New Treatments: Sitagliptin

Sitagliptin is a once-daily oral medication in the depeptidyl-peptidase-4 (DPP-4) inhibitor class of medications. Data from a phase 3 non-inferiority trial of sitagliptin vs. glipizide was presented. This was a double-blind randomized multicenter trial conducted in 1172 patients with type 2 diabetes. Patients who were not controlled on metformin monotherapy were randomized to either sitagliptin 100 mg/day or glipizide up to 20 mg/day. After 52 weeks of treatment, 63% of the sitagliptin group and 59% of the glipizide group had HbA1c values <7%; sitagliptin thus met the criteria for non-inferiority. The glipizide group, however, had a significantly higher occurrence of hypoglycemia (32.0% vs. 4.9%, respectively; $p<0.001$). Patients taking sitagliptin lost significantly more weight over the 52 weeks when compared to those taking glipizide (-1.5 kg vs. + 1.1 kg respectively; $p<0.001$). Although the primary endpoint was measured at 52 weeks, the study will continue for a total of 104 weeks.

The safety profile of sitagliptin was determined by combining data from four different clinical trials. No clinically significant differences were observed between sitagliptin and placebo in adverse events, incidence of hypoglycemia, body weight, or laboratory values in these studies. The most frequently reported (≥3% and greater than placebo) adverse events with sitagliptin were stuffy or runny nose and sore throat, headache, diarrhea, upper respiratory tract infection, joint pain, and urinary tract infection. Although not considered clinically significant, small rises in uric acid and neutrophil count and slight reductions in alkaline phosphatase values were observed in comparison to placebo-treated patients.

Sitagliptin is currently under review by the US Food and Drug Administration; regulatory filings in other countries are pending.

New treatments: Liraglutide

Liraglutide is a long-acting analog of glucagon-like-peptide-1 (GLP-1). Currently in phase 3 trials, this agent shows promise in the treatment of type 2 diabetes. A large, randomized, placebo controlled phase 2 trial was conducted in 165 patients with type 2 diabetes. Participants discontinued their previous medications and were randomized to either placebo or once-daily doses of 0.65 mg, 1.25 mg or 1.9 mg liraglutide. The primary outcome measure was the change in the baseline level of HbA1c at the final visit.

At Week 14, HbA1c levels in all 3 liraglutide groups were significantly lower compared to placebo ($p<0.0001$). This improvement in glycemic control was not associated with major or minor episodes of hypoglycemia. Patients taking liraglutide also had a decrease in body weight, with those in the 1.9 mg/day group losing approximately 3 kg vs. 1.2 kg on placebo after 14 weeks of treatment. The most common adverse events reported with liraglutide were nausea and diarrhea.

A subgroup of 39 patients was studied to determine first-phase insulin secretion and maximal beta cell insulin secretory capacity. Patients in the 1.25 mg/day and 1.9 mg/day groups had significantly higher maximal beta cell insulin secretory capacity and first phase insulin secretion when compared to placebo (all $p<0.05$). "We are excited by these results as they demonstrate that liraglutide monotherapy significantly improves blood glucose control without risk of major or minor hypoglycemia, is well-tolerated, lowers body weight, and may help improve the body's ability to produce insulin," said study investigator Sten Madsbad, MD, DMSc of the University of Copenhagen.