A JOINT MODEL-BASED META-ANALYSIS (MBMA) QUANTIFYING THE RELATIONSHIP BETWEEN PASI75 AND PASI SCORE IN PSORIASIS STUDIES

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Objectives: A longitudinal, joint MBMA of psoriasis (PsO) treatments quantified PASI75 response (Proportion of patients achieving ≥75% improvement in PsO Area and Severity Index score), and PASI change from baseline endpoints. The results were used to estimate predictive correlation of PASI score at week 4 to PASI75 at week 12.

Methods: A systematic literature review of PsO randomized controlled trials containing PASI75 and/or PASI score yielded 50 utilizable studies, including 22,733 subjects. The analysis used the regulatory approved or most common doses; depending on the approval status. Injectable drugs were adalimumab, alefacept, guselkumab, brodalumab, etanercept, infliximab, ixekizumab, secukinumab, ustekinumab, and oral drugs were apremilast, methotrexate, and tofacitinib. Data were analyzed using a parametric model with placebo and drug effects, implemented in NONMEM, version 7.3. Random effect terms quantified the between-study-variability. Residual error and off-diagonal matrix terms quantified the within-study-variability and correlation of time points within each arm, respectively. Residual errors were weighted by a factor (proportional to SE) to accommodate study size differences.

Results: The joint model adequately described predicted PASI75 (blue) and PASI score (black) time-course for PsO treatments shown in figure below:

Tofacitinib was predicted to have a higher mean Wk 12 response for PASI75 and PASI change from baseline, (56.1%, and -14.2; 10 mg BID) compared with other oral agents (methotrexate: 32.0%, and -8.86; apremilast: 27.4% and -9.29, respectively). Among the injectable drugs; guselkumab, secukinumab, and brodalumab had the highest Wk 12 PASI75 responses; 80.5% to 87.3%, and -19.2 to -22.3 points change from baseline PASI score respectively (no available information for guselkumab PASI score).

Conclusions: The longitudinal joint MBMA quantified the time-course of clinical responses across the range of compounds, as well as the correlation of PASI score and PASI75% to understand the predictive value of early time course PASI scores.