Best of the TCT Scientific Sessions 2006

Highlights from the Transcatheter Cardiovascular Therapeutics Scientific Symposium, October 22-27, 2006, Washington, DC

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Key words: Bifurcation lesions • Angioplasty • Contrast-induced nephropathy • Drug-eluting stents • Bare-metal stents • Autologous bone-marrow cells

The 2006 Transcatheter Cardiovascular Therapeutics (TCT) meeting in Washington, DC, provided a forum for the presentation of important new data regarding interventional cardiology. Following are discussions of late-breaking clinical trials, the DEScover (Drug-Eluting Stent) registry, and new platforms of drug-eluting stents (DES).

Late-Breaking Trials

The late-breaking clinical trials presented at the TCT focused on topics such as treatment of bifurcation lesions, pharmacologic strategies in angioplasty patients, selection of contrast to prevent contrast-induced nephropathy (CIN), new data on DES, and use of autologous bone-marrow cells to restore myocardial function after ST-segment elevation myocardial infarction (STEMI).

Treatment of Bifurcation Lesions

How best to treat coronary bifurcation lesions often generates impassioned debate. The majority of the controversy concerns optimal management of the sidebranch (whether to treat with angioplasty alone or with a second DES). In this regard, the results of the Nordic Bifurcation Study—the largest randomized study of bifurcation lesions to date—were presented by Andrejs Erglis, MD, PhD (P. Stradins Clinical University Hospital, Riga, Latvia).[1] This trial included 413 patients with angina pectoris and 2 bifurcation lesions: one of at least 2.5 mm in diameter in the main vessel and one of at least 2.0 mm in the sidebranch. Subjects were randomized to receive a DES in both the main vessel and the sidebranch (2-stent strategy) or a stent in the main vessel with provisional stenting of the sidebranch (single-stent strategy). In the single-stent strategy group, the criterion for balloon dilation of the sidebranch was any abnormality in Thrombolysis In Myocardial Infarction (TIMI) flow, with stenting only if the artery had TIMI 0 flow after angioplasty (remarkably, only 2.7% of patients in the single-stent strategy arm received a sidebranch stent).

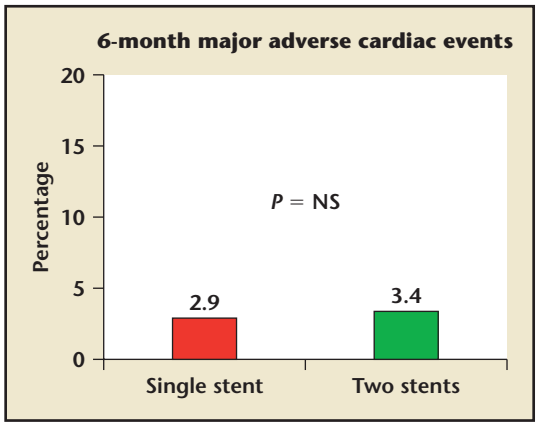


Figure 1. *Six-month major adverse cardiac events from the Nordic Bifurcation Study.*

Treatment success was similar in both groups, and the rate of the primary endpoint of 6-month major adverse composite events (MACE) was comparable in both groups (3.4% in the 2-stent strategy group vs 2.9% in the single-stent strategy group, Figure 1). At 8-month angiographic follow-up, the rate of binary restenosis (diameter stenosis greater than 50%) when assessed in the entire bifurcation lesion was similar in both groups (22.5% with the single-stent strategy vs 16.0% with the 2-stent strategy, $P = .15$).

In summary, in this well-conducted randomized trial of a single stent versus a 2-stent strategy for the treatment of bifurcation lesions, patients had very low rates of overall MACE and appeared to derive equal benefit from the simpler single-stent strategy. However, the patients enrolled in this study had relatively simple bifurcation lesions, and the sidebranch was rarely diffusely diseased. Further subset analyses are required to determine if there are certain lesion types that may benefit from a 2-stent strategy.

Pharmacologic Strategies in Angioplasty Patients

Patients undergoing percutaneous coronary intervention (PCI) are treated with a variety of antithrombotic and antiplatelet therapies to reduce ischemic events. Unfortunately, these therapies are associated with bleeding complications, which in recent studies have been found to predict mortality at least to the same extent as peri-procedural myocardial infarction. Two studies presented at TCT, the Acute Catheterization and Urgent Intervention Triage Strategy Trial-PCI Subgroup (ACUITY-PCI) and CIAO—A Prospective, Randomized, Placebo-Controlled, Single-Center Trial of Heparin vs No Heparin in Patients Undergoing Percutaneous Coronary Intervention, tested strategies designed to minimize bleeding risk while attempting to preserve a low rate of ischemic complications during PCI.

