

Case Study

Treating Acute Uncomplicated Influenza with a Novel, One-Dose Intravenous Neuraminidase Inhibitor

THE CHALLENGE:

During the influenza season, which typically peaks in the winter months, doctors' offices and emergency rooms see a great influx in patients presenting with influenza-like illness. Typically, the only available treatment option is to prescribe a multi-dose antiviral neuraminidase inhibitor which can alleviate the symptoms of influenza (headache, myalgias, fever, fatigue, cough, sore throat, and nasal congestion), on average, about a day sooner than standard of care. Many people are able to quickly recuperate from influenza; however, some segments of the population are at a higher risk of developing serious complications from the flu, leading to significant morbidity, hospitalizations, and even death.

THE CASE:

A 62-year-old male smoker with chronic bronchitis who was doing well prior to “catching a virus” presents with 12-hour history of fever, myalgia, sore throat, cough, and nausea. He states that he was feeling well the day before, but upon awakening that morning he “felt hot, had a cough, was nauseated and felt like every single muscle in his body was achy”. He called his doctor's office but they were closed and the answering service advised him to go directly to the emergency department of his local hospital. Upon presentation to the emergency department, the patient denied any chest pain, dizziness or shortness of breath and reported that he had not been vaccinated this year for the flu. He states that he had the flu a couple years ago and was given an oral medication but admits he started feeling better a couple days after getting the prescription and did not complete the treatment course. Patient's COPD is controlled with medication, and he does not require supplementary oxygen. His exam was notable for high fever and muscle aches and his chest X-ray was consistent with chronic COPD but showed no evidence of pneumonia.

Important Safety Information

Rapivab™ (peramivir injection) is indicated for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than 2 days.

- Efficacy of Rapivab was based on clinical trials in which the predominant influenza virus type was influenza A; a limited number of subjects infected with influenza B virus were enrolled.
- Influenza viruses change over time. Emergence of resistance substitutions could decrease drug effectiveness. Other factors (for example, changes in viral virulence) might also diminish clinical benefit of antiviral drugs. Prescribers should consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use Rapivab.
- Efficacy could not be established in patients with serious influenza requiring hospitalization.

Rapivab[™]
peramivir injection

THE RESULTS:

Patient was treated with one dose of Rapivab™ (peramivir injection), the complete treatment course for uncomplicated flu; this was deemed preferable due to his nausea and previous inability to comply with a multi-day oral antiviral regimen. The patient was also given IV hydration since he was not eating or drinking. The patient was then observed for the next ten hours and began to feel better, with diminished fever, and improvement in fatigue. His vital signs were stable, po intake was initiated, and he was able to ambulate. He was discharged from the emergency department's observation unit with instructions to call his outpatient physician should symptoms not resolve completely over the next few days.

THE CONCLUSION:

The CDC and IDSA recommend that among outpatients presenting with influenza-like illness during flu season, early (within the first 48 hours of onset of symptoms) antiviral treatment with a neuraminidase inhibitor is recommended for all persons who are at higher risk for influenza complications because of age or underlying medical conditions. Some selected high risk conditions include:

- persons with chronic pulmonary (including asthma), cardiovascular (except hypertension alone), renal, hepatic, hematological (including sickle cell disease), metabolic disorders (including diabetes mellitus) or neurologic and neurodevelopment conditions (including disorders of the brain, spinal cord, peripheral nerve, and muscle such as cerebral palsy, epilepsy [seizure disorders], stroke, intellectual disability [mental retardation], moderate to severe developmental delay, muscular dystrophy, or spinal cord injury);
- adults aged 65 years and older;
- persons with immunosuppression, including that caused by medications or by HIV infection;
- American Indians/Alaska Natives;
- persons who are morbidly obese (ie, BMI is 40 or greater); and
- residents of nursing homes and other chronic-care facilities.

Important Safety Information

Contraindications

None

Warnings and Precautions

- Rare cases of serious skin reactions, including Stevens-Johnson syndrome and erythema multiforme have occurred with Rapivab. Appropriate treatment should be instituted if a serious skin reaction occurs or is suspected.
- Patients with influenza may be at an increased risk of hallucinations, delirium and abnormal behavior early in their illness. There have been post-marketing reports (from Japan) of delirium and abnormal behavior leading to injury in patients with influenza who were receiving neuraminidase inhibitors, including Rapivab. Because these events were reported voluntarily during clinical practice, estimates of frequency cannot be made, but they appear to be uncommon. These events were reported primarily among pediatric patients. The contribution of RAPIVAB to these events has not been established. Patients with influenza should be closely monitored for signs of abnormal behavior.
- Serious bacterial infections may begin with influenza-like symptoms or may coexist with or occur as complications during the course of influenza. Rapivab has not been shown to prevent such complications.

