Mepolizumab for Severe Eosinophilic Asthma (DREAM): A Multicentre, Double-Blind, Placebo-Controlled Trial


PURPOSE OF THE STUDY. To elucidate the efficacy, safety, and patient characteristics of responsiveness to mepolizumab (a humanized monoclonal antibody against interleukin 5). Previous small, proof-of-concept studies in subjects with severe, eosinophilic asthma revealed that mepolizumab decreased exacerbation rates.

STUDY POPULATION. From 81 multinational centers, 621 patients were enrolled. Major inclusion criteria included: age 12 to 74 years, asthma diagnosis with objective measures, ≥2 asthma exacerbations requiring oral corticosteroids in the last year, refractory asthma as defined by the American Thoracic Society criteria, and signs of eosinophilic inflammation (sputum eosinophil count ≥3%, an exhaled nitric oxide concentration ≥50 ppb, peripheral blood eosinophil count ≥0.3 × 10⁹/L, or prompt deterioration of asthma control with inhaled or oral steroid weaning). Smokers, present or former (≥10 pack-years), were excluded.

METHODS. Subjects were randomized to receive placebo or 1 of 3 doses of mepolizumab (75, 250, or 750 mg). Every 4 weeks for 13 cycles, patients received infusions. Asthma symptom scores, objective lung testing results, and blood eosinophil counts were collected at baseline and follow-up visits. The primary outcome of verified, clinically significant exacerbations during treatment and 4 weeks thereafter was defined a priori.

RESULTS. All mepolizumab-treated groups demonstrated a significant decrease in clinically significant exacerbations (75 mg: −48% [P < .0001]; 250 mg: −39% [P = .005]; 750 mg: −52% [P < .0001]). Visits to emergency departments and admissions also decreased; however, no significant changes in spirometry or asthma control scores were noted. No treatment-associated deaths occurred, and other potential adverse events were equivocal in the placebo and treatment groups.

CONCLUSIONS. Mepolizumab is generally safe and reduces exacerbation rates in select patients with asthma who have the severe, refractory, eosinophilic subtype.

IMMUNOTHERAPY

Efficacy of Subcutaneous and Sublingual Immunotherapy With Grass Allergens for Seasonal Allergic Rhinitis: A Meta-Analysis-Based Comparison


PURPOSE OF THE STUDY. To compare the efficacy of subcutaneous (SCIT) and sublingual immunotherapy (SLIT) to grass by meta-analysis of double-blind, placebo-controlled trials.

STUDY POPULATION. Among 36 studies selected for this meta-analysis, 14 included children.

METHODS. An electronic literature search identified 36 randomized controlled trials (RCTs) comparing SCIT and SLIT to placebo for grass pollinosis. All the studies assessed symptom scores and 31 assessed medication scores as outcome measures. To standardized comparative studies, the authors used the “standard mean difference” method (SMD) to compare SCIT or SLIT versus placebo. A “fail-safe” number (the number of insignificant or missing studies that would need to be added to a meta-analysis to reduce a significant result to insignificance) calculation was performed.

RESULTS. The 36 RCTs (22 SLIT [10 drops, 12 tablets], 14 SCIT) included 3014 treated patients and 2768 patients given placebo. Nine SLIT studies and 5 SCIT studies included children. There was great variation in the
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Pediatrics 2013;132;S48
DOI: 10.1542/peds.2013-2294BBBB

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