COVID-19 in tralokinumab-treated patients with moderate-to-severe atopic dermatitis: case series from the ECZTEND long-term extension trial

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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,[1] characterized by eczematous skin lesions and multiple symptoms, including pruritus, sleep disturbance, and depression[2-4]
- Tralokinumab is a high-affinity, fully human, monoclonal antibody designed to specifically neutralize interleukin-13, a key driver of the underlying inflammation in AD[5-7]
- 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

- 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
- Here, 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

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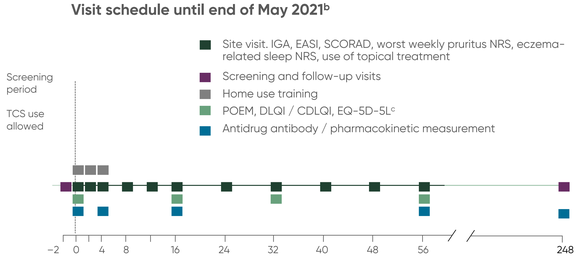
Figure 1. ECZTEND open-label extension trial design.



[a]Previous treatment regimens in parent trials included tralokinumab q2w, q4w, or placebo +/- TCS
[b]After May 2021, some site visits will be switched to telephone visits. [c]Patients from the parent trial ECZTRA 6 will not perform the EQ-5D-5L.
[c]DLQI, 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 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 Case Series (N=51)
Age	
Mean (range)	37.7 (19-70)
Sex	
Male, n (%)	22 (43%)
Female, n (%)	29 (57%)
Baseline BMI	
Mean (range)	27.6 (16.3-50.8)
Geographic region	
North America, n (%)	15 (29%)
Europe, n (%)	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 Case Series (N=51)
PYE tralokinumab (parent trial + ECZTEND)	
Mean	2.3
History of:	
Diabetes mellitus, n (%)	1 (2%)
Cardiovascular disease, n (%)	2 (4%)
Hypertension, n (%)	5 (10%)
COPD, n (%)	1 (2%)
Asthma, n (%)	30 (59%)

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

Concluding Remarks

In the present study, 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 tralokinumab[10]

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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, and a paid speaker for AbbVie
- **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
- **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 Celgene, UCB, Eli Lilly, Pfizer, Janssen, Novartis, Sanofi-Genzyme and MSD
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