The ACUITY-PCI study, presented by Gregg W. Stone, MD (New York-Presbyterian Hospital/Columbia University Medical Center and the Cardiovascular Research Foundation, New York, NY), was a prespecified subgroup analysis of PCI-treated patients in the ACUITY trial in which upstream bivalirudin with or without glycoprotein (GP) IIb/IIIa inhibitors was compared to heparin (either unfractionated or enoxaparin) plus GP IIb/IIIa inhibitors in patients with moderate- and high-risk acute coronary syndromes.[2] Among the 7789 PCI patients, the 30-day rates of composite ischemia (death, myocardial infarction, or unplanned revascularization for ischemia) were similar among the 3 groups (ranging from 8.2% to 9.3%), but major bleeding complications unrelated to coronary artery bypass grafting (CABG) occurred less frequently among patients treated with bivalirudin monotherapy (3.5%, $P < .001$ for comparison to heparin plus GP IIb/IIIa) compared to both groups receiving GP IIb/IIIa inhibition (6.8% for heparin plus GP IIb/IIIa and 7.5% for bivalirudin plus GP IIb/IIIa). As a result, composite net clinical outcomes (composite ischemia or non-CABG major bleeding) tended to occur least frequently in the bivalirudin-only group (Figure 2). The results were similar in troponin-positive and troponin-negative patients.

There are no placebo-controlled randomized trials demonstrating the benefit of heparin in PCI patients. CIAO, presented by Eugenio Stabile, MD, PhD (Clinica Montevergine, Mercogliano, Italy), sought to determine whether PCI could be performed in low-risk patients with no antithrombin agent.[3] The trial randomized 600 patients undergoing elective PCI for stable angina to 70 U/kg of heparin versus saline placebo during PCI (catheters were flushed with heparinized saline in both study arms). All patients were pretreated with aspirin and a thienopyridine, and patients did not receive GP IIb/IIIa inhibitors. Although the time of manual compression following immediate sheath removal was less in the no-heparin group (5.4 minutes vs 13.1 minutes, $P < .05$), there were no cases of catheter thrombosis in either group, and the incidence of in-hospital, 30-day, and 6-month clinical outcomes were similar in both groups.

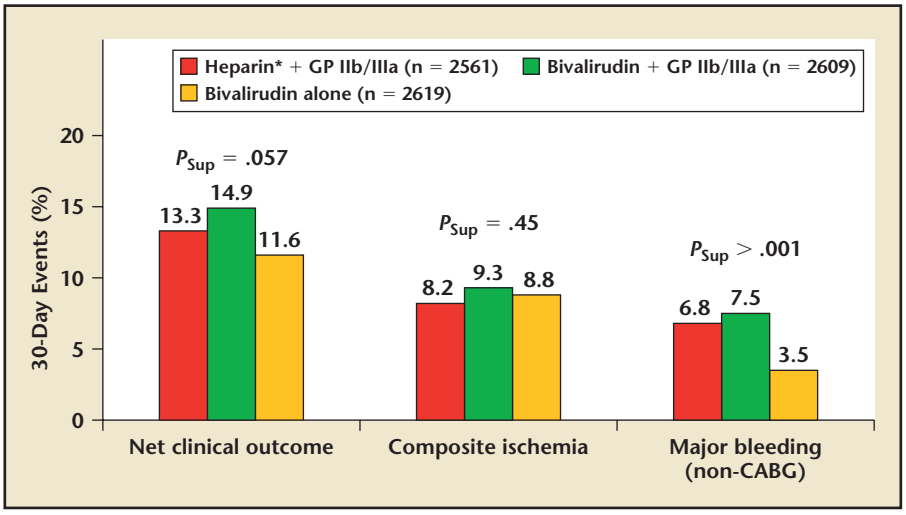


Figure 2. *Primary endpoint measures in percutaneous coronary intervention in the Acute Catheterization and Urgent Intervention Triage Strategy Trial-PCI Subgroup (ACUITY-PCI) study. The 3 study arms consisted of heparin plus GP IIb/IIIa, bivalirudin plus GP IIb/IIIa, and bivalirudin alone. *Heparin was unfractionated or enoxaparin. GP, glycoprotein; CABG, coronary artery bypass graft.*

The overall rate of coronary complications was 5.2% in the heparin arm versus 2.2% in the no-heparin arm ($P < .05$), and there were no major bleeding events in either study arm, with low rates of minor bleeding (0.9% in the heparin arm and 0.3% in the no-heparin arm, Figure 3). The very short duration of procedures performed in CIAO (mean 11 minutes) reflects the very low risk of the patients studied.

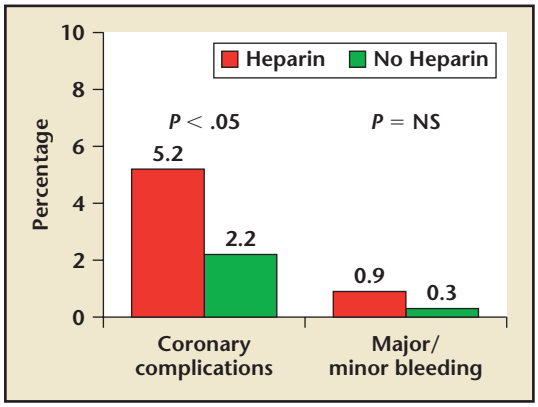
Taken together, these 2 trials emphasize the current interest in balancing the anti-ischemic effects of current antithrombotic therapies used in PCI with an additional focus on minimizing bleeding complications. The results of the large-scale ACUITY-PCI trial demonstrate that bivalirudin monotherapy is an attractive treatment to minimize hemorrhagic complications while effectively suppressing ischemia in high-risk patients with unstable angina and non–STEMI undergoing PCI, particularly when thienopyridines are administered prior to intervention. Although the CIAO trial suggests that heparin may not be needed in the lowest-risk PCI patients, this trial was relatively small and should be considered hypothesis-generating.

