

613 Reslizumab improves FVC and FEF_{25%-75%} in severe eosinophilic asthma: results from a pooled analysis



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RATIONALE: IV reslizumab (RES), a humanized anti-interleukin-5 monoclonal antibody, demonstrated significant improvement in FEV₁ at 52 weeks in patients aged 12–75 years with inadequately controlled asthma and blood eosinophils ≥ 400 cells/ μ L (110mL [95% CI: 67, 150mL]) (Castro et al., *Lancet Respir Med* 2015;3:355–66). It is previously unreported whether reslizumab treatment results in improvement in additional lung function parameters.

METHODS: Data were pooled from two 52-week placebo-controlled trials of IV reslizumab 3mg/kg (Q4wks) in patients with uncontrolled asthma and elevated blood eosinophils (≥ 400 cells/ μ L). Outcomes measured included FVC and FEF_{25%-75%}.

RESULTS: Patients were treated with placebo (n=476) or reslizumab (n=477). Mean treatment difference for reslizumab relative to placebo over 16 and 52 weeks in FVC was 108mL (95% CI: 55, 161; p<0.0001) and 104mL (95% CI: 51, 158; p=0.0001), respectively. At the first scheduled assessment 4 weeks after the first dose, reslizumab treatment resulted in FVC improvement of 128mL (95% CI: 69, 186; p<0.0001) compared with placebo. Mean treatment difference for reslizumab relative to placebo over 16 and 52 weeks in FEF_{25%-75%} was: 102mL (95% CI: 42, 161; p=0.0008) and 99mL (95% CI: 39, 158; p=0.0012), respectively. There was improvement in FEF_{25%-75%} as early as 4 weeks: treatment difference 102mL (95% CI: 34, 171; p=0.0034).

CONCLUSIONS: Patients with inadequately controlled asthma and elevated blood eosinophils treated with reslizumab showed clinically meaningful improvement in FVC and FEF_{25%-75%}. The increase observed may be indicative of a reduction in air trapping and recruitment of small peripheral airways.

614 Impact of Baseline IgE levels on Exacerbations and Asthma Symptom Control After Omalizumab Initiation



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RATIONALE: IgE is important in asthma pathogenesis; omalizumab is the only biologic to specifically target IgE, with dosing in asthma customized to IgE levels. However, confusion abounds as to whether IgE is a biomarker for response.

METHODS: Patients ≥ 12 y/o identified as omalizumab candidates by their treating physicians and with access to treatment through insurance or other funding were enrolled in PROSPERO (n=801); US-based, multicenter, prospective, 48-week observational study of patients with allergic asthma initiating treatment with omalizumab. Asthma-related exacerbations and ACT scores were recorded over 48 weeks. Outcomes were analyzed by baseline IgE level in 100IU/mL intervals (<100 to >700).

RESULTS: At baseline median (range) IgE levels were 193.3IU/mL (1.1–68,628). Patients reported mean (SD) 3.0 (3.28) exacerbations in the 12 months prior to study entry and 0.78 (1.37) exacerbations at the end of the study. Reductions in exacerbations were consistent regardless of baseline IgE levels (Spearman's corr. = -0.05, p=0.18). Patients reported poorly controlled asthma at baseline, mean (SD) ACT 13.94 (4.98), which improved to 18.37 (4.85) at the end of the study irrespective of IgE levels (Spearman's corr. = 0.06, p=0.08). Average change in ACT exceeded the

MID (3) in all IgE subgroups. Adverse events were consistent with the safety profile described in the current product label.

CONCLUSIONS: In a real-world setting, patients treated with omalizumab had improved asthma control with decreased asthma exacerbations and increased ACT scores regardless of baseline IgE levels suggesting that although important in omalizumab dosing, IgE may not be a predictive biomarker for response to omalizumab.

615 Pulmonary Innate Lymphoid Cell Responses During Rhinovirus-Induced Asthma Exacerbations



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RATIONALE: Preclinical models show that type 2 innate lymphoid cells (ILC2) produce type 2 cytokines, while type 1 ILCs (ILC1) produce IFN γ . Analogous ILC populations have been identified in man; however, the role of ILCs during viral exacerbations of asthma is unknown. This study aimed to characterise pulmonary ILC responses in asthma during experimental rhinovirus infection.

METHODS: Patients with moderate-severe asthma and healthy volunteers were inoculated with rhinovirus-16 and underwent bronchoscopy at baseline, and Days 3 and 8 post inoculation. Pulmonary ILC1s and ILC2s were sorted from bronchoalveolar lavage by FACs.

RESULTS: At baseline, ILC2s were increased in patients with asthma vs healthy volunteers ($P<0.05$), with no difference in ILC1 levels. In asthma, there was a significant increase in ILC2s at Day 8 from baseline ($P<0.05$). ILC2s at Day 8 were significantly greater in asthma vs healthy volunteers ($P<0.05$). In healthy volunteers, there was an early increase in ILC1s at Day 3 ($P<0.001$), whereas in asthma, there was a delayed increase in ILC1s at Day 8 ($P<0.05$). Patients with asthma had a significantly higher ratio of ILC2:ILC1 at baseline ($P<0.05$) and Day 8 ($P<0.01$), with a similar trend observed at Day 3 ($P=0.059$). Increased ILC2:ILC1 ratio in asthma correlated with clinical markers of exacerbation severity and type 2 cytokines.

CONCLUSIONS: This is the first study to show increased ILC2 recruitment in the lower airways during rhinovirus infection in asthma and delayed ILC1 recruitment compared with healthy volunteers. These results indicate that an ILC2-predominant inflammatory profile is associated with increased severity and duration of respiratory viral infections in asthma.