

Program Title:
Clinical Trial Results: SCAI-ACCi2 Summit 2008
Educational Lecture Series

CME Program Audience

A variety of current topics in cardiology and disease management were captured during the 2008 Society for Cardiovascular Angiography and Interventions (SCAI) and the American College of Cardiology (ACC) joint annual meeting held in Chicago. The purpose of this activity is to assist cardiologists in improving patient outcomes by providing insights from recent and late-breaking clinical trials concerning the pharmacological management of atrial fibrillation, heart failure, and thrombosis associated with PCI.

Needs summary

The SCAI-ACCi2 2008 Summit represents a premiere opportunity for cardiovascular specialists and invasive and interventional cardiologists to collaborate and learn from some of the most compelling figures in cardiovascular medicine today. Central in this educational process is the presentation of data from late-breaking clinical trials. These trial data inform the cardiovascular professional of the latest practices, knowledge, and clinical outcomes which help determine the standard for treatment for a variety of cardiovascular diseases.

Program Learning Objectives

With the needs summary clearly identified, the following learning objectives have been developed and supported by practice gaps.

At the end of the program, participants should be able to:

Objective 1: Describe the current status of antiarrhythmic drug therapy for atrial fibrillation, specifically for the treatment of atrial fibrillation after valvular or coronary artery bypass (CABG) surgery.

*"It is reasonable to administer antiarrhythmic medications in an attempt to maintain sinus rhythm in patients with recurrent or refractory postoperative AF, as recommended for other patients who develop AF. (Class IIa, level of evidence: B.)"*¹

Source: Fuster V, Ryden LE, Cannom DS, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation. *J. Amer. Col. Cardiol.* 2006;48(4):854-906.

*"Up to 40% of patients who undergo coronary artery bypass graft (CABG) or valvular surgeries often experience AF (characterized by an irregular heart rhythm and a high heart rate), which has a significant effect on both the intensive care unit and overall hospital length of stay."*²

Source: WebMD heartwire news service. An interview with Dr. Peter R. Kowey, available at: <http://www.medscape.com/viewarticle/566030>.

*"Roughly 80% of patients with AF in the US today are treated with electrical cardioversion. Cardioversion works well, but it's not a trivial procedure. If half the patients who would otherwise require electrical cardioversion can be fixed by a relatively brief infusion of a drug, under careful monitoring, but not with a risk of large complications, that's a worthwhile addition to what we have available."*²

Source: WebMD heartwire news service. An interview with Dr. Peter R. Kowey, available at: <http://www.medscape.com/viewarticle/566030>.

Objective 2: Evaluate the potential benefit of cardiac resynchronization therapy (CRT) with or without an implantable cardioverter-defibrillator (ICD) on disease progression over 12 months in patients with asymptomatic and mildly symptomatic heart failure and ventricular dyssynchrony.

“CRT therapy is one of only two treatments capable of reducing sudden death due to either fatal arrhythmia or electromechanical failure in HF; the second being β -blockers in combination with angiotensin-converting-enzyme (ACE) inhibitors.”³

Source: Kass DA. “Does cardiac resynchronization therapy reduce the long-term mortality risk in patients with heart failure?” *Nature Clinical Practice Cardiovascular Medicine*. 2007; 4:190-191.

“Although there is some evidence that CRT therapy can benefit patients with more severe HF, the benefits of CRT therapy for symptomatic HF patients resulting from systolic dysfunction is unknown.”³

Source: Kass DA. “Does cardiac resynchronization therapy reduce the long-term mortality risk in patients with heart failure?” *Nature Clinical Practice Cardiovascular Medicine*. 2007; 4:190-191.

“In the COMPANION trial, reduced mortality was demonstrated in patients receiving CRT with an internal defibrillator, while in the CARE-HF study, mortality reduction was observed with CRT alone.”⁴

Source: Bristow MR et al. “Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure.” *N Engl J Med*. 2004;350:2140-2150.

