Best of TCT 2005

Highlights from the Transcatheter Cardiovascular Therapeutics Meeting, October 16-21, 2005, Washington, DC

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Key words: ENDEAVOR III • ISAR-TEST • LE MANS • PLAATO • Platelet Resistance • SISR • TENACITY

The 2005 Transcatheter Cardiovascular Therapeutics (TCT) provided an excellent opportunity to garner new information on advances in a wide variety of techniques, ranging from complex coronary and peripheral percutaneous interventions to percutaneous treatment of cardiac valvular abnormalities, as well as subjects including cardiac imaging, platelet biology, and the relationship between chronic kidney disease and coronary artery disease. Our editorial board has reviewed some of the most important presentations of this meeting and how they can impact physician practice.

Reviewed by David P. Faxon, MD, FACC, FAHA, The University of Chicago Pritzker School of Medicine, Chicago, IL; Alice K. Jacobs, MD, FACC, FAHA, Boston University Medical Center, Boston, MA; Norman E. Lepor, MD, FACC, FAHA, The David Geffen School of Medicine at UCLA, Cedars-Sinai Medical Center, Los Angeles, CA; Alan C. Yeung, MD, Stanford University School of Medicine, Stanford, CA

ISAR-TEST Trial

An issue of great interest with regard to the short- and long-term safety and efficacy of drug-eluting coronary stents is whether those that utilize a polymer for drug delivery induce chronic inflammation, which may be associated with delayed re-endothelialization and associated stent thrombosis. It has also been observed that when stents are expanded, the polymer can partially unfold off the stent and create a web at the implant site. The Intracoronary Stenting and Angiographic Restenosis: Test Equivalence Between 2 Drug-Eluting Stents (ISAR-TEST) study compared the Yukon rapamycin-eluting stent (polymer-free microporous coated) and the Yukon Express^2 paclitaxel-eluting stent (both Translumina GmbH, Munich, Germany). Dr. Adnan Kastrati of the Deutches Herzzentrum in Munich, Germany, presented the results of this trial.

Patients (n = 450) were randomized to the polymer-free or polymer-based stents. Eighty one percent of patients underwent follow-up coronary angiography at 6 to 8 months

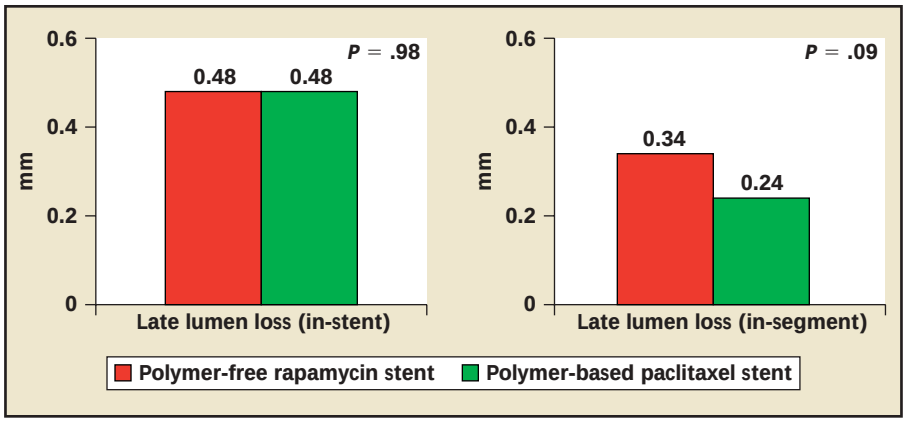

Figure 1. *Late loss results from the ISAR-TEST trial of the Yukon polymer-free drug-eluting stent versus the Yukon Express[2] polymer-based stent (both Translumina GmbH, Munich, Germany).*

