TCT 2009: New Findings Pave the Way for Novel Approaches to Treating Cardiovascular Disease

Highlights From the 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium, September 21-25, 2009, San Francisco, CA

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The annual Transcatheter Cardiovascular Therapeutics (TCT) symposium is the world's largest meeting at which interventional cardiologists, cardiac surgeons, and vascular medicine specialists gather to hear the latest data from key clinical trials and to observe live cases focusing on coronary artery disease, peripheral vascular disease, and structural heart disease. The conference enables these clinicians to incorporate the most advanced minimally invasive techniques for treating cardiovascular (CV) disease into their everyday practices. Here we examine important, late-breaking studies presented at TCT 2009 regarding current and future drug-eluting stents (DES) as well as conventional and emerging pharmacologic and catheter-based strategies.

Reviewed by Jason Kahn, MA, Gregg W. Stone, MD, FACC, FSCAI, Martin B. Leon, MD, George D. Dangas, MD, PhD, Caitlin E. Cox, MA, Kim Dalton, MA, Laura A. McKeown, BA, Gary S. Mintz, MD, Columbia University Medical Center and the Cardiovascular Research Foundation, New York, NY

Current and Next-Generation Stents

SPIRIT IV

Two large randomized trials (Clinical Evaluation of the XIENCE V® Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions [SPIRIT IV] and Second-Generation Everolimus-Eluting and Paclitaxel-Eluting Stents in Real-Life Practice [COMPARE]) compared the clinical outcomes of the XIENCE V (Abbott Laboratories, Abbott Park, IL) everolimus-eluting stent versus the paclitaxel-eluting TAXUS® Liberté® and TAXUS® Express$^{2®}$ (Boston Scientific, Natick, MA) stents in a broad cross-section of patients with coronary artery disease followed for 1 year (without routine angiographic follow-up).

TCT Course Director Gregg W. Stone, MD, of Columbia University Medical Center (New York, NY), presented the results of the 3687-patient randomized SPIRIT IV trial, showing that XIENCE V significantly reduced target lesion failure (a composite measure of cardiac death, target-vessel myocardial infarction [MI], or target lesion revascularization, the study's primary endpoint) at 1-year follow-up compared with TAXUS

Express[2] (XIENCE V 4.2% vs TAXUS 6.8%), in the SPIRIT IV trial.[1]

SPIRIT IV also demonstrated significant reductions in target vessel failure and major adverse cardiac events (MACE) for patients who received XIENCE V (n = 2458) versus TAXUS (n = 1229) through 1 year (Table 1).

XIENCE V was also superior compared with TAXUS for the secondary endpoint of ischemia-driven target lesion revascularization (TLR), with a relative risk reduction of 45% (relative risk [RR] = 0.55; 95% confidence interval [CI], 0.38-0.78). For another secondary endpoint, the composite of cardiac death or target vessel MI at 1 year, the difference between the 2 stents did not reach statistical significance (RR = 0.69; 95% CI, 0.46-1.04). XIENCE V did, however, reduce the rates of Academic Research Consortium (ARC)–defined definite or probable stent thrombosis by 77% compared with the TAXUS stent (0.3% vs 1.1%; *P* = .003).

COMPARE

The results of the 1800-patient randomized COMPARE trial, presented after SPIRIT IV, demonstrated that in an all-comer population, XIENCE V significantly reduced MACE compared with the TAXUS Liberté stent, according to presenter Peter C. Smits, MD, PhD, of Maasstad Ziekenhuis (Rotterdam, The Netherlands).[2] Superiority of XIENCE V was reached mainly due to less TLR, MI, and stent thrombosis.

In COMPARE, the XIENCE V was superior to TAXUS for the primary 1-year endpoint of combined all-cause death, nonfatal MI, and target vessel revascularization (TVR) at 1 year with a rate of 9.1% in the TAXUS group (n = 903) versus 6.2% (*P* = .023) in the XIENCE V group (n = 897). All-cause death and cardiac death, meanwhile, were not significantly different between groups (*P* = .58 and *P* = .81, respectively). TVR and ischemia-driven TLR were lower with XIENCE V (*P* = .0001 and *P* = .0002, respectively).

XIENCE V also outperformed TAXUS in the trial's secondary endpoint of MACE (4.9% vs 8.2%; *P* = .005). There was also less MI (2.8% vs 5.4%; *P* = .007) and stent thrombosis (ARC-defined definite and probable) (0.7% vs 2.6%; *P* = .002) at 1 year in the XIENCE V group versus the TAXUS group, respectively. Thus, the results of SPIRIT IV and COMPARE were remarkably consistent.

