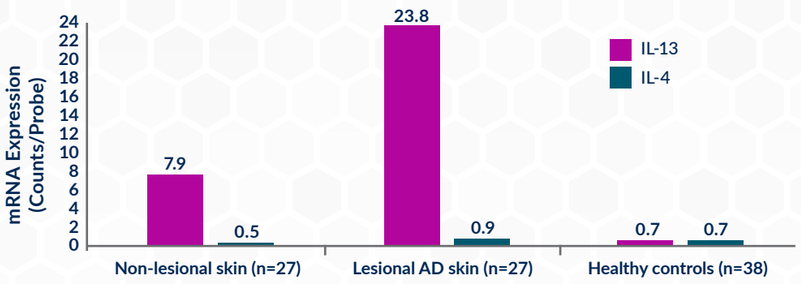
Lebrikizumab▼: Short and Long-Term Disease Control in Moderate-to-Severe AD Through Selective IL-13 Inhibition

Citation: EMJ. 2024;9[3]:46-47. https://doi.org/10.33590/emj/BUHL9841.

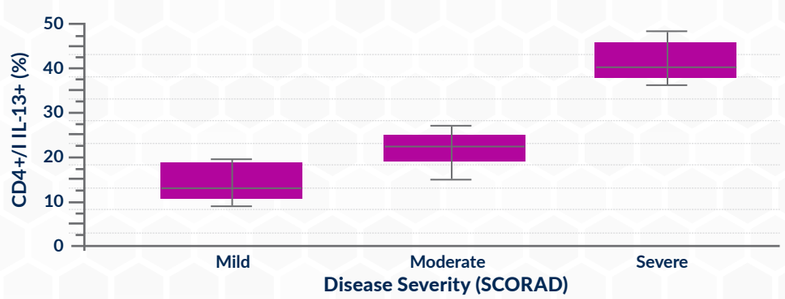
The publication of this infographic was funded by almirall

IL-13 is the key cytokine in the skin of patients with AD[1]

1. IL-13, but not IL-4, shows increased gene expression in AD skin[1]

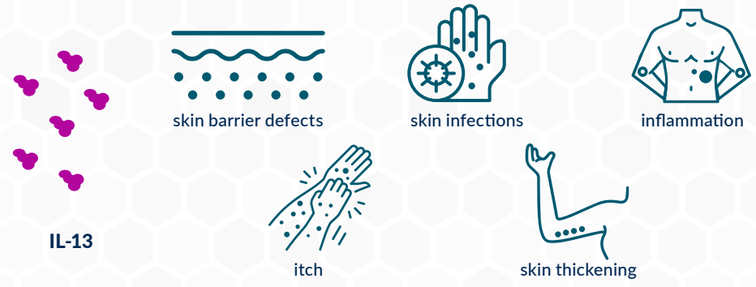


2. IL-13-producing CD4+ cells are increased in AD[2], with levels correlating with disease severity in the skin[2]



Adapted from La Grutta S et al. 2005[2]

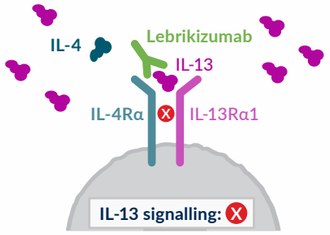
3. IL-13 drives several key signs and symptoms of atopic dermatitis[3,4]



Mechanism of Action of Lebrikizumab

Lebrikizumab selectively targets IL-13 and inhibits its signalling[3,5,6]

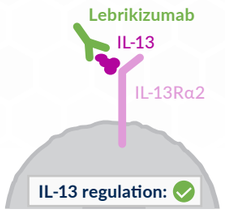
Lebrikizumab binds to IL-13 with high affinity and slow off-rate, thereby blocking the downstream effects of IL-13 with high potency[7]



Type II receptor
Skin structural cells and myeloid cells

Lebrikizumab does not interfere with the IL-13 endogenous regulation mechanism of the decoy receptor[3,5,6]

The IL-13+lebrikizumab complex can still bind to IL-13Rα2



Decoy receptor
Skin structural cells

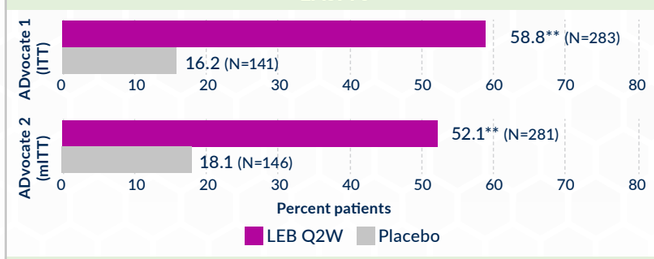
Key Lebrikizumab Data: Monotherapy ADvocate 1 and ADvocate 2 trials[8,9]

