Drugs in development and new data on established drugs: Highlights from the American Diabetes Association 81st Scientific Sessions

The American Diabetes Association 81st Scientific Sessions were conducted virtually from 25th to 29th June, with participants attending from across the world for the five-day programme. Despite the difficulties posed by the COVID-19 pandemic in conducting and concluding clinical trials, a wealth of data was presented on recent and developmental diabetes therapies. In this meeting report, Pam Brown highlights the key findings and relates them to current clinical practice. A brief summary is presented on this page, with more detailed analysis following.

Quick overview: Drugs in development and new data on established drugs

GRADE study: Head-to-head comparison of different diabetes drugs

Preliminary data were published from the long-awaited GRADE study, a head-to-head comparison of second-line (after metformin) use of the dipeptidyl peptidase-4 inhibitor sitagliptin, the sulfonylurea glimepiride, the glucagon-like peptide-1 receptor agonist (GLP-1 RA) liraglutide and insulin glargine in people with less than 10 years' type 2 diabetes duration (mean 4.2 years in those recruited), who were followed for an average of 5 years.

In the diverse population enrolled, the two injectable therapies demonstrated better glucose-lowering and ability to keep HbA_{1c} less than 7.0% (53 mmol/mol), while liraglutide and sitagliptin were associated with more weight loss. Liraglutide had the most gastrointestinal side effects and glimepiride was associated with the most hypoglycaemia.

The cardiovascular data remain to be fully adjudicated, but at this stage liraglutide appears to have demonstrated a reduction in cardiovascular risk compared with the other therapies. Sodium–glucose cotransporter 2 (SGLT2) inhibitors and thiazolidinediones were not included.

SURPASS: Phase 3 studies of new GIP/GLP-1 RA

Three different doses (5 mg, 10 mg and 15 mg) of tirzepatide, a once-weekly dual receptor agonist of glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 ("twincretin") that is currently in development, were studied across the SURPASS programme. Data from four of the phase 3 studies were presented at the meeting.

In SURPASS-1, tirzepatide achieved significantly better HbA_{1c} and weight reduction compared with placebo, while in SURPASS-2 it improved glycaemic control and weight loss compared with semaglutide. Tirzepatide also achieved superior glycaemic control versus insulin glargine in SURPASS-3 and compared to degludec in SURPASS-5.

AMPLITUDE-O: Cardiovascular outcomes trial of new GLP-1 RA

In AMPLITUDE-O, efpeglenatide, an exendin-based, injectable, once-weekly GLP-1 RA, demonstrated significant reductions in 3-point MACE and CKD progression when used as an add-on to metformin. There were no differences in outcomes with or without a co-prescribed SGLT2 inhibitor.

SOLOIST and SCORED: Sotagliflozin in people with comorbid heart failure or renal disease

An update on the SOLOIST and SCORED studies, previously published in the *New England Journal of Medicine*, exploring the effects of sotagliflozin, a dual SGLT1/SGLT2 inhibitor, demonstrated improved outcomes in people with type 2 diabetes and comorbid heart failure (HF) and chronic kidney disease (CKD), respectively.

SOLOIST confirmed that sotagliflozin was safe when initiated in patients recently hospitalised for worsening HF, reducing the risk of cardiovascular death and hospitalisation or urgent visits for HF by 33% across a range of ejection fractions, including in those with preserved ejection fraction. Data from SCORED demonstrated a significant reduction in myocardial infarction and stroke across the full range of albuminuria in those with type 2 diabetes and CKD.

Sotagliflozin is not currently licensed in the UK or US for treatment of type 2 diabetes.

DARE-19: Dapagliflozin in people with COVID-19

The DARE-19 study demonstrated the safety of dapagliflozin in patients admitted with COVID-19, although there was no significant benefit on mortality or other outcomes in this population who were carefully monitored during admission.

In particular, there was no evidence of any increased risk of diabetic ketoacidosis or acute kidney injury, suggesting that, if it is important to continue these drugs during acute infection and hospitalisation (for example, if used to treat HF), then with careful monitoring there is no need to stop the drug and lose the benefits. However, experts stressed it was important for the drug to be continued in an environment where careful monitoring of venous blood gases and renal function could take place, so this does not change current sick day guidance.

Click here to read Kevin Fernando's full analysis of DARE-19.

