Updates on COVID-19 Cases and SARS-CoV-2 Vaccinations during Tralokinumab Treatment in Moderate-to-Severe Atopic Dermatitis from the ECZTEND Long-Term Extension Trial

Richard Langley,[1] Andrew Pink,[2] Margitta Worm,[3] Antonio Costanzo,[4] Le Gjerum,[5] Emilie Jorgensen,[5] Joshua Corriveau,[6] Shannon Schneider,[6] Emma Guttman-Yassky,[7] Andrew Blauvelt[8]

[1]Division of Clinical Dermatology and Cutaneous Science, Dalhousie University, Halifax, NS, Canada; [2]St. John's Institute of Dermatology, Guy's and St. Thomas' Hospitals, London, UK; [3]Division of Allergy and Immunology, Department of Dermatology, Venereology and Allergy, Charité – Universitätsmedizin Berlin, Berlin, Germany; [4]Dermatology Unit Department of Biomedical Sciences, Humanitas University, Milan, Italy and Skin Pathology Laboratory, Humanitas Research Hospital IRCCS, Milan, Italy; [5]LEO Pharma A/S, Ballerup, Denmark; [6]LEO Pharma Inc., Madison, NJ, USA; [7]Department of Dermatology and the Immunology Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [8]Oregon Medical Research Center, Portland, OR, USA

Introduction

- There is interest in COVID-19 and SARS-CoV-2 vaccination experience in individuals with chronic inflammatory skin diseases, such as atopic dermatitis (AD), being treated with immunomodulatory therapies, including biologics
- Tralokinumab is a high-affinity, monoclonal antibody that neutralizes interleukin (IL)-13, a key driver of inflammation in AD[1-3]
  - Phase 3 trials have established the efficacy and safety of tralokinumab for up to 52 weeks in adult patients with moderate-to-severe AD[4,5]
- The ECZTRA 5 vaccine study showed that non-live vaccines–Tdap and meningococcal–could be safely administered on the same day as tralokinumab and elicit normal immune responses in AD patients treated with tralokinumab[6]
- 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
  - Efficacy and safety data from a 2-year interim analysis of ECZTEND has been previously presented[7,8]

Objective

- To describe outcomes of confirmed COVID-19 cases in adult AD patients being treated with tralokinumab in ECZTEND
- To present a case series of tralokinumab-treated adult AD patients who were vaccinated against SARS-CoV-2 while participating in ECZTEND

Materials and Methods

- ECZTEND is an ongoing, up to 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)
  - Over 1600 patients with moderate-to-severe AD across Canada, USA, Europe, and Japan
  - Primary endpoint is number of adverse events (AEs) during the treatment period up to Week 268
  - Patients received subcutaneous tralokinumab 300 mg Q2W plus optional topical corticosteroids (TCS) after 600-mg loading dose

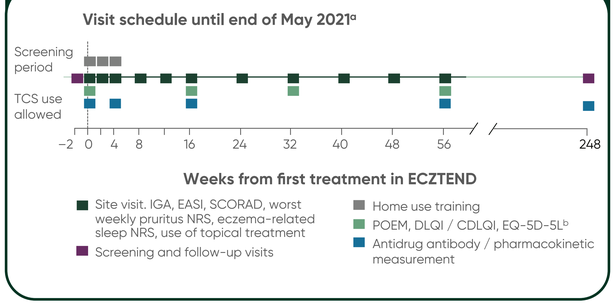
Key inclusion criteria

- Completed treatment period(s) in a tralokinumab parent trial without any safety concerns
- Complied with 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 ≥14 days before baseline

Study design (Figure 1)

- We report on adult patients who had confirmed cases of COVID-19 during treatment with tralokinumab
  - Patients were not required to discontinue tralokinumab treatment following COVID-19 infection, if continuation was deemed appropriate by the investigator
- Additionally, we report on adult patients with moderate-to-severe AD who were vaccinated against SARS-CoV-2 during treatment with tralokinumab
  - During the trial, subjects are permitted to receive non-live vaccines, such as SARS-CoV-2 vaccines
- This is an interim analysis of data collected through April 30, 2021

Figure 1. ECZTEND open-label extension trial design



[a]After May 2021, some site visits will be switched to telephone visits. [b]Patients 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 corticosteroids

