American Diabetes Association 66th Annual Scientific Sessions

Washington DC, USA, 9–13 June 2006

Sitagliptin gives same glucose-lowering effect as glipizide

Study results released at the *American Diabetes Association* (ADA) *66th Annual Scientific Sessions* show that sitagliptin (Januvia; Merck Sharp & Dohme, Hoddesdon) was non-inferior to glipizide in reducing blood glucose levels when added to metformin monotherapy in people with inadequately controlled type 2 diabetes. The data presented were based on a 52-week study period, with the trial due to continue for another 52 weeks.

This double-blind study randomised 1172 people to receive either once-daily 100 mg sitagliptin (an investigational dipeptidyl peptidase-4 [DPP-4] inhibitor) or glipizide at the maximum titrated dose. HbA_{1c} was observed to decrease by 0.67 percentage points versus baseline in each study arm ($P<0.001$) and similar proportions of participants achieved HbA_{1c} <7% in each group.

However, participants in the sitagliptin group exhibited significant weight loss (–1.5 kg) while the glipizide-treated people gained weight (+1.1 kg; $P<0.001$ between treatments). In addition, hypoglycaemic episodes were experienced by a smaller proportion of the sitagliptin group compared with the glipizide-treated group (4.9% versus 32.0%, respectively; $P<0.001$).

Study examines effects of insulin detemir in routine practice

Results from the German cohort of the international PREDICTIVE (Predictable Results and Experience in Diabetes through Intensification and Control to Target: an International Variability Evaluation) study confirm that insulin detemir (Levemir; Novo Nordisk, Crawley) improves glycaemic control and reduces the risk of hypoglycaemia. The new data were released in a poster presentation at the ADA Scientific Sessions.

The results are based on data from 10 276 participants taking part in the German arm of the 12-week, prospective, non-interventional, open-label observational study which was designed to evaluate the safety and efficacy of insulin detemir in routine clinical practice.

The beneficial effects of the insulin were seen regardless of the particular basal insulin treatment that participants were using before switching to insulin detemir, said the investigators. The effects were also noted in people who had not previously used insulin.

Commenting on these results, Dr Malcolm Nattrass of University Hospital Birmingham said: 'This insight into how [insulin detemir] is being used in clinical practice to manage diabetes successfully without weight gain is very positive for healthcare professionals and patients alike.'

Campaign for UN resolution on diabetes launched

The International Diabetes Federation (IDF) launched 'Unite for Diabetes' at the ADA meeting, a campaign aiming to highlight the alarming rise of diabetes worldwide and to secure a United Nations resolution on diabetes.

New data from the IDF suggest that more than 230 million people worldwide (nearly 6% of the population) now live with diabetes, with this figure estimated to rise to 350 million by 2025.

Despite these alarming statistics, the IDF says, little political effort has been made to tackle diabetes. Reversing the current trend will require a 'whole-of-government approach and the attention of the international community'.

'The diabetes epidemic will overwhelm healthcare resources everywhere if governments do not wake up and take action now,' said Professor Martin Silink, IDF's President-Elect.

It is hoped that a UN declaration on diabetes will be declared on or around World Diabetes Day 2007.

Phase III data demonstrate efficacy of ruboxistaurin

Analysis of data from two phase III clinical trials presented in Washington DC demonstrates that use of the investigational protein-kinase-C-beta inhibitor ruboxistaurin mesylate (Arxxant; Eli Lilly, Basingstoke) reduces the relative risk of sustained moderate vision loss (SMVL) compared with placebo in people with moderate-to-severe non-proliferative diabetic retinopathy.

SMVL occurred in 6.1% of people treated with ruboxistaurin over 3 years compared to 10.2% of those receiving placebo ($P=0.011$).

Insulin initiation delayed for 4–6 years in type 2 diabetes

Data from a study of UK patient records presented at the ADA meeting show that more than half of a group of 2501 patients from more than 100 general practices delayed starting insulin for at least 4–6 years after their oral therapies failed to be effective.

A statement from Pfizer says that these findings counter the preliminary NICE opinion on inhaled insulin therapy that using injected insulin is 'not usually a concern for the majority of people with diabetes'.

A similar analysis in the US of 4365 patient records spanning 8 years found that only half of patients taking two oral hypoglycaemic agents (a sulphonylurea and metformin) achieved targeted control of blood sugar levels.

Meetings

Skipping breakfast linked to increased risk of obesity

Investigators from Santa Barbara, California, reported the results of a cross-sectional study showing that skipping breakfast was associated with a rate of obesity similar to that associated with having a family history of diabetes.

