Head-to-Head Study Showed Prasugrel Statistically Superior to Clopidogrel in Reducing Recurrent Cardiovascular Events

New analysis of landmark study showed patients taking prasugrel had lower risk of combined endpoint of recurrent heart attack, stroke or cardiovascular death after first event than those taking clopidogrel

TOKYO and INDIANAPOLIS, Aug 21, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- A new, pre-specified analysis of the landmark Phase III head-to-head TRITON-TIMI 38 study showed patients who took prasugrel for acute coronary syndromes (ACS) managed with an artery-opening procedure known as percutaneous coronary intervention (PCI) and had survived their first cardiovascular event and then suffered a subsequent event, were 35 percent less likely to have a recurrent event (composite endpoint of heart attack, stroke or cardiovascular death) than those who took clopidogrel (10.8% vs. 15.4%; P=0.016). These data appear as a special advance access online publication from the European Heart Journal.

The recurrence of subsequent events assessment was part of the larger TRITON-TIMI 38 trial, the primary measure of which showed that prasugrel taken with aspirin reduced the relative risk of the combined endpoint of cardiovascular death, non-fatal heart attacks or non-fatal stroke by 19 percent more than clopidogrel (Plavix(R)/Iscover(R)) taken with aspirin. These benefits were accompanied by an increased risk of serious bleeding with prasugrel overall, some of which may be life threatening. Overall, for every 1,000 people treated, there were six more TIMI major bleeding events, but 23 fewer heart attacks in patients taking prasugrel compared with patients taking clopidogrel.(1) The risk of cardiovascular death overall in the study was not statistically different between treatment groups [prasugrel (2.0%) compared with clopidogrel (2.2%)].

Additional data from this further analysis of recurrent events showed:

-- The reduction in recurrent events among prasugrel patients persisted over the duration of the trial (15 months).

-- Among patients taking prasugrel, there were 58 recurrent events compared with 115 recurrent events in the clopidogrel group.

-- The risk of cardiovascular death after a heart attack while on therapy was significantly reduced with prasugrel (3.7%) compared with clopidogrel (7.1%).

-- Diabetics treated with prasugrel showed a risk reduction of 60 percent in subsequent events (P=0.003).

-- Even after adjusting for variables such as age, gender, tobacco use and other health conditions, those taking prasugrel still showed a statistically significant reduction of 34 percent in recurrent events (P=0.024).

-- While recurrent bleeding events occurred infrequently among patients with at least one TIMI non-CABG major or minor bleeding (17 in the prasugrel group and 13 in the clopidogrel group), the analysis noted the high percentage of discontinuation following an initial major bleeding event, which were similar among those patients taking prasugrel (42%) and those taking clopidogrel (43%).

"Not only do multiple heart events increase healthcare costs due to additional hospitalizations, tests and physician visits, but they also result in higher morbidity for many patients," said Elliott Antman, M.D., director of the Samuel A. Levine Cardiac Unit at Brigham and Women's Hospital (BWH) in Boston and principal investigator with the BWH-based TIMI Study Group for the TRITON-TIMI 38 clinical trial.

Methodology

TRITON-TIMI 38 was a Phase III, randomized, double-blind, head-to-head clinical trial comparing the effects of prasugrel versus clopidogrel in patients with ACS who were managed with PCI, a procedure to open blockages in heart arteries, including the use of coronary stenting. The study enrolled 13,608 patients at 707 trial sites in 30 countries.

The primary endpoint of the study was to compare the effects of prasugrel to clopidogrel on the combined incidence of cardiovascular death, non-fatal heart attack or non-fatal stroke during a median period of at least 12 months following PCI. Patients were randomly assigned to one of two treatment groups and given a loading dose of either prasugrel 60 mg or the

approved loading dose of clopidogrel 300 mg, followed by a daily maintenance dose of either prasugrel 10 mg or clopidogrel 75 mg. All patients also received a daily low dose of aspirin.

To measure the risk of recurrent events, a Poisson regression analysis was performed to compare the number of occurrences of cardiovascular events over a period in patients who had suffered at least one primary endpoint.

About Acute Coronary Syndromes

Acute coronary syndromes (ACS), which is comprised of heart attacks and unstable angina (chest pain), affects more than 1.4 million people in the United States annually.(2) Coronary heart disease, which can result in ACS, is the single most common cause of death in the European Union, accounting for more than 741,000 deaths in the EU each year.(3) Coronary artery disease occurs when the arteries become narrowed or clogged by cholesterol and fat deposits and cannot supply enough blood to the heart. In some cases, a blood clot may partially or totally block the blood supply to the heart resulting in ACS.(4) Many ACS patients are managed with PCI, which usually includes a stent placement.

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 syndromes who are managed with 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 Company, Limited

Daiichi Sankyo Company, Limited, established in 2005 after the merger of two leading century-old Japanese pharmaceutical companies, is a global pharmaceutical innovator, continuously generating innovative drugs that enrich the quality of life for patients around the world. The company uses its cumulative knowledge and expertise in the fields of cardiovascular disease, cancer, metabolic disorders, and infection as a foundation for developing an abundant product lineup and R&D pipeline.

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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