BIOCRYST

PHARMACEUTICALS, INC.

PERAMIVIR

BCX1812-301

A Phase 3, Multicenter, Randomized, Double-Blind, Controlled Study to Evaluate the Efficacy and Safety of Peramivir Administered Intravenously in Addition to Standard of Care Compared to Standard of Care Alone in Subjects Who Are Hospitalized Due to Influenza

Indication studied:	Hospitalized patients with acute influenza
Developmental phase of study:	Phase 3
First subject enrolled:	17 NOV 2009
Last subject completed:	16 NOV 2012
Release date of report:	11 OCT 2013

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1.1. SIGNATURE PAGE

This trial was conducted in accordance with the ethical principles of Good Clinical Practice, according to the ICH Harmonized Tripartite Guideline.

William P. Sheridan, MB BS — Date: 05 Nov 2013

Chief Medical Officer and Senior Vice President

Elliott Berger, PhD — Date: 05 Nov 2013

Senior Vice President Regulatory Affairs

2. SYNOPSIS

Name of Sponsor/Company: BioCryst Pharmaceuticals, Inc.	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use Only)*
Name of Finished Product:		
Name of Active Ingredient: Peramivir		

Title of Study:

A Phase 3, multicenter, randomized, double-blind, controlled study to evaluate the efficacy and safety of peramivir administered intravenously in addition to standard of care compared to standard of care alone in subjects who are hospitalized due to influenza.

Principal Investigator: Menno de Jong, MD, PhD

Investigators: Multi-center

Study center(s): Multi-center, Multinational

Publications (reference): None

Studied period (years):	**Phase of development:**
Date first patient enrolled: 17 NOV 2009 Date last patient completed: 16 NOV 2012	3

Objectives:

Primary:

- To evaluate the effect of treatment with peramivir plus standard of care (SOC) compared to placebo plus SOC on time to clinical resolution in subjects who are hospitalized with influenza.

Secondary:

- To evaluate the safety and tolerability of peramivir plus SOC compared to placebo plus SOC in subjects who are hospitalized with influenza.
- To evaluate changes in viral shedding associated with treatment with peramivir plus SOC compared to placebo plus SOC in subjects who are hospitalized with influenza.
- To evaluate the effect on time to alleviation of symptoms, time to resumption of usual daily activities, time to hospital discharge, incidence and duration of intensive care unit (ICU) admission after initiation of treatment, incidence of influenza-related complications and mortality associated with treatment with peramivir plus SOC compared to placebo plus SOC in subjects who are hospitalized with influenza.
- To evaluate changes in viral phenotype and genotype between baseline and post-treatment samples associated with treatment with peramivir plus SOC compared to placebo plus SOC in subjects who are hospitalized with influenza.
- To describe the pharmacokinetics of peramivir in subjects who are hospitalized with influenza infection.
- To evaluate pregnancy outcome and infant health and development in the first 12 months in

pregnant women who receive peramivir.

Methodology:

This was a multinational, randomized, double-blind, controlled study comparing the efficacy and safety of peramivir vs placebo administered intravenously once daily for 5 days in addition to the institution's SOC in subjects 6 years of age and older who were hospitalized due to influenza.

Subjects with signs and symptoms compatible with influenza infection were evaluated for participation. Enrollment was to continue until 160 subjects with confirmed influenza who had not received a neuraminidase inhibitor (NAI) as part of their SOC regimen (the "Non-NAI SOC subgroup") were enrolled. Up to 600 subjects in total may have been enrolled into the study in order to enroll 160 subjects with confirmed influenza in the Non-NAI SOC subgroup. Eligible subjects were unequally randomized 2:1 (Treatment Group 1: Treatment Group 2) to receive 1 of 2 treatments:

Treatment Group 1:

- Adults (≥ 18 years): Peramivir (BCX1812) 600 mg, administered intravenously, once daily (every 24 hours) for 5 days (5 doses) in addition to the institution's SOC.
- Adolescents (> 12 to < 18 years): Peramivir (BCX1812) 10 mg/kg (not to exceed a maximum dose of 600 mg), administered intravenously once daily (every 24 hours) for 5 days (5 doses) in addition to the institution's SOC.
- Children (≥ 6 to < 12 years): Peramivir (BCX1812) 12 mg/kg (not to exceed a maximum dose of 600 mg), administered intravenously once daily (every 24 hours) for 5 days (5 doses) in addition to the institution's SOC.

