PK-PD Analysis of PASI with Data at Boundary: BI 655066 an Anti-IL-23A mAb for the Treatment of Psoriasis

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Objectives: Psoriasis is a chronic, immunologically-mediated, inflammatory disease with scaly, erythematous, indurated skin of the scalp, trunk and limbs represented by an area severity index (PASI). This analysis describes longitudinal PASI scores from two studies (n=156) combining data from a single and ongoing multiple dose administrations of IL-23 antagonist BI 655066 with data at the boundary to estimate PASI response rates.

Methods: A two compartment model adequately described the PK of BI 655066; individual level parameters were the input for an indirect response PK-PD model (IRM) of PASI scores. Drug concentrations were assumed to inhibit the formation of psoriatic lesions (kin) [1-2]. PASI scores were normalized to a zero-to-one scale and modeled using an augmented beta distribution [3-4]. This distribution was parameterized with three location parameters (the probability of a lower and upper boundary score and the conditional mean given that one is not on the boundary), functionally related to each other via logit link functions. Model performance was assessed using residuals, visual and numeric predictive checks (fraction of observations at boundary).

Results: The model adequately describes the observed PASI time course and proportion of subjects across three (or fewer) administered doses of BI 655066 in patients completing at least 24 weeks of treatment. Predictive checks of the observed and predicted PASI scores and derived change from baseline or PASI rates indicate an acceptable performance of the model.

Conclusions: The augmented beta regression approach implemented in NONMEM appears to be a viable approach for the analysis of PASI data from early studies, capturing the distributional properties of PASI scores.

References: