

Nasal and Pharyngeal Concentrations of Peramivir Following Intramuscular and Intravenous Administration in Healthy Volunteers. W.J. ALEXANDER¹, L.A. HARMAN¹, P.J. COLLIS¹, J. ELDER¹, J.M. KILPATRICK¹ G. ATIEE², E. MEAD³,
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Background: The concentration of neuraminidase inhibitor at respiratory mucosal sites is likely important for effective treatment of acute influenza and concentrations above the IC₅₀ at sites of influenza virus replication may be a strategy for preventing emergence of viral resistance. Peramivir is a potent neuraminidase inhibitor with potential efficacy in treatment of human influenza infections.

Methods: Healthy subjects (n=27) received peramivir (single doses of 75 mg, 150 mg, or 300 mg) by both i.v. and i.m. routes in a randomized crossover design. At 1, 12, and 24 hours following single doses of peramivir, nasal wash samples and throat gargle samples were obtained. Peramivir concentrations (corrected) in the samples were calculated based on results of time-matched urea nitrogen values in sample and in serum.

Results: Mean concentrations (ng/mL) of peramivir in nasal washes and throat gargles at post-dose times shown in table:

Nasal Wash				
Dose (mg)	Route	2 hr	12 hr	24 hr
75	i.m.	223.9	7.9	nd
	i.v.	222.6	20.7	nd
150	i.m.	602.4	44.5	nd
	i.v.	475.1	25.9	nd
300	i.m.	786.8	101.7	nd
	i.v.	1139.5	95.4	nd

nd= not detected

Throat Gargle				
Dose (mg)	Route	2 hr	12 hr	24 hr
75	i.m.	86.6	26.6	3.6
	i.v.	93.0	4.0	3.4
150	i.m.	210.1	7.3	2.8
	i.v.	158.2	6.4	2.5
300	i.m.	191.3	41.0	4.6
	i.v.	171.2	21.0	5.1

Conclusions: These data demonstrate that single parenteral doses of peramivir provide drug concentrations at mucosal sites in the upper respiratory tract that may exceed the IC₅₀ of influenza A and influenza B strains for up to 24 hours. Clinical studies to evaluate the efficacy and safety of peramivir in the treatment of acute influenza are in progress.