Saxagliptin Aids Type 2 Disease Glucose Control

BY MIRIAM E. TUCKER
Senior Writer

Washington — Once-daily saxagliptin added to metformin resulted in statistically significant reductions in hemoglobin A1c, fasting plasma glucose, and postprandial glucose levels for up to 24 weeks in a placebo-controlled trial involving 743 patients with type 2 diabetes who were inadequately controlled with metformin alone.

Results of the multicenter phase III study were reported in a poster at the annual meeting of the American Association of Diabetes Educators by Dr. Shoba Ravichandran, an endocrinologist with Bristol-Myers Squibb and Laureen MacEachern, director of scientific communications for the company.

Saxagliptin is a dipeptidyl peptidase-4 (DPP-4) inhibitor jointly developed by Bristol-Myers Squibb and AstraZeneca PLC, which cosponsored the study.

At baseline, the patients had a mean diabetes duration of 6.5 years; 83% had hemoglobin A1c of 8.0%, fasting plasma glucose of 176 mg/dL, and 2-hour postprandial glucose of 286 mg/dL.

All of the patients were on stable doses of metformin—between 1,500 and 2,550 mg/day—for at least 8 weeks prior to the study, and remained on the same dosage during the study. They were randomly assigned to one of four groups: saxagliptin in daily doses of 2.5, 5, or 10 mg, or placebo.

The investigators found statistically significant reductions in both HbA1c and fasting plasma glucose were seen with all the saxagliptin doses, but the maximal benefit occurred with the 5.0-mg/day dose.

At week 24, placebo-corrected mean significant reductions in baseline in HbA1c were 0.73, 0.81, and 0.72 percentage points for the 2.5-, 5-, and 10-mg/day doses, respectively. Placebo-corrected PPG was reduced from baseline by 16, 23, and 22 mg/dL, respectively.

Reductions in PPG were observed as early as week 2, Dr. Ravichandran and Ms. MacEachern said.

The investigators also reported significant placebo-adjusted reductions in 2-hour postprandial glucose levels from baseline—44, 40, and 32 mg/dL, for the 2.5-, 5-, and 10-mg, respectively.

Saxagliptin did not have a significant impact on body weight, with mean reductions from baseline at week 24 of 1.4, 0.9, 0.5 kg, respectively, and of 0.9 kg in the placebo group.

Saxagliptin was generally well-tolerated. A total of 74% of patients in the three treatment groups and 65% of the placebo group reported at least one adverse event, including nasopharyngitis in 9% of the saxagliptin patients and 8% of the placebo group, headache in 13%, and diarrhea in 7% vs. 11%, respectively.

The incidence of hypoglycemia was similar in the saxagliptin plus metformin patients (3.7%) and the placebo plus metformin patients (3.0%).

Events of hypoglycemia that were confirmed by a fingerstick glucose value of 70 mg/dL or less were 0.5% for the saxagliptin group and 0.6% with placebo, the investigators reported.

In July, Bristol-Myers Squibb and AstraZeneca announced the submission of a New Drug Application to the U.S. Food and Drug Administration and validation of a Marketing Authorization Application to the European Medicines Agency for saxagliptin under the proposed trade name Onglyza.

Hypoglycemia Can Induce Visual Disturbances in Diabetics

BY MICHELE G. SULLIVAN
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San Francisco — Visual disturbances—including blurred vision, floaters, central scotoma, and even complete loss of vision—can be a symptom of hypoglycemia in some patients with diabetes, according to Dr. Mukhtar Khan.

Although not all those with diabetes experience visual disturbances during a hypoglycemic event, those who are susceptible might experience two or more, which resolve soon after blood glucose stabilizes, Dr. Khan wrote in a poster presented at the annual meeting of the Endocrine Society.

"Most clinicians are usually concerned about hyperglycemia and its effects," he said in an interview. "It is also important to keep the effects of hypoglycemia in mind because, in addition to the visual effects these can have devastating consequences in diabetic patients in situations such as operating a motor vehicle." His observational study enrolled 40 patients with diabetes (mean age 46 years) who had a history of visual symptoms during hypoglycemic episodes. Most of the patients (26) had type 1 diabetes; the rest had type 2 diabetes. Nineteen were on insulin pumps, while 21 were on various insulin regimens, including glargine, lispro, aspart, and mixtures.

The mean duration of the patients (57%), visual symptoms occurred when blood glucose dropped to 30-50 mg/dL. For 25%, symptoms occurred at a glucose level of 51-65 mg/dL, while a minority (10%) experienced them at a level of 66-80 mg/dL. The remaining patients were unable to document their blood glucose level at the onset of visual symptoms.

Blurred vision was the most common symptom (77%). About half of the group (47%) reported seeing floaters. Dimming of vision occurred in 37%; central scotoma (a black spot or "hole" in the central visual field) in 32%; and double vision in 22%. A few patients (8%) reported a complete loss of vision during hypoglycemia. Most (67%) reported more than one symptom during the episode.

The visual symptoms resolved after blood glucose stabilized, Dr. Khan said. "After hypoglycemia correction, the symptoms resolved within 5-15 minutes in 16 subjects; 20-30 minutes in 17 subjects; and 35-90 minutes in three subjects. Two subjects, who experienced a complete loss of vision at a blood glucose level in the 30- to 40-mg/dL range, reported gradual resolution of visual symptoms in 180 minutes and 300 minutes after improvement in the glucose level.”

Two patients did not report the time to resolution of their symptoms, noted Dr. Khan of the State University of New York, Syracuse.

"Patients with diabetes should be counseled about recognition and early management of visual effects of hypoglycemia," Dr. Khan said. "Prevention of hypoglycemia should be given as much importance as hyperglycemia during management of diabetes.”