Treatment Group 2:

- Placebo Peramivir (BCX1812) administered intravenously at a volume matched with that of the active drug, once daily (every 24 hours) for 5 days (5 doses) in addition to the institution's SOC.

Two subjects were randomized to Treatment Group 1 for every 1 subject randomized to Treatment Group 2. Randomization was stratified according to the following factors:

1. Duration of illness: ≤ 48 hours or > 48 to ≤ 72 hours;
2. Standard of care received: NAI-containing antiviral therapy, non-NAI-containing antiviral therapy or no antiviral therapy;
3. Laboratory diagnosis of influenza at entry: positive influenza A; positive influenza B; or Rapid Antigen Test (RAT) negative.
4. Whether the subject was admitted to the ICU at the time of randomization.

Each dose of peramivir or placebo was administered intravenously over a period of 15-30 minutes in all subjects. Peramivir doses were adjusted in subjects with renal impairment. Concomitant use of oseltamivir, zanamivir, amantadine, rimantadine, and/or ribavirin was permitted during administration of study drug and in the post-treatment follow-up period, where this was in accordance with the institution's SOC.

Subjects who had not met the protocol-defined criteria of clinical resolution on Day 5 or who had detectable virus by reverse transcriptase (RT) polymerase chain reaction (PCR) from a sample collected on Study Day 4 after dosing continued their assigned treatment for a further 5 days. Once allocated to a treatment regimen, subjects completed the entire treatment course (5 or 10 days) without respect to clinical status before the prescribed end of treatment.

Hospital discharge was expected to occur once the subject had met the local hospital practice criteria for discharge. The Investigator arranged for the subject to receive continuation of intravenous study

treatment as an outpatient in a clinic setting or in a medical facility, if required.

Subjects who at the time of enrollment had evidence of moderate or severe renal impairment or who developed moderate or severe renal impairment during the study were allowed to continue in the study, but the dose of peramivir was adjusted. Subjects with improvement of renal function during therapy had the dose of peramivir adjusted for the improved renal function. For example, an adult subject with severe renal impairment who received a peramivir dose of 100 mg/day received a dose of 150 mg/day when the renal impairment became moderate, or a dose of 600 mg/day if the renal impairment became mild. These dose adjustments were made no more frequently than once daily.

Number of patients (planned and analyzed):

A total of 160 subjects with confirmed influenza were planned to be enrolled. Data from 405 subjects were analyzed.

Diagnosis and main criteria for inclusion:

Inclusion Criteria:

1. Age ≥ 6 years of age or age ≥ 12 years (rest of world), male or female.
2. Provided informed consent/assent, or for whom consent may be provided by guardian, unless informed consent provided by a guardian or a legally authorized representative was not consistent with applicable local or ethical concerns, procedures, directives and/or guidelines.
3. Subject must have had at least one of the following clinical presentations at Screening:

   a. Oral temperature ≥ 38.0 °C (≥ 100.4 °F), ≥ 38.6°C (≥ 101.4 °F) tympanic or rectal

   OR

   b. Oxygen saturation < 92%, OR

   c. Two out of the following 3 vital signs:

   - Respiration rate > 24/minute in adults (≥ 18 years of age) and adolescents (≥ 12 to < 18 years of age), > 30/minute in children (6 to < 12 years of age)
   - Heart rate > 100 beats/minute in adults and adolescents, > 110 beats/minute in children
   - Systolic blood pressure < 90 mmHg in adults and adolescents, < 80 mmHg in children
4. Presence of at least 1 respiratory symptom (cough, sore throat, or nasal congestion) of any severity (mild, moderate, or severe).
5. Presence of at least 1 constitutional symptom (headache, myalgia, feverishness, or fatigue) of any severity (mild, moderate, or severe).
6. Onset of illness no more than 72 hours before presentation. Note: Time of onset of illness was defined as the earlier of either: 1) the time when the temperature was first measured as elevated, OR 2) the time when the subject experienced the presence of at least 1 respiratory symptom AND the presence of at least 1 constitutional symptom.
7. Either:
8. Severity of illness that, in the Investigator's judgment, justified hospitalization of the subject for supportive care.

   OR

   Presence of **1 or more** of the following factors:

- Age ≥ 60 years.
- Presence of chronic obstructive pulmonary disease or other chronic lung disease requiring daily pharmacotherapy.

- Current history of congestive heart failure or angina.
- Presence of diabetes mellitus, clinically stable or unstable.
- Transcutaneous oxygen saturation < 94% without supplemental oxygen for at least 5 minutes, or a medically significant decrease in oxygen saturation from an established baseline value (an investigative site at altitude > 2000 feet above sea level will utilize different criteria for oxygen saturation).
- History of chronic renal impairment not requiring peritoneal dialysis.
- Serum creatinine > 2.0 mg/dL or > 177 μmol/L.

