Selections from international journals

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Pimecrolimus in atopic dermatitis: consensus on safety and the need to allow use in infants.

Luger T, Boguniewicz M, Carr W, Cork M, Deleuran M, Eichenfield L, Eigenmann P, Fölster-Holst R, Gelmetti C, Gollnick H, Hamelmann E, Hebert AA, Muraro A, Oranje AP, Paller AS, Paul C, Puig L, Ring J, Siegfried E, Spergel JM, Stingl G, Taieb A, Torrelo A, Werfel T, Wahn U.

Atopic dermatitis (AD) is a distressing dermatological disease, which is highly prevalent during infancy, can persist into later life and requires long-term management with anti-inflammatory compounds. The introduction of the topical calcineurin inhibitors (TCIs), tacrolimus and pimecrolimus, more than 10 yr ago was a major breakthrough for the topical anti-inflammatory treatment of AD. Pimecrolimus 1% is approved for second-line use in children (e2 yr old) and adults with mild-to-moderate AD. The age restriction was emphasized in a boxed warning added by the FDA in January 2006, which also highlights the lack of long-term safety data and the theoretical risk of skin malignancy and lymphoma. Since then, pimecrolimus has been extensively investigated in short- and long-term studies including over 4000 infants (<2 yr old). These studies showed that pimecrolimus effectively treats AD in infants, with sustained improvement with long-term intermittent use. Unlike topical corticosteroids, long-term TCI use does not carry the risks of skin atrophy, impaired epidermal barrier function or enhanced percutaneous absorption, and so is suitable for AD treatment especially in sensitive skin areas. Most importantly, the studies of pimecrolimus in infants provided no evidence for systemic immunosuppression, and a comprehensive body of evidence from clinical studies, post-marketing surveillance and epidemiological investigations does not support potential safety concerns. In conclusion, the authors consider that the labelling restrictions regarding the use of pimecrolimus in infants are no longer justified and recommend that the validity of the boxed warning for TCIs should be reconsidered.

J Allergy Clin Immunol. 2015;136(2):258-611

Consensus communication on early peanut introduction and the prevention of peanut allergy in high-risk infants1

Fleischer DM, Sicherer S, Greenhawt M, Campbell D, Chan E, Muraro A, Halken S, Katz Y, Ebisawa M, Eichenfield L, Sampson H, Lack G, Du Toit G, Roberts G, Bahnson H, Feeney M, Hourihane J, Spergel J, Young M, As'aad A, Allen K, Prescott S, Kapur S, Saito H, Agache I, Akdis CA, Arshad H, Beyer K, Dubois A, Eigenmann P, Fernandez-Rivas M, Grimshaw K, Hoffman-Sommergruber K, Host A, Lau S, O'Mahony L, Mills C, Papadopoulos N, Venter C, Agmon-Levin N, Kessel A, Antaya R, Drolet B, Rosenwasser L1

The purpose of this brief communication is to highlight emerging evidence to existing guidelines regarding potential benefits of supporting early, rather than delayed, peanut introduction during the period of complementary food introduction in infants. This document should be considered as interim guidance based on consensus among the following organizations: American Academy of Allergy, Asthma & Immunology, American Academy of Pediatrics, American College of Allergy, Asthma & Immunology, Australasian Society of Clinical Immunology and Allergy, Canadian Society of Allergy and Clinical Immunology, European Academy of Allergy and Clinical Immunology, Israel Association of Allergy and Clinical Immunology, Japanese Society for Allergology, Society for Pediatric Dermatology, and World Allergy Organization. More formal guidelines regarding early-life, complementary feeding practices and the risk of allergy development will follow in the next year from the National Institute of Allergy and Infectious Diseases-sponsored Working Group and the European Academy of Allergy and Clinical Immunology.