ISAR-DESIRE 2

The open-label Intracoronary Stenting and Angiographic Results: Drug-Eluting Stents for In-Stent Restenosis (ISAR-DESIRE) 2 trial randomly assigned 450 patients with in-stent restenosis after initial sirolimus-eluting stent implantation to additional sirolimus-eluting stents (n = 225) or paclitaxel-eluting stents (n = 225).[3] Baseline clinical characteristics were well matched between the 2 groups. About one-third of the study population had diabetes. Vessel size was 2.75 mm in both groups. As presented by Robert A. Byrne, MD, from the Deutsches Herzzentrum (Munich, Germany), the primary endpoint (late lumen loss at 6-8 mo) was equivalent between the 2 groups (0.40 mm vs 0.38 mm; *P* = .75). Binary restenosis (19.0% vs 20.6%; *P* = .69) and target lesion revascularization (16.6% vs 14.6%; *P* = .52) were also similar in both groups.

There were no significant differences between groups regarding death, MACE, MI, or stent thrombosis rates at 30 days. At 1 year, the composite endpoint of death, MI, or TLR, and the composite endpoint of death, MI, or stent thrombosis were also not different (Table 2).

Thus, for most patients with in-stent restenosis of sirolimus-eluting stents, treatment with either additional

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Table 1
SPIRIT IV, Outcomes at 1 Year

	XIENCE V® (%)	TAXUS® (%)	*P* Value
TVF[a]	5.6	7.9	.009
TLF[b]	4.2	6.8	.001
MACE[c]	4.2	6.9	.0009

MACE, major adverse cardiac events; MI, myocardial infarction; SPIRIT IV, Clinical Evaluation of the XIENCE V Everolimus Eluting Coronary Stent System in the Treatment of Subjects With de Novo Native Coronary Artery Lesions; TLF, target lesion failure; TLR, target lesion revascularization; TVF, target vessel failure; TVR, target vessel revascularization.
[a]TVF = cardiac death, MI, or TVR.
[b]TLF = cardiac death, target vessel MI, or TLR.
[c]MACE = cardiac death, MI, or TLR.
XIENCE V® is manufactured by Abbott Laboratories (Abbott Park, IL); TAXUS® is manufactured by Boston Scientific (Natick, MA).

Table 2
ISAR-DESIRE 2, Composite Clinical Outcomes at 1 Year

	Sirolimus-Eluting Stents (%)	Paclitaxel-Eluting Stents (%)	*P* Value
Death, MI, or stent thrombosis	6.1	6.3	.98
Death, MI, or TLR	20.4	19.6	.71

ISAR-DESIRE, Intracoronary Stenting and Angiographic Results: Drug-Eluting Stents for In-Stent Restenosis; MI, myocardial infarction; TLR, target lesion revascularization.

sirolimus-eluting stents or paclitaxel-eluting stents would appear to provide comparable outcomes, although the 1-year absolute event rates in both groups are relatively high, pointing to the need for new approaches after drug-eluting stent restenosis.

LEADERS

Follow-up data from the Limus Eluted From A Durable Versus Erodable Stent Coating (LEADERS) trial, which randomized 1700 patients with stable angina or acute coronary syndromes to a biolimus-eluting stent (BES) with an abluminal bioabsorbable polymer or a sirolimus-eluting stent (SES) with a durable polymer, were presented by Volker Klauss, MD, of University Hospital Munich (Munich, Germany).[4] The previously reported 1-year noninferiority of BES compared with SES for the primary endpoint of MACE (composite of cardiac death, MI, and clinically indicated TVR) was sustained at 2 years. Rates of cardiac death or MI and TVR were also similar for the 2 stents (Table 3).

In a subgroup analysis, patients with ST-segment elevation myocardial infarction (STEMI) experienced reduced MACE with BES compared with SES (8.1% vs 19.3%; *P* for superiority < .01).

Despite the all-comers nature of the cohort, very late stent thrombosis (beyond 1 year) was uncommon in both BES and SES groups (0.2% and 0.5%, respectively). Whether the theoretical advantages of the bioabsorbable polymer of the BES will further differentiate the late safety characteristics of these 2 stents will depend on the results of longer-term follow-up studies or additional larger studies.

