EA DV CONGRESS
BERLIN 11-14 OCTOBER 2023
EUROPEAN ACADEMY OF DERMATOLOGY AND VENEREOLOGY

Abstract N°: 4607

Efficacy and safety of IL-22RA1 inhibition in patients with moderate-to-severe atopic dermatitis: results from a Phase 2a monotherapy trial

Diamant Thaçi[1], Vivian Laquer[2], Charles Lynde[3], Adam Reich[4], Weily Soong[5], Margitta Worm[6], Petra Arlert[7], Berith Hagen[7], Britta Martel[7], Ole Soerensen[7], Melinda Gooderham[8]

[1]Institute and Comprehensive Center for Inflammation Medicine, University of Lübeck, Lübeck, Germany,[2]First OC Dermatology Research, Fountain Valley, CA, United States, [3]The Lynde Institute for Dermatology and Lynderm Research, Markham, Ontario, Canada, and Department of Medicine, University of Toronto, Ontario, Canada, [4]Department of Dermatology, University of Rzeszow, Rzeszow, Poland,[5]AllerVie Health-Alabama Allergy and Asthma Center, Birmingham, AL, United States, [6]Division of Allergy and Immunology, Department of Dermatology, Venereology and Allergy, Charité –Universitätsmedizin Berlin, Berlin,, Germany, [7]LEO Pharma A/S, Ballerup, Denmark, [8]SKiN Centre for Dermatology, Queen's University and Probity Medical Research, Peterborough, ON,, Canada

Introduction & Objectives: Atopic dermatitis (AD) is a chronic, inflammatory skin disease in which IL-22 expression is increased and thought to contribute to epidermal hyperplasia and barrier defects. Previous data have shown that targeting the IL-22 cytokine benefits a subset of AD patients. LEO 138559 is a monoclonal antibody that specifically targets the IL-22 receptor subunit alpha-1 (IL-22RA1). Here we evaluate the efficacy and safety of IL-22RA1 inhibition in a Phase 2a study in adult patients with moderate-to-severe atopic dermatitis. As IL-20 and IL-24 partially signal via the IL-22RA1, we used an in vitro system to further understand how targeting the IL-22RA1 influences not only IL-22, but also IL-20 and IL-24 signaling.

Materials & Methods: A phase 2a, randomized, double-blind, placebo-controlled, multi-site, proof of concept trial (NCT04922021) was conducted in which patients were randomized 1:1 to receive LEO 138559 or placebo every 2 weeks for 16 weeks with an additional dose at Week 1, followed by an additional 16 weeks of safety follow-up. The primary endpoint was change in EASI from baseline to Week 16. In vitro experiments were conducted assessing the effect of LEO 138559 on IL-20, IL-22, and IL-24 signaling using HEK293 cells transfected with IL-22 receptor complex or IL-20 receptor type 2 complex.

Results: Baseline and clinical characteristics were similar between the LEO 138559 (N=29) and placebo (N=29) groups. Mean change in EASI from baseline to Week 16 was significantly greater for LEO 138559 compared with placebo (-15.3 vs. -3.5; P=0.003). The benefit of LEO 138559 with respect to EASI was evident by Week 4. At Week 16, greater proportions of patients receiving LEO 138559 relative to placebo achieved EASI-75 (41.6% vs. 13.7%; P=0.011), EASI-90 (30.8% vs. 3.5%; P=0.003), EASI-100 (20.9% vs. 0%; P=0.006), and vIGA-AD 0/1 (27.3% vs. 7.0%; P=0.035). LEO 138559 was well-tolerated with no safety signals observed. LEO 138559 was shown in vitro to not only block IL-22 signaling, but also IL-20 receptor type 2-dependent IL-20 and IL-24 signaling.

Conclusion: In this Phase 2a study, targeting IL-22RA1 with LEO 138559 for 16 weeks improved the signs and symptoms of AD compared to placebo and was well-tolerated. These data are the first to demonstrate the efficacy and safety of an IL-22RA1 targeting antibody for the treatment of moderate-to-severe AD. In vitro data showing LEO 138559 blocked IL-20 receptor type 2-dependent IL-20 and IL-24 signaling, in addition to IL-22 signaling, suggest that the mechanism of action of LEO 138559 in AD goes beyond inhibition of IL-22-mediated skin inflammation.