A Longitudinal PKPD Model Describing the Effect of Ixekizumab on static Physician’s Global Assessment score (sPGA) in Patients with Moderate-to-Severe Plaque Psoriasis

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Background and Objectives: Ixekizumab selectively binds and neutralizes interleukin 17A and has shown high levels of efficacy in the treatment of psoriasis \cite{1}. The sPGA score is used to evaluate the severity and extent of psoriasis and ranges from 0 (no disease) to 5 (most severe disease). The aim of this work is to describe the effect of ixekizumab on all 6 sPGA categories in patients with psoriasis using a longitudinal PKPD model.

Methods: Data from Phase 2 (N=141 patients) and Phase 3 (N=1297) were included in the analysis. Phase 2: Ixekizumab was administered subcutaneously (SC) at doses from 10 to 150 mg at weeks 0, 2, 4, 8, 12, and 16. Phase 3: Ixekizumab 80mg SC was dosed every 2 or 4 weeks (Q2W or Q4W) up to Week 12, with a starting dose of 160 mg. At week 12, patients were assigned to 80 mg Q4W, Q12W, or placebo. Sequential PKPD modeling was conducted (NONMEM® version 7.3). Posthoc ixekizumab concentrations and area under the curve (AUC) estimates were used as inputs to an indirect latent variable response model.

Results: The drug effect was best described by two components: an Emax effect on the latent variable model, and an AUC effect on the logit model for cumulative probabilities. The placebo effect was included as another latent variable model. Simulation of the approved dosing regimen showed high levels of response by week 12 (80\% were sPGA(0,1) responders) that were maintained through week 60 (84\% were sPGA(0,1) responders) and were in agreement with observed data.

Conclusions: The PKPD model well described the time course of sPGA responses with good agreement between model-predicted and observed response rates. It characterizes all 6 sPGA categories and includes a different approach to describe the drug and placebo effects compared with published models \cite{2,3}.

References: \cite{1} Griffiths. Lancet. 2015;386(9993):541-51. \cite{2} Choi. ACOP7 \cite{3} Hu. JPKPD. 2011:38(2):237-60