Table 3
LEADERS, 2-Year Outcomes for BES Versus DES

	BES (%)	DES (%)	*P* Value*
MACE	13.0	15.4	.18
Cardiac death or MI	8.3	9.1	.59
TVR	7.7	8.8	.37

BES, biolimus-eluting stent; DES, drug-eluting stent; LEADERS, Limus Eluted From A Durable vs Erodable Stent Coating; MACE, major adverse cardiac events; MI, myocardial infarction; TVR, target vessel revascularization.
**P* for superiority.

SIRTAX-LATE

Results from the Sirolimus-Eluting Versus Paclitaxel-Eluting Stents for Coronary Revascularization (SIRTAX)-LATE trial showed that the superiority of CYPHER® (Cordis Corporation, New Brunswick, NJ) sirolimus-eluting stents compared with TAXUS paclitaxel-eluting stents for the composite of death, MI, and TLR at 9 months observed in the original SIRTAX trial was lost at 5-year follow-up (Table 4).[5] The early CYPHER advantage of reduced TLR was replaced by a higher rate of revascularization after about 2 years.

In addition, as reported by Lorenz Räber, MD, of University Hospital (Bern, Switzerland), although in-stent late loss favored CYPHER at 8 months (0.12 mm vs 0.25 mm; $P < .001$), minimal lumen diameter continued to decline with both stents, though somewhat more so with CYPHER, such that by year 5, there were no significant differences in late loss between CYPHER and TAXUS stents (0.30 mm vs 0.37 mm; $P = .21$). Moreover, low but steady rates of definite stent thrombosis were seen over the 5-year study period. Together, these findings suggest that vascular healing in response to first-generation stents is ongoing at 5 years after implantation, Dr. Räber observed. Studies are ongoing to determine whether the long-term outcomes with second generation DES are improved.

DEBATER

The duel goals of the Comparison of Drug Eluting and Bare Metal Stents With or Without Abciximab in ST-Elevation Myocardial Infarction (DEBATER) trial were to evaluate DES versus bare metal stents (BMS) and abciximab versus no abciximab in STEMI patients undergoing primary percutaneous coronary intervention (PCI).[6] In the stent arm of this 871-patient randomized trial, BMS or CYPHER sirolimus-eluting stents were assigned in a 1:1 ratio. The primary endpoint of target-vessel

Table 4
SIRTAX-LATE, Outcomes at 5 Years

	CYPHER® (%) (n = 488)	TAXUS® (%) (n = 486)	*P* Value
MACE[a]	21.3	24.2	.21
Death or MI	16.9	14.9	.46
TLR	14.9	17.9	.16

MI, myocardial infarction; SIRTAX-LATE, Sirolimus-Eluting Stent Compared With Paclitaxel-Eluting Stent for Coronary Revascularization-LATE; TLR, target lesion revascularization.
CYPHER® is manufactured by Cordis Corporation (New Brunswick, NJ); TAXUS® is manufactured by Boston Scientific (Natick, MA).
[a]Composite of death, MI, and TLR.

Table 5
DEBATER Stent Comparison, 1-Year Outcomes

	DES (%)	BMS (%)	*P* Value
TVF	8	12	.029
MACCE	13	20	.006

BMS, bare metal stent; DEBATER, Comparison of Drug Eluting and Bare Metal Stents With or Without Abciximab in ST-Elevation Myocardial Infarction; DES, drug-eluting stent; MACCE, major adverse cardiovascular and cerebrovascular events; TVF, target vessel failure.

failure as well as the secondary endpoint of major adverse cardiac and cerebrovascular events (MACCE), were reduced in the DES arm at 1 year (Table 5).

In the drug arm of the trial, patients receiving abciximab were given a bolus of 0.25 mg/kg 10 to 60 minutes before PCI, and an infusion of 0.125 µg/kg/min for 12 hours afterward. Patients receiving abciximab experienced a reduction in the primary endpoint of target vessel failure (TVF) at 30 days (2% vs 8%; $P = .001$), whereas rates of MACCE at 1 year were not significantly different (16% with abciximab vs 18% with no abciximab; $P = .31$). Rolf Michels, MD, PhD, of Catharina Ziekenhuis (Eindhoven, The Netherlands), who presented the results, indicated that the decrease in TVF with abciximab was driven by a lower incidence of stent thrombosis, but that patients receiving the drug experienced increased bleeding. These results were similar to what was previously seen in the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) trial.

