ABSTRACT

The minimal PBPK model is a valuable tool for simulating pharmacokinetic (PK) and therapeutic effects of IgG molecules in humans. This study aimed to develop a mathematically-based pharmacokinetic (PBPK) model for simulating pharmacokinetics (PKs) of therapeutic mAbs in humans, with the following features:

- Simultaneous modeling of the IgG and mAb.
- Incorporation of physiologically realistic system parameters.
- A model to account for the effect of FcRn recycling on IgG kinetics.
- Incorporation of a model to allow the effect of targeted medetomidine disposition to be accounted for in either interstitial or plasma space.
- Initial efforts focused on a minimal PBPK model to allow rapid simulation speeds to be achieved.

RESULTS

The minimal PBPK model is very sensitive to the IgG-FcRn Kf value (Figures 2a and 2b). The reported values for wild type IgG-FcRn binding vary widely in the literature (Table 2). To cope with this variability we adopted a value for Kf for IgG-FcRn binding for a given mAb was calibrated against the binding of WT IgG to FcRn measured under identical conditions.

CONCLUSION

The minimal PBPK model allows a better understanding of the pharmacokinetics and therapeutic efficacy of IgG and mAbs. This model could be used to predict the plasma levels and behavior of endogenous IgG and the mAbs for future therapeutic development.

REFERENCES