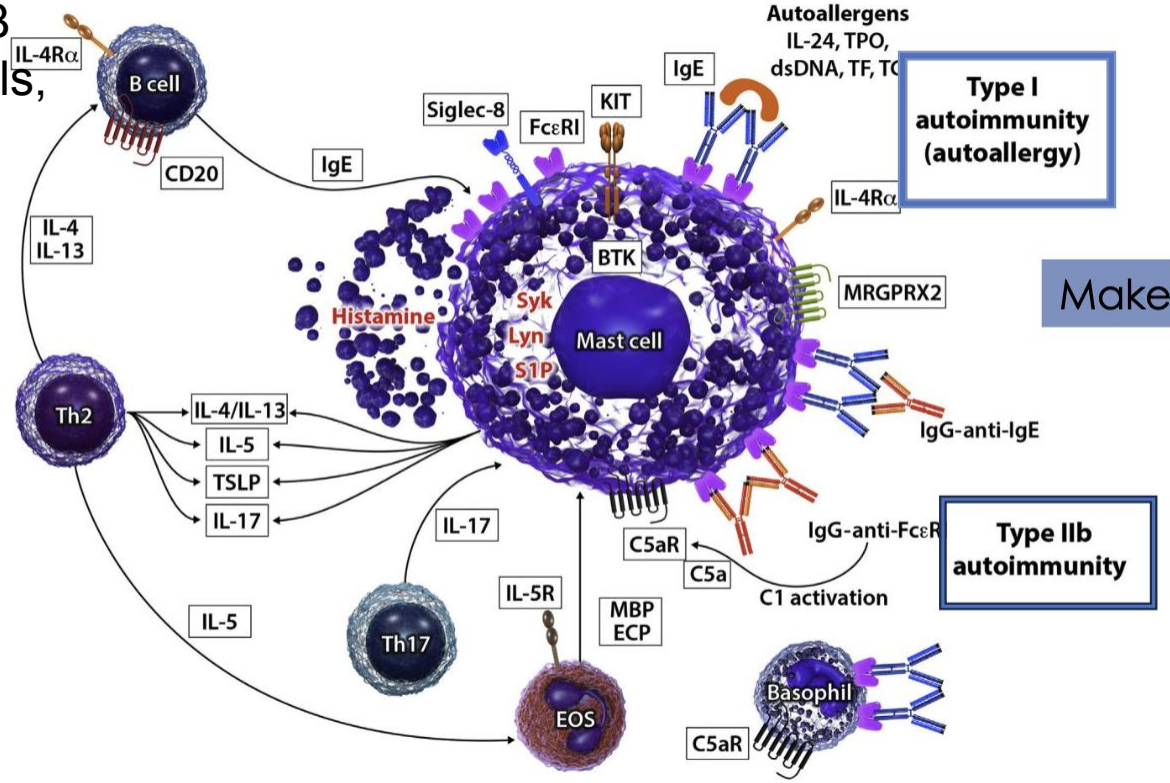
- Skin biopsy (when wheals last greater than 24 hours, bruise or scar)
- C4, C1-INH (level + function)
  - Recurrent angioedema without urticaria
- Serum tryptase
  - Anaphylaxis, flushing or fixed pigmented lesions
- ANA, complement, Urinalysis
  - Vasculitis suspected
- SPEP
  - Consider SPEP if Schnitzler features (nonpruritic or burning urticaria, fever, bone pain, arthralgias)

Allergy testing?

- Resist the broad allergy panel. Food-IgE testing in CSU mostly creates false positives and unnecessarily restrictive diets.

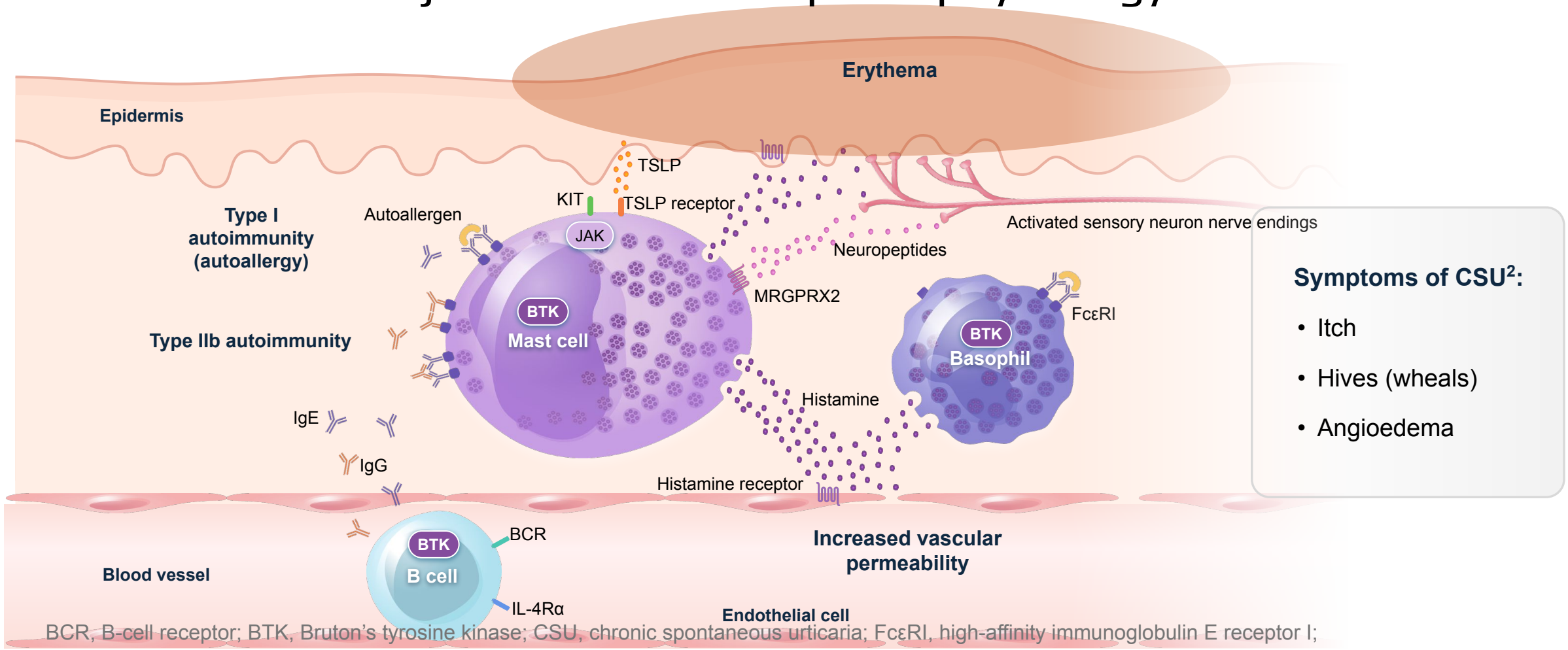
Urticaria is a MAST CELL Driven Disorder

- But the triggers that activate mast cells are heterogenous, diverse, and vary from patient to patient
- Non-mast cell players include: T cells, B cells, Eosinophils, Basophils, Neutrophils, Macrophages, Sensory nerves



Make up >50% of cases

Mast cells are major drivers of CSU pathophysiology[1-3]



