

A Single Intramuscular Injection of Peramivir Demonstrates Anti-influenza Activity Against Recently Isolated Pandemic Flu Virus H1N1 (A/CA/04/2009)

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Background: Peramivir is a potent and selective inhibitor of influenza neuraminidase. Here we demonstrate the efficacy of a single intramuscular (IM) injection of peramivir in mice infected with recently isolated pandemic flu virus H1N1 A/CA/04/09 (swine origin).

Methods: In the treatment model peramivir was administered as a single IM injection at 50 mg/kg dose and oseltamivir was given orally at 10 mg/kg/d bid for 5 days. In the prophylaxis model, peramivir was given as a single IM injection. Each infected, drug treated group contained 9-10 mice and the saline treated groups contained 10-15 mice.

Results: Peramivir potently inhibits the neuraminidase enzyme N1 from H1N1 (A/CA/04/09) in vitro with an IC₅₀ of 0.43 ± 0.07 nM (n=2). A single IM injection of peramivir, given 1 hr prior to infection (prophylaxis model), significantly reduced weight loss and mortality in mice infected with pandemic Influenza A/H1N1 virus (Table). In the therapeutic treatment model, peramivir given 24, 48 and 72 hrs after infection as a single IM injection at 50 mg/kg dose, showed significant protection against lethality. There was 13% survival in the vehicle treated group whereas in the peramivir treated group at 24, 48, and 72 hrs, the survival was 100, 40, and 50%, respectively. Survival in the oseltamivir groups at 24, 48 and 72 hrs was 90, 30 and 20%, respectively.

Conclusion: These data demonstrate efficacy of parenterally administered peramivir against the recently isolated pandemic flu virus.

Table: Effect of peramivir treatment (IM) on weight loss and survival in mice infected with H1N1 virus (Prophylaxis model)

Treatment	Dose Level (mg/kg)	Percent (%) Survival	Mean Weight change (± SEM) Day 4
Vehicle, uninfected	0	100	0.32 ± 0.22
Vehicle, infected Saline treated	0	20	- 3.41 ± 0.17
Peramivir	1.0	60*	- 2.11 ± 0.22**
Peramivir	3.0	60*	- 1.51 ± 0.33**
Peramivir	10.0	90**	- 1.84 ± 0.19**
Peramivir	30.0	100**	-1.83 ± 0.17**

*p<0.03, **p<0.001 vs. vehicle, infected control group;