

**Table 2** Parameter estimates of base model and final covariate model.

Parameter	Base model		Final model	
	Estimate	RSE (%)	Estimate	RSE (%)
OFV	-143.006		-159.539	
CL/F Sub-population 1, L/h	8.50	6.0	9.88	4.6
CL/F Sub-population 2, L/h	2.17	13.8	2.26	12.5
V/F, L	159.52	29.9	260.92	29.2
$k_a$ , h <sup>-1</sup>	0.7 FIX	-	0.7 FIX	-
%CV ETA-CL/F	39.46	27.4	30.12	18.4
ETA Covariance	0.1612	59.4	0 FIX	-
%CV ETA-V/F	55.47	68.8	0 FIX	-
SD RUV	0.14	18.2	0.14	18.7
Probability of Sub-population 1	0.86	4.2	0.80	4.9
Smoking status on CL/F	-	-	1.39	25.0
Weight on CL/F	-	-	0.75 FIX	-
Weight on V/F	-	-	1.00 FIX	-

CL/F: oral clearance; CV: coefficient of variation; ETA: interindividual random effect;  $k_a$ : absorption rate constant; OFV: objective function value; RSE: relative standard error; RUV: residual unexplained variability; SD: standard deviation; V/F: apparent volume of distribution.