11-NOV-2024

Statistical analyses plan – the BAR-MEDS study

Trough concentrations (C_0; measured immediately before intake of the daily dose), maximum serum concentrations (C_{max}) and the times to achieve C_{max} (t_{max}) will be obtained directly from the measured values. Other pharmacokinetic variables will be calculated using the pharmacokinetic program package Kinetica.

AUC from 0 to 24 hours (AUC_{0-24}) will be calculated using a mixed log-linear model. Apparent clearance (Cl/F) will be calculated as dose/AUC. By applying a non-compartment model, the parameter estimate describing the decrease of the log-concentration (λ_z) will be calculated using the best-fit log-linear regression line of the samples representing the elimination phase. The elimination half-life ($t_{1/2}$) will be calculated as $\ln 2/ \lambda_z$. Apparent volume of distribution (V_d/F) will be calculated as $(Cl/F)/ \lambda_z$.

The primary outcome will be changes in systemic drug exposure, as reflected by AUC_{0-24}, compared to baseline. Other pharmacokinetic variables will be considered secondary outcomes. Relative changes in percent from baseline will be calculated for relevant pharmacokinetic and body composition variables. When a sufficient number of individuals are available, relative changes in AUC_{0-24}, V_d/F and if relevant, other pharmacokinetic variables, will be correlated to relative changes for relevant body composition variables with appropriate correlation tests. Repeated measures Analysis of Variance (ANOVA) analyses for pharmacokinetic variables will be performed when relevant.