

**Pharmacokinetic and Safety Evaluations of Escalating Doses of Peramivir Administered Intravenously in Healthy Volunteers.** J. BEIGEL<sup>1</sup>, L.A. HARMAN<sup>2</sup>, P.J. COLLIS<sup>2</sup>, A. McCULLOUGH<sup>2</sup>, J.M. KILPATRICK<sup>2</sup>, D. RUFF<sup>3</sup>, E. MEAD<sup>4</sup>, W.J.ALEXANDER<sup>2</sup> <sup>1</sup>Clinical Research Section, Laboratory of Immunoregulation, NIAID, NIH, Bethesda, MD, <sup>2</sup>BioCryst Pharmaceuticals, Birmingham, AL and RTP, NC; <sup>3</sup>Healthcare Discoveries, Inc., San Antonio, TX; <sup>4</sup>Encorium Group, Inc., Wayne, PA

**Background:** Peramivir is a potent neuraminidase inhibitor with potential efficacy in treatment of uncomplicated and severe human influenza infections.

**Methods:** In 3 Phase 1 studies, healthy subjects received peramivir or placebo. The initial group of subjects (n=8) received single doses of peramivir (0.5 mg/kg) or placebo. A second group (n=8) received peramivir 0.5 mg/kg BID on one day or placebo. Additional subjects (n=68) received placebo or single peramivir doses of 1, 2, 4, and 8 mg/kg; 4 mg/kg BID on one day; and 2 mg/kg or 4 mg/kg BID for 10 days. Plasma and urine samples for pharmacokinetic analyses were collected as were serial laboratory assessments during and after treatment.

**Results:** A total of 84 subjects were enrolled and 61 subjects received peramivir. Plasma concentrations of peramivir increased linearly in a dose-dependent manner. Mean  $C_{max}$  ranged from 1925ng/mL (0.5 mg/kg) to 44667 ng/mL (8 mg/kg). The  $AUC_{0-72\text{ hr}}$  ranged from 4994 hr•ng/mL (0.5 mg/kg) to 90507 hr•ng/mL (8 mg/kg). The mean  $t_{1/2\lambda z}$  for doses of 2 mg/kg to 8 mg/kg ranged from 15.9 hr to 20.8 hr. Peramivir clearance was similar across all dose groups and no significant accumulation occurred with dosing for 10 days. No serious adverse events occurred. With dosing over 10 days, the overall incidence of treatment-emergent adverse events was similar among subjects who received peramivir (n=18) compared with subjects receiving placebo (n=9). There were no significant changes in clinical laboratory test results for those subjects who received peramivir.

**Conclusions:** This study provides important pharmacokinetic data and suggests that intravenous administration of peramivir at doses up to 8 mg/kg/day for 10 days may be well-tolerated.