Anti-IL-17 nanobody: A future option in treatment of psoriasis

An improved understanding of the pathogenesis of psoriasis has led to the development of multiple new potential targets for therapy. The first pathway targeted by new biologics focus on the p40 subunit that is shared by interleukin (IL)-12 and IL-23. Second new strategy focuses IL-17 or its receptor. Secukinumab is fully human monoclonal G1κ antibody targeting IL-17A, approved in EU for the first-line systemic therapy of moderate-to-severe plaque psoriasis. New IL-17 inhibitors, Ixekizumab and Brodalumab achieved very good efficacy and are currently in administration approved review. We demonstrate the preliminary results of the anti-IL-17 A/F bispecific nanobody that neutralize the pro-inflammatory cytokines IL-17A and IL-17F. We present results of multicentric, phase I, randomized, double-blind, placebo controlled study investigated multiple ascending doses of anti-IL-17 A/F nanobody (M1095) in patients with moderate-to-severe psoriasis. Body surface area (BSA) ≥10%, Psoriasis Area and Severity Index (PASI) ≥12 and static Physician’s Global Assessment (sPGA) ≥3 were evaluated. Patients received 30, 60, 120 or 240 mg anti-IL-17 A/F nanobody or placebo every two weeks subcutaneously for 6 weeks. Primary endpoints were safety, tolerability, immunogenicity and pharmacokinetics. Secondary endpoints were pharmacodynamics, efficacy and histological analysis. On day 85, 6 weeks after the last dose of the drug, PASI 75 was achieved in 7/8 patients (88%) receiving 30 or 60 mg, 8/8 (100%) receiving 120 mg and 9/9 (100%) receiving 240 mg of drug. PASI 90 was achieved in 4/8 (50%), 7/8 (88%) and 9/9 (100%) patients receiving 30 mg, 60 mg, 120 mg or 240 mg, respectively. PASI 100 was achieved in 1/8 (13%), 2/8 (25%), 4/8 (50%) and 5/9 (56%) patients receiving 30 mg, 60 mg, 120 mg or 240 mg, respectively. Improved PASI scores were seen 7 days post-first dose in all 4 cohorts. Biopsy assessment of skin lesion showed complete reversal of disease pathology in majority of patients in high dose groups. Conclusion can be drawn that Anti-IL-17 A/F bispecific nanobody presents a new treatment option well tolerated and effective in patients with moderate-to-severe psoriasis associated with skin clearance improvement in all indices of psoriasis studied.

Biography

Danka Svecova is presently a Professor of Dermatovenerology, Head of Bullous Disorders Unit, Department of Dermatovenerology, University Hospital and Faculty of Medicine, Comenius University, Slovakia. She is a Board Member of Committee for Dermatovenerology and Immunology dissertation for PhD at Comenius University and a Member of Committee for Probation of Specialization for Dermatovenerology at Comenius University and University of JP Safarik in Kosice. She has participated in research on Skin Allergology and Immunology under the supervision of Professor Akira Ohkawara at Hokkaido University in Sapporo, Japan. She wrote two monographs about blistering disorders-Pemphigus vulgaris autoimmune disease and Pemphigus.

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