Latest news: ADA 2019 special

Stay abreast of the latest news that could impact diabetes nursing. In this issue, we summarise the key presentations from the American Diabetes Association 79th Scientific Sessions.

The American Diabetes Association's 79th Scientific Sessions were held on 7–11 June in San Francisco, California. Here we summarise the key presentations and publications.

New CVOT data

Data from three cardiovascular outcome trials (CVOTs), shedding light on dulaglutide, linagliptin and glimepiride, were presented at the Sessions.

REWIND: Dulaglutide improves cardiovascular outcomes

The once-weekly glucagon-like peptide-1 (GLP-1) receptor agonist dulaglutide reduced the risk of the composite endpoint of three-point major adverse cardiac events (MACE; cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) by 12% compared with placebo. The trial, which is notable for having a large proportion of participants without previous cardiovascular disease (CVD), also showed renal benefits with dulaglutide.

In the REWIND trial, 9901 people with type 2 diabetes aged at least 50 years and with high cardiovascular risk were randomised to once-weekly dulaglutide or placebo, both in conjunction with the standard of care. Only 31.5% had a history of CVD. Over a relatively long median follow-up of 5.4 years, the primary outcome occurred in 12.0% of the dulaglutide group versus 13.4% of the placebo group (hazard ratio [HR], 0.88; 95% confidence interval [CI], 0.79–0.99), with the effect starting to emerge within the first year. The cardiovascular benefits were similar when comparing participants with and without previous CVD. These findings are exciting as they suggest that GLP-1 analogues are effective for primary prevention of CVD as well as secondary prevention.

The composite renal outcome (new macroalbuminuria, ≥30% decline in eGFR or need for renal replacement therapy) was also reduced (HR, 0.85; 95% CI, 0.77–0.93), and there were modest reductions in HbA_{1c}, weight, LDL-cholesterol and systolic blood pressure.

The results were simultaneously published in the *Lancet*; click here to read.

Learn more about the GLP-1 analogues with the PCDS Clinical Hubs. Featuring CPD modules, resources and patient leaflets – all for free. Click here to access.

CARMELINA: Linagliptin safe across all ages and levels of renal function

Subanalyses of the CARMELINA trial, which previously showed the cardiovascular safety of the dipeptidyl peptidase-4 (DPP-4) inhibitor linagliptin, have confirmed its effects are consistent across all age groups, and even in people who already have kidney disease. Linagliptin is the only DPP-4 inhibitor that is not excreted renally and so can be given irrespective of kidney function.

Among 6991 participants randomised to linagliptin or placebo, there was no difference between the groups in either three-point MACE or the composite renal outcome. This latest analysis showed that the results did not differ by age, including among those aged ≥75 years, or by renal function, even in those with an eGFR <30 mL/min/1.73 m^2). In addition, progression to albuminuria was reduced with linagliptin in all but the lowest eGFR subgroup. HbA_{1c} was modestly reduced without increased risk of hypoglycaemia, regardless of kidney function.

These findings suggest that linagliptin is safe in a broad population of high-risk patients with type 2 diabetes, including older people and those with chronic kidney disease (CKD), in whom treatment options are limited.

CAROLINA: Glimepiride vs linagliptin

The cardiovascular safety of sulfonylureas has been a matter of debate for decades. Results from the CAROLINA trial appear to vindicate glimepiride, which showed no increased cardiovascular risk compared with linagliptin.

CAROLINA is unique among CVOTs so far, in that it had a active comparator, linagliptin, rather than placebo. A total of 6033 people with type 2 diabetes and CVD or high cardiovascular risk were randomised to daily linagliptin or glimepiride, in addition to standard care. After a median follow-up of 6.3 years, the risk of three-point MACE was the same for linagliptin and glimepiride (HR, 0.98; 95% CI, 0.84–1.14).

However, there were other safety concerns with glimepiride, which showed an increased risk of hypoglycaemia (37.7% vs 10.6% of participants) and severe hypoglycaemia (2.2% vs 0.3%). Glimepiride recipients also gained 1.5 kg more in weight than the linagliptin group. There was no difference in HbA_{1c} between the groups.

CREDENCE trial: Canagliflozin effective for primary cardiovascular protection

As we recently reported, canagliflozin was shown to improve renal outcomes in people with type 2 diabetes and CKD, with a relative risk reduction of 30% for the composite renal outcome of end-stage kidney disease, doubling of serum creatinine, or renal or cardiovascular death, compared with placebo. In addition, the relative risk of three-point MACE was reduced by 20%.

