Post-Hoc Analyses Support Efficacy of Lebrikizumab in Patients With Moderate-to-Severe Uncontrolled Eosinophilic Asthma and Prior Exacerbations

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OBJECTIVE

- To describe post hoc analyses of exacerbation rate reduction and lung function improvement in adults with uncontrolled eosinophilic asthma (baseline elevated fractional exhaled nitric oxide [FeNO] and/or elevated blood eosinophils) with a history of ≥1 asthma exacerbation in the past 12 months from the LAVOLTA I and LAVOLTA II clinical trials

CONCLUSIONS

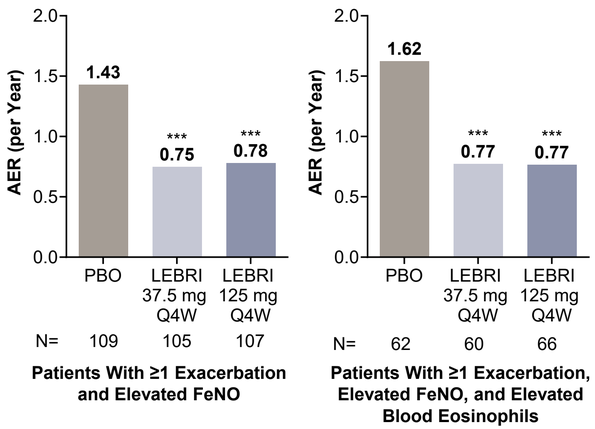
- This post hoc analysis demonstrates that lebrikizumab could be beneficial in patients with uncontrolled asthma with type 2 inflammation (elevated FeNO and/or elevated eosinophils) and a history of recent exacerbations
- Limitations of this study include small sample sizes and post hoc analyses are not multiplicity controlled

Fall Clinical 2024; Las Vegas, USA; 24-27 October 2024

BACKGROUND

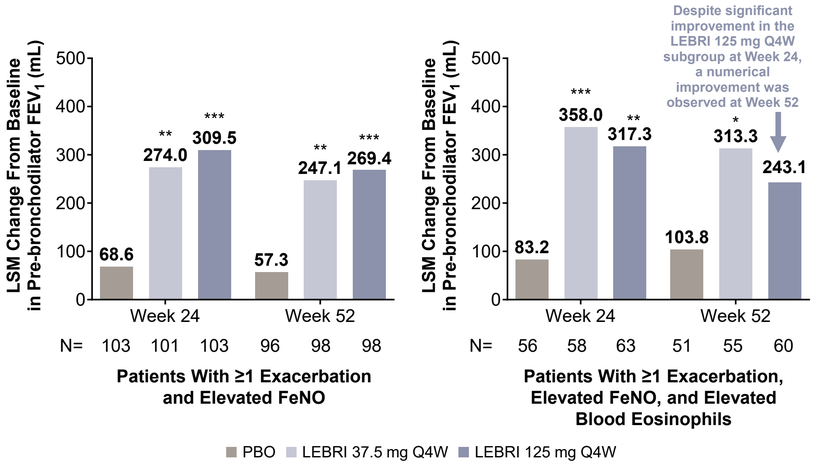
- Lebrikizumab, a novel, high-affinity monoclonal antibody selectively targeting interleukin-13, has demonstrated efficacy and safety in Phase 3 and 3b studies for moderate-to-severe AD at doses of 250 mg Q2W for induction and 250 mg Q4W for maintenance
- The Phase 3 LAVOLTA I (NCT01867125) and LAVOLTA II (NCT01868061) clinical trials of lebrikizumab in moderate-to-severe uncontrolled asthma that were completed in 2016, have not demonstrated consistent reductions in exacerbations,[1,2] possibly due to suboptimal patient selection and premature understanding of asthma phenotypes[2]
  - These trials studied doses of 37.5 mg and 125 mg Q4W

Lebrikizumab Significantly Reduced AER Compared With Placebo at Week 52



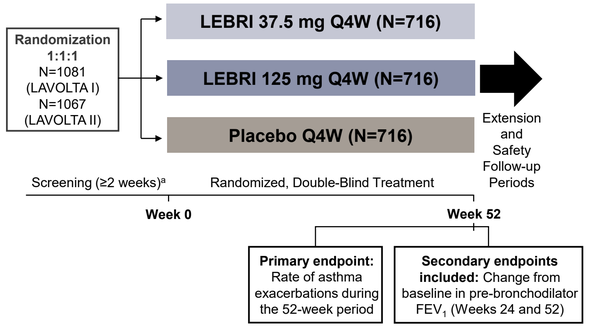
***p<0.001 vs. PBO.

