



Impressions from EASD 2018

Dr Caroline Day reports from the European Association for the Study of Diabetes 54th annual meeting in Berlin, Germany, 1–5 October 2018

Introduction

The 2018 EASD meeting, held at the Messe Berlin Exhibition Halls in Berlin-Charlottenburg – a short rail journey from the city centre – was the largest EASD since 2014, with 15,699 on-site delegates from 32 countries. Nevertheless, there were 2,428 fewer delegates than when the meeting was last held here in 2012. However, there were more than 10,000 online participants at this meeting. This year almost 20% of on-site delegates came from the nine countries that border Germany, and the host nation provided most delegates. The UK fell into third place this year with 980 delegates, being usurped by the USA, which was represented by just over 6% of delegates.

Abstracts and access

There were 48 fewer abstracts for presentation at this meeting than last year. This year abstracts 1–264 were presented in 48 oral sessions and abstracts 265–1218 were presented across six poster events. Abstracts and electronic posters can be viewed via the EASD virtual meeting, and abstracts can also be accessed via the meeting app (downloadable from Google play and the App store) and in the EASD journal *Diabetologia* – available free as a pdf.^{1,2} Efficient use of the virtual meeting can be facilitated by viewing the programme-at-a-glance webpage to check out the EASD study groups and non-commercial satellite symposia as well as the scientific programme sessions.³ Some oral presentations (OP) and symposia (S) are noted below. The industry-sponsored symposia, meet-the-expert sessions and their programmes are listed online (scroll down the page).⁴ Several of the EASD live TV interviews can be seen on YouTube. Many presentations were accompanied by simultaneous full publication online; where possible, full publications are cited herein.

SGLT inhibition

Sodium glucose co-transporter (SGLT) inhibitors received extensive attention at the meeting (eg, OP13, OP19, S17, S21, S25, S26), and a special issue of *Diabetologia*

Table 1 Award lectures at EASD 2018

Prize	Lecturer	Title (<i>day of presentation</i>) and link to EASD interview
50th Claude Bernard Lecture	Jaakko Tuomilehto (Finland, Kuwait)	Prevention of type 2 diabetes: the dream that came true
33rd Camillo Golgi Lecture	Peter P Nawrot (Heidelberg, Germany)	Diabetic complications – an alternative view on diabetes
12th Albert Renold Lecture	Rohit N Kulkarni (Boston, USA)	<i>Epitranscriptomics</i> (RNA methylation): a new level of regulation in islet biology and metabolism
4th EASD-Novo Nordisk Foundation Diabetes Prize for Excellence	Gokhan S Hotamisligil (Boston, USA)	A quarter century of immunometabolism
53rd Minkowski Lecture	Fredrik Bäckhed (Gothenburg, Sweden)	The gut microbiota – a forgotten organ – that contributes to glucose metabolism (see <i>Virtual Meeting, Thursday</i>) https://www.youtube.com/watch?v=QvRdGj931xM

was printed to accompany the meeting – a notable feature is a paucity of European authors.⁵ Amongst the presentations this year, particular attention was given to the potential use of SGLT inhibitors as adjuncts to insulin in type 1 diabetes. In the phase 3 EASE-2 and EASE-3 trials, overweight adults with type 1 diabetes (>1 year; eGFR >30 mL/min/1.73 m²) were given empagliflozin 10 mg or 25 mg as an adjunct to insulin, and in EASE-3 patients were also assigned to empagliflozin 2.5 mg plus intensified insulin therapy (S26). The primary endpoints were assessed at week 26 in both studies and, in EASE-2 patients, were additionally followed to week 52. Empagliflozin decreased HbA_{1c}, body weight, insulin dose and systolic blood pressure (consistent with previous studies in which SGLT inhibitors were added to insulin-treated type 2 patients). Continuous glucose monitoring (CGM) showed that patients spent more time in target glucose range. Genital infections were commoner in empagliflozin treated patients. Severe hypoglycaemia was rare and diabetic ketoacidosis (DKA) occurred more with empagliflozin 25 mg

and 10 mg, but was similar between empagliflozin 2.5 mg and placebo.⁶

The oral dual SGLT1 and SGLT2 inhibitor sotagliflozin is in clinical development. In the European inTandem2 study, addition of sotagliflozin 200 mg or 400 mg as an adjunct to optimised insulin therapy in adults with type 1 diabetes (>1 year; eGFR >45 mL/min/1.73m²) for 52 weeks decreased HbA_{1c}, body weight and insulin dose and increased time in target glucose range. Diarrhoea and genital infections were commoner with sotagliflozin, but there were fewer episodes of documented and severe hypoglycaemia in people taking sotagliflozin, although there were more cases of DKA (~3%) compared with placebo.⁷

A secondary analysis of data from the CANVAS programme showed reductions in HbA_{1c} progressively diminished with declining renal function, but the relative effects of canagliflozin on body weight and most cardiovascular (CV) and renal outcomes were similar across the eGFR subgroups.⁸

The CVD-REAL session (S25) highlighted comparative effectiveness of SGLT2 inhibitors on CV outcomes and the utility of

