ORIGINAL ARTICLE

Secukinumab is superior to ustekinumab in clearing skin of subjects with moderate-to-severe plaque psoriasis up to 1 year: Results from the CLEAR study

Andrew Blauvelt, MD, MBA,[a] Kristian Reich, MD,[b] Tsen-Fang Tsai, MD,[c] Stephen Tyring, MD, PhD,[d] Francisco Vanaclocha, MD,[e] Külli Kingo, MD, PhD,[f] Michael Ziv, MD, BSc,[g] Andreas Pinter, MD,[h] Ronald Vender, MD, FRCPC,[i] Sophie Hugot, MSc,[j] Ruquan You, MSc,[k] Marina Milutinovic, MD,[j] and Diamant Thaçi, MD[l]

Portland, Oregon; Hamburg, Frankfurt and Lübeck, Germany; Taipei, Taiwan; Houston, Texas; Madrid, Spain; Tartu, Estonia; Afula, Israel; Ontario, Canada; Basel, Switzerland; and Shanghai, China

Background: Secukinumab demonstrated superior efficacy to ustekinumab at week 4 and week 16 of the CLEAR study, with comparable safety, in subjects with moderate-to-severe plaque psoriasis.

Objective: To compare the efficacy and safety of secukinumab and ustekinumab use over 52 weeks.

Methods: Analysis of 52-week data from CLEAR, a randomized, double-blind, phase 3b study.

Results: Among 676 randomized subjects, secukinumab demonstrated superiority to ustekinumab at week 52 in the proportion of subjects with ≥90% improvement in Psoriasis Area and Severity Index (PASI 90) (76% vs 61% [$P < .0001$]); PASI 100 responses were 46% versus 36% ($P = .0103$) and Investigator's Global Assessment responses of clear/almost clear skin were 80% versus 65% ($P < .0001$). Subjects on secukinumab reported

From the Oregon Medical Research Center, Portland[a]; Dermatologikum Hamburg and SCIderm Research Institute[b]; National Taiwan University Hospital, National Taiwan University College of Medicine[c]; University of Texas Health Science Center at Houston, Center for Clinical Studies[d]; Hospital Universitario 12 de Octubre, Madrid[e]; Dermatology Clinic, Tartu University Hospital[f]; Emek Medical Center, Afula[g]; Goethe Universität Frankfurt am Main[h]; McMaster University, Hamilton, Ontario[i]; Novartis Pharma AG, Basel[j]; Novartis Beijing Novartis Pharma Co. Ltd, Shanghai[k]; and Comprehensive Center for Inflammation Medicine, University Hospital Schleswig-Holstein, Lübeck[l].

Supported by Novartis Pharma AG, Basel, Switzerland.

Disclosure: Dr Blauvelt has served as a scientific consultant and clinical study investigator for AbbVie, Amgen, AstraZeneca, Boehringer Ingelheim, Celgene, Dermira, Eli Lilly, Genentech, GSK, Janssen, MedImmune, Merck, Novartis, Pfizer, Regeneron, Sandoz, Sanofi, UCB, and Valeant and as a paid speaker for Eli Lilly. Dr Reich has served as a consultant and/or paid speaker for and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie, Amgen, Biogen-Idec, Celgene, Centocor, Covagen, Eli Lilly, Forward Pharma, GSK, Janssen-Cilag, Leo Pharma, Medac, MSD, Novartis, Pfizer, Vertex, Takeda, and Xenoport. Dr Tsai has served as a consultant and/or paid speaker for and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of psoriasis, including AbbVie, Celgene, Eli Lilly, Janssen-Cilag, Leo Pharma, Galderma, Novartis, and Pfizer. Dr Tyring has received grants from Novartis. Dr Vanaclocha has served as a principal investigator in clinical studies sponsored by Celgene, Janssen, Merck, and Novartis. Dr Kingo has served as a principal investigator in clinical studies sponsored by Celgene, Mitsubishi Pharma, Novartis, Merck, Regeneron, and Sandoz. Dr Ziv has served as a paid speaker/consultant/clinical trials investigator for AbbVie, Coherus Biosciences, Janssen-Cilag, Novartis, and Pfizer. Dr Pinter has served as a clinical study investigator, scientific consultant, and/or paid speaker for AbbVie, Amgen, Biogen-Idec, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen-Cilag, Leo Pharma, Merck, Novartis, Pfizer, and Regeneron. Dr Vender has been a speaker for AbbVie, Amgen, Celgene, Galderma, Janssen, Leo Pharma, Novartis, and Pfizer and an investigator for AbbVie, Amgen, Celgene, Galderma, Janssen, Leo Pharma, Lilly, Merck, Novartis, and Pfizer. Ms Hugot, Mr You, and Dr Milutinovic are employees of and/or own stock in Novartis. Dr Thaçi has received research support from AbbVie, Almirall, Amgen, Astellas, Biogen-Idec, Boehringer-Ingelheim, Celgene, Dignity, Eli-Lilly, Forward-Pharma, GSK, Leo, Janssen-Cilag, Maruho, Mitsubishi Pharma, MSD, Novartis, Pfizer, Roche, and Sandoz and honoraria from AbbVie, Biogen-Idec, Celgene, Janssen, Leo, Mundipharma, Novartis, Pfizer, and Roche-Possay. He has acted as a consultant for AbbVie, Biogen-Idec, Celgene, Dignity, Galapagos, Maruho, Mitsubishi, Novartis, Pfizer, and Xenoport and sat on scientific advisory boards for AbbVie, Amgen, Biogen-Idec, Celgene, GSK, Leo Pharma, Janssen, Lilly, Mundipharma, Novartis, Pfizer, and Sandoz.