Current and Emerging Pharmacologic Strategies

PLATO Invasive

The Platelet Inhibition and Patient Outcomes (PLATO) study analyzed outcomes with ticagrelor versus clopidogrel therapy in 18,624 patients with STEMI and non-STEMI. Ticagrelor is a new non-thienopyridine adenosine diphosphate (ADP) analogue, which is a more rapid and potent inhibitor of ADP-induced platelet activation than clopidogrel. As reported by Christopher P. Cannon, MD, of Brigham and Women's Hospital (Boston, MA), in the PLATO Invasive substudy, 13,408 patients with acute coronary syndromes (ACS) in whom an early invasive strategy was intended were randomized to ticagrelor (n = 6732) or clopidogrel (n = 6676) for 6 to 12 months.[7] The primary endpoint was the composite of CV death, MI, or stroke.

The investigators found a 16% reduction in the primary composite endpoint at 1 year with ticagrelor versus clopidogrel (9.02% vs 10.65%; $P = .0025$). Dr. Cannon also reported a significant 19% decrease in all-cause mortality as well as reductions in CV death and MI with ticagrelor (Table 6).

Patients with any stents who were assigned to ticagrelor also had lower rates of definite stent thrombosis (1.0% vs 1.6%; $P = .003$). No differences were reported in the overall rates of major bleeding, life-threatening bleeding, or fatal bleeding. Dyspnea was higher with ticagrelor versus clopidogrel (15.4% vs 10.4%; $P < .0001$), but was self-limited in most patients.

Thus, compared with clopidogrel, ticagrelor appears to effectively suppress adverse ischemic events without significantly increasing major bleeding. This favorable balance results in improved cardiac and all-cause mortality. Ticagrelor is currently undergoing US Food and Drug

Table 6
PLATO Invasive, 1-Year Outcomes

	Ticagrelor (%)	Clopidogrel (%)	*P* Value
All-cause death	3.9	5.1	.01
CV death	3.4	4.3	.025
MI	5.3	6.6	.002

CV, cardiovascular; MI, myocardial infarction; PLATO, Platelet Inhibition and Patient Outcomes.

Administration review for potential approval for sale in the United States.

CURRENT-STEMI PCI

Doubling the dose of clopidogrel before and for 1 week after primary PCI in STEMI patients appears beneficial, according to results from the Double-Dose Versus Standard-Dose Clopidogrel in ACS Patients Undergoing PCI for STEMI (CURRENT-STEMI PCI) trial, a postrandomization analysis of the Clopidogrel Optimal Loading Dose Usage to Reduce Recurrent Events/Optimal Antiplatelet Strategy for Interventions (CURRENT OASIS)-7 trial.[8] The double-dose group (n = 3171) received 600 mg of clopidogrel as a loading dose followed by 150 mg/d, stepped down to 75 mg/d after 7 days. The standard-dose group (n = 3175) received a 300-mg loading dose, then 75 mg/d. All patients then underwent PCI.

At 30 days, as reported by principal investigator Shamir Mehta, MD, MSc, from McMaster University (Hamilton, Ontario, Canada), efficacy outcomes favored the double-dose group with regard to stent thrombosis and MI, but with no significant differences in CV death or stroke (Table 7).

There was no significant difference between the 2 groups in major or severe bleeding.

In looking at stent type, the researchers found a relative risk reduction of 37% favoring the double dose of clopidogrel in patients receiving BMS (hazard ratio [HR] 0.63; 95% CI, 0.43-0.94) and 50% in patients receiving DES (HR 0.50; 95% CI, 0.30-0.85).

These data suggest a potential role for a higher dose of clopidogrel in patients with STEMI undergoing PCI. However, because these results represent a nonrandomized subgroup analysis from the entire 25,000 patient CURRENT OASIS-7 trial, they should be considered hypothesis generating.

COGENT

Nonrandomized studies have suggested that a significant interaction may exist between proton pump inhibitors and clopidogrel. At TCT 2009, Deepak L. Bhatt, MD, MPH, from the Thrombolysis in Myocardial Infarction (TIMI) Study Group (Boston, MA) reported the results from the randomized, controlled Clopidogrel and the Optimization of Gastrointestinal Events (COGENT) trial.[9] COGENT randomized 3627 patients receiving dual antiplatelet therapy (clopidogrel and aspirin) to either omeprazole or placebo. Omeprazole was formulated with clopidogrel to delay its release, thereby minimizing the chance of an interaction with clopidogrel metabolism. Patients were followed out to a median of 133 days (maximum of 362), during which there were 136 adjudicated CV events and 105 adjudicated gastrointestinal (GI) events.