Selection of Contrast to Prevent CIN

The development of CIN, a frequent occurrence in patients with diabetes mellitus and chronic kidney disease, is associated with a poor prognosis among patients undergoing angiography and PCI. At TCT, the results of 2 randomized trials of contrast agents for use during angiography and PCI were presented. The Cardiac Angiography in Renally Impaired Patients (CARE) trial, presented by Richard Solomon, MD (University of Vermont, Burlington, VT), was a 414-patient randomized trial comparing the non-ionic low-osmolar agent iopamidol to the non-ionic iso-osmolar agent iodixanol in patients at high risk of CIN who were undergoing coronary angiography.[4] All patients were treated with intravenous sodium bicarbonate, with N-acetyl-cysteine used in 41% of patients. At baseline, the mean estimated glomerular filtration rate was 50 mL/min/1.73 m^2. Diabetes was present in 41% of patients, and PCI was performed in 39% of patients. Mean contrast volume used was similar in both groups (133.7 mL for iopamidol vs 136.4 mL for iodixanol). The incidence of the primary CIN endpoint, defined by an increase in serum creatinine of 25% or greater, was similar in both treatment groups (9.8% for iopamidol vs 12.4% for iodixanol, $P = .44$, Figure 4). Similar results were observed in the subgroups of patients with diabetes, those undergoing PCI, and those treated with N-acetyl-cysteine.

The Ionic Versus Nonionic Contrast to Obviate Worsening of

Figure 3. *Data from CIAO—A Prospective, Randomized, Placebo-Controlled, Single-Center Trial of Heparin vs No Heparin in Patients Undergoing Percutaneous Coronary Intervention.*



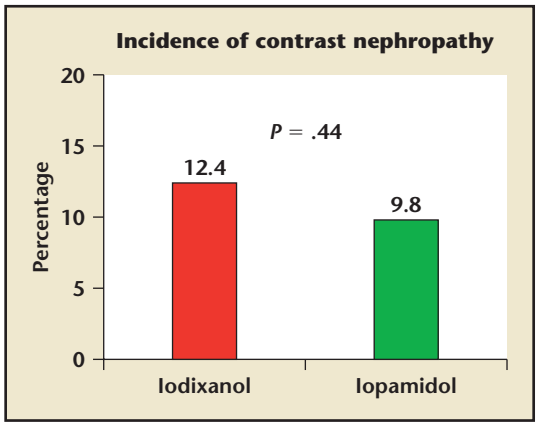


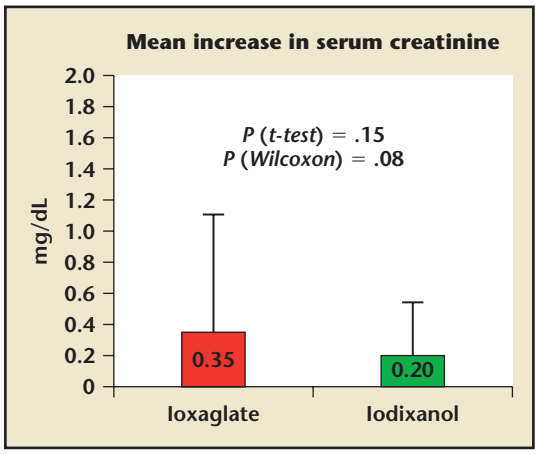
Figure 4. *Incidence of contrast nephropathy in the results from the Cardiac Angiography in Renally Impaired Patients (CARE) trial.*

Nephropathy After Angioplasty in Chronic Renal Failure Patients (ICON) trial, presented by Roxana Mehran, MD (New York-Presbyterian Hospital/Columbia University Medical Center and the Cardiovascular Research Foundation, New York, NY), was a randomized comparison of the low-osmolar, ionic agent ioxaglate versus iodixanol in 145 patients undergoing angiography and/or intervention.[5] The patients were high risk, with a 46% prevalence of diabetes, mean creatinine clearance of 45 mL/min, and 204 mL of contrast used in the ioxaglate group versus 217 mL in the iodixanol group (P = NS). The primary endpoint of an increase in serum creatinine after the procedure was similar in both treatment groups (0.35 mg/dL with ioxaglate vs 0.20 mg/dL with iodixanol, P = .08, Figure 5), although, given the modest sample size, a difference between the 2 groups cannot be excluded. There were also no differences in the incidence of adjudicated acute renal failure or in any other in-hospital or 30-day outcomes between treatment groups. In summary, the 2 trials demonstrated similar safety rates for a low-osmolar non-ionic contrast agent (iopamidol) and a low-osmolar ionic contrast agent (ioxaglate) as compared to the iso-osmolar non-ionic contrast agent iodixanol among higher risk patients undergoing angiography and intervention. Although the majority of head-to-head trials of contrast agents thus far have been negative studies, larger trials with harder clinical endpoints are necessary to fully examine the clinical events associated with the use of these agents in high-risk populations.