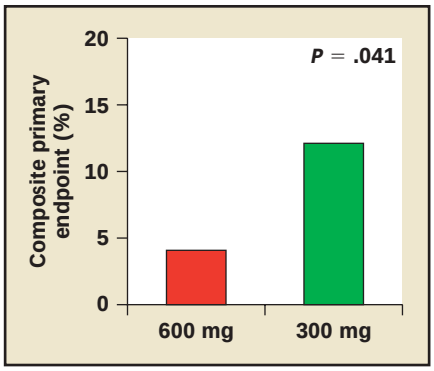

Figure 2. *Results of the ARMYDA-2 trial of clopidogrel prior to PCI for patients with non-ST-elevation myocardial infarction. The primary endpoint was a composite of cardiac death, MI, or target vessel revascularization, and was seen more commonly in the 300 mg clopidogrel group than the 600 mg clopidogrel group. It seems clear that the larger bolus dose of 600 mg of clopidogrel is associated with better outcomes in this relatively low-risk population of patients.*

with all patients followed up clinically after 9 months. Baseline characteristics were similar between the 2 study groups. The primary endpoint of in-stent late loss was similar in the 2 groups (Figure 1). There was no difference in stent occlusion (0.4% vs 0.9%), death (0.9% vs. 1.3%), or the composite of death or myocardial infarction between the polymer-based and polymer-free groups (4.4% vs. 4.0%, respectively). In addition, there was no significant difference in angiographic restenosis (14.2% vs. 15.5%; $P = 0.73$) and clinical restenosis (9.3% in both groups). The results of this study would seem to mollify some of the concern regarding the use of this particular polymer-based system in regard to complications, including stent thrombosis.

Platelet Resistance

Three trials were presented that showed the inferiority of the 300 mg dose of clopidogrel for anti-platelet therapy, when compared to the 600 mg dose. They also demonstrated a lack of incremental benefit at a dosage of 900 mg.

ARMYDA-2 Trial

The Anti-platelet Therapy for Reduction of Myocardial Damage During Angioplasty (ARMYDA-2) trial results were presented by Germano Di Sciascio, MD, of the Universita Campus Bio-Medico in Rome, Italy. This trial randomized 329 patients with stable angina or non-ST segment elevation myocardial infarction (NSTEMI) to receive clopidogrel at a dose of 300 mg or 600 mg prior to percutaneous coronary intervention (PCI). The overall patient population studied was relatively low risk with 75% having chronic stable angina and only 25% presenting with acute coronary syndromes. Mean left ventricular ejection fractions measured between 52% and 54%, blood creatinine levels averaged 1.0 mg/dL, and fewer than 33% of subjects had multivessel coronary artery disease. The oral clopidogrel bolus was given at a mean of 6 hours prior to PCI. The primary endpoint (a composite of cardiac death, MI, or target vessel revascularization) was seen more commonly in the 300 mg group than the 600 mg group (Figure 2). It seems clear that the larger bolus dose of 600 mg of clopidogrel is associated with better outcomes in this relatively low-risk population of patients that did not include those with STEMI.

In real life situations where patients are taken urgently to the catheterization lab for treatment of NSTEMI or STEMI, we cannot be certain that 600 mg doses of clopidogrel, given less than 6 hours prior to PCI, will provide the level of protection that was observed with an imposed 6-hour interval from dosing to intervention. Therefore, the question of whether novel thienopyridines, such as prasugrel, with more rapid onset of action and increased ability to block platelet activation, will provide even more protection during the interval from 0 to 6 hours between dosing and intervention, needs to be answered. In addition, if optimal platelet-activation blockade cannot be achieved with clopidogrel within the 6 hours following its dosing in order to block the platelet proaggregatory effects of unfractionated heparin (UFH), then serious consideration for the concomitant use of a GP IIb/IIIa inhibitor such as abciximab or replacement of UFH with the direct thrombin inhibitor bivalirudin, which does not exert this effect, should be considered.

ISAR-CHOICE Trial

Dr. Kastrati also presented the results of the Intracoronary Stenting and Antithrombotic Regimen:

Choose Between 3 High Oral Doses for Immediate Clopidogrel Effect (ISAR-CHOICE) trial comparing the pharmacokinetics and pharmacodynamics of 3 loading doses of clopidogrel: 300 mg, 600 mg, and 900 mg. Sixty patients with suspected or documented coronary artery disease admitted for coronary angiography were included in this trial. They were allocated to 1 of the 3 clopidogrel loading doses in a double-blinded, randomized manner. Plasma concentrations of the active thiol metabolite, unchanged clopidogrel, and the inactive carboxyl metabolite of clopidogrel were determined before and serially after drug administration. Optical aggregometry was performed before and 4 hours after drug administration. Loading with 600 mg resulted in higher plasma concentrations of the active metabolite, clopidogrel, and the carboxyl metabolite compared with loading with 300 mg ($P < .03$) as well as lower values for adenosine diphosphate-induced platelet aggregation, 4 hours after drug administration ($P = 0.01$ and 0.004). With administration of 900 mg, no further increase in plasma concentrations of active metabolite and clopidogrel and no further suppression of adenosine diphosphate-induced platelet aggregation were achieved, when compared with administration of the 600 mg bolus.

