Ticagrelor With Invasive Strategy Cut Deaths

BY MICHELE G. SULLIVAN

Patients with acute coronary syndrome who received ticagrelor before an invasive cardiovascular procedure were 16% less likely to die from heart attack or stroke over the course of 1 year than were those given clopidogrel, according to a new subanalysis of the PLATO trial.

The benefit accrued without a significantly increased risk of bleeding and, unlike other early antithrombotic treatments, occurred in patients both with and without ST-segment elevation MI, investigators reported.

"This mortality benefit compared with clopidogrel is similar in magnitude to other major advances such as streptokinase or aspirin versus placebo, tissue plasminogen activator, and primary percutaneous intervention in care of patients with ST-elevation myocardial infarction," wrote Dr. Christopher P. Cannon of Brigham and Women's Hospital, Boston, and his co-authors (Lancet 2010; DOI:10.1016/S0140-6736(09)62191-7).

"We estimate the use of ticagrelor instead of clopidogrel for 1 year in 1,000 patients with acute coronary syndromes who are planned to undergo an invasive strategy at the start of drug treatment would lead to 11 fewer deaths, 13 fewer myocardial infarctions, and six fewer cases of stent thrombosis," they wrote.

VITALS

Major Finding: ACS patients with a planned invasive strategy who received ticagrelor had a 16% reduction in risk of cardiovascular death, MI, or stroke, compared with patients given clopidogrel over 1 year.

Data Source: 13,408 ACS patients in the PLATO trial who were scheduled for invasive procedures.

Disclosures: Funding by AstraZeneca, which makes ticagrelor. Dr. Stone, Dr. Cannon, and all of the study authors but one reported financial relationships with AstraZeneca.

In an accompanying editorial, Dr. Gregg W. Stone called the results a "landmark event that should redefine the care of patients with acute coronary syndromes."

However, he cautioned against adopting them as a cookbook recipe for all ACS patients. "A personalized approach to drug selection should be used, wherein each patient's individualized risk of ischemia versus bleeding is considered," wrote Dr. Stone of Columbia University Medical Center, New York. "Clopidogrel might still be appropriate for selected patients who are at relatively low risk of myocardial infarction or stent thrombosis and/or high risk of major bleeding and/or for whom noncompliance with ticagrelor because of cost or other considerations (such as twice-daily dosing) is a concern" (Lancet 2010: DOI:10.1016/S0140-6736(10)60070-0).

The PLATO (Platelet Inhibition and Patient Outcomes) study comprised 18,758 patients hospitalized for acute coronary symptoms and randomized to either clopidogrel plus placebo or ticagrelor plus placebo. This subanalysis focused on safety and efficacy in a subgroup of 13,408 patients for whom an invasive strategy was planned. Of these, 6,732 received ticagrelor (180 mg loading dose followed by 90 mg twice daily) and 6,676 received clopidogrel (300- to 600-mg loading dose followed by 75 mg/day). All patients received 75-100 mg aspirin/day. The follow-up period was 1 year.

The patients' mean age was 61 years; most were white (91%) and male (75%). About half had STEMI, 38% had non-STEMI, and 13% had unstable angina. For most, the invasive therapy included a coronary angiography (97%) and a primary percutaneous intervention (77%).

The primary efficacy end point was cardiovascular death, MI, or stroke. By the end of the follow-up period, the primary end point had been reached in 569 (9%) of the ticagrelor group and 668 (11%) of the clopidogrel group, showing a hazard ratio of 0.84 for the ticagrelor patients.

Ticagrelor was also significantly more effective than clopidogrel in a secondary composite end point of MI, stroke, and all cause-mortality (9% vs. 11%; HR 0.84).

It was significantly better than clopidogrel in patients with non-STEMI, reducing the risk of death by 17%. The 14% risk reduction seen in STEMI patients (8% vs. 9.5%) did not quite reach statistical significance. Both drugs similarly reduced the overall rate of stroke to 1%.

The rate of definite stent thrombosis was significantly lower in patients receiving ticagrelor (HR 0.64). Patients with a bare-metal stent reaped most of that benefit, experiencing a 38% reduction, compared with a 31% reduction in patients with a drug-eluting stent.

There were no significant between-group differences in the incidence of major bleeding (11.5% ticagrelor vs. 11.6% clopidogrel) or in life-threatening, fatal, or intracranial bleeding. ■

PCI for Complex CAD Ups Revascularization Risk in Diabetes

BY KERRI WACHTER

Similar mortality rates for endovascular and surgical treatment of complex coronary artery disease suggest that drug-eluting stents may be a viable treatment for selected diabetes patients, though revascularization rates are greater for these patients.