9. Diagnosis of Influenza by satisfying one of the following:

a. Clinical Influenza with Positive Diagnostic Test. Subjects who had a positive RAT for influenza A and/or influenza B (using a Sponsor-approved test kit), or positive test (using other methodology) for influenza A and/or B virus antigen or RNA performed in a clinical laboratory at the screening/enrollment evaluation are eligible for enrollment.

OR

b. Clinical Influenza with Negative Rapid Antigen Test. Subjects with a negative RAT test were allowed to be enrolled once the site had been approved by the Sponsor to enroll such subjects, based on documentation of an outbreak of influenza in the community. An influenza outbreak was documented in the catchment area of the hospital via one of the following methods: 1) local confirmation of influenza A or B infection in the current influenza season by a) the institution's local laboratory, or b) the local public health system, or c) the national public health system, or d) a laboratory of a recognized multinational influenza surveillance scheme such as the European Influenza Surveillance Network; 2) prior enrollment of a RAT positive subject into this study at the same institution in the current influenza season.

Exclusion Criteria:

1. Subjects who had been hospitalized for greater than 24 hours (not including time spent in the Emergency Department).
2. Treatment with any dose(s) of rimantadine, amantadine, ribavirin, zanamivir, or oseltamivir in the previous 7 days.
3. Blood platelet count of < 20 x 10^9/L at the time of the screening evaluation.
4. Serum bilirubin > 6 mg/dL or > 102.6 μmol/L at time of screening evaluation.
5. Serum alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 5 times the upper limit of normal at time of screening evaluation.
6. Congestive heart failure of New York Heart Association Class III or Class IV functional status.
7. Serum creatinine > 5.0 mg/dL or > 442 μmol/L at time of screening evaluation.
8. Subjects who required peritoneal dialysis.
9. Altered neurologic status as defined by a Glasgow Coma Score of ≤ 9, unless medically induced.
10. Females who were pregnant (excluded from sites outside the US) or breastfeeding (all sites).
11. Actively undergoing systemic chemotherapy or radiotherapy treatment for a malignancy. Subjects who have completed treatment 30 days prior to enrollment were not excluded. Hormone treatment for cancer was also not excluded.
12. Prior hematopoietic stem cell transplantation or solid organ transplant during the previous 4 months.

13. HIV infection with a known CD4 count < 200 cells/mm^3 unless on a stable highly active antiretroviral therapy for at least 6 months.
14. Presence of a pre-existing chronic infection that is undergoing or requiring medical therapy (eg, tuberculosis). Subjects with chronic osteomyelitis or Hepatitis B or C not requiring treatment were not excluded.
15. Presence of any pre-existing illness that, in the opinion of the investigator, would place the subject at an unreasonably increased risk through participation in this study.
16. Previous treatment with intravenous or intramuscular peramivir.
17. Participation as a subject in any study of an experimental treatment for any condition within the 30 days prior to the time of the screening evaluation.
18. Subjects diagnosed with cystic fibrosis.
19. Subjects with confirmed clinical evidence of acute non-influenza infection at the time of screening evaluation.
20. Subjects who, in the judgment of the investigator, would be unlikely to comply with the requirements of this protocol.

Test product, dose and mode of administration, batch number:

Peramivir injection is a liquid for parenteral administration and was supplied as a 10 mg/mL stock solution in 20-mL single-use glass vials. Peramivir was administered intravenously according to the dose regimens described above.

Each dose of peramivir was administered intravenously over a period of 15 to 30 minutes. Peramivir doses were adjusted in subjects with renal impairment in accordance with subject's renal status using the dose adjustment guidelines provided in the protocol.

The following lot numbers of peramivir were used in this study: C0267 and C0299.

Duration of treatment:

Treatment was administered once daily for 5 days. Subjects who had not met criteria of clinical resolution on Day 5 of treatment or who had detectable virus on Day 4 continued treatment for 5 more days for a total of 10 days.

Reference therapy, dose and mode of administration, batch number:

Placebo was supplied in matching 20-mL single-use glass vials containing sterile saline (0.9%) for infusion. Placebo was administered intravenously over a period of 15 to 30 minutes.

The following lot numbers were used in this study: 7441, C0389, and C0644.