The study found no difference in the likelihood of survival free from CV events (composite of CV death, nonfatal MI, coronary artery bypass graft [CABG] or PCI, or ischemic stroke) between the placebo and treatment groups (HR 1.02; 95% CI, 0.70-1.51). The incidence of composite GI events, including GI bleeding, symptomatic ulcer disease, obstruction, or perforation, was significantly lower in the omeprazole group, which had 38 events compared with 67 in the placebo arm (HR 0.55; 95% CI, 0.36-0.85; $P = .007$).

The results of COGENT are preliminary because researchers are still evaluating some patients. The trial was halted early for financial reasons. Nonetheless, these results are the best evidence to date suggesting that omeprazole may be beneficial in patients requiring dual antiplatelet therapy without a significant adverse CV interaction.

HORIZONS-AMI

Two-year data from Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction (HORIZONS-AMI) showed that STEMI patients undergoing PCI fare best with bivalirudin and TAXUS stents.[10]

HORIZONS-AMI was a randomized, multicenter trial that compared bivalirudin with heparin plus a glycoprotein (GP) IIb/IIIa inhibitor in 3602 STEMI patients. Of these patients, 3006 were eligible for

Table 7
CURRENT-STEMI PCI, 30-Day Outcomes

	Standard Clopidogrel (%) (n = 3175)	Double Clopidogrel (%) (n = 3171)	*P* Value
Definite ST	1.8	1.0	.006
All ST	3.5	2.5	.024
MI	1.9	1.2	.025
CV death	3.2	3.1	.73
Stroke	0.5	0.4	.58

CURRENT-STEMI PCI, Double-Dose Versus Standard-Dose Clopidogrel in ACS Patients Undergoing PCI for STEMI; CV, cardiovascular; MI, myocardial infarction; ST, stent thrombosis.

randomization, in a 3:1 ratio, to either TAXUS paclitaxel-eluting stents or Express BMS.

As presented by Dr. Stone, at 2 years bivalirudin significantly reduced non-CABG major bleeding by 36%, reinfarction by 25%, cardiac mortality by 41%, and all-cause mortality by 25% (Table 8). The bivalirudin and heparin plus GP IIb/IIIa arms had comparable rates of stent thrombosis, TVR, and stroke.

In the stent analysis, TAXUS significantly reduced ischemic TLR and TVR by 42% and 34%, respectively, compared with Express BMS, with no evidence of late catch-up (Table 9). Rates of all-cause mortality, CV mortality, reinfarction, and stent thrombosis were comparable between the 2 groups.

Of the 4 possible treatment combinations, the lowest cumulative 2-year mortality was observed in patients assigned to bivalirudin plus TAXUS (3.8%), and the highest was seen in those randomized to heparin plus a GP IIb/IIIa inhibitor and Express (6.1%).

TRITON-TIMI 38 Economic Substudy

The newly approved antiplatelet agent prasugrel was shown to be more cost effective than clopidogrel in patients with ACS undergoing PCI, according to the results of an economic analysis from the Trial to assess Improvement in Therapeutic Outcomes by Optimizing Platelet Inhibition With Prasugrel Thrombolysis In Myocardial Infarction (TRITON-TIMI) 38 study.[11] The subanalysis compared the total medical costs among 6705 patients randomized to receive 1 of the 2 drugs.

As presented by David Cohen, MD, from St. Luke's Hospital and the Mid America Heart Institute (Kansas City, MO), index hospitalization costs were similar with the 2 drugs ($19,752 with clopidogrel vs $19,740 with prasugrel), but rehospitalization costs were slightly higher with clopidogrel ($4982 vs $4465). However, the acquisition cost of prasugrel was higher: $1862 versus $1554 for clopidogrel.

Added together, the overall cost savings with prasugrel totaled $221 per 0.102 years of life expectancy gained when compared with clopidogrel. The savings were greater over the first 30 days of the trial (cost savings of $192 for 0.056 years of life expectancy gained) than those observed from day 31 to the end of the trial (cost savings of $28 for 0.053 years of life expectancy gained).

Table 8
HORIZONS AMI 2-Year Outcomes, Drug Arm Analysis

	Bivalirudin (%) (n = 1800)	Heparin (%) (n = 1802)	*P* Value
Major bleeding	6.4	9.6	< .001
Reinfarction	5.1	6.9	.038
Cardiac mortality	2.5	4.2	.005
All-cause mortality	4.6	6.1	.049

HORIZONS-AMI, Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction.

