

[Title] Impact of P-glycoprotein-mediated active efflux on drug distribution into lumbar cerebrospinal fluid in nonhuman primates

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Supplemental Table 2. Comparison of $K_{p,uu,lumbar\ CSF}$ values with $C_{CSF}/C_{u,plasma}$ at 24 hours after starting infusion

The $K_{p,uu,lumbar\ CSF}$ values were compared with the C_{CSF} -to- $C_{u,plasma}$ ratios ($C_{CSF}/C_{u,plasma}$) at 24 hours after starting infusion in animal study Part 1 (A) and Part 2 (B). The correlation is graphically shown in (C). The $K_{p,uu,lumbar\ CSF}$ values were obtained from Table 1 or Table 2.

(A) Part 1

Test compounds	$K_{p,uu,lumbar\ CSF}$	$C_{CSF}/C_{u,plasma}$ at 24 h	Fold difference
Antipyrine	1.10 ± 0.15	0.924 ± 0.323	1.2
Carbamazepine	1.34 ± 0.10	1.87 ± 1.07	0.7
Lamotrigine	0.990 ± 0.066	1.06 ± 0.07	0.9
Ondansetron	0.885 ± 0.259	0.784 ± 0.350	1.1
E2074	1.05 ± 0.11	1.01 ± 0.76	1.0
Risperidone	0.458 ± 0.074	0.206 ^a	2.2
Verapamil	0.406 ± 0.058	0.266 ± 0.158	1.5
Paliperidone	0.226 ± 0.061	0.258 ± 0.100	0.9
Desloratadine	0.195 ± 0.006	0.227 ± 0.066	0.9
Quinidine	0.278 ± 0.029	0.194 ± 0.052	1.4

^aData from single animal because the C_{CSF} at 24 hours was below the quantification limit (< 0.1 ng/mL) in two out of three animals.

$K_{p,uu,lumbar\ CSF}$ and $C_{csf}/C_{u,plasma}$ at 24 h are represented as mean ± SD.

(B) Part 2 (with and without zosuquidar co-treatment)

Test compounds	Zosuquidar (-)			Zosuquidar (+)		
	$K_{p,uu,lumbar\ CSF}^a$	$C_{CSF}/C_{u,plasma}$ at 24 h ^a	Fold difference	$K_{p,uu,lumbar\ CSF}^b$	$C_{CSF}/C_{u,plasma}$ at 24 h ^a	Fold difference
Antipyrine	1.05 ± 0.04	1.11 ± 0.19	1.0	1.07 (1.05, 1.08)	1.04 ± 0.16	1.0
Ondansetron	0.861 ± 0.096	0.422 ± 0.156	2.0	1.08 (0.968, 1.19)	0.880 ± 0.297*	1.2
Desloratadine	0.151 ± 0.026	0.144 ± 0.026	1.0	0.250 (0.264, 0.235)	0.268 ± 0.087	0.9
Quinidine	0.239 ± 0.011	0.271 ± 0.153	0.9	0.987 (0.916, 1.06)	1.57 ± 0.86**	0.6

^aMean ± SD of three animals.

^bMean of two animals with individual values given in the parenthesis.

*: $P < 0.05$, **: $P < 0.01$ (Paired t test vs Zosuquidar (-))

(C) Correlation

