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ASSESSMENT OF PHARMACOKINETIC LINEARITY AFTER REPEATED DRUG ADMINISTRATION

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Seminarraum Center for Medical Data Science (previously CeMSIIS),
Spitalgasse 23, Room 88.03.513
Medical University of Vienna, 1090 Wien

Host: Martin Wolfsegger

ABSTRACT

The prediction of drug concentration time courses after different dosing scenarios is greatly facilitated if the pharmacokinetics (PK) can be assumed linear. The assumption of linear PK thus needs careful evaluation for any new drug in development. Under linear PK, exposure is proportional to dose (linear PK across doses) and exposure at steady state can be predicted from a single dose based on the superposition principle (linear PK over time). While investigation of dose-proportionality is common practice, evaluation of time dependent PK has received less attention in the literature. In particular, the superposition principle can be used to assess whether the observed extent of accumulation after repeated administration is expected under the premise of linear PK. This work emphasizes the importance of the time related aspect of linear PK by introducing the predictability ratio (PR). Linear PK over time can be concluded if $PR = 1$. Accumulation is higher than expected if $PR > 1$, and lower if $PR < 1$. If PK data from multiple dose cohorts are available, the PR is assessed for each dose cohort and a supportive hypothesis test can be applied to test for potential differences between doses in PR.