

(AQLQ), where higher scores (range 1–7) indicate better HRQoL. Changes from baseline were analyzed using mixed-effect models with repeated

Results: At baseline, dupilumab and placebo groups had mean ACQ-5 scores of 2.42 and 2.58 and mean AQLQ scores of 4.38 and 4.31. In the dupilumab group, ACQ-5 scores improved by Week 2 (LS mean change from baseline – 0.57, $P=0.002$ vs. placebo) with further improvements by Week 12 (– 1.01, $P=0.001$ vs. placebo), which were sustained to Week 24 (– 1.05, $P=0.002$ vs. placebo). AQLQ scores improved by first assessment at Week 12 (0.76, $P=0.14$ vs. placebo) and continued to improve to Week 24 (0.89, $P=0.008$ vs. placebo). Similar trends were observed in patients who achieved $\geq 50\%$ OCS dose reduction or discontinued OCS use. Overall, the most frequent treatment-emergent AE occurring in dupilumab- vs. placebo-treated patients was eosinophilia (14% vs. 1%).

Conclusion: Dupilumab vs. placebo improved asthma control and HRQoL in patients with OCS-dependent, severe asthma. Dupilumab was generally well tolerated.

#3

Targeting the IL-5 pathway in eosinophilic asthma: a comparison of mepolizumab to benralizumab in the reduction of peripheral eosinophil counts

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Background: Mepolizumab and benralizumab are biologics approved for severe eosinophilic asthma. Mepolizumab is an anti-IL-5 antibody while benralizumab is an anti-IL-5R α antibody targeting the IL-5 receptor on eosinophils. Both therapies reduce oral steroid requirements and asthma exacerbations. However, no head-to-head studies have been published. We compared these agents in their efficacy in peripheral eosinophil reduction.

Methods: A retrospective chart review was conducted on patients with severe eosinophilic asthma who were approved for either IL-5 agent. Patients with noted non-compliance or those who were on fluctuating doses of steroids for non-asthma related illnesses were excluded. The last detectable eosinophil count for each patient prior to start of therapy was compared to the highest eosinophil count noted after therapy start.

Results: Thirty-six patients taking mepolizumab and 19 patients taking benralizumab met the inclusion criteria and had both pre-treatment and post-treatment eosinophil counts. There was no statistically significant difference between the age and sex of the patients taking mepolizumab versus benralizumab. The mean pre-therapy serum eosinophil count did not statistically differ between patients on mepolizumab (611.1 cells/ μ L) compared to benralizumab (526.3 cells/ μ L), $p=0.3222$. While both therapies resulted in a significant decrease in eosinophil count ($p<0.0001$); the mean decrease did not statistically differ between patients taking mepolizumab compared to those on benralizumab, $p=0.7420$. Nonetheless, 100% of patients receiving Benralizumab had undetectable eosinophil counts post-therapy compared to 25% of patients receiving Mepolizumab ($p<0.0001$).

Conclusion: Both mepolizumab and benralizumab are potent targets of the IL-5 pathway with the ability to significantly reduce peripheral eosinophil counts. While there is no statistical difference in the magnitude of eosinophil reduction offered by each agent, benralizumab is superior in decreasing peripheral eosinophil counts to 0 cells/ μ L.

*This study was approved by the Hamilton Integrated Research Ethics Board-5437-C.

#4

Controlled dander aerosolization in a naturalistic exposure chamber

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Background: A naturalistic exposure chamber housing two neutered male cats has been developed (Red Maple Trials, Ottawa) to test allergic responses of subjects during controlled exposures to Fel d 1. To improve upon traditional methods of dander aerosolization in which bedding is shaken resulting in transient levels of allergen, we have developed an automated delivery system with adjustable flow, using a modified robotic vacuum cleaner. Here, we present the range of Fel d 1 and particle concentrations produced by our system.

