Ann Allergy Asthma Immunol xxx (2024) xxx-xxx

Contents lists available at ScienceDirect

ELSEVIER

Annals of Allergy, Asthma & Immunology

LATE-BREAKING ABSTRACTS

Allergy diagnostics and immunotherapy
LBA001

COMPELLING PHASE III EFFICACY AFTER ONLY 6 PRE-SEASONAL INJECTIONS OF POLLINEX QUATTRO GRASS

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Background: Pollinex Quattro (PQ) Grass 27600 SU cumulative dose is a short-course (6 pre-seasonal injections) modified subcutaneous grass immunotherapy product under development for the treatment of allergic rhinitis. RESONATE was the pivotal phase III randomized double-blind, placebo-controlled clinical trial performed to evaluate the efficacy and safety of PQ Grass.
Methods: RESONATE applied an adaptive group sequential trial design with 1 pre-defined interim analysis, conducted simultaneously in the United States and Europe. The primary efficacy endpoint was the "combined symptom" and "medication score" as proposed by the European Academy of Allergy and Clinical Immunology averaged over the peak grass pollen season.
Results: RESONATE could be stopped for success after the randomization of 555 subjects at the interim stage, as superiority in favor of PQ Grass compared with placebo was demonstrated. The primary endpoint combined symptom and medication score as proposed by the European Academy of Allergy and Clinical Immunology during peak grass pollen season showed a relative difference of −20.3% (95% CI: −31.00% to −9.49%, $P = .0005$). Highly consistent beneficial results were obtained for PQ Grass on all key secondary endpoints. Patients showing high compliance (>90%) received all 6 injections and, more than 95% completed the 6-month safety follow-up. The PQ Grass was well tolerated, and there were no unexpected safety signals.
Conclusion: This pivotal phase III trial demonstrated a significant and clinically meaningful effect on the primary endpoint. The study is pivotal and allows progress toward the application for registration of PQ Grass 27600 SU.

Angioedema/urticaria
LBA002

DUPILUMAB SIGNIFICANTLY IMPROVES ITCH AND HIVES IN PATIENTS WITH CHRONIC SPONTANEOUS URTICARIA (CUPID STUDY C)

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Background: Chronic spontaneous urticaria (CSU) can be difficult to manage with many patients experiencing inadequate disease control despite treatment with H1-antihistamines.
Methods: LIBERTY-CSU CUPID Study C (NCT04180488), a randomized, placebo-controlled, double-blind 24-week phase III trial compared dupilumab with placebo treatment in omalizumab-naive patients with symptomatic CSU despite standard-of-care H1-antihistamines treatment (up to 4-fold approved dose) ($n = 151$, age ≥ 6 years). Patients were randomized to receive add-on dupilumab 300 mg (adults and adolescents ≥ 60 kg) or 200 mg (adolescents < 60 kg, children ≥ 30 kg) ($n = 74$) or matching placebo ($n = 77$) subcutaneously every 2 weeks. Efficacy endpoints included Itch Severity Score over 7 days (ISS7, range: 0-21) and Urticaria Activity Score over 7 days (UAS7, range: 0-42). Safety and tolerability were assessed.
Results: Dupilumab significantly improved ISS7 and UAS7 vs placebo at week 24 (least squares mean change in ISS7 from baseline: −8.6 dupilumab vs −6.1 placebo; difference: −2.5, $P = .02$; least squares mean change in UAS7: −15.9 dupilumab vs −11.2 placebo; difference: −4.7, $P = .02$). A higher proportion of patients receiving dupilumab achieved well-controlled disease status (UAS ≤ 6: 41% dupilumab vs 23% placebo, odds ratio = 2.7, $P = .005$) or complete response (UAS = 0: 30% dupilumab vs 18% placebo, odds ratio = 2.7, $P = .02$) at week 24 compared with placebo. Overall rates of participants with treatment-emergent adverse events were the same for both groups (53%). Safety was generally consistent with the known safety profile of dupilumab.
Conclusion: Dupilumab significantly reduced itch and urticaria in patients with CSU who were uncontrolled with H1-antihistamine therapy. This research was sponsored by Sanofi and Regeneron Pharmaceuticals Inc and was compliant with GPPG.

LBA003

POSITIVE EFFICACY AND FAVORABLE SAFETY OF BARZOLVOLIMAB IN CHRONIC INDUCIBLE URTICARIA: PHASE II TRIAL RESULTS

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Background: Chronic inducible urticaria (CIndU) is characterized by mast cell-mediated wheals elicited in response to definite triggers. Barzolvolimab (monoclonal anti-KIT antibody) specifically inhibits the activation of KIT by stem cell factors, which control the survival and activity of mast cells. We reported efficacy and safety through 12W from a phase II study on patients with CIndU refractory to antihistamines (NCT05405660).
Methods: This ongoing, double-blind, placebo-controlled trial randomized patients with cold urticaria (ColdU) and symptomatic dermographism (SD) to receive barzolvolimab subcutaneous at 150 mg every 4 weeks, 300 mg every 8 weeks, or placebo during a 20W placebo-controlled period with 24W follow-up. The primary endpoint was the percentage of patients with negative provocation tests (ColdU: TempTest < 4°C, SD: FricTest: 0 pins) at 12W. Secondary endpoints included the Worst Itch Numeric Rating Scale and safety.
Results: A total of 196 patients enrolled: 97 with ColdU and 99 with SD. Mean baseline provocation thresholds for TempTest ranged from 18.6°C to 20.7°C and 3.55 to 3.64 pins for FricTest. At 12W, the percentage of patients with negative TempTest was 46.9% (P = .0023), 53.1% (P = .0011), and 12.5%, and negative FricTest was 57.6% (P < .0001), 42.2% (P = .0003), and 3.2% for 150 mg every 4 weeks, 300 mg every 8 weeks and placebo, respectively. Barzolvolimab was well-tolerated with hair color changes with grade I to II neutropenia being the most common adverse events.
Conclusion: The study met the primary endpoint with unprecedented, clinically meaningful, and statistically significant complete response rates (negative provocation test) in patients with ColdU and SD at 12W. This phase II barzolvolimab study is the first large, randomized placebo-controlled study to achieve a successful outcome for CIndU and supports advancing to phase III registrational studies.

