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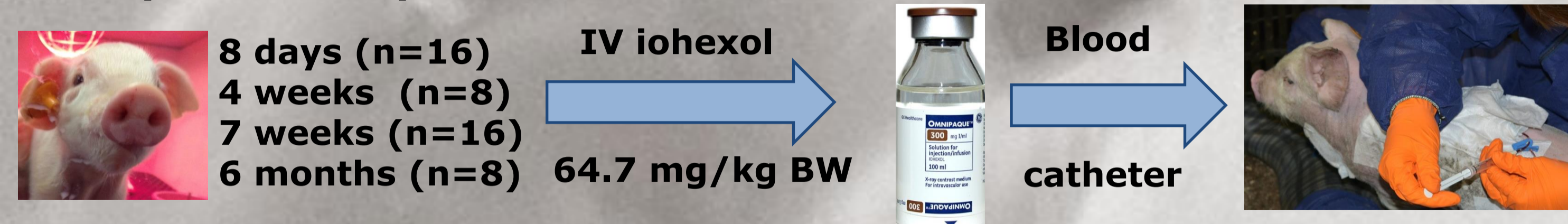
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## BACKGROUND

Development of appropriate animal models that take growth and maturation into account is pivotal for pediatric preclinical pharmacokinetic research. To determine if the conventional pig (Landrace x Large White) is such a potential animal model, the ontogeny of the different elimination processes need to be unraveled. The kidneys play a pivotal role in the PK and PD of various drugs. The glomerular filtration rate (GFR) is considered as one of the most important estimators of the renal function. Over the last decade, iohexol has proven to be a sensitive and selective marker for GFR. Iohexol is a non-radiolabeled contrast medium, which is cleared solely by glomerular filtration. It has already been successfully applied in both human and veterinary medicine and seems to be of particular interest in the pediatric population as well. Since the renal function of adult pigs and humans display great similarities, the aim of this study was to determine the GFR in growing piglets using nonlinear mixed-effects modeling and correlate the data with the GFR data obtained in humans.