Methods: Circuitry was added to the vacuum, enabling full control of its suction power level to achieve a range of allergen levels. Controlled remotely, the vacuum passed throughout the chamber (floor area = 15.1 m²) for up to 2 h, aspirating dander that naturally collected on the floor and venting it through a custom exhaust tube. Air samples were obtained using portable air sampling pumps (Gilliam 5000) at three locations across the chamber and for multiple time intervals. Fel d 1 deposited on glass fiber filters was quantified using ELISA. Numbers and sizes of dander particles were measured in real time using a time-of-flight particle size distribution analyser (PSD 3603, TSI Incorporated). Tests were performed for a range of suction power levels and for operation with and without brushes.

Results: A fivefold increase in particle aerosolization was observed from the lowest to the highest power setting. A significant range of Fel d 1 concentrations was also measured. The vacuum's brushes significantly increased the airborne particulate and allergen level.

Conclusion: A novel automated system to aerosolize animal dander has been developed with controls to generate a range of allergen concentrations. This provides a means of better controlling subject exposure to allergen for cat allergy studies, while maintaining a naturalistic environment.

#5

Validation of a cat dander Naturalistic Exposure Chamber (NEC™)

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Background: A naturalistic cat exposure chamber (NEC) with allergen concentrations similar to homes with cats can provide a relevant model to test allergy medications in a controlled environment with stable Fel d 1 levels. We report here on the technical and clinical validation of the NEC.

Methods: Allergen buildup was assessed over 2 years to assess stability of allergen levels. Walls and floor were swabbed using glass fiber filters (Millipore) for sampling, while airborne allergen was measured at 3 points using portable air sampling pumps (Gilliam 5000) at 4 L/min with glass fiber filters. Fel d 1 was quantified by ELISA (Indoor Biotechnologies). Six subjects (4 allergic and 2 non-allergic) underwent two 60-min challenges 1 week apart during which cat bedding was shaken every 15 min. Nasal, ocular and respiratory symptoms were captured every 5 min using a 4-point severity scale and spirometry was performed every 15 min. The study was approved by Advarra Ethics Board, approval number Pro 00023880. NCT03414801.

Results: Two-year averages for Fel d 1 were: floor 20.2 ± 14.7 μ g/m³, walls 2.3 ± 1.67 μ g/m³. Variation was due to build up and cleaning. Airborne Fel d 1 was below the limit of detection without disturbance.

During subject challenges, room Fel d 1 was 189.5 ± 183.4 ng/m³; personal samplers reported 63.4 ± 51.2 ng/m³. Rhinoconjunctivitis symptoms for the two challenges in the 4 cat-allergic subjects were similar (6.5 ± 1.7 vs. 6.25 ± 3.36). Nasal symptoms predominated (5.25 ± 2.1 , Challenge 1; 4.0 ± 2.4 , Challenge 2). Allergic subjects reported modest respiratory discomfort during the challenges although none experienced a fall in FEV1. The 2 non-cat allergic subjects experienced no nasal, ocular or respiratory symptoms.

Conclusion: With disturbance, the NEC maintains airborne Fel d 1 levels similar to homes and induces reproducible symptoms in allergic subjects while non-allergic subjects remain asymptomatic.

#6

Prevalence and predictive factors of pollen food syndrome in a Canadian cohort of birch, grass and/or ragweed allergic individuals

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Background: Pollen food syndrome (PFS) is an IgE-mediated food allergy that occurs in aeroallergen sensitized individuals, due to cross-reactivity of plant proteins with homologous proteins present in food. In North America, culprit aeroallergens include: birch, grass and ragweed. Few prognostic factors for PFS have been identified, and there is limited data on the epidemiology of this condition in Canada.

Methods: A retrospective chart review was completed of patients seen in a single Canadian allergy clinic in Kingston, ON, Canada. Adult patients with allergic rhinitis and sensitization to birch, grass and/or ragweed pollen, based on positive skin prick testing, who were seen between 2009 and 2018 were included in our study. Patients were considered to have PFS based on physician diagnosis. Variables of interest such as multiple aeroallergen sensitization were assessed with a Pearson's Chi-square test. The relationship between skin prick test size of aeroallergens of interest and the presence of PFS was assessed using a binomial logistic regression. The study was approved by Queen's University Ethics Board.