Criteria for evaluation:

Efficacy:

Efficacy was evaluated through assessments of body temperature, oxygen saturation, vital signs, influenza virus titers, clinical symptoms of influenza, usual daily activities, time to hospital discharge, incidence of influenza-related complications, incidence and duration of ICU admission after initiation of treatment, requirement for continued antiviral treatment beyond Day 5, 30-day mortality following treatment, and changes in viral sensitivity to other antiviral drugs.

Body temperature measurements were recorded once at Screening/Baseline, 3 times per day while hospitalized, twice daily after discharge (if discharged before Day 9), and once daily from Day 10 through Day 14. To avoid the confounding effects of antipyretic medications, temperature measurements were taken, whenever possible, at least 4 hours after administration of the antipyretic medication. Temperature measurements that were recorded for the purpose of analyzing efficacy in this study < 4 hours after administration of the antipyretic medication, regardless of the dose, were not counted in the efficacy analyses.

Oxygen saturation was measured by transcutaneous oximetry once at Screening/ Baseline and 3 times per day, approximately 8 hours apart while hospitalized, once at hospital discharge, and once during the follow-up clinic visits. Oxygen saturation levels were adjusted for altitude.

The subject was asked to provide an assessment of 7 influenza symptoms (1. cough; 2. sore throat; 3. nasal congestion; 4. myalgia [aches and pains]; 5. headache; 6. feverishness; and 7. fatigue) on a 4-point severity scale (0, absent; 1, mild; 2, moderate; 3, severe) twice daily during the hospitalization period, beginning predose on Day 1. Following discharge, signs and symptoms of influenza were recorded twice daily by the subject through Day 9 and once daily on Day 10 through Day 14.

Subjects or parents/guardians were asked to provide a daily assessment of the subject's ability to perform usual daily activities using a 0-10 visual analogue scale, where 0 = unable to perform usual activities at all, and 10 = able to perform usual activities fully.

An adequate specimen was collected by swab from the anterior nose (bilateral) and posterior pharynx for virologic laboratory culture and analysis by $\log_{10}$ $TCID_{50}$ of influenza virus, RT-PCR assay, and viral resistance assays. Samples were collected at Screening/Baseline and at the following time points after initiation of study drug on Day 1: 12, 24, 36, 48, 60, 72, 84, 96, and 108 hours and again at the Day 10 follow-up visit. In any subject who was intubated or who required a clinically indicated bronchoscopy, additional virology specimens were collected from the lower respiratory tract via an appropriate method such as endotracheal aspiration or bronchoalveolar lavage, at the same times specified above for the nasopharyngeal specimens.

Virology laboratory tests included phenotypic characterizations of influenza virus recovered (hemagglutinin and neuraminidase) and viral susceptibility to peramivir, oseltamivir, and zanamivir, and genotypic analysis of primary virus isolates.

Serum samples were collected at Screening (acute sample) and Day 14 (convalescent sample) for purposes of determining antibody titers against influenza A or B. These data were used to confirm the presence of influenza.

Safety:

Safety was evaluated through assessments of adverse events (AEs), laboratory analyses (clinical chemistry, hematology, and urinalysis), vital signs, electrocardiograms (ECGs), physical examinations, and pregnancy outcome and infant health and development in the first 12 months in pregnant women who received blinded study drug.

Adverse events were assessed and recorded at least once daily during the period of study drug administration in the hospital, during any period while the subject remained hospitalized after interruption of study drug (if applicable), and at each follow-up visit until the study completion visit at Day 14 or later. Adverse events were graded through use of the Division of Acquired Immune Deficiency Syndrome Tables for Grading Adult and Pediatric Adverse Experiences. Any Grade 3 and Grade 4 clinical AEs or laboratory abnormalities that were judged to be possibly, probably, or definitely related to blinded study treatment were promptly (within 72 hours) reported to the study medical monitor. Influenza-related complications were not considered AEs unless they met the criteria for serious adverse events (SAEs).

Clinical chemistry profiles included a chemistry 20 panel (includes sodium, potassium, chloride, total CO_2 [bicarbonate], creatinine, glucose, urea nitrogen, albumin, total calcium, total magnesium, phosphorus, alkaline phosphatase, ALT, AST, total bilirubin, direct bilirubin, lactate dehydrogenase [LDH], total protein, total creatine kinase, and uric acid).