These results showed a ceiling of effect at the 600 mg dose, as there was no incremental increase in serum blood concentration or ability to inhibit platelet activity going from the 600 mg to the 900 mg dose. There was speculation that the inability of the 900 mg dose to show enhanced pharmacokinetics beyond that observed with the 600 mg dose may be due to limits of intestinal absorption. It is therefore unlikely that the 900 mg dose will be useful in overcoming the platelet resistance to lower doses of clopidogrel observed in some patients.

ALBION Trial

Higher doses of clopidogrel prior to PCI may improve outcomes in patients with stable angina or non-ST-elevation MI, according to Gilles Montalescot, MD, PhD, from the Department of Cardiology at Pitié-Salpêtrière Hospital in Paris, France. Results of the Assessment of the Best Loading Dose of Clopidogrel to Blunt Platelet Activation, Inflammation, and On-Going Necrosis (ALBION) trial demonstrated the superiority of clopidogrel when administered at 600 mg or 900 mg doses.

In comparison to the 300 mg dose of clopidogrel, the 600 mg and 900 mg doses were associated with more rapid and higher levels of inhibition of platelet aggregation and greater reductions in platelet activation, particularly when given in the first 24 hours following a cardiac event (Figure 3). However there was

Figure 3. *Troponin I-level **(A)** and platelet-inhibition **(B)** results from the ALBION trial of clopidogrel prior to percutaneous coronary intervention (PCI) in patients with stable angina or non-ST-elevation myocardial infarction. Comparing the 300 mg, 600 mg, and 900 mg doses of clopidogrel, there was no significant change in the levels of troponin release at day 2 following PCI. However, in comparison to the 300 mg dose, the 600 mg and 900 mg doses were associated with more rapid and higher levels of inhibition of platelet aggregation and greater reductions in platelet activation, particularly when given in the first 24 hours following a cardiac event.*

