SL05 Can PBPK Help to Individualise Drug Dosage?

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The application of physiologically-based pharmacokinetic (PBPK) modelling has come of age in drug development and regulation, reflecting significant advances over the past 15 years in the predictability of key pharmacokinetic parameters from human *in vitro* data and in the availability of dedicated software platforms and associated data bases. With respect to understanding co-variates and variability, focus in applying PBPK has been on anticipating the quantitative impact of drug-drug interactions, age, genetics, racial differences, disease, food effects and pharmaceutical formulation. These extensions of PBPK modelling, along with the incorporation of the PK of biologicals and moves towards linking PBPK to pharmacodynamic (PD) outcome, are clearly of benefit in understanding extremes of risk in different patient populations as part of the process of drug development. Indeed, mechanistic PBPK modelling is the only efficient methodology that can anticipate the combined effects of many patient variables acting simultaneously. The next challenge for PBPK-PD is its direct application in health care, concentrating on the individual rather than the population, as an educational tool and for the provision of computerised, 'point of care' advice on personalised drug dosage. The safe and effective management of multi-drug treatment of the complex patient with multiple diseases and multiple prescribers requires an integrated view of pharmacology and therapeutics. In this context, linking the real patient to his/her 'virtual twin' and a PBPK-PD model in the cloud through a tablet is technically feasible and promises to predict appropriate, rapid individualised drug dosage, and to avoid undesired complex multiple drug-drug interactions. Practical issues related to making this proposition a reality will be discussed including the availability of sufficient patient input data (electronic medical records, demographics, genotypes, co-medication, biomarkers), the availability of a sufficient range of unit dose preparations, physician and Pharma resistance, the relationship of dose prediction (PBPK) to dose adjustment (TDM/adaptive feedback), evidence of cost-benefit for payers and regulatory approval.