Further analysis of the cardiovascular outcomes in this trial were presented at the Sessions, suggesting that the sodium–glucose cotransporter 2 (SGLT2) inhibitor was effective not only for secondary cardiovascular protection but also primary prevention.

Overall, 49.6% of the study cohort had no previous CVD. The HR for three-point MACE in this group was 0.68 (compared with 0.85 in the subgroup with existing CVD). Similarly the risk of the combined endpoint of cardiovascular death or hospitalisation for heart failure was reduced in both subgroups (HR, 0.74 for primary prevention; 0.66 for secondary prevention).

With these findings, and the results for dulaglutide in REWIND, we have growing evidence to support the primary cardioprotective effects of both the GLP-1 receptor agonist and the SGLT2 inhibitor classes.

ABCD FreeStyle Libre audit results

The Association of British Clinical Diabetologists (ABCD) began its audit of the FreeStyle Libre flash glucose monitoring system in November 2017. The first results were presented at the Sessions, and showed improvements in HbA_{1c}, hypoglycaemia and diabetes distress, as well as reduced hospital admissions.

A total of 114 centres across the UK participated in the audit, providing details on 4709 Libre users. Almost all had type 1 diabetes, with a mean diabetes duration of 20 years. After a median follow-up of 6 months, mean HbA_{1c} fell from 66 to 60 mmol/mol (8.2% to 7.6%). Users with a higher HbA_{1c} at baseline had larger reductions.

Hypoglycaemia was also improved, with 79% reporting reduced time in the hypoglycaemic range, 31% reducing the number of hypos and 39% reducing nocturnal hypoglycaemia. In addition, 9% reported reversal of hypo unawareness, as assessed by the Gold score. Diabetes distress scores also fell significantly. Finally, the rate of hospital admissions due to hypoglycaemia or diabetic ketoacidosis fell from 7.3% to 1.9%.

Many Clinical Commissioning Groups has resisted uptake of the FreeStyle Libre, citing a lack of evidence. Although not from a randomised controlled trial, these data provide solid evidence from a large real-world cohort of NHS users to support the use of the device in appropriate patients.

PIONEER trials: Oral semaglutide

A new oral, once-daily formulation of the GLP-1 analogue semaglutide is undergoing Phase 3 evaluation in the PIONEER series of trials. Data from three studies from this series were presented at the Sessions.

In PIONEER 2, an open-label comparison conducted in 822 people with type 2 diabetes inadequately controlled on metformin, semaglutide was found to have a greater effect on HbA_{1c} than the SGLT2 inhibitor empagliflozin at 6 months (reductions of 14 vs 10 mmol/mol [1.3% vs 0.9%]). Both drugs also resulted in a mean weight loss of around 3.8 kg at 6 and 12 months.

In PIONEER 4, oral semaglutide was non-inferior to liraglutide and superior to placebo in terms of HbA_{1c}, and led to greater weight loss than both comparators. The most common adverse effect was nausea, which occurred in around 20% of users of either GLP-1 analogue.

Finally, in PIONEER 6, oral semaglutide was shown to be non-inferior to placebo in terms of cardiovascular safety. In a relatively small cohort of 3183 participants with type 2 diabetes and high cardiovascular risk, and after a short follow-up of just under 16 months, there was no significant difference in three-point MACE. However, there was a significant reduction in cardiovascular death (HR, 0.49; 95% CI, 0.27–0.92) and all-cause death (HR, 0.51; 95% CI, 0.31–0.84).

A common barrier to GLP-1 analogue use is the fact that, until now, they have only been available in injectable form. Although not yet approved by the European Medicines Agency, an oral formulation might well be preferable for many patients if it is proven to be as safe and effective as the injectable varieties.

CGM in type 1 pregnancy reduces costs over capillary testing alone

Offering women with type 1 diabetes continuous glucose monitoring (CGM) in pregnancy could save the NHS thousands of pounds per pregnancy and birth, according to a cost-effectiveness analysis.

Adding CGM to capillary blood glucose testing had previously been shown in the CONCEPTT trial to reduce the risk of maternal and neonatal complications, hospital length of stay, and the number and length of neonatal intensive care admissions.

Using data from CONCEPTT and modelling the costs of complications and hospital stay, based on an average of 1441 pregnancies in women with type 1 diabetes a year, the potential annual cost savings to the NHS were estimated to be £9 560 461, this despite the increased cost of routinely adding CGM to therapy between 10 and 38 weeks' gestation. ■

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