Table 9
HORIZONS-AMI 2-Year Outcomes, Stent Arm Analysis

	TAXUS® DES (%) (n = 2257)	Express® BMS (%) (n = 749)	*P* Value
TLR	6.8	11.6	< .001
TVR	8.9	13.3	< .001

BMS, bare metal stent; DES, drug-eluting stent; HORIZONS-AMI, Harmonizing Outcomes With Revascularization and Stents in Acute Myocardial Infarction; TLR, target lesion revascularization; TVR, target vessel revascularization.
TAXUS® and Express® BMS are manufactured by Boston Scientific (Natick, MA).

Improving Current Practice

FAME

Two-year results from the Fractional Flow Reserve Versus Angiography for Guiding PCI in Patients With Multivessel Coronary Artery Disease (FAME) trial confirm and extend the 1-year results reported at TCT 2008, namely that patients with multivessel disease experience a significant decrease in major adverse events if they undergo PCI guided by angiography plus fractional flow reserve (FFR) measurements compared with those who undergo standard angiography alone.

The new results presented by William F. Fearon, MD, of Stanford University Medical Center (Stanford, CA), showed that the total number of MACE was 105 in the FFR group and 139 in the angiography alone group.[12] This translated into significantly lower rates of MI and death/MI; there was also a strong trend for lower

death/MI/CABG/repeat PCI with FFR-guided treatment (Table 10).

The average number of indicated lesions per patient was 2.8 in the FFR group and 2.7 in the standard angiography group. The average number of stents per patient was 1.9 in the FFR group and 2.7 in the standard angiography group. Thus, by avoiding unnecessary stent implantation in non-ischemia–producing lesions, the use of FFR may improve long-term outcomes in patients undergoing PCI.

Symplicity I

Catheter-based renal denervation by radiofrequency ablation resulted in substantial and sustained blood pressure reduction without serious adverse events in patients with refractory hypertension, according to extended data from the first-in-human Symplicity I trial (Symplicity® Catheter System [Ardian Inc., Palo Alto, CA]) reported by Henry Krum, MD, of Monash University (Melbourne, Australia).[13] Investigators studied 70 patients with a systolic blood pressure (BP) ≥ 160 mm Hg despite taking ≥ 3 antihypertensive medications, including a diuretic.

A total of 89% of patients were considered responders, defined as experiencing ≥ 10 mm Hg reduction in systolic BP. Follow-up office-based assessments showed reductions from baseline in both systolic BP (−18 mm Hg) and diastolic BP (−11 mm Hg) beginning at 1 month and sustained through 12 months (−27 mm Hg systolic and −13 mm Hg diastolic; $P < .0001$).

The procedure was considered safe, with CT and magnetic resonance angiography of 38 patients at 6 months showing no chronic vascular complications. In addition, no significant declines in kidney function were seen after 12 months.

PROSPECT

The Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPECT) trial was the first prospective, multimodality imaging natural history study of atherosclerosis, enrolling 700 patients with ACS—either STEMI within 24 hours (30.3%), non-STEMI (65.6%), or unstable angina with electrocardiographic changes (4.2%)—who underwent successful PCI in 1 or 2 major coronary arteries at 37 centers in the United States and Europe.[14] The investigators performed quantitative coronary angiography of the entire coronary tree, intravascular ultrasound (IVUS), and virtual histology (VH).

Dr. Stone reported that over a median follow-up period of 3.4 years, culprit lesions (those originally treated) and nonculprit lesions (untreated areas of the coronary tree which were expected to remain stable) led to similar levels of MACE, a composite of cardiac death, cardiac arrest, MI, unstable angina, and increasing angina. Half of the events occurred within 1 year and half between 1 and 3 years.

Baseline clinical and angiographic factors were poor predictors of nonculprit lesion-related events. IVUS characteristics and VH plaque type, however, were much more informative. Among them, multivariable analysis found 3 independent predictors of lesion-level events (Table 11).

According to Dr. Stone, the prospective identification of nonculprit lesions prone to develop MACE within 3 years can be enhanced by characterization of underlying plaque morphology, with virtual histology-thin-cap fibroatheromas (VH-TCFA) representing the highest-risk lesion type. Specifically, the combination of large plaque burden detected by IVUS and a large necrotic core without a visible cap (ie, a VH-TCFA) identifies lesions that are at especially high risk for future adverse CV events.

