Conference news: Highlights from the 83rd Scientific Sessions of the American Diabetes Association

The American Diabetes Association's 83rd Scientific Sessions were held on 23–26 June in San Diego and virtually. Some of the key presentations from a diabetes nursing perspective are summarised in our report.

Bempedoic acid effective for primary prevention of cardiovascular events in statin-intolerant individuals

Bempedoic acid is a new cholesterol-lowering drug that has recently been demonstrated to lower LDL-cholesterol and improve cardiovascular outcomes in people at high cardiovascular risk who are intolerant to statin therapy in the CLEAR Outcomes trial (see summary in *Diabetes Distilled*). In this subanalysis of CLEAR Outcomes, Steven Nissen (Cleveland Clinic, OH, USA) and colleagues presented data on the effects of bempedoic acid in the subgroup of participants who had risk factors for heart disease but had not previously had a cardiovascular event.

Among the 4206 participants, 67% of whom had diabetes, the mean LDL-cholesterol level was reduced by 22.7% at 6 months in the bempedoic acid group, compared to a 1.4% reduction in the placebo group. High-sensitivity C-reactive protein levels, another cardiovascular risk marker, also fell significantly, by 25%, versus no change in the placebo group.

Over a median follow-up of 40 months, significant risk reductions were seen in the primary endpoint of 4-component major adverse cardiovascular events (hazard ratio [HR], 0.70), as well as secondary endpoints of myocardial infarction (HR, 0.64), cardiovascular death (HR, 0.61) and death from any cause (HR, 0.73).

Adverse effects of bempedoic acid included gout (2.6% vs 2.0% of participants), gallstones (2.5% vs 1.1%), and increases in serum creatinine, uric acid and hepatic enzyme levels.

The study was simultaneously published in *JAMA*.

Tirzepatide achieves 15% weight loss in people with type 2 diabetes and obesity

Tirzepatide, a dual GIP/GLP-1 receptor agonist, has previously been shown to reduce body weight and HbA_{1c} in people with type 2 diabetes. People with type 2 diabetes typically have a lesser weight-loss response to obesity drugs than those without type 2 diabetes.

Results from the SURMOUNT-2 study, designed to assess the effects of tirzepatide on weight loss over 6 years in people with type 2 diabetes, were presented at the Sessions. A total of 938 participants with type 2 diabetes who were either obese or overweight were randomised to tirzepatide 10 mg, 15 mg or placebo.

At 72 weeks, average weight loss in the pooled tirzepatide groups was 14.8 kg. Around 80% of tirzepatide recipients achieved ≥5% weight loss, compared with 33% in the placebo group, while ≥15% weight loss was achieved by 40%, 48% and 3% in the tirzepatide 10 mg, 15 mg and placebo groups, respectively.

Mean HbA_{1c} in the pooled tirzepatide groups fell from 64 mmol/mol (8.0%) at baseline to 41 mmol/mol (5.9%) at 72 weeks, and 80% of tirzepatide recipients achieved an HbA_{1c} ≤48 mmol/mol (6.5%), compared with only 20% of placebo recipients. Clinically significant improvements in risk factors such as blood pressure and lipids were also observed in the tirzepatide groups.

The adverse event profile was similar to those of other incretin-based drugs, with gastrointestinal side effects being the most common. The rate of serious adverse events was similar between the tirzepatide and placebo groups.

The study was simultaneously published in *The Lancet*.

A more detailed summary can be read in *Diabetes Distilled*.

A glut of new obesity drugs in the pipeline

New and updated weight loss medications dominated the final day of the sessions, with Robert Gabbay, Chief Scientific and Medical Officer for the ADA, describing the studies presented as "game changers in the way we customise treatment for individuals with obesity and those with type 2 diabetes".

Orforglipron, a developmental oral GLP-1 receptor agonist without the restrictions on food and drink intake that are required with oral semaglutide, was evaluated in 272 people with obesity or excess weight, but without diabetes, and resulted in a weight loss of 9.4%–14.7%, depending on dose, at 36 weeks, compared with a loss of 2.3% with placebo. The study was simultaneously published in *The New England Journal of Medicine*.

Another phase 2 study of orforglipron, published in *The Lancet*, was conducted in 383 people with type 2 diabetes. At

26 weeks, from a mean of 65 mmol/mol (8.1%) at baseline, HbA_{1c} fell by 23 mmol/mol (2.1%) in the pooled orforglipron group, versus a 5 mmol/mol (0.4%) reduction with placebo and a 12 mmol/mol (1.1%) reduction with the active comparator dulaglutide. Mean weight loss was 10.1 kg, 2.2 kg and 3.9 kg in the orforglipron, placebo and dulaglutide arms, respectively.