## METHODS

### Experimental protocol



### Analytical protocol

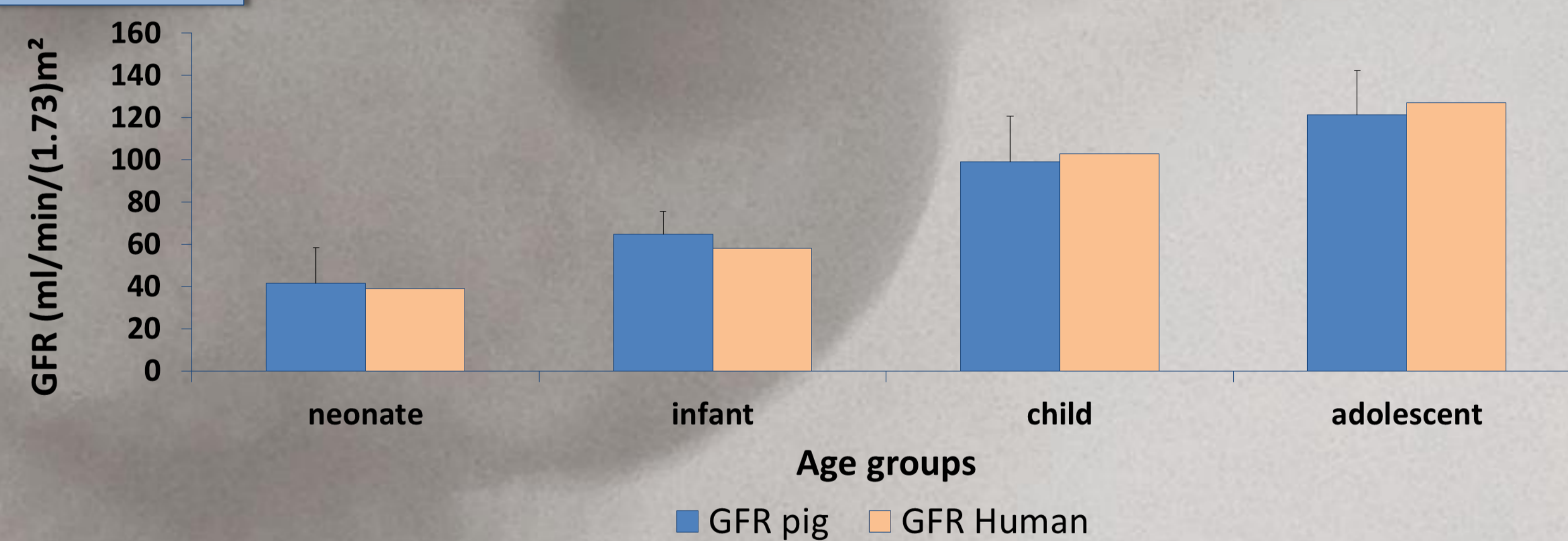
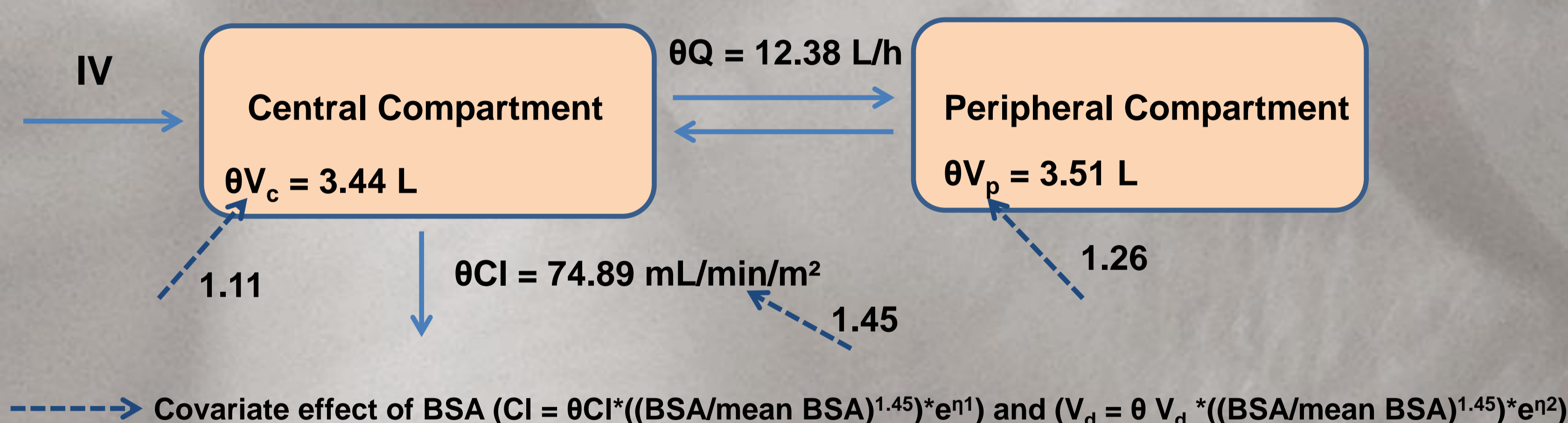


### Population PK analysis

Nonlinear mixed-effects modeling was performed using Quasi Random Parametric Expectation Maximization (QRPEM) as an estimation method in Phoenix NLME®.

- Structural model: two-compartmental with first order absorption and elimination.
  - Interindividual variability: exponential error model
  - Covariates tested: age, bodyweight, body surface area
- Model selection was based on the smaller values of -2LL, AIC and BIC, better precision of estimates, and superior goodness-of-fit plots

## RESULTS



## CONCLUSION

Iohexol plasma concentration is best described using a two-compartmental model in pig, with BSA as covariate. The GFR values obtained in the current study were comparable to humans. Therefore, the pig could be a convenient juvenile animal model for studying the GFR in the pediatric subpopulation, and to evaluate the PK of renally excreted drugs.

## ACKNOWLEDGMENTS

The SAFE-PEDRUG project (IWT-SBO 130033) is supported by the Agency for Innovation by Science and Technology in Flanders (IWT). Software license for Phoenix® was provided by Certara USA, Inc. (Princeton, NJ) as part of their Centers of Excellence program.

