Optimal sampling design for a pediatric pharmacokinetic study of an anti-influenza A monoclonal antibody, MHAA4549A, with prior information from adults

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Objectives: MHAA4549A is a human monoclonal IgG1 antibody being developed for the treatment of hospitalized patients with severe influenza A infection. The objective of this study was to design an optimal sampling scheme for a pediatric pharmacokinetic (PK) trial of MHAA4549A, using prior serum PK data from adults.

Methods: MHAA4549A serum PK data from three clinical studies in adults were used to build an adult population PK model. The covariate effects of body weight (BW), age, sex, creatinine clearance, albumin, total protein and infection status were evaluated. Similar body-size-adjusted PK parameters were observed in pediatrics and adults for mAb with linear PK. Therefore, the established adult PK model, together with the pediatric BW distribution from oseltamivir pediatric trials, were implemented in the software PFIM to identify optimal sampling scheme for age groups of 0 to 23 months and 2 to 12 years old. Pediatric trials with sampling times corresponding to the design scheme were then simulated to further evaluate the design, by re-estimating PK parameters and calculating relative bias and relative standard errors for each PK parameter.

Results: A two-compartment PK model with BW as a covariate on clearance and volume of distribution of the central compartment was established. A sparse sampling design (0.5 hour after the end of IV infusion on day 1, days 4, 15 and 120) was proposed for pediatric patients in both age groups. With this design, the pediatric PK parameters were well estimated in simulated trials with adult PK parameters as a prior.

Conclusions: Appropriate sampling design is critical for precisely characterizing PK parameters in a pediatric population with limited number of samples. This study illustrates an example of leveraging adult PK information to design a sampling scheme for a pediatric PK study.

References: