Updates on COVID-19 cases and SARS-CoV-2 vaccinations during tralokinumab treatment in moderate-to-severe atopic dermatitis from ECZTEND long-term extension trial

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Introduction. There is special interest in real-word experience of COVID-19 and SARS-CoV-2 vaccination in individuals with chronic inflammatory skin diseases being treated with immunomodulatory therapies, including biologics. Tralokinumab is a fully human immunoglobulin G4 monoclonal antibody that specifically binds with high affinity to IL-13, thereby inhibiting subsequent downstream signaling and improving the signs and symptoms of atopic dermatitis (AD), a type 2-mediated disease. We present an overview of confirmed COVID-19 cases in AD patients being treated with tralokinumab in a long-term extension trial, ECZTEND (NCT 03587805), and describe outcomes of tralokinumab-treated AD patients who were vaccinated against SARS-CoV-2 while participating in the trial.

Methods. Approximately 1600 patients with moderate-to-severe AD across Canada, the United States, Europe, and Japan are participating in the ongoing open-label ECZTEND trial. The primary endpoint for the trial is safety of long-term tralokinumab treatment. During the trial, subjects are permitted to receive non-live vaccines, such as SARS-CoV-2 vaccines. We present a case series of patients with moderate-to-severe AD who were vaccinated against SARS-CoV-2 during treatment with tralokinumab. In addition, we report on patients who have confirmed cases of COVID-19. Patients are 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 April 30, 2021.

Results. The ECZTEND study has been collecting data related to COVID-19 cases and vaccination against SARS-CoV-2 among participants. As of April 30, 2021, there were 77 (37 male and 40 female) patients with confirmed COVID-19 infection. Baseline and clinical characteristics of patients with COVID-19 infection are shown in the table. COVID-19 severity, according to the investigator's clinical judgment, was predominantly mild (68%) or moderate (30%). 97% of patients with mild or moderate disease had recovered fully as of April 30, 2021. 2 patients who experienced severe disease (3%)

had multiple risk factors and comorbidities, including obesity and hypertension; both recovered following hospitalized (one with sequelae), and neither was reported as related to tralokinumab treatment. Two of the 77 (3%) COVID-19 cases were reported as possibly related to tralokinumab treatment; both were mild or moderate cases in patients under the age of 30 years that resolved within 22 days. All patients (100%) continued tralokinumab treatment following COVID-19 infection; most (78%) did not interrupt tralokinumab dosing. 99% of COVID-19 cases occurred in patients who were unvaccinated at the time of infection. One case (1%) was reported in a partially vaccinated patient. 231 patients (129 male and 102 female) 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% of patients were in North America, 49% in Europe, and 2% in Japan. 93 of these patients (40%) are confirmed fully vaccinated and 136 (59%) are confirmed partially vaccinated. No patients had adverse events leading to permanent discontinuation of tralokinumab treatment after receiving the SARS-CoV-2 vaccine as per data cut-off.

Conclusions. IL-13 is not thought to be a major contributor to host defense mechanisms against viral infection. The ECZTRA 5 vaccine study showed that non-live vaccines, specifically tetanus/diphtheria/pertussis (Tdap) and meningococcal vaccines, could be safely administered on the same day as tralokinumab and can elicit normal immune responses in AD patients treated with tralokinumab (Merola J, et al. *J Am Acad Dermatol.* 2021;85:71-78).

Baseline characteristics of patients with a confirmed Covid-19 case through April 30, 2021 n=77

Characteristic	**COVID-19 Cases (n=77)**
Mean age, y (range)	38 (19-70)
Male, n (%)	37 (48)
Mean baseline BMI (range)	28 (16-51)
Geographic region	
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 (eg, 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 co-morbidity as a risk factor (Centers for Disease Control and Prevention. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html#anchor_1618433687270