In the diabetes subgroup analysis of the SYNTAX trial, the 1-year major adverse cardiac and cerebrovascular event rate was significantly greater in medically treated diabetic patients with left main and/or three-vessel disease who underwent percutaneous coronary intervention with paclitaxel-eluting stents (PES), than in those who had coronary artery bypass grafting. However, this increase in the primary end point of the trial appears to be driven largely by an increased rate of repeat revascularization.

"For patients with medically treated diabetes, PES treatment was a significant predictor of repeat revascularization" but not death, cerebrovascular event, or MI, Dr. Adrian P. Banning and his associates wrote in a study published online Jan. 13 (J. Am. Coll. Cardiol. 2010 Jan. 13 [doi:10.1016/j.jacc.2009.09.057]).

In a related commentary, Dr. Harold L. Dauerman noted that many clinicians are already performing multivessel PCI in diabetic patients, "many of whom investigators believe could not be served at all with CABG because of a variety of comorbidities (risk of stroke) or anatomic challenges (diffuse distal vessel disease, poor conduits).

"The SYNTAX study diabetes analysis does not tell those clinicians to stop doing PCI in diabetic patients," said Dr. Dauerman, professor of cardiology at the University of Vermont in Burlington. Instead, the results suggest that PCI is a viable option given the caveat that diabetic patients undergoing PCI with [drug-eluting stents] remain at greater risk for repeat revascularization with PCI versus CABG.

VITALS

Major Finding: Endovascular treatment with paclitaxel-eluting stents significantly increased the risk of revascularization, compared with CABG treatment, in diabetic patients with left main and/or three-vessel disease but does not increase the rates of death, cerebrovascular accident, or MI in these patients.

Data Source: A diabetes subgroup analysis of the SYNTAX trial.

Disclosures: Funded by Boston Scientific, which makes the Taxus stent. Dr. Banning and four coauthors have financial ties to the company. Dr. Banning is partially funded by the National Health Research Institute's Biomedical Research Center in Oxford.

The SYNTAX (Synergy Between [PCI] With Taxus and Cardiac Surgery) study included 1,800 patients with de novo left main and/or three-vessel disease, with or without diabetes. Patients were randomized to undergo CABG or PCI using paclitaxel-eluting stents (PES). The diabetes substudy included the 452 patients with medically treated diabetes, of whom 71% had three-vessel disease and 29% had left main disease. Beyond that, 79% of patients with left main disease had concurrent two- or three-vessel disease. Of the 452 diabetes patients, 231 underwent PCI and 221 underwent CABG. Most (94%) of the diabetes patients had type 2 disease.

The researchers used a composite end point of all-cause death, cerebrovascular accident, MI, or repeat revascularization (any subsequent PES of CABG procedure in any coronary vessel). Among diabetic patients, the 1-year event rate was significantly greater after PES (26%), compared with CABG (14%), for a relative risk of 1.83. However, among nondiabetic patients, the 1-year event rate was slightly higher for the PES group, though this was not significant—15% vs. 12%, relative risk 1.28.

"The number needed to treat CABG to avoid 1 [major adverse coronary event] is 9 for diabetic patients and 31 for nondiabetic patients," wrote Dr. Banning, a consultant cardiologist at the John Radcliffe Hospital in Oxford, England, and his coauthors.

There were no significant differences between CABG and PES in terms of the composite safety end point (death, cerebrovascular accident, or MI) for either diabetic or nondiabetic patients in SYNTAX. Neither was there a significant difference in terms of symptomatic graft occlusion or stent thrombosis for patients with or without diabetes.

Repeat revascularization appears to have driven the significantly greater event rate for diabetic patients treated with PES. Repeat revascularization was greater for the PES group, regardless of diabetes status. The PES revascularization rate for diabetic patients was 20% compared with 6% for diabetic patients who underwent CABG.

Likewise, the PES revascularization rate for nondiabetic patients was 11% compared with 6% for nondiabetic patients who underwent CABG. Repeat revascularization following PES was also greater for diabetic patients than for nondiabetic patients. This was not true for CABG patients.

"Medically treated diabetes was a significant independent predictor of revascularization the PES arm (odds ratio of 2.93) but not in the CABG arm," the investigators wrote.

However, the degree of glycemic control was not a significant predictor of 1-year outcomes for diabetic patients.

Among diabetic patients, there were no differences in death, MI or cerebrovascular accident between PES and CABG groups in either those treated with insulin (182) or those treated with oral hypoglycemics (270).

The authors cautioned that the 1-year results may not yet reflect the true long-term differences between CABG and PES treatments of diabetic patients.

Dr. Dauerman reported significant financial relationships with Abbott Laboratories and Medtronic Inc. ■