



Hospitalist News

www.ehospitalistnews.com

THE LEADER
IN NEWS
AND
MEETING
COVERAGE

VOL. 2, No. 4

The Leading Independent Newspaper for the Hospitalist

APRIL 2009



COURTESY DR. DAVID C. HESS

The new paradigm for rural stroke care “is drip and ship,” said Dr. David C. Hess (yellow tie), with members of the network.

Telemedicine Consult Aids Stroke Patients

BY DOUG BRUNK

SAN DIEGO — Physicians in rural Georgia are achieving the optimal window for administration of tissue plasminogen activator to stroke patients, thanks to a telemedicine network spearheaded by the Medical College of Georgia, Augusta.

Called the Georgia REACH Telestroke Network, it involves the use of phone consultations, videoconferencing, remote review of images, and other elements of telemedicine delivered by a neurologist to clinicians in rural hospitals who don't have a neurologist on staff or on call when a stroke patient presents to the emergency department.

“The idea is that you're getting TPA use out to community hospitals or to sites where it would not be normally administered because there is a lack of expertise,” Dr. David C. Hess said at the International Stroke Conference.

According to the American Hospital Association, there were 2,003 rural hospitals in the United States in 2006. Of these, about half have fewer than 100 beds and most likely are not equipped to administer TPA to stroke patients, said Dr. Hess, professor and chairman of the department of neurology at the Medical College of Georgia. “They are neurologically underserved. This doesn't just happen at rural or suburban hospitals. Some of our urban hospitals in the United States don't give TPA and are outside the loop of up-to-date, quality stroke care. We can extend our expertise by using telemedicine.”

Other trends in the medical field are complicating efforts to provide optimal stroke care. Many emergency department physicians are reluctant to use TPA without the presence or guidance of a neurologist. And “many neurologists are abandoning emergency department call altogether,” Dr. Hess said.

A drop in the number of doctors choosing careers in vascular neurology isn't helping. According to the Accreditation Council for Graduate Medical Education, the number of residents in vascular neurology fell from 100 in 2000 to 60 in 2007.

See **Telemedicine** page 11

INSIDE

Postop Consults

Screening system flags high complication risk before patients undergo surgery.

PAGE 4



Mandatory Vaccination

Immunizing all staff against influenza can help protect patients.

PAGE 8

Comparing Quality

Expanded data expected to make online hospital ratings ‘harder to ignore.’

PAGE 12



Watching Hand Washing

Wireless badges can track hand-hygiene compliance.

PAGE 10

Statin Before PCI Established as Standard of Care

Evidence for extra doses is preliminary.

BY MITCHEL L. ZOLER

ORLANDO — Ensuring that patients have a statin on board when they arrive at the coronary catheterization laboratory for an interventional procedure is now the standard of care, based on results from a fourth report documenting the safety and efficacy of early initiation of statin treatment in patients not already on a statin.

The major lingering question is the optimal statin dosage. Findings from another study reported at the annual meeting of the American College of Cardiology showed that loading a patient already on a daily statin

regimen with two extra doses of atorvastatin during the 12 hours preceding a percutaneous coronary intervention (PCI) worked better than relying on the patient's background statin level, especially in patients with acute coronary syndrome (ACS). But this first test of such a reloading strategy was limited to about 350 patients, and the results were judged too preliminary to immediately change practice, said Dr. Germano Di Sciacio, professor of cardiology at the Bio-Medico University in Rome and lead investigator on the statin redosing study.

Those findings “add to a body of evidence that a statin regimen is already on a daily statin

See **Statin** page 2

FDA Panel Backs Approval Of Oral Anticoagulant

BY ELIZABETH MEHCATIE

ADELPHI, MD. — A federal panel agreed that data on the oral anticoagulant rivaroxaban indicate that the drug's benefits in preventing venous thromboembolic events after hip and knee replacement surgery outweigh its potential risks of excess bleeding and potential risk of severe hepatotoxicity.

The Food and Drug Administration's Cardiovascular and Renal Drugs Advisory Committee voted 15-2 that data from four

clinical trials showed that rivaroxaban has a favorable risk-benefit profile for the proposed indication—prophylaxis of venous thromboembolism (VTE) in patients undergoing hip or knee replacement surgery. The recommended dosage schedule is 10 mg once daily, for 35 days after hip surgery or 14 days after knee replacement.

Most panelists agreed that potential hepatotoxicity should not preclude approval, although long-term data on hepatotoxicity are critically needed. Panelists, however, voted 15-2 that data from four

See **Anticoagulant** page 3

Medical
News Net

Want Daily Medical
News and Commentary?

Follow us on **Twitter**
Twitter.com/MedicalNewsNet

Printed Standard
U.S. Postage
PAID
Permit No. 384
Lebanon, Ky.

HOSPITALIST NEWS
60 Columbia Rd., Bldg. B, 2nd Fl.
Morristown, NJ 07960
CHANGE SERVICE REQUESTED

Rivaroxaban Assessed

Anticoagulant from page 1

who were concerned about off-label use of the drug, emphasized the importance of advising clinicians to avoid prescribing the drug for longer periods and for other uses, and of continuing to follow patients on rivaroxaban in clinical trials and clinical practice for hepatotoxicity.

If approved, rivaroxaban, an oral, direct Factor Xa inhibitor made by Johnson & Johnson Pharmaceutical Research & Development LLC, would be marketed as Xarelto. It would be the first oral anticoagulant approved for these indications, as well as the first oral anticoagulant approved since warfarin. The drug works by inhibiting direct Factor Xa, which lowers thrombin production and prolongs prothrombin time. The FDA usually follows the recommendations of its advisory panels.

The proposed regimen was compared with enoxaparin in four international studies of more than 12,000 patients (6,183 patients on rivaroxaban) after total hip or knee replacement surgery. Patients with significant liver disease were excluded. The composite end point of venographic evidence of deep vein thrombosis (DVT), nonfatal pulmonary embolus (PE), or death was significantly lower in those treated with rivaroxaban, but patients on the drug had a higher rate of bleeding. The major bleeding rate was 0.4% in those on rivaroxaban and 0.2% in those on enoxaparin. The one bleeding-related death in the studies was in a patient on rivaroxaban.

Serious ALT elevations were more common with rivaroxaban (0.3% vs. 0.2%), as was a composite marker of liver injury (an ALT greater than three times the upper limit of normal with a total bilirubin greater than two times the upper limit of normal, in 0.15% vs. 0.11%), but these were not significant differences.

The consumer representative on the panel was Dr. Sidney Wolfe, director of the Public Citizen Health Research Group. He voted no on the risk-benefit question and said he was concerned about the bleeding risk and was "very uncomfortable about the certainty of long-term use and the absence of long-term safety data on hepatotoxicity." Because there is no need for a regular blood test, as there is with warfarin, he expects it will be used "massively" for off-label indications for which there are no data.

The panel chair, Dr. A. Michael Lincoff, professor of medicine at the Cleveland Clinic Foundation, who was among the majority in favor of the risk-benefit profile, said that "the liver issue is not completely resolved, but I believe the signal for liver injury is very weak" but should be followed.

Rivaroxaban is also being studied for other indications in ongoing trials, including acute coronary syndromes, secondary prevention and long-term treatment of patients who have had a DVT or PE, and prevention of stroke and non-central nervous system embolism in patients with nonvalvular atrial fibrillation. ■

ADVISER'S VIEWPOINT

Anticoagulation in Hospitalized Patients

Once the oral anticoagulant rivaroxaban becomes available, I believe it will revolutionize the way that U.S. hospitalists manage patients who require an anticoagulant in the hospital.

The drug, already approved in Canada and the European Union, is expected to be approved by the Food and Drug Administration following a 15-2 vote by the FDA's Cardiovascular and Renal Drugs Advisory Committee that the drug has a favorable risk-benefit profile for prophylaxis of venous thromboembolism (VTE) in patients undergoing hip or knee replacement surgery. This is the first indication reviewed by the FDA; other indications are being studied in phase III trials, including a multinational study of VTE prevention in medically ill hospitalized patients. I am familiar with rivaroxaban in my role as principal investigator in this study at the University of Miami, one of the study sites.

The drug is important for hospitalists because we work closely with orthopedic surgeons in caring for patients undergoing hip and knee replacement. It will provide an alternative to existing drugs for preventing VTE, a common complication in these patients, including warfarin (Coumadin); low-molecular-weight heparin (LMWH), such as enoxaparin sodium (Lovenox); and fondaparinux sodium (Arixtra). About half of these patients receive LMWH for prophylaxis, about 30%-40% receive warfarin, and a smaller proportion receive fondaparinux.

Promising data were reported in a study published last year, which compared rivaroxaban to enoxaparin after hip arthroplasty. The VTE rate was a little over 3.5% among those on enoxaparin, but was closer to 1% among those on 10 mg of rivaroxaban a day, a significant difference. Rivaroxaban was associated with an absolute risk reduction in VTE of approximately 2.6%, and the number of patients needed to treat to prevent one case of VTE was about 38 (*N. Engl. J. Med.* 2008;358:2765-75).

In addition to its efficacy, a great benefit of this drug is that it's taken once daily and, unlike LMWH, is not given parenterally. Compliance decreases when patients must take a drug twice a day or more often. Also, no monitoring is needed, so rivaroxaban has several advantages over warfarin, the only other oral anticoagulant available. Warfarin has a narrow therapeutic index, requires regular INR monitoring, interacts with many drugs and with some food, and is cleared by the cytochrome P450 system.

More patients are undergoing surgery than ever before, and joint replacement surgeries are becoming ever more frequent, so rivaroxaban holds great promise for our aging population.

Excess bleeding and potential hepatotoxicity were the adverse events considered in the FDA panel's discussion of the drug's risk-benefit profile. Although the risk of major bleeding may be slightly increased, the rate of major bleeding in pooled clinical trials was 0.4% in those on rivaroxaban and 0.2% in those on enoxaparin, which was not a significant difference. Signs of potential hepatotoxicity also were uncommon (0.15% in rivaroxaban-treated patients vs. 0.11% in those on enoxaparin, not a significant difference). I don't believe that hepatotoxicity will be an issue with this drug.

The recommended dose of rivaroxaban is 10 mg a day, its onset of action is anywhere from 2.5 to 4 hours, it lasts for 24 hours, and it has a half-life of 6-9 hours. It is cleared by the kidneys, and patients with creatine clearances under 3 mL/min were not enrolled in trials. Rivaroxaban should be avoided in patients on drugs that inhibit the cytochrome P450 3A4 (CYP 3A4), such as ketoconazole and protease inhibitors, and vice versa. Rivaroxaban should be avoided in patients with severe renal disease (creatinine clearance below 30 mL/min) or severe liver disease.

We have just enrolled our first patient in the study that is comparing 10 mg of rivaroxaban a day (for up to 39 days) with 40 mg of enoxaparin once a day (for up to 14 days) for preventing VTE in medically ill hospitalized patients. Also, as one of the sites for a study of rivaroxaban for treating deep vein thrombosis and pulmonary embolism, we plan to start enrolling patients in that trial soon. For now, the FDA is looking at approving rivaroxaban only for VTE prevention in patients undergoing hip or knee replacement. But this indication itself will make the drug the first new oral anticoagulant since warfarin was discovered to treat VTE more than 50 years ago. ■

DR. JAFFER is chief of the division of hospital medicine at the University of Miami Miller School of Medicine. He has received research funding for the rivaroxaban study from Bayer HealthCare AG, which is working with Johnson & Johnson to develop rivaroxaban, and has served as a consultant and a speaker for enoxaparin manufacturer Sanofi-Aventis. He had no other disclosures to report.



BY AMIR K. JAFFER, M.D.

Panel Supports Prasugrel Approval With Few Conditions

BY ELIZABETH MEHCATIE

SILVER SPRING, MD. — With unanimous support by an expert panel of prasugrel, the Food and Drug Administration is poised to approve the antiplatelet drug for treating patients with acute coronary syndrome who present with unstable angina, non-ST-segment elevation myocardial infarction, or ST-elevation MI.

All nine voting members of the FDA's Cardiovascular and Renal Drugs Advisory Committee agreed that prasugrel, a thienopyridine developed by Eli Lilly & Co. and Daiichi Sankyo Inc., has a favorable benefit-to-risk profile, based on clinical trial data.

Prasugrel, given as a 60-mg loading dose followed by 10 mg/day, was compared with clopidogrel, administered at a 300-mg loading dose followed by 75 mg/day, in the Trial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition with Prasugrel-Thrombolysis in Myocardial Infarction (TRITON-TIMI

38), an international double-blind study of 13,608 patients with moderate to high-risk ACS, scheduled to have percutaneous coronary intervention. They had unstable angina, non-ST-segment elevation myocardial infarction (NSTEMI), or STEMI. All patients were on aspirin.

Over a mean of 12 months, the primary end point—a composite of cardiovascular death, MI, or nonfatal stroke—occurred in 12.1% of patients on clopidogrel and 9.9% of those on prasugrel, a significant reduction.

The rate of strokes in both groups was 0.9%. The overall risk of cardiovascular death was also not significantly different between the two groups.

The main risk was bleeding. The rate of major bleeding was 2.2% in those on prasugrel, compared with 1.7% in those on clopidogrel; the rates were 1.3% and 0.8% for life-threatening bleeding, including fatalities; 0.3% and 0.1% for fatal bleeding; and 0.3% and 0.2% for intracranial hemorrhage.

An FDA analysis showed that for every 1,000 patients

with ACS treated with prasugrel, the treatment prevents 21 nonfatal MIs and 3 cardiovascular deaths, with no strokes, but at a cost of 2 fatal hemorrhages, 3 nonfatal major hemorrhages, 5 minor hemorrhages, and 19 minimal hemorrhages.

All panelists agreed that labeling should discourage physicians from prescribing prasugrel to treat patients with a history of stroke or TIA.

Among patients over age 70 years, bleeding was not more common with prasugrel, but the sequelae were more serious. The company has proposed that a lower dose be used in patients over age 75 years, and in people who weigh less than 60 kg, who also were at a greater risk of hemorrhage.

The panel recommended that the drug not be taken around the time of CABG.

The FDA usually follows the recommendations of its advisory committee. If approved, prasugrel will be marketed as Effient. ■