Trial abbreviations	
EASE	Empagliflozin as adjunctive to insulin therapy in type 1 diabetes
ELIXA	Evaluation of cardiovascular outcomes in patients with type 2 diabetes after acute coronary syndrome during treatment with AVE0010 (Lixisenatide)
EXSCEL	EXenatide Study of Cardiovascular Event Lowering
CANVAS	CANagliflozin cardioVascular Assessment Study
CARMELINA	Cardiovascular and Renal Microvascular outcome study with LINagliptin in patients with type 2 diabetes mellitus
HARMONY	Albiglutide QW cardiovascular outcome trial
LEADER	Liraglutide Effect and Action in Diabetes: Evaluation of cardiovascular outcome Results
PIONEER	Oral semaglutide trial
RISE	Restoring Insulin Secretion

real-world evidence. The OBSERVE-4D study, a retrospective real-world analysis across four databases (>720,000 new users of glucose lowering agents), showed that the SGLT2 inhibitors conferred a similarly reduced risk of hospitalisation for heart failure, including patients with established CV disease. There was no evidence of increased risk of lower limb amputations with canagliflozin compared with other SGLT2 inhibitors and non-SGLT2 inhibitors in the overall population and in those with established CV disease.⁹

Incretin action

Among reports of cardiovascular outcome trial (CVOT) data, the HARMONY study (S04) with albiglutide (a once-weekly injectable glucagon-like peptide-1 receptor agonist (GLP-1RA)) showed superiority to usual care ($p=0.0006$), reducing major adverse cardiovascular events (MACE) by 22%. Adverse events were similar in both groups.¹⁰ In June 2018, marketing of albiglutide was discontinued for commercial reasons, but it is possible that another company will consider returning it to the European market.

Several presentations described further analyses from CVOTs including ELIXA,¹¹ EXSCEL and LEADER (eg, OP07, OP13, S17). The session on the PIONEER programme (S19) showed that, at 26 weeks, once-daily oral semaglutide (titrated to 3 mg, 7 mg or 14 mg) as monotherapy or as combination therapy reduced HbA_{1c} and body weight more effectively than comparator treat-

ments and was as effective as the injection. Adverse events were consistent with those shown with injected semaglutide.

Glucose-dependent insulinotropic polypeptide (GIP) acts on the beta cell to potentiate nutrient-induced insulin secretion – offering a novel therapeutic approach. The concept of ‘twincetins’ (combination of GIP and a GLP-1RA), supported by a phase 2 trial, was considered in S53 and other novel combinations were presented in OP28.¹²

CARMELINA is the latest CVOT with a dipeptidyl peptidase-4 (DPP4) inhibitor to report (S35). Like the other DPP4 inhibitors, linagliptin was non-inferior to standard treatment with regard to MACE and renal outcomes, although a relatively high proportion (62%) of patients had renal disease (eGFR <60 mL/min/1.73m²). Linagliptin had neutral effects on hospitalisation for heart failure and adverse events were consistent with those known for the class.

Symposia etc

The invited symposium to reprise the UKPDS (S15) set the scene leading to Professor Robert Turner designing the UKPDS (his widow Dr Jenny Turner was a guest of EASD at the symposium), highlighted the cumulative observations which occurred during the 20 years (1977–1997) of this study – there were five simultaneous publications when the study reported at EASD 1998 – and considered the impact of this study which sought to assess policy rather than individual drugs (of which five new classes have become available in the UK since the

UKPDS reported). The UKPDS is the only large trial of newly diagnosed type 2 diabetes. It addressed the issue of early glycaemic control (additionally vindicated by the post-trial follow-up data) and is the evidential cornerstone of clinical practice in the first years of treatment. The international impact of UKPDS is apparent throughout the EASD meeting and is manifest in the ADA-EASD consensus guidance – the most recent version of which was presented on the last morning of the meeting (S41).¹³

The CV safety of the serotonin 2C receptor agonist lorcaserin in overweight/obese people with or at high CV risk was investigated in the CVOT CAMELLIA (S33). This appetite suppressant improved weight loss (vs diet/lifestyle) and did not increase MACE.¹⁴ Lorcaserin-induced weight loss decreased incident diabetes, improved glycaemic control and some patients achieved remission of diabetes.¹⁵ Lorcaserin is available in the USA, but has not been approved in Europe.

The RISE study is investigating a range of interventions to determine their impact on the preservation or improvement of beta-cell function in youths and adults with pre-diabetes or early type 2 diabetes. In a dedicated session (S09) it was concluded that weight loss may be an effective way to reduce the severe insulin resistance of puberty.¹⁶ Adults treated for 2 years with metformin or adjustable gastric band (Lap-Band®) achieved a 1.7 kg and 10.6 kg weight loss, respectively, but there were no significant differences between the treatments for indices of glycaemic control, despite gastric banding improving the acute beta-cell response to glucose.¹⁷

Technological advances continue apace in glucose monitoring and insulin delivery, including closed-loop systems and their utility, as well as studies on beta-cell replacement (eg, OP10, OP15, OP18, S24).¹⁸

Advocacy

The St Vincent Declaration was launched in 1989 as an initiative to set targets at a national level to aid healthcare systems to improve outcomes for people with diabetes.¹⁹ The European Diabetes Forum (EUDF) has been launched as a follow-on from the 1989 initiative to address the landscape of diabetes care in Europe and influence policy.²⁰ The Parliamentarians for Diabetes Global Network continues to champion the cause of diabetes across the political spectrum and EUDF should further support diabetes policy development at government level.²¹

Forward planning

From 16 to 19 September the Fira de Barcelona, Av. Joan Carles I (about 10 km from the airport and 8 km from La Rambla) is the venue for EASD 2019. September is an optimal month to visit Barcelona with temperatures ranging from 19°C to 27°C – so an opportunity to top up vitamin D reserves.

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Correspondence: Dr Caroline Day,
Visiting Fellow, Diabetes Group,
Aston University, Birmingham B4 7ET, UK
E-mail: cday@mededuk.com

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