Lebrikizumab Improved FEV_1 Compared With Placebo at Weeks 24 and 52



*p<0.05, **p<0.01, ***p<0.001 vs. PBO.

Study Design: LAVOLTA I and LAVOLTA II



[a]To prospectively determine that patients met eligibility criteria and to obtain periostin concentrations for stratified randomization and blood eosinophil counts.

Key Eligibility Criteria

- Adults aged 18-75 years
- Uncontrolled asthma, defined by a 5-item Asthma Control Questionnaire score ≥1.5 with ≥1 of the following:
  - Symptoms >2 days/week
  - Nighttime awakenings ≥1 time/week
  - Use of short-acting β-agonist rescue medication >2 days/week
  - Interference with normal daily activities
- Pre-bronchodilator forced expiratory volume in 1 second (FEV_1) 40-80% predicted and improvement in FEV_1 after bronchodilator of ≥12%
- Daily treatment with inhaled corticosteroids (500-2000 µg/day fluticasone propionate or equivalent) for ≥6 months
- ≥1 additional controller medication
- Patients were enrolled irrespective of asthma exacerbation history

Analysis Population

- Post hoc analysis of pooled observed data from LAVOLTA I and II in the subgroup of patients with ≥1 asthma exacerbation in the past 12 months and:
  - Baseline elevated FeNO (≥50 mean ppb)
  - Baseline elevated FeNO (≥50 mean ppb) and baseline elevated blood eosinophils (≥300 cells/µL)

Outcomes

- Annualized adjusted exacerbation rate (AER) vs. placebo at Week 52
  - Exacerbation events were defined as any new or increased asthma symptoms that led to treatment with systemic corticosteroids or to hospitalization
- Least squares mean (LSM) difference in pre-bronchodilator FEV_1 vs. placebo at Weeks 24 and 52
  - Asthma therapies with the potential to affect FEV_1 were withheld until pre-bronchodilator FEV_1 measurements were completed

Statistical Analyses

- AER: Poisson regression model included treatment and adjusted for over-dispersion with the following covariates in addition to log (patient-years) as an offset: number of asthma exacerbations within the last 12 months, baseline asthma medications, and geographic region
- FEV_1: Mixed model for repeated measures included treatment, and adjusted baseline FEV_1, visit, baseline FEV_1 × visit, treatment × visit, number of asthma exacerbations within the last 12 months, baseline asthma medication, and geographic region
- All analyses are considered post hoc, with no multiplicity adjustment

References: 1. Hanania NA, et al. *Lancet Respir Med*. 2016;4:781-796. 2. Corren J, et al. *J Allergy Clin Immunol Pract*. 2024;12:1215-1224.

Abbreviations: *AD=atopic dermatitis; AER=adjusted exacerbation rate; FeNO=fractional exhaled nitric oxide; FEV_1=forced expiratory volume in 1 second; LEBRI=lebrikizumab; LSM=least squares mean; PBO=placebo; ppb=parts per billion; Q2W=every 2 weeks; Q4W=every 4 weeks*