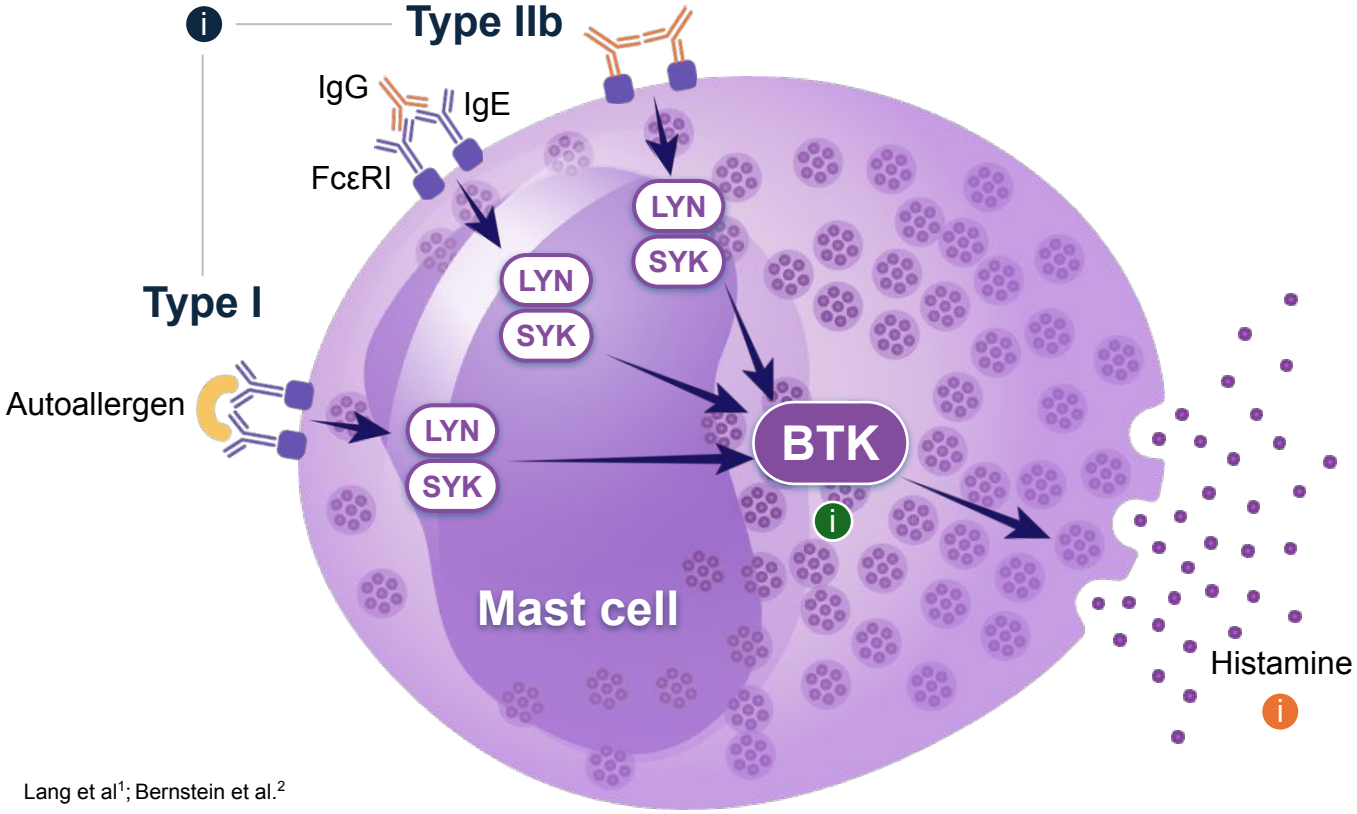
Symptoms of CSU[2]:

- Itch
- Hives (wheals)
- Angioedema

BCR, B-cell receptor; BTK, Bruton's tyrosine kinase; CSU, chronic spontaneous urticaria; FcεRI, high-affinity immunoglobulin E receptor I; Ig, immunoglobulin; IL-4Rα, interleukin-4 receptor alpha; JAK, Janus kinase; KIT, receptor tyrosine kinase; MRGPRX2, Mas-related G protein–coupled receptor X2; TSLP, thymic stromal lymphopoietin.

1. Bernstein JA et al. *J Allergy Clin Immunol.* 2024;153(5):1229-1240. **2.** Kolkhir P et al. *Nat Rev Dis Primers.* 2022;8(1):61. **3.** Kolkhir P et al. *JAMA.* 2024;332(17):1464-1477.

BTK phosphorylation and FcεRI crosslinking are involved in mast cell activation



Lang et al[1]; Bernstein et al.[2]

Two autoimmune endotypes of CSU have been identified **(Type I and Type IIb),** which involve crosslinking of FcεRI[1]

Bruton's tyrosine kinase (BTK) is a component of the complex network of cytoplasmic signaling proteins **downstream of FcεRI**[2]

BTK phosphorylates downstream targets to induce **mast cell activation and degranulation**[2]

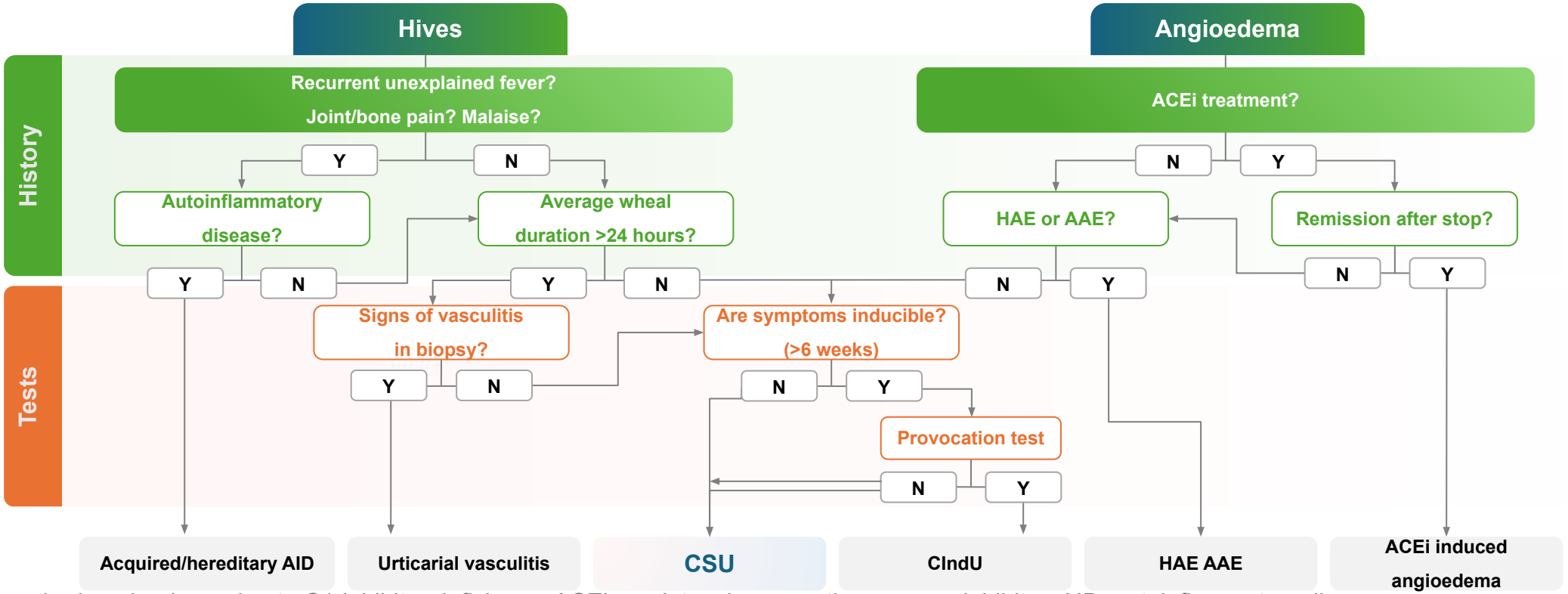
BTK and **FcεRI** play key roles in inducing mast cell activation and degranulation[3]

CSU, chronic spontaneous urticaria; FcεRI, high-affinity immunoglobulin E receptor; Ig, immunoglobulin; LYN, Lck/Yes- related novel tyrosine kinase; SYK, spleen tyrosine kinase.