DES Comparisons

Several head-to-head comparisons of the sirolimus-eluting Cypher® stent (Cordis Corporation, Miami Lakes, FL) and the paclitaxel-eluting Taxus® stent (Boston Scientific, Natick, MA) in patients undergoing PCI have been performed and previously reported. Two additional unique randomized trials, SORT OUT II: A Prospective, Multicenter, Large-Scale Randomized Trial of Paclitaxel-Eluting and Sirolimus-Eluting Stents in Real-World Lesions: 9-Month Clinical Results, presented by Anders M. Galløe, MD, PhD (Copenhagen County Hospital, Gentofte University Hospital, Hellerup, Denmark), and Percutaneous Treatment of Long Native Coronary Lesions with Drug-Eluting Stent–II: Cypher versus Taxus (LONG DES II), presented by Seung-Jung Park, MD, PhD (Asan Medical Center, Seoul, South Korea), were presented at the TCT. The SORT OUT II, in Denmark, was a trial of 2098 unselected PCI patients randomized to receive either the Cypher or Taxus stent.[6] It is the largest comparative trial of these 2 devices performed to date. The primary endpoint was 9-month MACE (the composite of death, MI, or target vessel revascularization [TVR]). It is important to note that routine angiographic follow-up was not performed. The incidence of 9-month MACE was similar in both groups (7.8% with Cypher and 8.6% with Taxus, P = NS, Figure 6), and there

Figure 5. *Mean increase in serum creatinine in the Ionic Versus Nonionic Contrast to Obviate Worsening of Nephropathy After Angioplasty in Chronic Renal Failure Patients (ICON) trial.*



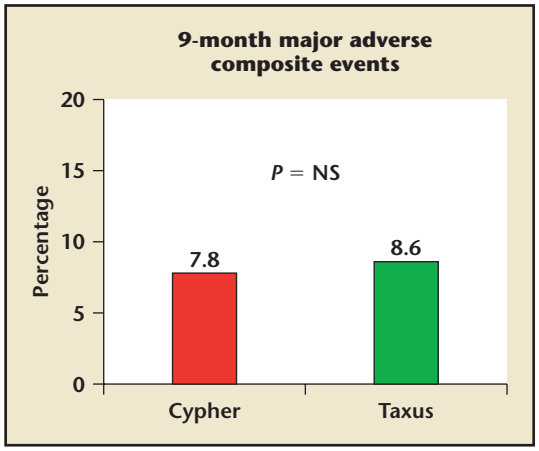


Figure 6. *Major adverse composite events in the Prospective, Multicenter, Large-Scale Randomized Trial of Paclitaxel-Eluting and Sirolimus-Eluting Stents in Real-World Lesions: 9-Month Clinical Results (SORT OUT II) trial.*

were no differences in the individual components of the endpoint.

LONG DES II was a randomized trial of the Cypher versus Taxus stent among 500 patients with long coronary lesions (mean of 33.9 mm in the Cypher group and of 34.5 mm in the Taxus group) in native coronary arteries.[7] The rate of the primary angiographic endpoint of 6-month in-segment binary restenosis was significantly lower among Cypher-treated patients (3.3% vs 14.6% in Taxus-treated patients, $P < .001$, Figure 7), and Cypher-treated patients with restenosis had a more focal pattern of in-stent restenosis (100% vs 53.3% focal in Taxus-treated patients, $P = .03$). The rate of target TVR at 9 months was lower among Cypher-treated patients (3.2% vs 7.6%, $P = .03$), with similar rates of death and myocardial infarction in both groups.

There were several presentations of novel DES platforms at TCT 2006. ZOMAXX I, a comparison of the ZoMaxx™ zotarolimus-eluting stent (Abbott Laboratories, Abbott Park, IL) and the Taxus paclitaxel-eluting stent, was presented by Bernard R. Chevalier, MD (Centre Cardiologie du Nord, Saint-Denis Cedex, France), at a late-breaking clinical trials session.[8] In this 401-patient trial, the ZoMaxx stent failed to meet its primary non-inferiority endpoint of 9-month angiographic in-segment late loss (mean 0.43 mm for ZoMaxx vs 0.25 mm for Taxus, Figure 8). In-stent late loss was similarly higher with the ZoMaxx stent compared with the Taxus stent, as were rates of binary angiographic restenosis (16.5% vs 6.9%, $P = .007$).

Taken together, these 3 studies demonstrate that both currently approved DES platforms (Cypher and Taxus) perform very well across a broad spectrum of simple and complex lesions, with low overall rates of TVR. Angiographic endpoints seem to favor the Cypher stent, which is associated with a lower overall late loss, but rates of clinical endpoints such as TVR, particularly when assessed in trials that do not mandate angiographic follow-up, are low with both stent platforms. In contrast, binary angiographic restenosis was more frequent with the ZoMaxx

Figure 7. *In-segment restenosis in the Percutaneous Treatment of Long Native Coronary Lesions with Drug-Eluting Stent—II: Cypher versus Taxus (LONG DES II) trial.*