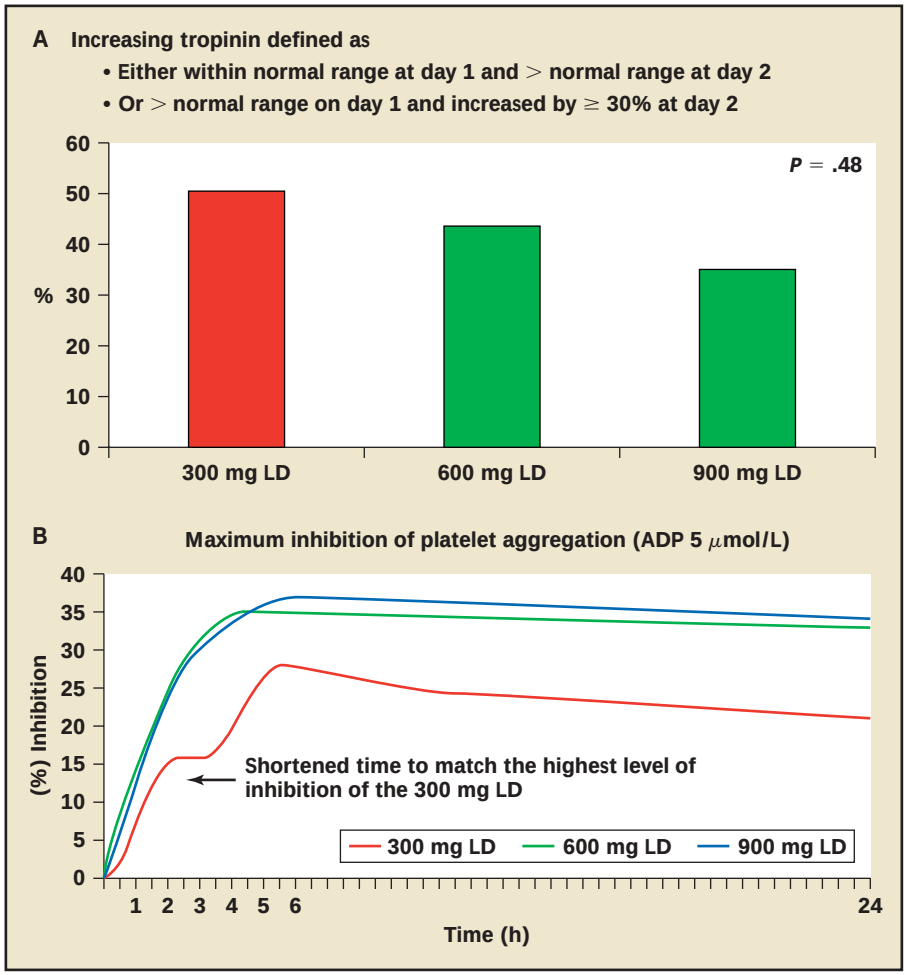

Figure 4. *Illustration of the Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO) device (Appriva Medical, Sunnyvale, CA) for implantation in atrial fibrillation patients in whom warfarin is contraindicated.*

no difference between the 600 mg and 900 mg doses of clopidogrel. Comparing the 300 mg, 600 mg, and 900 mg doses of clopidogrel, there was no significant change in the levels of troponin release at day 2 following PCI.

PLAATO Trial

The Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO) device trial evaluated the percutaneous, trans-septal implantation of a self-expanding nitinol cage covered with expanded polytetrafluoroethylene, in 111 atrial fibrillation patients in the United States and Europe, in whom the use of warfarin was contraindicated. (Figure 4). Evelyn Fischer, MD, of the CardioVasculares Centrum Sankt Katharien, Frankfurt/Main, Germany, found that PLAATO (Appriva Medical, Sunnyvale, CA) reduced the annual incidence of stroke from 6.3% to 3.6%. There were three patients in whom the device could not be implanted. During the peri-implant period, four patients experienced cardiac tamponade. These findings could represent an important development in the treatment of atrial fibrillation, particularly in patients at high risk for hemorrhagic complications from anticoagulation with warfarin.

[Norman E. Lepor, MD, FACC, FAHA]

Table 1
Angiographic and IVUS Results at 8 Months in the ENDEAVOR III Trial

Endpoints	Endeavor™ (zotarolimus) (n = 282)	Cypher® (sirolimus) (n = 94)	*P* Value
In-stent mean lumen diameter (mm)	2.08	2.52	< .001
In-segment mean lumen diameter (mm)	1.92	2.16	< .001
In-stent diameter stenosis (%)	24.3	11.0	<.001
In-segment diameter stenosis (%)	29.9	23.9	< .001
In-stent binary restenosis (%)	9.2	2.1	.02
In-segment binary restenosis (%)	11.7	4.3	.04
In-stent late loss (mm)	**0.60**	**0.15**	**< .001**
In-segment late loss (mm)	**0.34**	**0.13**	**< .001**

IVUS, intravascular ultrasound.
Endeavor,™ Abbott Laboratories, Abbott Park, IL; Cypher®, Cordis Cardiology, Miami Lakes, FL.

ENDEAVOR III Trial

As currently marketed drug-eluting stents (DES) have fulfilled their promise to significantly decrease restenosis in comparison to bare metal stents, new stents utilizing new drug elutions with the potential to be at least as effective as those currently in use continue to be evaluated. One such stent, a cobalt-alloy metal coated with the compound formerly known as ABT-578 (another "-limus" agent), was evaluated in ENDEAVOR III, a prospective, randomized trial comparing zotarolimus with the sirolimus-eluting stent, which was presented by David Kandzari, MD, of the Duke University Medical Center in Durham, NC.

At 30 sites, 436 patients underwent percutaneous coronary intervention in native lesions between 14 mm and 27 mm in length and vessel diameters between 2.5 mm and 3.5 mm. Patients were randomized to the zotarolimus- or sirolimus-eluting stent in a 3:1 single blind design. The primary endpoint of the study was late lumen loss at 8 months. The study was designed to show that the zotarolimus-eluting stent was statistically non-inferior to the sirolimus-eluting stent. Secondary endpoints included rates of target lesion and target vessel revascularization (TLR/TVR) and target vessel failure (TVF) at 9 months.

