Snippets from EASD 2023

Dr Caroline Day reports on the European Association for the Study of Diabetes 59th annual meeting, Hybrid EASD 2023



Introduction

The annual EASD meeting for 2023 was held in Hamburg (2-6 October) for the first time in its 59-year history. The conference centre, in the shadow of the telecoms tower in the heart of Hamburg, had the benefit of being opposite the picturesque Planten un Blomen Park which offered a tranguil escape from the city and conference bustle and a short cut to the old town. As in 2022 this was a hybrid event, with onsite presentations and delegate participation possible both physically and virtually. It was a lively meeting, with most of the >11,000 registrants being on-site. The meeting was also viewed live from 739 locations worldwide, 6.5% of them in the UK. How many people might have shared a screen? Total registrant numbers were similar to last year (but >20% fewer than at the last pre-Covid meeting in 2019) and the top four countries were, as previously, Germany (again No. 1), the US, Denmark and the UK, which had dropped to 4th place with fewer than 700 registrants. Exclusive registrant access to webcasts was available until 3rd November 2023.

Engaging with the event

Industry symposia were held all day Monday (9am-5pm), after the scientific sessions on Tuesday and Wednesday and for early risers three symposia were held from 7.45am on the Tuesday. During the three breaks in the daily scientific sessions an industry-sponsored hot topic lecture was delivered on the Spotlight Stage.

A flipbook and pdf of the full programme (programme at a glance p24-31; scientific sessions p32-136; short orals p137-235; satellite symposia p252-265; industry-sponsored sessions p268-317) can be downloaded from the EASD website, and the link to the programme overview offers interactive access to individual abstracts (https:// www.easd.org/annual-meeting/easd-2023.html). The supplement to *Diabetologia* offers an opportunity for

Table 1. Award lectures at EASD 2023

| Prize | Lecturer | Title (day and time of presentation) |
|--|---------------------------|--|
| 55th Claude Bernard Lecture | Ake Lernmark Sweden | Dissecting etiologies of autoimmune type 1 diabetes <i>Tuesday 9.30am</i> |
| 38th Camillo Golgi Lecture | Stephan Herzig Germany | Diabetes complications: from classical to emerging <i>Tuesday 5.15pm</i> |
| 17th Albert Renold Lecture | Yuval Dor Israel | Disrupted RNA editing as a path to type 1 diabetes Wednesday, 9am |
| 9th EASD-Novo Nordisk Foundation Diabetes Prize for Excellence | Roman Hovorka UK | Automated insulin delivery – diabetes tech at its best <i>Wednesday, 5.30pm</i> |
| 58th Minkowski Lecture | Timo Muller Germany | Novel insights into regulation of energy and glucose metabolism by GIP and GIPR:GLP-1R co-agonists <i>Thursday, 5.30pm</i> |
| 2nd EASD-Lilly Centennial Anniversary Prize Lecture | Gerald Shulman USA | The role of ectopic lipid in insulin resistance and cardiometabolic disease Friday, 9.00am |

perusal of the content of the 56 oral presentation sessions (Abstracts 1-308) and 96 short oral discussion sessions of nearly 700 abstracts (Abstract 309-1007).¹

The EASD media centre hosts recordings of presentations at the annual meetings (https://www.easd.org/mediacentre/ home.html) and the EASD YouTube channel has interviews with several of this year's EASD celebrities.

Highlights

Symposia and debates are usually worth attending. Examples this year included 'Is lasting remission of type 2 diabetes feasible in the real-world setting?' (Wednesday 5.30pm) and 'Precision medicine in diabetes: complexity and pragmatism' (Thursday 9am). 2-5 The EASD/ADA symposium: 'Hyperglycaemic crises in adult patients with diabetes consensus report' is worth a visit (some useful decision graphics) to get the latest recommendations for diagnosis and care of these patients (including those with euglycaemic DKA) - publication of the consensus was awaited at the time of writing. As usual, the award lectures were highlights of the meeting (Table 1).

