

# Diabetes research news

## Exenatide once weekly

Exenatide is a glucagon-like peptide-1 (GLP-1) receptor agonist that stimulates glucose-dependent insulin secretion, reduces glucagon secretion, decreases food intake, and slows gastric emptying. Twice-daily exenatide improves glycaemic control and induces weight loss. Now a once-weekly formulation of exenatide has been compared with insulin for the treatment of type 2 diabetes in an international trial published in the *Lancet*.

A total of 456 patients with type 2 diabetes not adequately controlled on blood-glucose-lowering drugs (metformin with or without a sulphonylurea) were randomised at 72 centres to add s.c. exenatide 2 mg once weekly, or insulin glargine once daily, with dose adjusted according to blood glucose measurement, to their usual treatment. The change in HbA<sub>1c</sub> level from baseline at 26 weeks was significantly greater with exenatide (-1.5% vs -1.3%). More patients on exenatide (5% vs 1%) discontinued treatment because of adverse events. Further follow-up is in progress.

Once weekly exenatide may be a valid addition to the treatment of type 2 diabetes especially for obese patients and those for whom hypoglycaemia is a problem.

## Dapagliflozin plus metformin for type 2 diabetes

An international trial of dapagliflozin (a selective inhibitor of sodium-glucose cotransporter 2 [SGLT2] that inhibits renal glucose reabsorption) has been reported in the *Lancet*.

A total of 546 adults with type 2 diabetes inadequately controlled on metformin were randomised at 80 centres in North and South America to added dapagliflozin 2.5 mg, dapagliflozin 5 mg, dapagliflozin 10 mg, or placebo, all orally once daily. At 24 weeks, mean HbA<sub>1c</sub> had decreased by 0.30% (percentage points) on placebo, 0.67% on dapagliflozin 2.5 mg, 0.70% on dapagliflozin 5 mg, and 0.84% on dapagliflozin 10 mg. Symptoms of hypoglycaemia occurred in 2-4% of each group. Genital infection occurred in 5% (placebo), 8% (dapagliflozin 2.5 mg) 13% (5 mg), and 9% (10 mg). Significant weight loss occurred in all of the dapagliflozin groups. Serious adverse events occurred in four patients in each of the dapagliflozin groups and five in the placebo group.

Addition of dapagliflozin may be a new option for the treatment of type 2 diabetes not satisfactorily controlled on metformin alone.

## Inhaled insulin plus insulin glargine versus biaspart insulin for type 2 diabetes

Inhaled insulin is rapidly absorbed, rapidly active, and short acting. Compared with injected short-acting insulins it might be expected to reduce early post-prandial hyperglycaemia and lessen the risk of late post-prandial hypoglycaemia.

Now a regimen including inhaled insulin has been compared with twice-daily biaspart insulin for the treatment of type 2 diabetes in a trial in ten countries in North and South America and Europe.

A total of 677 patients with type 2 diabetes inadequately controlled on insulin therapy with or without oral antidiabetes drugs were randomised to prandial inhaled insulin (Technosphere) plus bedtime insulin glargine (II/IG) or twice-daily biaspart insulin (70% insulin aspart protamine suspension/30% insulin aspart [BAI]). The trial was discontinued by 107 patients in the II/IG group and 85 in the BAI group, the excess in the II/IG being mainly due to persisting cough. The change in HbA<sub>1c</sub> with II/IG from baseline at week 52 was similar and non-inferior to that with BAI (-0.68% vs -0.76%). Weight gain was less and episodes of hypoglycaemia fewer in patients in the II/IG group. Cough was more frequent in the II/IG group.

These researchers conclude that inhaled insulin could provide improved glycaemic control with lower weight gain and less risk of hypoglycaemia. More follow-up is needed to establish safety.

## Cell found that may lead to kidney failure in diabetes

A particular cell in the kidney has been identified by scientists trying to understand why diabetes patients can also suffer from kidney failure. Although kidney disease in diabetes patients was thought to be mostly due to the high blood glucose levels harming small blood vessels in the kidney, this study, published in *Cell Metabolism*, has discovered that a cell in the kidney called the podocyte is a key element in the development of kidney failure in diabetes.

The researchers showed that kidney failure was unrelated to the effects of high glucose levels on the podocyte, but due to a lack of sensitivity to insulin.

The scientists experimented on mice that genetically had the insulin receptor removed from their podocytes, which made only this cell unresponsive to insulin in the body, in order to discover whether insulin signalling in podocytes affects kidney function. They showed that those mice that developed kidney disease had many similarities to that seen in diabetic patients, apart from the fact that the mice all had normal blood glucose levels.

## Lack of sleep may lead to diabetes

People who sleep for less than 6 hours a night are more likely to develop diabetes, new research has revealed. It was found that those who sleep for less than 6 hours a night during the working week were three times more likely to have higher blood glucose levels than people who sleep for between 6 and 8 hours.