TARGET: Do Tirosiban And ReoPro Give Similar Efficacy Trial?

Eric J. Topol et al

There is considerable debate about the choice of intravenous platelet glycoprotein IIb/IIIa inhibitors for percutaneous coronary intervention, after a meta-analysis of 7 trials and 16,771 patients has shown a 38% reduction in death or non-fatal MI 30 days after the index procedure. At 149 hospitals in 18 countries throughout North America, Europe, and Australia, 4810 patients were randomized between 12,699 and 9,025/900,000 min infusion. Patients qualified by baseline angiography for "intent-to-stem" lesions addressed by percutaneous revascularization, and were not with evolving ST-elevation MI or with serum creatinine exceeding 1.5 mg/dl. The primary endpoint was 30 death or non-fatal MI and the trial has 80% power to determine non-inferiority for the EPISTENT Trial. The primary endpoint data will be presented along with the key subgroups such as diabetics. Follow-up data for the trial to 1 year will also be performed.

Late Breaking Science: Linking Genes to Function in the Heart and Vasculature

BASIC ABSTRACTS

Exogenous Hematopoietic Stem Cells Can Regenerate Infarcted Myocardium

Donald Orlic, Jan Kajstura, Stefano Chimienti, Baooshing Li, Stacie Anderson, David Bodine, James Pickel, Annarose Furnari, Anne-Marie Galarneau, Pier Aversa, New York Medical College, Valhalla, NY; NHS/NIH, Bethesda, MD

To determine whether hematopoietic stem cells (HSC) can transform into cardiomyocytes with the potential to repair dead myocardium after infarction. Lin-ki-F4 HSC were harvested from transgenic mice expressing green fluorescent protein (GFP) and injected in the region bordering the infarct, 3-5 hours after coronary artery occlusion in mice. A band of closely packed cells that were double positive to GFP and c-kit was identified in 17 days in the left ventricular myocardium in nearly 50% of hearts injected, between the endocardial and epicardial surface of the infarcted ventricle. This band occupied 50 of the damaged portion of the wall. c-kit/GFP positive HSC were found in the infarcted area shortly after coronary ligation and were still detectable at 7 days. c-kit stained HSC were not labeled by markers for c-kit+ myoblasts, c-kit+ smooth muscle cells, factor VIII, and myocytes (a marker of cell proliferation). Injection was performed using adult mouse myocyte progenitor cells that contain Kit and KitLigand, a growth factor that is required for hematopoietic stem cell proliferation. The band of tissue included in the infarcted zone was 30 death or non-fatal MI and the trial has 80% power to determine non-inferiority for the EPISTENT Trial. The primary endpoint data will be presented along with the key subgroups such as diabetics. Follow-up data for the trial to 1 year will also be performed.

Mutations in the Human δ-Sarcoglycan Gene in Familial and Sporadic Dilated Cardiomyopathy, a Disease of the Cytoskeleton and Sarcolemma

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Background: Dilated cardiomyopathy (DCM) is a significant cause of morbidity and mortality due to congestive heart failure and rhythm abnormalities. Approximately 30% of cases are familial and can be traced back generational systems. Mutations in the δ-sarcoglycan (δ-Sgc) gene are the most common form of DCM, although X-linked disease is also well described. Two mutations have been identified for the X-linked forms (dystrophin and tafazzin), whereas three genes have been identified in autosomal dominant DFCM (actin, lamin A/C, desmin). We have hypothesized that DCM is a disease of the cytoskeleton and sarcolemma and have focused our studies on cardiac sarcolemma. When the δ-Sgc gene was found in these structures, we hypothesized that DCM was caused by mutations in this gene. We identified a dominant δ-Sgc mutation in 50 sporadic cases, a total of 11 known and 10 uncharacterized molecules. These data show, for the first time, (i) that PKCδ forms signaling complexes with multiple proteins in multiple subcellular compartments, suggesting heretofore-unrecognized functions of PKCδ isozyme; and (ii) that cardioprotection is coupled with dynamic modulation of PKCδ-associated proteins and recruitment of signaling molecules to PKCδ complexes. Functional proteomic analysis of PKCδ complexes is a crucial step toward understanding PKCδ-dependent signaling architecture and cardioprotection.
Exogenous Hematopoietic Stem Cells Can Regenerate Infarcted Myocardium
Donald Orlic, Jan Kajstura, Stefano Chimenti, Baosheng Li, Stacie Anderson, David Bodine, James Pickel, Annarosa Leri, Bernardo Nadal-Ginard and Piero Anversa

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