Following several years of receiving the headline results of the latest cardiovascular

outcome trial, the delivery of sub-studies and re-visiting of data via varied comparisons and calculations failed to elicit excitement. In T2NOW, a 26-week phase 3 trial in 245 children (10-17 years) with type 2 diabetes (T2DM) (HbA_{1c} 6.5-10%) treated with metformin, insulin or both, patients were assigned to treatment with placebo or dapagliflozin (5mg) or saxagliptin (2.5mg). At week 12 if $HbA_{1c} > 7\%$ the patients on active treatment regimens had their study drugs uptitrated (dapagliflozin 10mg; saxagliptin 5mg), and at week 26 a safety extension period of 26 weeks was implemented (Abstract 691). The study achieved its primary endpoint by showing a greater reduction in HbA_{1c} (by 1.03%) for dapagliflozin than saxagliptin (by 0.44%) compared to placebo. Rates of severe hypoglycemia were similar for the two oral drug groups (4.9% and 4.5%, respectively) compared to 9.8% for placebo. Adverse events were similar across the groups, the commonest being headache (dapagliflozin 14.8%, placebo 5.3%).6

Old and new

Thanks to the DCCT, it is now accepted that good glycaemic control reduces microvascular complications in type 1 diabetes (T1DM). The ongoing impact of

DCCT/EDIC (the follow-on observational study) after 40 years is that glycaemia is recognised as the strongest modifiable risk factor in reducing complications (lipid and blood pressure control are also useful, of course). Over the duration of DDCT/EDIC the cumulative reduction in HbA_{1c} was greater in those who had originally been in the intensively treated arm. These patients experienced fewer microvascular and cardiovascular complications and had a mortality risk similar to people without diabetes (Wednesday 9am). The UKPDS showed that tight blood pressure control in T2DM improved outcomes (e.g. reduced microvascular disease, stroke and diabetesrelated death), and has become good practice. However, but during the 10-year post-trial monitoring phase these benefits were attenuated, with the exception of peripheral vascular disease which improved (p=0.02). Use of NHS administrative data to extend follow-up for the surviving cohort to a maximum of 34 years showed that initial tight blood pressure control bequeathed no persisting beneficial or detrimental effects (Abstract 179).

ASPREE was a double-blind study in people ≥65 years without cardiovascular disease who were randomised to 100mg enteric-coated aspirin daily (n=8,086) or placebo (n=8,123) with a median follow-up of 4.7 years (Abstract 175). The aspirin group, compared with placebo, had a 15% reduction in incident diabetes (p=0.01) and a slower rate of increase in fasting plasma glucose (p=0.004). This currently maligned ancient agent may yet have new utility.

Real-world data from the ABCD international audit substantiated the seasoned observation that testosterone replacement therapy improves glycaemia in men with T2DM (of whom about 40% are testosterone-deficient).⁷ Testosterone lowered HbA_{1c} from baseline within three months of starting therapy (p<0.001) and further reductions in HbA_{1c} were evident after 24 months of treatment (p<0.0001) (Abstract 704).

Several abstracts were devoted to studies with the once-weekly basal insulin analogue icodec. These reported the phase 3a trials (ONWARDS 1-6) which assessed its efficacy and safety versus once-daily insulin comparators (degludec, U100 glargine) in T1DM and T2DM

(Abstracts 8,9, 775-782). Overall, icodec improved HbA_{1c} and 'time in range' (by CGM) versus comparators and more patients achieve HbA_{1c} <7%. Similar or smaller increases in level 2 and 3 hypoglycaemia were observed with icodec, there were no differences in weight gain and icodec was associated with greater patient treatment satisfaction. Pharmacokinetic studies demonstrated that no specific dose adjustment was required in patients with hepatic or renal impairment (Abstract 737, 738).

