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Bioresorabable Vascular Scaffolds

Dissolvable Stents Are The Next Major Breakthrough in Coronary Care

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The technology involved in reopening clogged coronary arteries has come a long way since Andreas Grüntzig introduced coronary balloon angioplasty in 1977. A procedure that began by inflating a tiny balloon to expand a partially blocked artery evolved over the years to include a wide variety of bare metal stents and drug-eluting stents designed to hold arteries open after balloon angioplasty treatment.

The widespread use of stents has significantly reduced the need for open-heart bypass operations and repeated angioplasty treatments. However, some patients receiving stents have suffered recurrent blockages (known as restenosis) and a complication called stent thrombosis, which is caused by the development of blood clots within the stent. These adverse events have been linked to the polymer that carries the drug, as well as other components used to make drug-eluting stents. These risks are uncommon, but to reduce them further stent makers are working to develop bioresorbable polymers, polymer-free metal platforms and, ultimately, completely resorbable scaffolds.

Preventing Stent Thrombosis

Although rare, stent thrombosis is a medical emergency that can lead to heart attacks (myocardial infarction) and death. Ironically, the very properties of drug-eluting stents that help prevent recurrent blockages also may be responsible for promoting blood clot formation. The medications that flow from drug-eluting stents sometimes can result in delayed or incomplete stent healing, which can lead to exposed or "bare" metal stent struts within the coronary artery. These exposed struts can trigger thrombosis.

Some polymer substances used to deliver medications from drug-eluting stents also may promote thrombosis. Concerns about blood clot formation in drug-eluting stents have led to recommendations that patients continue anti-platelet therapy for at least one year. Anti-platelet therapy combines aspirin with other platelet-blocking drugs such as Plavix, Effient or Brillinta. Some scientists believe anti-platelet therapy may be needed even longer than a year. Large-scale clinical trials are evaluating whether two years of combination anti-platelet therapy is more advantageous than one year. Careful study is needed because long-duration anti-platelet therapy sometimes causes serious internal bleeding.

Late Adverse Events

Late adverse events—those occurring more than a year after receiving a stent—include the development of recurrent blockages and the need for repeated angioplasty procedures. These events have been linked to polymer-related inflammation and metal scaffold exposure within the coronary artery. The metal scaffold may also interfere with normal arterial responses to physical exertion and atherosclerosis, commonly known as hardening of the arteries. In addition, metallic scaffolds may stimulate new plaque development within the stented coronary segment. The ideal coronary stent would be one that delivers medication to prevent early recurrent blockages, holds the artery open long enough to assure longer-term success—and then dissolves away.

Bioresorbable Vascular Scaffolds

Manufacturers are working to develop bioresorbable vascular scaffolds that could offer several advantages over current drug-eluting stents. A scaffold that can be resorbed could remove triggers for stent thrombosis, which may in turn reduce the need for potentially risky long-term anti-platelet therapy. The lack of a permanent metallic stent or permanent polymer residue also would avoid the risk of triggering new plaque formation. Bioresorbable vascular scaffolds may allow coronary arteries to return to normal function, including the ability to increase blood flow in response to exercise. They also would avoid potential complications should a patient later need another angioplasty procedure or bypass surgery. Bioresorbable vascular scaffolds could eliminate problems that occur when stents cover small coronary side branches. They also would not interfere with post-treatment imaging tests such as CT or MRI scans.

The most extensively studied polymer for this purpose has been Poly-L Lactic Acid (PLLA), a substance already used to produce resorbable sutures, soft tissue implants and kidney dialysis media. Over time, PLLA slowly converts into carbon dioxide and water, which are then resorbed by the body. Currently, the most extensively evaluated product using PLLA is Absorb, a bioresorbable vascular scaffold made by the health care company Abbott.

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Absorb Approved in Europe

Abbott's Absorb product includes a PLLA scaffold coated with Poly-D, L-Lactide (PDLLA) and everolimus, an anti-proliferative medication to prevent further blockages. The bioresorbable vascular scaffold is mounted on a balloon catheter and delivered to the coronary artery blockage much like a stent. PDLLA provides controlled release of everolimus similar to that observed with the metallic XIENCE and PROMUS drug-eluting stents. In the first two trials, the patients receiving Absorb experienced no stent thrombosis events, and follow-up by ultrasound and CAT scans has indicated the device is resorbing as intended. Some patients have been followed for more than two years and have shown normal coronary function. Based on clinical trials performed in Europe, Australia and New Zealand, Absorb has been approved for use in Europe and countries in Asia and Latin America.

Abbott intends to initiate a clinical trial in the U.S. to obtain U.S. FDA approval. The trial is designed to evaluate 2,000 patients, who will receive either the Absorb bioresorbable vascular scaffold or the XIENCE/PROMUS metallic drug-eluting stent. The devices will be compared according to risks such as heart attacks, the need for repeated treatment, or death through one-year follow-up.

Leading the Way

Physicians working at The Lindner Research Center and The Christ Hospital Heart and Vascular Center are leading the way with respect to this exciting new technology. The national principal investigators for the U.S. ABSORB trial are Dean J. Kereiakes, MD, Medical Director of The Christ Hospital Heart and Vascular Center, and Steve Ellis, MD, Section Head, Invasive and Interventional Cardiology, The Cleveland Clinic Foundation. The site principal investigator for the trial at The Christ Hospital is Thomas M. Broderick, MD, President of The Christ Hospital Medical Staff. ■

POTENTIAL BENEFITS OF BIORESORBABLE VASCULAR SCAFFOLDS

1. Preserve arterial capacity for responding to the demands of exercise or stress.
2. Preserve arterial ability to accommodate atherosclerosis.
3. Improve microcirculatory function.
4. Prevent new plaque formation.
5. Reduce need for longer-term anti-platelet therapy.
6. Eliminate impediments to future procedures.
7. Avoid interference with CT and MRI scans.

ODYSSEY TRIAL

PHASE III STUDIES OF PROMISING MONOCLONAL ANTIBODY THERAPY NOW ENROLLING PATIENTS WITH HIGH CHOLESTEROL LEVELS

As recently presented at the annual 2012 American College of Cardiology Meeting, the new human monoclonal antibody therapy, SAR236553, reduced LDL-C (bad cholesterol) levels by up to 72 percent when given in addition to statin lipid-lowering therapy in Phase II trials. The 150 mg dose, delivered subcutaneously (subQ) every two weeks, was found to be most beneficial and well tolerated.

ODYSSEY, a Phase III clinical trial program, is now enrolling patients and will include more than 10 clinical trials with 22,000 patients. The ODYSSEY program will examine the long-term safety and efficacy of SAR236553 in multiple treatment strategies and patient types, such as those who are at elevated cardiovascular risk, are unable to tolerate statin therapy, or have a family history of high cholesterol.

This new therapy will help many patients with high cholesterol levels reach clinical practice guideline recommended targets that have been associated with better clinical outcomes.

For more information, call The Lindner Research Center at 513-585-1777.