1. Lang et al. *Ann Allergy Asthma Immunol.* 2025;134(4):408-417.e3. **2.** Bernstein JA et al. *J Allergy Clin Immunol.* 2024;153(5):1229-1240. **3.** Segú-Vergés C et al. *J Allergy Clin Immunol.* 2023;151(4):1005-1014.

Diagnostic algorithm for CSU

International (**EAACI/GA²LEN/EuroGuiDerm/APAAACI**) Guidelines



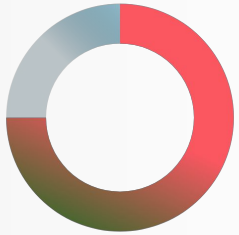
AAE, acquired angioedema due to C1-inhibitor deficiency; ACEi, angiotensin-converting enzyme inhibitor; AID, autoinflammatory disease; APAAACI, Asia Pacific Association of Allergy, Asthma and Clinical Immunology; CIndU, chronic inducible urticaria; CSU, chronic spontaneous urticaria;
EAACI, European Academy of Allergy and Clinical Immunology; GA^{2}LEN, Global Allergy and Asthma European Network; HAE, hereditary angioedema.

Zuberbier T et al. *Allergy*. 2022;77(3):734-766.

Corticosteroids are used frequently in patients with CSU despite guidance as rescue medication only

Up to

75%



of patients with CSU reported use of oral corticosteroids following diagnosis[1-3]

Corticosteroid use is associated with higher health care costs due to side effects[4]

Adverse events associated with short-term (5–30 days) oral corticosteroid use[5,*]

5.3x increased risk of **sepsis**

IRR (95% CI): 5.30 (3.80–7.41)

3.3x increased risk of **VTE**

IRR (95% CI): 3.33 (2.78–3.99)

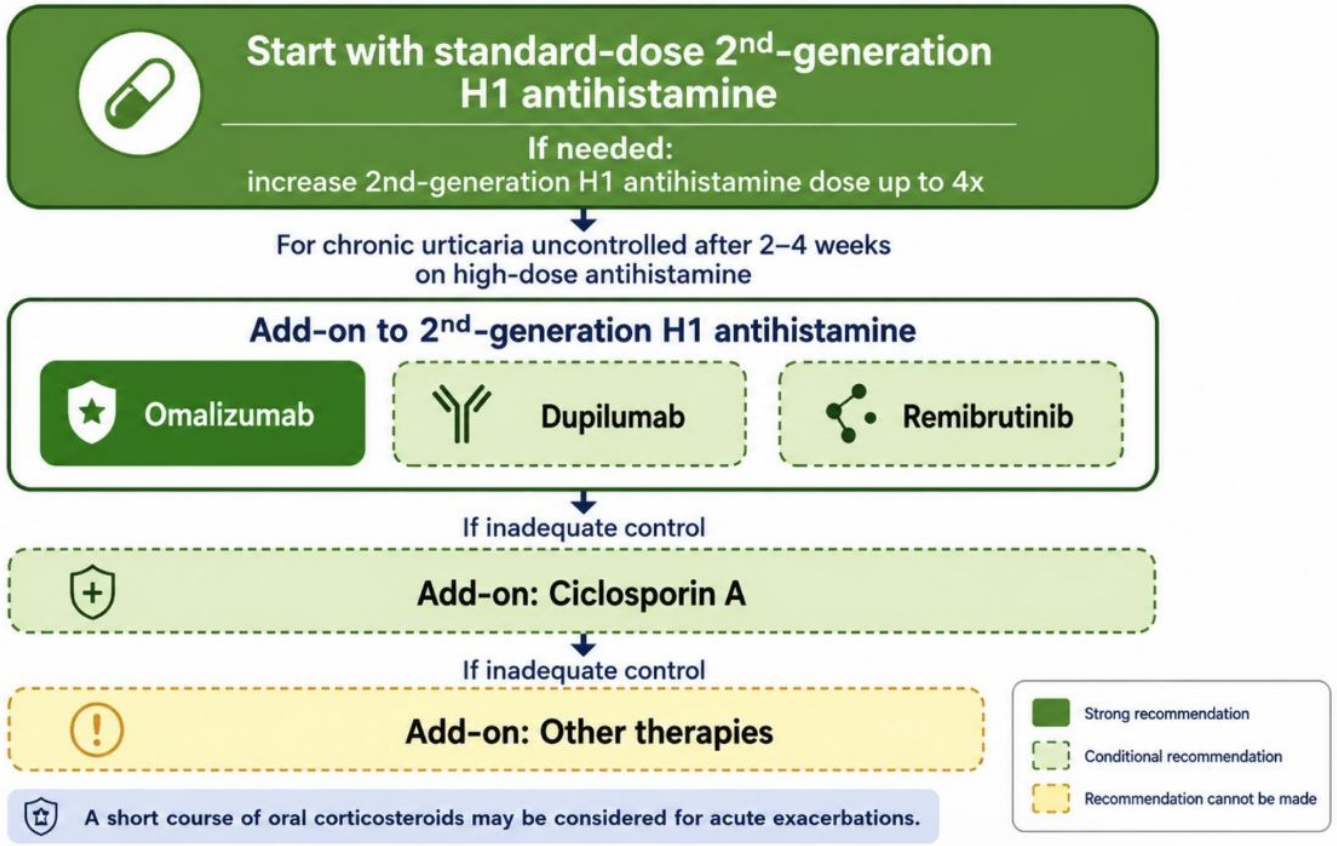
1.9x increased risk of **fracture**

IRR (95% CI): 1.87 (1.69–2.07)

CI, confidence interval; CSU, chronic spontaneous urticaria; IRR, incidence rate ratio; VTE, venous thromboembolism.
*Based on a median of 6 days using oral corticosteroids. Incidence rates were significantly higher in short-term vs non-users of oral corticosteroids (*P*<.001 for all).

1. Riedl MA et al. *Ann Allergy Asthma Immunol.* 2025;134(3):324-332.e4. **2.** Broder MS et al. *Am J Clin Dermatol.* 2015;16(4):313-321. **3.** Soong W et al. *World Allergy Organ J.* 2023;16(12):100843. **4.** Ledford D et al. *Allergy Asthma Proc.* 2016;37(6):458-465. **5.** Waljee AK et al. *BMJ.* 2017;357:j1415.

Updated 2026 Guidelines



Zuberbier T, et al. *Allergy*. 2026;1–51.

Second generation H1 Antihistamines

Agent	Minimum Age of Indication (US)	Sedation Potential	Practical Safety Notes
Cetirizine	≥ 6 months	Higher (more sedating)	• Effective and commonly used; may cause more sedation than some other second-generation agents
Levocetirizine	≥ 6 months	Higher (more sedating)	• Similar to cetirizine; somnolence/ fatigue can occur
Fexofenadine	≥ 6 months (suspension); tablets depend on formulation	Low (least sedating)	• Generally considered least sedating; favorable daytime tolerability
Desloratadine	≥ 6 months	Low (low sedation burden)	• Usually well tolerated; low sedation burden
Loratadine	≥ 2 years in older Rx labeling; OTC self-use often starts at ≥ 6 years	Low (low sedation burden)	• Generally well tolerated; low sedation burden

SEDATION POTENTIAL (color key)

- Higher — More likely to cause drowsiness
- Moderate — Some drowsiness possible
- Low — Least likely to cause drowsiness

MINIMUM AGE (color key)

- ≥ 6 months
- ≥ 2 years

KEY TAKEAWAY

Second-generation antihistamines are preferred over first-generation agents due to better tolerability and less cognitive/sedating burden.

