Coronary Artery Disease Treatment in the Catheterization Laboratory: The Promise of an Evolving New Pharmaco-Mechanical Approach

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Supplement Editors, *Coronary Artery Disease Treatment in the Catheterization Laboratory: The Promise of an Evolving New Pharmaco-Mechanical Approach*
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MedReviews, LLC and *Reviews in Cardiovascular Medicine* are pleased to present this very important educational initiative to you. We appreciate the support of the Guidant Corporation, which has asked us to develop this timely, comprehensive, contemporary, and objective presentation of coronary artery restenosis and its pathology, prevention, and treatment. We have assembled a distinguished panel of international authorities including Drs. Drachman, Eigler, Schwartz, and Waksman. In this supplement we provide a platform for their important discussions.

Coronary stent implantation was touted as an improved treatment for restenosis following percutaneous transluminal coronary angioplasty. We traded in negative remodeling for intimal proliferation. Just when we thought stents were becoming a commodity, clinical trials have shown that not all stents are created equal. Stent design plays a significant role in short and long-term outcomes, as in the case of the MULTI-LINK®, which may induce less intimal proliferation than the others. The new cobalt chrome stent, VISION™, seems to offer more hope of being able to reduce restenosis rates than a "plain old stent."

In the stent era, diffuse in-stent restenosis (ISR) became the Achilles heel of the coronary interventionalist. Intravascular radiation therapy (IRT) has provided us with a tool to reduce ISR to acceptable levels. Limitations of IRT include the logistical inconvenience of assembling radiation therapists and physicists, late thrombosis, and edge effects. The GALILEO® system allowed the physician to use

a centering catheter to achieve more uniform dosing and maintain coronary perfusion during therapy, which is an incremental improvement in intracoronary radiation therapy.

Now as we enter the drug-eluting stent era, we will have at our disposal new technology to prevent and perhaps treat coronary artery restenosis. The two agents furthest along in clinical trials are sirolimus and paclitaxel.

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At the Transcatheter Cardiovascular Therapeutics (TCT) 2002 conference held September 24–28, the results of the completed U.S. Multicenter, Randomized, Double-Blind Study of the Sirolimus-Eluting Stent in De Novo Native Coronary Lesions (SIRIUS) and TAXUS II trial were presented along with the DELIVER trial safety data. SIRIUS assessed the safety and effectiveness of the sirolimus-eluting Bx Velocity™ stent in reducing target vessel failure (TVF) compared to the uncoated Bx Velocity™ stent. The primary endpoint of this trial was TVF, defined as the composite of cardiac death, myocardial infarction (MI), or target vessel revascularization (TVR) at 9 months post-procedure. The primary endpoint of TVF was reached in 8.6% of patients in the sirolimus (S) group and 21.0% in the control (C) group ($P < .001$). The incidence of major adverse cardiac events (MACE) at 9 months was 7.1% in group S and 18.9% in group C ($P < .001$). There was a relationship between tertiles of vessel diameter and ISR in both the S and C arms, with a 1.9% and 30.2% incidence, respectively, in the largest tertile group (mean 3.3 mm) and 18.6% and 42.9% in the smallest tertile (mean 2.3 mm). There was no difference at 8-month angiographic follow-up in the incidence of perforation, embolization, or aneurysm formation. The 36% restenosis rate observed in SIRIUS with the non–drug-eluting Bx Velocity™ population is certainly higher than the restenosis rates of 15.7% and 17.5% seen with the VISION™ and PENTA™ non-coated stents.

The TAXUS II trial was an international (non-U.S.) randomized, double-blind trial of slow- and medium-release paclitaxel (1 mcg/mm^2) on the NIRx™ stent in de novo lesions in vessels with reference diameters ≥ 3.0 mm and ≤ 3.5 mm and lesion length ≤ 12 mm. Subjects in this group represented a low-restenosis risk population. The primary endpoint of this trial was percentage of in-stent net volume obstruction at 6 months, which was reduced by over 60% in the TAXUS group compared to control (23.17% vs 7.85%, $P < .0001$). Six-month target lesion revascularization (TLR) occurred in 12.0% of patients in the control arm and 4.6% of those in the TAXUS arm ($P = 0.043$).

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The 30-day safety data of the Evaluation of the RX ACHIEVE™ Drug-Eluting Stent System (DELIVER) trial were also presented at TCT 2002. The objective of this trial was to evaluate the safety and effectiveness of the ACHIEVE™ Drug-Eluting Coronary Stent System in the treatment of patients with de novo native coronary artery lesions ≤ 25 mm in length in vessels ≥ 2.5 mm and ≤ 4.0 mm in diameter in the 1043 patients enrolled in the United States. Paclitaxel stabilizes microtubules and inhibits cell processes that require microtubule turnover, including mitosis, migration, and secretion, and is applied directly to a specially prepared stent surface (INTERLOCK™) metal stent as a durable coating without the need for a polymer. In this evaluation, 3.0 mcg/mm^3 of paclitaxel was loaded on RX PENTA™ stents of 15, 18, 23, and 28 mm in length. The unblinded data show no difference in MACE (death, MI, TLR) between the two groups, consistent with the safety of the ACHIEVE™ Drug-Eluting Coronary Stent System. The effectiveness data will be presented in the near future.

