TARGET Trial*

We are in the midst of enrolling patients in TARGET (Tirofiban and Reopro Give Similar Efficacy Outcomes Trial), which directly compares the use of tirofiban and abciximab in percutaneous coronary intervention (PCI) for "intent-to-stent" patients. The criteria for both patient and angiographic entry are the same as were used in the Evaluation of Platelet IIb/IIIa Inhibition for Stenting (EPISTENT) trial, the first to document a strong benefit of glycoprotein (GP) IIb/IIIa inhibition in patients undergoing stenting, compared with placebo. Transcending the placebo-controlled era, we believe it is critically important to establish whether the less expensive, easy-to-use tirofiban strategy is "not inferior" to the accepted standard, abciximab.

Approximately 5000 patients will be randomly assigned on a double-blind, double-dummy basis, with the primary end point of 30-day death, myocardial infarction, or urgent target vessel revascularization. Patients receive preprocedural dual oral antiplatelet therapy with aspirin and clopidogrel as well as weight-adjusted heparin titrated to activated clotting time during the intervention. Sites from 4 continents/18 countries are participating. The enthusiasm to conduct this trial is remarkably robust, with the fastest enrollment of patients in a clinical trial in the history of the field of interventional cardiology.

This "fever" for comparing the 2 agents is fueled, at least in part, by the concern whether it is necessary to use abciximab if GPIIb/IIIa inhibition is obligatory in patients undergoing PCI. Obviously, if this were the case, the financial implications in catheterization laboratories around the world would be profound. Since we know that ischemic events with stenting are driven largely by the platelet response to microparticulate embolization, the hypothesis that tirofiban can achieve similar protection from major ischemic events is sound. The not-inferior design for the primary end point at 30 days compares point estimates for the event rates for either treatment as well as an absolute difference and 95% confidence intervals wrapped around that difference. If the event rate is 5.3% in the abciximab group (as it was in EPISTENT) and 5.8% in the tirofiban arm, then tirofiban would be declared not inferior to abciximab by the way in which the trial is designed. This is not only based on statistical considerations but also is viewed from a medical perspective—that tirofiban preserved more than 90% of the benefit, compared with placebo. This is calculated from knowing that the event rate for stent-placebo in EPISTENT was 10.3% and that the hypothetical absolute difference of 0.5% between abciximab and tirofiban is divided by the absolute difference of the validated abciximab versus placebo, or 5.5%.

Enough on statistics and hypothetical numbers. The field of interventional cardiology has been through an explosive growth phase, with incorporation of stenting in more than 80% of patients undergoing PCI and use of GPIIb/IIIa inhibition in approximately 50% of patients (in the United States). This has occurred in a very rapid time frame, with intensive refinement of the engineering of stents and, now in parallel, the thorough assessment of optimal pharmacologic antiplatelet adjunctive therapy. During the past 5 years, as GPIIb/IIIa inhibitors were undergoing clinical development, there has been an evolution of the debate from "IIb or not IIb" to "which IIb?" This is a very healthy sign of progression in a field in which transformation of adjunctive pharmacology intrinsically receives less priority than device and catheter selection. We are fortunate to be in the position, and essentially right on target, to be the first to determine whether there is any clinically meaningful differentiation between abciximab and tirofiban. No matter what we find, we hit a bull's-eye in advancing the field of PCI and the beyond-placebo era of using GPIIb/IIIa inhibitors for patients with coronary artery disease.

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