Urticaria Activity Score over 7 days (UAS7)

0	Urticaria-free
1–6	Well controlled
7–15	Mild urticaria
16–27	Moderate
28–42	Severe

Daily scoring

HSS = Hives severity score	
0	None
1	**Mild** (<20 wheals/24 h)
2	**Moderate** (20–50 wheals/24 h)
3	**Intense** (>50 wheals/24 h or large confluent areas)

ISS = Itch severity score	
0	None
1	**Mild** (present but not troublesome)
2	**Moderate** (troublesome, no interference with daily activity or sleep)
3	**Intense** (interferes with daily activity or sleep)

Daily UAS = HSS (0–3) + ISS (0–3) = 0–6

UAS7 = sum of 7 daily scores = 0–42

2 questions/day | 7 days | 0–42 points

Zuberbier T, et al. *Allergy*. 2022

Urticaria Control Test (UCT)

UCT = 16
Complete control
Consider step-down

UCT = 12–15
Well controlled
Continue / optimize

UCT < 12
Uncontrolled
Step up therapy

Over the last 4 weeks...

1 How much have you suffered from the **physical symptoms** of urticaria (itch, hives, swelling)?				
0 Very much	1 Much	2 Somewhat	3 A little	4 Not at all
2 How much has your **quality of life** been affected by urticaria?				
0 Very much	1 Much	2 Somewhat	3 A little	4 Not at all
3 How often was the **treatment** for your urticaria in the last 4 weeks **not enough** to control your symptoms?				
0 Very often	1 Often	2 Sometimes	3 Seldom	4 Not at all
4 Overall, how well have you had your urticaria **under control** in the last 4 weeks?				
0 Not at all	1 A little	2 Somewhat	3 Well	4 Very well
TOTAL UCT SCORE (0–16)				

4 questions • 0–16 points • Last 4 weeks

Score 16 = complete control
< 12 = poorly controlled

Zuberbier T, et al. *Allergy*. 2022.

CSU pearls

- Only allow 2-4 weeks of up-dosed AH before moving on to other therapy
- Fexofenadine will likely induce less somnolence than cetirizine when up-dosing.
- No one sgAH has been shown to be significantly better than another
- Remind your pt that CSU is NOT caused by allergy
- Some things can exacerbate CSU: heat, stress, exercise, NSAIDS, tight clothing
- If your pat does not improve all all with appropriate therapy, may need to consider another diagnosis

CSU pearls

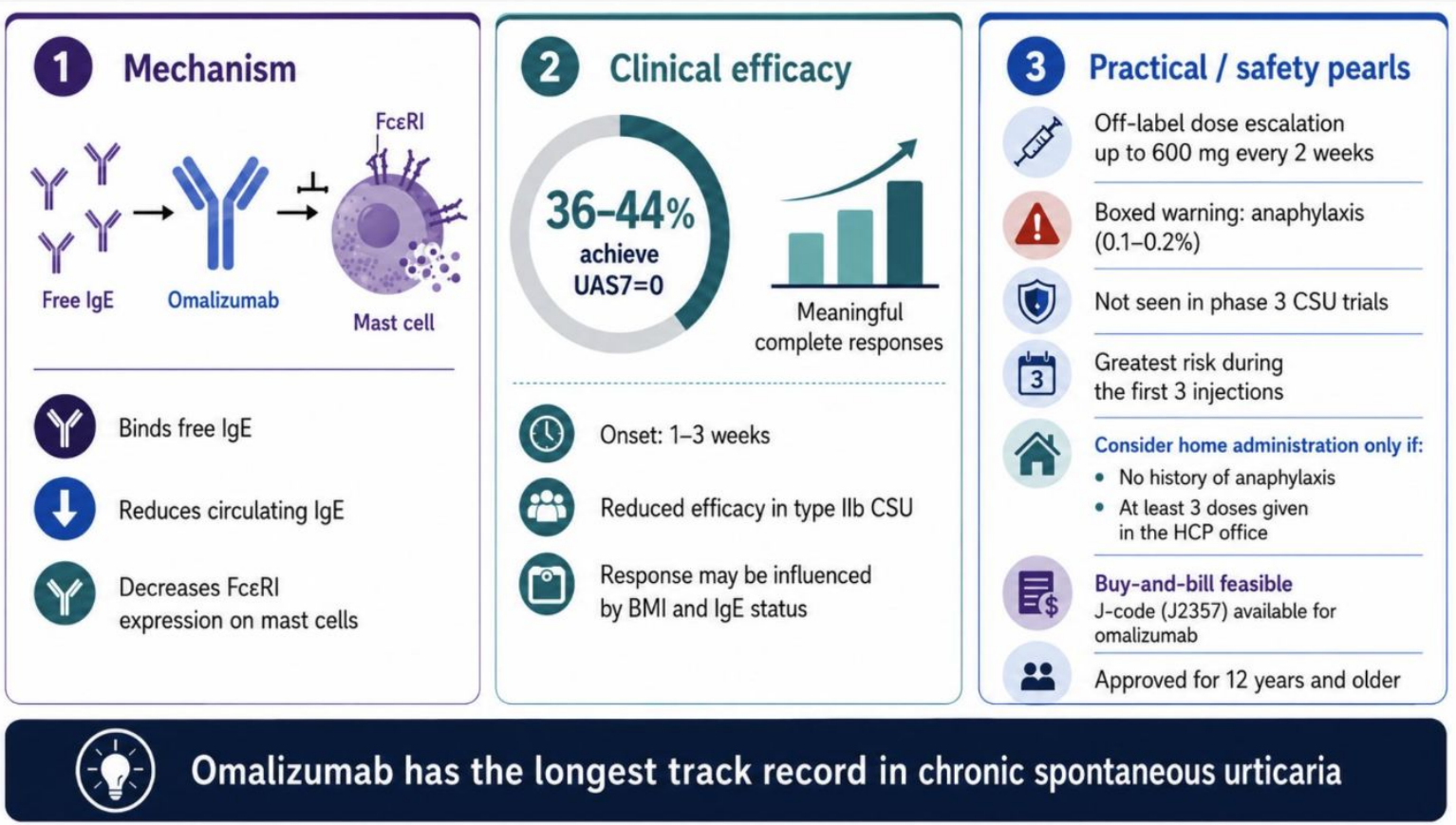
- When moving up the treatment ladder, do NOT stop the AH (at least not right away)
- If you pt is completely clear- continue treatment for 6-12 months before tapering slowly off to look for remission

Patient Reported Disease Control in Patients Receiving Up dosing of AH

- Outcomes following up-dosing
  - 72% partial improvement
  - 16% complete improvement
  - 12% no improvement

- Side effects following up-dosing
  - 51% no new side effects
  - 40% more drowsiness
  - 9% other new side effects

