Conference news: Highlights from the 2024 EASD Annual Meeting

The European Association for the Study of Diabetes Annual Meeting was held on 10–13 September in Madrid and virtually. In this report, we summarise the key presentations from a diabetes nursing perspective.

New once-weekly insulin shows promise in type 2 diabetes, but hypoglycaemia remains a concern in type 1 diabetes

Results of two phase 3 studies of insulin efsitora alfa, a once-weekly basal insulin in development by Eli Lilly, were presented at the meeting and published simultaneously. In the QWINT-2 study, once-weekly efsitora was compared with daily insulin degludec in people with type 2 diabetes insufficiently controlled on multiple oral diabetes medications and who had not yet begun insulin therapy.

A total of 928 participants were randomised to efsitora or degludec. After 1 year, the primary endpoint of mean HbA_{1c} decreased by 1.26% with efsitora and by 1.17% with degludec, a statistically significant treatment difference that demonstrated non-inferiority between efsitora and degludec. In addition, the proportion of time spent in the target glycaemic range was 64.3% with efsitora and 61.2% with degludec.

The rate of combined clinically significant or severe hypoglycaemia was similar between the two agents, at 0.58 and 0.45 events per person-year of exposure with efsitora and degludec, respectively. No severe hypoglycaemia was reported with efsitora, while six episodes were reported with degludec. The incidence of adverse events was similar in the two groups.

In the QWINT-5 study, weekly efsitora was compared with daily degludec, both in combination with meal-time insulin lispro, in 692 adults with type 1 diabetes. Again, after 1 year, efsitora was shown to be non-inferior to degludec; however, hypoglycaemia was more of a concern, with level 2–3 hypoglycaemia occurring at rates of 14.0 versus 11.6 events per person-year of exposure (estimated rate ratio 1.21), with the highest rates in the first 3 months of treatment. Severe hypoglycaemia was also more common in the efsitora group (10% vs 3% of participants over the 52-week study period).

These findings suggest that once-weekly insulin efsitora alfa may be a useful therapy for adults with type 2 diabetes; however, more research may be needed to evaluate efsitora dose initiation and optimisation of basal–bolus insulin dosing to balance efficacy with risk of hypoglycaemia.

The full studies can be read in the *New England Journal of Medicine* and the *Lancet* (open access; login required):

- QWINT-2
- QWINT-5

Liraglutide effective for weight loss in under-12s

The GLP-1 receptor agonist liraglutide is a safe and effective treatment for weight loss in children under 12 years of age, according to the SCALE Kids study, the results of which were presented at the meeting and published simultaneously. Children aged 6 to <12 years who took liraglutide for just over a year experienced a reduction in BMI of 7.4% compared with placebo and experienced improvements in blood pressure and glycaemia.

In the 56-week phase 3 study, 82 children (53.7% male, mean age 10 years, none with diabetes) were randomised 2:1 to receive liraglutide (3 mg or maximum tolerated dose) or placebo once daily, alongside individualised counselling at every visit to encourage adherence to a healthy diet and 60 minutes per day of moderate- to high-intensity exercise.

At study initiation, mean body weight was 70.2 kg, mean BMI was 31.0 kg/m^2 and 54.9% of participants had one or more obesity-related complication, such as insulin resistance or early puberty. At 56 weeks, the mean change in BMI was –5.8% for liraglutide and +1.6% for placebo (estimated treatment difference 7.4%; P<0.01). A reduction in BMI of at least 5% was observed in 46.2% of children receiving liraglutide versus 8.7% of those receiving placebo. Diastolic blood pressure and HbA_{1c} also improved more with liraglutide than with placebo. BMI and body weight increased in both groups after treatment stopped.

Side effects were in line with what has previously been observed in adolescents and adults taking liraglutide, and were common, occurring in almost 90% of participants in both groups. Gastrointestinal side effects were the most common, occurring in 80.4% and 53.8% of the liraglutide and placebo groups, respectively. Serious adverse events occurred in 12.5% of liraglutide recipients and 7.7% of placebo recipients. Four of the seven events in the liraglutide group were gastrointestinal in nature and 10.7% of participants in the liraglutide group discontinued treatment due to side effects, versus none in the placebo group.

Liraglutide is currently approved as an adjunct to lifestyle therapy in adults

and adolescents with obesity, but not in children under 12. Commenting on the findings, lead author Professor Claudia Fox (University of Minnesota Medical School), said: "The backbone of obesity treatment is lifestyle therapy – changes in diet and physical activity – but when used alone, the effect is modest and, as yet, no medication is approved for the treatment of general obesity in children who are younger than 12. Now with the possibility of a medication that addresses the underlying physiology of obesity, there is hope that children living with obesity can live healthier, more productive lives."

The full study can be read in the *New England Journal of Medicine* (open access; login required).

Rapid control of blood glucose in gestational diabetes can reverse the risk of obesity in offspring

Gestational diabetes (GDM) is known to confer an increased risk of obesity in the offspring. However, swiftly achieving glycaemic control after diagnosis can reduce the baby's risk to levels similar to that of children whose mothers did not have GDM, according to findings presented at the meeting.

The authors studied 258 064 women who gave birth in the US between 2011 and 2023 and their children. In total, 17 316 of the women had GDM. The trajectory of glycaemic control after diagnosis was divided into four groups:

1. Stable in the optimal range (optimal glycaemic control achieved soon after diagnosis and maintained throughout pregnancy) – 39.2% of participants.
2. Rapidly improving to optimal (optimal glycaemic control achieved within 4–6 weeks of diagnosis and maintained throughout pregnancy) – 32.3%.
3. Slowly improving to near-optimal – 16.7%.
4. Slowly improving to suboptimal – 11.8%.

