Lebrikizumab Provides Clinically Meaningful Improvements in Atopic Dermatitis in Patients Previously Treated With Dupilumab

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Linda Stein Gold,[1] Jan Gutermuth,[2] David Adam,[3-5] Carsten Flohr,[6] Stephan Weidinger,[7] Amber Reck Atwater,[8] Evangeline Pierce,[8] Fan Emily Yang,[8] Sherry Chen,[9] Ignasi Pau-Charles,[10] Lisa A. Beck[11]

[1]Dermatology Clinical Research, Henry Ford Health System, Detroit, USA; [2]Vrije Universiteit, Brussel, Belgium; [3]CCA Medical Research, Ajax, Canada; [4]University of Toronto, Temerty Faculty of Medicine, Division of Dermatology, Toronto, Canada; [5]Probity Medical Research, Waterloo, Canada; [6]St. John's Institute of Dermatology, London, UK; [7]University Hospital Schleswig-Holstein, Kiel, Germany; [8]Eli Lilly and Company, Indianapolis, USA; [9]Tigermed, Somerset, USA; [10]Almirall, S.A., Barcelona, Spain; [11]University of Rochester Medical Center, Rochester, USA

BACKGROUND

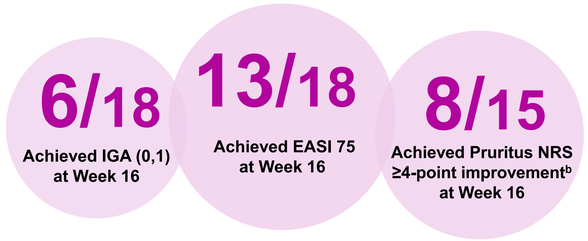
- AD is a chronic skin disease that can be a serious burden, affecting sleep, daily activities, and social relationships[1]
- Dupilumab is used to treat moderate-to-severe AD; however, not all patients treated with dupilumab achieve and maintain clinically meaningful response[2]
- Lebrikizumab is a novel monoclonal antibody targeting IL-13 that selectively prevents the formation of the IL-13Rα1/IL-4Rα heterodimer receptor signaling complex[3]
- Lebrikizumab has demonstrated efficacy and a positive benefit-risk profile:
  - As a monotherapy in patients with moderate-to-severe AD at the 16-week primary endpoint in the 2 Phase 3, randomized, double-blind, placebo-controlled trials (ADvocate1 and ADvocate2)[4]
  - In a TCS combination study in patients with moderate-to-severe AD at the 16-week endpoint in the Phase 3, randomized, double-blind, placebo-controlled ADhere study (NCT04250337)[5]

OBJECTIVE

- To evaluate the efficacy of lebrikizumab in the subset of patients with prior dupilumab exposure and moderate-to-severe AD in the ADhere TCS combination study

SUMMARY OF KEY FINDINGS

Of patients[a] with prior dupilumab exposure who were treated with **LEB 250 mg Q2W + TCS**:



This analysis suggests that patients with prior dupilumab exposure may respond to treatment of moderate-to-severe AD with lebrikizumab + TCS

[a] With non-missing values at Week 16; [b] In patients who had Pruritus NRS ≥4 points at baseline

CONCLUSIONS

- Patients[a] with prior dupilumab exposure showed improvement at Week 16 when treated with lebrikizumab + TCS in:
  - IGA (0,1) response with ≥2-point improvement
  - EASI 75
  - Pruritus NRS ≥4-point improvement[b]
- The results of this subpopulation analysis suggest that patients with moderate-to-severe AD and prior dupilumab exposure may respond to lebrikizumab + TCS combination therapy

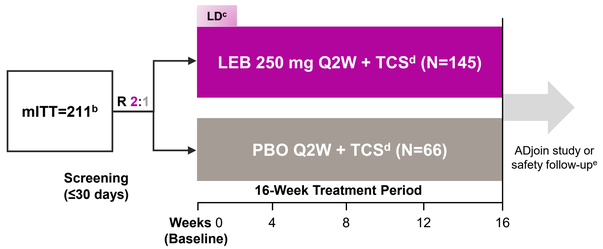
[a] With non-missing values at Week 16; [b] In patients who had Pruritus NRS ≥4 points at baseline

