EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
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Inhaled anti-TSLP antibody fragment, ecleralimab, blocks responses to allergen in mild asthma

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Shareable abstract (@ERSpublications)
Ecleralimab significantly attenuated allergen-induced airway responses and inflammation in subjects with mild asthma. It was generally safe and well tolerated, suggesting anti-TSLP may be a promising, new therapeutic class for inhaled asthma treatment. https://bit.ly/3U294EA

Cite this article as: Gauvreau GM, Hohlfeld JM, FitzGerald JM, *et al*. Inhaled anti-TSLP antibody fragment, ecleralimab, blocks responses to allergen in mild asthma. *Eur Respir J* 2023; 61: 2201193 [DOI: 10.1183/13993003.01193-2022].

This article has an editorial commentary: https://doi.org/10.1183/13993003.02389-2022

Received: 10 June 2022
Accepted: 24 Oct 2022

Abstract

Background Thymic stromal lymphopoietin (TSLP) is a key upstream regulator driving allergic inflammatory responses. We evaluated the efficacy and safety of ecleralimab, a potent inhaled neutralising antibody fragment against human TSLP, using allergen inhalation challenge (AIC) in subjects with mild atopic asthma.

Methods This was a 12-week, randomised, double-blind, placebo-controlled, parallel-design, multicentre allergen bronchoprovocation study conducted at 10 centres across Canada and Germany. Subjects aged 18–60 years with stable mild atopic asthma were randomised (1:1) to receive 4 mg once-daily inhaled ecleralimab or placebo. Primary end-points were the allergen-induced change in forced expiratory volume in 1 s (FEV_1) during the late asthmatic response (LAR) measured by area under the curve ($AUC_{3–7h}$) and maximum percentage decrease (LAR%) on day 84, and the safety of ecleralimab. Allergen-induced early asthmatic response (EAR), sputum eosinophils and fractional exhaled nitric oxide (F_{ENO}) were secondary and exploratory end-points.

Results 28 subjects were randomised to ecleralimab (n=15) or placebo (n=13). On day 84, ecleralimab significantly attenuated LAR $AUC_{3–7h}$ by 64% (p=0.008), LAR% by 48% (p=0.029), and allergen-induced sputum eosinophils by 64% at 7 h (p=0.011) and by 52% at 24 h (p=0.047) post-challenge. Ecleralimab also numerically reduced EAR $AUC_{0–2h}$ (p=0.097) and EAR% (p=0.105). F_{ENO} levels were significantly reduced from baseline throughout the study (p<0.05), except at 24 h post-allergen (day 43 and day 85). Overall, ecleralimab was safe and well tolerated.

Conclusion Ecleralimab significantly attenuated allergen-induced bronchoconstriction and airway inflammation, and was safe in subjects with mild atopic asthma.