As expected, based on the results of ENDEAVOR II, late lumen loss (Table 1) was significantly higher as were in-stent (9.2% vs 2.1%) and in-segment (11.7% vs 4.3%) binary restenosis rates in the zotarolimus- compared with the sirolimus-eluting stent. However, there were no differences in TLR, TVR, or TVF between groups and non-Q wave myocardial infarction occurred significantly less often in patients treated with the zotarolimus-eluting stent (Table 2).

Comments

The reasons for the difference in late loss between these 2 "-limus" stents are unclear but differing elution kinetics or different molecular properties of the drugs have been implicated. Whether the increase in late

Table 2
Clinical Results at 9 Months in the ENDEAVOR III Trial

Endpoints	Endeavor™ (zotarolimus) (n = 316)	Cypher® (sirolimus) (n = 113)	*P* Value
MACE (%)	7.6	7.1	NS
Target lesion revascularization (%)	**6.3**	**3.5**	**NS**
Non-Q-wave MI (%)	0.6	3.5	0.04
Target vessel revascularization (%)	**6.0**	**5.3**	**NS**
Target vessel failure (%)	**12.0**	**11.5**	**NS**

MACE, major adverse cardiac events; MI, myocardial infarction.
Endeavor,™ Abbott Laboratories, Abbott Park, IL; Cypher®, Cordis Cardiology, Miami Lakes, FL.

loss will translate into greater late TVR rates will require further study. However, despite these differences in the surrogate endpoint, ongoing enthusiasm for ENDEAVOR IV is fueled by the similar clinical outcomes, the excellent deliverability of the zotarolimus-eluting stent, and the potential that more late loss may translate into less stent thrombosis long-term. ENDEAVOR IV will compare incidence of TVR utilizing the zotarolimus stent versus a paclitaxel-eluting stent.

SISR Trial

Sirolimus-Eluting Stent Versus Intravascular Brachytherapy in the Treatment of Patients with In-Stent Restenotic Coronary Lesions

To date, intravascular brachytherapy is the only approved therapy for treatment of in-stent restenosis, based on its ability to significantly reduce neointimal hyperplasia within the treated lesion. Due to the potential of drug-eluting stents to achieve similar results in this setting and to the cumbersome nature and logistical considerations inherent in the delivery of brachytherapy, the results of the SISR trial, as presented by David Holmes, MD, of the Mayo Clinic, Rochester, MN, comparing brachytherapy with the sirolimus-eluting stent in reducing in-stent restenosis have been long awaited.

SISR was a multicenter, randomized trial designed to demonstrate either superiority or non-inferiority of the sirolimus-eluting stent in the treatment of native coronary artery in-stent (bare metal) restenotic lesions. In 384 patients with lesions between 15 mm and 40 mm in length and in vessels between 2.5 mm and 3.5 mm in diameter, the sirolimus-eluting stent (Cypher, Cordis Cardiology) or intravascular brachytherapy (beta or gamma radiation) were randomly assigned in a 2:1 fashion. The primary endpoint of the trial was target vessel failure (TVF) at 9 months.

As expected, baseline clinical, angiographic, and procedural characteristics were similar between groups, with the exception of a higher prevalence of renal insufficiency and of totally occluded lesions in the sirolimus-eluting stent group. Procedural, lesion, and device success were also similar in both groups. The primary endpoint, TVF at 9 months, occurred in 12.4% and 21.6% ($P = .023$) of patients in the sirolimus-eluting stent and brachytherapy groups, respectively. Target lesion and target vessel revascularization rates were also significantly lower in the sirolimus-eluting stent group (Table 3).

Although angiographic analysis at 6 months revealed similar late lumen loss for the analysis segment and proximal edge, at the distal edge patients in the sirolimus-eluting stent group had significantly less lumen loss in comparison to the brachytherapy group (0.04 vs 0.21 mm, $P < .001$). In the analysis segment, diameter stenosis was 32.35% versus 40.97%, $P < 0.001$, and in the injury segment was 21.13% versus 29.73%, $P = .004$ in the sirolimus-eluting stent and vascular brachytherapy groups, respectively (Table 4). There were two cases of stent thrombosis in the sirolimus-eluting stent group and none in the brachytherapy group.

