Background: Psoriatic arthritis is a chronic inflammatory condition which can be associated with extra-articular manifestations and metabolic morbidity. The high-affinity monoclonal antibody ixekizumab, selectively targets IL-17A and improves physical function & disease activity in bDMARD-naive patients with active PsA. Here we present data from a phase 3 study (SPIRIT-P2: NCT02349295) with ixekizumab in patients with active PsA, who showed inadequate response to prior biologics.

Methods: In this double-blind, placebo-controlled study, patients received subcutaneous placebo or ixekizumab 80mg every two (Q2W) or four weeks (Q4W), following a 160mg initial dose at w0. Patients who showed inadequate response received rescue therapy at week 16. Primary endpoint was the 24-week ACR20. Categorical variables were analysed through logistic regression models, while mixed models for repeated measurement were used for continuous variables. Analyses of skin outcomes were conducted on the Intent-to-Treat population with baseline body surface area of at least 3%. Safety outcomes were compared using Fisher’s exact tests.

Results: 363 patients were randomised: 52 years average age, female (53%), white (92%), and with inadequate response to one or two TNF-inhibitors (204 [56.2%], 128 [35.3%], respectively) or TNF-intolerant (31 [8.5%]). The majority (87%) completed the 24wk, double-blind period. At w24, significantly more ixekizumab- vs. placebo-treated patients achieved ACR20 (65 [53.3%], 59 [48.0%] vs. 23 [19.0%], Q4W, Q2W, placebo, respectively), ACR50 (43 [35.2%], 41 [33.3%] vs. 6 [5.1%], Q4W, Q2W, placebo, respectively), ACR70 (27 [22.1%], 15 [12.2%] vs. 0, Q4W, Q2W, placebo, respectively). MDA (34 [27.9%], 29 [23.6%] vs. 4 [3.4%], Q4W, Q2W, placebo, respectively) and reductions in functional disability (HAQ-DI): A significantly higher proportion of IxE-QGW- vs. placebo-treated patients reached complete resolution of dactylitis (LDI-B=0). Enthesitis improved from baseline with ixekizumab. Significantly more ixekizumab-treated patients with ≥3% BSA achieved PASI75 vs. placebo. The proportion of patients achieving an itch numeric rating scale of zero was significantly higher in ixekizumab groups (16 [23.5%] for Q4W, 16 [23.5%] for Q2W) vs. placebo (0). Achieving itch resolution or a DLQI score of zero or one was significantly more frequent in ixekizumab-treated patients (22 [32.4%] for Q4W, 18 [26.5%] for Q2W) vs. 2 (3.0%) for placebo-treated patients. Ixekizumab-treated patients showed significantly greater improvements in patient-reported outcomes (SF-36 PCS, MCS; EQ-5D VAS; WPAl-SHP) than placebo-treated patients. There was a higher incidence of injection site reactions in the ixekizumab treatment groups, with the majority being mild otherwise the incidence of treatment emergent adverse events was similar across groups (83 [68.0%], 90 [73.2%] vs. 76 [64.4%]; Q4W, Q2W, placebo, respectively).

Conclusion: Ixekizumab improved arthritis, physical function, psoriasis and DLQI compared to placebo with no unexpected safety findings in patients with active PsA who had inadequate response or intolerance with prior TNF-inhibitors. This study was sponsored by Eli Lilly and Company.

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