Accepted for publication August 2, 2016.

Reprints not available from the authors.

Correspondence to: Andrew Blauvelt, MD, MBA, Oregon Medical Research Center, 9495 SW Locust St, Suite G, Portland, OR 97223. E-mail: ablauvelt@oregonmedicalresearch.com.

Published online September 20, 2016.

0190-9622/$36.00

http://dx.doi.org/10.1016/j.jaad.2016.08.008

greater reductions in psoriasis-related pain, itching, and scaling, and greater improvement across all quality-of-life measures evaluated (Dermatology Life Quality Index [DLQI], EuroQoL 5-Dimension Health Questionnaire, Work Productivity and Activity Impairment Questionnaire-Psoriasis, and Health Assessment Questionnaire-Disability Index). At week 52, 72% of subjects on secukinumab versus 59% on ustekinumab ($P = .0008$) reported no impact of skin disease on their lives (DLQI 0/1 response). Safety and tolerability was comparable.

Limitations: There was no placebo arm.

Conclusion: In this head-to-head, double-blind study, secukinumab demonstrated sustained superior efficacy in comparison with ustekinumab in clearing skin through week 52, greater improvement in quality of life, and a favorable and comparable safety profile. (J Am Acad Dermatol http://dx.doi.org/10.1016/j.jaad.2016.08.008.)

Key words: psoriasis; secukinumab; ustekinumab; clinical trial; Psoriasis Area and Severity Index (PASI); efficacy; safety.

Secukinumab—a first-in-class, fully human, anti–interleukin (IL)-17A monoclonal antibody—has demonstrated strong and sustained efficacy with a favorable safety profile in the treatment of patients with moderate-to-severe plaque psoriasis, psoriatic arthritis (PsA), and ankylosing spondylitis[1-6] and has been approved for these indications.[7,8] Given the availability of biologics with different mechanisms of action, providing data from a single trial of multiple agents can facilitate informed decision-making by physicians. Secukinumab demonstrated superior efficacy to that of the anti-tumor necrosis factor agent etanercept with a similar safety profile in the comparative, 52-week FIXTURE trial (NCT01358578).[1] More recently, in the 16-week primary analysis of the CLEAR study (NCT02074982), secukinumab demonstrated superior efficacy.[9] Here, the CLEAR study's key secondary objective of comparing long-term efficacy (52 weeks) of secukinumab and ustekinumab is reported.

CAPSULE SUMMARY

- Secukinumab has demonstrated superior efficacy to ustekinumab at weeks 4 and 16 in subjects with plaque psoriasis (CLEAR study).
- This superior efficacy is sustained over 52 weeks, with greater improvement in health-related quality of life and comparable safety.
- This study provides head-to-head data that will inform clinical decisions on long-term management of psoriasis.

METHODS

Study design

CLEAR was a phase 3b, randomized, double-blind, head-to-head study comparing secukinumab and ustekinumab to week 52. Study methods were described in detail in the primary 16-week study publication.[9]

In brief, subjects were randomized 1:1 to receive subcutaneous injections of secukinumab or ustekinumab (Fig 1). Both treatments were administered as recommended.[7,8,10,11] Subjects assigned to secukinumab received a 300 mg dose at baseline and weeks 1, 2, and 3, and then every 4 weeks from week 4 onward. Ustekinumab was dosed at 45 mg in subjects with a baseline weight ≤100 kg and at 90 mg in those >100 kg and given at baseline, week 4, and then every 12 weeks. Placebo injections (matching the secukinumab dose regimen) were given to subjects in the ustekinumab group to maintain blinding. Randomization was stratified by body weight (≤ and >100 kg).

Study population

Key inclusion criteria were age ≥18 years and diagnosis (≥6 months before randomization) of moderate-to-severe plaque psoriasis, which was defined as having a Psoriasis Area and Severity Index (PASI) score of ≥12, an Investigator's Global Assessment, 2011 modified version (IGA mod 2011), score of 3 (moderate) or 4 (severe), and ≥10% of the body surface area affected. Subjects were eligible if their psoriasis had been poorly controlled with topical treatment, phototherapy, systemic therapy (conventional or biologic), or a combination of these therapies.

Key exclusion criteria included nonplaque-type psoriasis; previous exposure to biologics directly targeting IL-17A, IL-17 receptor A, or IL-12/IL-23; history of malignancy within 5 years; any medical or psychiatric condition that in the investigator's opinion would preclude adherence to the protocol.