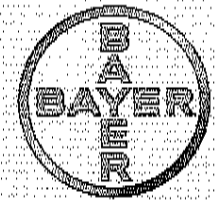


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## Investor News

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### **Trasylol (Aprotinin Injection) Reduced Bleeding and Transfusion Requirements in Patients on Clopidogrel who Required Coronary Artery Bypass Graft (CABG) Surgery**

New study addresses critical days prior to CABG surgery when stopping antiplatelet therapy may delay operation and expose patients to risk of cardiac events

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**Leverkusen / September 19, 2005** – Patients who received clopidogrel in the days prior to coronary artery bypass graft (CABG) surgery lost less blood and required fewer blood transfusions when they received Trasylol<sup>®</sup> during their CABG procedure. These findings, published in the September supplement of *Circulation – Journal of the American Heart Association*, represent an important development for people who benefit from antiplatelet therapy to prevent major adverse cardiac events, including heart attack, stroke and death and who may at some point undergo CABG surgery.<sup>1</sup>

About 13 million people have coronary artery disease (CAD)<sup>2</sup> and antiplatelet drugs are a foundational treatment for many of them, especially those with unstable angina and heart attacks. Multiple studies indicate that antiplatelet medications such as aspirin and clopidogrel can prevent cardiac events by reducing the formation of blood clots by keeping platelets in the blood from sticking together. Additionally, antiplatelet therapy has been associated with improvement in perioperative outcomes.<sup>3,4,5,6</sup> In a recent study involving more than 1,600 patients undergoing first-time CABG surgery, Mayo Clinic researchers found that administering aspirin within five days before the procedure was associated with a lower risk of postoperative in-hospital mortality (1.7 percent vs. 4.4 percent for placebo).<sup>6</sup>

However, previous research had suggested that receiving antiplatelet therapy less than five days prior to CABG surgery could lead to a greater need for blood transfusion.<sup>7</sup> While the number of patients requiring CABG surgery who are exposed to antiplatelet therapy continues to increase, surgeons are left to balance the risk of increased

operative blood loss against the risks of discontinuing antiplatelet treatment or delaying surgery.<sup>1,8,9</sup>

“Discontinuing antiplatelet therapy and delaying surgery exposes patients to the risks that they started antiplatelet therapy to avoid in the first place,” said Dr. Jan van der Linden, study investigator and professor of cardiac anesthesia, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden. “When you stop antiplatelet therapy, you increase the risk of heart attack, stroke and other potentially serious ischemic events.”

In the study published in *Circulation*, patients were allowed to continue antiplatelet therapy prior to surgery. A key to reducing blood loss and transfusion needs in this challenging population was the use of Trasylol. Patients lost 37 percent less blood and received fewer units of red blood cells, platelets and total number of blood products.<sup>1</sup>

Trasylol is the only drug approved by the FDA to reduce bleeding and the need for blood transfusions in patients undergoing cardiopulmonary bypass (CPB) in the course of CABG surgery.<sup>10</sup>

“The combination of continuing antiplatelet therapy prior to surgery and using Trasylol to reduce bleeding and the need for a blood transfusion during the procedure is an effective strategy for CABG patients,” said Dr. van der Linden. “This study adds to a growing body of emerging clinical evidence showing that we can use antiplatelet medication to reduce the risk of cardiac events during the critical days leading up to surgery without complicating the surgery itself.”

### **About the Study**

The study, *Aprotinin Decreases Postoperative Bleeding and Number of Transfusions in Patients on Clopidogrel Undergoing Coronary Artery Bypass Graft Surgery*, investigated acute unstable angina patients (n=75) who were ineligible for percutaneous coronary intervention (PCI), scheduled for surgery, and whom were started on low molecular weight heparin, aspirin, and an oral starting dose of 300 mg of clopidogrel followed by daily intake of clopidogrel 75 mg. Only patients in whom clopidogrel was discontinued less than five days prior to surgery were eligible for study.

Before the start of the surgery, patients were randomized to either receive Trasylol (n=37) or saline solution (n=38). Tranexamic acid was given to both groups at the

discretion of the anesthesiologist. There was no significant difference between groups with respect to patients receiving aspirin and low molecular weight heparin (LMWH) within 24 hours of surgery. Three patients in each group underwent off-pump CABG surgery because of severe arteriosclerosis. One patient in the Trasyolol group underwent concomitant mitral valve repair.

