Case study: Focus on compliance with therapy

One-dose intravenous neuraminidase inhibitor in patients who are nonadherent to a multiday treatment course

THE CHALLENGE:

During the influenza season, which usually peaks between the months of December and March, doctors' offices and emergency departments (EDs) see a great influx in patients presenting with influenza-like illness. Although previously healthy individuals often recuperate from influenza within 5 to 8 days without treatment, some are at a higher risk of serious complications from the flu, which may lead to significant morbidity, hospitalizations, and even death. A common treatment option is a multidose antiviral neuraminidase inhibitor that may alleviate the symptoms of influenza, on average, about a day sooner than standard of care.

Problems with multidose antiviral neuraminidase inhibitor treatments arise when patients have difficulty complying with a multiday treatment regimen. Patients who have difficulty with adherence and those vulnerable patients at higher risk of complications from the flu (e.g., people 65 years and older) may benefit from an alternative treatment option like Rapivab® (peramivir injection). Rapivab provides a complete antiviral course of influenza therapy in a one-dose infusion, providing assurance to the physician that the patient is appropriately treated.

THE CASE:

A 68-year-old male smoker with chronic bronchitis, who was well prior to "catching a virus," presented with a 12-hour history of fever, myalgia, sore throat, cough, and nausea. He stated that he "felt hot, had a cough, was nauseated, and like every single muscle in his body was achy" upon awakening that morning. He called his doctor's office but it was closed, and the answering service advised him to go directly to the ED of his local hospital.

Upon presentation to the ED, he denied any chest pain, dizziness, or shortness of breath and reported that he had not been vaccinated this year for the flu. He said that he had the flu a couple years ago and was given an oral medication but admitted to 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 examination was notable for high fever and muscle aches, and his chest x-ray was consistent with COPD but showed no evidence of pneumonia.

THE RESULTS:

Patient was treated with one dose of Rapivab, a complete antiviral treatment course for uncomplicated flu, which was deemed preferable due to his nausea and previous inability to comply with a multiday oral antiviral regimen. The patient was observed for the next 10 hours. His vital signs were stable and he was able to ambulate. He was discharged from the ED's observation unit with instructions to call his outpatient physician should symptoms not resolve completely over the next few days.

THE CONCLUSION:

Nonadherence with medication is a multidimensional health care problem. While the most common form of noncompliance is patients simply forgetting to take a prescribed medicine, almost one-third of patients stop taking their medicine earlier than instructed. Overall, nearly 75% of adults are nonadherent in one or more ways.

Some patients have difficulty complying with the 5-day treatment regimen required by oral and inhaled influenza treatments. In a study, it was estimated that up to 55% of patients were noncompliant when prescribed oral antiviral influenza medication. Several patient-related issues that lead to medication nonadherence include the following:

- Psychological problems
- Cognitive impairment
- Medication side effects
- Inadequate follow up or discharge planning
- Lack of belief in benefit of treatment

Medication adherence becomes particularly challenging in older adults as their cognitive abilities decline. Older patients tend to have more chronic conditions and therefore receive a greater number of prescription medications. Also, older adults have a higher prevalence of physical impairments that may affect medication adherence.

For patients with acute uncomplicated influenza who may be noncompliant or have difficulty with medication adherence, treatment with one-dose peramivir helps ensure that patients receive a full course of antiviral influenza therapy.

Neuraminidase inhibitors are most effective for the treatment of acute uncomplicated influenza when administered within 48 hours of onset of influenza-like illness 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 and resolution of fever a median of 12 hours when compared with placebo.

Rapivab has a demonstrated safety profile. The single-dose intravenous (IV) delivery of Rapivab makes it optimal for patients presenting with symptoms precluding them from taking oral antiviral therapy or for patients requiring IV hydration. Additionally, for patients who do not adhere well to a multiday oral treatment regimen, a one-dose IV option like Rapivab may be the most fitting choice.

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.

Contraindications

Rapivab is contraindicated in patients with known serious hypersensitivity or anaphylaxis to peramivir or any component of the product. Severe allergic reactions have included anaphylaxis, erythema multiforme, and Stevens-Johnson syndrome.

Warnings and Precautions

- Rare cases of serious skin reactions, including erythema multiforme, have been reported with Rapivab in clinical studies and in postmarketing experience. Cases of anaphylaxis and Stevens-Johnson syndrome have been reported in postmarketing experience with Rapivab. Discontinue Rapivab and institute appropriate treatment if anaphylaxis or a serious skin reaction occurs or is suspected. The use of Rapivab is contraindicated in patients with known serious hypersensitivity or anaphylaxis to Rapivab.
- Patients with influenza may be at an increased risk of hallucinations, delirium, and abnormal behavior early in their illness. There have been postmarketing 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.

Adverse Reactions

The most common adverse reaction was diarrhea (8% Rapivab vs 7% placebo).

Lab abnormalities (incidence ≥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 >160 mg/dL (5% vs 3%), elevated CPK at least 6 times the upper limit of normal (4% vs 2%), and neutrophils $<1.0 \times 10^9$/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 Rapivab within 2 weeks after or 48 hours before administration of LAIV unless medically indicated.

Please see accompanying 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.

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Rapivab® peramivir injection