Omalizumab: Anti-IgE Monoclonal Antibody

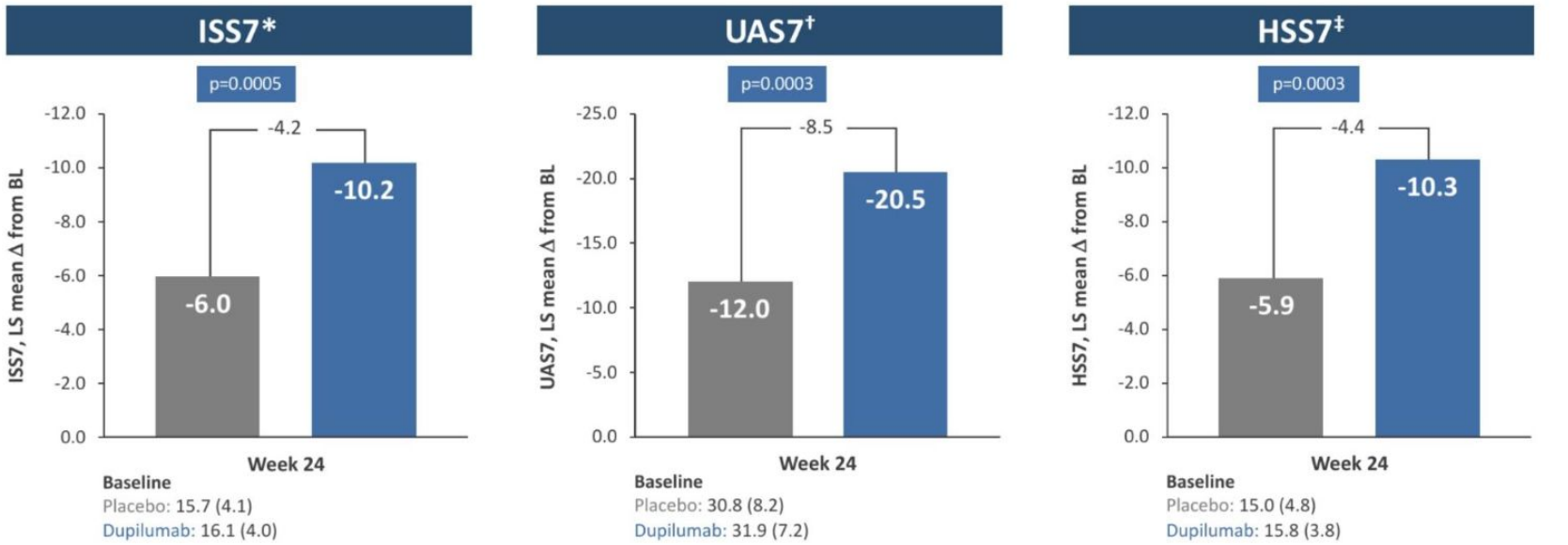


Dupilumab for CSU- Approved April 2025

- Approved in adolescents 12-17 and in adults
- Adult dosing 600 mg loading dose, then 300 mg q2 weeks
- Liberty-Cupid Study C: At 24 weeks, 41% of pts had well controlled disease and 30% had complete remission
  - Safety Summary: Overall TEAEs reported in greater than or equal to 5% of pats in any tx group were comparable for placebo and dupilumab.

Dupilumab: LIBERTY-CSU CUPID Study A (anti-IgE Naïve)

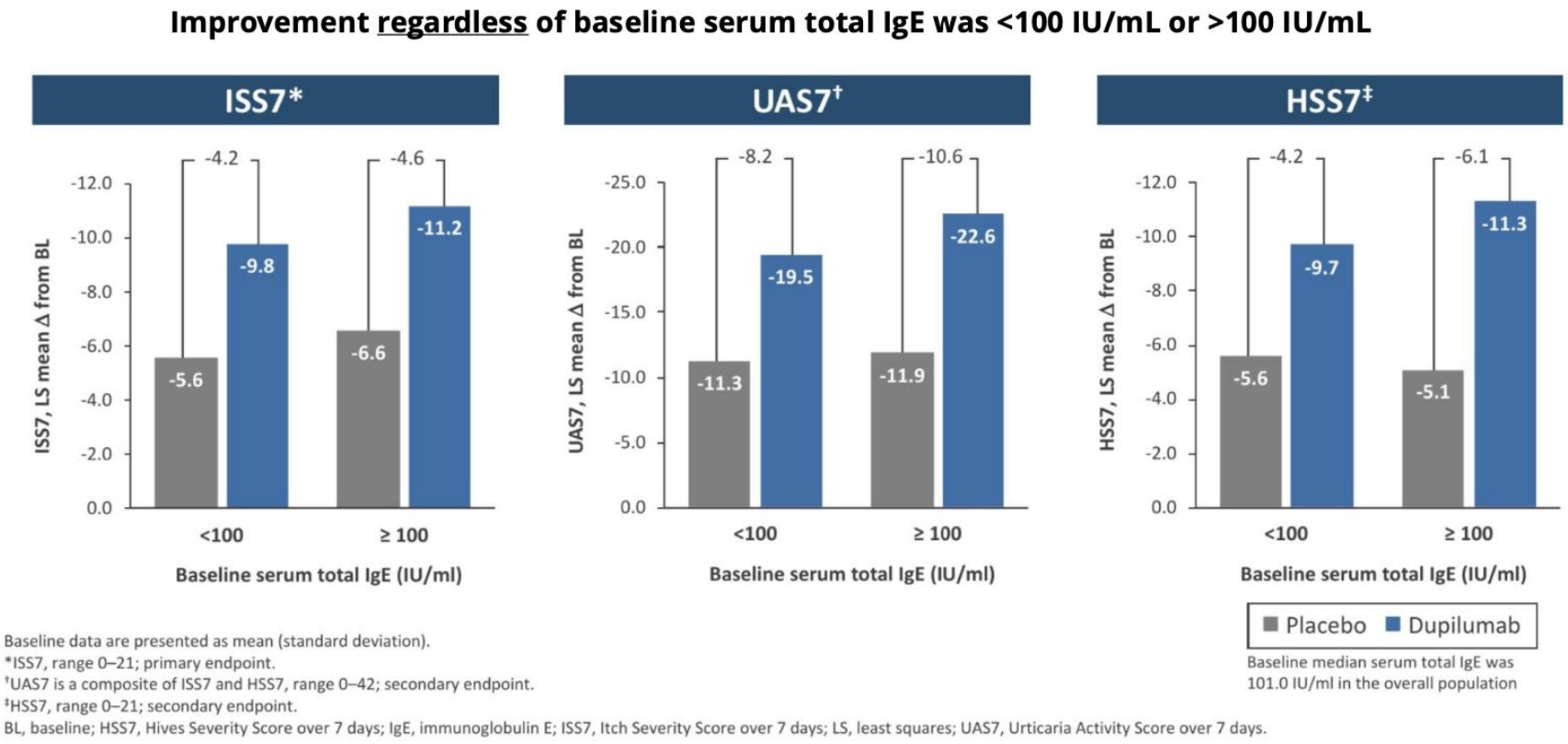
Itch Severity Score over 7 days (ISS7), Urticaria Activity Score summed over 7 days (UAS7), and Weekly Hives Severity Score, (HSS7)



Baseline data are presented as mean (standard deviation).
*ISS7, range 0–21; primary endpoint.
†UAS7 is a composite of ISS7 and HSS7, range 0–42; secondary endpoint.
‡HSS7, range 0–21; secondary endpoint.
BL, baseline; HSS7, Hives Severity Score over 7 days; ISS7, Itch Severity Score over 7 days; LS, least squares; UAS7, Urticaria Activity Score over 7 days.

Casale TB, et al. Presented at 2022 Annual Scientific Meeting of Advancing Allergy and immunology. November 10-14, 2022. Louisville, KY.