The results of the newest generation of stent technology, a stent with a cobalt chromium alloy, were presented at TCT 2002. This device, the VISION™ stent, has a multicellular design and reduced strut thickness (which is believed to provide enhanced deliverability), scaffolding, and visibility, yet it maintains a similar restenosis rate compared with the MULTI-LINK® stent (see Figures 1 and 2). The study was a prospective, open-label, multicenter, global registry enrolling 265 patients with de novo coronary lesions in vessels 3.0–4.0 mm in diameter and ≤ 25 mm in length. The lesions approached in the registry were relatively complex, with 40% classified

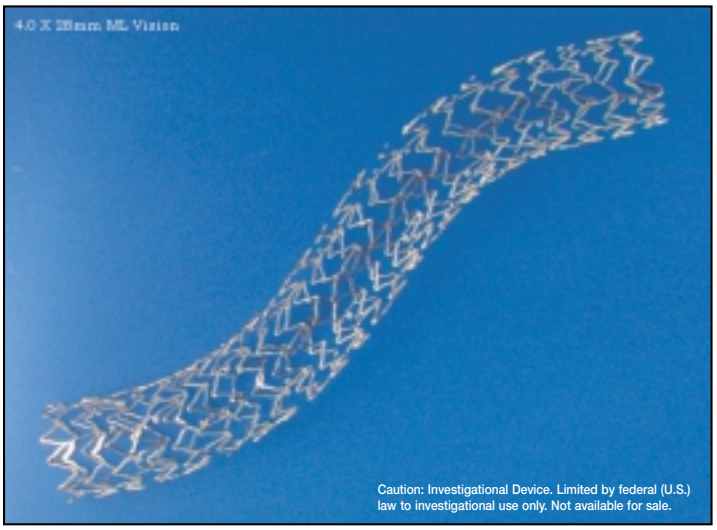

Figure 1. *MULTI-LINK® VISION™ stent.*

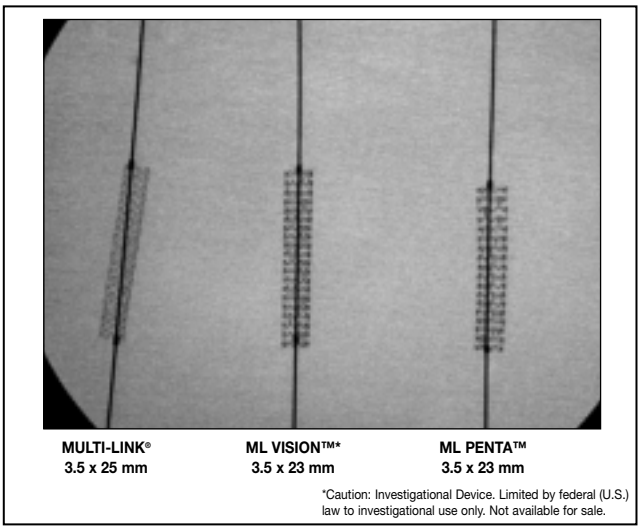

Figure 2. *Thin struts with radiopacity.*

as B2/C by the American College of Cardiology/American Heart Association classification system. The 30-day and 180-day MACE rates (death, MI, or TVR) were 1.9% and 6.2%, respectively. Low rates of 180-day TVR (5.1%) and binary restenosis (15.7%) were observed. The low restenosis rate, observed despite being evaluated in a higher-risk lesion set, makes the VISION™ a significant incremental improvement in stent performance over currently available devices.

The true test of time does not yet allow us to consider the drug-eluting stent to be a panacea. Initial results are very encouraging, and clinical trials are either being designed or are in progress to answer many more important questions. Brachytherapy will probably maintain a place in the cardiac catheterization laboratory in the treatment of restenosis and drug-eluting stent failures. Improved bare metal stent technology, such as that seen with VISION™, and future generation stents will also keep "plain old stenting" an option in certain patient/lesion subsets as well.

It is clear that in order to maximize the clinical and economic benefit of drug-eluting stent technology, interventional cardiologists will have to become experts on stent design, drug delivery platforms, and the pharmacology of eluting agents. Meticulous attention to implantation techniques to maximize vessel wall apposition and to avoid trauma outside the drug delivery field will be mandatory. Selecting a drug-eluting stent for a particular lesion will involve a more complex process than we have been using with "plain old stenting." Our goal is that this supplement will provide the information that will assist you in using this wonderful new technology in a most effective way.

We hope you enjoy reading this supplement, and we look forward to receiving your comments. Our appreciation goes to the folks at the Guidant Corporation for being an inspirational force in bringing this project to life. ■