Table 3
SISR: 9-Month Clinical Outcomes

Endpoint	Sirolimus-eluting stent (%) (n = 259)	Brachytherapy (%) (n = 125)	*P* value
Target vessel failure*	**12.4**	**21.6**	**.023**
Target vessel revascularization	10.8	21.6	.008
Target lesion revascularization	8.5	19.2	.004

*Primary endpoint.

Table 4
SISR: 6-Month Late Loss

Endpoint	Sirolimus-eluting stent (n = 259)	Brachytherapy (n = 125)	*P* value
Analysis-segment late loss (mm)	0.27	0.33	NS
Proximal-edge late loss (mm)	0.10	0.15	NS
Distal-edge late loss (mm)	0.04	0.21	<.001

Comments

The results of this trial, which lag behind clinical practice, provide the evidence upon which to enthusiastically support use of the sirolimus-eluting stent in the treatment of in-stent restenosis in native coronary lesions. The differences between the sirolimus-eluting stent and vascular brachytherapy groups translate into better lumen dimensions and clinical outcomes with use of the sirolimus-eluting stent. Safety issues concerning rates of stent thrombosis, the observed trend toward reduction in TVF at 9 months in a subgroup analysis of diabetic patients, and the optimal treatment of drug-eluting in-stent restenosis must await further study before the few remaining institutions performing intravascular brachytherapy definitively discard their brachytherapy equipment.

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

Left Main PCI: Results of the LE MANS Trial

Left main (LM) coronary artery disease has been decisively shown to lead to more negative long-term outcomes than other types of coronary artery disease, including three vessel disease. Early trials of coronary bypass surgery demonstrated that revascularization of patients with severe LM disease (> 70% stenosis) was far more effective at improving outcomes than medical therapy. Thus it has become standard practice to treat LM disease with coronary artery bypass grafting (CABG) whenever it is discovered, regardless of patient symptoms. Early experience with angioplasty for LM disease was disappointing, yielding high rates of mortality and restenosis. Even with new techniques, such as atherectomy and bare metal stent placement, outcomes were unfavorable. However, in the current era of drug-eluting stents, this may be changing.

Three recently published, non-randomized studies have shown very low rates of mortality and restenosis incidence over follow-up periods of 6 months to 1 year. In addition, recent experiences in Europe and Asia have confirmed favorable short and intermediate outcomes seen with drug-eluting stents. In the US, the experience has been limited, largely confined to the treatment of patients with protected left main disease or those with unprotected left main disease who are considered to be at too high a risk for surgery. American College of Cardiology/American Heart Association guidelines make the Class 1 recommendation that patients with unprotected left main disease, who are candidates for surgery, be treated with CABG. Surgery has been highly effective in improving outcomes in these patients and improvements in surgical technique have reduced rates of operative mortality and improved long-term outcomes. Given these advances in CABG and those in percutaneous coronary intervention (PCI) with the utilization of drug-eluting stents, a randomized comparison of the two techniques in left main disease is sorely needed. The Prospective, Randomized Trial of Stent Implantation versus Bypass Graft Surgery in Patients with Left Main Coronary Artery Disease (LE MANS) trial is the first of a number of such comparisons and was recently reported at this year's TCT meeting.

Dr. Pawel Buszman, of the University of Silesia, Katowice, Poland, and colleagues reported the results of this first randomized trial of PCI compared to CABG in patients with left

Table 5
Design and Study Populations in the LE MANS Randomized Trial

	PCI Group	CABG Group
Total patients	163	184
Patients randomized to treatment	52	53
Distal left main lesions	58%	62%
Average EuroScore	3.3	3.0
Mean number of vessels treated	2.3 (35% via DES)	2.9 (79% via LIMA)
Average in-hospital days per patient	6.8	12

CABG, coronary artery bypass graft; DES, drug-eluting stent; LIMA, left internal mammary artery graft; PCI, percutaneous coronary intervention.

