Inhaled anti-TSLP antibody fragment, ecleralimab, blocks responses to allergen in mild asthma

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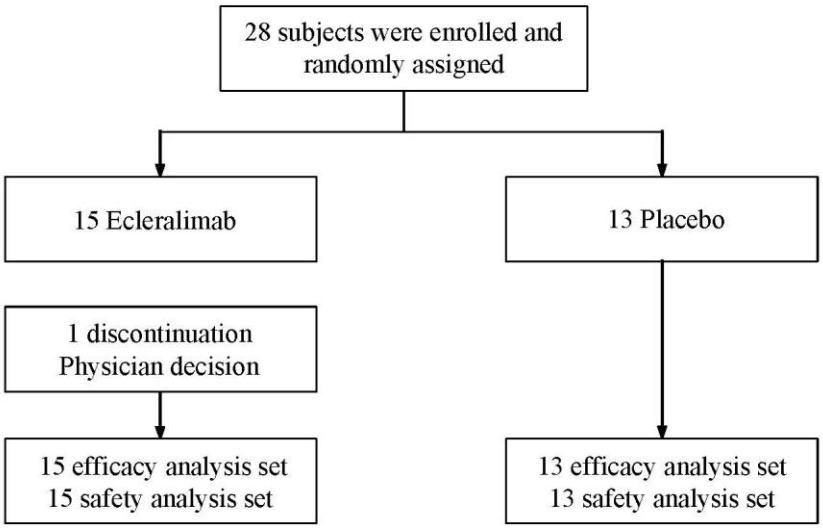
Methods:

Allergen inhalation challenge (AIC)

AIC was conducted using one of several standardized and commercially available aero-allergen extracts. The allergen for inhalation was selected based on the results of a skin prick test panel including pollens (grass, trees, ragweed), animals (cat, dog, horse, muse, cattle, rat, bird), house dust mite (Dermatophagoides farinae, Dermatophagoides pteronyssinus), and crops. The dose of allergen was determined during the screening AIC and the starting concentration was calculated using the results of an allergen skin titration and the methacholine PC20.[1,2] Doubling doses of the selected allergen extract were inhaled for 2 minutes from a Wright nebulizer (Canadian sites) or DeVilbiss nebulizer at 12-minute intervals until FEV_1 fell by 20%. The FEV_1 was then measured at regular intervals for 7 hours to identify subjects with positive LAR. AIC at days 42 and 84 administered the highest 3 doses that were administered at screening, 12 minutes apart.

Results:

Supplementary Figure 1: Subject disposition



Supplementary Table 1. Effect of ecleralimab on EAR and LAR at Day 42 and Day 84 (Efficacy set)

	Ecleralimab group (mean)	**Placebo group**	**Difference (Ecleralimab-Placebo**	**90% CI***	**p value†**
EAR% fall					
Day 42	27.9%	32.6%	−4.70%	−13.10 to 3.69	0.172
Day 84	25.5%	30.9%	−5.41%	−12.62 to 1.79	0.105
EAR AUC$_{(0\text{-}2h)}$					
Day 42	15.1%	16.1%	−1.02%	−6.06 to 4.01	0.364
Day 84	12.8%	17.1%	−4.26%	−9.72 to 1.21	0.097
EAR$_{min}$					
Day 42	2.35L	2.20L	0.15L	−0.14 to 0.45	0.186
Day 84	2.42L	2.25L	0.17L	−0.08 to 0.42	0.130
LAR% fall					
Day 42	13.11%	15.75%	−2.64%	−9.02 to 3.74	0.243
Day 84	9.28%	17.70%	−8.42%	−15.66 to −1.18	0.029
LAR AUC $_{(3\text{-}7h)}$					
Day 42	6.46%	9.36%	−2.90	−7.43 to 1.62	0.141
Day 84	4.20%	11.38%	−7.18	−11.92 to −2.44	0.008
LAR$_{min}$					
Day 42	2.84L	2.75L	0.09L	−0.19 to 0.37	0.293
Day 84	2.96L	2.69L	0.27L	−0.00 to 0.55	0.050

AUC, area under curve; EAR, early asthmatic response; LAR, late asthmatic response

*two sided CI; †one sided p-value

The endpoint was analysed using an Analysis of Covariance (ANCOVA) model for repeated measures, to compare the ecleralimab group with placebo.