Patients in the treatment group bled 37 percent less and received fewer units of blood products than patients in the control group. Patients in the control group received an average total of 4.8 units of blood products as compared with 1.8 units in patients treated with Trasyolol. Approximately 80 percent of patients in the control group received blood transfusions versus 53 percent in the Trasyolol group.

No significant differences between groups in mortality, stroke, peak serum creatinine, re-exploration for bleeding or myocardial infarction were observed. There were three deaths in the treatment group versus one in the control group. All deaths were related to complications – such as stroke or myocardial infarction – known to occur in this high-risk population. <sup>1</sup>

#### **About Coronary Artery Bypass Graft (CABG) Surgery**

CABG surgery is a form of heart surgery that redirects blood around clogged arteries to increase blood flow and oxygen to the heart. <sup>11</sup> A patient may undergo one, two, three or more bypasses depending on how many coronary arteries are blocked. CABG surgery is the most commonly performed major surgery, with approximately 500,000 procedures conducted in the United States each year. <sup>11,12</sup> Complications associated with CABG surgery include stroke, heart attack, abnormal heart beat, bleeding, and death. <sup>13</sup>

#### **About Trasyolol**

Trasyolol, a broad-spectrum proteinase inhibitor, modulates the systemic inflammatory response associated with cardiopulmonary bypass (CPB) in the course of CABG surgery.

Approved by the FDA in 1993, Trasyolol is the only product indicated for prophylactic use to reduce perioperative blood loss and the need for blood transfusion in patients undergoing CPB in the course of CABG surgery. Full prescribing and warning information is also available at [www.Trasyolol.com](http://www.Trasyolol.com).

The effects of Trasylol use in CPB involves a reduction of inflammatory response to surgery, reduced bleeding and decreased re-exploration for bleeding, which translates into a decreased need for allogeneic (blood donated from another individual) blood transfusions.<sup>10</sup>

An important part of Bayer Pharmaceuticals Corporation's Specialty Pharmaceuticals portfolio, Trasylol has remained a category leader for several years.

### **Important Safety Considerations**

Anaphylactic or anaphylactoid reactions are possible when Trasylol<sup>®</sup> is administered. Hypersensitivity reactions are rare in patients with no prior exposure to aprotinin. The risk of anaphylaxis is increased in patients who are reexposed to aprotinin-containing products. The benefit of Trasylol<sup>®</sup> to patients undergoing primary CABG surgery should be weighed against the risk of anaphylaxis should a second exposure to aprotinin be required. (See WARNINGS and PRECAUTIONS in the Trasylol<sup>®</sup> prescribing information.)

Trasylol is generally well tolerated. Graft patency, myocardial infraction, renal or hepatic dysfunction and mortality were comparable to placebo.

Anaphylactic reactions are possible. In clinical studies, hypersensitivity and anaphylactic reactions were:

- rare (<0.1%) in patients with no prior exposure to Trasylol
- 2.7% overall reaction rate upon re-exposure
  - within 6 months, the incidence was 5 percent
  - after 6 months, the incidence was 0.9 percent<sup>10</sup>

### **About Bayer Pharmaceuticals Corporation**

Bayer Pharmaceuticals Corporation ([www.bayerpharma.com](http://www.bayerpharma.com)) is part of the worldwide operations of Bayer HealthCare AG, a subsidiary of Bayer A.G.

Bayer HealthCare, with sales of approximately 8.5 billion Euro in 2004, is one of the world's leading, innovative companies in the health care and medical products industry. The company combines the global activities of the divisions: Animal Health, Biological Products, Consumer Care, Diagnostics and Pharmaceuticals. Bayer HealthCare employed 35,300 people worldwide in 2004.

Bayer HealthCare's aim is to discover and manufacture innovative products that will improve human and animal health worldwide. Our products enhance well-being and quality of life by diagnosing, preventing and treating disease.

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**Forward-looking statements**

This news release contains forward-looking statements based on current assumptions and forecasts made by Bayer Group management. Various known and unknown risks, uncertainties and other factors could lead to material differences between the actual future results, financial situation, development or performance of the company and the estimates given here. These factors include those discussed in our public reports filed with the Frankfurt Stock Exchange and with the U.S. Securities and Exchange Commission (including our Form 20-F). The company assumes no liability whatsoever to update these forward-looking statements or to conform them to future events or developments.

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