

Early and sustained improvements in patient-reported outcomes with tralokinumab in combination with topical corticosteroids as needed in moderate-to-severe atopic dermatitis

Boni E. Elewski,¹ Sonja Ständer,² Matthew Zirwas,³ Juan Francisco Silvestre,⁴ Sunil Kalia,^{5,6} Jan Gutermuth,⁷ Thomas Mark,⁸ Ann-Marie Tindberg,⁸ Jonathan I. Silverberg⁹

¹The University of Alabama at Birmingham, Birmingham, AL, USA; ²Department of Dermatology and Interdisciplinary Competence Center Chronic Pruritus (KCP), University Hospital Münster, Münster, Germany; ³Probit Medical Research, Columbus, OH, USA; ⁴Dermatology Department, Hospital General Universitario de Alicante, Alicante, Spain; ⁵Department of Dermatology and Skin Science, University of British Columbia, Vancouver, British Columbia, Canada; ⁶Vancouver Coastal Health & BC Children's Hospital Research Institutes, Vancouver, British Columbia, Canada; ⁷Department of Dermatology, Universitair Ziekenhuis Brussel and Vrije Universiteit Brussel, Brussels, Belgium; ⁸LEO Pharma A/S, Ballerup, Denmark; ⁹Department of Dermatology, The George Washington University School of Medicine and Health Sciences, Washington, DC, USA

Introduction: Atopic dermatitis is a chronic, inflammatory skin disease characterized by eczematous skin lesions associated with intense itch, sleep loss, impaired quality of life (QoL), anxiety, and depression.¹ Interleukin (IL)-13 is a key driver of the underlying type 2 inflammation and skin barrier dysfunction in atopic dermatitis.² Tralokinumab is a fully human monoclonal antibody that specifically binds to the IL-13 cytokine with high affinity, preventing interaction with the IL-13 receptor and subsequent downstream IL-13 signaling. The pivotal ECZTRA 3 trial (NCT03363854) investigated the efficacy and safety of tralokinumab plus topical corticosteroids (TCS) as needed in adults with moderate-to-severe

atopic dermatitis.³ This analysis assessed the effects of treatment with tralokinumab plus TCS as needed on patient-reported outcomes over 32 weeks.

Methods: ECZTRA 3 was a double-blind, placebo plus TCS-controlled, Phase 3 trial.³

Adults with moderate-to-severe atopic dermatitis were randomized 2:1 to subcutaneous tralokinumab 300 mg every 2 weeks (q2w) plus TCS (mometasone furoate 0.1% cream applied once daily to active lesions as needed; n=252) or placebo plus TCS (n=126) for 16 weeks. Hereafter, tralokinumab-treated patients continued on either q2w or every 4 weeks q4w + TCS for an additional 16 weeks. Worst daily pruritus Numeric Rating Scale (NRS) and eczema-related sleep interference NRS were recorded daily via eDiary, and Patient Oriented Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), and Hospital Anxiety and Depression Scale (HADS) were recorded during scheduled visits. *Post hoc* analyses of week 16–32 data were conducted by pooling all patients who were randomized to tralokinumab in the initial treatment period, irrespective of tralokinumab dosing regimen beyond week 16. Statistical analyses followed pre-specifications, i.e. mixed model for repeated measures with fixed effects of planned treatment, region, and baseline Investigator’s Global Assessment (IGA), as well as interactions between treatment and visit and baseline value and visit for continuous endpoints. Data after rescue medication or permanent discontinuation of trial product was set to missing and a compound symmetric covariance matrix was assumed for repeated measures of a patient.

Results: At week 16, mean worst daily pruritus NRS (weekly average) improved by –4.1 versus baseline with tralokinumab q2w plus TCS and by –3.0 with placebo plus TCS (difference –1.1; [95% confidence interval (CI) –1.6, –0.7]; $P<0.001$), mean eczema-related sleep interference NRS improved by –4.4 with tralokinumab q2w plus TCS versus –3.2 with placebo plus TCS (–1.2 [–1.7, –0.7]; $P<0.001$), and mean POEM improved by –11.8 with

tralokinumab q2w plus TCS versus -7.8 with placebo plus TCS (-4.0 [$-5.6, -2.4$]; $P<0.001$). Least square mean (standard error [SE]) HADS total score improved from 11.6 (0.3) at baseline to 7.2 (0.3) at week 16 with tralokinumab q2w versus 9.2 (0.4) with placebo plus TCS (-2.0 [$-3.1, -1.0$]; $P<0.001$). Least square mean DLQI total score was reduced from 17.4 (0.3) at baseline to 5.6 (0.3) at week 16 with tralokinumab q2w plus TCS versus 8.3 (0.5) with placebo plus TCS (-2.7 [95% CI $-3.9, -1.5$]; $P<0.001$). Early separation in all patient-reported outcomes between tralokinumab plus TCS and placebo plus TCS was observed from week 2 or 3 onwards. At weeks 15–16, tralokinumab-treated patients used approximately 50% less TCS versus placebo-treated patients ($P=0.002$). Continued tralokinumab q2w/q4w + TCS was associated with sustained improvements versus baseline at week 32 in worst daily pruritus NRS (estimated mean change [SE] of -4.6 [0.1]), eczema-related sleep interference NRS (-4.9 [0.1]), and POEM (-12.4 [0.5]). Similarly, sustained improvements were observed at week 32 in DLQI (estimated total score [SE] of 5.1 [0.3]) and HADS (6.4 [0.3]).