Results: Of 400 patients identified with sensitization to an aeroallergen of interest, 82 (21%) had a concomitant physician diagnosis of PFS. PFS occurred significantly more frequently in those patients with multiple aeroallergen sensitization ($p < 0.001$) and birch and alder sensitization, compared to birch sensitization alone ($p = 0.002$). Larger skin prick test size to birch was associated with the presence of PFS ($OR = 1$).

Conclusion: Our data, similarly to previous studies, suggests that multiple aeroallergen sensitization is associated with PFS. Additionally, birch and alder co-sensitization were associated with higher rates of PFS than birch sensitization alone, and larger skin prick test size to birch was correlated with PFS. In our Canadian cohort of patients, the rate of PFS was 21%.

#7

Dupilumab improved lung function despite exacerbation events in patients with uncontrolled, moderate-to-severe asthma during the LIBERTY ASTHMA QUEST study

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Background: Dupilumab, a fully human monoclonal antibody, blocks the shared receptor component for IL-4/IL-13, key drivers of type 2 inflammation in multiple diseases. In the USA, dupilumab is approved for patients aged ≥ 12 years with moderate to severe eosinophilic or oral corticosteroid-dependent asthma and for patients aged ≥ 12 years with inadequately controlled, moderate-to-severe atopic dermatitis. In the phase 3 QUEST study (NCT02414854), dupilumab 200 mg/300 mg every 2 weeks, vs. matched placebo, reduced severe exacerbations and improved pre bronchodilator FEV1 and quality-of-life in uncontrolled, moderate-to-severe asthma patients. This post hoc analysis assessed dupilumab's effect on lung function by number of exacerbations during the 52-week study period.

Methods: LS mean change from baseline in pre- and post-bronchodilator FEV1 at Week 52, adjusted for baseline FEV1, was assessed in patients experiencing 0, 1, 2, ≥ 3 exacerbations.

Results: More dupilumab- than placebo-treated patients had 0 exacerbations during the study. At Week 52, dupilumab 200 mg/300 mg vs. matched placebo significantly improved pre-bronchodilator FEV1 by 0.20 L (95% CI: 0.12, 0.27)/0.11 L (0.03, 0.18) and post-bronchodilator FEV1 by 0.20 L (0.13, 0.26)/0.13 L (0.06, 0.20), respectively, in patients experiencing 0 exacerbations (all $P < 0.01$). At Week 52, LS mean difference in change from baseline post-bronchodilator FEV1 was 0.14 L (0.02, 0.26)/0.01 L (-0.11 , 0.14), 0.12 L (-0.08 , 0.32)/0.10 L (-0.09 , 0.30), and 0.12 L (-0.14 , 0.37)/0.13 L (-0.09 , 0.35) in patients experiencing 1, 2, and ≥ 3 exacerbations, for dupilumab 200 mg/300 mg vs. matched placebo, respectively. Similar trends in pre-bronchodilator FEV1 at Week 52 were observed in these subgroups. The most frequent AE in dupilumab-treated patients vs. matched placebo was injection-site reaction (15%/18% vs. 5%/10%).

Conclusion: Most dupilumab-treated patients had 0 exacerbations during the study. In placebo-treated patients, lung function worsened with increasing numbers of exacerbations. Dupilumab-treated patients had improved post-bronchodilator FEV1, though the magnitude of improvement diminished with increasing exacerbations. These data highlight the relationship between exacerbations and lung function preservation in moderate-to-severe asthma.

#8

The SQ tree SLIT-tablet reduces rhinoconjunctivitis symptoms and medication use during the tree pollen season (hazel, alder and birch pollen seasons): results from a large multi-center phase III trial

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Background: The SQ tree SLIT-tablet (ALK, Denmark) is being developed for treatment of moderate-to-severe allergic rhinitis and/or conjunctivitis induced by pollen from the birch homologous group. We report the results of a phase III trial.