PSORIASIS

# SECUKINUMAB TREATMENT NORMALIZES INFLAMMATORY MARKERS AND IMMUNE RESPONSE AND LEADS TO CLINICAL IMPROVEMENT IN PATIENTS WITH PSORIASIS: FINDINGS FROM THE PRIMARY ANALYSIS OF THE OBEPSO-S STUDY

*James Krueger [1] - David Pariser [2] - Patricia Lee [3] - Jerry Bagel [4] - April Armstrong [5] - Elisa Muscianisi [6] - Farid Kianifard [6] - Rajendra Sarkar [7] - Jennifer Steadman [6] - Andrew Blauvelt [8]*

*The Rockefeller University, Laboratory For Investigative Dermatology, New York, United States [1] - Eastern Virginia Medical School, Department Of Dermatology, Norfolk, United States [2] - Center For Clinical Studies, Dermatology, Webster, United States [3] - Windsor Dermatology, Psoriasis Treatment Center Of Central New Jersey, East Windsor, United States [4] - Keck School Of Medicine Of The University Of Southern California, Department Of Dermatology, Los Angeles, United States [5] - Novartis Pharmaceuticals Corporation, Us Clinical Development And Medical Affairs, East Hanover, United States [6] - Novartis Healthcare Pvt Ltd, Novartis Business Services, Hyderabad, India [7] - Oregon Medical Research Center, Dermatology, Portland, United States [8]*

Introduction: Psoriasis is associated with skin and systemic inflammation due to cytokines released following an altered immune response. Secukinumab, a fully human monoclonal antibody that selectively targets interleukin 17A, has demonstrated efficacy in moderate-to-severe psoriasis with a favorable safety profile. We report results from the primary analysis of ObePso-S, a study investigating cellular and molecular changes in patients with psoriasis treated with secukinumab.

Objective: To explore the effect of secukinumab on skin and systemic inflammation in patients with moderate-to-severe psoriasis.

Materials and Methods: ObePsO-S is a randomized, double-blind, phase 4 trial (NCT03055494) investigating modulation of skin inflammation and changes in subcutaneous adipose tissue in patients with moderate-to-severe plaque psoriasis. Patients were randomized 2:1 to receive secukinumab 300 mg or placebo. The primary efficacy variables were absence of keratin 16 (K16, a marker of keratinocyte hyperproliferation) expression and a ≥90% reduction from baseline in Psoriasis Area and Severity Index score (PASI90 response), at week 12.

Results: Overall, 82 patients were randomized (secukinumab, n=54; placebo, n=28). At week 12, absence of K16 expression was seen in a greater proportion of patients receiving secukinumab than placebo (79.6% vs 3.6% [95% CI: 63.3%, 88.8%]). Absence of K16 expression in skin of patients treated with secukinumab was associated with clinical response; K16 was not expressed in 27/29 (93.1%) and 14/14 (100%) patients with PASI90 and PASI100 responses, respectively. Secukinumab also decreased other biomarkers and immune cell counts (eg, C-reactive protein, leukocytes).

Conclusions: Secukinumab led to substantial clinical improvement and rapid inhibition of K16 expression. Complete suppression of K16 was seen in patients achieving PASI100 response, suggesting an association between clinical improvement and K16 inhibition. Reductions in systemic inflammation markers were also observed. Overall, secukinumab led to complete or near-complete disease clearance and normalization of inflammatory biomarkers and immune cell counts in patients with moderate-to-severe psoriasis.