Retatrutide, a triple agonist of the GIP, GLP-1 and glucagon receptors, was evaluated in 338 adults with obesity (type 2 diabetes excluded), in a phase 2 study published in *The New England Journal of Medicine*. At 48 weeks, significant weight reductions, as high as 24.2% with the highest (12 mg) dose, were seen with all doses of retatrutide compared with the placebo arm, which saw a 2.1% reduction. A weight loss of ≥15% was achieved by 83% of participants who received the highest dose of retatrutide, compared with 2% of placebo recipients. In a separate phase 2 study, conducted in people with type 2 diabetes and published in *The Lancet*, retatrutide 8 mg and 12 mg reduced HbA_{1c} by 20–21 mmol/mol (1.9%–2.0%), significantly greater reductions than with both placebo and dulaglutide.

Survodutide, a dual GLP-1/glucagon receptor agonist in development, resulted in mean weight loss ranging from 6.2% to 14.9%, depending on dose, in a 46-week phase 2 study conducted in 387 adults with obesity. Weight loss of ≥5% was achieved by 83% of recipients of the highest dose, compared with 26% in the placebo group.

High-dose oral semaglutide (50 mg) was also evaluated as a treatment for obesity in the phase 3 OASIS 1 study, simultaneously published in *The Lancet*. In 667 participants with obesity but no diabetes, semaglutide resulted in a 15.1% mean weight reduction at 68 weeks, while 54% of semaglutide recipients achieved ≥15% weight loss.

Successful approaches to improve diabetes distress

Data from the EMBARK randomised controlled trial demonstrate clinically significant reductions in diabetes distress in adults with type 1 diabetes undergoing one of three structured intervention programmes. Three hundred adults with a T1-DDS score of ≥2.0 (indicating at least moderate distress; maximum score 6) were randomised to one of the following programmes:

- Streamline, a diabetes educator-led education and management programme.
- TunedIn, a psychologist-led programme focused exclusively on reducing DD.
- FixIt, an integration of the other two programmes.

All interventions were conducted remotely in groups of eight to twelve members and included initial workshops, one-to-one phone calls and follow-up meetings over a 4-month period.

The results showed significant reductions in diabetes distress in all three study arms at follow-up, with 35% of participants no longer reporting elevated distress and 74% reporting a clinically meaningful reduction in distress. From a mean of 2.8 at baseline, T1-DDS scores fell by 0.88, 0.59 and 0.48 in the Fixit, TunedIn and Streamline interventions, respectively, with significantly greater reductions in FixIt compared with Streamline ($P<0.05$).

Outcomes at 12 months' follow-up will be reported later in the year to determine whether these effects are sustained, as well as whether there are any effects on glycaemic outcomes.

Weekly insulin icodec in insulin-naïve patients with type 2 diabetes

Results from the ONWARDS 1 phase 3a, open-label, randomised controlled trial of a developmental once-weekly basal insulin, insulin icodec, demonstrated superior glycaemic control in insulin-naïve individuals with type 2 diabetes compared with once-daily insulin glargine U100.

The two treatment groups each comprised 492 participants with an HbA_{1c} at baseline of 53–97 mmol/mol (7.0–11.0%). At 52 weeks, mean HbA_{1c} was reduced by 17 versus 15 mmol/mol in the icodec versus glargine groups ($P<0.001$ for non-inferiority and $P=0.02$ for superiority of insulin icodec). Time in target glycaemic range was also significantly higher in the icodec group (72% vs 67%).

However, the rate of severe hypoglycaemia was significantly higher in the icodec group, at 0.30 versus 0.16 events per person-year of exposure at 83 weeks of follow-up (estimated rate ratio, 1.63). No new safety signals were identified and incidences of adverse events were similar in the two groups.

The study was simultaneously published in *The New England Journal of Medicine*.

Further discussion of insulin icodec, and the ONWARDS 2 trial conducted in people with insufficient glycaemic control whilst already on insulin therapy, can be found in *Diabetes Distilled*. ■

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Citation: Conference news: Highlights from the 83rd Scientific Sessions of the American Diabetes Association. *Journal of Diabetes Nursing* **27**: JDN297