Results

Patient characteristics

- Among adult patients in ECZTEND, 82 patients had reported COVID-19 infections through April 30, 2021
  - 5 of these cases are reported as suspected COVID-19 infection and are not included below
- The 37 male and 40 female patients with confirmed COVID-19 infections through April 30, 2021 are described in **Table 1**
  - Percentages of patients with confirmed COVID-19 with different established or probable risk factors for severe COVID-19 according to CDC classification[9] are shown in **Table 1**
  - Mean patient-years of exposure to tralokinumab (parent trial + ECZTEND) was 2.4

Table 1. Baseline demographic and clinical characteristics for patients in ECZTEND with confirmed cases of COVID-19 through April 30, 2021

	COVID-19 Cases (n=77)
Mean age, years (range)	38 (19-70)
Male, n (%)	37 (48)
Mean baseline BMI (range)	28 (16-51)
Geographic region, n (%)	
North America	19 (25)
Europe	58 (75)
History of, n (%)*	
Cancer	1 (1)
Chronic kidney disease	1 (1)
Lung disease	2 (3)
Diabetes	2 (3)
Down syndrome	1 (1)
Overweight or obesity (BMI≥25)	51 (66)
Asthma†	42 (55)
Hypertension†	10 (13)

*Additional risk factors (e.g. pregnancy, organ transplant, and HIV) fall under trial exclusion criteria. No patients with confirmed cases of COVID-19 had history of cerebrovascular disease, heart conditions, or liver disease†
†Mixed evidence supporting this comorbidity as a risk factor[9]
BMI, body-mass index

- 129 male and 102 female patients received at least one dose of vaccine against SARS-CoV-2 through April 30, 2021
  - Mean age was 45 years (range 18–84 years); mean patient-years of exposure to tralokinumab (parent trial + ECZTEND) was 2.7
  - 49% (113/231) of patients were in North America, 49% (114/231) in Europe, and 2% (4/231) in Japan

COVID-19 infection in patients in ECZTEND

- COVID-19 severity, according to the investigator's clinical judgment, was predominantly mild (52/77, 68%) or moderate (23/77, 30%) **(Table 2)**
  - 75/77 (97%) patients with mild or moderate disease had recovered fully as of April 30, 2021
  - 2 patients who experienced severe disease (2/77, 3%) had multiple risk factors and comorbidities, including obesity and hypertension
    - Both recovered following hospitalized (one with sequelae)
    - Neither was reported as related to tralokinumab treatment
- Only 2 of the 77 (3%) COVID-19 cases were reported as possibly related to tralokinumab treatment
  - Both were mild or moderate cases in patients under age of 30 that resolved within 22 days
- All (77/77, 100%) patients continued tralokinumab treatment following COVID-19 infection
  - The majority (60/77, 78%) did not interrupt tralokinumab dosing
- 76/77 (99%) COVID-19 cases occurred in patients who were unvaccinated at the time of infection
  - 1 (1%) case was reported in a partially vaccinated patient (1 dose of Pfizer-BioNTech)

Table 2. Adverse event details for patients in ECZTEND with confirmed cases of COVID-19 through April 30, 2021

	COVID-19 Cases (n=77)
Disease course	
Mild, n (%)	52 (68)
Moderate, n (%)	23 (30)
Severe, n (%)	2 (3)
Mean disease duration in days (range)	17 (1-190)
Recovery, n (%)	
Full	74 (96)
With sequelae	1 (1)
Not recovered by April 30, 2021	2 (3)
Serious adverse events	
Hospitalization, n (%)	3 (4)
Mean duration of stay, days (range)	8 (5-10)
Possibly related to treatment, n (%)	2 (3)
Tralokinumab continuation, n (%)	
No dose interruption	60 (78)
Dose interruption	17 (22)
Vaccination status at time of COVID-19 infection, n (%)	
Unvaccinated	76 (99)
Partially vaccinated*	1 (1)

