

# Off-Pump CABG Improves Outcomes in Women

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Denver Bureau

SAN DIEGO — Performing coronary artery bypass graft surgery off pump rather than on the heart-lung machine narrows the historic gender gap in operative mortality, stroke, MI, and other critical outcomes, Dr. John D. Puskas said at the annual meeting of the Society of Thoracic Surgeons.

His retrospective observational study, which involved 42,477 consecutive patients who underwent nonemergent

**The 24% relative risk reduction in mortality in OPCAB-treated women was twice the size of the risk reduction seen in OPCAB-treated men.**

CABG at 63 experienced North American centers in 2004-2005, earned the J. Maxwell Chamberlain Memorial Award for the meeting's top adult cardiac surgery study.

The study, which utilized

the Society of Thoracic Surgeons (STS) national cardiac database, demonstrated that the 16,245 off-pump coronary artery bypass (OPCAB) patients had significantly lower major morbidities and mortality than did the on-pump patients after adjustment for 32 potential confounding variables, including height, weight, body mass index, diabetes, and use of internal mammary artery grafts.

For 30 years, studies have shown that CABG outcomes are worse in women. This study was no exception: The nearly 12,000 female CABG patients had an unadjusted mortality fully twice that of the 1.4% figure in men. Women also had significantly higher rates of stroke (1.8% vs. 1.1%) and MI (1.5% vs. 1.1%).

After the extensive risk adjustment, OPCAB patients had a highly significant 17% reduction in mortality, compared with the on-pump population. OPCAB benefits were greater in women.

For example, the 24% relative risk reduction in mortality in OPCAB-treated women, compared with on-pump women, was twice the size of the risk reduction seen in OPCAB-treated as compared with on-pump men. Among on-pump patients, women had a 47% greater mortality risk than did men; among OPCAB patients, however, there was no significant gender disparity in mortality, ex-

plained Dr. Puskas, associate chief of cardiothoracic surgery at Emory University, Atlanta.

The unique strengths of this study were its great size, the unusually complete data in the STS archive, and the fact that information on emergent intraoperative conversions from OPCAB to on-pump surgery was included in the STS database starting in 2004.

As a result, the 2.2% of OPCAB patients who were urgently converted to on-pump

bypass—with an associated very high operative mortality of 6.5%—were counted on the OPCAB side of the equation. This permitted the first-ever intent-to-treat analysis of OPCAB, providing the truest picture to date of the procedure's pluses and minuses, the surgeon said.

The discussion period made it clear that OPCAB remains a contentious issue among surgeons.

"Off-pump surgery has not become the standard of care. It is one of the choices

that's currently available in coronary revascularization," said discussant Dr. Bruce W. Lytle, president of the American Association for Thoracic Surgery.

"We still are betwixt and between with regard to the use of off-pump surgery, as evidenced by the fact that the percentage of cases performed off pump in America appears to have settled out at 20%-25%," added Dr. Lytle, chair of the department of thoracic and cardiovascular surgery at the Cleveland Clinic.

**Newly published data vs rosuvastatin**

## What mean LDL-C reduction did and rosuvastatin did not?

- ▶ VYTORIN 10/40 mg was superior to atorvastatin 40 mg at lowering LDL-C (57% vs 48%,  $P<0.001$ ).<sup>1</sup>
- ▶ VYTORIN 10/40 mg and 10/80 mg were both superior to atorvastatin 80 mg at lowering LDL-C (57% and 59% vs 53%, respectively,  $P<0.001$ ).<sup>1</sup>

<sup>1</sup>Mean percent change in LDL-C from untreated baseline in a multicenter, double-blind, randomized, active-controlled, 8-arm, parallel-group study (6 weeks of active treatment) (N=1,902). Patients with hypercholesterolemia who had not met their LDL-C goal as defined by NCEP ATP III were randomized to VYTORIN 10/10, 10/20, 10/40, or 10/80 mg or atorvastatin 10, 20, 40, or 80 mg. Mean pooled baseline LDL-C values for VYTORIN and atorvastatin were 178 mg/dL and 179 mg/dL, respectively. VYTORIN 10/10 mg reduced LDL-C by 47% from baseline vs 36% with atorvastatin 10 mg ( $P<0.001$ ).<sup>1</sup>

- ▶ The dosage should be individualized according to baseline LDL-C level, the recommended goal of therapy, and the patient's response.