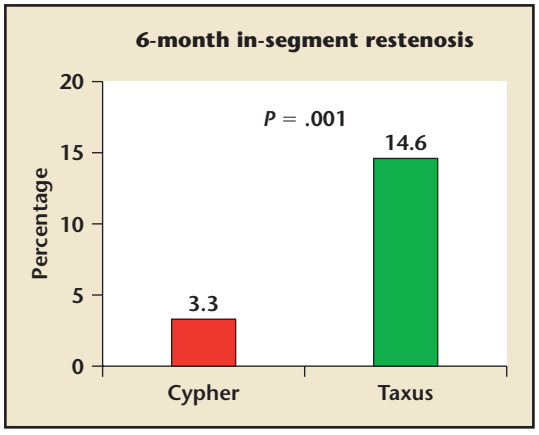
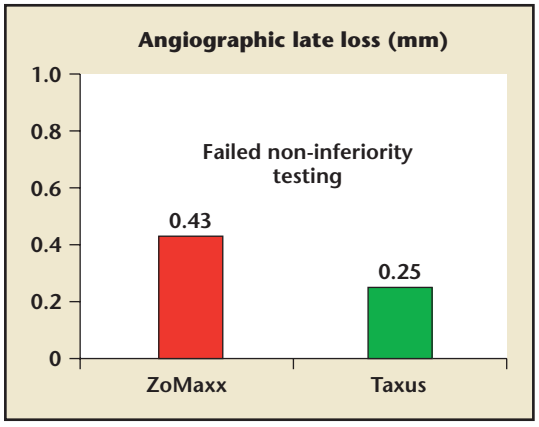


Figure 8. *Angiographic late loss in the ZOMAXX I trial.*



stent than with Taxus, which would have been expected to translate into greater clinical restenosis (TVR) in a larger trial; the manufacturer has therefore elected to discontinue this program. Further study is required to determine if there is indeed a clinical advantage of lower late loss in complex lesions, as suggested in LONG DES II. Larger studies are also required to assess the relative safety of the Cypher and Taxus stents in simple and complex lesions.

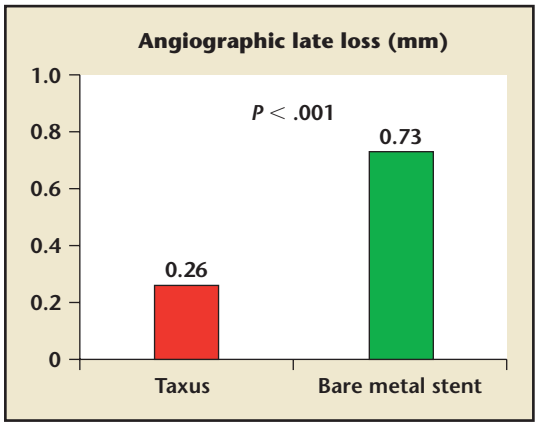


Figure 9. *Angiographic late loss in the Helsinki Area Acute Myocardial Infarction Treatment Reevaluation (HAAMU-STENT) study.*

DES in STEMI

Several prior studies have demonstrated that DES decrease rates of TVR and restenosis among stable patients, but the data in patients with acute STEMI are less conclusive. For example, the recently published Paclitaxel-Eluting Stent versus Conventional Stent in Myocardial Infarction with ST-Segment Elevation (PASSION) trial, which did not have mandatory angiographic follow-up, demonstrated a trend toward lower rates of serious adverse events with the Taxus stent compared to bare metal stents (BMS), whereas rates of TVR were not different between DES and BMS.[9] The Helsinki Area Acute Myocardial Infarction Treatment Reevaluation (HAAMU-STENT) study, presented at TCT by Ilkka Tierala, MD (Helsinki University Central Hospital, Helsinki, Finland), further examined this question, by randomizing 164 patients undergoing primary or facilitated PCI for STEMI to the Taxus stent or a BMS.[10] Upon angiographic follow-up at 9 months, the Taxus stent was associated with lower late loss (mean 0.26 mm vs 0.73 mm, $P < .001$, Figure 9) as well as a larger in-stent minimal luminal diameter (mean 2.5 mm vs 2.0 mm, $P < .001$). Although the study was not adequately powered to assess clinical events, the rate of TVR trended lower in patients treated with the Taxus stent (3.7% vs 11.0%, $P = .072$). Overall, these data suggest that neointimal hyperplasia is suppressed to a greater degree with the Taxus stent as compared to BMS in patients with STEMI. Whether this greater suppression of neointimal hyperplasia is consistent with improved clinical outcomes among patients not undergoing routine angiographic follow-up remains open to debate and is the subject of further study in the ongoing large-scale Harmonizing Outcomes with Revascularization and Stents-Acute Myocardial Infarction (HORIZONS-AMI) trial.

Autologous Bone-Marrow Cells to Restore Myocardial Function After STEMI

Patients with STEMI are often left with significant reductions in ventricular function due to ischemic necrosis of the infarct territory. Recent trials of myocardial regeneration therapies for patients with ischemic heart disease have had mixed results. The 12-month clinical results of the largest such trial, Reinfusion of Enriched Progenitor Cells and Infarct Remodeling in Acute MI (REPAIR AMI), were presented by Andreas M. Zeiher, MD (University Hospital Medical Center, Frankfurt, Germany). This trial randomized 204 patients to an intracoronary infusion of autologous bone-marrow cells versus placebo at 3 to 7 days following revascularized STEMI.[11] The rates of the composite occurrence of death, reinfarction, or rehospitalization for heart failure (2% vs 12%, $P = .006$) and death, reinfarction, or revascularization (24% vs 42%, $P = .009$) were both lower among patients receiving bone marrow cells compared to placebo (Figure 10). In multivariable analyses, randomization to bone marrow cells was the only significant predictor of freedom from death, reinfarction, or revascularization. Results from this large randomized clinical trial suggest a favorable effect of bone marrow progenitor cells. A large, multicenter trial is being planned to confirm these results and to determine the subgroups of patients who could benefit the most from intracoronary autologous bone marrow infusions.