Objective 3: Describe the potential benefit for patients who are at high-risk for developing cardiovascular disease related to treatment with either telmisartan or telmisartan and ramipril combined therapy.

“In patients who have vascular disease or high-risk diabetes without heart failure, angiotensin-converting-enzyme (ACE) inhibitors reduce mortality and morbidity from cardiovascular causes, but the role of angiotensin-receptor II blockers (ARBs) in such patients is unknown.”⁶

Source: The Heart Outcomes Prevention Evaluation Study Investigators. “Effects of angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients.” *N Engl J Med*. 2000;342(3):146-153.

“Alternatives to ACE inhibitor therapy are desired, as ACE inhibitors are not tolerated by 15% to 25% of patients.”⁷

Source: Bart BA, et al. “Contemporary management of patients with left ventricular systolic dysfunction: results from the Study of Patients Intolerant of Converting Enzyme inhibitors (SPICE) registry.” *Eur Heart J*. 1999;20:1182-1190.

Objective 4: Explain the current status regarding the safety and efficacy of a further loading dose of clopidogrel given to patients already taking chronic clopidogrel, specifically in patients undergoing percutaneous coronary intervention (PCI).

“Many patients, including ACS patients, who go to a cardiac catheterization laboratory for a PCI procedure, are already taking 75mg of clopidogrel each day to prevent blood clots. Previous studies have indicated that further platelet inhibition can be achieved with clopidogrel in addition to that provided by currently recommended loading and maintenance doses, and that higher doses might be warranted after assessment of their clinical efficacy and safety.”⁸

Source: Kastrati A, et al. “Loading with 600 mg clopidogrel in patients with coronary artery disease with and without chronic clopidogrel therapy.” *Circulation*. 2004;110(14):1916-1919.

Objective 5: Define the current status regarding the safety and efficacy prasugrel + aspirin versus clopidogrel + aspirin in ACS patients who will undergo a PCI procedure, in particular patients who will receive stents.

“Dual-antiplatelet therapy with aspirin and a thienopyridine is a cornerstone of treatment to prevent thrombotic complications of ACS and PCI. Prasugrel is a thienopyridine that is more potent, more rapid in onset, and more consistent in inhibition of platelets than clopidogrel. In addition, an alternative to clopidogrel is needed as some patients exhibit a resistance to its action.”⁹

Source: Wiviott SD, Antman EM. “Clopidogrel Resistance: A New Chapter in a Fast-Moving Story.” *Circulation*. 2004;109:3064-3067.

“The TRITON-TIMI 38 study is designed to compare prasugrel with clopidogrel in moderate to high-risk patients with ACS.”¹⁰

Source: Stephen D. Wiviott, et al. “Evaluation of prasugrel compared with clopidogrel in patients with acute coronary syndromes: design and rationale for the TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet Inhibition with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38).” *Am Heart J*. 2006;152(4):627-635.

Objective 6: Describe the current state regarding the safety and efficacy of increased initial loading doses of clopidogrel in patients who will undergo PCI.

“Pretreatment doses of clopidogrel have been shown to reduce periprocedural MI in patients undergoing PCI.”¹¹

Source: Patti G, et al. “Randomized Trial of High Loading Dose of Clopidogrel for Reduction of Periprocedural Myocardial Infarction in Patients Undergoing Coronary Intervention Results From the ARMYDA-2 (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty) Study.” *Circulation*. 2005;111:2099-2106.

“The Clopidogrel for the Reduction of Events During Observation (CREDO) trial examined the effects of a loading dose (300 mg) of clopidogrel before PCI followed by maintenance dosing versus maintenance alone and found a significant reduction of early events only when pretreatment was given >6 hours before PCI.”¹¹

Source: Patti G, et al. “Randomized Trial of High Loading Dose of Clopidogrel for Reduction of Periprocedural Myocardial Infarction in Patients Undergoing Coronary Intervention Results From the ARMYDA-2 (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty) Study.” *Circulation*. 2005;111:2099-2106.