**VYTORIN is indicated as adjunctive therapy to diet** for the reduction of elevated TOTAL-C, LDL-C, Apo B, TG, and non-HDL-C, and to increase HDL-C in patients with primary (heterozygous familial and nonfamilial) hypercholesterolemia or mixed hyperlipidemia when diet alone is not enough.

**Contraindications:** hypersensitivity to any component of this medication; active liver disease; unexplained persistent elevations of serum transaminases; and women who are pregnant, nursing, or may become pregnant.

VYTORIN contains 2 active ingredients: ezetimibe and simvastatin.

No incremental benefit of VYTORIN on cardiovascular morbidity and mortality over and above that demonstrated for simvastatin has been established.

The clinical impact of comparative differences in lipid changes between products is not known.

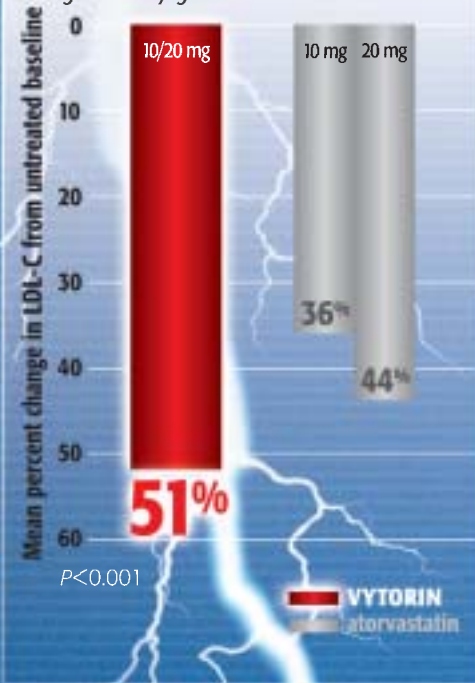
### SELECTED CAUTIONARY INFORMATION

**Skeletal Muscle:** Myopathy sometimes takes the form of rhabdomyolysis with or without acute renal failure secondary to myoglobinuria, and rare fatalities have occurred. The risk of myopathy/rhabdomyolysis is dose related. Tell patients to promptly report muscle pain, tenderness, or weakness. Discontinue drug if myopathy is suspected or CPK levels rise markedly.

**Myopathy Caused by Drug Interactions:** Use of VYTORIN with itraconazole, ketoconazole, erythromycin, clarithromycin, telithromycin, HIV protease inhibitors, nefazodone, or large quantities of grapefruit juice (>1 quart daily) should be avoided because of the increased risk of myopathy, particularly at higher doses.

### VYTORIN vs atorvastatin<sup>1</sup>

Significantly greater LDL-C reduction\*



### VERBATIM

*'We have been kicking this can down the road for the past 5 years.'*

Dr. Cecil Wilson, on fixing the sustainable growth rate, p. 47



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Dr. J. Scott Rankin questioned the clinical relevance of the benefits seen with OPCAB in this study. If stroke or MI occurs in about 1.5% of on-pump patients, and if OPCAB reduces that risk by one-third, that's only a 0.5% absolute difference, noted Dr. Rankin, a cardiothoracic surgeon who practices in Nashville.

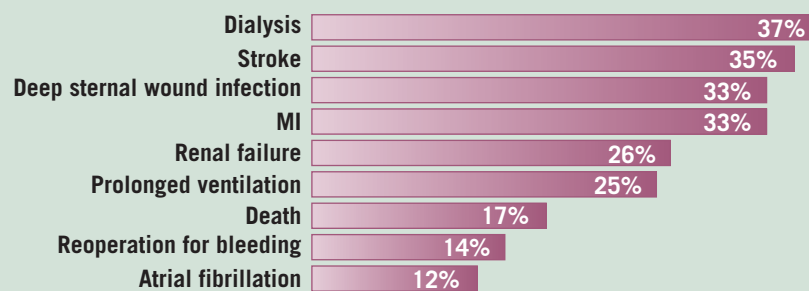
"I would argue that's clinically relevant," replied Dr. Puskas. "I think if I could reduce by 30% the number of bereaved families I have to talk to after heart surgery, I would consider that an excellent thing."

In an interview, he called his study "a wake-up call" for cardiac surgeons. There

are understandable reasons why 80% of CABGs still happen on-pump—the procedure is more familiar and technically easier, and few good OPCAB training programs now exist—but surgeons need to be thinking about how to move increasingly to OPCAB because the outcomes are better.

He added that OPCAB will provide superior results in all patient subgroups at high risk of morbidity and mortality with on-pump CABG. Besides women, this would include the very elderly, patients with extensive aortic atherosclerosis, and those with renal or pulmonary failure.

