

Tables

<i>Characteristic</i>	Value
<i>No. of Patients / no. of samples</i>	152 / 443
<i>Age (years)</i>	15 (12 – 18)
<i>Male, n (%)</i>	64 (42)
<i>Weight (kg)</i>	50 (39 – 97)
<i>Body mass index (kg/m²)</i>	20 (14.3 – 34.4)
<i>Body surface area (m²)</i>	1.48 (1.27 – 2.15)
<i>Smoking status</i>	
<i>Smoker, n (%)</i>	2 (1.3)
<i>Ethnic origin</i>	
<i>Caucasian, n (%)</i>	31 (20)
<i>Black-African, n (%)</i>	85 (56)
<i>Asian, n (%)</i>	28 (18)
<i>Other, n (%)</i>	8 (5.9)
<i>Albumin (g/L)</i>	45 (36 – 52.2)
<i>Alpha-1 glycoprotein (g/L)</i>	0.66 (0.25 – 1.47)
<i>Alkaline phosphatase (UI/L)</i>	202 (41 – 718)
<i>Alanine amino-transferase (UI/L)</i>	12 (5 – 1765)
<i>Aspartate amino-transferase (UI/L)</i>	19 (11 – 1039)
<i>Total bilirubin (mg/dL)</i>	0.3 (0.09 – 2.52)
<i>Creatinine (mg/dL)</i>	0.63 (0.4 – 1.37)

Table 1. Population baseline characteristics at the start of the PK sub-study (i.e. 4 weeks after the start of the SMILE trial).

Values expressed as median (range) where applicable.

Parameters	Value	Relative Standard Error (%)
Population Effects		
Darunavir		
k_{DRV} (h^{-1})	0.43	21
$CL/F_{DRV,u}$ (L/h)	168.6	4
AUC_{RTV} effect on $CL/F_{DRV,u}$	- 0.5	21
$V/F_{DRV,u}$ (L)	2601	18
N_{AAG}	1	fixed
$K_{d,AAG}$ ($* 10^{-3}$ mmol/L)	0.85	10
Θ_{HSA} (L/mmol)	5.54	25
Ritonavir		
k_{RTV} (h^{-1})	0.18	17
CL/F_{RTV} (L/h)	21.6	5
Weight effect on CL/F_{RTV}	0.75	fixed
V/F_{RTV} (L)	105.7	18
Weight effect on V/F_{RTV}	1	fixed
Inter-individual variability (CV%)		
$CL/F_{DRV,u}$	29.3	9
$V/F_{DRV,u}$	76.1	15
CL/F_{RTV}	41.7	9
Proportional error model (%)		
Unbound DRV concentrations	40	4
Total DRV concentrations	34	4
RTV concentrations	50	5

Table 2. Pharmacokinetic parameter estimates of the final joint model. k_{DRV} is the absorption constant of DRV, $CL/F_{DRV,u}$ the apparent clearance of unbound DRV. AUC_{RTV} the ritonavir AUC between 0 and 24h post-dose at steady state, $V/F_{DRV,u}$ apparent volume of distribution of unbound DRV, $K_{d,AAG}$ the dissociation constant of AAG for DRV, N_{AAG} the number of binding site on AAG for DRV, Θ_{HSA} the binding constant of HSA for DRV, k_{RTV} the absorption constant of RTV, CL/F_{RTV} the apparent clearance of RTV, V/F_{RTV} the apparent volume of distribution of RTV. Relative Standard Error is the standard error divided by the parameter estimate, expressed as a percentage.

PK parameter	ODIN trial (N = 280)	SMILE trial (N = 152)
Trough C_{DRV} (mg/L)	1.90 (0.18 – 7.88)	1.76 (0.05 – 6.98)
AUC _{0-24h, DRV} (mg*h/L)	87.8 (45.5 – 236.9)	80.2 (28 – 199)

Table 3. Trough concentrations and exposures of darunavir in adults and adolescents of 12 years and older. Results are expressed as median (range). SMILE outcomes are individual predictions, ODIN outcomes are observations.