Asthma, other lower airway disorders

LBA004

BATURA: A FULLY VIRTUAL RANDOMIZED CONTROLLED STUDY OF AS-NEEDED ALBUTEROL-BUDESONIDE VS ALBUTEROL IN MILD ASTHMA

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Background: In MANDALA, rescue therapy with as-needed albuterol-budesonide 180/160 µg (ALB-BUD) pressurized metered-dose inhaler reduced severe exacerbation risk by 28% vs as-needed albuterol 180 µg (ALB) pressurized metered-dose inhaler, in patients aged 18 years or older with moderate-to-severe asthma. Information is limited on as-needed ALB-BUD use in patients with mild asthma, despite this population bearing substantial exacerbation risk and burden. The BATURA study (NCT05505734) examined the efficacy and safety of ALB-BUD vs ALB in participants with mild asthma.
Methods: BATURA, a fully virtual, phase IIIb, double-blind, event-driven study, randomized participants aged 12 years and older with mild asthma (using as-needed short-acting β_2-agonists ± low-dose inhaled corticosteroids/leukotriene modifiers) 1 to 1 to ALB-BUD or ALB, as-needed for symptoms, for 12 to 52 weeks. All trial-related visits were virtual. We reported severe exacerbation risk, measured as time-to-first severe exacerbation (defined as an exacerbation resulting in 3 days or longer systemic corticosteroid use, an emergency-room/urgent care visit for asthma requiring systemic corticosteroids, hospitalization, or death; primary endpoint) and safety.
Results: The BATURA study enrolled 2421 participants (1209 randomized to ALB-BUD and 1212 to ALB); the mean (SD) age was 42.7 (14.50) years; 2.8% were 12 to 17 years old and 68.3% female. Compared with ALB, ALB-BUD reduced severe exacerbation risk by 47% in a time-to-first-severe-exacerbation analysis (hazard ratio = 0.535, 95% CI: 0.392-0.730, P < .001). Similar percentages of participants experienced adverse events in both groups (Table 1).
Conclusion: In participants with mild asthma, the use of ALB-BUD as-needed rescue therapy for symptoms reduced the risk of a severe exacerbation by 47% compared with ALB. Both treatment groups had comparable safety profiles.

Table 1 Overall Adverse Event Profile During the On-Treatment Period, in Patients Receiving As-Needed Albuterol-Budesonide 180/160 µg vs As-Needed Albuterol 180 µg

Patients with AEs during on-treatment period, n (%)	Albuterol-budesonide 180/160 µg (N=1,209)	Albuterol 180 µg (N=1,212)
Any AE	435 (36.0)	461 (38.0)
Any serious AE	29 (2.4)	31 (2.6)
Any AE leading to treatment discontinuation	17 (1.4)	31 (2.6)
Any treatment-related AE	40 (3.3)	41 (3.4)
Any AE with an outcome of death	1 (0.1)	1 (0.1)
Most common AEs		
Upper respiratory tract infection	56 (4.6)	67 (5.5)
COVID-19	50 (4.1)	59 (4.9)
Nasopharyngitis	41 (3.4)	32 (2.6)

AEs, adverse events; COVID-19, coronavirus disease 2019.

LBA005

EFFECTIVENESS OF NIRSEVIMAB IN INFANTS AGAINST RESPIRATORY SYNCYTIAL VIRUS AND RELATED EVENTS

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Background: Nirsevimab is Centers for Disease Control and Prevention–recommended for infants to prevent respiratory syncytial virus (RSV) disease, the most common cause of lower respiratory tract disease (LRTD). Previously published nirsevimab effectiveness has been limited to the hospital setting. This study assessed nirsevimab's effectiveness against RSV, LRTD, and associated medical encounters across all settings in an integrated healthcare delivery system between 2023 and 2024.
Methods: Nirsevimab administration started on October 19, 2023. We included healthy-term infants born in April 2023 or later and excluded infants with high-risk conditions or whose mothers were RSV-vaccinated. The primary endpoint was a polymerase chain reaction positive RSV LRTD diagnosis by the International Classification of Diseases, 10th Revision code in any setting. Nirsevimab effectiveness against RSV LRTD was assessed by Cox regression and estimated as (1-hazard ratio). We estimated the association of nirsevimab treatment with the mean number of encounters per episode by linear regression and the odds of hospitalization by logistic regression.

Results: The study included 31,900 infants; 15,647 of whom received nirsevimab. There were 35 RSV LRTD episodes (6.1/1000 person-years) among nirsevimab-treated infants compared with 462 episodes (58.5/1000 person-years) among untreated infants. The adjusted nirsevimab effectiveness estimate against RSV LRTD was 87.2% (CI: 81.7%-91.1%). Nirsevimab-treated infants with RSV LRTD had a lower mean number of encounters (2.1 vs 2.7, $P = .001$) and lower hospitalization odds (odds ratio = 0.11, CI: 0.01-0.85).

Conclusion: In this large study, nirsevimab reduced the risk of RSV LRTD by 87% across all healthcare settings. Compared with untreated infants, those who had RSV LRTD after nirsevimab had significantly fewer medical encounters and were less likely to be hospitalized.