

COVID-19 in Tralokinumab-Treated Patients with Moderate-to-Severe Atopic Dermatitis: Case Series from the ECZTEND Long-Term Extension Trial

Andrew Blauvelt,¹ Andrew Pink,² Margitta Worm,³ Richard Langley,⁴ Antonio Costanzo,⁵ Le Gjerum,⁶ Emilie Jorgensen,⁶ Joshua Corriveau,⁷ Shannon Schneider,⁷ Emma Guttman-Yassky⁸

¹Oregon Medical Research Center, Portland, OR, USA; ²St. John's Institute of Dermatology, Guy's and St. Thomas' Hospitals, London, UK; ³Charité-Universitätsmedizin Berlin, Berlin, Germany; ⁴Dalhousie University, Halifax, NS, Canada; ⁵Humanitas University and Humanitas Research Hospital IRCCS, Milan, Italy; ⁶LEO Pharma A/S, Ballerup, Denmark; ⁷LEO Pharma, Madison, NJ, USA; ⁸Icahn School of Medicine at Mount Sinai, New York, NY, USA

Introduction

- There is special interest in the impact of COVID-19 on individuals with chronic immune-mediated diseases such as atopic dermatitis (AD), including concerns that patients treated with immunomodulatory therapies for these diseases may have increased risk of developing COVID-19 or more severe disease with worse outcomes following infection with SARS-CoV-2
- AD is a chronic inflammatory disease characterized by eczematous skin lesions and multiple symptoms, including pruritus, sleep disturbance, and depression¹⁻⁴
- Tralokinumab is a high-affinity, fully human, monoclonal antibody designed to specifically neutralize interleukin-13, a key driver of the underlying inflammation in AD⁵⁻⁷
- Phase 3 trials have established the efficacy and safety of tralokinumab for up to 52 weeks in adult patients with moderate-to-severe AD^{8,9}
- An ongoing, open-label extension trial, ECZTEND (NCT03587805) is investigating the long-term safety and efficacy of tralokinumab in patients with AD who participated in previous tralokinumab trials

Objective

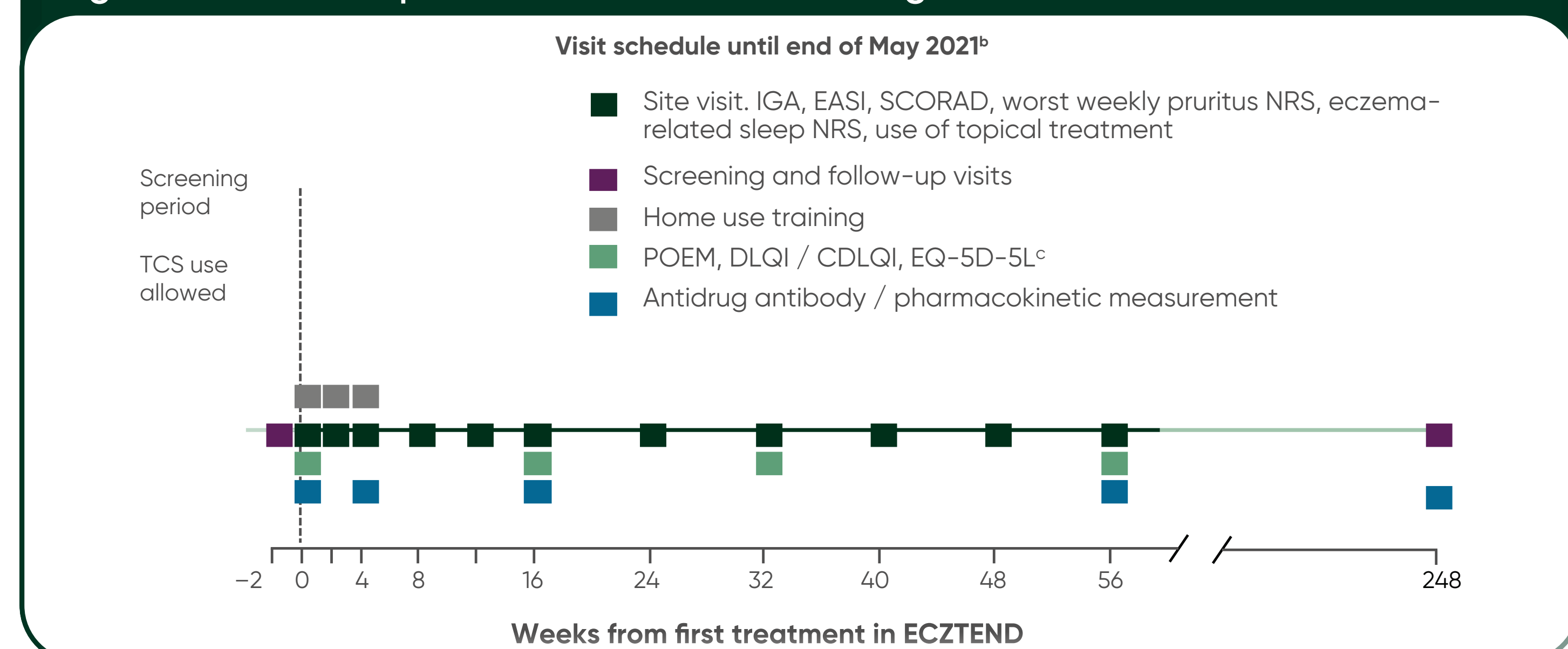
- To describe the outcomes of adult patients diagnosed with COVID-19 while participating in the tralokinumab long term extension trial, ECZTEND