Adolescents (n=2701) from two high schools participated in the study, which involved a physical examination and lifestyle questionnaire which asked if breakfast was eaten on school days.

In an age-, sex- and ethnicity-controlled logistical analysis, breakfast skipping and family history of diabetes were each significantly linked to obesity (odds ratios 1.87 and 2.26, respectively).

The investigators reported that obesity could have resulted from breakfast skipping, or the students could have skipped breakfast in an attempt to lose weight. However, they concluded, breakfast could be of major importance to obesity prevention, as it is a potentially modifiable lifestyle factor.

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International endorsement for UK diabetes strategy

A poster from a group in Coventry, UK, outlined the results of a questionnaire collected from 179 diabetes centres in 32 different countries, assessing the possibility of these centres implementing the investigators' 'Alphabet Strategy' to diabetes care. The questionnaire was returned by doctors, nurses and people with diabetes.

The strategy is based on the mnemonic **A**dvice, **B**lood pressure, **C**holesterol, **D**iabetes control, **E**yes, **F**eet and **G**uardian drugs.

Nearly 90 % of the survey respondents thought the strategy was practical, and 85 % agreed that it was evidence-based. More than 80 % of the respondents felt positive about the scheme's posters and care plans. Overall, nearly 70 % of respondents felt that they were likely to adopt it in their own area.

The authors concluded that the strategy has the potential to be widely adopted as an evidence-based and practical scheme for diabetes management.

Continuous glucose monitoring system safe and efficacious

The results of two studies examining a continuous glucose monitoring system (FreeStyle Navigator; Abbott Laboratories Ltd, Maidenhead), presented during poster sessions in Washington DC, show that it is accurate, safe and efficacious.

The first study, which examined the system's use in 30 children (mean age 11 years) with type 1 diabetes in both inpatient and outpatient settings, concluded that the system's accuracy and precision were sustained for up to 5 days of use and were similar in different insertion locations (arm, abdomen or hip).

The second study examined the use of the system in the home environment in 123 people with type 1 or type 2 diabetes. The overall mean difference between values from the continuous monitoring system and simultaneous reference blood glucose values was 14.4 ± 13.4 %.

In a Clark error-grid analysis, 96.8 % of the system's values fell in zone A (meaning that the results were clinically accurate and consistent with the laboratory reference values).

'These data are promising and suggest the potential value of [the system] in the management of type 1 diabetes both in children and adults,' said Peter Chase, Professor of Paediatrics at the University of Colorado Health Sciences Center.

Type 2 diabetes increases Parkinson's disease risk

Investigators from Finland reported the results of a study of over 51 000 men and women which found that type 2 diabetes is a significant risk factor for the development of Parkinson's disease.

The researchers examined a cohort of people aged 25–74 years without a history of Parkinson's disease at baseline. During a mean follow-up period of 18.0 years and 927 736 person-years, over 630 people developed the condition. In people with a history of diabetes at baseline, the sex- and multivariate-adjusted hazard ratio of developing Parkinson's disease was 1.78 (95 % confidence interval, 1.18–2.70) compared to those people without diabetes.

This association was observed in sub-groups aged 25–44 years and those aged 45–54 years, in both sexes and in people who smoked and people who had never smoked.

Antidepressants and diabetes

A sub-analysis of the Diabetes Prevention Programme, reported in a poster presentation at the meeting, found that the use of antidepressant drugs was associated with the development of type 2 diabetes in people already at risk of the condition.

This effect was observed in those people also receiving placebo or undertaking lifestyle intervention, but interestingly was not seen in those taking metformin. Depression at baseline did not predict development of diabetes.

'This occurred in a population at very high risk for diabetes, so we don't know whether the findings would apply to the general population,' said Dr Richard Rubin (John Hopkins University School of Medicine, Baltimore), one of the investigators in the study.

Benefits of exenatide in those receiving a glitazone

New study data announced at the ADA show that 16 weeks' treatment with exenatide (Byetta; Eli Lilly, Basingstoke, and Amylin, San Diego) provided improvements in HbA_{1C} and fasting and postprandial blood glucose levels in people with type 2 diabetes not achieving glycaemic targets despite receiving a glitazone with or without metformin.

Sixty-two per cent of the people taking exenatide in combination therapy versus 16% of those receiving placebo reached an HbA_{1C} target of <7% (P<0.0001). The investigators also found that exenatide treatment was associated with a larger reduction in body weight compared with placebo (1.5kg versus 0.2kg, respectively; P<0.001).

