



Lebrikizumab Dosed Every Four Weeks Maintained Durable Skin Clearance in Lilly's Phase 3 Monotherapy Atopic Dermatitis Trials

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- *New, late-breaking data show lebrikizumab responders reported long-lasting results at one year of treatment across measures of improvement in skin clearance, itch and disease extent and severity*
- *Results suggest less frequent, every four week dosing of lebrikizumab provided similar improvements to every two week dosing*
- *Regulatory submissions for U.S. and EU planned for this year*

INDIANAPOLIS, Sept. 8, 2022 /PRNewswire/ -- New detailed results from Eli Lilly and Company's (NYSE: LLY) Phase 3 monotherapy studies in atopic dermatitis (AD) showed investigational lebrikizumab provided robust and durable improvements in skin clearance and itch for patients who achieved a clinical response* at Week 16 through one year of treatment. Lebrikizumab, a high-affinity and potent IL-13 inhibitor, delivered similar results when dosed once every four weeks or once every two weeks after Week 16. These data were featured in a late-breaking, oral presentation at the 31st European Academy of Dermatology and Venerology (EADV) Congress. The company previously announced topline results of these one-year analyses of ADvocate 1 and ADvocate 2 in June 2022.

"Despite available treatment options, many patients with atopic dermatitis experience distressing symptoms every day over the course of years. Thus, there is a clear need for new therapies that maintain long-term results," said Andrew Blauvelt, M.D., board-certified dermatologist, president of Oregon Medical Research Center and lead author of the ADvocate analyses. "Lebrikizumab helped patients reduce the impact of atopic dermatitis by maintaining long-lasting skin clearance and itch relief with dosing at every four weeks in the ADvocate studies. These data help deepen our understanding of the role lebrikizumab may play in treating atopic dermatitis and will assist practitioners to improve clinical outcomes for their patients with this chronic disease."

Efficacy with every four week dosing, after a 16-week induction period with lebrikizumab every two weeks, was similar to that of every two week dosing.

	Lebrikizumab Week 52 Results		Lebrikizumab Week 52 Results	
	ADvocate 1		ADvocate 2	
	Lebrikizumab 250 mg Q4W	Lebrikizumab 250 mg Q2W	Lebrikizumab 250 mg Q4W	Lebrikizumab 250 mg Q2W
IGA (0,1) and ≥2-point improvement	74 %	76 %	81 %	65 %
EASI-75	79 %	79 %	85 %	77 %
Pruritus ("Itch") NRS ≥4-point improvement	80 %	81 %	88 %	90 %

EASI=Eczema Area and Severity Index; EASI-75=75% improvement in EASI; IGA=Investigator's Global Assessment 0 or 1 ("clear" or "almost clear"); Q2W=every 2 weeks; Q4W=every 4 weeks

Safety among patients at 52 weeks was consistent with the induction phase of the trials and prior lebrikizumab studies in AD. The incidence rate of treatment-emergent adverse events remained stable over time in patients with lebrikizumab. The proportion of lebrikizumab-treated patients who reported an adverse event in ADvocate 1 and ADvocate 2 through Week 52 was 58% and 68%, respectively. Most adverse events across the two studies were mild or moderate in severity, nonserious and did not lead to treatment discontinuation. The most commonly reported adverse events were conjunctivitis, common cold and headache.

"Based on the robust and clinically meaningful results from our clinical trial program in atopic dermatitis, we believe lebrikizumab, if approved, could become a first-line treatment for dermatologists and many of their patients with moderate-to-severe disease who suffer from debilitating symptoms and seek new treatment options and prefer less frequent dosing," said Lotus Mallbris, M.D., Ph.D., vice president of global immunology development and medical affairs at Lilly.

Full results from the Phase 3 studies will be published in a peer-reviewed journal. Lilly and Almirall S.A. plan to submit regulatory applications to U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) respectively for lebrikizumab in AD this year. The FDA granted lebrikizumab Fast Track designation in AD in December 2019.

"The detailed data that were presented today demonstrate the potential role lebrikizumab could play in the treatment of AD. Living with atopic dermatitis means facing a complex condition that impacts quality of life and overall wellbeing. We look forward to working with Lilly and regulators on bringing to market this important medicine," said Karl Ziegelbauer, Ph.D., Almirall's Chief Scientific Officer.

Lilly has exclusive rights for development and commercialization of lebrikizumab in the United States and the rest of the world outside Europe. Almirall has licensed the rights to develop and commercialize lebrikizumab for the treatment of dermatology indications, including AD, in Europe.

* Responders were defined as those achieving a 75% reduction in the Eczema Area and Severity Index from baseline (EASI-75) or an IGA 0 or 1

("clear" or "almost clear") with a 2-point improvement and without rescue medication use at Week 16. At Week 16, responders were re-randomized to lebrikizumab 250 mg every two weeks or four weeks or placebo for an additional 36 weeks.

