FDA Approves Prasugrel as Antiplatelet Agent

BY ELIZABETH MECHCATIE

Last month, the Food and Drug Administration approved the antiplatelet agent prasugrel to reduce the risk of clotting during percutaneous coronary intervention, with labeling that includes a boxed warning about the potential for significant and sometimes fatal bleeding associated with the drug.

Specifically, prasugrel, a thienopyridine, was approved for reducing thrombotic cardiovascular events, including stent thrombosis, in the following patients with acute coronary syndrome who will be managed with percutaneous coronary intervention (PCI): those with unstable angina or non-ST elevation myocardial infarction (NSTEMI) and those with ST-elevation MI (STEMI), when managed with either primary or delayed PCI.

In the pivotal phase III TRITON-TIMI 38 trial of 13,608 patients with a threatened or actual myocardial infarction who were about to undergo angioplasty, prasugrel (Effient) was more effective than clopidogrel (Plavix) at reducing subsequent nonfatal myocardial infarction (9.1% vs. 7%). Patients with a history of stroke were more likely to have a repeat stroke on prasugrel, however. There was also a greater risk of significant bleeding events with prasugrel.

Because of that higher risk, prasugrel's labeling includes a boxed warning about the bleeding, which advises against using the drug in patients with active pathological bleeding, a history of transient ischemic attacks or stroke, or urgent need for surgery, including coronary artery bypass graft surgery.

"Effient offers physicians an alternative treatment for preventing dangerous blood clots from forming and causing a heart attack or stroke during or after an angioplasty procedure," Dr. John Jenkins, director of the Office of New Drugs at the FDA's Center for Drug Evaluation and Research, said in a statement. "Physicians must carefully weigh the potential benefits and risks of Effient as they decide which patients should receive the drug."

Prasugrel offers 'an alternative treatment for preventing dangerous blood clots from forming and causing a heart attack or stroke during or after an angioplasty procedure.'

In February 2009, the FDA's Cardiovascular and Renal Drugs Advisory Committee voted unanimously that the drug's benefits outweighed its risk and backed prasugrel's approval. The drug was developed by Eli Lilly & Co. and Daiichi Sankyo Inc., and is available in 5-mg and 10-mg tablets. Treatment is started with a 60-mg single oral loading dose, followed by 10 mg once daily. The label says that 5 mg per day should be considered for patients who weigh less than 60 kg and advises that patients should also take 75-325 mg of aspirin a day.

Because of the large number of patients now receiving stents, "achieving a consistent and effective level of platelet inhibition is paramount to preventing stent thrombosis and myocardial ischemic events," Dr. Curtiss Stinis, an interventional cardiologist at Scripps Clinic and Research Foundation, La Jolla, Calif., said in an interview. Noting that the effectiveness of clopidogrel can vary widely across individual patients, and that some patients do not have an adequate response to clopidogrel, despite increasing the dose, he said that for such patients, "prasugrel offers an alternative." Dr. Stinis is director of peripheral interventions in the division of cardiovascular diseases at the Scripps Foundation.

In his own practice, Dr. Stinis said he expects that prasugrel will "definitely be useful" in patients who had had an inadequate response to clopidogrel by blood test assay, or who have already had an episode of stent thrombosis. He added, however, that it was likely that he would still routinely prescribe clopidogrel to patients who have an adequate response to that drug, and to elderly patients or patients with a previous stroke who are likely at a higher risk of bleeding with prasugrel.

Dr. Stinis said that he has been a speaker for Eli Lilly in the past. ■

Alicia Ault contributed to this report.

Data Support Aggressive A-Fib Protocol

BY BRUCE JANCIN

NEW ORLEANS — Treatment of acute-onset atrial fibrillation or flutter using the Ottawa Aggressive Protocol for rapid emergency department rhythm control yielded a 91% conversion rate in a large consecutive patient series.

"To extrapolate, widespread use of the Ottawa Protocol could lead to a significant decrease in hospital admissions for acute atrial fibrillation or atrial flutter where that's the local practice, and otherwise to rapid disposition of patients who can quickly resume normal activities of daily life," Dr. Ian G. Stiell said at the annual meeting of the Society for Academic Emergency Medicine.

'Use of the Ottawa Protocol could lead to a significant decrease in hospital admissions.'

