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Title: Penetration and pharmacokinetics of peramivir in upper and lower airway epithelia and plasma

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Body: INTRODUCTION: Peramivir is an only available neuraminidase inhibitor agent allowing intravenous infusion approved in Japan and South Korea for the treatment of influenza. The purpose of the current study was to describe the pharmacokinetic profile and determine the level of penetration of peramivir into pharyngeal epithelial lining fluid (ELF), bronchial ELF and plasma in healthy volunteers. METHODS: Six healthy volunteers were studied. After plasma was sampled, peramivir was infused over 30 minutes intravenously. Then ELFs of upper and lower airway and plasma were obtained as follows, at the time of finishing infusion, at 0.5hr, 1.0hr, 1.5hr, 2.0hr, 2.5hr, 3.0hr, 4.0hr and 5.0hr after infusion by bronchoscopic microsampling. The concentrations of peramivir in ELFs and those in plasma were measured by LC-MS-MS technique. Pharmacokinetic analysis was performed. RESULTS:Intravenous administration of peramivir was well tolerated, and no adverse effects were observed. Pharmacokinetics parameters are shown in Table 1.

Pharmacokinetics parameters of peramivir

	Bronchus	Pharynx	Plasma
Cmax(μg/mL)	9.60±2.30	0.99±0.43	50.52±17.51
AUC(0→∞) (μg·hr /mL)	24.36±3.21	3.048±2.67	59.69±9.35
t1/2 (hr)	1.51±0.49	3.39±4.31	1.60±0.12
CL(0→∞) (L/hr)	-	-	5.13±0.84

Cmax of bronchus, pharynx and plasma are 25056±6003 nmol/L, 2583.9±1122.3 nmol/L and

1318572±457011 nmol/L respectively. Those sufficiently exceed the geometric mean of previously reported IC50 (0.38 to 3.96 nmol/L) for the peramivir[1]. CONCLUSION: Peramivir in bronchial and pharyngeal ELF would reach enough levels to treat for influenza viral pneumonia. REFERENCES: 1. Ikematsu H et al. J Infect Chemother 2012;18:529–533.