Meeting report: ADA 80th Scientific Sessions

Stay abreast of the latest news that could impact diabetes nursing. In this issue, we summarise the key presentations from the American Diabetes Association 80th Scientific Sessions.

The American Diabetes Association's 80th Scientific Sessions were held on 11–16 June 2020. Owing to the COVID-19 pandemic, the Sessions were held virtually. Here we summarise the key presentations and publications.

VERTIS-CV: Cardiovascular safety of ertugliflozin

Results of the cardiovascular outcomes trial (CVOT) of the sodium–glucose cotransporter 2 (SGLT2) inhibitor ertugliflozin were presented at the Sessions. The data confirmed the CV safety of the drug; however, the CV benefits that had been expected based on the CVOTs of other SGLT2 inhibitors were not observed.

VERTIS-CV randomised people with type 2 diabetes and established CV disease to ertugliflozin (5 mg or 15 mg; *n*=5499) or placebo (*n*=2747), in addition to standard therapy. After a median follow-up of 3 years, there was no difference between the groups in terms of the primary outcome (CV death, non-fatal myocardial infarction or non-fatal stroke), confirming the CV safety of the drug.

However, ertugliflozin failed to meet its secondary endpoints of superiority in terms of CV death; a composite of hospitalisation for heart failure (HHF) and CV death; and a composite of renal death, dialysis/transplant, or doubling of serum creatinine from baseline. Indeed, the only CV benefit observed was a reduction in HHF (hazard ratio [HR], 0.70; 95% confidence interval [CI], 0.54–0.90). However, due to non-significance in earlier secondary endpoints in the hierarchical analysis, this finding was not statistically valid.

Compared with placebo, ertugliflozin reduced HbA_{1c}, body weight and systolic blood pressure. There was a greater risk of genital mycotic and urinary tract infections, in keeping with the class; however, there was no increase in risk of lower limb amputation, acute kidney injury, fracture or Fournier's gangrene. Diabetic ketoacidosis (DKA) rates were increased but not significantly so.

SGLT2 inhibitor amputation rates: canagliflozin exonerated?

In this database study of 43 017 people with type 2 diabetes who were initiated on SGLT2 inhibitors, no significant difference in amputation rates was identified between empagliflozin, dapagliflozin and canagliflozin.

Over a mean follow-up of 16.7 months, compared with empagliflozin, the adjusted incident rate ratio (IRR) was 1.31 (95% CI, 0.72–2.36) for dapagliflozin and 1.26 (95% CI, 0.81–1.97) for canagliflozin. The only significant predictors were prior amputation (IRR, 21.44; 95% CI, 11.88–36.69) and a Diabetes Complication Severity Index score of 3 or higher (IRR, 8.44; 95% CI, 5.55–12.82).

Given that a significantly increased amputation risk with canagliflozin has only been observed in one study cohort, the present results support the hypothesis that this was a chance finding.

Flash monitoring halves DKA rates

Use of the FreeStyle Libre flash glucose monitoring system has been found to halve the rate of hospitalisation for DKA in a nationwide database study from France.

The RELIEF study retrospectively reviewed the records of 33 203 people with type 1 diabetes and 40 955 with type 2 diabetes who initiated the Libre in the last 5 months of 2017. DKA rates were reviewed one year before and after initiation.

Overall, yearly DKA rates were reduced by 52% in people with type 1 diabetes and by 47% in those with type 2 diabetes. The reduction was greatest in those who had not used self-monitoring of blood glucose in the prior year (60% and 51% reductions in those with type 1 and type 2 diabetes, respectively); however, marked reductions were also seen in those who had previously tested their blood glucose five or more times per day (59% and 52% reductions).

Explaining the findings, lead author Ronan Roussel (chief of endocrinology, diabetes, and nutrition at Hôpital Bichat, Paris) said: "It is plausible that the use of the FreeStyle Libre system allowed people to detect and limit persistent hyperglycemia, and subsequently prevent ketoacidosis. Although preventing ketoacidosis has traditionally relied on intensive self-monitoring of blood glucose, there is growing literature that shows this has not helped reduce the overall incidence of diabetic ketoacidosis."

New cholesterol-lowering drug safe and effective in people with and without diabetes

The cholesterol-lowering drug bempedoic acid, which was approved for use in the EU in April 2020, has been shown to lower cholesterol levels without worsening glycaemic control or increasing the risk of developing diabetes, according to a pooled analysis of data from four Phase 3 trials.

