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Title: Omalizumab in allergic eosinophilic asthma and lung eosinophil numbers: A 78-week randomized controlled trial

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Body: A biopsy study has previously shown significant anti-inflammatory activity of omalizumab (OMA) in mild asthma, but how these results apply to more severe disease is uncertain. We studied the impact of OMA on airway inflammation and remodelling in persistent moderate-to-severe allergic eosinophilic asthma. Patients with allergic asthma and high sputum eosinophils, treated with ICS/LABA, were randomized 2:1 to OMA or placebo for 78 weeks. Bronchial biopsy was performed at baseline (BL) and end of treatment (EOT). Primary endpoint was change from BL (Δ) in total sub-epithelial eosinophils at EOT. Other outcomes included Δ in reticular basement membrane thickness (RBMT) and sub-epithelial IgE levels. Efficacy was assessed by physician's Global Evaluation of Treatment Effectiveness (GETE) and clinically significant exacerbations (CSE). 36 patients (mean age 43.1 years) were recruited (OMA, n=23; placebo, n=13). Response by GETE was 56.5% for OMA and 25.0% for placebo. Percentage of patients with ≥ 1 CSE was 26.1% for OMA and 41.7% for placebo. However, there were no significant between-group differences in primary outcome or RBMT. Sub-epithelial IgE suppression was demonstrated at EOT, but was not associated with changes in sub-epithelial eosinophil numbers. Consistent with past studies, OMA was clinically effective in moderate-to-severe allergic eosinophilic asthma, but a relationship between lung eosinophils and response was not apparent. Although inconclusive, this study questions whether the efficacy of OMA is independent of eosinophil suppression and suggests that further investigations should explore other anti-inflammatory mechanisms.