Source: text.

“Data strongly suggest that there is individual variability in response to clopidogrel in the setting of PCI after STEMI and more broadly that clopidogrel resistance may be a marker for increased risk of recurrent cardiovascular events.”¹¹

Source: Patti G, et al. “Randomized Trial of High Loading Dose of Clopidogrel for Reduction of Periprocedural Myocardial Infarction in Patients Undergoing Coronary Intervention Results From the ARMYDA-2 (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty) Study.” *Circulation*. 2005;111:2099-2106.

Objective 7: Evaluate the potential benefit of early administration of an increased bolus of tirofiban in MI patients prior to PCI.

“The relationship between the level of platelet aggregation inhibition in patients with acute myocardial infarction and their clinical outcome is unknown.”¹²

Source: Smit JJ, et al. "Platelet microaggregation inhibition in patients with acute myocardial infarction pretreated with tirofiban and relationship with angiographic and clinical outcome." *Am Heart J.* 2006;151(5):1102-1107.

*"We found no correlation between the level of platelet microaggregation inhibition after tirofiban and outcome, whereas only a modest increase in platelet microaggregation inhibition was observed after a commonly used dose of tirofiban."*¹²

Source: Smit JJ, et al. "Platelet microaggregation inhibition in patients with acute myocardial infarction pretreated with tirofiban and relationship with angiographic and clinical outcome." *Am Heart J.* 2006;151(5):1102-1107.

*"A higher bolus dose of tirofiban might provide better therapeutic value than the current dosing strategy."*¹²

Source: Smit JJ, et al. "Platelet microaggregation inhibition in patients with acute myocardial infarction pretreated with tirofiban and relationship with angiographic and clinical outcome." *Am Heart J.* 2006;151(5):1102-1107.

References:

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4. Bristow MR et al. "Cardiac-Resynchronization Therapy with or without an Implantable Defibrillator in Advanced Chronic Heart Failure." *N Engl J Med.* 2004;350:2140-2150.
5. Cleland JGF, et al. "The Effect of Cardiac Resynchronization on Morbidity and Mortality in Heart Failure." *N Engl J Med.* 2005;352:1539-1549.
6. The Heart Outcomes Prevention Evaluation Study Investigators. "Effects of angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients." *N Engl J Med.* 2000;342(3):146-153.
7. Bart BA, et al. "Contemporary management of patients with left ventricular systolic dysfunction: results from the Study of Patients Intolerant of Converting Enzyme inhibitors (SPICE) registry." *Eur Heart J.* 1999;20:1182-1190.
8. Kastrati A, et al. "Loading with 600 mg clopidogrel in patients with coronary artery disease with and without chronic clopidogrel therapy." *Circulation.* 2004;110(14):1916-1919.
9. Wiviott SD, Antman EM. "Clopidogrel Resistance: A New Chapter in a Fast-Moving Story." *Circulation.* 2004;109:3064-3067.
10. Stephen D. Wiviott, et al. "Evaluation of prasugrel compared with clopidogrel in patients with acute coronary syndromes: design and rationale for the TRial to assess Improvement in Therapeutic Outcomes by optimizing platelet Inhibition with prasugrel Thrombolysis In Myocardial Infarction 38 (TRITON-TIMI 38)." *Am Heart J.* 2006;152(4):627-635.
11. Patti G, et al. "Randomized Trial of High Loading Dose of Clopidogrel for Reduction of Periprocedural Myocardial Infarction in Patients Undergoing Coronary Intervention Results From the ARMYDA-2 (Antiplatelet therapy for Reduction of MYocardial Damage during Angioplasty) Study." *Circulation.* 2005;111:2099-2106.
12. Smit JJ, et al. "Platelet microaggregation inhibition in patients with acute myocardial infarction pretreated with tirofiban and relationship with angiographic and clinical outcome." *Am Heart J.* 2006;151(5):1102-1107.