Selections from international journals

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Allergy. 2013; 68(12):1520-31.
EAACI position statement on asthma exacerbations and severe asthma.

Custovic A, Johnston SL, Pavord I, Gaga M, Fabbri L, Bel EH, Le Souëf P, Lötvall J, Demoly P, Akdis CA, Ryan D, Mäkelä MJ, Martinez F, Holloway JW, Saglani S, O'Byrne P, Papi A, Sergejeva S, Magnan A, Del Giacco S, Kalayci O, Hamelmann E, Papadopoulos NG.

Asthma exacerbations and severe asthma are linked with high morbidity, significant mortality and high treatment costs. Recurrent asthma exacerbations cause a decline in lung function and, in childhood, are linked to development of persistent asthma. This position paper, from the European Academy of Allergy and Clinical Immunology, highlights the shortcomings of current treatment guidelines for patients suffering from frequent asthma exacerbations and those with difficult-to-treat asthma and severe treatment-resistant asthma. It reviews current evidence that supports a call for increased awareness of (i) the seriousness of asthma exacerbations and (ii) the need for novel treatment strategies in specific forms of severe treatment-resistant asthma. There is strong evidence linking asthma exacerbations with viral airway infection and underlying deficiencies in innate immunity and evidence of a synergism between viral infection and allergic mechanisms in increasing risk of exacerbations. Nonadherence to prescribed medication has been identified as a common clinical problem amongst adults and children with difficult-to-control asthma. Appropriate diagnosis, assessment of adherence and other potentially modifiable factors (such as passive or active smoking, ongoing allergen exposure, psychosocial factors) have to be a priority in clinical assessment of all patients with difficult-to-control asthma. Further studies with improved designs and new diagnostic tools are needed to properly characterize (i) the pathophysiology and risk of asthma exacerbations, and (ii) the clinical and pathophysiological heterogeneity of severe asthma.

Arthritis Rheumatol. 2014; 66(3):740-9.
Predictors of clinical improvement in rituximab-treated refractory adult and juvenile dermatomyositis and adult polymyositis.

Aggarwal R1, Bandos A, Reed AM, Ascherman DP, Barohn RJ, Feldman BM, Miller FW, Rider LG, Harris-Love MO, Levesque MC; RIM Study Group, Oddis CV.

OBJECTIVE: To identify the clinical and laboratory predictors of clinical improvement in a cohort of myositis patients treated with rituximab. METHODS: We analyzed data for 195 patients with myositis (75 with adult polymyositis [PM], 72 with adult dermatomyositis [DM], and 48 with juvenile DM) in the Rituximab in Myositis trial. Clinical improvement was defined as 20% improvement in at least 3 of the following 6 core set measures of disease activity: physician's and patient's/parent's global assessment of disease activity, manual muscle testing, physical function, muscle enzymes, and extramuscular disease activity. We analyzed the association of the following baseline variables with improvement: myositis clinical subgroup, demographics, myositis damage, clinical and laboratory parameters, core set measures, rituximab treatment, and myositis autoantibodies (antisynthetase, anti-Mi-2, anti-signal recognition particle, anti-transcription intermediary factor 1^3 [TIF-1^3], anti-MJ, other autoantibodies, and no autoantibodies). All measures were univariately assessed for association with improvement using time-to-event analyses. A multivariable time-dependent proportional hazards model was used to evaluate the association of individual predictive factors with improvement. RESULTS: In the final multivariable model, the presence of an antisynthetase, primarily anti-Jo-1 (hazard ratio [HR] 3.08, P < 0.01), anti-Mi-

2 (HR 2.5, P < 0.01), or other autoantibody (HR 1.4, P = 0.14) predicted a shorter time to improvement compared to the absence of autoantibodies. A lower physician's global assessment of damage (HR 2.32, P = 0.02) and juvenile DM (versus adult myositis) (HR 2.45, P = 0.01) also predicted improvement. Unlike autoantibody status, the predictive effect of physician's global assessment of damage and juvenile DM diminished by week 20. Rituximab treatment did not affect these associations. CONCLUSION: Our findings indicate that the presence of antisynthetase and anti-Mi-2 autoantibodies, juvenile DM subset, and lower disease damage strongly predict clinical improvement in patients with refractory myositis

Ann Allergy Asthma Immunol. 2014; 112(2):146-153.e2.
Efficacy and safety of grass sublingual immunotherapy tablet, MK-7243: a large randomized controlled trial.

Maloney J, Bernstein DI, Nelson H, Creticos P, Hébert J, Noonan M, Skoner D, Zhou Y, Kaur A, Nolte H.

BACKGROUND: In North America, few studies have evaluated sublingual immunotherapy for allergic rhinitis with or without conjunctivitis (AR/C); pediatric data are sparse. The authors report findings from the largest published immunotherapy trial yet conducted in adults and children. OBJECTIVE: To evaluate grass sublingual immunotherapy tablet (MK-7243) treatment in subjects with AR/C. METHODS: North American subjects (5-65 years old) with grass allergy were randomized 1:1 to once-daily MK-7243 (2,800 BAU Phleum pratense) or placebo. The first dose was given at the investigator's office; subsequent doses were self-administered at home. The primary end point was total combined score (TCS; rhinoconjunctivitis daily symptom score [DSS] plus daily medication score [DMS]) over the entire grass pollen season (GPS). Key secondary end points included entire-season DSS, DMS, peak-season TCS, and rhinoconjunctivitis quality-of-life questionnaire scores. Safety outcomes included adverse events (AEs). RESULTS: One thousand five hundred one subjects were randomized (85% polysensitized, 25% had asthma). MK-7243 yielded improvements vs placebo of 23% in entire-season TCS (median difference -0.98, P < .001), 29% in peak-season TCS (median difference -1.33, P < .001), 20% in entire-season DSS (median difference -0.64, P = .001), 35% in entire-season DMS (mean difference -0.48, P < .001), and 12% in peak-season rhinoconjunctivitis quality-of-life questionnaire (median difference -0.13, P = .027). Efficacy between children and adults was similar. Most AEs were transient local application-site reactions, with no serious treatment-related AEs or anaphylactic shock. Three subjects (1 placebo, 2 MK-7243) had moderate systemic allergic reactions. CONCLUSION: MK-7243 was effective in polysensitized grass-allergic North American children and adults with AR/C in this large trial, confirming previous research.

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Indications, protocols, and outcomes of drug desensitizations for chemotherapy and monoclonal antibodies in adults and children.

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Advances in the understanding of various malignancies and chronic inflammatory diseases has led to the development of better treatment options for prolonging patient survival and minimizing morbidity. The recognition of "first-line" chemotherapy and monoclonal agents for these conditions has given more urgency to the need to re-administer these drugs in cases of drug hypersensitivity reactions. Therefore, in these cases, not only is desensitization considered when there is no alternative therapy available but also when alternative treatments are considered therapeutically inferior and/or more toxic. In this article, we describe the steps involved in the evaluation of these patients, factors to consider before making a decision to desensitize, the implementation of desensitization protocols, and the outcomes of such procedures