Proof of concept for amylin in leptin responsiveness

Study results presented in a poster at the meeting showed that co-administration of the neurohormones amylin and leptin led to sustained, fat-specific weight loss in a leptin-resistant animal model of obesity.

These findings, said Alain Baron (Senior Vice President of Research at Amylin Pharmaceuticals), 'provide proof of concept that amylin can restore leptin responsiveness in obese leptin-resistant animals. The study further demonstrates the potential to treat obesity with a combination therapy that employs multiple weight-regulating neurohormones.'

A clinical study to investigate further is planned to begin before the end of 2006.

Discrete obesity sub-types identified

Researchers from Baton Rouge, Louisiana, presented gene expression data which they claim reveal the presence of two distinct sub-types of obesity.

The investigators performed adipose tissue and skeletal muscle biopsies in 72 obese men and women. The participants then received treatment with either placebo (n=20) or ephedra plus caffeine (n=52) and the biopsy tissue was analysed using microarray.

The investigators found that cluster analysis of the gene expression data revealed two distinct obesity sub-types and that cluster identity predicted weight loss upon treatment with caffeine and ephedra.

This, say the authors, could open the door to personalised treatment plans based on the diagnosis of distinct obesity sub-types that respond differently to therapeutic intervention.

Type 2 diabetes and old age: An explanation?

Researchers from Philadelphia presented results from studies on mice showing that beta-cell replication is highly limited in old age. If the findings are preserved in humans, diabetes could result from an inability of beta-cell mass to compensate for age-related increases in peripheral insulin resistance – potentially offering an explanation for the high incidence of type 2 diabetes in old age, say the investigators.

The study measured adaptive beta-cell replication in young, middle-aged and very old mice that had undergone partial pancreatectomy.

Other meetings

Pioglitazone shows early promise in Alzheimer's disease

Data presented at the *10th International Conference on Alzheimer's Disease and Related Disorders* in Madrid, Spain, in July suggest that the type 2 diabetes oral medication pioglitazone (Actos; Takeda, High Wycombe) may also be a useful treatment for Alzheimer's disease.

Researchers at US universities in Cleveland, Ohio, and Charlottesville, Viriginia, tested the drug in a placebo-controlled trial involving 25 people with mild-to-moderate Alzheimer's disease. While the treatment appeared to safely reduce the progression of the condition, the investigators say that the study was too small to be sure of the drug's possible effects on memory. However, based on these promising findings, larger studies are now planned.

'We believe that [pioglitazone] may reduce the body's inflammatory reaction to one of the toxic components that builds up in Alzheimer's disease, called amyloid plaque,' said Dr David Geldmacher (Associate Professor of Neurology at the University of Virginia).

Pioglitazone represents a novel approach to the treatment of Alzheimer's disease, said Dr Geldmacher. 'It could complement other treatments and become part of a multi-pronged approach to Alzheimer's treatment [if further research is successful].'

Up to 4.5 million older people in the USA are currently affected by Alzheimer's disease.

Seventy per cent LDL reduction with statin combination therapy

According to the investigators, a study on combination therapy comprising rosuvastatin (40mg) and ezetimibe (10mg) has produced the largest reduction in LDL-cholesterol ever observed in a statin clinical trial. The 70% reduction in LDL-cholesterol in high-risk patients after 6 weeks' therapy was announced at the recent *XIV International Symposium on Atherosclerosis* in Rome, Italy.

The study, known as EXPLORER1 (EXamination of Potential Lipid modifying effects Of Rosuvastatin in combination with Ezetimibe versus Rosuvastatin alone), randomised over 450 people with very high LDL-cholesterol (between 4.1 and <6.5 mmol/l) to receive either rosuvastation (40mg daily) alone or in combination with ezetimibe (10mg) for 6 weeks. The randomised phase followed a 6-week dietary lead-in period.

Mean LDL-cholesterol was lowered from 4.9 to 1.5 mmol/l in those receiving combination therapy (a 70% reduction), compared with a reduction of 4.9 to 2.1 mmol/l in those receiving rosuvastatin alone (a 57% reduction).

Compared with the monotherapy group, significantly more participants receiving combination therapy were able to achieve both the US and European LDL-cholesterol goals (79 versus 94% and 74 versus 94%, respectively; P<0.001). A similar increase in HDL-cholesterol was also seen between the two groups.