Drug-Eluting Stents Favored in ST-Elevation MI

BY PATRICE WENDLING    Chicago Bureau

Chicago — The rate of major adverse cardiac events was roughly halved at 8 months by the use of sirolimus-eluting stents, compared with bare-metal stents in a randomized trial of 743 patients who underwent percutaneous coronary intervention for ST-segment elevation MI. The Multicentre Evaluation of Single High-Dose Bolus Tirofiban vs. Abciximab with Sirolimus-Eluting Stent or Bare-Metal Stent in Acute Myocardial Infarction Study (MULTISTRATEGY) also found that tirofiban was noninferior to abciximab in resolving ST elevation at 90 minutes.

"These findings may provide a robust scientific rationale for high-dose tirofiban as an alternative to abciximab in patients with STEMI," Dr. Marco Valgimigli said in a statement.

The open-label, 2-by-2 factorial trial showed that at 8 months, major adverse cardiac events (MACE) occurred in 29 of 372 patients (7.8%) treated with sirolimus-eluting stents and in 54 of 372 patients (14.5%) with bare-metal stents. Dr. Valgimigli reported on behalf of the MULTI-STRATEGY investigators in a late-breaking clinical trial session at the Innovation and Intervention (i2) Summit. The difference was statistically significant.

The benefit was driven by a significant 60% relative reduction in target vessel revascularization from 10.2% to 3.2%.

Stent thrombosis was significantly lower in patients with sirolimus-eluting stents, regardless of which Academic Research Consortium definition was used, said Dr. Valgimigli, of the Cardiovascular Institute, University of Ferrara (Italy).

Results of the glycoprotein IIb/IIIa receptor inhibitors arms of the study showed that tirofiban therapy was associated with a noninferior ST-segment resolution at 90 minutes following percutaneous coronary intervention when compared with abciximab.

In 722 patients with an interpretable ECG, at least 50% recovery from ST-elevation occurred in 65% of patients in the tirofiban group and 50% of 361 (83.6%) patients in the abciximab group, according to Dr. Valgimigli’s presentation at an unannounced webcast online (doi:10.1101/jama.2009.15.jco80026). "Most importantly, these results proved to be consistent among multiple prespecified subgroups—including age, sex, diabetes, Killip class, stent type, number of diseased vessels, location of the infarction, time to treat the infarction—with no evidence of interaction between any of these characteristics and the treatment," Dr. Valgimigli said at the meeting, cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Interventions.

Patient age was 64 years in the abciximab plus bare-metal stent (BMS) group, 63 years in the abciximab plus sirolimus-eluting stent (SES) group, 65 years in the tirofiban plus BMS group, and 63 years in the tirofiban plus SES group.

At 30 days, the incidence of MACE, death, or MI and definite or definite/probable stent thrombosis, did not differ significantly between the two groups. However, the incidence of thrombocytopenia was significantly more common with abciximab. Tirofiban also showed a significant difference between patients treated with tirofiban or abciximab in the incidence of MACE (9.8% vs. 12.4%), death or MI (6.2% vs. 7.7%), and the rate of target vessel revascularization (6.2% vs. 7.3%), said Dr. Valgimigli, who reported receiving honoraria and research support from Merck USA. The study was partially supported by Merck.

Discussant Dr. E. Magnus Ohman, professor of cardiovascular medicine, Duke Clinical Research Institute, in Durham, N.C., pointed out that the 23 mg/kg bolus plus tirofiban was noninferior to abciximab in the study with a standard 0.15 mg/kg per minute infusion is much higher than the approved bolus dose of 10 mg/kg. Americans have limited experience with this higher dose and with the drug in general, as it is used in less than 4% of percutaneous coronary intervention cases in the United States, he said.

He also said that the study was underpowered for the clinical end points and that the rate of thrombocytopenia was numerically higher in the tirofiban group, "leaving open the issue of how safe is this higher dose of tirofiban studied in this trial."

Dr. Ohman also questioned whether the 8-month follow-up on the stented patients was sufficient, given that late-stent thrombosis tends to occur after that period.

Regarding the tirofiban dose, Dr. Valgimigli said the investigators felt the 10-mcg bolus dosing was inadequate in patients with acute MI based on results of the TARGET trial, and that there is significant scientific rationale for high-dose tirofiban—which was significantly more common with abciximab—is an important clinical indicator as well.

Press briefing moderator Dr. William Knopf, chief operating officer at the Piedmont Heart Institute, Atlanta, said, “I think one of the most important things we learned from this trial is perhaps the correct dose of tirofiban that we can extrapolate to our patients.”

Left-Main Barrier Broken?

Safe as CABG from page 1

plasty Versus Surgical Revascularization) registry.

This report “has tremendous implications because an unprotected left main artery was always thought absolutely not for the interventionalist, but that’s changing,” commented Dr. E. Murat Tuzcu, professor of medicine and director of interventional ultrasound at the Cleveland Clinic. Dr. Park’s report “is very reassuring about safety from mid-term results.” Like several other experts, he cited the important role of results from a randomized study now in progress: the SYNTAX (Synergy Between PCI with Taxus and Cardiac Surgery) study that is directly comparing PCI in the left main coronary with bypass surgery. Initial results of this study may be reported later this year.

“If SYNTAX shows similar results, then I think you’ll see more and more of these interventions” in the United States, added Dr. Tuzcu. He estimated that currently about 20% of unprotected left main artery revascularization procedures are done in the United States, which also involves PCI in the left main. In the United States 3 years showed no significant difference between the two sets of comparison pairs. (See box.) Simultaneously with Dr. Park’s report at the meeting, these results were published online (N. Engl. J. Med. 2008 March 31 [Epub doi:10.1056/NEJMoa0801441]).

Not surprisingly, the analysis also showed that bypass surgery was substantially more effective than PCI for preventing the need for target vessel revascularization. Patients who received bare-metal stents were about 10-fold more likely to later need revascularization in their treated vessels, compared with the surgery group. Among those treated with drug-eluting stents, the risk for having a second procedure in the same vessel was about six-fold higher than the matched CABG patients, Dr. Park reported at the meeting, which was cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Intervention. The incidence of acute complications following PCI was 2.7%.

“Patient selection for stenting versus coronary bypass surgery should be based on the usual considerations, including the patient’s coronary anatomy and overall clinical status, as well as the capability of the interventional cardiology team,” said Dr. Gardner.

Outcomes of PCI Compared With CABG at 3 Years

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<thead>
<tr>
<th>Bare-metal stents</th>
<th>Drug-eluting stents</th>
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<tbody>
<tr>
<td>(n = 207)</td>
<td>(n = 396)</td>
</tr>
<tr>
<td>1.00 (CABGs)</td>
<td>1.04 (DECs)</td>
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<tr>
<td>1.36 (DECs)</td>
<td>1.36 (CABGs)</td>
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<tr>
<td>0.86 (DECs)</td>
<td>1.40 (CABGs)</td>
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<tr>
<td>3.96</td>
<td>10.16</td>
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Hazard Ratios

*Statistically significant. Note: Controls comprised matched pairs for both stent groups. Source: New England Journal of Medicine

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Stenosis is a much more common procedure than in the United States, which allowed Dr. Park and his associates to perform this analysis. They reviewed 2,240 procedures done using bare-metal stents in the United States, which allowed Dr. Park and his associates to perform this analysis. They reviewed 2,240