Methods

Study Design

- As shown in Figure 1, ECZTEND is an ongoing, 5 year, open-label, single-arm, multicenter, long-term extension trial in patients with AD who participated in parent tralokinumab trials (ECZTRA 1-8 and TraSki)^a
 - Approximately 1600 patients with moderate-to-severe AD across Canada, the United States, Europe, and Japan are participating in ECZTEND
 - Patients received subcutaneous tralokinumab 300 mg Q2W plus optional TCS after a 300-mg or 600-mg loading dose of tralokinumab
 - Safety follow-up 16 weeks after last investigational medicinal product
- Key inclusion criteria for ECZTEND:
 - Completed treatment period(s) in a tralokinumab parent trial (ECZTRA 1-8 or TraSki) without any safety concerns
 - Complied with the clinical trial protocol in the parent trial
 - Able and willing to self-administer tralokinumab, or have it administered by a caregiver, at home after the initial 3 injection visits at trial site
 - Applied a stable dose of emollient (minimum twice daily) for at least 14 days before baseline
- We report a case series of 51 adult patients with moderate-to-severe AD who had confirmed cases of COVID-19 during treatment with tralokinumab every 2 weeks
 - Patients were not required to discontinue tralokinumab treatment following a COVID-19 diagnosis, if continuation was deemed appropriate by the investigator
 - This is an interim analysis of data collected through February 26, 2021

Figure 1. ECZTEND open-label extension trial design.



^aPrevious treatment regimens in parent trials included tralokinumab q2w, q4w, or placebo +/- TCS. After May 2021, some site visits will be switched to telephone visits. ^bPatients from the parent trial ECZTRA 6 will not perform the EQ-5D-5L. CDLQI, Children's Dermatology Life Quality Index; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EQ-5D-5L, EuroQol 5-Dimension Health Questionnaire 5-Level; IGA, Investigator's Global Assessment; NRS, Numeric Rating Scale; POEM, Patient-Oriented Eczema Measure; q2w, every 2 weeks; SCORAD, SCORing Atopic Dermatitis; TCS, topical corticosteroid.

Results

Patient Characteristics

- Twenty-two male and 29 female patients were diagnosed with COVID-19 through February 2021 (Table 1)
- The mean age was 37.7 years (range 19-70 years) and the mean body-mass index (BMI) was 27.6 (range 16.3-50.8)

Table 1. Baseline demographics for patients in ECZTEND with confirmed cases of COVID-19.

	COVID-19 Cases (n=51)
Age, y	
Mean (range)	37.7 (19-70)
Sex, n (%)	
Male	22 (43)
Female	29 (57)
Baseline BMI, kg/m ²	
Mean (range)	27.6 (16.3-50.8)
Geographic region, n (%)	
North America	15 (29)
Europe	36 (71)

- Regarding comorbidities that confer additional risk of severe COVID-19, 59% (n/N, 30/51) of patients had asthma and 10% (5/51) had hypertension; cardiovascular disease was present in 2 patients and chronic obstructive pulmonary disease (COPD) and diabetes mellitus were present in 1 patient each (Table 2)

Table 2. Clinical characteristics for patients in ECZTEND with confirmed cases of COVID-19.

	COVID-19 Cases (n=51)
PYE tralokinumab (parent trial + ECZTEND), mean	2.3
History of, n (%)	
Diabetes	1 (2)
Cardiovascular disease	2 (4)
Hypertension	5 (10)
COPD	1 (2)
Asthma	30 (59)

PYE, patient-years of exposure

- COVID-19 severity was predominantly mild (35/51, 68.6%) or moderate (14/51, 27.5%), and all patients with mild or moderate disease recovered fully (Table 3)
- The two patients who experienced severe cases (2/51, 3.9%) had multiple risk factors and comorbidities, including obesity, COPD, and cardiovascular disease. Both were hospitalized and subsequently recovered (one with sequelae); neither case was reported as related to tralokinumab treatment
- Mean duration of infection was 15 days (range 1-39 days)
- Only two of the 51 COVID-19 cases were reported as possibly related to tralokinumab treatment; both were mild or moderate cases occurring in patients under the age of 30
- All (51/51) patients continued tralokinumab treatment, the majority (38/51, 75%) without dose interruptions following COVID-19 diagnosis

Table 3. Adverse events details for patients in ECZTEND with confirmed cases of COVID-19.

