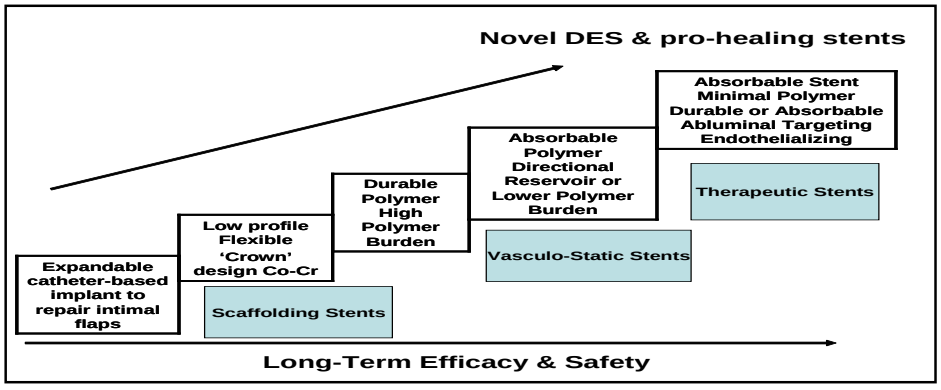
# Emerging Technologies: Stents

## New Drugs

Although many new drug eluting stent (DES) programs are underway, most are focusing on using existing drugs or their analogs with new stent technology (Figure 1). Thus, Eberhard Grube, MD, HELIOS Klinikum, Siegburg, Germany, does not see many new drugs on the horizon. One stent program that Prof. Grube felt was particularly promising involves using Biolimus A9® that is eluted from a biodegradable polylactic acid (PLA) polymer. Biolimus A9®, a rapamycin derivative, has immunosuppressive properties that are similar to those of sirolimus, but is more rapidly absorbed by the vessel wall, readily entering smooth muscle cell membranes and blocking cell proliferation [Grube & Buellesfeld. *Exp Rev Med Dev* 2006]. This stent is currently being tested in two clinical trials (STEALTH II and LEADERS).

**Figure 1. Evolution of Intracoronary Stents.**




## Nanotechnology

One of the most exciting areas in interventional cardiology is the development of new therapies, procedures, and devices that are derived from nanotechnology. Nanotechnology allows researchers to combine materials (eg, proteins and metals) on a scale that could not have been combined previously. According to Steven R. Bailey, MD, University of Texas, San Antonio, TX, the result of these combinations is nanosynthesized metals that have fewer surface impurities and provide improved endothelial coverage, decreased protein deposition, improved stress, and fracture resistance. In addition, nanoscaffolds and nanoporous surfaces actually change the surface of the stent so that polymers are no longer needed for drug delivery.

## Pro-Healing Approach

Endothelial progenitor cells (EPCs) are associated with new vessel formation and vessel repair. They accelerate the natural healing process after stent placement by forming an endothelial layer over the stent that provides protection against thrombus formation and restenosis. The e-Healing Study is a worldwide, prospective registry of patients (current enrollment ~5000) who have been treated with a bioengineered, antibody-coated stent that captures circulating EPCs. Data presented by Robbert J. de Winter, MD, Academic Medical Center, Amsterdam, The Netherlands, showed that use of the stent resulted in low rates of major cardiac adverse events at 6 and 12 months

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(Table 1). The use of these stents might reduce the duration of dual platelet therapy.

**Table 1. Clinical Events in Patients with 12-Month Follow-Up. Interim results as of Feb. 21, 2008, n=1640.**

| | 30 days | 6 months | 12 months | |
|---|---|---|---|---|
| Cardiac Death | 0.6% | 1.5% | 2.1% | |
| MI | 1.2% | 1.6% | 1.8% | |
| Q-wave | 0.1% | 0.2% | 0.2% | |
| Non Q-wave | 1.0% | 1.4% | 1.5% | |
| TLR (Clinically Driven) | 0% | 2.8% | 5.4% | |
| PCI | 0.1% | 2.6% | 5.1% | |
| CABG | 0.0% | 0.2% | 0.4% | |
| MACE | 1.9% | 5.9% | 9.3% | |
| Acute stent thrombosis | | | | 0.0% |
| Sub-acute stent thrombosis | | | | 0.5% |
| Late stent thrombosis | | | | 0.5% |

Patients treated before Aug 14, 2006. All events reported before Jan 15, 2008; all events adjudicated by CECWorst MACE per patient = cardiac death, MI, CABG, and clinically driven TLR.

## Bioabsorbable Stents

Bioabsorbable stents, called "The Holy Grail" by some, have several theoretical advantages over permanent stents, including no chronic inflammation, short duration of platelet therapy after stenting, and avoidance of late thrombosis. Although the initial experience is promising [Erbel R et al. *Lancet* 2007; Ormiston JA et al. *Lancet* 2008], according to Ron Waksman, MD, Georgetown University, Washington, DC, bioabsorbable stents are not ready for mainstream use. He sees the remaining challenges as restenosis, radial strength, biocompatibility, radioopacity, and ability to combine the kinetics of stent degradation with the kinetics of drug elution.

## Paclitaxel-Coated Balloon

Bruno Scheller, MD, Universität des Saarlandes, Homburg/Saar, Germany, presented results from several studies that evaluated the drug-eluting balloon (DEB), a new approach that is based on immediate, short-lasting drug release and homogeneous drug distribution along the vessel wall that can be used alone or in combination with a BMS. The DEB has been tested in patients with coronary in-stent restenosis and has shown positive results in terms of late lumen loss and event-free survival.

Many challenges remain in the development of new stent systems. It was clear, however, from the information presented at this session that researchers are well on their way to finding new and innovative solutions to some of the problems that are seen with the current generation of stents.

# Implications of COURAGE Data Discussed

A year after their initial presentation, the findings of the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial continue to generate debate and uncertainty. The session, "COURAGE in Perspective," was designed to help provide clarity about the trial results and their implications for specific subgroups of patients.

In brief, the findings of the COURAGE study demonstrated that routine percutaneous coronary intervention (PCI) in patients receiving optimal medical therapy (OMT) did not provide additional benefit compared with OMT alone in patients with chronic angina and stable coronary artery disease. There were no differences between the 2 treatment strategies in terms of overall mortality, hospitalization for acute coronary syndrome, or myocardial infarction (MI), although anginal symptoms were reduced for the first 3 years in the PCI group.

Questions have surrounded the implications of the COURAGE findings in terms of the age and gender of patients. William E. Boden, MD, State University of New York, Buffalo, NY, lead investigator of the COURAGE trial, said that although there were numerically higher death and death/MI rates in older patients (≥65 years) in the trial, there was no evidence that an initial strategy of PCI plus OMT was better than OMT alone in mitigating clinical events in this population. "These data support adherence to published American College of Cardiology/American Heart Association (ACC/AHA) treatment guidelines that recommend OMT as the preferred initial management strategy, regardless of age," he said. He added that PCI appeared to be of benefit for women in the overall trial, but a gender subset analysis indicated no significant differences between PCI plus OMT and OMT alone for major prespecified cardiovascular events in women. He explained that the subset analysis involved adjustments to account for differences in baseline clinical characteristics between the men and women in the study, which eliminated differences in outcomes between the genders.

Data from the nuclear substudy of COURAGE have begun to answer other questions about how the trial findings apply to varying degrees of ischemia [Shaw et al. *Circulation* 2008]. The results of this subanalysis indicated that PCI plus OMT was associated with a higher rate of ≥5% reduction in ischemic myocardium (33% vs 19%; p=0.0004), especially among patients who had moderate to severe ischemia