The model included treatment and visit as independent variables, treatment by visit interaction term and baseline by visit interaction term

Baseline values were measured following the AIC at Day −14

Supplementary Table 2. Incidence of AEs by preferred term - n (percent) of subjects (safety analysis set)

Preferred term	**Ecleralimab 4 mg N=15 n (%)**	**Placebo N=13 n (%)**	**Total N=28 n (%)**
Subjects with at least one AE	10 (66.7)	12 (92.3)	22 (78.6)
Preferred term			
Headache	4 (26.7)	3 (23.1)	7 (25.0)
Nasopharyngitis	2 (13.3)	3 (23.1)	5 (17.9)
Oropharyngeal Pain	2 (13.3)	3 (23.1)	5 (17.9)
Cough	2 (13.3)	2 (15.4)	4 (14.3)
Back Pain	1 (6.7)	2 (15.4)	3 (10.7)
Rhinitis	2 (13.3)	1 (7.7)	3 (10.7)
Vomiting	3 (20.0)	0	3 (10.7)
Abdominal Pain Upper	2 (13.3)	0	2 (7.1)
Diarrhea	2 (13.3)	0	2 (7.1)
Migraine	1 (6.7)	1 (7.7)	2 (7.1)
Nausea	2 (13.3)	0	2 (7.1)
Upper Respiratory Tract			
Infection	0	2 (15.4)	2 (7.1)
Vertigo	1 (6.7)	1 (7.7)	2 (7.1)
Abdominal Pain	1 (6.7)	0	1 (3.6)
Abdominal Pain Lower	0	1 (7.7)	1 (3.6)

Allergy To Arthropod Bite	1 (6.7)	0	1 (3.6)
Aphthous Ulcer	1 (6.7)	0	1 (3.6)
Bacterial Vaginosis	0	1 (7.7)	1 (3.6)
Blood Creatine Phosphokinase Increased	1 (6.7)	1 (3.6)	1 (3.6)
Bone Pain	1 (6.7)	0	1 (3.6)
Chest Discomfort	1 (6.7)	0	1 (3.6)
Conjunctivitis	0	1 (7.7)	1 (3.6)
Constipation	0	1 (7.7)	1 (3.6)
Depression	1 (6.7)	0	1 (3.6)
Dysmenorrhea	0	1 (7.7)	1 (3.6)
Dyspnea	1 (6.7)	0	1 (3.6)
Ear Discomfort	1 (6.7)	0	1 (3.6)
Eye Swelling	0	1 (7.7)	1 (3.6)
Fatigue	1 (6.7)	0	1 (3.6)
Infected Bite	0	1 (7.7)	1 (3.6)
Influenza	0	1 (7.7)	1 (3.6)
Insomnia	0	1 (7.7)	1 (3.6)
Lymph Node Pain	0	1 (7.7)	1 (3.6)
Malaise	1 (6.7)	0	1 (3.6)
Muscular Weakness	1 (6.7)	0	1 (3.6)
Myalgia	1 (6.7)	0	1 (3.6)
Non-Cardiac Chest Pain	1 (6.7)	0	1 (3.6)

Paronychia	0	1 (7.7)	1 (3.6)
Pruritus	1 (6.7)	0	1 (3.6)
Rash	0	1 (7.7)	1 (3.6)
Respiratory Tract			
Congestion	1 (6.7)	0	1 (3.6)
Rhinitis Allergic	1 (6.7)	0	1 (3.6)
Sneezing	1 (6.7)	0	1 (3.6)
Tachycardia	0	1 (7.7)	1 (3.6)
Throat Tightness	0	1 (7.7)	1 (3.6)
Thyroid Mass	0	1 (7.7)	1 (3.6)
Tonsillitis	1 (6.7)	0	1 (3.6)
Urinary Tract Infection	1 (6.7)	0	1 (3.6)
Vessel Puncture Site Pain	0	1 (7.7)	1 (3.6)

AE, adverse event

A subject with multiple AEs is counted only once in the “at least one AE” row

A subject with multiple AEs with the same preferred term is counted only once for that preferred term and treatment

Preferred terms are sorted in descending frequency, as reported in the "Total" column

Only adverse events occurring at or after first drug intake are included

References:

1. Boulet LP, Gauvreau G, Boulay ME, et al. The allergen bronchoprovocation model: an important tool for the investigation of new asthma anti-inflammatory therapies. Allergy 2007;62:1101–1110.
2. Cockcroft DW, Murdock KY, Kirby J, et al.Prediction of airway responsiveness to allergen from skin sensitivity to allergen and airway responsiveness to histamine. Am Rev Respir Dis 1987;135:264–267.