LIMITATIONS

- This subpopulation analysis included a small number of patients; therefore, these results must be interpreted with caution

METHODS

Study Design: ADhere[a]



[a] Patients in ADhere were permitted to use dupilumab ≥8 weeks prior to the ADhere study; [b] Efficacy analyses used the mITT population; [c] LEB-treated patients received a 500-mg LD at Weeks 0 and 2; [d] Use of TCS was required and TCS were provided within the trial; use could be tapered and stopped and then resumed as needed at the patient's discretion; [e] Patients completing the study could enter the ADjoin extension study or complete a safety follow-up 12 weeks after their last dose

Key Eligibility Criteria

- Adults or adolescents (≥12 to <18 years; weight ≥40 kg)
- Diagnosis of AD, as defined by the American Academy of Dermatology Consensus Criteria, for ≥1 year before screening
- Moderate-to-severe AD, defined as having all the following at the baseline visit:
  - EASI ≥16
  - IGA ≥3
  - BSA involvement ≥10%
- Candidate for systemic therapy

Outcomes

- IGA (0,1) with ≥2-point improvement from baseline, indicating clear or almost clear skin
- EASI 75, a measure of clinical impact according to the validated EASI scoring system
- Percentage of patients achieving ≥4-point reduction[a] in Pruritus NRS, an assessment of clinical impact[6]

[a] In patients with Pruritus NRS ≥4 at baseline

Analysis Population

- This analysis includes a subset of patients in the lebrikizumab treatment group (N=20) who had prior exposure to dupilumab
- Reasons for discontinuation of dupilumab included:
  - Loss of response or inadequate response (N=10)
  - Patient decision (N=4)
  - Intolerance to medication (N=1)
  - Other (N=5), including affordability, treatment availability, or unspecified reasons

Statistical Analyses

- ADhere efficacy analyses were performed on a modified population, excluding 17 patients (from a single study site) whose eligibility could not be confirmed
- All analyses were descriptive summaries using observed results
- Observed results excluded data collected after use of rescue medication or treatment discontinuation
- Patients with non-missing values were analyzed for each efficacy measure at Week 16

RESULTS

Baseline Demographics and Disease Characteristics

	ADhere Patients With Prior Dupilumab Use	ADhere Overall Population
	LEB 250 mg Q2W + TCS (N=20)	LEB 250 mg Q2W + TCS (N=145)
Age, years	46.0 (17.3)	37.5 (19.9)
Adults (≥18 years), n (%)	19	113 (77.9)
Adolescents (≥12 to <18 years), n (%)	1	32 (22.1)
Female, n (%)	7	70 (48.3)
Region, n (%)		
USA	19	103 (71.0)
Rest of world	1	42 (29.0)
Race, n (%)		
White	10	90 (62.1)
Asian	3	18 (12.4)
Black	2	19 (13.1)
Other	5	18 (12.4)
BMI, kg/m^2	28.8 (7.2)	26.5 (7.2)
Disease duration since AD diagnosis, years	27.0 (22.5)	21.0 (17.4)
Use of TCS, n (%)	20	145 (100)
IGA, n (%)		
3 (Moderate)	13	98 (67.6)
4 (Severe)	7	47 (32.4)
EASI	25.9 (8.1)	27.7 (11.1)
BSA % involvement	37.3 (15.7)	40.4 (21.9)
Pruritus NRS, n (%)		
<4	0[a]	9 (6.5)[b]
≥4	18 (100)[a]	130 (93.5)[b]

[a] N=18; [b] N=139

Note: Data are mean (SD) unless stated otherwise

IGA (0,1) in Lebrikizumab-Treated Patients With Prior Exposure to Dupilumab

6/18[a] patients treated with **LEB 250 mg Q2W + TCS** achieved IGA (0,1) with ≥2-point improvement at Week 16[b]

[a] Patients with non-missing IGA values at Week 16: N=18; [b] 57/130 (43.8%) patients (observed) achieved IGA (0,1) with ≥2-point improvement in the overall mITT ADhere LEB + TCS population

EASI 75 in Lebrikizumab-Treated Patients With Prior Exposure to Dupilumab

13/18 patients[a] treated with **LEB 250 mg Q2W + TCS** achieved EASI 75 at Week 16[b]