	COVID-19 Cases (n=51)
Disease duration, days	
Mean (range)	15.2 (1-39)
Disease course, n (%)	
Mild	35 (69)
Moderate	14 (27)
Severe	2 (4)
Hospitalizations	
n (%)	2 (4)
Mean duration of stay, days (range)	7 (5-9)
Possibly related to treatment, n (%)	
n	2 (4)
Recovery, n (%)	
Full	50 (98)
With sequelae	1 (2)
Not recovered	0
Tralokinumab continuation, n (%)	
No dose interruption	38 (75)
Dose interruption	13 (25)

- In the ECZTEND study, 19 patients have received the first dose of COVID-19 vaccine and 6 patients have received the second dose; no patients had adverse events leading to permanent discontinuation after receiving the vaccine as per data cut-off

Conclusions

In this ECZTEND trial interim analysis, COVID-19 cases were predominately mild or moderate (96%), and all patients continued tralokinumab treatment following COVID-19 diagnosis.

- Severe COVID-19 is characterized by release of pro-inflammatory cytokines, leading to pulmonary inflammation and impairment of lung function
- IL-13 is not thought to be a major contributor to host defense mechanisms against viral infections
- The recent ECZTRA 5 vaccine study showed that non-live vaccines could be safely administered and can elicit normal immune responses in patients treated with tralokinumab¹⁰

References

- Weidinger S, Novak N. *Lancet*. 2016;387:1109-22; 2. Eckert L, et al. *J Am Acad Dermatol*. 2017;77:274-9.e273; 3. Silverberg JI, et al. *Ann Allergy Asthma Immunol*. 2018;121:340-7; 4. Dalgard FJ, et al. *J Invest Dermatol*. 2015;135:984-91; 5. Bieber T. *Allergy*. 2020;75:54-62; 6. Tsoi LC, et al. *J Invest Dermatol*. 2019;139:1480-9; 7. Popovic B, et al. *J Mol Biol*. 2017;429:208-19; 8. Wollenberg A, et al. *Br J Dermatol*. 2021;184(3):437-449; 9. Silverberg JI, et al. *Br J Dermatol*. 2021;184(3):450-463; 10. Merola JF, et al. *J Am Acad Dermatol*. 2021;85:71-78.

Disclosures

Andrew Blauvelt is a scientific adviser and clinical study investigator for AbbVie, Aclaris, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Dermira, Eli Lilly, FLX Bio, Forte, Galderma, Janssen, LEO Pharma, Novartis, Ortho Derm, Pfizer, Regeneron Pharmaceuticals, Inc., Sandoz, Sanofi Genzyme, Sun Pharma, UCB Pharma, Novartis, and UCB; and personal fees from AbbVie, Almirall, Janssen, La Roche Posay Lilly, and Sanofi. Margitta Worm declares that she has received honoraria or consultation fees from ALK-Abelló Arzneimittel GmbH, Mylan Germany GmbH, LEO Pharma GmbH, Sanofi-Aventis Deutschland GmbH, Regeneron Pharmaceuticals, Inc., DBV Technologies S.A, Stallergenes GmbH, HAL Allergie GmbH, Allergopharma GmbH & Co. KG, Bencard Allergie GmbH, Aimmune Therapeutics UK Limited, Actelion Pharmaceuticals Deutschland GmbH, Novartis AG and Biotest AG. Richard Langley has served and has received compensation in the form of grant funding and or honoraria as principal investigator for and is on the scientific advisory board or has served as a speaker for AbbVie, Amgen, Boehringer Ingelheim, Celgene, Janssen, LEO Pharma, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharma, and UCB. Antonio Costanzo has served on advisory boards for Celgene, UCB, Eli Lilly, Pfizer, Janssen, Novartis, Sanofi-Genzyme and MSD. Le Gjerum, Emilie Jorgensen, and Joshua Corriveau, and Shannon Schneider are employees of LEO Pharma. Emma Guttman-Yassky has received honoraria for consultant services from AbbVie, Almirall, Amgen, Asana Biosciences, Boehringer Ingelheim, Cara Therapeutics, Celgene, Concert, DBV, Dermira, DS Biopharma, Lilly, EMD Serono, Escalier, Galderma, Glenmark, Kyowa Kirin, LEO Pharma, Mitsubishi Tanabe, Pfizer, RAPT Therapeutics, Regeneron, Sanofi, Sienna Biopharma, and Union Therapeutics and received research grants for investigator services from AbbVie, Almirall, Amgen, AnaptysBio, Asana Biosciences, Boehringer Ingelheim, Celgene, Concert, Dermavant, Dermira, DS Biopharma, Lilly, Glenmark, Galderma, Innovaderm, Janssen, Kiniska, Kyowa Kirin, LEO Pharma, Novan, Pfizer, Ralexar, Regeneron, Sienna Biopharma, UCB, and Union Therapeutics.

Acknowledgments

The ongoing ECZTEND clinical trial is sponsored by LEO Pharma A/S Ballerup, Denmark. Originally presented at Revolutionizing Atopic Dermatitis (RAD), June 13, 2021