

Safety and Antiviral Effect of Multi-Day Therapy with IV Peramivir 300mg BID or 600mg QD in Hospitalized Influenza Subjects.

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BACKGROUND: Influenza causes > 200,000 hospitalizations/year in the US. Few studies have focused on patients hospitalized with influenza.

METHODS: Subjects were ≥ 12 yr old, hospitalized with influenza symptoms, and met eligibility criteria in the 2009/10 pandemic in 5 countries. Quantitative virology was done on nasopharyngeal specimens at regular intervals. TCID₅₀/mL (BL to 48 hours) was the primary endpoint. Secondary endpoints included change from BL in quantitative PCR, a composite endpoint (Time To Clinical Resolution, 4 vital signs and oxygen (O₂) saturation measured 3 times daily, met if 4 of the 5 measures normalized for at least 24 hrs), and other clinical and virologic endpoints. Safety was assessed by reports of adverse events and laboratory results.

RESULTS: 234 subjects were randomized to 5 to 10 days of therapy with intravenous (IV) peramivir 300 mg twice daily (BID, n = 117), or 600 mg once daily (QD, n = 117). Analyses focused on 127 subjects with confirmed influenza (mean age 46 yr; range 14-92). More subjects in the QD arm needed O₂ therapy or ICU care at BL vs. the BID group (74% and 21% vs. 61% and 16%). For the primary or secondary virologic endpoints, there were no differences between treatment groups (Table). After adjustment for significant BL variables there were also no differences between treatment groups in the secondary clinical endpoints, including safety and survival. All isolates were susceptible to NAIs at BL. One isolate had a high IC₅₀ post BL.

ENDPOINT (median ± 95% CI)		Peramivir 300 mg IV BID	Peramivir 600 mg IV QD	
Δ in Viral Titer (BL to 48 hrs) (log ₁₀ TCID ₅₀ /mL) Influenza A & B (n = 44)		-1.66 (-2.32,-0.61)	-1.47 (-1.89, -0.75)	
Δ in PCR Titer (BL to 48 hrs) (log ₁₀ vp/mL) Influenza A & B (n = 86)		-1.00 (-1.52,-0.77)	-1.07 (-1.24, -0.67)	
TTCR (hrs) O ₂ therapy needed at BL (n = 87)		165.9 (65.6, NA)	177.0 (115.9, 283.2)	
TTCR (hrs) No O ₂ therapy needed at BL (n = 39)		29.1 (18.8, 42.2)	20.1 (12.4, 173.0)	
Time to Resumption of Usual Activities (days) n = 112		27.7 (17.8, NA)	24.9 (13.5, 28.8)	
Time To Hospital Discharge (days) n = 127 (57 300 BID, 70 600 QD)		6.0 (5.0,8.0)	6.0 (6.0, 11.0)	
Influenza Virus Type	All subjects	BL values NAI Assay IC ₅₀ nM Median (Min, Max)		
		Peramivir	Oseltamivir	Zanamivir
2009 H1N1 Influenza A	N = 47	0.1 (0.01,0.1)	0.4 (0.2, 1.3)	0.2 (0.02, 0.6)

CONCLUSIONS: Peramivir IV at 300 mg IV BID or 600 mg IV QD demonstrated generally similar tolerability and efficacy based on virologic and clinical endpoints. Further study of the efficacy and safety of peramivir in hospitalized subjects is warranted.