Table 6
Outcome Results from the LE MANS Randomized Trial

Outcome (30 days)	PCI (n = 52)	CABG (n = 53)	*P* value
Death	0	2	
MI	1	2	
CVA	0	2	
MACE	2 (3.8%)	9 (20.7%)	< .02
Outcome (1-12 months)			
Death	1	2	
MI/CVA	0	0	
Revascularization	8	7	
MACE	11 (21%)	11 (20%)	ns

CABG, coronary artery bypass graft; MI, myocardial infarction; CVA, cardiovascular accident; MACE, major adverse coronary event; PCI, percutaneous coronary intervention.

main disease (Tables 5 and 6). They randomized 52 of 163 eligible patients to PCI and 53 of 184 eligible patients to CABG. The primary endpoint of the study was left ventricular ejection fraction along with functional capacity and anginal status. The secondary endpoints were major adverse cardiac events and survival. Fifty percent to 60% of these patients had distal left main lesions. Only left main vessels less than 3.8 mm in diameter were included in the study. In general, the patients were low risk as shown by low EuroScores, a measure of operative risk. Most of the patients had multi-vessel disease with mean 2.3 to 2.9 vessels treated. The majority (79%) of the patients undergoing CABG had a left internal mammary artery graft. Drug-eluting stents were used in 35% of the patients receiving PCI.

The study demonstrated an average increase in ejection fraction from 55% to 60% in the PCI group but no change in the CABG group. Angina status and exercise test results were similar. The MACE rates were significantly lower in the PCI group at 30 days but by 1 year they were similar in the 2 groups.

The study is of interest because it is the first of a series of trials on this topic. However, it can be criticized on a number of points. First, it is a very small study, underpowered to look at any endpoint other than MACE. The use of DES in only 35% of the PCI patients would also be expected to result in poorer outcomes in that group. The primary endpoint of left ventricular ejection fraction is unusual and would not be considered in most trials. Nevertheless, a significant difference would be clinically relevant in the selection of the type of revascularization. The overall group was very low risk and may not reflect the current clinical practice of PCI and CABG. Clearly more and larger trials are necessary.

The SYNTAX trial is currently ongoing and will randomize 1500 patients with either left main disease or three vessel disease. The primary endpoint is MACE at one year but patients will be followed for 5 years. The COMBAT trial is a 1500 patient study, conducted primarily in Asia, that will randomize only left main disease and will look at MACE at 2 years with a 5-year follow-up as well. The results of these 2 larger trials will need to be examined before PCI can be accepted as an alternative for patients with left main disease. In addition, the optimal technique to be used in bifurcation lesions, as well as the types of patients who would be the best candidates for PCI, remains to be determined.

[David P. Faxon, MD, FACC, FAHA]

TENACITY Trial

The Final Word

Thus far, the only head-to-head comparison trial of glycoprotein (GP) IIb/IIIa inhibitors in PCI, the TARGET Trial, has shown that tirofiban was inferior to abciximab when comparing the primary endpoint of death, myocardial infarction, or urgent TVR at 30 days (7.6% vs 6.0%, $P = .038$). Since those results were announced, however, it has become clear that the dose of tirofiban studied was insufficient to achieve the desired level of platelet inhibition during PCI and a new trial, the Tirofiban Evaluation of Novel Dosing vs. Abciximab with Clopidogrel and Inhibition of Thrombin Study (TENACITY) was organized, with the aim of studying a higher dose of tirofiban versus abciximab. Patients were administered the 2 drugs for head-to-head comparison, then further randomized to receive heparin or bivalirudin concomitantly (Figure 5). All patients studied had moderate- to high-risk clinical and angiographic profiles. Tirofiban was administered in a 25 μg/kg bolus (instead of the 10 μg/kg used in TARGET) and infused continually at 0.15 μg/kg/min for 12 hrs. Abciximab was given in the standard dose. Unfortunately, this trial, which was designed to randomize 8000 patients, was terminated due to a loss of funding, as reported by Dr. David J. Moliterno of