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peramivir injection

Neuraminidase inhibitors are the most effective treatment for acute uncomplicated influenza when given within 48 hours of onset of symptoms. Rapivab™, specifically, has been clinically shown to reduce the total time to alleviation of symptoms of influenza by a median of 21.5 hours sooner and resolution of fever a median of 12 hours sooner when compared to placebo. Also, the safety profile of RAPIVAB is comparable to placebo. The single dose, intravenous delivery of Rapivab makes it optimal for patients presenting to the emergency room with symptoms precluding them from taking oral antiviral therapy or for patients requiring IV hydration. Additionally, a high percentage of patients do not adhere to oral, multi-day neuraminidase inhibitor treatment making a one dose option like Rapivab™ the most fitting choice.

Important Safety Information

Adverse Reactions

The most common adverse reaction was diarrhea (8% Rapivab vs 7% placebo). Lab abnormalities (incidence $\geq 2\%$) occurring more commonly with Rapivab than placebo were elevated ALT 2.5 times the upper limit of normal (3% vs 2%), elevated serum glucose greater than 160 mg/dL (5% vs 3%), elevated CPK at least 6 times the upper limit of normal (4% vs 2%) and neutrophils less than $1.0 \times 10^9/L$ (8% vs 6%).

Concurrent use with Live Attenuated Influenza Vaccine

Antiviral drugs may inhibit viral replication of a live attenuated influenza vaccine (LAIV). The concurrent use of Rapivab with LAIV intranasal has not been evaluated. Because of the potential for interference between these two products, avoid use of LAIV within 2 weeks before or 48 hours after administration of Rapivab unless medically indicated.

Please see full prescribing information for Rapivab.

You are encouraged to report negative side effects of prescription drugs to the FDA.

Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Rapivab™
peramivir injection

The first-and-only ONE-DOSE IV TREATMENT FOR INFLUENZA



It's About Time

- An IV neuraminidase inhibitor that exhibits broad activity against influenza A and B viruses
- Effective in patients 18 years and older who have been symptomatic for less than 48 hours
- Provides a full course of treatment in one 15-30 minute infusion



RAPIVAB™ (peramivir injection), for intravenous use
Initial U.S. Approval: 2014

BRIEF SUMMARY OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use RAPIVAB safely and effectively. See full prescribing information for RAPIVAB.

INDICATIONS AND USAGE

RAPIVAB is an influenza virus neuraminidase inhibitor indicated for the treatment of acute uncomplicated influenza in patients 18 years and older who have been symptomatic for no more than two days.

Limitations of Use:

- Efficacy based on clinical trials in which the predominant influenza virus type was influenza A; a limited number of subjects infected with influenza B virus were enrolled.
- Consider available information on influenza drug susceptibility patterns and treatment effects when deciding whether to use.
- Efficacy could not be established in patients with serious influenza requiring hospitalization.

DOSAGE AND ADMINISTRATION

- Administer as a single dose within 2 days of onset of influenza symptoms.
- Recommended dose is 600 mg, administered by intravenous infusion for a minimum of 15 minutes.
- Renal Impairment: Recommended dose for patients with creatinine clearance 30-49 mL/min is 200 mg and the recommended dose for patients with creatinine clearance 10-29 mL/min is 100 mg.
- Hemodialysis: Administer after dialysis.
- RAPIVAB must be diluted prior to administration.
- See the Full Prescribing Information for drug compatibility information.

DOSAGE FORMS AND STRENGTHS

Injection: 200 mg in 20 mL (10 mg/mL) in a single-use vial.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

- Serious skin/hypersensitivity reactions such as Stevens-Johnson syndrome and erythema multiforme have occurred with RAPIVAB.
- Neuropsychiatric events: Patients with influenza may be at an increased risk of hallucinations, delirium and abnormal behavior early in their illness. Monitor for signs of abnormal behavior.

ADVERSE REACTIONS

Most common adverse reaction (incidence >2%) is diarrhea.

To report SUSPECTED ADVERSE REACTIONS, contact BioCryst Pharmaceuticals, Inc. at 1-844-273-2327 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

DRUG INTERACTIONS

Live attenuated influenza vaccine (LAIV), intranasal: Avoid use of LAIV within 2 weeks before or 48 hours after administration of RAPIVAB, unless medically indicated.

USE IN SPECIFIC POPULATIONS

- Pregnancy: Use if benefit outweighs risk.
- Nursing mothers: Caution should be exercised when administered to a nursing woman.

Based on December 2014 Version

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