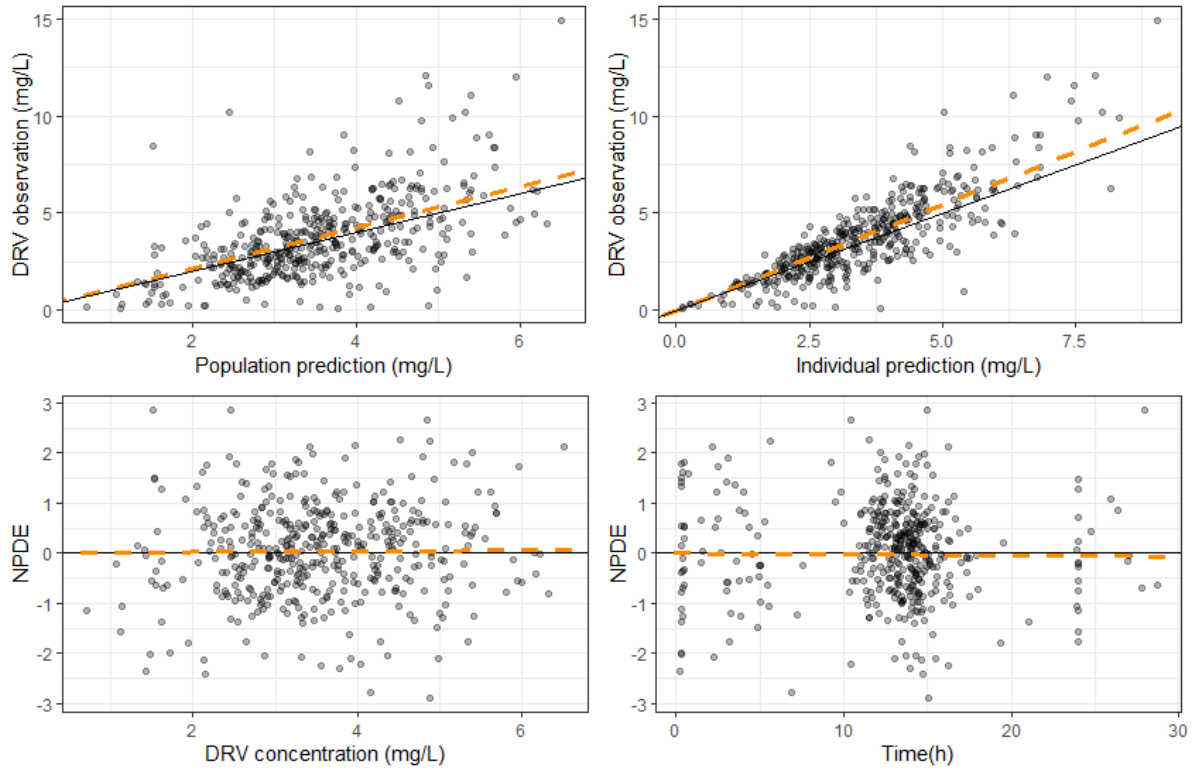
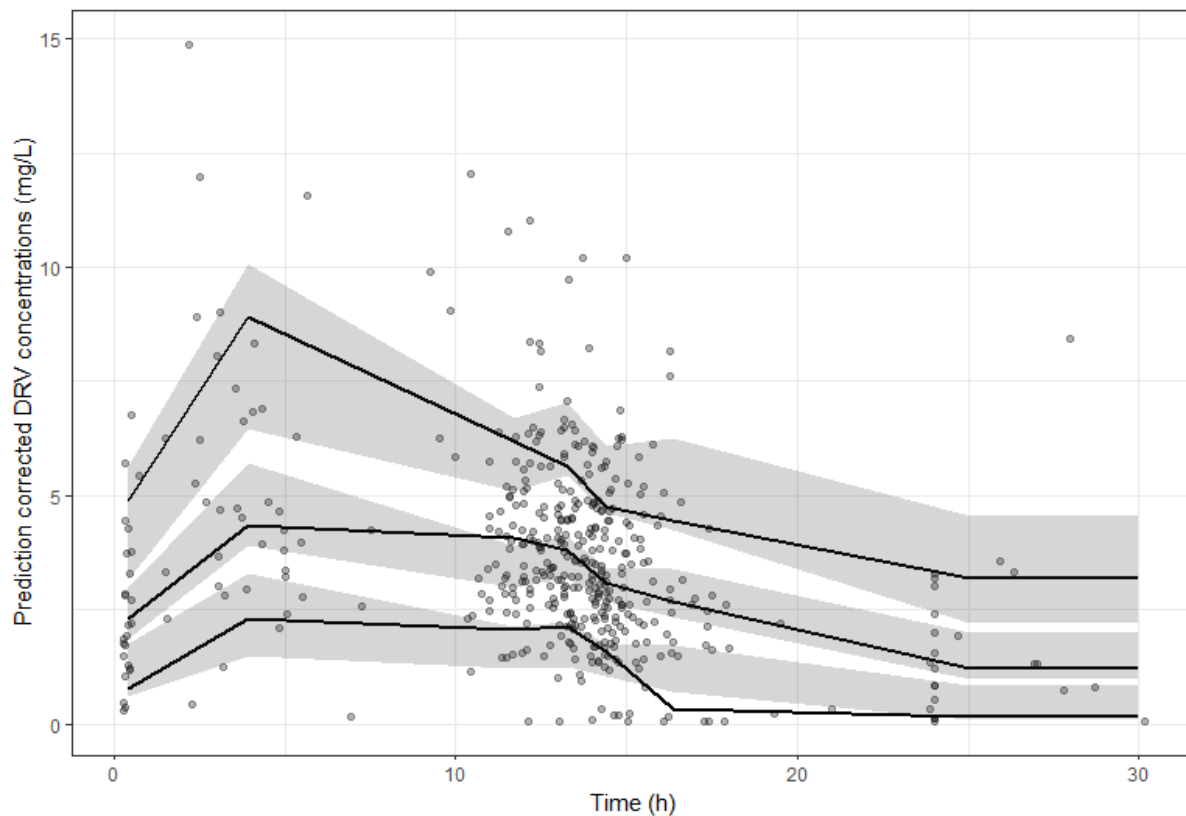