Short-term efficacy from ADvocate 1 and ADvocate 2 trials:

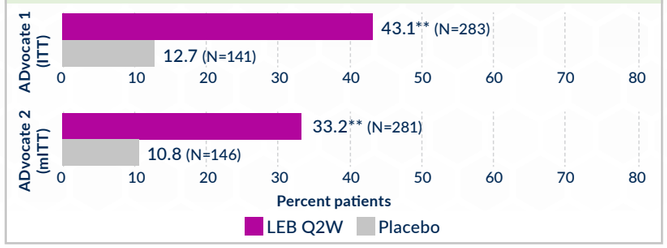
>50% patients achieved EASI-75 at Week 16

Week 16*

EASI-75



IGA (0/1) with ≥2 point reduction from baseline



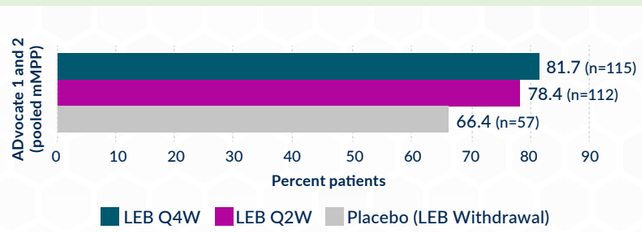
*Missing data due to lack of efficacy or data after rescue medication usage were imputed with NRI. Other missing data were imputed with MI.
**P<0.001 versus placebo

Long-term efficacy from ADvocate 1 and ADvocate 2 trials:†

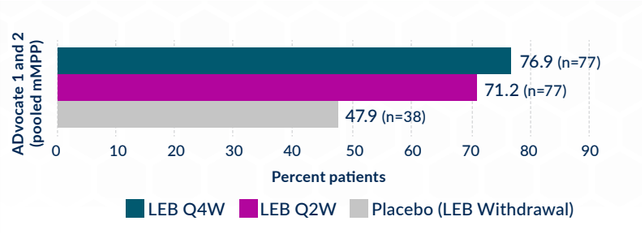
More than 80% of Week 16 per-protocol responders maintained EASI-75 with Q4W monotherapy between Weeks 16 and 52

Week 52*

Maintenance of EASI-75 at Week 52 in lebrikizumab Week 16 responders



Maintenance of IGA (0/1) with ≥2 point reduction from baseline at Week 52 in lebrikizumab Week 16 responders



†Lebrikizumab per-protocol responders were re-randomised to continue lebrikizumab Q2W, or move to lebrikizumab Q4W or a placebo-withdrawal arm. Per protocol-specified criteria for having a response to lebrikizumaban: IGA score of 0 or 1 with a reduction of ≥2 points from baseline or a 75% improvement in the EASI score without rescue medication use.

The most common adverse reactions are conjunctivitis (6.9%), injection site reactions (2.6%), conjunctivitis allergic (1.8%), and dry eye (1.4%). The safety profile of lebrikizumab as monotherapy through Week 52 or in combination with TCS through Week 56 is consistent with the safety profile observed up to Week 16.[10]

Indication and Posology[10]

- Lebrikizumab is indicated for the treatment of moderate-to-severe AD in adults and adolescents ≥12 years with a body weight ≥40 kg who are candidates for systemic therapy.
- Recommended dose of lebrikizumab is 500 mg (two 250 mg injections) at both Week 0 and Week 2, followed by 250 mg administered subcutaneously every other week up to Week 16. Once clinical response is achieved, the recommended maintenance dose of lebrikizumab is 250 mg every fourth week.

Abbreviations
AD: atopic dermatitis; CD4: cluster of differentiation 4; EASI: Eczema Area and Severity Index; IL-13: interleukin-13; IL-13Rα: interleukin-13 receptor subunit alpha; IL4Rα: interleukin-4 receptor alpha; IGA: Investigator Global Assessment; ITT: intention-to-treat; JAK: Janus kinase; LEB: lebrikizumab; mMPP: modified maintenance primary population; mITT: modified intention-to-treat; Q2W: every 2 weeks; Q4W: every 4 weeks; Rα: receptor α; SCORAD: SCORing Atopic Dermatitis; TCS: topical corticosteroids.

References:
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UK Prescribing Information can be found here

Lebrikizumab:

- Selectively binds IL-13 with high affinity and inhibits its downstream signalling
- Has demonstrated short- and long-term efficacy in signs and symptoms of moderate to severe AD
- Shows a consistent safety profile in short- and long-term use[7]
- Is administered every 4 weeks as maintenance therapy

UK-EBG-2400049 | August 2024