

## Bardoxolone Upped eGFR in Diabetic CKD

BY M. ALEXANDER OTTO

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF NEPHROLOGY

A 24-week course of bardoxolone methyl, an experimental antioxidant inflammation modulator, improved estimated glomerular filtration rates in chronic kidney disease patients with type 2 diabetes, according to a randomized phase IIb study funded by Reata Pharmaceuticals Inc.

A phase III study slated to start next year will test whether the mean eGFR improvement of 10.1 mL/minute per 1.73 m<sup>2</sup> leads to better patient outcomes, according to nephrologist Pablo Pergo-

### VITALS

**Major Finding:** Bardoxolone methyl improved eGFR in diabetic CKD patients by a mean of 10.1 mL/minute per 1.73 m<sup>2</sup>.

**Data Source:** Phase IIb randomized, double-blind, placebo-controlled trial enrolling 227 patients.

**Disclosures:** The study was funded by the drug's sponsor, Reata Pharmaceuticals. The lead investigator said he had no conflicts of interest.

la of the University of Texas Health Science Center, San Antonio.

"You want to make sure this drug will be associated with a clinical outcome," said Dr. Pergola, the lead investigator of the phase IIb study.

Patients in the randomized, double-blind, placebo-controlled trial were assigned to 25-mg, 75-mg, or 150-mg daily doses of bardoxolone or to placebo. Each group had 57 subjects, except the 150-mg group, which had 56.

In addition to type 2 diabetes, subjects had stage 3b or 4 chronic kidney disease (CKD), with an eGFR of 20-45 mL/minute per 1.73m<sup>2</sup>.

Their median age was 67 years, and all were on standard-of-care therapy – 98% of patients took ACE inhibitors or angiotensin-receptor blockers.

At 24 weeks, bardoxolone patients had a mean eGFR gain of 10.1 mL/minute per 1.73 m<sup>2</sup>, with improvements noted in each group ranging from 8.3 to 11.5 mL/minute per 1.73 m<sup>2</sup>, a significant difference from the 0.1–mL/minute per 1.73 m<sup>2</sup> gain with placebo.

About 73% (124) of patients in each bardoxolone group had at least a 10% eGFR increase; 25% (43) had more than a 50% increase.

Increased eGFRs also correlated with decreased blood-urea-nitrogen levels, decreased serum phosphorous and uric acid levels, and improved CKD stage.

Adverse events were more common in the bardoxolone groups; 49% reported muscle spasms, compared with 12% in the placebo group. The spasms were thought to be treatment related, as were nausea, hypomagnesemia, and diminished appetite. ■

## Intensive Control Curbed Renal Events

BY MIRIAM E. TUCKER

FROM THE ANNUAL MEETING OF THE EUROPEAN ASSOCIATION FOR THE STUDY OF DIABETES

STOCKHOLM – An intensive glucose control regimen aiming for a hemoglobin A<sub>1c</sub> level of 6.5% or lower significantly reduced the incidence of renal events in patients with established type 2 diabetes, according to findings from a large Australian study.

The total number of renal events in 5,571 patients randomized to intensive treatment was reduced by 11% (26.9% vs. 30%), compared with 5,569 patients who followed a standard glucose control regimen, Dr. Sophia Zoungas said at the meeting.

The data come from the glucose-lowering arm of the multinational ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicon-MR Controlled Evaluation) study, which ex-

amined the effects of both blood pressure lowering with perindopril/indapamide and glucose-lowering gliclazide MR in a total of 11,140 patients. Primary trial findings were reported in 2007 and 2008 ([www.advance-trial.com](http://www.advance-trial.com)).

The current analysis evaluated the incidence of renal events at a median follow-up of 5 years, when the mean HbA<sub>1c</sub> level achieved was 6.5% in the intensive treatment arm and 7.3% in the standard control group, reported Dr.

### Easy to teach<sup>1</sup>

– Can be used in 6 straightforward steps

### Easy to use<sup>1</sup>

– Only long-acting insulin pen in which dose can be set from 1 to 80 units in 1-unit steps, dialed both up and down  
– Once opened, Lantus<sup>®</sup> SoloSTAR<sup>®</sup> can be used for up to 28 days and is not refrigerated

### Easy to inject<sup>1</sup>

– Dose cannot be dialed past the number of units left in the pen  
– It is important to keep the injection button pressed all the way in and to **slowly count to 10 before withdrawing the needle from the skin**. After a full injection, the number in the dose window will return to zero. These steps help ensure that the full dose has been delivered  
– To help ensure an accurate dose each time, patients should follow all steps in the Instruction Leaflet accompanying the pen; otherwise they may not get the correct amount of insulin, which may affect their blood glucose

## Important Safety Information for Lantus<sup>®</sup>

### Contraindications

Lantus<sup>®</sup> is contraindicated in patients hypersensitive to insulin glargine or one of its excipients.

### Warnings and precautions

Monitor blood glucose in all patients treated with insulin. Insulin regimens should be modified cautiously and only under medical supervision. Changes in insulin strength, manufacturer, type, or method of administration may result in the need for a change in insulin dose or an adjustment in concomitant oral antidiabetic treatment.

Do not dilute or mix Lantus<sup>®</sup> with any other insulin or solution. If mixed or diluted, the solution may become cloudy, and the onset of action/time to peak effect may be altered in an unpredictable manner. Do not administer Lantus<sup>®</sup> via an insulin pump or intravenously because severe hypoglycemia can occur. Insulin devices and needles must not be shared between patients.

Hypoglycemia is the most common adverse reaction of insulin therapy, including Lantus<sup>®</sup>, and may be life-threatening.

Severe life-threatening, generalized allergy, including anaphylaxis, can occur.

A reduction in the Lantus<sup>®</sup> dose may be required in patients with renal or hepatic impairment.

### Drug interactions

Certain drugs may affect glucose metabolism, requiring insulin dose adjustment and close monitoring of blood glucose. The signs of hypoglycemia may be reduced in patients taking anti-adrenergic drugs (e.g., beta-blockers, clonidine, guanethidine, and reserpine).

### Adverse reactions

Other adverse reactions commonly associated with Lantus<sup>®</sup> are injection site reaction, lipodystrophy, pruritus, and rash.

## Indications and Usage for Lantus<sup>®</sup>

Lantus<sup>®</sup> is a long-acting insulin analog indicated to improve glycemic control in adults and children (6 years and older) with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus. Lantus<sup>®</sup> should be administered once a day at the same time every day.

Important Limitations of Use: Lantus<sup>®</sup> is not recommended for the treatment of diabetic ketoacidosis. Use intravenous short-acting insulin instead.

Lantus<sup>®</sup> SoloSTAR<sup>®</sup> is a disposable prefilled insulin pen.

**Please see brief summary of full prescribing information for Lantus<sup>®</sup> on the next page.**

References: 1. Data on file, sanofi-aventis U.S. LLC. 2. Lantus Prescribing Information. September 2009.