Conclusions: Patients with moderate-to-severe atopic dermatitis receiving tralokinumab plus TCS as needed, reported early and sustained improvements in itch, sleep interference, POEM, anxiety, depression, and QoL. The impact of atopic dermatitis on patients' QoL was reduced from having a very large effect (mean DLQI total score ≥ 11) at baseline to a small effect (mean DLQI total <6) at week 32. In addition, symptoms of anxiety and depression, as reported by the patients, improved from abnormal (mean HADS total score ≥ 11) to normal (mean <8) at week 32.

1. Silverberg JI, et al. Br J Dermatol 2019;181:554–565.
2. Bieber T. Allergy 2020;75:54–62.
3. Silverberg JI, et al. Br J Dermatol 2020. doi:10.1111/bjd.19573.

Funding and acknowledgments: The ECZTRA 3 trial was sponsored by LEO Pharma A/S. Medical writing and editorial support were provided by Kathryn Woods, PhD, and Jane Beck, MA, of Complete HealthVizion, funded by LEO Pharma A/S.

Conflicts of interest:

Boni E. Elewski reports receiving honoraria as a consultant for Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, LEO Pharma, Lilly, Menlo Therapeutics, Novartis, Pfizer, Sun, Valeant (Ortho Dermatologics), and Verrica; and has received research funding from AbbVie, AnaptysBio, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Incyte, LEO Pharma, Lilly, Menlo Therapeutics, Merck, Novartis, Pfizer, Regeneron, Sun, Valeant (Ortho Dermatologics), and Vanda.

Sonja Ständer reports personal fees from Almirall, Bayer, Beiersdorf, Bellus Health, Cara Therapeutics, Clexio Biosciences, Dermasence, Escient, Galderma, Kiniksa, LEO Pharma, Menlo Therapeutics, Novartis, Pfizer, Sanofi, Trevi Therapeutics, and Vifor.

Matthew Zirwas has acted as a consultant for AbbVie, Aclaris, Arcutis, Asana, Aseptic MD, Avillion, DS Biopharma, Fitbit, Foamix, Genentech, Incyte, Janssen, LEO Pharma, Lilly, L'Oreal, Menlo, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi, and UCB.

Juan Francisco Silvestre has received honoraria as a consultant/advisor for AbbVie, Lilly, LEO Pharma, Novartis, Pfizer, Regeneron, and Sanofi Genzyme.

Sunil Kalia serves as the President of the Dermatology Society of the British Columbia. He is the current Chair of the Sun Awareness Group, Canadian Dermatology Association. He has acted as an advisor/consultant and received honorarium from: Amgen, Abbvie, Aralez, Celgene, Galderma, Eli Lilly, La Roche Posay, La Bausche, Johnson and Johnson, Novartis, Pfizer, Sanofi-Genzyme, UCB. Dr. Kalia has conducted clinical trials that have received

funding from Abbvie, Corbus, Merck, La Bausch, Janssen, Amgen, Eli Lilly, LEO Pharma, Novartis, Pfizer, and UCB. He is the co-director of the Clinical Trials Unit, Skin Care Centre, Vancouver General Hospital. Intellectual property includes Raman Clinical Skin Database, with a commercial interest by Vita Imaging LLC. He has received grant funding and honoraria from educational lectures from Eczema Society of Canada. He also has received honoraria for education lectures by SPH CME and BC Cancer Skin Tumor Group. He has acted as a consultant for BC Pharmacare and Canadian Agency for Drugs and Technology in Health. He is an advisor for the Drug Benefit Adjudication Advisory Committee, Pharmacare Benefits Branch, Ministry of Health, British Columbia. Dr. Kalia's salary is funded by the Photomedicine Institute, Vancouver, and UBC Hospital Foundation and the Michael Smith Foundation for Health Research.

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.

Thomas Mark is an employee of LEO Pharma.

Ann-Marie Tindberg is an employee of LEO Pharma.

Jonathan I. Silverberg reports honoraria as a consultant/advisory board member from LEO Pharma; and has acted as a consultant for, and/or received grants/honoraria from, AbbVie, AnaptysBio, Asana Biosciences, Galderma Research and Development, GlaxoSmithKline, Glenmark, Kiniksa, LEO Pharma, Lilly, MedImmune, Menlo Therapeutics, Pfizer, PuriCore, Regeneron, and Sanofi.