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A systematic approach to investigate the impact of variable fragment (Fv) charge on antibody PK

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PK characterization is a key step in the drug development process. In preclinical studies approximately 40% of therapeutic monoclonal antibodies (mAbs) tested in cynomolgus monkeys has atypically fast clearance. There are currently efforts to understand and mitigate the lead selection process to improve translational success in the clinic. One approach has been to investigate how antibody variable fragment (Fv) charge impacts PK and bioavailability of therapeutic antibodies. An empirical model was used to test the role of antibody Fv charge on PK properties by systematic amino acid substitutions in the Fv region of two mAbs, rhuMAbX and rhuMAbY. We compared the PK results of the parental mAbs and Fv charge variants to test our prediction for non-specific clearance. Given the large number of samples and low volumes we selected the Gyros platform for PK assay development and sample analysis. PK assays were developed and qualified successfully for the two parental mAbs and their two variants in three preclinical species (Cynomolgus monkey, Rat and Mouse). We present our results as well as our strategy in utilizing micro-sampling and the Gyros technology as a cost and time effective approach to streamline and improve efficiency for screening and selection of therapeutic mAb lead candidates for clinical development.

Biography

Yong Ying has completed her Medicine degree from Shanghai Second Medical University, Shanghai China and was a Physician. She has worked for Children's Hospital of Los Angeles, University of Southern California, School of Medicine, Abbott Laboratories and currently employed by Genentech as a Senior Scientific Researcher since 9 years.

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