Latest news: Draft ADA/EASD advice, more data on tirzepatide, dulaglutide in paediatric T2D, and tech-assisted remission

Stay abreast of the latest news in diabetes. This issue, we cover the headlines from the American Diabetes Association 82nd Scientific Sessions, held in New Orleans and online from 3rd to 7th June.

Draft 2022 ADA/EASD consensus: Focus on holistic, patient-centred care, weight management and equity of access

The Chairs and writing group members presented the 2022 draft of the ADA/EASD consensus report on the management of hyperglycaemia in type 2 diabetes on the penultimate day of the Sessions. The draft builds on the 2018 consensus and its 2019 update, based on evidence from the last 3 years.

John Buse, summing up the presentation, called for action, highlighting the major opportunities to improve diabetes outcomes by effective implementation of the available evidence, with everyone having a role to play. He stressed the importance of individualising care to ensure that the right person gets the right therapy at the right time, independent of their social determinants of health (SDOH).

Significant differences proposed include the following.

- An updated holistic approach to patient-centred care:
  - Assess key person characteristics, including SDOH.
  - Consider specific factors impacting choice of treatment.
  - Shared decision-making to create a management plan.
  - Agree on a management plan.
  - Implement the management plan, with focus on avoiding clinical inertia by healthcare professionals.
  - Ongoing support and monitoring.
  - Review and agree on management plan.
- Healthy lifestyle behaviours, structured education and support, and addressing SDOH are the basis of care.
- Equal importance given to management of the four areas of care (glycaemic control, weight management, cardiovascular risk factors and cardiorenal protection), reflected in the updated treatment algorithm, with no longer any need to choose between them.
- Importance of 24-hour physical behaviours:
  - **Sitting** – break up every 30 minutes.
  - **Stepping** – add at least 500 steps per day.
  - **Sweating** – 150 minutes of moderate-to-vigorous activity per week.
  - **Strengthening** – 2–3 strength sessions per week.
  - **Sleep** – new focus on quality and quantity (>6 and <9 hours per night) and chronotype.
- Drug treatment guidance now includes benefits and side effects of oral semaglutide, higher-dose GLP-1 RAs, GLP-1 RA/insulin combinations, and mitigating weight gain with pioglitazone by combining with SGLT2 inhibitors or GLP-1 RAs.
- Recommendations for those at high cardiorenal risk updated:
  - Established or high risk of ASCVD: GLP-1 RA or SGLT2 inhibitor. If needed, add the other class or a TZD.
  - Heart failure: SGLT2 inhibitor (advice unchanged).
  - CKD: if albuminuria >200 mg/g (22.6 mg/mmol), SGLT2 inhibitor is preferred. If albuminuria <200 mg/g, manage increased cardiovascular risk using either an SGLT2 inhibitor or a GLP-1 RA.

The webinar session is available to watch here, and feedback on the draft consensus is open to everyone by emailing adacomments@diabetes.org until 21st June. The final consensus will be presented at the EASD meeting in September 2022 and published in *Diabetes Care* and *Diabetologia*.

New data on tirzepatide

New data on the effects of tirzepatide, a once-weekly dual GIP/GLP-1 receptor agonist that was approved by the US Food and Drug Administration in May for the treatment of type 2 diabetes, were presented at the Sessions. In particular, new findings on the effects of tirzepatide on obesity and chronic kidney disease (CKD) were presented.

Obesity

SURMOUNT-1 was a phase 3 trial evaluating the safety and efficacy of tirzepatide for the treatment of obesity. A total of 2539 adults with obesity but no type 2 diabetes (40.6% with prediabetes) were randomised 1:1:1:1 to tirzepatide (5 mg, 10 mg or 15 mg) or placebo. The mean BMI at baseline was 38 kg/m^2.

After 72 weeks of treatment, mean body weight was reduced by 15.0%, 19.5% and 20.9% in the tirzepatide 5 mg, 10 mg and 15 mg groups, respectively. In comparison, the placebo group lost 3.1% of body weight. Around 90% of tirzepatide recipients lost ≥5% of body weight, compared with 35%

of placebo recipients. Among participants with prediabetes, over 95% saw their blood glucose levels normalise in the tirzepatide groups. Clinically significant improvements in lipid levels and blood pressure were also observed with the study drug.