BCIS-1

In the Balloon-pump Assisted Coronary Intervention-1 (BCIS-1) study, 301 high-risk PCI patients with

Table 10
FAME, 2-Year Outcomes

	Angiography Alone (n = 496)	Angiography Plus FFR (n = 509)	*P* Value
Total MACE	139	105	
Individual endpoints			
Death	19 (3.8)	13 (2.6)	.25
MI	48 (9.7)	31 (6.1)	.03
CABG or Re-PCI	61 (12.3)	53 (10.4)	.35
Composite endpoints			
Death or MI	63 (12.7)	43 (8.4)	.03
Death, MI, CABG, or Re-PCI	110 (22.2)	90 (17.7)	.07

CABG, coronary artery bypass graft; FAME, Fractional Flow Reserve Versus Angiography for Guiding PCI in Patients With Multivessel Coronary Artery Disease; FFR, fractional flow reserve; MACE, major adverse cardiac events; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Table 11
PROSPECT, Independent Predictors of Nonculprit Lesion Level MACE

Variable	OR (95% CI)	*P* Value
$PB_{MLA} \geq 70\%$	4.99 (2.54-9.79)	< 0.0001
VH-TCFA	3.00 (1.68-5.37)	.0002
MLA ≤ 4.0 mm^2	2.77 (1.32-5.81)	.007
Lesion length ≥ 11.6 mm	1.97 (0.94-4.16)	.07

CI, confidence interval; MACE, major adverse cardiac events; MLA, minimal luminal area; OR, odds ratio, PB_{MLA}, plaque burden at the minimal luminal area; PROSPECT, Providing Regional Observations to Study Predictors of Events in the Coronary Tree; VH-TCFA, virtual histology-thin-cap fibroatheroma.

impaired left ventricular function (ejection fraction ≤ 30%) and extensive myocardium at risk were randomized to elective use of intra-aortic balloon pump (IABP) or "no planned" IABP use.[15] Simon Redwood, MD, of St. Thomas' Hospital (London, United Kingdom) reported that there were no significant differences between the 2 strategies for the primary endpoint of MACCE at hospital discharge (14.6% for IABP vs 15.3% for no-IABP; $P = .35$) or for the individual endpoints of all-cause death, MI, stroke, or revascularization at hospital discharge. Likewise, 6-month mortality was similar for the 2 groups (4.6% for IABP vs 7.3% for no-IABP; $P = .32$). The incidence of procedural complications was lower in patients who received planned IABP.

In the no-planned IABP group, 18 patients (12%) received bailout IABP, most because of hypotension (72%); 4 of these patients (22%) suffered MACCE. Dr. Redwood underlined the "acceptable" in-hospital mortality of 1.3% and 6-month mortality of 6.0% in these patients despite poor left ventricular function and severe coronary disease.

CHARISMA Genomics

The Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management and Avoidance (CHARISMA) Genomics study sought to determine the effect of CYP2C19 polymorphisms on CV death, MI, or stroke in stable CV patients randomly assigned to clopidogrel or placebo.[16] Of 15,603 participants who were enrolled in the CHARISMA trial, 4862 consented to genotyping for CYP2C19*2, *3, and *17 alleles.

According to Dr. Bhatt, the CYP2C19*2 variant allele was not associated with an increase in CV events or bleeding in patients receiving clopidogrel therapy. Compared with the normally occurring CYP2C19 alleles, the *2/*2 variant was associated with an increased risk of CV death, MI, or stroke (HR 2.383; 95% CI, 1.14-5.00) among patients taking clopidogrel. However, there was also an increased risk among carriers of the same polymorphism in the placebo arm (HR 1.852; 95% CI, 0.74-4.65).