*1 dose of 2-dose regimen vaccine

SARS-CoV-2 vaccination of patients in ECZTEND

- In the ECZTEND study, 231 adult patients received ≥1 dose of COVID-19 vaccine through April 30, 2021 **(Table 3)**
  - 93 of these patients are confirmed fully vaccinated and 136 are confirmed partially vaccinated
  - 58% received the Pfizer-BioNTech, 15% received the AstraZeneca, and 13% received the Moderna vaccine
- No patients had AEs leading to permanent discontinuation of tralokinumab treatment after receiving the SARS-CoV-2 vaccine as per data cut-off

Table 3. Clinical characteristics of patients in ECZTEND with confirmed vaccination against SARS-CoV-2

	SARS-CoV-2 Vaccination Cases (n=231)
Vaccination status, n (%)	
At least 1 dose	231 (100)
Fully vaccinated	93 (40)
1 dose of Johnson & Johnson	7 (3)
2 doses of 2-dose regimen	86 (37)
Partially vaccinated	136 (59)
Assumed fully vaccinated*	2 (1)
Type of vaccine, n (%)	
AstraZeneca (Vaxzeveria)	35 (15)
Johnson & Johnson	7(3)
Moderna	29 (13)
Pfizer-BioNTech (Comirnaty)	133 (58)
Unspecified	27 (12)

*More than 13 weeks elapsed since first dose

Conclusions

- These data describe adult patients with reported COVID-19 infection or vaccination against SARS-CoV-2 during targeted inhibition of IL-13 with tralokinumab in the long-term extension study ECZTEND
- As of April 30, 2021, reported COVID-19 cases in ECZTEND were predominately mild or moderate (98%)
  - All patients continued tralokinumab treatment following COVID-19 infection, the majority (78%) without dose interruptions
- 231 patients had received ≥1 dose of vaccine against SARS-CoV-2, and 40% of these patients were fully vaccinated
  - As of the data cutoff, no patients had AEs leading to permanent discontinuation of tralokinumab treatment after receiving the SARS-CoV-2 vaccine
  - Only 1 COVID-19 infection was reported in a partially vaccinated patient; no cases were reported following full vaccination

References

1. Bieber T. *Allergy*. 2020;75:54–62; **2.** Tsoi LC, et al. *J Invest Dermatol*. 2019;139:1480–9; **3.** Popovic B, et al. *J Mol Biol*. 2017;429:208–19; **4.** Wollenberg A, et al. *Br J Dermatol*. 2021;184:437–449; **5.** Silverberg JI, et al. *Br J Dermatol*. 2021;184:450–463; **6.** Merola JF, et al. *J Am Acad Dermatol*. 2021;85:71–78; **7.** Blauvelt et al. Long-term improvements observed in tralokinumab-treated patients with moderate-to-severe atopic dermatitis: an ECZTEND interim analysis. Oral presentation at AAD VMX 2021; **8.** Blauvelt et al. Long-term efficacy, safety, and adherence to tralokinumab treatment in moderate-to-severe atopic dermatitis for up to 3 years: interim readout of ECZTEND, a Phase 3, long-term extension trial. Poster presentation at AAD VMX 2021; **9.** Centers for Disease Control and Prevention. Underlying medical conditions associated with high risk for severe COVID-19: Information for healthcare providers. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html#anchor_1618433687270 (Accessed on August 24, 2021).

Disclosures

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. **Andrew Pink** reports personal fees and nonfinancial support from LEO Pharma, Novartis, and UCB; and personal fees from AbbVie, Almirall, Janssen, La Roche Posay Lilly, and Sanofi. **Margitta Worm** declares that she has receipt honoraria or consultation fees by 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. **Antonio Costanzo** has served on advisory boards Celgene, UCB, Eli Lilly, Pfizer, Janssen, Novartis, Sanofi-Genzyme and MSD. **Le Gjerum, Emilie Jorgensen**, **Joshua Corriveau** and **Shannon Schneider** are employees of LEO Pharma A/S. **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. **Andrew Blauvelt** is a scientific adviser and clinical study investigator for AbbVie, Abcentra, Aligos, Almirall, Amgen, Arcutis, Arena, Aslan, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Evommune, Forte, Galderma, Incyte, Janssen, Landos, LEO Pharma, Novartis, Pfizer, Rapt, Regeneron, Sanofi Genzyme, Sun Pharma, and UCB Pharma.

Acknowledgements

The ongoing ECZTEND clinical trial is sponsored by LEO Pharma A/S, Ballerup, Denmark