

Online Resource 2

Manuscript: Comprehensive Pharmacokinetic, Pharmacodynamic and Pharmacogenetic Evaluation of Once Daily Efavirenz 400 mg and 600 mg in Treatment-Naïve HIV-Infected Patients at 96 Weeks: Results of the ENCORE1 Study

Journal: Clinical Pharmacokinetics

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Online Resource 2 Mean individual predicted PK parameters stratified by dose and composite *CYP2B6* 516G>T/983T>C/*CYP2A6**9B/*17 genotype (defined as extensive, intermediate, slow) estimated by the population PK model (n=568 patients)*. Data presented as median (range).

	Efavirenz 400mg once daily			Efavirenz 600mg once daily		
	Extensive (n=119)	Intermediate (n=128)	Slow (n=48)	Extensive (n=107)	Intermediate (n=127)	Slow (n=39)
<i>CL/F (L/h)</i>	10.7 (4.69-25.6)	8.05 (2.14-27.3)	4.12 (1.45-45.9)	12.4 (5.11-69.7)	8.93 (2.98-65.4)	3.55 (1.69-58.2)
<i>CV (%)</i>	33	37	124	55	62	155
<i>AUC₀₋₂₄ (mg.h/L)</i>	37.6 (17.6-85.4)	49.9 (14.8-187)	97.5(20.7-285)	49.2 (8.61-117)	67.6 (12.4-202)	171 (19.2-359)
<i>CV (%)</i>	32	37	49	34	38	47
<i>T_{max} (h)</i>	3.98 (3.35-4.22)	4.08 (3.28-4.32)	4.27 (3.11-4.39)	3.93 (2.23-4.23)	4.04 (2.64-4.32)	4.27 (2.74-4.38)
<i>CV (%)</i>	3.5	3.4	5.1	6.3	4.4	7.1
<i>C_{max} (mg/L)</i>	1.97 (0.95-4.14)	2.51 (1.10-8.34)	4.38 (1.38-12.2)	2.80 (1.53-5.79)	3.71 (1.69-9.03)	7.80 (1.75-15.6)
<i>CV (%)</i>	28	32	45	27	32	42
<i>C₂₄ (mg/L)</i>	0.970 (0.305-2.79)	1.46 (0.169-7.00)	3.54 (0.341-11.3)	1.28 (0.00247-3.94)	1.94 (0.0789-7.55)	6.24 (0.243-14.1)
<i>CV (%)</i>	44	48	56	47	51	52
<i>C₁₂ (mg/L)</i>	1.60 (0.734-3.65)	2.14 (0.579-7.89)	4.13 (0.845-12.0)	2.11 (0.119-5.02)	2.90 (0.377-8.52)	7.25 (0.684-15.09)
<i>CV (%)</i>	32	37	49	35	38	47

<i>Half-life (h)</i>	17.5 (7.71-37.0)	22.8 (6.09-69.1)	48.0 (8.78-152)	15.9 (2.13-40.4)	20.5 (3.70-68.6)	49.4 (4.92-125)
<i>CV (%)</i>	31	36	49	34	39	46

* 37/605 with missing composite genotype (n=15 400mg EFV; n=22 600mg EFV)

PK: pharmacokinetic; CL/F: apparent oral clearance; AUC₀₋₂₄: area under the curve over the 24 hour dosing interval; T_{max}: time of maximum concentration; C_{max}: maximum concentration; C₂₄: trough concentration, 24 hours post-dose; C₁₂: concentration 12 hours post-dose representing the mid-dose interval; CV: co-efficient of variation

Data in this Table also presented in Dickinson L, Amin J, Else L, et al., on behalf of the ENCORE1 Study Group. Pharmacokinetic and Pharmacodynamic Comparison of Once-Daily Efavirenz (400 mg vs. 600 mg) in Treatment-Naïve HIV-Infected Patients: Results of the ENCORE1 Study. Clin Pharmacol Ther. 2015. doi: 10.1002/cpt.156. **Open Access**, available at: <http://onlinelibrary.wiley.com/doi/10.1002/cpt.156/abstract>