A new treatment hope is the use of oral antivirals in new-onset T1DM. In one study, 96 children (6-15 years) were randomly assigned to pleconaril and ribavirin or placebo within three weeks of diagnosis and treated for 26 weeks, with a further 26 week off-treatment (and an ongoing 2-year follow-up). Patients were monitored at 3, 6 and 12 months. Endogenous insulin production at 12 months (the primary endpoint) was assessed via the 2-h area under the C-peptide curve during a mixed meal tolerance test. The C-peptide curve was decreased by 11% in the treated group and 24% in the placebo group, indicating some preservation of beta-cell function in the treated group (Abstract 105).8

Incretin crazy

The interest in incretins continues, notably with tirzepatide (e.g. Abstracts 46, 527, 542, 620-627, 659, 660, 665, 673), including a session on the SURPASS trials in obese T2DM (Abstracts 1-6) and the SURMOUNT-4 trials which were designed primarily to assess weight management (Thursday 5.30pm). Tirze-patide continued to give impressive weight loss and glucose lowering in all studies. As for other incretins, dual and triple agonists, novel combinations and formulations, checking the programme is the simplest way to find direction in this year's meeting. This year's EASD Diabetologia special issue 'Incretins in metabolic disease: pathophysiology and therapy' is recommended reading - print copies disappeared as soon as they were displayed and there was a void on the shelf for most of the meeting.9

Diary date

The 60th annual EASD meeting will take place at the IFEMA Convention Centre

(Feria de Madrid) Avda. del Partenón, 5, 28042 Madrid, on 9-13 September 2024. At 543-846 metres above sea level Madrid is the highest European capital (after Andorra la Vella) and reputed to be one of Europe's sunniest capitals.

References

- Abstracts of the 59th EASD Annual Meeting,2-6 October 2023. *Diabetologia* 2023,66(Suppl1): S1–S536. https://doi.org/ 10.1007/s00125-023-05969-6 (downloadable pdf)
- Franks PW, Cefalu WT, Dennis J, et al. Precision Medicine 1. Precision medicine for cardiometabolic disease: a framework for clinical translation. Lancet Diabetes Endocrinol October 2023. https://doi.org/ 10.1016/S2213-8587(23)00165-1
- Misra S, Aquilar-Salina CA, Chikowore T, et al. Precision Medicine 2. The case for precision medicine in the prevention, diagnosis, and treatment of cardiometabolic diseases in low-income and middle-income countries. Lancet Diabetes Endocrinol October 2023. https://doi.org/ 10.1016/S2213-8587(23)00164-X
- Leslie RD, Ma RCW, Franks PW, et al. Understanding diabetes heterogeneity: key steps towards precision medicine in diabetes. Lancet Diabetes Endocrinol October 2023. https://doi.org/10.1016/ S2213-8587(23)00159-6
- Szczerbinski L, Florez JC. Precision medicine of obesity as an integral part of type 2 diabetes management – past, present, and future. Precision medicine 4. Lancet Diabetes Endocrinol October 2023. https://doi.org/10.1016/S2213-8587 (23) 00232-2
- Shehadeh N, Barrett T, Galassetti P, et al.
 Dapagliflozin or saxagliptin in pediatric type 2 diabetes. A phase 2 randomized trial New Engl J Med Evidence 2023. https://doi.org/10.1056/ EVIDoa2300210
- ABCD worldwide audit of testosterone deficiency in men with type 2 diabetes http://www.diabetologists-abcd.org.uk/ Testosterone/ Testosterone_Deficiency_ Diabetes_Nationwide_Audit.htm
- Krogvold L, Mynarek IM, Ponzi E, et al. Pleconaril and ribavirin in new-onset type 1 diabetes: a phase 2 randomized trial. Nature Med October 2023. https://doi.org/10.1038/s41591-023-02576-1
- Incretins in metabolic disease: pathophysiology and therapy. Special Issue. *Diabetologia*; 66: pp107.

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