Blood samples and urine samples were collected at Screening/Baseline, at Day 3, at hospital discharge (if other than Day 5), at Day 5, Day 10, Day 14 or at the Early Termination Visit, and at Day 28 if required, for analysis by a central laboratory. If the Day 3 or hospital discharge clinical chemistry laboratory result for any analyte was abnormal and/or unexplained, repeat testing was obtained at periodic intervals as deemed appropriate by the Investigator. Hematology profiles included complete

blood count with differential. Routine urinalysis evaluations included dipstick evaluations for protein, glucose, ketones, hemoglobin, and specific gravity.

Females of childbearing potential were evaluated for pregnancy at Screening/Baseline using a urine or serum pregnancy test performed locally. At Day 14 and, if required, at Day 28, a serum pregnancy test was performed via the study central laboratory, unless the subject was pregnant when enrolled. In order to obtain more information on the outcomes of pregnancies and infants exposed to blinded study drug in utero, there was enhanced data collection for pregnant women enrolled in this trial. Pregnant women enrolling in the trial were asked to give consent for this enhanced data collection, which was provided by their obstetrical provider and the infant's pediatric provider.

Vital signs (blood pressure, heart rate, respiration rate) were measured once at Screening/Baseline, 3 times per day approximately 8 hours apart during the inpatient treatment period, once at hospital discharge, and once during the follow-up visits. If a subject was discharged prior to completion of study treatment (either 5 days or 10 days if treatment for more than 5 days is required), vital signs were recorded on each day that the subject returned for study treatment on an out-patient basis.

A 12-lead ECG was obtained from all subjects at Screening/Baseline. The Principal Investigator was responsible for interpretation of the Screening ECG. If the ECG was interpreted as being abnormal, and, in the opinion of the Investigator, would have placed the subject at an unreasonably increased risk through participation in this study, the subject was not enrolled.

The Investigator performed a physical examination at Screening/Baseline, at Day 5 or at hospital discharge (if prior to Day 5), at Day 10 and at Day 14 or at completion of the study follow-up, whichever occurred later. As part of scheduled physical examinations and as deemed medically necessary at other times, study personnel were provided with an influenza-related complications checklist to evaluate the subject for the presence of clinical signs and/or symptoms of the following influenza-related complications: sinusitis, otitis, bronchitis, and pneumonia. Signs and symptoms referable to influenza-related complication signs and/or symptoms were not reported as adverse events unless they met criteria for an SAE.

Statistical methods:

A SAP describing all analyses performed for this study was written and approved prior to unblinded review of any data.

Data from a previous Phase 2 study of multiple-day treatment with IV peramivir in subjects hospitalized with influenza (BCX1812-201) showed a median time to clinical resolution of 24.3 hours (21.2, 47.5) for subjects who met the inclusion criteria and intent to treat infected (ITTI) definition proposed for this trial and were treated with 400 mg peramivir; the median time to clinical resolution for subjects randomized to receive oseltamivir was 35.5 hours (23.3, 37.9). Based on this difference of 11.2 hours and the increased dose of peramivir in this study, it was anticipated that the improvement in the time to clinical resolution for subjects treated with peramivir + SOC that does not contain an NAI compared to placebo + SOC that does not contain an NAI would be at least 18 hours. Using this assumption and the observed time to clinical resolution from study BCX1812-201, a hazard ratio (HR) of 0.57 was expected.

Using a log-rank statistic and a significance level of $\alpha = 0.049$, a sample size of 106 subjects in the peramivir + SOC treatment arm who did not receive an additional NAI and 53 subjects in the placebo + SOC treatment arm who did not receive an additional NAI was sufficient to detect an HR of 0.57 with a power of 90% (SAS v9.1.3). As the sample size required was dependent on the HR, an interim analysis was planned to reassess the sample size based on observed data. Up to 600 subjects in total were permitted to be enrolled into the study in order to enroll a maximum of 320 subjects with confirmed influenza who had not received an NAI as part of their SOC regimen.

The populations for analysis included the Safety, Intent-to-Treat (ITT), ITTI, ITTI-Non-NAI-Containing SOC (ITTI-Non-NAI), and Exposure-Response populations.

The Safety population included all randomized subjects who received at least one dose/infusion of study treatment. Subjects who received therapy other than that intended were analyzed according to the therapy received. The Safety population was the primary population for all analyses of safety data.

The ITT population included all randomized subjects. Subjects were analyzed in the treatment group to which they were randomized. The ITT population was the primary population for analyses of demography and subject accountability.

The ITTI population included all subjects who were randomized, received at least one dose/infusion of study drug, and had confirmed influenza by primary viral culture, PCR, or paired acute and convalescent serology specimens demonstrating at least a 4-fold increase in antibody titer against influenza A or B. Subjects who met the above criteria but had significant Good Clinical Practice inconsistencies that could call into question the validity of their efficacy data were not included in the ITTI population.

