

# PCI Raises 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, wrote Dr. Adrian P. Banning and his associates (*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.

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 pa-

tients with diabetes 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 MACCE 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.



## Same Name. New Size.

### Introducing 3 mL of Humalog® and Humulin® R U-100 in a Smaller Vial\*

#### The New Smaller Vial, Another Insulin Delivery Option

**Intended To:** Give hospitals more flexibility when evaluating insulin storage and distribution (floor stock vs individual patient supply), in addition to the 10 mL vial and Humalog® KwikPen™.

- Same Bar-Coding Technique, New Size
- Same Color-Differentiating System, New Size
- National Drug Code (NDC)

Humalog - NDC Number - 0002-7510-17

Humulin R U-100 - NDC Number - 0002-8215-17

#### Indication

Humalog is for use in patients with diabetes mellitus for the control of hyperglycemia. Humalog should be used with longer-acting insulin, except when used in combination with sulfonylureas in patients with type 2 diabetes.

#### Select Safety Information

Hypoglycemia is the most common adverse effect associated with insulins, including Humalog.

When used as a mealtime insulin, Humalog should be given within 15 minutes before or immediately after a meal.

\*3 mL of Humalog and Humulin R U-100 are in a 5 mL vial.

Pens are for single-patient use only and should not be shared among patients.

**Please see Important Safety Information on adjacent page and accompanying Brief Summary of full Prescribing Information.**

*Humalog*  
insulin lispro injection (rDNA origin)

#### 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 did 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. 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.

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 diabetic or nondiabetic patients.

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 patients with diabetes.

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.

SYNTAX was funded by Boston Scientific Corporation, which makes the Taxus paclitaxel-eluting stent. Dr. Banning and two of his coauthors have received grant support from Boston Scientific and two other coauthors are employed by the company.

Dr. Banning also received funding from the National Health Research Institute's Biomedical Research Center in Oxford.

Dr. Dauerman indicated that he has significant financial relationships with Abbott Laboratories and Medtronic Inc. ■

## Indication

Humalog (insulin lispro injection [rDNA origin]) is for use in patients with diabetes mellitus for the control of hyperglycemia. Humalog should be used with longer-acting insulin, except when used in combination with sulfonylureas in patients with type 2 diabetes.

## Important Safety Information

Humalog is contraindicated during episodes of hypoglycemia and in patients sensitive to Humalog or one of its excipients.

Humalog differs from regular human insulin by its rapid onset of action as well as a shorter duration of action. Therefore, when used as a mealtime insulin, Humalog should be given within 15 minutes before or immediately after a meal.

Due to the short duration of action of Humalog, patients with type 1 diabetes also require a longer-acting insulin to maintain glucose control (except when using an insulin pump). Glucose monitoring is recommended for all patients with diabetes.

The safety and effectiveness of Humalog in patients less than 3 years of age have not been established. There are no adequate and well-controlled clinical studies of the use of Humalog in pregnant or nursing women.

**Starting or changing insulin therapy should be done cautiously and only under medical supervision.**

## Hypoglycemia

Hypoglycemia is the most common adverse effect associated with insulins, including Humalog. Hypoglycemia can happen suddenly, and symptoms may be different for each person and may change from time to time. Severe hypoglycemia can cause seizures and may be life-threatening.

## Other Side Effects

Other potential side effects associated with the use of insulins include: hypokalemia, weight gain, lipodystrophy, and hypersensitivity. Systemic allergy is less common, but may be life-threatening. Because of the difference in action of Humalog, care should be taken in patients in whom hypoglycemia or hypokalemia may be clinically relevant (eg, those who are fasting, have autonomic neuropathy or renal impairment, are using potassium-lowering drugs, or taking drugs sensitive to serum potassium level).

**For additional safety profile and other important prescribing considerations, see accompanying Brief Summary of full Prescribing Information.**

**Please see full user manual that accompanies the pen.**

Humalog® is a registered trademark of Eli Lilly and Company and is available by prescription only. Humalog® KwikPen™ is a trademark of Eli Lilly and Company and is available by prescription only. Humulin® is a registered trademark of Eli Lilly and Company.

*Humalog*  
KwikPen™  
insulin lispro injection (rDNA origin)

**Humulin® R**  
Regular human insulin  
(recombinant DNA origin)