GRADE study: Comparison of various diabetes medications

The preliminary data from the long-awaited GRADE (Glycaemia Reduction Approaches in Diabetes: a comparative Effectiveness) study, designed to compare the effectiveness of a variety of diabetes therapies, demonstrated improved glucose-lowering and ability to keep HbA_{1c} <7.0% (53 mmol/mol) for longest in those treated with liraglutide or insulin glargine, compared to treatment with sitagliptin or glimepiride.

Study design

GRADE was a head-to-head study which recruited more than 5000 participants, comparing the second-line (after metformin) use of the dipeptidyl peptidase-4 inhibitor sitagliptin, the sulfonylurea glimepiride, the glucagon-like peptide-1 (GLP-1) receptor agonist liraglutide and insulin glargine in those with less than 10 years' type 2 diabetes duration (average 4 years in those recruited).

The participants were followed for a median of 5 years (maximum 7 years) and had an average age of 57 years, a baseline HbA_{1c} of ≤8.5% (69 mmol/mol) and were treated with at least 1000 mg per day of metformin at enrolment. The population was designed to be as diverse as possible, with 20% Black and 18% Latino participants.

Drug classes were included which were in common use in the US at the time of the study initiation, and specific drugs were selected by the investigators based on experience, tolerability and safety. Thiazolidinediones (TZDs) were not included as there were safety concerns, and neither were sodium–glucose cotransporter 2 (SGLT2) inhibitors as the first drug in this class was newly approved with limited experience of use. Although participants could not be masked to treatments since there were injectable and oral therapies in use, the staff and outcome adjudicators were masked.

The primary metabolic outcome was time to HbA_{1c} ≥7.0%, confirmed on a second HbA_{1c} test, on the maximal dose of study medication, with secondary outcomes including time to HbA_{1c} >7.5% (58 mmol/mol, again confirmed on second measurement). In the study protocol, when HbA_{1c} rose above 7.5%, glargine would be added if not already in use, or insulin would be intensified.

Results

Liraglutide and insulin glargine both demonstrated improved glucose-lowering and ability to keep HbA_{1c} <7.0% for longest, compared to treatment with sitagliptin or glimepiride, with liraglutide achieving this for a mean of 2.4 years, 72 days longer than the mean with glimepiride (2.2 years), 185 days longer than with sitagliptin (1.9 years) and 21 days shorter than with glargine.

Liraglutide and sitagliptin were associated with more weight loss; liraglutide-treated patients had the most gastrointestinal side effects, although there was only a 10% difference compared with the other drugs; and glimepiride was associated with the most hypoglycaemia. The cardiovascular (CV) data remain to be fully adjudicated, but at the time of the presentation, liraglutide demonstrated a reduction in CV risk compared with the other therapies.

Serious adverse events were rare and there was no difference between treatment groups. Rates of severe hypoglycaemia were low, occurring in 2.3% of participants with glimepiride, 1.4% with glargine, 0.9% with liraglutide and 0.7% with sitagliptin.

David Matthews (University of Oxford), who delivered the independent commentary on the study, congratulated the investigators on achieving study completion despite the restrictions posed by COVID-19. He challenged the fact that participants had had type 2 diabetes for differing durations, up to 10 years, at baseline, as well as the failure to include TZDs and SGLT2 inhibitors, the use of glimepiride rather than gliclazide, and the fact that the study was undertaken in a US population only. He highlighted that although hypoglycaemia numbers were small, they were 2–3 times more common in those treated with glimepiride than with liraglutide or sitagliptin. He concluded that GRADE was a good study but that there were very few findings to guide individualisation of therapy. Nonetheless, he outlined his key take-home messages from the study:

- The upward trend in the trajectory of HbA_{1c} over time seen in other studies (e.g. ACCORD and UKPDS) was confirmed.
- It would have been good to include SGLT2 inhibitors.
- Glimepiride works well early but then fails.
- Sitagliptin does not seem to work in those whose HbA_{1c} is >7.3% on metformin.
- Liraglutide appeared to reduce CV outcomes compared with the other treatments studied, although 10% of CV outcomes have yet to be adjudicated.
- The study is underpowered to answer questions about major adverse CV events and heart failure.

Tirzepatide versus semaglutide: SURPASS-2

GLP-1 receptor agonists are recommended in guidelines for their glucose-lowering, weight-reducing and cardioprotective effects, and work by stimulating insulin secretion during hyperglycaemia, suppressing glucagon secretion, delaying gastric emptying, decreasing appetite and reducing body weight. Another incretin hormone, glucose-dependent insulinotropic polypeptide (GIP), also promotes insulin secretion in response

to nutrient intake and modulates glucagon release, inhibiting it when hyperglycaemia occurs and increasing it in hypoglycaemia. Thus, therapies that increase the activity of both incretin hormones might be expected to further improve glycaemic control while reducing the risk of hypoglycaemia.

