

# Rosiglitazone Improved Glycemic Control

Adverse events were not increased and cardiovascular markers were decreased.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

**T**he addition of rosiglitazone to insulin in difficult-to-control patients led to reductions in HbA1c, according to a report at the American Diabetes Association 65th Annual Meeting and Scientific Sessions in San Diego.

"Similar to prior rosiglitazone investigations, adding the agent also led to a significant reduction in serum cardiovascular risk biofactors," said Priscilla Hollander, MD, from Baylor Medical Center, during the presentation.

Type 2 diabetes is a progressive disease characterized by insulin resistance and declining beta-cell function, Dr. Hollander said. "To maintain optimal glucose control, most patients with type 2 diabetes will ultimately need insulin therapy," she said. "However, insulin alone may not allow achievement of appropriate glucose goals in these patients."

## GLITAZONE SIDE EFFECTS

Previous studies have shown that adding an insulin sensitizer can significantly improve glucose control in a majority of patients. While glitazones are effective, they have been associated with edema, weight gain and anemia.

In this study, two low-dose rosiglitazone treatments were evaluated in type 2 diabetic patients whose glucose was inadequately controlled by insulin therapy. Researchers assessed changes in HbA1c, fasting plasma glucose and the percent of patients who achieved HbA1c below the ADA goal of 7%. The investigators also looked at lipids and cardiovascular-related biomarkers.

"Importantly, we also wanted to analyze safety and tolerability – to be judged by the general safety profile – including adverse effects," Dr. Hollander said. "We included a substudy to assess cardiovascular risk that consisted of dobutamine stress echocardiograms."

Patients were on insulin for  $\geq 6$  months, had an HbA1c  $> 8\%$ , and had no history of congestive heart failure or edema. A 2-week screening period was followed by a 2-week placebo run-in. The 630 patients in this multicenter trial were then randomized in a 1:1 ratio to placebo or a 2- or 4-mg dose of rosiglitazone. "In terms of the 4-mg

arm, patients were actually placed on 2 mg for 8 weeks and then titrated up to the 4-mg dose," Dr. Hollander said.

There were an equal number of men and women in the trial, and the group was about 60% white and 25% black. A small percentage were Asian. The average age of patients was mid-50s and the duration of diabetes was about 12 years. These patients had a significant number of comorbidities, the average HbA1c was about 9%, and they were on an average of about 2.5 injections of insulin daily.

There was a 3.8% change in HbA1c in the 4-mg group over the course of the 24-week trial and a 0.26% change in the 2 mg group. Both were significant.

"There was a parallel fall over the first 8 weeks when both treatment groups were on the 2-mg dose," Dr. Hollander said. "When the additional 2 mg was added, we saw an additional extension of the fall in HbA1c for the 4-mg group, and the 2-mg group hit a plateau."

Approximately 15% of patients in the 4-mg group reached an HbA1c of 7%. Fewer achieved the goal in the 2-mg group. The average HbA1c dropped from 9% to 8.2%. "The percentage of patients who reached the ADA goal was not as robust as we would like to see, but this was a difficult population who started the trial with elevated levels of HbA1c," she said.

There was a significant reduction in the cardiovascular biomarkers of CRP, fibrinogen and MMP9.

Hypoglycemia was similar in patients receiving insulin alone and insulin plus rosiglitazone. There was no increased frequency of edema-related adverse events in patients taking rosiglitazone. In summary, low-dose rosiglitazone added to insulin significantly improved glycemic control without increasing the risk of hypoglycemia or fluid-related adverse events in patients with poorly controlled glycemia. ■

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