Dupixent: LIBERTY-CSU CUPID Study A Based on IgE Level

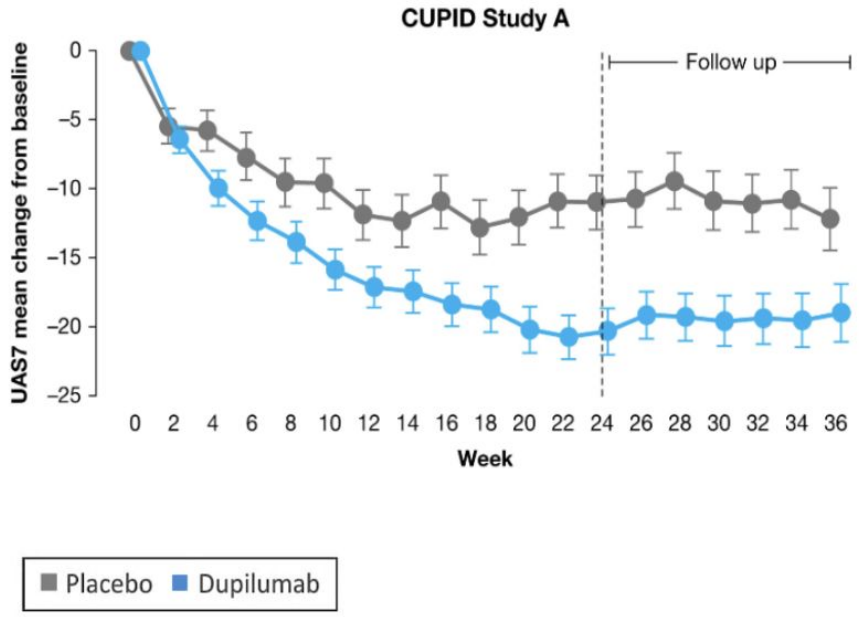


Baseline data are presented as mean (standard deviation).
*ISS7, range 0–21; primary endpoint.
†UAS7 is a composite of ISS7 and HSS7, range 0–42; secondary endpoint.
‡HSS7, range 0–21; secondary endpoint.
BL, baseline; HSS7, Hives Severity Score over 7 days; IgE, immunoglobulin E; ISS7, Itch Severity Score over 7 days; LS, least squares; UAS7, Urticaria Activity Score over 7 days.

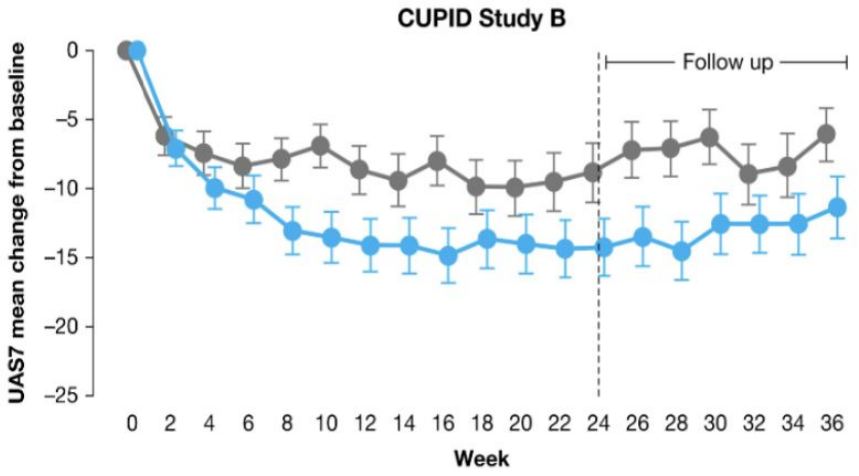
Casale TB, et al. Presented at 2022 Annual Scientific Meeting of Advancing Allergy and immunology. November 10-14, 2022. Louisville, KY.

Dupilumab: LIBERTY-CSU CUPID A/B Through Week 36

Omalizumab-naive



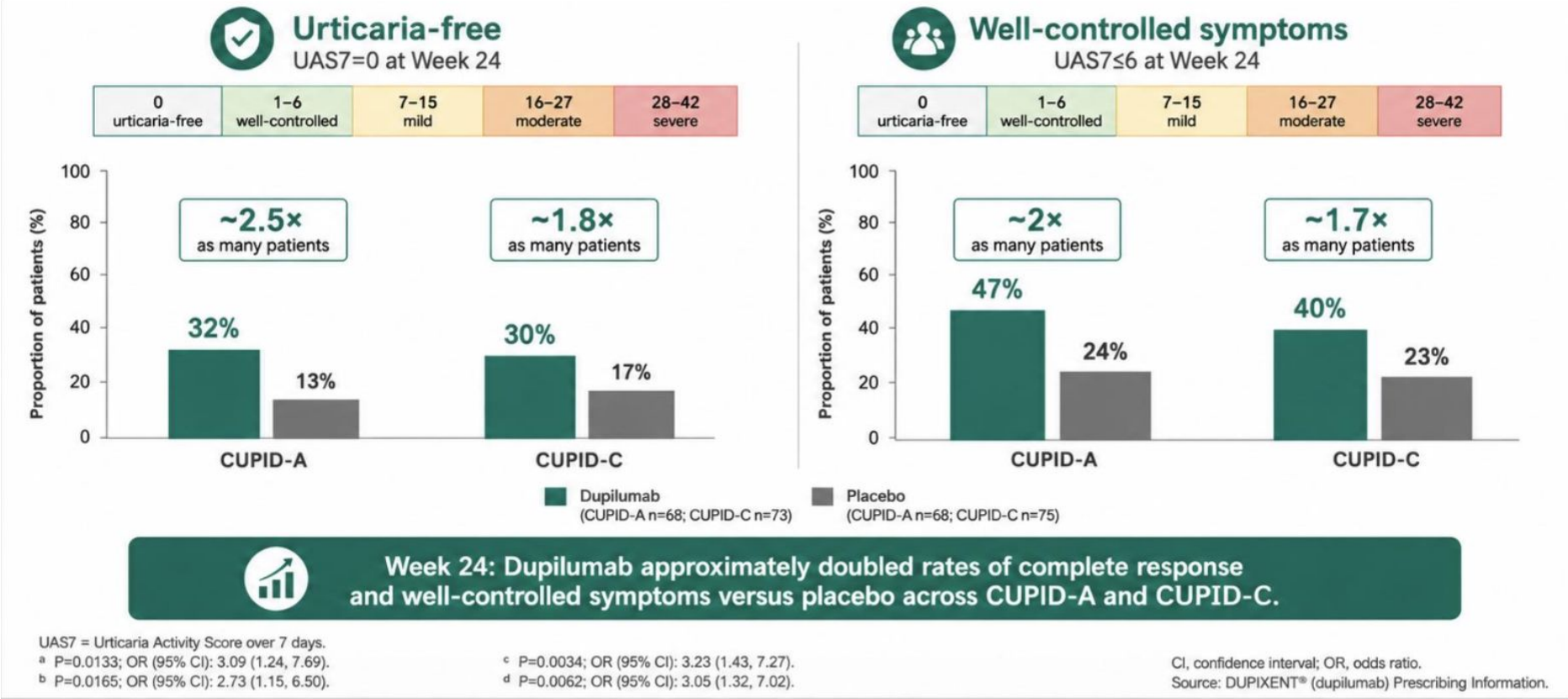
Omalizumab non-responders



UAS marginally significant
ISS not significant

Maurer M, et al. *J Allergy Clin Immunol.* 2024;154(1):184-194.

More Patients Achieved Complete or Well-Controlled Symptoms on Dupilumab



UAS7 = Urticaria Activity Score over 7 days.

[a] P=0.0133; OR (95% CI): 3.09 (1.24, 7.69).

[b] P=0.0165; OR (95% CI): 2.73 (1.15, 6.50).

[c] P=0.0034; OR (95% CI): 3.23 (1.43, 7.27).

[d] P=0.0062; OR (95% CI): 3.05 (1.32, 7.02).

CI, confidence interval; OR, odds ratio.

Source: DUPIXENT® (dupilumab) Prescribing Information.