SURPASS-2 was an open-label, phase 3, randomised, active-control study of tirzepatide, a dual GIP/GLP-1 receptor agonist (a "twincretin"), currently in development for the treatment of type 2 diabetes. The study compared three once-weekly doses of tirzepatide (5 mg, 10 mg and 15 mg) with once-weekly semaglutide 1 mg, the current highest licensed dose for glucose-lowering, in 1879 participants who were overweight or obese, with type 2 diabetes inadequately controlled on at least 1500 mg of metformin.

The primary endpoint was HbA_{1c} change from baseline to week 40, with secondary endpoints including change in body weight, attainment of HbA_{1c} <53 mmol/mol (7.0%) and <39 mmol/mol (5.7% – the lower end of the prediabetes/non-diabetic hyperglycaemia range in the US).

At baseline, mean HbA_{1c} was 67 mmol/mol (8.3%), weight 93.7 kg, diabetes duration 8.6 years and age 56.6 years. The study used two "estimands" – or precisely defined estimates of treatment effect – and the published results discussed here represent the "treatment-regimen estimand", which includes the effects of all treatments in those randomised, even if study drugs were discontinued, and including additional drugs added to therapy.

Mean changes in HbA_{1c} were both noninferior and superior to semaglutide in those treated with all three doses of tirzepatide, with a 25 mmol/mol (2.3%) reduction in those treated with tirzepatide 15 mg compared to a 20 mmol/mol (1.86%) reduction with semaglutide 1 mg.

Weight reduction with tirzepatide was dose-dependent, with mean reductions of 7.6 kg, 9.3 kg and 11.2 kg with the 5 mg, 10 mg and 15 mg doses, respectively, over the 40-week study, compared with a 5.7 kg loss with semaglutide. Depending on the dose, 65–80% of those receiving tirzepatide achieved at least 5% weight loss. There was no plateauing of weight loss at study end in any of the groups. Lipid profiles and blood pressure also improved in many participants.

Adverse events were the main reason for early discontinuation in both treatment groups, and these were more common in participants treated with tirzepatide. Although there were 13 deaths during the trial, with four in each of the tirzepatide groups and one in the semaglutide group, all the deaths were adjudicated and none were considered to be related to the study drugs. The ongoing SURPASS-CVOT study is comparing cardiovascular outcomes with tirzepatide versus dulaglutide in people with type 2 diabetes and atherosclerotic cardiovascular disease.

Other studies of higher-dose semaglutide

In the phase 3 SUSTAIN FORTE study, also presented at the Sessions, treatment with semaglutide 2 mg was compared with the current top licensed dose of 1 mg, in 961 adults with type 2 diabetes and an average baseline HbA_{1c} of 74 mmol/mol (8.9%). Those treated with semaglutide 2 mg achieved HbA_{1c} reductions of 24 mmol/mol (2.2%) after 40 weeks (12 weeks' titration and 28 weeks at full dose) in those using it as directed, compared to 21 mmol/mol (1.9%) in those taking semaglutide 1 mg. A significantly greater weight loss of 6.9 kg was achieved with the higher dose, compared to a 6 kg reduction with the 1 mg dose. Reduced appetite was identified in 6.1% of those on 2 mg, compared with 3.8% of those on 1 mg, but rates of nausea, diarrhoea and vomiting were not significantly increased with the higher dose. The 2 mg dose is not licensed for use in the UK.

Weight loss achieved with a 2.4 mg dose of semaglutide used in the STEP trial programme was discussed by Kevin Fernando in a previous *Diabetes Distilled*.

The SURPASS-2 study was presented at the Sessions and published simultaneously in the *New England Journal of Medicine*. Click here to read the study in full.