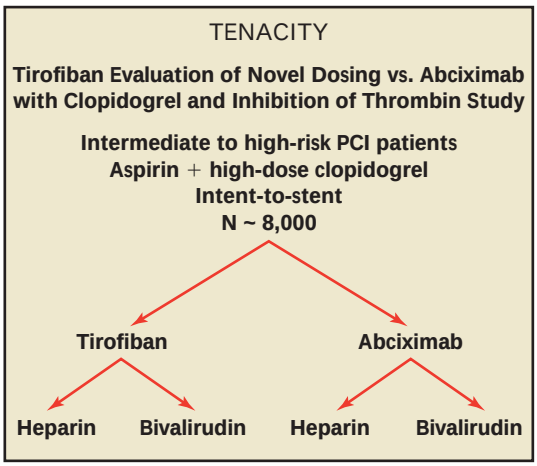

Figure 5. *Intended study design for the TENACITY trial. Only 383 patients were randomized before the trial was terminated.*

the University of Kentucky in Lexington, KY.

Before the trial was terminated, 383 patients were enrolled into the 2 arms. The 30-day MACE of death, MI, and urgent TVR was 6.9% versus 8.8% (tirofiban and abciximab, respectively, $P = 0.5$). The overall heparin versus bivalirudin event rates were 8.1% and 7.6%, respectively ($P = 0.86$). Bleeding rates were lower in the bivalirudin arm, consistent with the findings of the REPLACE-2 trial. Further stratification into abciximab/heparin, abciximab/bivalirudin, tirofiban/heparin, and tirofiban/bivalirudin arms resulted in MACE rates of 8.1%, 9.5%, 8.1% and 5.6% respectively. Adding major bleeding to the above yielded statistics of 9.1%, 10.5%, 10.1%, and 5.6% respectively. The statistical significance is unknown as each of these subsets is too small in number.

It is unfortunate that this trial will never be completed. The preliminary results are encouraging and support the notion that if the same amount of platelet inhibition can be achieved, the clinical outcomes among GP IIb/IIIa inhibitors will be very similar. The data also suggest that the use of a small molecule GP IIb/IIIa inhibitor plus bivalirudin, in this higher-risk patient subset, may be a very good alternative as adjuvant therapy for PCI. More information will become available regarding the treatment of higher-risk patients with the release of results from the ongoing ACUITY trial. ■

[Alan C. Yeung, MD]

Main Points

- The results of three trials (ARMYDA-2, ISAR-CHOICE, and ALBION) showed a ceiling of effect at a 600 mg dose of clopidogrel as anti-platelet therapy in patients undergoing percutaneous coronary intervention (PCI). This effect was seen in measures of both anti-aggregatory efficacy and levels of absorption of the active metabolite.
- A trial of the Percutaneous Left Atrial Appendage Transcatheter Occlusion (PLAATO) device evaluated the percutaneous, trans-septal implantation of a self-expanding nitinol cage covered with expanded polytetrafluoroethylene, in atrial fibrillation patients in whom the use of warfarin was contraindicated; it showed a reduced annual incidence of stroke, from 6.3% to 3.6%, with use of the device.
- In the ENDEAVOR III trial of a new zotarolimus-eluting stent versus a sirolimus-eluting stent for PCI in native lesions, late lumen loss was significantly higher as were in-stent and in-segment binary restenosis rates with the zotarolimus-eluting stent. However, there were no differences in TLR, TVR, or TVF between groups and non-Q wave myocardial infarction occurred significantly less often in patients treated with the zotarolimus-eluting stent.
- In the SISR trial, although angiographic analysis at 6 months revealed similar late lumen loss for the analysis segment and proximal edge, at the distal edge patients in the sirolimus-eluting stent group had significantly less lumen loss in comparison to the brachytherapy group.
- The LE MANS trial, comparing percutaneous coronary intervention (PCI) to coronary artery bypass grafting in patients with left main disease, showed an advantage to treatment with PCI at 30 days but no difference at 1-year-follow-up. It was a small study, underpowered to look at any endpoint other than major adverse coronary events; more and larger trials are necessary to definitively recommend one therapy over the other in these patients.
- Preliminary results of the TENACITY trial are encouraging and support the notion that if the same amount of platelet inhibition can be achieved, the clinical outcomes among GP IIb/IIIa inhibitors will be very similar. The data also suggests that the use of a small molecule GP IIb/IIIa inhibitor plus bivalirudin, in this higher-risk patient subset, may be a very good alternative as adjuvant therapy for PCI.