Conclusion

The late-breaking trials presented at TCT 2006 represent a broad sampling of areas of current interest in interventional cardiology. Notably, several of these randomized studies were performed by independent and relatively new collaborative study groups outside the United States. This fact alone portends a healthy future for evidence-based medicine

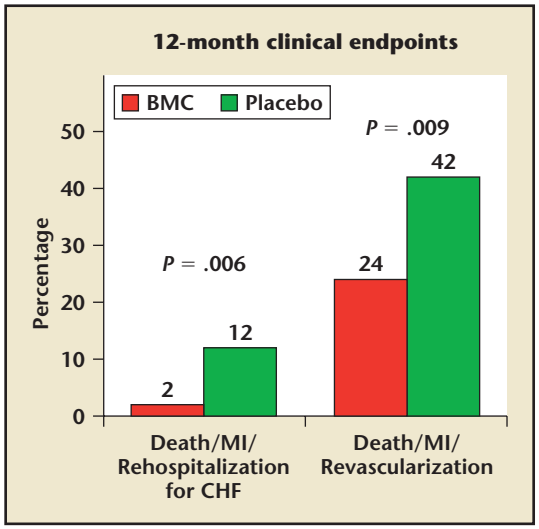


Figure 10. *Results from the Reinfusion of Enriched Progenitor Cells and Infarct Remodeling in Acute MI (REPAIR AMI) trial. MI, myocardial infarction; CHF, coronary heart failure; BMC, bone-marrow cells.*

in interventional cardiology in the years to come. In addition to these 10 trials, 15 "First Report" investigations were presented, consisting of novel new devices and therapies, "first-in-man" experiences, and large, multicenter registries. These studies will be the subject of a future report.

[Ajay J. Kirtane, MD, SM, Gregg W. Stone, MD, FACC]

The DEScover Registry

During the past 15 years, the number of PCI procedures performed annually has continued to increase, as has the proportion of these procedures that include the use of stents. Similarly, since the introduction of DES into clinical practice, the proportion of stent procedures that include the use of a DES has continued to rise, and it is estimated that DES are used in more than 85% of PCI procedures. Yet, early randomized clinical trials that compared the ability of DES and BMS to significantly decrease restenosis and TVR rates following a successful procedure were performed only in relatively low-risk patients without complex coronary anatomy.[12,13] Given the extension in the use of DES to patient and lesion subsets that were excluded from these trials, it is important to understand current clinical practice and to evaluate the outcomes of DES in an unselected patient cohort.

The DEScover Registry was designed to characterize and evaluate patients undergoing contemporary PCI using DES in the United States. Accordingly, 6906 patients at 140 medical centers were enrolled in this registry and were compared on the basis of treatment with BMS (n = 397), sirolimus-eluting stents (SES, n = 3873), or paclitaxel-eluting stents (PES, n = 2636). The findings were presented by David O. Williams, MD (Rhode Island Hospital, Providence, RI).[14] Patients receiving BMS were significantly older and had a higher prevalence of triple vessel disease, totally occluded vessels, and comorbid disease, and a higher incidence of STEMI as the indication for the procedure in comparison with patients receiving DES. Left ventricular ejection fraction was significantly lower in BMS patients (mean 49.5% vs 52.7% SES and 52.8% PES). Despite more triple vessel disease, multi-lesion intervention was performed less often in the BMS group (25.5% vs 34.7% SES and 32.3% PES, $P = .0005$). In addition, bypass grafts were more often treated with BMS (15.9% vs 6.5% for both SES and PES, $P < .0001$).

At 1 year, mortality was 5.9% in the BMS group and 3.1% in the DES

Table 1
Outcomes at 1-Year in Patients Treated With BMS and DES

Clinical Event	BMS (n = 397)	DES (n = 6509)	*P* Value	SES (n = 3873)	PES (n = 2636)	*P* Value
Death (%)	5.9	3.1	.005	3.3	2.8	.45
MI (%)	3.5	2.4	.19	2.2	2.6	.20
Stent thrombosis (%)	.8	0.6	.67	.5	.8	.06
Repeat PCI (%)	9.3	8.4	.62	8.7	7.9	.37
CABG (%)	3.5	1.4	.0007	1.3	1.5	.53
TVR (%)	9.5	6.0	.007	6.3	5.5	.20
Death/ MI (%)	9.0	5.2	.002	5.2	5.3	.64

BMS, bare-metal stents; DES, drug-eluting stents; SES, sirolimus-eluting stents; PES, paclitaxel-eluting stents; MI, myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft surgery; TVR, target vessel revascularization.

group (P = .005). There was no difference in the rate of myocardial infarction (3.5% vs 2.4%) or repeat PCI (9.3% vs 8.4%) in the BMS and DES groups, respectively, although coronary bypass surgery was performed more frequently in the BMS group (3.5%) compared to the DES group (1.4%) (P = .0007). Importantly, there was no difference in the rate of stent thrombosis (0.8% BMS, 0.5% SES, 0.8% PES) (Table 1). In an adjusted analysis, there was no difference in death or myocardial infarction (hazard ratio, 0.74; 95% CI, 0.52-1.07) between groups. Of note, patient selection and clinical outcomes at 1 year were similar between subjects receiving SES and PES.