The safety profile of tirzepatide was consistent with the GLP-1 RA class. Adverse events were principally gastrointestinal in nature, with up to one third of tirzepatide recipients experiencing nausea (compared with 10% of the placebo group). They occurred primarily during dose titration.

The findings were published simultaneously in the *New England Journal of Medicine* (click here to access).

CKD

The open-label, phase 3 SURPASS-4 trial had previously demonstrated that tirzepatide improved glycaemic control compared with insulin glargine in people with type 2 diabetes inadequately controlled on oral medications (including SGLT2 inhibitors) and high cardiovascular risk (Del Prato et al, 2021). This prespecified analysis evaluated the effects of tirzepatide on renal outcomes (primary outcome: a composite of ≥40% eGFR decline, new-onset macroalbuminuria, renal death or progression to end-stage renal disease [ESRD]).

A total of 1995 participants were enrolled and followed for up to 104 weeks (median, 85 weeks). At study end, the risk of the primary endpoint was significantly reduced in tirzepatide versus insulin recipients (hazard ratio [HR], 0.58; 95% CI, 0.43–0.80). However, this was largely driven by a reduction in new-onset macroalbuminuria (HR, 0.41), as the risk of 40% eGFR decline was not significantly reduced (although eGFR decline over time was slowed) and there were no renal deaths and only five people progressed to ESRD (all in the insulin group). These effects were consistent across high-risk population subgroups and background SGLT2 inhibitor use.

Presenting the findings, Dr Hiddo Heerspink (University Medical Center Groningen, the Netherlands) concluded that a renoprotective effect of tirzepatide was possible (rather than a deleterious effect of insulin glargine), and that the agent should be evaluated further.

Artificial intelligence-led precision nutrition advice results in type 2 diabetes remission

This randomised controlled trial offers a glimpse into the future of using data to provide precision nutritional and lifestyle advice to improve health outcomes. The Twin Precision Nutrition programme uses artificial intelligence to analyse daily data collected from continuous glucose monitors, sensor watches, blood pressure meters, smart scales and detailed patient food intake information to provide an individual with daily precision health guidance, including nutrition, exercise, sleep and breathing recommendations, delivered by an app and by health coaches.

Interim data on 262 individuals with type 2 diabetes who had participated in the trial for 180 days (199 randomised to the intervention and 63 to standard care) were available for analysis. At baseline, mean age was 45 years, diabetes duration 3.9 years and HbA_{1c} 75 mmol/mol (9.0%). After 180 days, 94.9% of participants in the intervention group had achieved an HbA_{1c} <48 mmol/mol (6.5%), including 83.9% who achieved this without taking metformin. Mean HbA_{1c} fell by 36 mmol/mol in the intervention group, compared with 4 mmol/mol in the standard care group.

The study is ongoing, and the authors acknowledged that further, longer-term study will be required.

Dulaglutide in paediatric type 2 diabetes

The once-weekly GLP-1 RA dulaglutide was shown to be a safe and effective treatment for paediatric type 2 diabetes in findings presented at the Sessions and published simultaneously in the *New England Journal of Medicine*.

In a double-blind randomised controlled trial, 154 young people with type 2 diabetes (age 10 to <18 years with a BMI over the 85th percentile), treated with diet and lifestyle and/or metformin, with or without basal insulin, were assigned to placebo or dulaglutide 0.75 mg or 1.5 mg.

After 26 weeks of treatment, compared with an increase of 6.6 mmol/mol in the placebo group, mean HbA_{1c} decreased by 6.6 and 9.8 mmol/mol in the dulaglutide 0.75 mg and 1.5 mg groups, respectively (P<0.001 for both comparisons). Overall, 51% of dulaglutide recipients (either dose) achieved an HbA_{1c} of <53 mmol/mol, compared with 14% of placebo recipients. There were no significant differences in BMI between the groups.

The overall safety profile of dulaglutide matched that in adults, with gastrointestinal symptoms (mostly mild) among the most common adverse events.

These findings could extend the list of treatment options for type 2 diabetes in young people, at a time when incidence is rising rapidly.

Click here to read the article in full. ■

Del Prato S, Kahn SE, Pavo I et al; SURPASS-4 investigators (2021) Tirzepatide versus insulin glargine in type 2 diabetes and increased cardiovascular risk (SURPASS-4): a randomised, open-label, parallel-group, multicentre, phase 3 trial. *Lancet* **398**: 1811–24

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