Remibrutinib- Approved September 2025

- Approved for Adult pts with CSU who have inadequate response to H1-antihistamines
- Oral medication – 25 mg BID
- Highly selective BTK inhibitor that inhibits the release of histamine by blocking mast cell and basophil degranulation
- Nearly half of the pts in the trial were completely symptoms free (UAS7=0) by week 52
- Safety: bleeding- mucocutaneous bleeding in 9% of pts- petechiae being the most common symptoms

Remibrutinib Safety Over 24 weeks

	Remibrutinib (n=58)	Placebo (n=57)
Median exposure, weeks	**24.0**	**24.0**
Any AEs, % (n)	**67.2 (39)**	**66.7 (38)**
Mild	39.7 (23)	43.9 (25)
Moderate	27.6 (16)	21.1 (12)
Severe	0	1.8 (1)[a]
Serious or other significant events, % (n)		
Serious AEs	0	3.5 (2)[b]
Treatment discontinuation due to AE(s)	3.4 (2)[c]	0
Treatment discontinuations due to SAE(s)	0	0
Deaths	0	0

Most Common AEs (≥5% Patients)

	Remibrutinib (n=58)	Placebo (n=57)
Nasopharyngitis	13.8 (8)	8.8 (5)
Headache	12.1 (7)	7.0 (4)
Upper respiratory tract infection	6.9 (4)	5.3 (3)
Nausea	5.2 (3)	0
Petechiae	**5.2 (3)**	**1.8 (1)**
Diarrhea	0	5.3 (3)

Select Safety Topics

Infection AEs, % (n)[d]	**37.9 (22)**	**28.1 (16)**
Nasopharyngitis	13.8 (8)	8.8 (5)
Upper respiratory tract infection	6.9 (4)	5.3 (3)
Gastroenteritis	3.4 (2)	1.8 (1)
COVID-19	3.4 (2)	1.8 (1)
Conjunctivitis	3.4 (2)	0
Herpes zoster	0	3.5 (2)
Cytopenia AEs, % (n)	**3.4 (2)**	**3.5 (2)**
Newly occurring liver enzyme abnormalities eALT or AST >3× ULN, n/N	**0/57[e]**	**0/57**

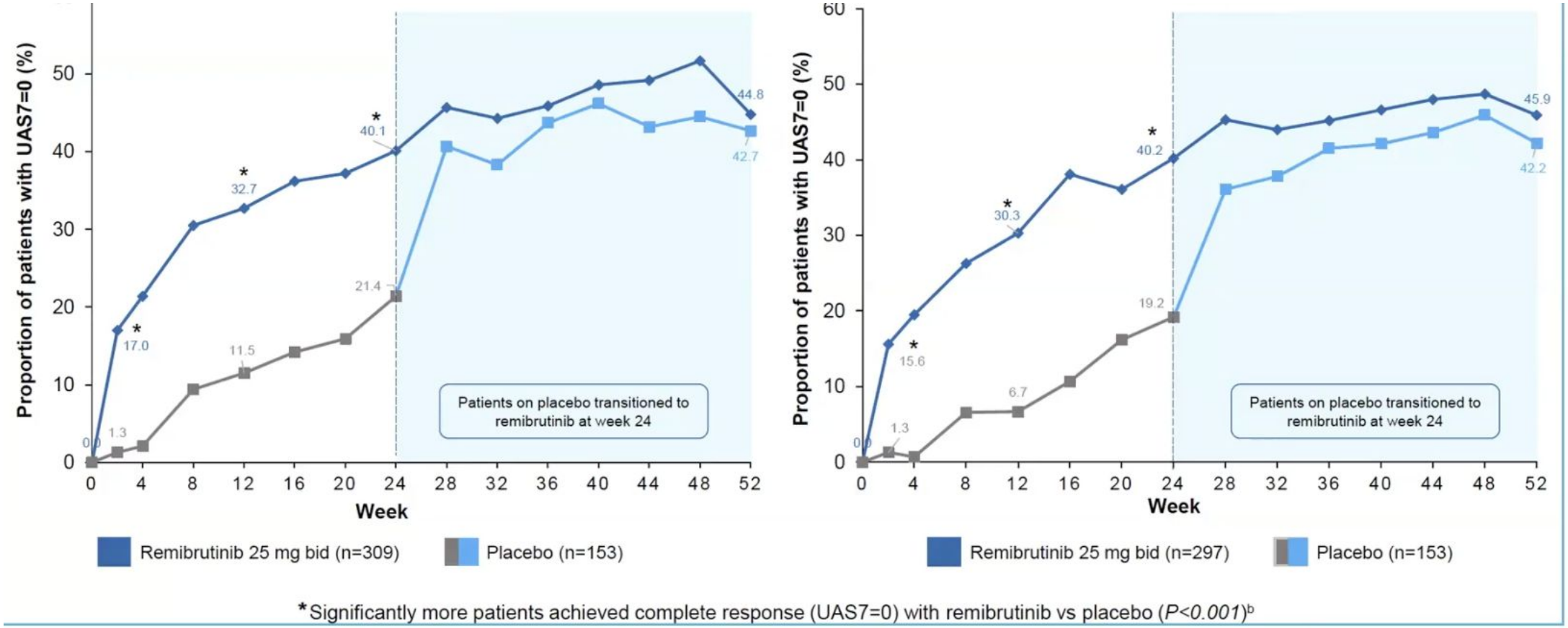
- Overall incidence of AEs was comparable between remibrutinib and placebo; AEs with remibrutinib were all mild or moderate.
- No SAEs occurred with remibrutinib; 2 SAEs (food poisoning and pneumonia) were reported with placebo.
- Petechiae occurred in 5.2% of patients with remibrutinib and 1.8% with placebo (all events were mild).

AE, adverse event; SAE, serious adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal.

[a] Migraine. [b] Food poisoning and pneumonia in 1 patient each. [c] Syncope and urticaria reported in 1 patient each. [d] Safety set. [e] 1 patient in the remibrutinib arm had elevated ALT that was not included.