AMPLITUDE-O: cardiovascular and renal outcomes with efpeglenatide in type 2 diabetes

AMPLITUDE-O, a cardiovascular outcome trial (CVOT) of efpeglenatide (a once-weekly, exendin-based, injectable GLP-1 receptor agonist) in those with previous cardiovascular disease (CVD) events or chronic kidney disease (CKD) and CV risk factors, demonstrated significant reduction in 3-point major adverse CV events (MACE) and a renal composite of CKD progression, compared to placebo over a median 1.8 years of follow-up. There were no differences in outcomes depending on baseline eGFR or co-prescribed metformin or SGLT2 inhibitors. An updated meta-analysis of GLP-1 RA CVOTs, including AMPLITUDE-O, demonstrated consistent benefits on MACE and slowing progression of CKD across the GLP-1 RA class.

The study randomised 4076 participants with type 2 diabetes and HbA_{1c} >7.0% (53 mmol/mol) who had either:

- a history of established CVD, or
- aged ≥50 years (male) or ≥55 years (female) with CKD (eGFR 25.0–59.9 mL/min/1.73 m^2), plus at least one other CV risk factor.

Mean age was 65.4 years, with nearly 50% aged <65 years; only 33% were female. Overall, 89.6% of participants had prior CVD and nearly one-third had an eGFR <60 mL/min/1.73 m^2; 21.8% had both established CVD and low eGFR.

Previous CVOTs of GLP-1 RAs did not include significant numbers of participants co-treated with SGLT2 inhibitors. AMPLITUDE-O, therefore, sought to clarify how combination treatment with the two drug classes would affect outcomes; 15.2% of participants were using an SGLT2 inhibitor at baseline. Use of other glucose-lowering and cardioprotective drugs was similar between those randomised to placebo and efpeglenatide. By study completion, 21.2% of those in the placebo group were prescribed an SGLT2 inhibitor compared with 17.5% of those receiving efpeglenatide at either dose.

Participants were randomised to receive efpeglenatide 4 mg or 6 mg or placebo, all delivered in identical syringes for subcutaneous injection, and randomisation was stratified according to SGLT2 inhibitor use. Efpeglenatide was initiated at 2 mg weekly, and the dose increased every 4 weeks until the randomised dose was achieved.

The primary outcome was first occurrence of MACE, consisting of CV death, non-fatal myocardial infarction or stroke.

Secondary outcomes, in hierarchical order of testing, included:

- Expanded MACE (including coronary revascularisation and hospitalisation for unstable angina).
- Composite renal outcome: new macroalbuminuria (ACR >300 mg albumen to creatinine in grams [>33.9 ACR measured in mg albumin to mmol creatinine as reported in the UK]); increase in ACR of ≥30% from baseline; sustained decrease in eGFR ≥40% for >30 days; renal replacement therapy for 90 days; or sustained eGFR <15 mL/min/1.73 m^2 for ≥30 days.
- MACE or death from non-CV causes.

Other pre-specified secondary endpoints included components of the expanded MACE or renal outcomes, death from any cause or hospitalisation for heart failure (HHF). A variety of additional pre-planned composite outcomes were also explored.

Results

There were 3.9 MACE events per 100 person-years in those treated with efpeglenatide compared to 5.3 events per 100 person-years in those receiving placebo (a significant 27% reduction), demonstrating the non-inferiority and superiority of efpeglenatide in reducing major adverse cardiovascular events, with a possible greater benefit for the higher dose of efpeglenatide versus the lower dose. In total, 46 similar patients would need to be treated with efpeglenatide for 1.8 years to prevent one major adverse CV event. There was also a significantly lower incidence of the expanded MACE composite event.

The composite renal outcome was significantly reduced by 32% in those receiving efpeglenatide versus placebo.

Results of the analyses of the other pre-specified secondary endpoints must be seen as exploratory only, due to the hierarchy of statistical testing. Despite attempts to achieve glycaemic equipoise, there was a 1.24% difference in HbA_{1c} between those treated with efpeglenatide compared to placebo, and small differences in blood pressure and weight, which the investigators concluded might contribute a small amount to the identified outcome differences.

As would be anticipated, gastrointestinal adverse events occurred more frequently with efpeglenatide than with placebo, but other pre-specified safety outcomes and adverse events were similar between the treatment and placebo groups. There was no signal for worsening of retinal disease, but those with severe retinal disease were excluded from the study.

Key take-home messages

In those with type 2 diabetes and high prevalence of CVD and CKD with high HbA_{1c} and moderate use of an SGLT2 inhibitor, efpeglenatide 4 mg or 6 mg once weekly significantly and safely reduced:

- MACE (including death from unknown causes) by 27%.
- Expanded MACE, including coronary revascularisation or unstable angina, by 21%.
- Renal composite by 32%.
- MACE or non-CV death by 27%.