In the studies, a total of 3623 patients on stable lipid-lowering therapy were randomised to bempedoic acid 180 mg or placebo for up to 52 weeks. Overall, 52% of participants had non-diabetic hyperglycaemia (NDH), 31% had diabetes and 17% had normoglycaemia.

Overall, mean LDL-cholesterol levels fell by around 20% at 12 weeks' follow-up in the bempedoic acid group, compared with a 1% increase in the placebo group. Reductions were greater in the subgroup of participants who were intolerant to statins (mean reduction, 24% vs 16% in those who tolerated statins). Significant reductions in total cholesterol, non-HDL-cholesterol, apolipoprotein B, and high-sensitivity C-reactive protein were also observed.

The effects did not differ by glycaemic status, nor did the safety profile, which was similar to that of placebo. The drug did not worsen measures of glycaemic control or increase the risk of new-onset diabetes compared with placebo.

It should be noted that these effects have not yet been translated into improved CV outcomes; however, a CV outcomes trial for the drug is currently underway. In a separate discussion of the potential role of bempedoic acid in the treatment armamentarium, John R Guyton (Duke University Medical Center, Durham, NC, USA) said that the drug would not be chosen in preference to a statin, ezetimibe, or PCSK9 inhibitor, but rather that its main role would be in people with statin intolerance and those with poor cholesterol control despite maximum tolerated lipid-lowering therapy.

Dapagliflozin cuts risk of new type 2 diabetes by a third

In this pre-planned analysis of the DAPA-HF trial (a Phase 3 study of dapagliflozin in people with chronic heart failure with reduced ejection fraction), dapagliflozin has been shown to reduce the incidence of new-onset type 2 diabetes by a third.

Of the 2605 participants who did not have type 2 diabetes when the study began, 1298 received dapagliflozin and 1307 received placebo. Over a median follow-up of 18.2 months, a total of 157 participants developed type 2 diabetes, of whom 150 had NDH at the study initiation. Overall, 4.9% of dapagliflozin recipients developed the condition, compared with 7.1% in the placebo group (HR, 0.68; 95% CI, 0.50–0.94).

The participants who developed type 2 diabetes had on average higher HbA_{1c} levels, greater BMI and lower estimated glomerular filtration rate at the beginning of the study.

Commenting on the findings, lead investigator Silvio Inzucchi (Yale University School of Medicine, New Haven, CT, USA) noted that the 32% risk reduction was similar to that observed with metformin in the US Diabetes Prevention Program. He added: "We will need to do more studies to see if this effect extends to patients without heart failure and reduced ejection fraction and to evaluate how durable the benefit might be and how long diabetes prevention persists after the discontinuation of therapy."

Insulin icodec: new once-weekly insulin safe and effective in early trials

Results of a Phase 2 trial of insulin icodec, a novel basal insulin analogue that can be taken once per week, showed that the medication was comparable to once-daily insulin glargine in terms of efficacy and safety.

In the double-blind trial, 247 insulin-naïve people with type 2 diabetes inadequately controlled with metformin plus or minus a DPP-4 inhibitor were randomised to icodec or glargine for 26 weeks. At follow-up, estimated mean HbA_{1c} had fallen by 14.5 mmol/mol and 12.6 mmol/mol in the icodec and glargine groups, respectively (*P*=non-significant).

Moderate-to-severe hypoglycaemia rates were comparable in the two groups (60.55 and 52.36 events per 100 person-years), and there were no unexpected safety findings.

Phase 3 clinical trials are now in development, and a co-formulation of insulin icodec and the GLP-1 receptor agonist semaglutide is also being tested in Phase 1 trials.

Diabetes Prevention Program shows a 20% reduction in new type 2 diabetes after 22 years

Long-term follow-up of more than 2000 people enrolled in the US Diabetes Prevention Program (DPP) Outcomes Study indicates a continued significant reduction in the participants' risk of developing type 2 diabetes.

As outlined previously, the original DPP, conducted in people with NDH, demonstrated that both lifestyle intervention, aimed at achieving weight loss, and metformin treatment reduced the risk of type 2 diabetes development, by 58% and 31%, respectively, compared with placebo after an average of three years.

The latest data, after an average of 22 years of study and including 75% of the participants who enrolled in the DPP who are still alive, show that the preventative effects in the treatment groups have persisted, with a 25% and 18% reduced risk of diabetes development with lifestyle intervention and metformin, respectively, compared with the original placebo group.

Those participants who did not develop diabetes had a significant 57% and 37% lower risk of developing the early changes of eye and kidney disease, respectively, and a 39% lower risk of major cardiovascular disease endpoints. The intensive lifestyle intervention group also had a long-term reduction in the development of frailty. ■

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