PSORIASIS

META-ANALYSIS OF FOUR PHASE 3 TRIALS BY MACHINE LEARNING REVEALED PREDICTORS THAT INDICATE ADDITIONAL BENEFIT OF SECUKINUMAB 300 MG OVER 150 MG IN PSORIATIC ARTHRITIS

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Introduction: Subcutaneous secukinumab 150mg and 300mg are approved doses for the treatment of psoriasis and psoriatic arthritis (PsA) with the higher dose recommended for PsA patients with anti-TNF inadequate response or moderate-to-severe psoriasis. Although traditionally multivariate logistic regression analysis has been used to predict if a specific group of patients can benefit from higher dose, machine learning surpasses these estimation-focused analyses with a higher area under the Receiver Operating Characteristic curve.

Objective: To investigate if machine learning reveals specific baseline clinical characteristics can be used to predict which patients gain additional benefit from the 300mg dose using pooled data from the secukinumab phase 3 studies.

Materials and Methods: Bayesian Elastic net was used to analyze 4 studies (FUTURE2-5) with 2148 patients investigating a total of 275 predictors (baseline demographic, disease characteristics in both main effects and interaction effects). Eleven endpoints were analyzed at Week 16 including ACR50, PASI 75, PASI 90, HAQ-DI and resolution of enthesitis at Week 16. For each endpoint, a complex algorithm involving ~40 predictors was developed, and key subgroups were identified for each endpoint. Missing responses were imputed as non-responders.

Results: No prior use of a biologic, 1 previous anti-TNF therapy, no use of concomitant methotrexate, and the presence of enthesitis at baseline were the strongest predictors for the additional benefit of secukinumab 300mg dose over the 150mg dose across multiple endpoints.

Conclusions: Machine learning on this large pooled dataset (2148 patients) provided new insights on predictors that indicated additional benefit of secukinumab 300mg against 150mg; this included patients who had prior treatment with only one anti-TNF agent, and patients on secukinumab monotherapy. Machine learning also confirmed previous clinical findings of secukinumab 300mg having additional benefit in PsA patients with moderate to severe psoriasis, and in patients with enthesitis at baseline.