Efficacy and safety of tralokinumab plus topical corticosteroids in patients with severe atopic dermatitis and prior history of dupilumab treatment: a post hoc subgroup analysis from ECZTRA 7 trial

Jan Gutermuth1, Andrew Pink2, Margitta Worm3, Lise Soldbro4, Thomas Mark4, Joshua Corriveau5, Christian Bjerrøgård Øland4, Stephan Weidinger6

1Department of Dermatology, Universitair Ziekenhuis Brussel and Vrije Universiteit Brussel, Brussels, Belgium
2St John’s Institute of Dermatology, Guy’s and St Thomas’ NHS Foundation Trust, London, UK
3Division of Allergy and Immunology, Department of Dermatology, Venereology and Allergy, Charité – Universitätsmedizin Berlin, Berlin, Germany
4LEO Pharma A/S, Ballerup, Denmark
5LEO Pharma Inc., Madison, NJ, USA
6Department of Dermatology and Allergy, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany

Introduction
Tralokinumab is a high affinity monoclonal antibody that specifically neutralizes the IL-13 cytokine. The Phase 3 ECZTRA 7 trial (NCT03761537) met its primary endpoint of EASI-75 at Week 16, confirming tralokinumab plus topical corticosteroids (TCS) is superior to placebo plus TCS in treating severe atopic dermatitis (AD) in patients not adequately controlled by, or with contraindications to, oral cyclosporine A. There can be inadequate disease control with currently available treatment options and many patients with severe AD continue to experience high disease burden. This post hoc analysis aims to describe the efficacy and safety of tralokinumab in a subgroup of ECZTRA 7 patients with prior history of dupilumab treatment.

Methods
ECZTRA 7 was a randomized, double-blinded, multicenter, placebo-controlled Phase 3 trial. Adult patients with AD for ≥1 year with inadequate response to topical or documented systemic medication, involvement of ≥10% BSA, and EASI ≥20 were randomized 1:1 to subcutaneous tralokinumab 300 mg every 2 weeks with TCS as needed or placebo with TCS as needed for a treatment period of 26 weeks. For this analysis, prior history of dupilumab treatment was confirmed and further details were collected via queries before trial unblinding. Dupilumab-experienced patients are defined as those with a confirmed history of dupilumab use prior to the trial. Cochran-Mantel-Haenszel with treatment as only strata was used for analysis.

Results
Dupilumab-experienced (n=14) and dupilumab-naïve (n=263) cohorts had comparable baseline characteristics, except that median (IQR) age was 51.5 (43.0, 57.0) years for dupilumab-experienced patients and 33.0 (25.0, 45.0) years for dupilumab-naïve patients. Median (IQR) EASI and percentage of patients with an IGA of 4 were 35.5 (24.8, 39.6) and 57.1% among dupilumab-experienced patients and 28.7 (22.4, 39.5) and 49.0% among dupilumab-naïve patients, respectively. Among dupilumab-experienced patients, baseline and clinical characteristics were similar between the tralokinumab + TCS as needed (n=6) and placebo +
TCS as needed (n=8) groups. Also, 50% of patients in each of these two groups discontinued dupilumab due to either lack of efficacy or safety concerns.

Among dupilumab-experienced patients at Week 16, 100% (n/N, 6/6) of patients receiving tralokinumab + TCS achieved EASI-75, compared to 50% (4/8) of those receiving placebo + TCS (difference [95% CI]: 50.0 [15.4, 84.6]). Numerically higher proportions of dupilumab-experienced patients receiving tralokinumab + TCS achieved IGA 0/1 (4/6, 66.7%; placebo + TCS: 3/8, 37.5%; difference: 29.2 [-21.3, 79.6]) and improvement in worst daily pruritus NRS (weekly average) ≥4 points (3/6, 50%; placebo + TCS: 3/8, 37.5%; difference: 12.5 [-39.7, 64.7]) at Week 16. Similarly, at Week 26, numerically higher proportions of dupilumab-experienced patients receiving tralokinumab + TCS achieved EASI-75 (6/6, 100%; placebo + TCS: 3/8, 37.5%; difference: 62.5 [29.0, 96.0]), IGA 0/1 (4/6, 66.7%; placebo + TCS: 2/8, 25%; difference: 41.7 [-6.5, 89.9]), and improvement in worst daily pruritus NRS (weekly average) ≥4 points (3/6, 50%; placebo + TCS: 3/8, 37.5%; difference: 12.5 [-39.7, 64.7]), compared to placebo + TCS.

Through the 26 weeks, 66.7% (4/6) of dupilumab-experienced patients receiving tralokinumab + TCS reported any adverse event, compared to 87.5% (7/8) of those receiving placebo + TCS. One placebo patient reported 2 events of conjunctivitis, 1 mild and 1 of moderate severity; 1 tralokinumab patient reported 1 mild event of conjunctivitis. No serious adverse events occurred in either treatment group. From a safety perspective, there were 2 patients who had previously discontinued dupilumab due to conjunctivitis; adverse events of conjunctivitis were not reported for either patient during 26 weeks of tralokinumab + TCS treatment.

Discussion
This post hoc subgroup analysis indicates that dupilumab-experienced patients can benefit from tralokinumab + TCS as needed. Overall frequencies of adverse events in dupilumab-experienced patients treated with tralokinumab + TCS as needed were consistent with the pooled analysis of tralokinumab Phase 2 and 3 trials. Due to the small sample size, further studies involving more patients are needed to confirm these findings.

References:
This analysis was sponsored by LEO Pharma A/S. Medical writing and editorial support from Alphabet Health by Clair Geary, PhD, was funded LEO Pharma A/S, Ballerup, Denmark.

**Disclosures:**

**Jan Gutermuth** reports honoraria as a consultant/advisory board member/speaker and/or received grants from AbbVie, Genzyme, LEO Pharma, Lilly, Pfizer, Regeneron, and Sanofi.

**Andrew E. Pink** has acted as an advisor/speaker for AbbVie, Almirall, Janssen, La Roche-Posay, LEO Pharma, Lilly, Novartis, Pfizer, Sanofi, and UCB.

**Margitta Worm** has served as a scientific advisor and/or clinical trial investigator and/or paid speaker for AbbVie, ALK, Allergopharma, Aimmune, Boehringer Ingelheim, Dermira, Eli Lilly, Galderma, Janssen, LEO Pharma, Mylan, Novartis, Pfizer, Regeneron and Sanofi-Genzyme.

**Lise Soldbro, Thomas Mark, Joshua Corriveau, and Christian Bjerregård Øland** are employees of LEO Pharma A/S.

**Stephan Weidinger** is co-principal investigator of the German Atopic Eczema Registry TREATgermany. He has received institutional research grants from Sanofi Deutschland GmbH, LEO Pharma, and La Roche-Posay, has performed consultancies for Sanofi-Genzyme, Regeneron, LEO Pharma, AbbVie, Pfizer, Eli Lilly, Kymab and Novartis, he has also lectured at educational events sponsored by Sanofi-Genzyme, Regeneron, LEO Pharma, AbbVie, Novartis and Galderma, and is involved in performing clinical trials with many pharmaceutical industries that manufacture drugs used for the treatment of psoriasis and atopic eczema.