A PKPD Model Describing the Effect of Ixekizumab on Absolute Psoriasis Area and Severity Index (PASI) score in Patients with Moderate to Severe Plaque Psoriasis

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Objectives: To describe and quantify the effect of ixekizumab on the absolute Psoriasis Area and Severity Index (PASI) score over time in patients with moderate to severe plaque psoriasis using a longitudinal PK/PD model.

Methods: Data from patients in a Phase 2 (N=115) and a Phase 3 (N=1247) study were included in this analysis. In the Phase 2 study, ixekizumab was administered subcutaneously (SC) at doses from 10 to 150 mg at weeks 0, 2, 4, 8, 12, and 16. In the Phase 3 study, ixekizumab 80mg SC was dosed every 2 weeks (Q2W) or every four weeks (Q4W) during an induction period (weeks 0 to 12); and Q4W or every 12 weeks (Q12W) during the maintenance period (weeks 12 to 60). A starting dose of 160 mg was administered at the beginning of this study. PASI score was modeled as a continuous covariate using an indirect response model. Drug and placebo effects were included in the model. All analyses were performed with the non-linear mixed-effect modeling software NONMEM® version 7.3.

Results: The PKPD model well describes the time course of PASI response. The model predicted that both doses of ixekizumab studied in Phase 3 resulted in significant improvements in PASI scores compared with the placebo group, and agreed with the observed data. Complete clearance of the disease (achievement of PASI100) was predicted for both Phase 3 doses in more than one-third of the treated patients by week 12 of treatment.

Conclusions: An indirect response model well described the time course of PASI score in patients with moderate to severe plaque psoriasis. This model could be adapted to describe PASI response for other treatments and for other indications e.g. Psoriatic Arthritis.