



Efient(R) Exhibited Greater Antiplatelet Activity than High Dose Clopidogrel in Type 2 Diabetes Mellitus Patients with Coronary Artery Disease

ORLANDO, Florida, Nov 15, 2009 (PR Newswire Europe via COMTEX News Network) -- Results from a new study showed patients with type 2 diabetes mellitus who also had coronary artery disease (CAD) and received a 60 mg loading dose and 10 mg maintenance dose of Efient(R) (prasugrel) achieved significantly greater platelet inhibition compared with a 600 mg loading dose and 150 mg maintenance dose of clopidogrel (Plavix(R)). These data were presented today at the American Heart Association 2009 Scientific Sessions.

The OPTIMUS-3 study, which evaluated 35 patients with type 2 diabetes who also had CAD and were taking aspirin, showed that within four hours, the level of platelet inhibition as measured using the VerifyNow(R) P2Y12 Test with a 60 mg loading dose of prasugrel was higher than observed with a 600 mg loading dose of clopidogrel (89 percent vs. 28 percent inhibition of platelet activation [IPA], respectively; $P < 0.0001$). In addition, one hour after the loading dose, patients who received prasugrel had 50 percent IPA compared with 13 percent in patients who received clopidogrel. The level of platelet inhibition achieved for each drug at four hours was unchanged over the following 24 hours. A 600 mg loading dose of clopidogrel is not currently approved for use.

"Previous research has shown that patients with type 2 diabetes mellitus have more active platelets, so might be more prone to clotting, than non-diabetics, and may have suboptimal response to therapies that reduce platelet activity," said Dominick Angiolillo, M.D., Ph.D., assistant professor of Medicine and director of Cardiovascular Research, Division of Cardiology, University of Florida, Jacksonville, Fla. "This study was designed to compare the antiplatelet activity of prasugrel used at standard doses with high doses of clopidogrel in patients with type 2 diabetes mellitus who also had coronary artery disease."

The study also looked at the maintenance doses of prasugrel and clopidogrel. After seven days, results showed that a 10 mg maintenance dose of prasugrel achieved greater platelet inhibition than a 150 mg maintenance dose of clopidogrel (62 percent vs. 44 percent IPA, respectively; $P < 0.0001$).

This study was performed in patients who did not have a specific indication for clopidogrel therapy (more than 12 months after an acute coronary event or bare metal stent placement and no drug eluting stent in place). The relationship between inhibition of platelet aggregation and clinical activity has not been established.

About OPTIMUS-3

OPTIMUS-3 (Third Optimising anti-Platelet Therapy In Diabetes MellitUS) evaluated the pharmacodynamic effects of prasugrel compared with clopidogrel in 35 patients with type 2 diabetes mellitus who also had CAD and were taking aspirin. The double-blind crossover study compared loading and maintenance doses of prasugrel (60 mg and 10 mg, respectively) with a higher 600 mg loading dose and a higher 150 mg maintenance dose of clopidogrel for one week, followed by a 14-day washout period before patients crossed over to receive the alternate study drug.

Measurements of platelet inhibition were taken at several time periods, including baseline, one hour, four hours and 24 hours post loading dose, as well as six to eight days post maintenance dose during each period of the study. Inhibition of platelet aggregation was measured using three separate methods: VerifyNow P2Y12 assay, light transmission aggregometry, and phosphorylation of vasodilator stimulated phosphoprotein.

About Type 2 Diabetes Mellitus in Patients with Coronary Artery Disease

At least 65 percent of people with diabetes mellitus eventually will die of some form of heart or blood vessel disease.(1) CAD is the major cause of mortality and morbidity in patients with type 2 diabetes mellitus.(2)

CAD is the chronic narrowing or hardening of the coronary arteries and is a condition linked to acute coronary syndrome (ACS). Over time, plaques build up in the arteries of patients with CAD. If a plaque ruptures and a clot forms in the artery, it may suddenly block blood supply to the heart, a condition known as ACS. (3)

About Prasugrel

Daiichi Sankyo Company, Limited, and Eli Lilly and Company co-developed prasugrel, an oral antiplatelet agent discovered by

Daiichi Sankyo and its Japanese research partner, Ube Industries, Ltd. Prasugrel helps keep blood platelets from clumping together and developing a blockage in an artery. The European Commission granted marketing authorisation for prasugrel for the prevention of atherothrombotic events in patients with ACS undergoing PCI.