About ADvocate 1 and ADvocate 2 and the Phase 3 Program

[ADvocate 1](#) and [ADvocate 2](#) are 52-week randomized, double-blind, placebo-controlled, parallel-group, global, Phase 3 studies designed to evaluate lebrikizumab as monotherapy in adult and adolescent patients (aged 12 to less than 18 years of age and weighing at least 40 kg) with moderate-to-severe AD.

During the 16-week treatment period, patients received lebrikizumab 500-mg initially and at two weeks, followed by lebrikizumab 250-mg or placebo every two weeks. In the maintenance period, patients with moderate-to-severe AD who achieved a clinical response after 16 weeks of lebrikizumab treatment were re-randomized to receive lebrikizumab every two weeks or four weeks or placebo for an additional 36 weeks. Patients who required rescue treatment during the induction period or who did not meet protocol-defined response criteria at 16 weeks received lebrikizumab every two weeks for an additional 36 weeks.

The primary endpoints were measured by an Investigator Global Assessment (IGA) score of clear (0) or almost clear (1) skin with a reduction of at least two points from baseline and at least 75 percent change in baseline in the Eczema Area and Severity Index (EASI-75) score at 16 weeks. EASI measures extent and severity of the disease. Key secondary endpoints were measured by IGA, EASI, the Pruritus Numeric Rating Scale, Sleep-Loss due to Pruritus and the Dermatology Life Quality Index.

The U.S. Food and Drug Administration (FDA) granted lebrikizumab Fast Track designation in AD in December 2019. The lebrikizumab Phase 3 program consists of five key global studies evaluating more than 2,000 patients, including two monotherapy studies (ADvocate 1 and 2), a combination study with topical corticosteroids (ADhere), as well as long-term extension (ADjoin) and adolescent open label (ADore) studies. Lilly has also initiated a first-of-its-kind [clinical study](#) dedicated to people of color living with AD. The study will further evaluate the efficacy and safety of lebrikizumab in people of color to generate additional data and disease information to help investigators and clinicians provide better diagnoses and treatment options.

About Lebrikizumab

Lebrikizumab is a novel, investigational, monoclonal antibody designed to bind IL-13 with high affinity, slow disassociation rate and high potency to specifically prevent the formation of the IL-13R α 1/IL-4R α heterodimer complex and subsequent signaling, thereby inhibiting the biological effects of IL-13 in a targeted and efficient fashion.^{1,2} AD is an IL-13 dominant disease in which IL-13 drives skin barrier dysfunction, itch, skin thickening, and susceptibility to infection.^{3,4}

About Lilly

Lilly unites caring with discovery to create medicines that make life better for people around the world. We've been pioneering life-changing discoveries for nearly 150 years, and today our medicines help more than 47 million people across the globe. Harnessing the power of biotechnology, chemistry and genetic medicine, our scientists are urgently advancing new discoveries to solve some of the world's most significant health challenges, redefining diabetes care, treating obesity and curbing its most devastating long-term effects, advancing the fight against Alzheimer's disease, providing solutions to some of the most debilitating immune system disorders, and transforming the most difficult-to-treat cancers into manageable diseases. With each step toward a healthier world, we're motivated by one thing: making life better for millions more people. That includes delivering innovative clinical trials that reflect the diversity of our world and working to ensure our medicines are accessible and affordable. To learn more, visit [Lilly.com](#) and [Lilly.com/newsroom](#) or follow us on [Facebook](#), [Instagram](#), [Twitter](#) and [LinkedIn](#). P-LLY

Lilly Cautionary Statement Regarding Forward-Looking Statements

This press release contains forward-looking statements (as that term is defined in the Private Securities Litigation Reform Act of 1995) about lebrikizumab as a potential treatment for patients with atopic dermatitis and reflects Lilly's current beliefs and expectations. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of research, development and commercialization. Among other things, there can be no guarantee that planned or ongoing studies will be completed as planned, that future study results will be consistent with the results to date, or that lebrikizumab will receive regulatory approvals, or be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's most recent Form 10-K and Form 10-Q filings with the United States Securities and Exchange Commission. Except as required by law, Lilly undertakes no duty to update forward-looking statements to reflect events after the date of this release.

¹ Simpson EL, et al. *J Am Acad Dermatol*. 2018;78(5):863-871.e11.

² Okragly A, et al. *Comparison of the Affinity and in vitro Activity of Lebrikizumab, Tralokinumab, and Cendakimab*. Presented at the Inflammatory Skin Disease Summit, New York, November 3-6, 2021.

³ Tsoi LC, et al. Atopic Dermatitis Is an IL-13-Dominant Disease with Greater Molecular Heterogeneity Compared to Psoriasis. *J Invest Dermatol*. 2019;139(7):1480-1489.

⁴ Bieber T. Interleukin-13: Targeting an underestimated cytokine in atopic dermatitis. *Allergy*. 2020;75:54-62.

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