Obesity prevalence at 2–4 years was 15.1% in children of women without GDM. In comparison, rates were 15.9%, 18.7%, 20.9% and 24.6% in children of women in groups 1–4, respectively. Adjusted relative risks were 1.01, 1.04, 1.13 and 1.23, respectively, and were significantly higher than controls in groups 3 and 4.

At 5–7 years, only children of women in group 1 had an obesity risk similar to that observed in children of individuals without GDM, while the relative risk was 1.18, 1.19 and 1.30 in groups 2–4, respectively.

These findings demonstrate further benefits of optimising blood glucose as soon as possible after GDM diagnosis, beyond reducing the risk of perinatal complications.

Post-marketing surveillance reassures about safety profile of tirzepatide

Analysis of real-world evidence from the US Food and Drug Administration's Adverse Event Reporting System (FAERS) database suggests that tirzepatide has similar gastrointestinal tolerability to other GLP-1 medications, without increased risk of diabetic retinopathy, medullary thyroid cancer or pancreatobiliary adverse events.

Randomised controlled trials have shown the safety profile of tirzepatide to be similar to that of GLP-1 receptor agonists, and mainly characterised by adverse gastrointestinal events. However, concerns about greater risks of pancreatitis, diabetic retinopathy, thyroid neoplasms, and cholecystitis and gallstones, have arisen. Therefore, authors from the University of Bari, Italy, analysed FAERS data and compared the risk of these adverse events versus those associated with SGLT2 inhibitors, insulin, metformin and other GLP-1 RAs.

Out of 20 409 reports referring to 1432 adverse events, the researchers analysed 7460 reports referring to 286 selected adverse events. Disproportionate reporting of several gastrointestinal events was detected with tirzepatide; specifically, eructation was 30-times more likely compared with other drugs overall, while nausea, dyspepsia, constipation and pancreatitis were four-times more likely. However, the risks were similar as those with other GLP-1 RAs. As expected, tirzepatide exhibited a greater risk of most gastrointestinal adverse events compared with insulin and SGLT2 inhibitors.

No disproportionate reporting of pancreatitis was observed with tirzepatide compared with SGLT2 inhibitors, but a greater risk was described compared with insulin and a lower risk compared with other GLP-1 RAs.

Medullary thyroid cancer had 13-times greater odds with tirzepatide compared to all other drugs (based on three events). The risk was similar to that with other GLP-1 RAs and SGLT2 inhibitors, but greater compared with insulin.

Similarly, reports of diabetic retinopathy (based on 12 events) were over three-times more likely with tirzepatide compared with all other drugs, but similar to that with SGLT2 inhibitors and lower compared with other GLP-1 RAs and insulin.

No disproportionate reporting of gallbladder and biliary-related adverse events was found, except for an increased risk of biliary colic with tirzepatide compared with other drugs overall and insulin. The risk of biliary colic was similar to that with other GLP-1 RAs and with SGLT2 inhibitors.

The study is limited by its observational nature, the relatively short experience with tirzepatide in everyday clinical use, non-randomised comparisons, potential data incompleteness and duplication, so the results should be interpreted cautiously.

The study was first published in August in the *Journal of Endocrinological Investigation* (open access).

GLP-1/amylin receptor agonist pill effective for weight loss in phase 1 trial

Amycretin, an oral dual agonist of the GLP-1 and amylin receptors in development by Novo Nordisk, results in weight loss of up to 13%, according to a phase 1, first-in-human study presented at the meeting.

After 12 weeks of therapy with amycretin (*n*=95) or placebo (*n*=29), the mean percentage body weight reduction was significantly higher with amycretin (10.4% with 50 mg once daily and 13.1% with 50 mg twice daily, versus 1.1% with placebo). Adverse events were similar to those observed with other GLP-1 receptor agonists and were more common during dose escalation.

Further study of this agent is planned.

Semaglutide's cardiovascular benefits are maintained in people with impaired kidney function

The benefits of semaglutide on preventing major adverse cardiovascular events (MACE) occur irrespective of whether the individual has impaired kidney function, according to a prespecified analysis of the SELECT trial presented at the meeting.

The study enrolled 17 604 adults (72% male) with overweight or obesity and established cardiovascular disease, but not type 1 or type 2 diabetes. Participants were randomised to semaglutide 2.4 mg or placebo for an average of 40 months. At randomisation, 11% of participants had an eGFR of <60 mL/min/1.73 m^2, and 13% had a urinary ACR of ≥30 mg/g (3.39 mg/mmol).

Over a median follow-up of 3.5 years, in participants with eGFR ≥60, the semaglutide group had an 18% reduction in MACE (a composite of cardiovascular death, non-fatal myocardial infarction or non-fatal stroke) compared with placebo (6.0% vs 7.3%), as well as an 18% reduction in the composite of MACE or death from any cause. The effects were more pronounced in participants with eGFR <60, in whom semaglutide was linked to a 31% reduction in MACE (9.7% vs 13.5%), and a 33% lower risk of MACE or death from any cause.

When ACR was used as a marker of kidney disease, semaglutide was linked to a 20% reduction in MACE both in those with ACR above and below 30 mg/g.

Among those with eGFR <60, serious adverse events were reported in 37% of those allocated to semaglutide compared to 46% of those on placebo.

Lead author Professor Helen Colhoun (University of Edinburgh) explained: "This new analysis found a similar percentage reduction in cardiovascular disease with semaglutide in those with and without poor kidney function in SELECT. Because those with poor kidney function have higher background risk of cardiovascular disease, the absolute benefit is greatest in this group.

"These findings have important clinical implications. People with impaired kidney function have increased risks of cardiovascular disease and the results show that semaglutide is safe and effective in reducing this risk substantially." ■

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