The authors concluded that differences in patient selection were apparent between BMS and DES groups in the DEScover Registry (Figure 11). Although DES use resulted in lower rates of repeat revascularization compared to BMS, rates of stent thrombosis were similar for both types of stents. Therefore, these data confirm the effectiveness and safety of both SES and PES in unselected patients.

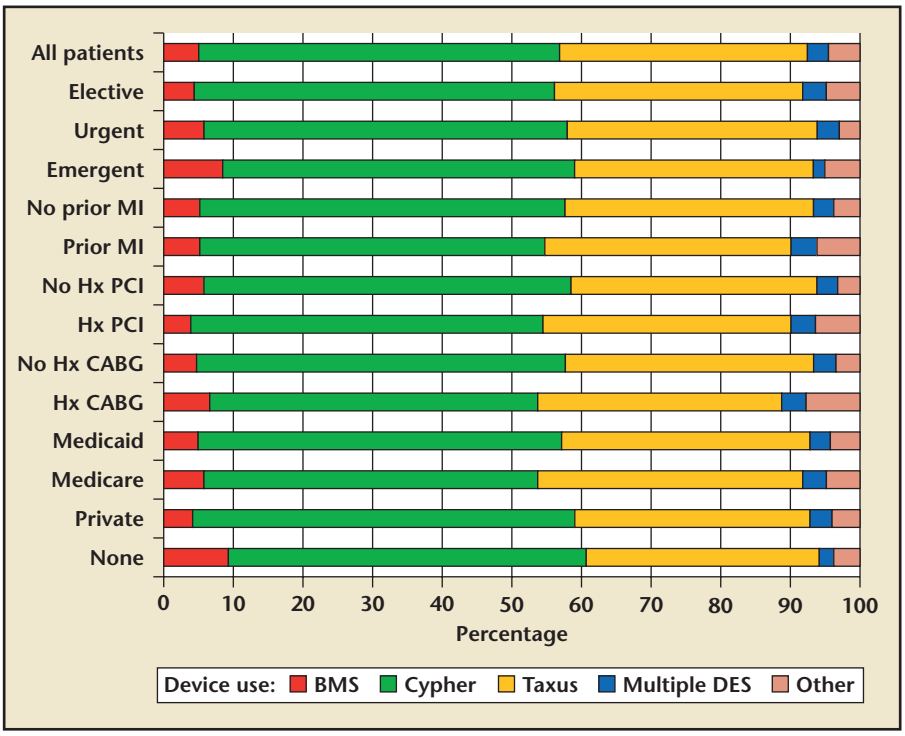


Figure 11. *Differences in patient selection between BMS and DES groups in the DEScover Registry. BMS, bare-metal stent; DES, drug-eluting stent; MI, myocardial infarction; Hx, history; PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft. Reprinted with permission from Williams DO.*[14]

Of note, patient selection and clinical outcomes at 1 year were similar between subjects receiving sirolimus-eluting stents and paclitaxel-eluting stents.

Comment

This important and timely report provides a glimpse into "real-world" practice from a multicenter experience that includes all patients undergoing PCI (with or without BMS or DES), and notes that stents are used in 96% of PCI procedures, of which 94% are DES. It also reveals the characteristics that are associated with the selection of BMS, such as vein graft stenoses that are perhaps chosen based on large vessel diameter, and use during PCI for STEMI, a choice perhaps based on the concern of DES thrombosis in this setting. The study also underscores the older age and higher risk features in patients treated with BMS. It is not unexpected that death and myocardial infarction at 1 year occurred more frequently among BMS-treated patients, but this difference disappeared after adjustment for the baseline differences between groups.

Importantly, the results of the DEScover Registry are consistent with other reports that demonstrate a reduction in the rate of TVR in DES compared with BMS-treated patients, although the benefit is less pronounced in this unselected population. Given the recent concern regarding increased rates of stent thrombosis associated with DES, the absence of a difference in the rate among BMS-, SES-, and PES-treated patients is reassuring, although it must be noted that the registry was not designed to detect a difference in thrombosis rates between SES and PES, and the study lacked precision for uncommon clinical events due to the relatively small number of BMS-treated patients. In addition, the registry did not collect outcomes beyond 1 year, when "very late" stent thrombosis in DES-treated patients has been noted, nor did it collect data regarding use of antiplatelet agents during follow-up.

[Alice K. Jacobs, MD, FACC, FAHA]

New Platforms of DES

DES have achieved unprecedented success in interventional cardiology since their 2003 launch in the United States. In the early part of 2006, up to 92% of all stents placed were drug-eluting. Recently, clinical follow-up (up to 4 years) in some of the early pivotal trials raises concern regarding the safety of these stents. There seems to be a slightly increased risk (0.4% to 0.5%) of very late stent thrombosis (> 1 year). The mechanism of this late stent thrombosis is unclear. The hypothesis has been that the polymer or the drug has induced delayed healing or hypersensitivity.

There are approximately 20 to 30 DES platforms in clinical release around the world. I will summarize the findings regarding these platforms presented at this year's TCT.