Disclosures: J. Corren has served as a speaker and/or consultant for and/or received research grants and/or clinical trial funds from: Amgen, AstraZeneca, Eli Lilly and Company, Genentech, Novartis, Optinose, Regeneron, and Sanofi; **S. J. Szefler** has consulted for: AstraZeneca, GlaxoSmithKline, Moderna, Propeller Health, Regeneron, and Sanofi; and has received research support from: the Colorado Department of Public Health and Environment's Colorado Cancer, Cardiovascular and Pulmonary Disease Program, the National Institutes of Health National Heart, Lung and Blood Institute, and Propeller Health; **E. Sher** has served as an advisor, speaker, researcher, and/or consultant for: AbbVie, Aimmune Therapeutics, ALK-Abelló, Allergy Therapeutics, Amgen, AstraZeneca, Eli Lilly and Company, Genentech, GlaxoSmithKline, Merck, Novartis, Optinose, Regeneron, Sanofi Genzyme, and Shionogi; **P. Korenblat** has nothing to declare; **W. Soong** has served as an investigator for: AbbVie, Allakos, Amgen, Dermavant, Eli Lilly and Company, Escient Pharmaceuticals, Galderma, GlaxoSmithKline, Incyte Corporation, LEO Pharma, Pfizer, Regeneron, Sanofi, Teva, and Upstream Bio; and as a consultant or speaker for: AbbVie, Amgen, Dermavant, Eli Lilly and Company, Genentech, GlaxoSmithKline, Incyte Corporation, LEO Pharma, Novartis, Pfizer, Regeneron, Sanofi, Teva, and UCB Pharma; **N. A. Hanania** has received honoraria for serving as an advisor or consultant for: Amgen, AstraZeneca, Genentech, GlaxoSmithKline, Novartis, Regeneron, Sanofi, and Teva; and his institution has received research grant support on his behalf from: AstraZeneca, Genentech, GlaxoSmithKline, Novartis, Sanofi, and Teva; **G. Berman** has received speaker fees from: Allergan, Alder BioPharmaceuticals, Amgen, Biohaven, Eli Lilly and Company, and Teva; and has consulted for: Alder BioPharmaceuticals, Biohaven, and electroCore; **G. Brusselle** has received fees for attending advisory boards and speaker fees from: AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Novartis, Merck Sharp & Dohme, and Sanofi Regeneron; **R. Zitnik** has served as a consultant for: Eli Lilly and Company; **C. R. Natalie**, **K. Siu**, and **W-S. Wu** are employees and shareholders of: Eli Lilly and Company; **M. Qiao** is an employee of: TigerMed Inc; **P. Lio** reports research grants and/or funding from: AbbVie, AOBiome, and Eczema Foundation; has been on speakers bureaus for: AbbVie, Eli Lilly and Company, Galderma, Hyphens Pharma, Incyte Corporation, La Roche-Posay/L'Oréal, MyOr, ParentMD, Pfizer, Pierre Fabre, and Sanofi Regeneron; has received consulting fees from and/or been on advisory boards for: AbbVie, Almirall, Amyris, Arbonne, Arcutis, ASLAN Pharmaceuticals, Bodewell, Boston Skin Science, Bristol Myers Squibb, Burt's Bees, Castle Biosciences, Codex Labs, Concerto Biosciences, Dermavant, Dermira, Dermveda, Eli Lilly and Company, Galderma, IntraDerm, Janssen, Johnson & Johnson, Kaleido Biosciences, Kimberly-Clark, L'Oréal, LEO Pharma, Lipidor, Menlo Therapeutics, Merck, Micreos, MyOr, Sanofi Regeneron, Sibel Health, Skinfix, Sonica, Theraplex, UCB Pharma, Unilever, Verrica Pharmaceuticals, and Yobee Care; has stock options with: LearnSkin/LearnHealth, Medable, Micreos, Modernizing Medicine, and Yobee Care; has a patent pending for: Theraplex product with royalties paid; and is a board member and scientific advisory committee member of: the National Eczema Association; **A. W. Armstrong** has served as a consultant, speaker, and/or investigator for: AbbVie, Almirall, Arcutis, ASLAN Pharmaceuticals, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Dermira, Eli Lilly and Company, EPI Health, Incyte Corporation, Janssen, LEO Pharma, Modernizing Medicine, Nimbus Therapeutics, Novartis, Ortho Dermatologics, PAREXEL, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma

Medical writing assistance was provided by Clare Weston, MSc, of ProScribe – Envision Pharma Group, and was funded by Eli Lilly and Company

This study was funded by Roche. Post-hoc statistical analyses were funded by Dermira, a wholly-owned subsidiary of Eli Lilly and Company. Eli Lilly and Company provided additional funding for statistical analyses.

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