For the primary endpoint of moderate to severe bleeding, there was no significant effect of genotype on the risk from clopidogrel. For all Global Use of Strategies to Open Occluded Coronary Arteries (GUSTO) bleeding, however, the HR was 0.329 (95% CI,

Main Points

- The results of SPIRIT IV and COMPARE trials were remarkably consistent, in that they both proved that the XIENCE V® drug-eluting stent (DES) outperformed the TAXUS® DES in clinically driven endpoints such as major adverse cardiac events, target vessel revascularization, and nonfatal myocardial infarction.
- The SIRTAX-LATE trial results suggest that vascular healing in response to first-generation DES is ongoing at 5 years after device implantation.
- The platelet aggregation inhibitor ticagrelor was superior to clopidogrel in treating patients with acute coronary syndromes. Investigators found a 16% reduction in the primary composite endpoint of cardiovascular death, MI, or stroke.
- The FAME trial showed that patients with multivessel disease experience a significant decrease in major adverse coronary events if they undergo percutaneous coronary intervention (PCI) guided by angiography plus fractional flow reserve (FFR) measurements compared with those who undergo standard angiography alone. By avoiding unnecessary stent implantation in non-ischemia–producing lesions, the use of FFR may improve long-term outcomes in patients undergoing PCI.

0.160-0.619; $P = 4 \times 10^{-4}$) in participants with the *2*2 polymorphism who were treated with clopidogrel. ■

References

1. Stone GW. SPIRIT IV: a prospective, randomized trial comparing an everolimus-eluting stent vs. a paclitaxel-eluting stent in patients with coronary artery disease: One-year clinical results. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 23, 2009; San Francisco, CA.
2. Smits PC. COMPARE: a prospective randomized trial of everolimus-eluting vs. paclitaxel-eluting stents. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 23, 2009; San Francisco, CA.
3. Byrne RA. ISAR-DESIRE 2: a prospective randomized trial of paclitaxel-eluting vs. sirolimus-eluting stents for treatment of coronary restenosis in sirolimus-eluting stents. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 23, 2009; San Francisco, CA.
4. Klauss V. LEADERS: a prospective, randomized, noninferiority trial comparing a biolimus-eluting stent with biodegradable polymer vs. a sirolimus-eluting stent with durable polymer: two-year clinical follow-up. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 23, 2009; San Francisco, CA.
5. Räber L. SIRTAX-LATE: five-year clinical and angiographic follow-up from a prospective randomized trial comparing sirolimus-eluting with paclitaxel-eluting stents. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 23, 2009; San Francisco, CA.
6. Michels R. DEBATER: a comparison of drug-eluting stents and bare metal stents with or without abciximab in ST-segment elevation myocardial infarction: the Eindhoven Reperfusion study. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 25, 2009; San Francisco, CA.
7. Cannon CP. PLATO Invasive: a prospective, randomized, placebo-controlled trial of ticagrelor vs. clopidogrel in patients with ACS managed with an invasive strategy. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 24, 2009; San Francisco, CA.
8. Mehta SR. CURRENT-STEMI PCI: double-dose vs. standard-dose clopidogrel in ACS patients undergoing PCI for STEMI. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 24, 2009; San Francisco, CA.
9. Bhatt DL. COGENT: a prospective, randomized, placebo-controlled trial of omeprazole in patients receiving aspirin and clopidogrel. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 24, 2009; San Francisco, CA.
10. Stone GW. HORIZONS AMI: two-year follow-up from a prospective randomized trial of heparin plus glycoprotein IIb/IIIa inhibitors vs. bivalirudin and paclitaxel-eluting vs. bare metal stents in STEMI. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 25, 2009; San Francisco, CA.
11. Cohen DJ. TRITON-TIMI 38 ECONOMIC SUBSTUDY: cost-effectiveness of prasugrel vs. clopidogrel from a prospective randomized trial of patients with ACS undergoing PCI. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 24, 2009; San Francisco, CA.
12. Fearon WF. FAME: two-year follow-up from a prospective randomized trial of FFR-guided vs. angiography-guided PCI in patients with multivessel coronary artery disease. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 23, 2009; San Francisco, CA.
13. Krum H. SYMPLICITY I: sympathetic renal denervation in resistant hypertension: one-year results. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 25, 2009; San Francisco, CA.
14. Stone GW. PROSPECT: a natural history study of atherosclerosis using multimodality intracoronary imaging to prospectively identify vulnerable plaque. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 25, 2009; San Francisco, CA.
15. Redwood S. BCIS-1: a prospective randomized trial of intra-aortic balloon pump counterpulsation in high-risk patients undergoing PCI. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 25, 2009; San Francisco, CA.
16. Bhatt DL. CHARISMA GENOMICS SUBSTUDY: evaluation of the CYP2C19 polymorphism in a prospective, randomized, placebo-controlled trial of chronic clopidogrel use for primary and secondary prevention. Paper presented at: 21st Annual Transcatheter Cardiovascular Therapeutics Scientific Symposium; September 24, 2009; San Francisco, CA.