



Editorial

Update on skin diseases

Urticaria, angioedema, and other skin disorders from the 2022 American College of Allergy, Asthma, and Immunology Annual Literature Review



Recent articles on allergic skin conditions indicate ongoing progress in the understanding of these conditions and advances in management strategies. These articles include studies with very practical and immediate application to the clinical management of patients, in addition to data on emerging therapeutic options. Starting with urticaria, De et al¹ conducted a study to evaluate the readability, quality, and timeliness of online patient educational content for urticaria. Of 35 websites analyzed, none scored “excellent,” and only 5 scored “good” using validated quality assessment instruments. The average readability grade level was 10.9, with only 4 sites below the ninth grade level. This shows that many online patient educational resources for urticaria are poor because of difficult readability and a lack of updated information, with improved online resources needed. Bizjak et al² published a multisite observational study on cold urticaria and investigated risk factors for cold-induced anaphylaxis, an associated life-threatening complication in a subset of patients. Of the 412 patients with confirmed cold urticaria, 37% had cold-induced anaphylaxis. Independent clinical risk factors for cold-induced anaphylaxis were a history of angioedema, oropharyngeal or laryngeal symptoms, itchy earlobes, concomitant asthma, or a previous systemic reaction to Hymenoptera sting. Self-injected epinephrine is recommended for patients with cold urticaria and any of these clinical findings or a history of cold-induced anaphylaxis. A study of laboratory biomarkers for autoimmune spontaneous chronic urticaria by Kolchir et al³ investigated data from 4 study sites and found that a combination of elevated anti-thyroid-peroxidase antibody levels (>34 kU/L) and low total immunoglobulin E levels (<40 IU/mL) strongly correlated with other, less available diagnostic markers of autoimmune chronic urticaria (ie, autologous serum skin testing, basophil activation assays, eosinopenia, basopenia). Patients with this laboratory biomarker profile were much more likely to be resistant to standard doses of second-generation antihistamines. Metz et al⁴ reported data from a phase 2 clinical study investigating the efficacy of fenebrutinib, an oral, potent, highly selective, reversible Bruton’s tyrosine kinase inhibitor, for the treatment of chronic urticaria. This 8-week treatment study showed significant improvements in Urticaria Activity Score summed over 7 days and in itch scores, including a subset of patients with evidence of autoimmune chronic urticaria, supporting fenebrutinib as a potentially beneficial future treatment for chronic spontaneous

urticaria. Study data on investigational therapies for hereditary angioedema (HAE) continue to emerge. Craig et al⁵ published phase 2 study data on garadacimab, a monoclonal antibody targeting Factor XIIIa for HAE prophylactic treatment. Subcutaneous dosing of garadacimab every 4 weeks over a 12-week period decreased the median number of monthly attacks by more than 90% compared with placebo. Results of a clinical study of donidalorsen, an antisense oligonucleotide targeting plasma prekallikrein for prophylactic treatment of HAE, were published by Fijen et al.⁶ This study indicated that subcutaneous dosing of donidalorsen every 4 weeks reduced the mean monthly HAE attack rate by 90% over 16 weeks of treatment. In the area of atopic dermatitis, Ryczaj et al⁷ investigated the prevalence of contact allergens in moisturizers used in clinical studies of atopic dermatitis. Of the 16 emollient preparations used in 12 studies, 75% contained at least 1 identified contact allergen, which may increase the risk of allergic contact dermatitis and promote atopic dermatitis. Bai et al⁸ reported a single-site retrospective study of patients diagnosed with atopic dermatitis but incomplete responses to dupilumab. In 50 patients who met the inclusion criteria, all were found to have a concomitant skin condition or an entirely different diagnosis, with allergic contact dermatitis found in more than 90%. Results of a study of upadacitinib, an oral, reversible, small molecule selective Janus kinase 1 inhibitor, vs dupilumab in the treatment of atopic dermatitis, were published by Blauvelt et al.⁹ The 24-week study showed improved EASI 75 for upadacitinib at week 16, indicating superiority to dupilumab for the treatment of adults with moderate-to-severe atopic dermatitis. Another study in atopic dermatitis investigated the efficacy of abrocitinib in patients who received previous dupilumab treatment¹⁰. These results, published by Shi et al,¹⁰ showed that with 12 weeks of abrocitinib treatment, patients with a previous response to dupilumab maintained most clinical benefits with abrocitinib treatment (Investigator’s Global Assessment 0/1 in > 76% of patients), and some patients who did not respond to dupilumab achieved clinical benefit with abrocitinib treatment (Investigator’s Global Assessment score 0/1 in at least 35% of patients). Finally, international evidence-based guidelines have been recently published for both urticaria¹¹ and hereditary angioedema,¹² which are useful updated references for clinicians managing these patients.