DR. STIELL

He presented a retrospective study of 385 consecutive patients who were managed in two Ontario EDs according to the Ottawa Aggressive Protocol (OAP). Fully 91.4% were discharged home in sinus rhythm after a median ED stay of 5.6 hours, with instructions to see a cardiologist within the next month.

During the next 30 days, 30% of patients had a recurrence of their atrial arrhythmia. Half were successfully cardioverted. A total of 16% of patients were admitted to the hospital. No cerebrovascular accidents or cardioversion-related adverse events occurred, according to Dr. Stiell of the University of Ottawa.

The OAP for ED management of acute atrial fibrillation or flutter was developed several years ago in response to a prevailing lack of consensus on the optimal way to manage these common arrhythmias in the ED.

The OAP entails an initial attempt at pharmacologic conversion using intravenous procainamide infused at 1 g over 1 hour. If the patient has a history of previous lack of efficacy for intravenous procainamide, an alternative intravenous antiarrhythmic agent may be used before moving on to electrical cardioversion in the ED. Patients with a history of multiple unsuccessful prior attempts at pharmacologic cardioversion using all available intravenous rhythm-control drugs proceed straight to electrical cardioversion.

Pharmacologic conversion was attempted in 65% of patients in this series, with a success rate of 42% in patients with acute atrial fibrillation and 27% for those with atrial flutter. Procainamide had a 43% success rate in converting patients to sinus rhythm, vernakalant had a 70% success rate, and amiodarone had a 9.5% success rate. Vernakalant's marketing application is now under review by the Food and Drug Administration.

Electrical cardioversion was attempted in 68% of patients, with a 90.3% success rate. Typically, one emergency physician oversaw the electrical cardioversion while another or a senior resident managed the sedation, consisting of a small dose of fentanyl followed by bolus propofol.

"We usually start at a pretty high energy level of 150 J biphasic. Our cardiologists tend to favor starting high and just doing it once," Dr. Stiell explained.

Under the OAP, patients are not anticoagulated prior to attempted electrical cardioversion. "Our standard is to focus on the time of onset. If it's clearly less than 48 hours, then we're comfortable in cardioverting without giving heparin, aspirin, or warfarin," Dr. Stiell said. "If the patients are converted, they'll typically go home without warfarin. They'd be encouraged to have follow-up with cardiology."

On the other hand, if the time since arrhythmia onset is unclear or is greater than 48 hours, emergency physicians won't proceed with electrical cardioversion unless they have access to a reassuring transesophageal echocardiogram.

In this series, mean duration of symptoms prior to presenting to the ED was just 4 hours, he added.

Some investigators assert that having a rate-control drug on board enhances the success rate of attempted electrical cardioversion. That wasn't the case in this study, according to Dr. Stiell: 47% of patients received intravenous rate-control drugs prior to attempting cardioversion, but they proved to have no effect on the direct-current cardioversion success rate. ■

Discharge Error Rate for Chest Pain: 1%-2% Seen as OK

NEW ORLEANS — What constitutes an acceptable rate of erroneous discharge of patients who present to the emergency department with chest pain?

Somewhere between 1% and 5%, according to a survey of experienced emergency physicians at two prestigious Boston academic medical centers. A narrow majority of responding physicians drew the boundary of acceptability more tightly at 1%-2%, Dr. John Nagurney reported at the annual meeting of the Society for Academic Emergency Medicine.

Whether to admit or discharge a patient who presents to the ED complaining of chest pain is a common dilemma. It has been estimated that up to 80% of patients with chest pain who are admitted to rule out acute coronary syndrome turn out not to have ACS. On the flip side, 2%-4% of ED patients with ACS are misidentified and erroneously discharged.

A figure of 1% has begun appearing in the literature as an "acceptable" erroneous discharge rate, but without any supporting evidence to show that physicians on the front lines actually agree it's a reasonable number, Dr. Nagurney said. To clarify the situation, he and his coinvestigators interviewed 31 emergency medicine faculty or fellows at two Harvard University–affiliated hospitals. Many were reinterviewed a few weeks later; if their answers were discordant, the results were averaged.

Sixteen physicians (52%) said that a 1%-2% erroneous discharge rate is acceptable. Another 8 (26%) indicated they considered an acceptable error rate to be 1%-5%, according to Dr. Nagurney, an internist at Massachusetts General Hospital, Boston.

—Bruce Jancin