[a] Patients with non-missing EASI values at Week 16: N=18; [b] 97/130 (74.6%) patients (observed) achieved EASI 75 in the overall mITT ADhere LEB + TCS population

Pruritus NRS With ≥4-Point Improvement in Lebrikizumab-Treated Patients With Prior Exposure to Dupilumab

8/15[a] patients treated with **LEB 250 mg Q2W + TCS** achieved ≥4-point improvement in Pruritus NRS at Week 16[b]

[a] Patients with non-missing Pruritus NRS values at Week 16, with Pruritus NRS ≥4 points at baseline: N=15; [b] 59/107 (55.1%) patients (observed) with Pruritus NRS ≥4 points at baseline achieved ≥4-point improvement in Pruritus NRS in the overall mITT ADhere LEB + TCS population

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ABBREVIATIONS

AD=atopic dermatitis; BMI=body mass index; BSA=body surface area; EASI=Eczema Area and Severity Index; EASI 75=75% improvement from baseline in EASI; IGA=Investigator's Global Assessment; IGA (0,1)=IGA response of clear or almost clear; IL=interleukin; LD=loading dose; LEB=lebrikizumab; mITT=modified Intent-to-Treat; NRS=Numeric Rating Scale; PBO=placebo; Q2W=every 2 weeks; R=randomization; SD=standard deviation; TCS=topical corticosteroid(s)

DISCLOSURES

- **L. Stein Gold** is an investigator and/or consultant and/or speaker for: AbbVie, Amgen, Arcutis, Bristol Myers Squibb, Dermavant, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, and UCB Pharma; **J. Gutermuth** has conducted clinical trials and/or has been an advisory board member and/or speaker for: AbbVie, Almirall, Eli Lilly and Company, Galderma, Janssen, LEO Pharma, Pfizer, Regeneron, and Sanofi Genzyme; **D. Adam** has been an investigator, speaker, or advisory board member for: AbbVie, Actelion, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cohenus BioSciences, Dermavant, Dermira, Eli Lilly and Company, Galderma, Incyte Corporation, Janssen, LEO Pharma, Merck, Novartis, Pfizer, Regeneron, Reistone Biopharma, Sanofi Genzyme, Sun Pharma, and UCB Pharma; **C. Flohr** is Chief Investigator of: the UK-Irish Atopic Eczema Systemic Therapy Register and the UK National Institute for Health Research–funded TREAT and SOFTER trials; Principal Investigator in: the European Union Horizon 2020–funded BIOMAP Consortium; leads: the EU Horizon 2020 Joint Program Initiative–funded Trans-Foods consortium; and/or has received funding from: Pfizer and Sanofi Genzyme; **S. Weidinger** is a speaker, advisory board member, and/or investigator for: AbbVie, Almirall, Boehringer Ingelheim, Eli Lilly and Company, Galderma, GlaxoSmithKline, Kymab, LEO Pharma, Novartis, Pfizer, Regeneron, and Sanofi; and has received research grants from: La Roche-Posay, LEO Pharma, Pfizer, and Sanofi; **A. R. Atwater**, **E. Pierce**, **F. E. Yang**, and **S. Chen** are employees and shareholders of: Eli Lilly and Company; **I. Pau-Charles** is a current employee and shareholder of: Almirall; **L. A. Beck** is an advisory board member or consultant for: Allakos, Amgen, Arena Pharmaceuticals, AstraZeneca, Cara Therapeutics, DermTech, Evelo Biosciences, Galderma, GlaxoSmithKline, Incyte Corporation, Janssen, LEO Pharma, Merck, Numab Therapeutics, Pfizer, RAPT Therapeutics, Regeneron, Ribon Therapeutics, Sanofi-Aventis, Sanofi Genzyme, Stealth BioTherapeutics, Trevi Therapeutics, UCB Pharma, UNION Therapeutics, and Xencor; data monitoring committee member for: Novartis; and Principal Investigator for clinical studies supported by: AbbVie, AstraZeneca, DermTech, Kiniksa, Pfizer, Regeneron, Ribon Therapeutics, and Sanofi
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