Disclosures: The author reports research support from Biocryst, Biomarin, CSL Behring, Ionis, Kalvista, Pharvaris, and Takeda; consulting for Astria, Biocryst, Biomarin, CSL Behring, Cycle Pharma, Grifols, Intellia, Ipsen, Kalvista, Ono Pharma, Pfizer, Pharming, Pharvaris, RegenxBio, Sanofi-Regeneron, Spark, and Takeda; and speaker presentations for Grifols, Pharming, and Takeda.

Funding: The author has no funding sources to report.

Marc A. Riedl, MD, MS
Division of Rheumatology, Allergy, and Immunology
Department of Medicine
University of California San Diego
San Diego, California
mriedl@ucsd.edu

References

1. De DR, Seivright J, Yee D, Hsiao JL, Shi VY. Readability, quality, and timeliness of patient online health resources for urticaria. *J Am Acad Dermatol.* 2022;86(5):1182–1185.
2. Bizjak M, Košnik M, Dinevski D, Thomsen SF, Fomina D, Borzova E, et al. Risk factors for systemic reactions in typical cold urticaria: results from the COLD-CE study. *Allergy.* 2022;77(7):2185–2199.
3. Kolkhir P, Kovalkova E, Chernov A, Danilycheva I, Krause K, Sauer M, et al. Autoimmune chronic spontaneous urticaria detection with IgG anti-TPO and total IgE. *J Allergy Clin Immunol Pract.* 2021;9(11):4138–4146.e8.
4. Metz M, Sussman G, Gagnon R, Staubach P, Tanus T, Yang WH, et al. Fenebrutinib in H1 antihistamine-refractory chronic spontaneous urticaria: a randomized phase 2 trial. *Nat Med.* 2021;27(11):1961–1969.
5. Craig T, Magerl M, Levy DS, Reshef A, Lumry WR, Martinez-Saguer I, et al. Prophylactic use of an anti-activated factor XII monoclonal antibody, garadacimab, for patients with C1-esterase inhibitor-deficient hereditary angioedema: a randomised, double-blind, placebo-controlled, phase 2 trial. *Lancet.* 2022;399(10328):945–955.
6. Fijen LM, Riedl MA, Bordone L, Bernstein JA, Raasch J, Tachdjian R, et al. Inhibition of prekallikrein for hereditary angioedema. *N Engl J Med.* 2022;386(11):1026–1033.
7. Ryczaj K, Dumycz K, Spiewak R, Feleszko W. Contact allergens in moisturizers in preventative emollient therapy - a systematic review. *Clin Transl Allergy.* 2022;12(6):e12150.
8. Bai H, Murase EM, Ashbaugh AG, Botto NB, Murase JE. Diagnostic testing of eczematous dermatitis with incomplete response to dupilumab. *J Am Acad Dermatol.* 2022;87:692–695.
9. Blauvelt A, Teixeira HD, Simpson EL, Costanzo A, De Bruin-Weller M, Barbarot S, et al. Efficacy and safety of Upadacitinib vs Dupilumab in adults with moderate-to-severe atopic dermatitis: a randomized clinical trial. *JAMA Dermatol.* 2021;157(9):1047–1055.
10. Shi VY, Bhutani T, Fonacier L, Deleuran M, Shumack S, Valdez H, et al. Phase 3 efficacy and safety of abrocitinib in adults with moderate-to-severe atopic dermatitis after switching from dupilumab (JADE EXTEND). *J Am Acad Dermatol.* 2022;87:351–358.
11. Zuberbier T, Abdul Latiff AH, Abuzakouk M, Aquilina S, Asero R, Baker D, et al. The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria. *Allergy.* 2022;77(3):734–766.
12. Maurer M, Magerl M, Betschel S, Aberer W, Ansotegui IJ, Aygören-Pürsün E, et al. The international WAO/EAACI guideline for the management of hereditary angioedema-The 2021 revision and update. *Allergy.* 2022;77(7):1961–1990.