Endeavor Stent

The Endeavor® stent (Medtronic, Minneapolis, MN) is based on the Driver® stent platform (Medtronic, Minneapolis, MN). The polymer, phosphorylcholine, is designed to mimic the cell membrane, thus making it biocompatible and potentially less thrombogenic. The drug used in this DES platform is zotarolimus, an analog of sirolimus, the drug used in the Cypher stent.

The Endeavor stent clinical program seems to show slightly higher late loss (0.6 mm), but the clinical efficacy (target lesion revascularization) is only marginally increased. What is intriguing so far is that there seems to be no late stent thrombosis after the first 30 days. Is this due to the small sample size or to a more biocompatible polymer?

Endeavor Resolute Stent

Data on the Endeavor Resolute stent (Medtronic, Minneapolis, MN) were presented by Ian Meredith, MD, PhD (Monash Medical Centre, Melbourne, Australia).[15] The Resolute stent also uses zotarolimus, but the polymer was changed to BioLinx, which is specifically designed for drug delivery. The drug is released over 90 to 100 days. This study enrolled 130 patients; 30 patients underwent a 4-month intravascular ultrasound (IVUS) and angiographic follow-up. The late loss was 0.12 mm, with an IVUS neointimal volume of 2.2%. Whether this stent will be as safe as the Endeavor is too early to tell.

ZoMaxx Stent

As mentioned above, ZOMAXX I is an international randomized trial using the ZoMaxx stent platform.[8] This DES uses the same drug and polymer as the Endeavor platform, except with a topcoat applied over the phosphorylcholine/drug mixture in order to slow down the release. The trial compared 200 patients treated with the ZoMaxx stent and 200 patients treated with the Taxus stent. The primary endpoint was in-segment late loss. The ZoMaxx had a late loss of 0.43 mm, whereas the late loss of Taxus was 0.25. Thus, the prespecified endpoint was not met. The in-stent late loss of ZoMaxx was 0.67 mm. The manufacturer decided not to commercialize the ZoMaxx stent platform and essentially terminated the ZoMaxx clinical program.

Xience Stent

The Xience™ stent (Abbott Laboratories, Abbott Park, IL) is based on the Vision® (Abbott Laboratories, Abbott Park, IL) BMS platform.[16] The drug is everolimus, with a durable polymer as the carrier. The STI571 ProspectIve RandomIzed Trial (SPIRIT) family of clinical trials is ongoing, and the SPIRIT II CE mark trial was a 3 to 1 randomized trial of 300 patients comparing Xience to the Taxus stent. The 6-month angiographic follow-up showed a late loss of 0.12 mm for the Xience stent and 0.37 mm for the Taxus stent. The TLR rate was 2.7% versus 6.5%, respectively. The pivotal US trial SPIRIT III is ongoing.

Biodegradable Stent

The current work on a completely biodegradable stent (Abbott Laboratories, Abbott Park, IL) is based on a polylactic acid platform.[15] The coating and its drug are absorbed over a 90-day period, and the polymer backbone is absorbed over 2 years. The first in-man trial is ongoing.

Conclusions

The current generation of DES has proven extremely efficacious in reducing restenosis. However, there seems to be a slight increase in late thrombosis with these stents, thus ameliorating some of the clinical benefits provided by the reduction in complications related to repeat revascularization. The new generation of stents will be targeted towards reproducing the same efficacy without sacrificing safety. Whether this goal is possible will not be known until long-term follow-up of these patients is performed. ■

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Main Points

- In a well-conducted randomized trial of a single stent versus a 2-stent strategy for the treatment of bifurcation lesions, patients had very low rates of overall major adverse coronary events and appeared to derive equal benefit from the simpler single-stent strategy.
- The results of the large-scale Acute Catheterization and Urgent Intervention Triage Strategy Trial-PCI Subgroup (ACUITY-PCI) trial demonstrate that bivalirudin monotherapy is an attractive treatment to minimize hemorrhagic complications while effectively suppressing ischemia in high-risk patients with unstable angina and non–ST-segment elevation myocardial infarction undergoing percutaneous coronary intervention, particularly when thienopyridines are administered prior to intervention.
- Two trials demonstrated similar safety rates for a low-osmolar non-ionic contrast agent and a low-osmolar ionic contrast agent as compared to an iso-osmolar non-ionic contrast agent among higher risk patients undergoing angiography and intervention.
- In a trial of myocardial regeneration therapies, rates of the composite occurrence of death, reinfarction, or rehospitalization for heart failure and death, reinfarction, or revascularization both were lower among patients receiving bone marrow cells compared to placebo.
- In the DEScover (Drug-Eluting Stent) registry, death and myocardial infarction at 1 year occurred more frequently among patients treated with bare-metal stents in comparison to drug-eluting stents, but this difference disappeared after adjustment for the baseline differences between groups.
- Both currently approved drug-eluting stent platforms (Cypher and Taxus) perform very well across a broad spectrum of simple and complex lesions, with low overall rates of target vessel revascularization (TVR). Angiographic endpoints seem to favor the Cypher stent, which is associated with a lower overall late loss, but rates of clinical endpoints such as TVR, particularly when assessed in trials that do not mandate angiographic follow-up, are low with both stent platforms.