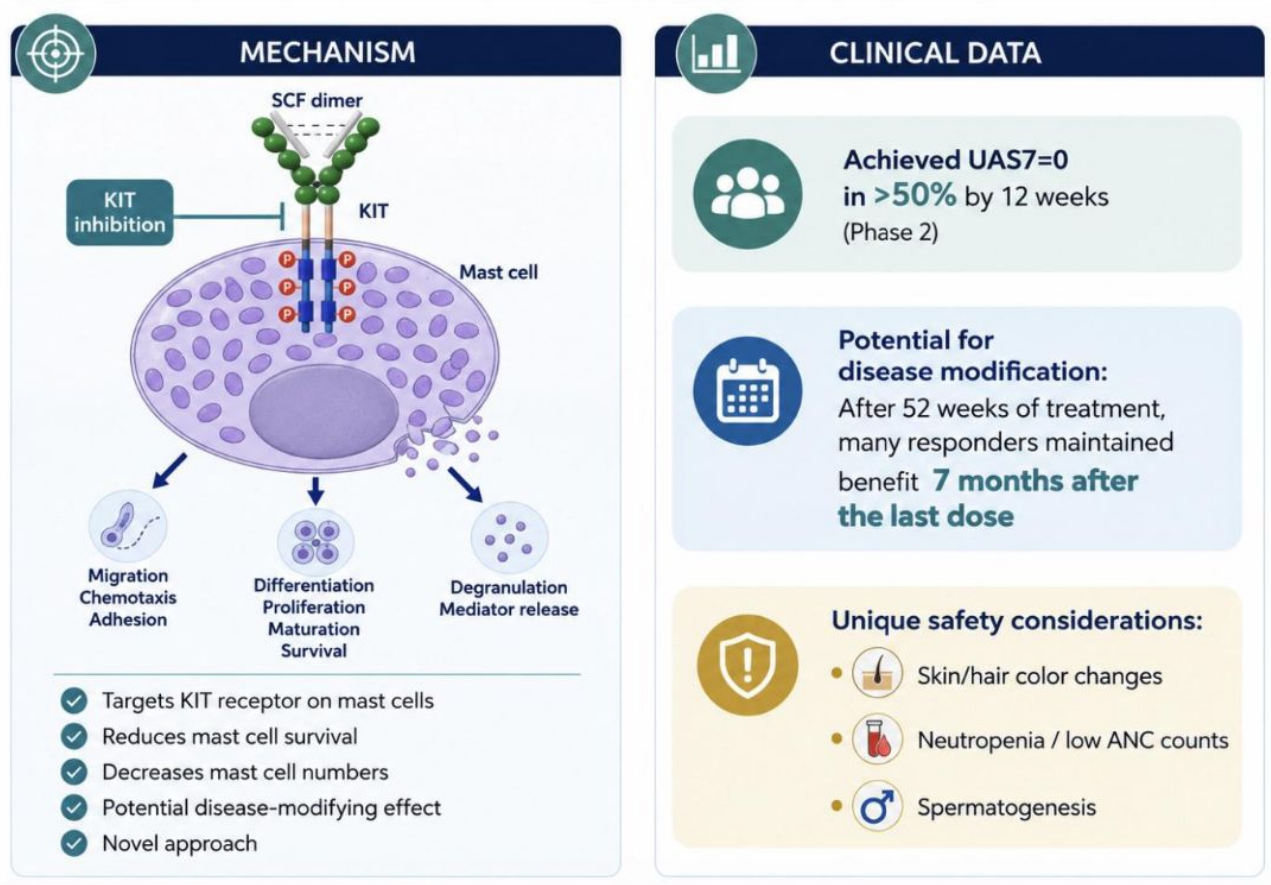
Türk M, et al. *Asia Pac Allergy.* 2026;16(2):107–122.

REMIX-1: Complete Response (USA7=0) Observed Early and Sustained to Week 52



*Significantly more patients achieved complete response (UAS7=0) with remibrutinib vs placebo (*P*<0.001)[b]

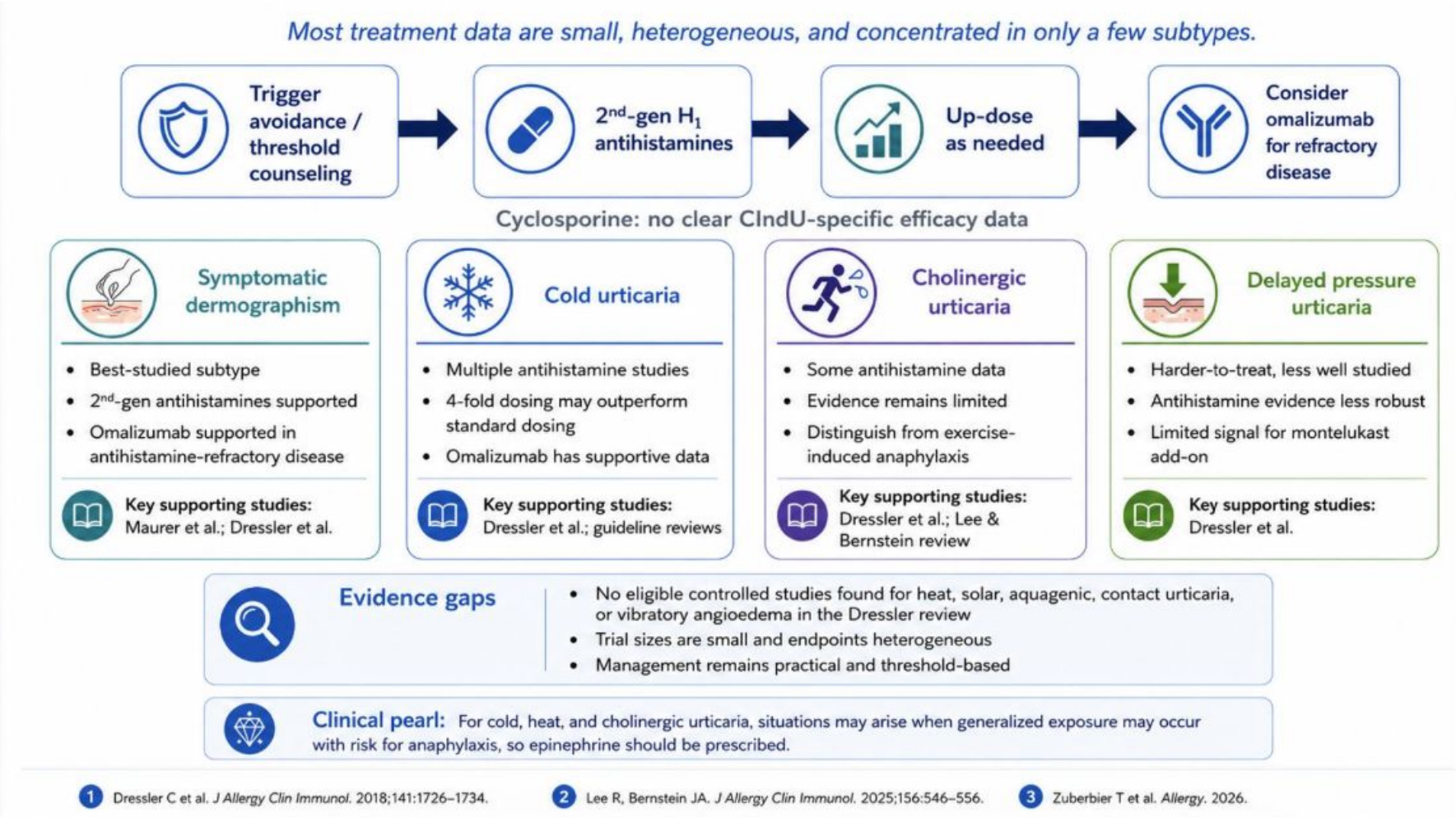
Barzolvolimab: Anti-KIT (Mast Cell Modulation)



Chronic Inducible Urticaria (CIndU)

- The Other Form of Chronic Urticaria
  - Dermatographism
  - Cholinergic
  - Cold
  - Solar
  - Aquagenic
  - Exercise
  - Delayed Pressure

Limited Treatment Evidence for CIndU



Remibrutinib Demonstrated Superior Efficacy vs Placebo With a Favorable Safety Profile in Patients With Symptomatic Dermographism in the Phase 3 RemIND Study

Giselle Mosnaim, Ana Maria Giménez-Arnau, Lindsey Finklea, Koremasa Hayama, Michihiro Hide, Johannes S Kern, Moisés Labrador-Horrillo, Philip H Li, Heike Rockmann, Sarbjit Saini, Sebastian Volc, Jinhua Xu, Bin Yang, Alis Burciu, Li Chen, Clarice Field, Sibylle Haemmerle, Karine Lheritier, Miriam Porter, Martin Metz

Summary

- Chronic Urticaria: >6 weeks of recurrent wheals or angioedema with individual lesions resolving in <24 hours
- Inducible?
- Minimal workup: CBC, CRP/ESR, IgE, TSH +/- anti-TPO
- New updated guidelines
  - 2^{nd}-gen H1 – up-dose- Omalizumab, Dupilumab, Remibrutinib
- Recent data shows promising results for remibrutinib in CindU

Thank you!

Questions?

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