



Simulated population:
Age/ weight/height/
creatinine clearance
(CrCL)



Monte Carlo simulations at steady state
with $Dose_{guidelines}$:
5 mg/kg once a day for GCV and
7*BSA*CrCL for VGCV, max 900mg)

Calculation of steady state $AUC_{0-24,ref}$
in simulations using
trapezoidal rule

Development of 4 ML algorithms to predict the
target (AUC_{0-24} in 40-60mg*h/L) and selection the
best algorithm (accuracy)

Calculation with the best ML algorithm of the
probability of having an AUC_{0-24} in the target (40-60
mg*h/L) for different doses from $0,1 * Dose_{guidelines}$ to
 $10 * Dose_{guidelines}$



Select the dose associated with the best probability =
 $dose_{ML}$



Calculation based on the $dose_{ML}$ selected of the

$$AUC_{0-24,ML} = \frac{AUC_{0-24,ref} \times Dose_{ML}}{Dose_{guidelines}}$$

$Dose_{POPPK}$ calculating using formula derived from
POPPK models and calculation of

$$the\ AUC_{0-24,POPPK} = \frac{AUC_{0-24,ref} \times Dose_{POPPK}}{Dose_{guidelines}}$$



Comparison of drug target attainment proportion
in the test set of simulated patients and in real
patients for $AUC_{0-24,ML}$ and $AUC_{0-24,POPPK}$

Simulated patients

Simulated patients and real patients