Parameters	Value	Relative Standard Error (%)
Population Effects		
Darunavir		
k_{DRV} (h^{-1})	0.41	24
CL/F_{DRV} (L/h)	9.7	3
<i>AUC_{RTV} effect on CL/F_{DRV}</i>	- 0.38	16
<i>AAG effect on CL/F_{DRV}</i>	- 0.73	10
V/F_{DRV} (L)	183	18
Ritonavir		
k_{RTV} (h^{-1})	0.17	18
CL/F_{RTV}	21.8	5
<i>Weight effect on CL/F_{RTV}</i>	0.75	fixed
V/F_{RTV}	107.6	18
<i>Weight effect on V/F_{RTV}</i>	1	fixed
Inter-individual variability (CV%)		
CL/F_{DRV}	17.7	15
V/F_{DRV}	65.52	18
CL/F_{RTV}	43.5	9
Proportional error model (%)		
<i>DRV concentrations</i>	37	4
<i>RTV concentrations</i>	50	4

S I. Parameters estimates of the “intermediate” AUC_{RTV} interaction model, using total DRV and RTV concentrations. k_a is the absorption constant rate, V/F the apparent volume of distribution and CL/F the apparent clearance of total DRV or RTV. Relative Standard Error is the standard error divided by the parameter estimate, expressed as a percentage.



S 2. Diagnostic plots of darunavir from the “intermediate” interaction model using total DRV and RTV concentrations. NPDE is the normalized prediction distribution error. Solid lines represent identity lines (top plots) or theoretical mean of NPDE (bottom plots). Orange dashed lines are the regression lines. (RTV diagnostic plots are similar to plots of the final model as the model part for RTV did not change).



S 3. pcVPC of darunavir from the “intermediate” AUC_{RTV} interaction model using total DRV and RTV concentrations. Black points represent observed concentrations. Solid black lines represent the 10th, 50th and 90th percentiles of observed concentrations. Grey areas represent the 95% confidence interval of the 10th, 50th and 90th percentiles of simulated concentrations. (RTV pcVPC plots is similar to plot of the final model as the model part for RTV did not change).