Meta-analysis and commentary

Professor Naveed Sattar (University of Glasgow) presented an updated meta-analysis of outcomes from the eight GLP-1 RA CVOTs, including AMPLITUDE-O. This demonstrated a 24% reduction in 3-component MACE, with no difference between human and exendin-based GLP-1 RA structures. There was a greater effect (17% reduction) on stroke than on myocardial infarction. The GLP-1 RAs demonstrated a decrease in all-cause mortality, plus additional evidence of reduced risk of HHF and renal dysfunction. There was no increased risk of severe hypoglycaemia, retinopathy or pancreatic adverse effects.

In her independent commentary on the study, Amanda Adler (Professor of Diabetic Medicine and Health Policy, University of Oxford) congratulated the investigators on placing the trial in the context of previous CVOTs, demonstrating the safety of efpeglenatide and that it lowered the risk of CV and renal disease compared with standard care. Those results that were only exploratory in respect of the statistical hierarchy were clearly labelled. She highlighted that this study was primarily a safety trial and, compared with other GLP-1 RA CVOTs, this study recruited those with a longer duration of type 2 diabetes (up to 15 years), eGFRs down to 25 mL/min/1.73 m^2, highest mean HbA_{1c} (8.9% [74 mmol/mol]) and the highest percentage of people on insulin (72%).

Professor Adler challenged the use of

placebo as the comparator in relation to the CV outcome, since she felt the real question is how this drug compares to other drugs in the class. However, for the renal outcome, she agreed placebo was the correct comparator, since the drug would be used mainly as add-on to an ACEi/ARB or sacubitril–valsartan, rather than instead of these. SGLT2 inhibitors are known to have cardioprotective effects, and people were stratified by use at baseline into current use, potential future use and neither current nor future use. She concluded that if there was an interaction between SGLT2 inhibitor use and efpeglenatide, then this study did not find it.

Data were presented at the Sessions, and the results from AMPLITUDE-O were simultaneously published in the *New England Journal of Medicine*. Click here to read in full.

SCORED and SOLOIST-WHF: updated data confirm significant benefits of sotagliflozin across the heart failure spectrum

An update on the SCORED and SOLOIST-WHF studies previously published in the *New England Journal of Medicine*, exploring effects of sotagliflozin (a dual SGLT1/SGLT2 inhibitor) versus placebo demonstrated improved outcomes in those with CKD or heart failure (HF). SCORED data demonstrate a significant reduction in myocardial infarction (MI) and stroke across the full range of albuminuria in those with type 2 diabetes and CKD compared to placebo. Sotagliflozin is not licensed in the UK or US for use in type 2 diabetes.

SOLOIST-WHF confirmed sotagliflozin was safe when initiated in patients recently hospitalised for worsening HF, reducing the risk of CV death, hospitalisation or urgent visits for HF by 33% across a range of ejection fractions, including in those with preserved ejection fraction (HFpEF).

SCORED

The SCORED (effect of Sotagliflozin on Cardiovascular and Renal Events in Patients with Type 2 Diabetes and Moderate Renal Impairment who are at Cardiovascular Risk) study was a double-blind, randomised controlled trial that recruited 10 584 people with type 2 diabetes and CKD (eGFR 25–60 mL/min/1.73 m^2 and CV risk factors) but no requirement for significant albuminuria, who were randomised to placebo or sotagliflozin 200 mg (increased to 400 mg, if tolerated), and followed for a median of 16 months.

The primary endpoint was changed in August 2002 prior to any unblinding, due to funding being withdrawn, and the trial duration shortened. The new primary endpoint, a composite of total CV deaths, hospitalisations for heart failure (HHF) or urgent HF visits, demonstrated a highly significant 26% reduction in those receiving sotagliflozin versus placebo. This translates to an absolute risk reduction of 1.9 events per 100 patient-years and 54 patient-years of treatment required to prevent one event. Sotagliflozin was demonstrated to provide benefit across the whole spectrum of albuminuria.

The original co-primary endpoints of first occurrence of 3-point major adverse CV events (CV death, non-fatal MI or stroke) and a composite of CV death or HHF were also both significantly reduced in those receiving sotagliflozin compared with placebo.

Presenting the renal data, the investigators outlined the impact of the trial shortening and lower event rates, which resulted in there no longer being statistical power to demonstrate significant reductions in the renal endpoints. Although investigator-reported events had to be used instead of adjudication, as this was a double-blind trial and the renal endpoints were judged to be unambiguous, the investigators concluded this was not a concern.

SOLOIST-WHF

The SOLOIST-WHF (Effect of Sotagliflozin on Cardiovascular Events in Patients with Type 2 Diabetes Post Worsening Heart Failure) trial recruited 1222 patients admitted with HF, with elevated BNP, who required intravenous diuretics and had been stabilised prior to randomisation to sotagliflozin or placebo initiation prior to or within 3 days of discharge. Those with end-stage HF, recent acute coronary syndrome, stroke, PCI or CABG, or eGFR <30 mL/min/1.73 m^2 were excluded. The primary endpoint was the same as in SCORED – total CV deaths, HHF and urgent HF visit.

As with SCORED, the Kaplan–Meier curves separated early and there was a significant 33% reduction in the primary endpoint in those treated with sotagliflozin compared with placebo, translating to an ARR of 25 events per 100 patient-years. One person would need to be treated for 4 years to prevent one event.

Independent commentary

In his independent commentary on SCORED and SOLOIST-WHF, Javed Butler (Professor and Chairman, Department of Medicine at the University of Mississippi, USA) reminded the audience of the CV and renal outcomes of earlier SGLT2 inhibitor studies, highlighting that differing renal-related composite endpoints in these studies make it difficult to compare trials but that all, except VERTIS CV, demonstrated significant positive renal outcomes. He outlined multiple confirmed and postulated mechanisms likely to confer cardio–renal–metabolic benefits and summarised the uniqueness of SCORED among SGLT2 inhibitor studies, in that it tested a combination of SGLT1 and SGLT2 inhibition and studied people with stage 4 CKD, who have not been studied previously, and those with stage 3b CKD, who have been under-represented in other

CV and renal outcome trials. SCORED is, therefore, important in assessing the generalisability of CV and renal benefits of SGLT2 inhibitors, as it included a broader range of people with CKD, including those with and without macroalbuminuria, those who were older (mean age 68 years) and a greater proportion of females (48%) than other studies.

Reviewing the data from 4500 patients with a history of HF included in SOLOIST-WHF and SCORED, Professor Butler highlighted the significant reduction in the primary outcome of CV death, HHF and urgent HF visits in patients with HF across the spectrum of ejection fraction (EF <40%, EF 40–50% and EF >50%), with absolute risk reductions of 9.1/100 patient-years, 11.1/100 patient-years and 5/100 patient-years, respectively, in those in the three ejection fraction groups.

Deepak Bhatt, the lead author of the published papers, speaking at the conference, concluded that the results of these two studies make it clear that most patients with type 2 diabetes and either kidney disease or HF should be on an SGLT2 inhibitor or an SGLT1/SGLT2 inhibitor.

Sotagliflozin is a dual SGLT1 and SGLT2 inhibitor. SGLT1 is the primary transporter for absorption of glucose and galactose in the gut, and inhibition would be expected to decrease glucose peaks post-prandially. Its action is independent of kidney function. SGLT2 is expressed in the kidney, where it is responsible for the reabsorption of 90% of filtered glucose, and inhibition by sotagliflozin requires adequate kidney function. Both the effects of SGLT1 and SGLT2 inhibition are insulin-independent.

Key take-home messages from the two trials

- Sotagliflozin was well tolerated in both studies, with increased diarrhoea, genital infections, volume depletion and DKA in SCORED, and higher rates of diarrhoea and severe hypoglycaemia in SOLOIST-WHF, compared to placebo.
- Sotagliflozin significantly reduced CV death, HHF and urgent HF visits when started during, or immediately following, admission for HF (SOLOIST-WHF) or in those with type 2 diabetes, CKD and CV risk factors (SCORED).
- Sotagliflozin provides glycaemic control even at the lower range of eGFR, unlike with conventional SGLT2 inhibitors.
- Early eGFR changes seen with sotagliflozin are similar to those seen with renin–angiotensin system blocking drugs and SGLT2 inhibitors.

Sotagliflozin is only currently licensed in the UK for use as an adjunct to insulin in those with type 1 diabetes, and is not licensed for use in type 2 diabetes.

The original data from the SCORED and SOLOIST-WHF trials were presented as late-breaking news at the American Heart Association Scientific Sessions and published in the *New England Journal of Medicine* early in 2021. Updated data, including the consequences of the funding withdrawal for the study, were presented at the ADA Scientific Sessions. ■

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