

**A Placebo-Controlled Evaluation of the Safety and Pharmacokinetics of Multiple-Dose Intravenous Administration of Peramivir to Healthy Elderly Subjects.**

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**Background:** Hospitalizations due to influenza occur more frequently in the elderly and the risks of complications are highest in this age group. Peramivir is a potent neuraminidase inhibitor suitable for parenteral administration that may be of benefit in the hospital setting.

**Methods:** Twenty (20) healthy subjects  $\geq$  65 yr received intravenous peramivir (4 mg/kg BID) on Day 1 and thereafter, two cohorts of 8 subjects each (6 peramivir; 2 placebo) received 4 mg/kg BID for either 5d or 10d. Samples for PK analyses were obtained and safety monitoring included assessment of adverse events and results of clinical laboratory tests, including 24-hour urine collections.

**Results:** Pharmacokinetic parameters are shown in the table. There was no evidence of drug accumulation over either 5 or 10 days. When data were compared with those of subjects aged 18-50 years in another study, elderly subjects had a 46% increase in dose-normalized AUC. This increase is likely attributed to reduced renal function in elderly subjects.

	<b>Day 1</b>	<b>Day 7 (post 5 day dosing)</b>	<b>Day 12 (post 10 day dosing)</b>
n	<b>20</b>	<b>6</b>	<b>6</b>
$C_{max}$ (ng/mL)	22647 $\pm$ 4823	22608 $\pm$ 4910	22933 $\pm$ 2951
AUC <sub>0-12</sub> (ng·h/mL)	61334 $\pm$ 8793	70465 $\pm$ 12236	61572 $\pm$ 8564
$T_{1/2\lambda z}$ (h)	ND	14.6 $\pm$ 1.8	16.3 $\pm$ 3.5

**Safety:** Serial ECG monitoring resulted in no findings considered related to treatment. Changes in clinical chemistry, hematology and urinalysis results were unremarkable. No serious adverse events were reported.

**Conclusions:** This study provides pharmacokinetic information in an elderly age group and suggests an acceptable safety profile with multiple-day, twice-daily intravenous administration of peramivir. Clinical studies to evaluate the efficacy and safety of peramivir in the treatment of influenza in the hospital setting are in progress.