## **Supplementary material**

# **Journal: Clinical Drug Investigation**

Paxlovid-Tacrolimus Drug-Drug Interaction in a 23-Year Old Female Kidney Transplant Patient with COVID-19

Short title: Paxlovid-Tacrolimus drug-drug interaction in a kidney transplant patient with Covid-19

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### **Supplementary Material**

# The prior model used for Bayesian maximum aposteriori probability (MAP):

1- Mean values of pharmacokinetic parameters adjusted to fat free mass (FFM) 
Clearance (CL) = 11.3 L/h 
Volume of Central compartment (Vc) = 82.23 L 
Intercompartmental clearance (Q) = 15.8 L/h 
Absorption rate =  $1.01 \text{ h}^{-1}$  
Volume of Peripheral compartment= 422.73L 
Lag time on absorption= 0.41 h

Clearance, Volume of Central compartment and Intercompartmental clearance were modeled as random effects, and absorption rate, Volume of Peripheral compartment were modeled as fixed effects.

 $2-\Omega$  matrix ( Variance-covariance matrix for random effects)

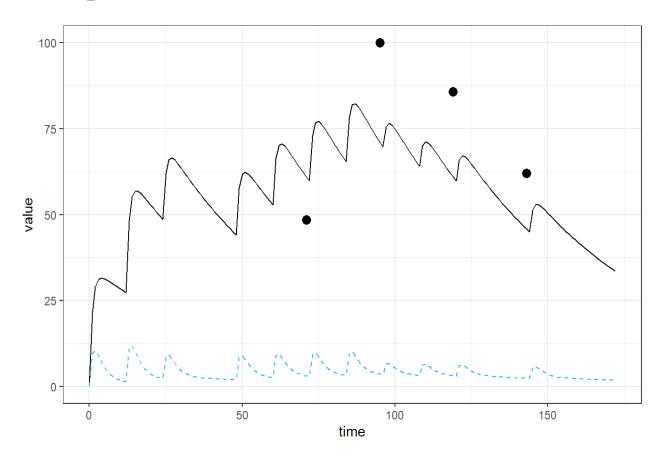
0.63 0.29 0.73 0.44 0 0.79

Elements on the diagonal are variances of CL [1,1], Vc [2,2] and Q [3,3]. Elements [2,1] and [3,1], are the covariance of CL with Vc, CL with Q, respectively.

#### R code for bayseian MAP estimation:

```
library (MASS)
library(mrgsolve)
library(mapbayr)
code <- "
$PARAM @annotated
TVCL: 11.3 : Clearance
TVVC: 82.23 : Central volume
V2 : 422.73 : Peripheral volume of distribution
    : 15.8 : Intercompartmental clearance
KA : 1.01 : Absorption rate (h-1)
TVALAG1: 0.41 : lag time on absorption
ETA1: 0 : Clearance (L/h)
ETA2: 0 : Central volume (L)
ETA3: 0: Intercompartmental clearance
$OMEGA @block
0.63
0.29 0.73
0.44 0 0.79
$SIGMA
0.149 // proportional
0 // additive
$CMT @annotated
DEPOT : Depot () [ADM]
CENTRAL: Central (mcg/L)[OBS]
PERIPH: Peripheral compartment ()
$TABLE
double DV = (CENTRAL/VC) * (1 + EPS(1)) + EPS(2);
$MAIN
double CL = TVCL * exp(ETA1 + ETA(1));
double VC = TVVC * \exp(ETA(2) + ETA2);
double Q = TVQ * exp(ETA(3) + ETA3);
double K12 = Q / VC ;
double K21 = Q / V2;
double K10 = CL / VC ;
$ODE
dxdt CENTRAL = KA * DEPOT+ K21 * PERIPH - (K10 + K12) * CENTRAL;
dxdt PERIPH = K12 * CENTRAL - K21 * PERIPH ;
dxdt DEPOT
           = -KA * DEPOT;
$CAPTURE DV CL VC Q
my model <- mcode("tac", code)</pre>
## Building tac ... done.
my_est <- my_model %>%
  adm lines(time = 0, amt = 1500) %>%
  adm lines(time = 12, amt = 1500) \%>%
  adm lines(time = 24, amt = 1000) %>%
  adm lines(time = 48, amt = 1000) %>%
  adm lines(time = 60, amt = 1000) %>%
  adm lines(time = 72, amt = 1000) \%>%
  adm lines(time = 84, amt = 1000) %>%
```

```
adm_lines(time = 96, amt = 500) %>%
adm_lines(time = 108, amt = 500) %>%
adm_lines(time = 120, amt = 500) %>%
adm_lines(time = 144, amt = 500) %>%
obs_lines(time = 71, DV = 48.5) %>%
obs_lines(time = 95, DV = 100) %>%
obs_lines(time = 119, DV = 85.8) %>%
obs_lines(time = 143, DV = 62) %>%
mapbayest()
plot(my_est)
```



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