Subjects were analyzed according to the treatment randomized. If a discrepancy was noted in the final database for any subject, such that the drug differed from the randomized treatment assignment, efficacy analyses were repeated with the subjects analyzed according to the treatment received. The ITTI population was used for secondary analyses of efficacy.

The ITTI-Non-NAI population included all ITTI subjects who received a SOC that did not contain an NAI at randomization. Subjects were analyzed according to the treatment randomized. If a discrepancy was noted in the final database for any subject, such that the drug differed from the randomized treatment assignment, efficacy analyses were repeated with the subjects analyzed according to the treatment received. The ITTI-Non-NAI population was used for primary analyses of efficacy.

The Exposure-Response population included all subjects in the ITTI population who had a quantifiable plasma concentration of peramivir and at least one postbaseline efficacy assessment. This population was used for all exposure-response analyses.

To control for any potential inflation of type I error that was incurred from the interim analysis, an administrative penalty of 0.001 was applied to the final analysis of the primary efficacy endpoint (eg, the final primary efficacy analysis was conducted at $\alpha = 0.049$ to ensure that the overall type I error rate was 0.05).

The ITTI-Non-NAI population was used for primary analyses of efficacy. The ITTI-Non-NAI population included all ITTI subjects who received an SOC that did not contain an NAI at randomization. Subjects were analyzed according to the treatment randomized. If a discrepancy was noted in the final database for any subject, such that the drug differed from the randomized treatment assignment, efficacy analyses were repeated with the subjects analyzed according to the treatment received.

The primary efficacy endpoint and selected secondary endpoints were summarized separately by SOC regimen (NAI-containing or non-NAI-containing), duration of illness at randomization, age (adults versus adolescents and children), gender, ICU admission, influenza season, need for supplemental oxygen at baseline, viral subtype (influenza A or B, influenza A seasonal H1, seasonal H3, or 2009 H1N1, and influenza A H1) at Screening using descriptive statistics by treatment group and study day, where appropriate. Statistical testing of treatment differences within subgroups was performed.

SUMMARY – CONCLUSIONS

EFFICACY RESULTS:

The primary efficacy endpoint for this study was the time to clinical resolution. For this endpoint, no significant differences were seen between treatment groups for the ITTI-Non-NAI population; similar results were seen for the ITTI population. The overall time to clinical resolution was strongly correlated with time to resolution of fever. In addition, no significant differences were seen for the secondary and tertiary endpoints for either the ITTI-Non-NAI population or the ITTI population. In a post hoc analysis, a multiple regression statistical model identified the Baseline characteristics of

region (Eastern Europe vs India; US/Canada vs India), duration of illness, gender, oxygen saturation < 94%, and history of congestive heart failure or angina to be significant predictors of time to clinical resolution. Among subjects who participated in full PK sampling, the PK findings were generally consistent with prior studies, with a geometric mean C_{max} of 30,798 ng/L, a geometric mean $AUC_{0\text{-last}}$ of 83,729 ng•hr/mL, and a geometric mean $T_{1/2}$ of 18.5 hours.

SAFETY RESULTS:

Intravenous peramivir at 600 mg QD was generally safe and well tolerated in this population of hospitalized subjects. No clinically relevant differences in safety outcomes were noted between the placebo and peramivir treatment groups.

By design, this study enrolled subjects who were hospitalized with influenza. Adverse events reported by these subjects were consistent with those expected for a hospitalized influenza population. Overall, the incidence of AEs, drug-related AEs, serious AEs, and deaths was similar between the placebo and peramivir treatment groups. Very few subjects discontinued the study due to AEs. No preferred term was reported by more than 5% of subjects who received peramivir. The incidence of laboratory toxicities was similar between treatment groups. No safety signals were identified in this study.

Four subjects died during the study: 3 subjects who received placebo and 1 subject who received peramivir. The preferred terms that were experienced as SAEs were consistent with serious complications of influenza; no single preferred term was reported as an SAE by more than 2 subjects in either treatment group.

CONCLUSION:

This study failed to demonstrate a significant difference between treatment with placebo + SOC and treatment with peramivir (600 mg IV, QD for 5 or 10 days) + SOC for the primary endpoint of time to clinical resolution. In this population of subjects hospitalized with influenza, peramivir 600 mg QD was generally safe and well tolerated.

Date of the report:

11 OCT 2013