Leveraging Pharmacometrics in Selecting Proper Dose Regime for Nulojix in Pediatric Patients

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Objectives: Nulojix® (Belatacept) is a selective T-cell costimulation blocker indicated for prophylaxis of organ rejection in adults receiving a kidney transplant. The objective of the present study was to characterize the pharmacokinetic (PK) profile of belatacept in pediatric subjects age 12 to 17 years old using a population pharmacokinetic (PPK) approach.

Methods: A phase 1 belatacept pediatric study is currently ongoing to guide future pediatric dose selection. A single-dose of 7.5 mg/kg was administered to 7 subjects in the on-going study, which was based on the allometric exploration of the adult PPK model [1]. The available pediatric PK data, collected by semi-intensive serial blood sampling, were compared with the PPK model simulations using pediatric demographics. The pediatric PPK model were further optimized to describe the observed pediatric PK data, and assess the effects of individual-specific covariate factors (e.g., demographics, disease status) on variability of belatacept disposition.

Results: The modeling results show that the adult PPK model underestimates the exposure in pediatric subjects. The best pediatric PPK model was identified when the age covariate on clearance was removed from the established adult model. The external predictive check suggested that this updated model adequately predicted the median observed belatacept PK in pediatric subjects aged 12 to 17 years old. This alteration to the model is also physiologically reasonable considering the age effect on clearance in addition to body weight was meant to describe an older aged transplant population, which may not be relevant to a pediatric population.

Conclusions: Available belatacept pediatric concentration data were well described by a linear, two compartment, zero-order infusion, and first-order elimination model. Body-weight and disease status are significant covariates on the clearance and volume of belatacept PK thereby adequately explaining the observed variability in serum concentrations.

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