Stability of long-term therapeutic responses to tralokinumab in adults with moderate-to-severe atopic dermatitis

Andrew Blauvelt[1], H. Chih-ho Hong[2], Ketty Peris[3], Norito Katoh[4], Marie Tauber[5], Mahreen Ameen[6], Melinda Gooderham[7], Christian Bjerregård Øland[8], Ann-Marie Tindberg[8], Le Gjerum[8], Kristian Reich[9]

[1]Oregon Medical Research Center, Portland, OR, USA; [2]University of British Columbia, Vancouver, BC, Canada; [3]Dermatologia, Università Cattolica del Sacro Cuore, Rome, Italy; [4]Kyoto Prefectural University of Medicine Graduate School of Medical Science, Kyoto, Japan; [5]Department of Allergology and Clinical Immunology, Lyon Sud Hospital and Inserm U1111 CIRI, Lyon, France; [6]Royal Free London National Health Services Foundation Trust, London, UK; [7]SKiN Centre for Dermatology, Peterborough, ON, Canada; Department of Medicine, Queen's University, Kingston, ON, Canada; [8]LEO Pharma A/S, Ballerup, Denmark; [9]Translational Research in Inflammatory Skin Diseases, Institute for Health Services Research in Dermatology and Nursing, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Objective

- To determine the proportion of tralokinumab-treated patients with AD who exhibit a stable long-term response, by conducting a post hoc analysis of clinical trial data from patients treated for up to 4 years in parent trial + ECZTEND

Results

- More than 70% of patients who continued treatment with tralokinumab in ECZTEND maintained stable EASI ≤7 (no to mild disease) at ≥80% of the days (**Table 1, Figures 1 and 2**)
- Over half of responders maintained stable EASI ≤7 at 100% of the days (**Figure 2**)

Table 1. Proportions of patients achieving endpoints during ECZTEND Week 16-152.

Outcome	≥80% of visits with outcome (Week 16-152)	≥80% of days with outcome (Week 16-152)	
% responders (95% CI)	AO (N=332)	AO (N=332)	MI[a] (N=347)
EASI ≤2	34.0	32.2 (27.4, 37.4)	30.7 (26.0, 35.9)
EASI ≤7	70.2	71.4 (66.3, 76.0)	69.1 (63.9, 73.9)
DLQI ≤5	NA	61.2 (55.8, 66.3)	59.1 (53.6, 64.4)
Worst weekly pruritus NRS ≤4	52.7	48.5 (43.2, 53.9)	46.5 (41.2, 51.9)
EASI ≤7 + (DLQI ≤5 OR Pruritus NRS ≤4)	60.5	53.9 (48.5, 59.2)	52.5 (47.1, 57.9)

[a]**2-step MI: (1)** Missing data up to 1 year in ECZTEND imputed using a standard regression-based MI method; **(2)** Missing data post 1 year imputed by carrying forward the within-patient AUC of days in-response [estimated between scheduled visits using the last observed year's data (only using data post the Week 16 visit due to the re-normalization of patients)]. AO = as observed.

Figure 1. Proportions of patients with ≥80% of days with target outcome AO during ECZTEND Week 16-152.

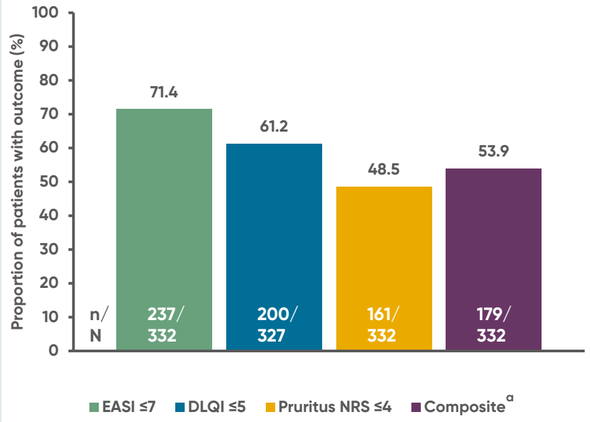
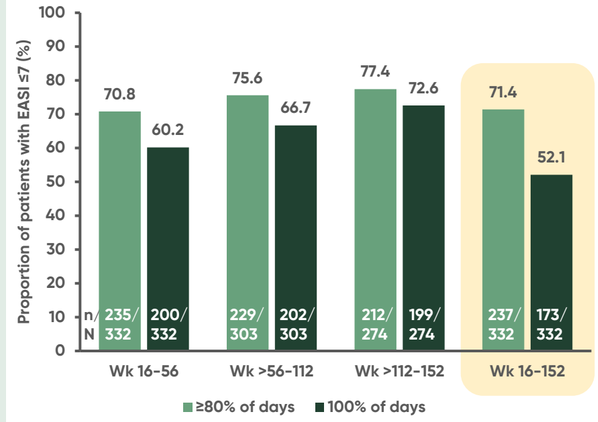


Figure 2. Proportions of patients achieving EASI ≤7 (no to mild disease) AO in subperiods of ECZTEND Week 16-152.



[a]**Composite:** EASI ≤7 and either DLQI ≤5 or Pruritus NRS ≤4.

Conclusions

- **High proportions of patients maintained a stable response with minimal or no fluctuations in physician- and patient-reported outcomes when continuing treatment with tralokinumab Q2W ± optional TCS for up to 3 years in ECZTEND**
- **These data show that it is possible to transition from flare-driven treatment with topical therapies to stable disease control with long-term tralokinumab treatment in adult patients with moderate-to-severe AD**

Background

- Maintaining disease stability and preventing fluctuations is crucial for patients with AD to effectively manage their condition
- Recently published consensus reports have defined optimal long-term treatment targets to ensure minimal residual disease or relapses[1,2]
- Tralokinumab is a high-affinity monoclonal antibody that specifically neutralizes interleukin-13
- ECZTEND (NCT03587805) is an ongoing open-label, 5-year extension trial investigating the long-term safety and efficacy of tralokinumab[3]

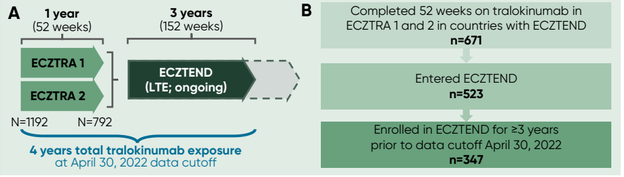
Methods

- Included 347 patients who were continuously treated with tralokinumab ± optional TCS for 52 weeks in the parent trial ECZTRA 1 or ECZTRA 2 and have been treated for up to 152 weeks in ECZTEND as of the April 30, 2022 data cutoff (**Figure 3**)

Assessments

- Assessments focused on timepoints after Week 16 in ECZTEND to allow for re-normalization of response rates due to variable time between last treatment in parent trial and first treatment in ECZTEND
- Stability of response was assessed as:
  - proportions of patients with the target endpoints at ≥80% of the attended visits AO and at ≥80% of the days in ECZTEND Week 16-152
    - EASI ≤2; EASI ≤7; DLQI ≤5; worst weekly pruritus NRS ≤4
    - Treat-to-target composite[1]: EASI ≤7 and either DLQI ≤5 or worst weekly pruritus NRS ≤4
  - proportions of patients with EASI ≤7 at 100% of the days in ECZTEND Week 16-152
- Proportions of days in response estimated using the AUC between scheduled visits AO, with missing data imputed using a 2-step MI approach mitigating survival bias

Figure 3. ECZTEND (**A**) study design and (**B**) patient disposition.



Abbreviations: %, percentage; AD, atopic dermatitis; AE, adverse event; AO, as observed; AUC, area under the curve; CI, confidence interval; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IQR, interquartile range; LTE, long-term extension; MI, multiple imputation; n, number of patients achieving the indicated metric; N, number of patients with recorded observation; NA, not available; NRS, numerical rating scale; Pruritus NRS, Worst Weekly Pruritus NRS; Q, quartile; Q2W, every 2 weeks; SCORAD, SCORing Atopic Dermatitis; TCS, topical corticosteroids; w/, with; Wk, week.

Baseline demographics and characteristics

- Median EASI improved from 26.7 at parent trial baseline (inclusion criteria, EASI ≥16) to 4.7 at ECZTEND baseline (**Table 2**)

Table 2. Baseline demographics and characteristics.

	ECZTEND interim efficacy analysis set (n=347)	
	Parent Trial Baseline	ECZTEND Baseline
Age (ECZTEND baseline) Median years (IQR)		42.0 (30.0; 53.0)
Male % (n)		59.1 (205)
Race % (n)[a]		
White		74.6 (259)
Black		5.8 (20)
Asian		16.1 (56)
Age at onset of AD Median years (IQR)		3.0 (1.0; 15.0)
Duration of AD (ECZTEND baseline) Median years (IQR)		29.0 (19.0; 43.0)
IGA severity % (n)		
Clear/Almost clear (score=0/1)	-	28.2 (98)
Mild (score=2)	-	35.4 (123)
Moderate (score=3)	49.6 (172)	30.5 (106)
Severe (score=4)	50.4 (175)	5.8 (20)
Median EASI (IQR)	26.7 (19.7; 38.4)	4.7 (2.2; 12.4)
Median SCORAD (IQR)	68.1 (60.8; 78.1)	32.8 (20.6; 46.9)
Median DLQI (IQR)	17.0 (11.0; 23.0), *n*=344	5.0 (2.0; 10.0), *n*=333
Worst weekly pruritus NRS[a] Median (IQR)	7.9 (6.9; 8.9), *n*=346	5.0 (3.0; 8.0), *n*=347

[a]In the parent trials, worst pruritus NRS was assessed daily; in ECZTEND, worst pruritus NRS was assessed based on recall of the previous week before the visit.

