Use of Pharmacokinetic and Pharmacodynamic Knowledge of Bilastine for the Optimal Design of the First Pediatric Trial

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Background: Bilastine is a non-sedating H\textsubscript{1} antihistamine for the treatment of allergic rhinoconjuntivitis and urticaria. The approved therapeutic dose in adults, supported by its pharmacokinetics and pharmacodynamics (PK/PD), is 20 mg/day via the oral route. Bilastine has favorable characteristics for its use in pediatrics. Currently trials in pediatrics are ongoing to determine the PK and PD and confirm the dose predicted by the model presented here.

Aims: (1) Develop a predictive model of bilastine PK and PD for pediatrics by integrating current knowledge. (2) Use the model for optimal design (bilastine dose, number of patients and sample selection) of a pharmacokinetic study in 2 to 11 years old. (3) Confirm the model predictability in the first recruited children.

Methods: A semi-physiological approach was applied in predicting pediatric PK parameters (age ranges in predictions were 2-6 and 6-11 years). The PD assumed that the H\textsubscript{1} antihistamine effect of bilastine in children is substantially similar to that in adults. The time evolution of the plasma levels and the wheal and flare effects after 5, 10, 20 mg/day bilastine were simulated. Model and study design confirmation was performed with data from the first seven children recruited to ensure that plasma levels were in line with the predictions above.

Results: Simulations indicated an adequate efficacy profile with the dose of 10 mg/day in children from 2 up to 11 years of age. Results from the first recruits confirmed the dose and design, hence trial continuation.

Conclusion: The developed model was successfully used to predict bilastine PK behavior in children using the previously available information in adults. The PK parameters predicted in children were used to aid the selection of an optimal dose and the sampling times for the first pediatric trial, increasing the efficiency of the process.