Important Safety Information about Prasugrel

In the EU prasugrel label, the risk of non-coronary artery bypass graft (non-CABG) major bleeding, including fatal bleeding, was higher with prasugrel (2.2 percent incidence) compared with clopidogrel (1.7 percent incidence). Compared with the overall study population, a higher risk of serious bleeding among prasugrel patients was most evident in three distinct patient populations that are readily identifiable: patients who weighed less than 60 kg (132 lbs), patients who were 75 years of age or older and patients who have had a prior transient ischemic attack (TIA) or stroke. Patients who weighed less than 60 kg, or were 75 years of age or older had increased exposure with prasugrel. In the EU prasugrel label, a 5 mg maintenance dose is recommended for patients who weigh less than 60 kg. Prasugrel is generally not recommended for use in patients 75 years or older; if treatment is deemed necessary in this age group, a 5 mg maintenance dose should be prescribed. Patients with prior TIA or stroke should not be treated with prasugrel.

The EU prasugrel label includes a contraindication for patients with a history of TIA or stroke, as well as a warning for patients who weighed less than 60 kg (132 lbs) and patients who are 75 years of age or older. For the patients in TRITON-TIMI 38 without these risk factors, the efficacy of prasugrel compared with clopidogrel on the primary composite endpoint of CVD, nonfatal MI, or nonfatal stroke was 8.3 percent vs. 11.0 percent, respectively, and consistent with the significant efficacy benefit observed with prasugrel in the overall study population. In these same patients, the risk of serious bleeding was reduced but still higher with prasugrel compared with clopidogrel (2.0 percent vs. 1.5 percent, respectively).

An analysis weighing the risk of major bleeding and the reduction in heart attacks found an overall benefit favouring prasugrel compared with clopidogrel. For every 1,000 patients treated with prasugrel as compared with clopidogrel, there were 22 fewer patients with heart attacks and five more with non-CABG-related major bleeding events.

About Daiichi Sankyo

A global pharmaceutical innovator, Daiichi Sankyo Co., Ltd., was established in 2005 through the merger of two leading Japanese pharmaceutical companies. This integration created a more robust organisation that allows for continuous development of novel drugs that enrich the quality of life for patients around the world. Areas of primary focus for Daiichi Sankyo research and development are thrombotic disorders, malignant neoplasm, diabetes mellitus, and autoimmune disorders. Equally important to the company are hypertension, hyperlipidemia or atherosclerosis and bacterial infections. For more information, visit www.daiichisankyo.com.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organisations. Headquartered in Indianapolis, Ind., Lilly provides answers - through medicines and information - for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

This press release contains certain forward-looking statements about Efient for the reduction of thrombotic cardiovascular events (including stent thrombosis) in patients with acute coronary syndromes who are managed with percutaneous coronary intervention and reflects Daiichi Sankyo's and Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialisation. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that the product will be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filing with the United States Securities and Exchange Commission and Daiichi Sankyo's filings with the Tokyo Stock Exchange. Daiichi Sankyo and Lilly undertake no duty to update forward-looking statements.

Efient(R) is a registered trademark of Eli Lilly and Company.

Plavix(R) is a registered trademark of Sanofi-Aventis Corp.

VerifyNow(R) is a registered trademark of Accumetrics.

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1 American Heart Association. Diabetes Mellitus-Statistics-2009 Update.
<http://www.americanheart.org/downloadable/heart/1236357007811FS12DIAB08.pdf>

2 Young, L, Cardiac Outcomes After Screening for Asymptomatic Coronary Artery Disease in Patients With Type 2 Diabetes: The DIAD Study: A Randomized Controlled Trial. JAMA, 2009;301(15):1547-1555.

3 Cleveland Clinic. Understanding Coronary Artery Disease. Available at: <http://my.clevelandclinic.org/heart/disorders/cad/understandingcad.aspx>. Last accessed on October 29, 2009.

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