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Prasugrel Head-to-Head Study Showed Reduced Cardiovascular Events in Diabetes Patients by 30 Percent Compared with Clopidogrel

Sub-group analysis of landmark trial showed prasugrel substantially reduced risk of heart attack and stent thrombosis compared with clopidogrel among ACS patients with diabetes

MUNICH, Germany (August 31, 2008) – Patients who were diabetic and diagnosed with acute coronary syndromes (ACS) were 40 percent less likely to suffer a heart attack if they were treated with prasugrel vs. clopidogrel, according to a sub-group analysis of the TRITON-TIMI 38 trial (8.2 percent vs. 13.2 percent, $P < 0.001$). In addition, according to this same analysis, the combined rate of cardiovascular death, non-fatal heart attack and non-fatal stroke was reduced by 30 percent in diabetes patients treated with prasugrel compared to those treated with clopidogrel (12.2 percent vs. 17.0 percent, $P < 0.001$). In patients without diabetes, there was also improvement in outcomes with prasugrel, with

the primary endpoint occurring in 9.2 percent of patients treated with prasugrel and 10.6 percent of patients treated with clopidogrel (P=0.02).

The diabetic sub-group analysis was presented today by Stephen Wiviott, M.D., Assistant Professor of Medicine at Harvard Medical School and investigator with the Thrombolysis in Myocardial Infarction (TIMI) Study Group, Brigham & Women's Hospital, Boston, USA, at the Congress of the European Society of Cardiology (ESC) in Munich, Germany. In addition, the manuscript was simultaneously published online in *Circulation*, the medical journal of the American Heart Association (AHA).

"The results observed from this sub-group analysis showed that antiplatelet therapy with prasugrel resulted in significantly greater reduction of cardiovascular events among patients with diabetes when compared to those who were treated with clopidogrel," said Wiviott.

The reduction of cardiovascular events was consistent across the sub-group of diabetes patients regardless of diabetic therapies (insulin versus no insulin). The study showed a significant relative risk reduction in the primary endpoint of cardiovascular death, non-fatal heart attack and non-fatal stroke with prasugrel, 37 percent for insulin treated and 26 percent (P=0.001) for non-insulin treated diabetics. There was also a significantly lower rate of stent thrombosis among diabetes patients treated with prasugrel, resulting in a 48 percent relative risk reduction in stent thrombosis compared with clopidogrel (3.6 percent vs. 2.0 percent, P=0.007).

"These findings are interesting in view of previous studies that showed higher levels of platelet aggregation in insulin-treated diabetes patients after dual antiplatelet therapy compared to diabetes patients not treated with insulin," said Dr. Wiviott.

The main TRITON-TIMI 38 clinical trial, previously published in the *New England Journal of Medicine* in November 2007 (Vol. 357, No. 20), compared prasugrel with clopidogrel in patients with ACS undergoing percutaneous coronary intervention (PCI). In the primary analysis of the trial, prasugrel reduced the risk of the composite endpoint of cardiovascular death, heart attack or stroke by 19 percent, with an increased risk of major bleeding compared with clopidogrel (2.4 percent vs. 1.8 percent).¹

In this sub analysis, the rates of major bleeding events were similar for prasugrel (2.5 percent) and clopidogrel (2.6 percent) among patients with diabetes, regardless of diabetes therapies (insulin versus no insulin).

About Diabetes in Patients with ACS

Among patients with ACS, those with diabetes are at a higher risk for subsequent cardiovascular events, including death.² Several mechanisms may increase the risk of events in patients with diabetes, including greater frequency of other cardiac risk factors, a greater burden of narrowing of the arteries (atherosclerotic disease), high blood sugar (hyperglycemia), inflammation, and a greater tendency toward blood clots (thrombosis).^{3,4,5}

About Prasugrel

Daiichi Sankyo Company, Limited (TSE: 4568) and Eli Lilly and Company (NYSE: LLY) are co-developing prasugrel, an investigational oral antiplatelet agent invented by Daiichi Sankyo and its Japanese research partner Ube Industries, Ltd., as a potential treatment, initially for patients with acute coronary syndrome undergoing PCI. Prasugrel works by inhibiting platelet activation and subsequent aggregation by blocking the P2Y₁₂ adenosine diphosphate (ADP) receptor on the platelet surface. Antiplatelet agents prevent platelets from clumping or sticking together, which can result in clogged arteries and may lead to heart attack or stroke.

About Daiichi Sankyo

A global pharma innovator, **Daiichi Sankyo Co., Ltd.**, was established in 2005 through the merger of two leading Japanese pharmaceutical companies. This integration created a more robust organization that allows for continuous development of novel drugs that enrich the quality of life for patients around the world. A central focus of Daiichi Sankyo's research and development is cardiovascular disease, including therapies for dyslipidemia, hypertension, diabetes, and acute coronary syndrome. Equally important to the company is the discovery of new medicines in the areas of infectious diseases, cancer, bone and joint diseases, and immune disorders. For more information, visit www.daiichisankyo.com.

Daiichi Sankyo, Inc. (www.dsus.com) headquartered in Parsippany, New Jersey, is the U.S. subsidiary of Daiichi Sankyo Co., Ltd.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers – through medicines and information – for some of the world’s most urgent medical needs.

This press release contains certain forward-looking statements about the potential of the investigational compound prasugrel (CS-747, LY640315) and reflects Daiichi Sankyo’s and Lilly’s current beliefs. However, as with any pharmaceutical compound under development, there are substantial risks and uncertainties in the process of development and regulatory review. There is no guarantee that the compound will receive regulatory approval, that the regulatory approval will be for the indication(s) anticipated by the companies, or that later studies and patient experience will be consistent with study findings to date. There is also no guarantee that the compound will prove to 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.

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¹ Wiviott, S, Braunwald, E, et al. Prasugrel versus Clopidogrel in Patients with Acute Coronary Syndromes. *New England Journal of Medicine*. November 2007;357:2001-15.

² Donahoe SM et al. Diabetes and mortality following acute coronary syndromes. *JAMA* 2007; 298(7):765-775.

³ Angiolillo DJ. Antiplatelet therapy in type 2 diabetes mellitus. *Curr Opin Endocrinol Diabetes Obes*. 2007;14(2):124-131.

⁴ Sabatine MS, Braunwald E. Will diabetes save the platelet blockers? *Circulation*. 2001;104(23):2759-2761.

⁵ Sobel BE. Optimizing cardiovascular outcomes in diabetes mellitus. *Am J Med*. 2007;120(9 Suppl 2):S3-11.