Transition to ECZTEND and treatment duration

- Median time between last treatment in parent trial and first treatment in ECZTEND was 63.0 days (IQR 21.0; 105.0)
- Median treatment duration from first dose to discontinuation was 155.6 weeks (IQR 132.1; 174.4)
  - The most common reasons for discontinuation were lack of efficacy (7.5%), other reasons (6.1%), AEs (5.8%), and withdrawal by patient (5.8%)

References: **1.** Yeung J et al. *J Am Acad Dermatol.* 2023;89(2):372-375. **2.** De Bruin-Weller M, et al. *Acta Derm Venereol.* 2021;101(2):adv00402. **3.** Blauvelt A. et al. *J Am Acad Dermatol.* 2022;87(4):815-824.

Disclosures: **AB** has served as a speaker (received honoraria) for AbbVie, Bristol-Myers Squibb, Eli Lilly and Company, Pfizer, Regeneron, and Sanofi, served as a scientific adviser (received honoraria) for AbbVie, Abcentra, Actoris, Affibody, Aligos, Almirall, Alumis, Amgen, Anaptysbio, Arcutis, Arena, Aslan, Athenex, Bluefin Biomedicine, Boehringer Ingelheim, Bristol-Myers Squibb, Cara Therapeutics, Dermavant, EcoR1, Eli Lilly and Company, Escient, Evelo, Evommune, Forte, Galderma, Highlight Pharma, Incyte, InnoventBio, Janssen, Landos, LEO Pharma, Merck, Novartis, Pfizer, Pani, Rapt, Regeneron, Sanofi Genzyme, Spherix Global Insights, Sun Pharma, TLL Pharmaceutical, TrialSpark, UCB Pharma, Union, Viblome, and Xencor, and has acted as a clinical study investigator (institution has received clinical study funds) for AbbVie, Acelyrin, Almirall, Alumis, Amgen, Arcutis, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Concert, Dermavant, Eli Lilly and Company, Evelo, Evommune, Galderma, Incyte, Janssen, Leo, Merck, Novartis, Pfizer, Regeneron, Sun Pharma, and UCB Pharma. **HCH** is a researcher, consultant, and/or advisor for AbbVie, Amgen, Arcutis, Bausch Health, Boehringer Ingelheim, Celgene, Dermavant, Dermira, DS Biopharma, Galderma, GlaxoSmithKline, Incyte, Janssen, LEO Pharma, Lilly, MedImmune, Novartis, Pfizer, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, and UCB. **KP** reports grants or personal fees for participation in advisory boards from AbbVie, Almirall, Galderma, Lilly, LEO Pharma, Novartis, Pierre Fabre, Sanofi, Sun Pharma, and Janssen. **NK** has received honoraria as a speaker/consultant for Sanofi, Maruho, AbbVie, Eli Lilly, Japan, Mitsubishi Tanabe Pharma, Jansen Pharma, Taiho Pharmaceutical, Torii Pharmaceutical, Kyowa Kirin, Celgene Japan, and LEO Pharma, and has received grants as an investigator from Maruho, Eli Lilly Japan, Sun Pharma, Taiho Pharmaceutical, Torii Pharmaceutical, Boehringer Ingelheim Japan, Kyowa Kirin, Jansen Pharma, Eisai, A2 Healthcare, AbbVie, and LEO Pharma. **MT** has served as an investigator for AbbVie, Boehringer Ingelheim, Eli Lilly, Galderma, LEO Pharma, Pierre Fabre, and Sanofi-Regeneron; a consultant or advisory board for Sanofi-Regeneron, AbbVie, Eli Lilly, MEDAC, Jansen Pharma and Almirall. **MA** has served as a consultant and/or scientific advisor and/or principal investigator of clinical trials with Regeneron, Sanofi Genzyme, LEO Pharma, Pfizer, AbbVie, and Eli Lilly. **MG** has been an investigator, speaker and/or advisor for AbbVie, Amgen, Akros, Anaptysbio, Aslan, Arcutis, Aristea, Bausch Health, BMS, Boehringer Ingelheim, Celgene, Dermira, Dermavant, Eli Lilly, Galderma, GSK, Incyte, Janssen, Kyowa Kirin, LEO Pharma, Medimmune, Merck, Meiji, Moonlake, Nimbus, Novartis, Pfizer, Reistone, Regeneron, Roche, Sanofi Genzyme, Sun Pharma, and UCB. **CBD, AT,** and **LG** are employees and shareholders of LEO Pharma. **KR** has served as advisor and/or paid speaker for and/or participated in clinical trials sponsored by Abbvie, Almirall, Amgen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Forward Pharma, Gilead, Galderma, Janssen-Cilag, Kyowa Kirin, LEO Pharma, Lilly, Medac, Novartis, Ocean Pharma, Pfizer, Sanofi, UCB; Professor Reich is co-founder of Moonlake Immunotherapeutics.

Acknowledgements: Medical writing and editorial assistance were provided by Juliel Espinosa, PhD from Alphabet Health, funded by LEO Pharma A/S, according to Good Publication Practice guidelines (https://www.ismpp.org/gpp-2022). The authors thank Jens-Kristian Slott Jensen for help with programming the statistical analyses. This work was previously presented at AAD 2024.