#### Relative Risk Reduction in Outcomes of Off-Pump vs. On-Pump CABG



Note: Based on a study of 42,477 patients who underwent nonemergent CABG. Source: Dr. Puskas

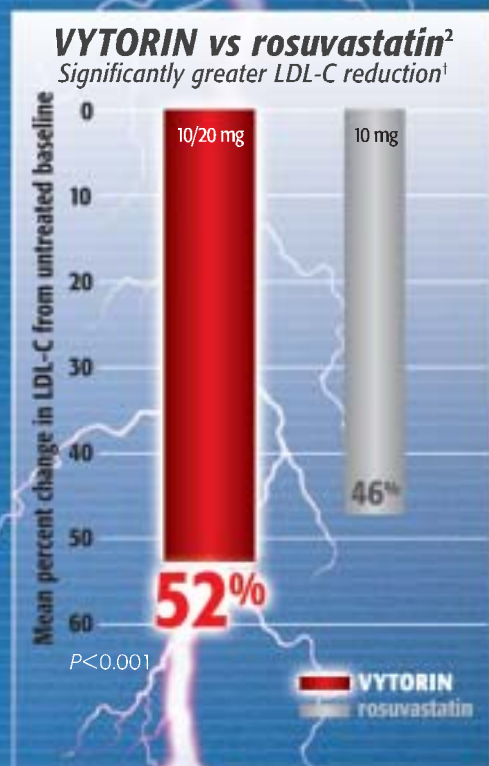
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enough, in 2 separate head-to-head studies

# VYTORIN provide that atorvastatin

# 50% at a usual starting dose<sup>1,2,3</sup>

mean LDL-C reduction



- VYTORIN 10/40 mg lowered LDL-C more than rosuvastatin 20 mg (55% vs 52%,  $P=0.001$ ).<sup>2</sup>
- VYTORIN 10/80 mg lowered LDL-C more than rosuvastatin 40 mg (61% vs 57%,  $P<0.001$ ).<sup>2</sup>

<sup>†</sup> Data from a multicenter, randomized, double-blind, active-controlled, 6-arm, parallel-group study designed to evaluate the efficacy and safety of VYTORIN vs rosuvastatin over a 6-week period. Patients with hypercholesterolemia (N=2,959) were randomized to 1 of 6 treatment groups: VYTORIN 10/20, 10/40, or 10/80 mg or rosuvastatin 10, 20, or 40 mg. Mean baseline LDL-C level for both VYTORIN 10/20 mg and rosuvastatin 10 mg was 172 mg/dL.<sup>2</sup>

#### SELECTED CAUTIONARY INFORMATION (cont)

The concomitant use of VYTORIN and fibrates (especially gemfibrozil) should be avoided. Although not recommended, the dose of VYTORIN should not exceed 10/10 mg if used with gemfibrozil. The benefit of further alterations in lipid levels by the combined use of VYTORIN with niacin should be carefully weighed against the potential risks of myopathy. The dose of VYTORIN should not exceed 10/10 mg daily in patients receiving cyclosporine or danazol, and 10/20 mg daily in patients receiving amiodarone or verapamil.

**Liver:** It is recommended that liver function tests be performed before the initiation of treatment and thereafter when clinically indicated. Additional tests are recommended prior to and 3 months after titration to the 10/80-mg dose, and semiannually for the first year thereafter.

VYTORIN is not recommended in patients with moderate or severe hepatic insufficiency.

In clinical trials, the most commonly reported side effects, regardless of cause, included headache (6.8%), upper respiratory tract infection (3.9%), myalgia (3.5%), influenza (2.6%), and extremity pain (2.3%).

Please read the brief summary of Prescribing Information on the adjacent page.

References: 1. Ballantyne CM, Abate N, Yuan Z, King TR, Palmisano J. Dose-comparison study of the combination of ezetimibe and simvastatin (Vytorin) versus atorvastatin in patients with hypercholesterolemia: the Vytorin Versus Atorvastatin (VIVA) Study. *Am Heart J*. 2005;149:464-473. 2. Catapano AL, Davidson MH, Ballantyne CM, et al. Lipid-altering efficacy of the ezetimibe/simvastatin single tablet versus rosuvastatin in hypercholesterolemic patients. *Curr Med Res Opin*. 2006;22:2041-2053. 3. IMS HEALTH, NPA Plus<sup>™</sup>, NRx, July 2006.

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**VYTORIN**  
(ezetimibe/simvastatin)  
tablets