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Efficacy and safety of tocilizumab in patients with polyarticular-course juvenile idiopathic arthritis: results from a phase 3, randomised, double-blind withdrawal trial1

Brunner HI, Ruperto N, Zuber Z, Keane C, Harari O, Kenwright A, Lu P, Cuttica R, Keltsev V, Xavier RM, Calvo I, Nikishina I, Rubio-Pérez N, Alexeeva E, Chasnyk V, Horneff G, Opoka-Winiarska V, Quartier P, Silva CA, Silverman E, Spindler A, Baildam E, Gámir ML, Martin A, Rietschel C, Siri D, Smolewska E, Lovell D, Martini A, De Benedetti F; Paediatric Rheumatology International Trials Organisation PRINTO; Pediatric Rheumatology Collaborative Study Group (PRCSG).
Collaborators (35) Espada G, Allen R, Chaitow J, Joos R, Wouters C, Knupp S, Sztajnbok F, Cabral D, Houghton K, Roth J, Schmeling H, Job-Deslandre C, Jorgensen C, Paut IK, Minden K, Weller-Heinemann F, Gerloni V, Zulian F, Burgos-Vargas R, Salazar CD, Solis-Vallejo E, Calvo A, Chavez J, Zavaler MF, Gruenpeter A, Kobusinska K, Sarychev A, Zholobova E, Ramanan A, Woo P, Goodman S, Gedalia A, Kimura Y, Onel K, Schikler K1

OBJECTIVE: To evaluate the interleukin-6 receptor inhibitor tocilizumab for the treatment of patients with polyarticular-course juvenile idiopathic arthritis (pcJIA). METHODS: This three-part, randomised, placebo-controlled, double-blind withdrawal study (NCT00988221) included patients who had active pcJIA for e6 months and inadequate responses to methotrexate. During part 1, patients received open-label tocilizumab every 4 weeks (8 or 10 mg/kg for body weight (BW) <30 kg; 8 mg/kg for BW e30 kg). At week 16, patients with eJIA-American College of Rheumatology (ACR) 30 improvement entered the 24-week, double-blind part 2 after randomisation 1:1 to placebo or tocilizumab (stratified by methotrexate and steroid background therapy) for evaluation of the primary end point: JIA flare, compared with week 16. Patients flaring or completing part 2 received open-label tocilizumab. RESULTS: In part 1, 188 patients received tocilizumab (<30 kg: 10 mg/kg (n=35) or 8 mg/kg (n=34); e30 kg: n=119). In part 2, 163 patients received tocilizumab (n=82) or placebo (n=81). JIA flare occurred in 48.1% of patients on placebo versus 25.6% continuing tocilizumab (difference in means adjusted for stratification: -0.21; 95% CI -0.35 to -0.08; p=0.0024). At the end of part 2, 64.6% and 45.1% of patients receiving tocilizumab had JIA-ACR70 and JIA-ACR90 responses, respectively. Rates/100 patient-years (PY) of adverse events (AEs) and serious AEs (SAEs) were 480 and 12.5, respectively; infections were the most common SAE (4.9/100 PY). CONCLUSIONS: Tocilizumab treatment results in significant improvement, maintained over time, of pcJIA signs and symptoms and has a safety profile consistent with that for adults with rheumatoid arthritis.

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Phenotypes and endotypes of rhinitis and their impact on management: a PRACTALL report1

Papadopoulos NG1, Bernstein JA, Demoly P, Dykewicz M, Fokkens W, Hellings PW, Peters AT, Rondon C, Togias A, Cox LS1

Rhinitis is an umbrella term that encompasses many different subtypes, several of which still elude complete characterization. The concept of phenotyping, being the definition of disease subtypes on the basis of clinical presentation, has been well established in the last decade. Classification of rhinitis entities on the basis of phenotypes has facilitated their characterization and has helped practicing clinicians to efficiently approach rhinitis patients. Recently, the concept of endotypes, that is, the definition of disease subtypes on the basis of underlying pathophysiology, has emerged. Phenotypes/endotypes are dynamic, overlapping, and may evolve into one another, thus rendering clear-cut definitions difficult. Nevertheless, a phenotype-/endotype-based classification approach could lead toward the application of stratified and personalized medicine in the rhinitis field. In this PRACTALL document, rhinitis phenotypes and endotypes are described, and rhinitis diagnosis and management approaches focusing on those phenotypes/endotypes are presented and discussed. We emphasize the concept of control-based management, which transcends all rhinitis subtypes.