Diabetes Ther (2020) 11:1–6
https://doi.org/10.1007/s13300-019-00714-y

EDITORIAL

European Association for the Study of Diabetes 2019 Conference: Podcast Overview of the Conference

Uazman Alam · Shazli Azmi

Received: October 9, 2019 / Published online: October 31, 2019

Keywords: Cardiovascular; Continuous glucose monitoring; Diabetes; Diabetic neuropathy; GLP1; Precision medicine; Renal; Research; SGLT2i; Technology

VG: Victoria Glasson (Managing Editor of *Diabetes Therapy*)
UA: Uazman Alam (Editorial Board Member of *Diabetes Therapy*)

Abstracts from all the sessions can be found at https://link.springer.com/article/10.1007/s00125-019-4946-6.

Enhanced Digital Features To view enhanced digital features for this article go to: https://doi.org/10.6084/m9.figshare.9959123.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s13300-019-00714-y) contains supplementary material, which is available to authorized users.

U. Alam (✉)
Diabetes & Endocrinology Research, Department of Eye & Vision Sciences, Institute of Ageing and Chronic Disease and the Pain Research Institute, University of Liverpool and Liverpool University Hospitals NHS Foundation Trust, Liverpool, UK
e-mail: uazman.alam@liverpool.ac.uk

U. Alam
Division of Diabetes, Endocrinology and Gastroenterology, Institute of Human Development, University of Manchester, Manchester, UK

SA: Shazli Azmi (Editorial Board Member of *Diabetes Therapy*)

VG: Hello, my name is Victoria Glasson and I am the editor for *Diabetes Therapy*. Today we are live from the EASD conference (2019) [1] with Dr. Shazli Azmi and Dr. Uazman Alam who are going to speak about their most interesting sessions from the conference and their take-home messages.

UA: Hello, my name is Uazman Alam. I am currently a consultant and a senior clinical lecturer at the University of Liverpool and Aintree University Hospital (Liverpool University Hospital Trust), and I am a member of the Editorial Board for *Diabetes Therapy*.

SA: Hi, my name is Shazli Azmi; I am consultant in diabetes and endocrinology at Manchester foundation trust and I am a member of the Editorial Board for *Diabetes Therapy*.

S. Azmi (✉)
Institute of Cardiovascular Science, University of Manchester and Manchester Diabetes Centre, Manchester Foundation Trust, Manchester, UK
e-mail: shazli.azmi@manchester.ac.uk

We've spent the last few days at the EASD conference in Barcelona and attended quite a few sessions. It's been really productive. I think overall there has been quite a lot of data, especially cardiovascular and renal outcomes.

UA: Yes, certainly I think the really big important session, which had quite a lot of impressive data, was CREDENCE [ClinicalTrials.gov number NCT02065791]. This trial was on the use of canagliflozin in a renal population.

SA: I think that was the one that we were the most excited by, because of renal failure being an important issue that we see in clinic. The majority of patients (we see with type 2 diabetes) do have CKD (chronic kidney disease) stage 3, especially in secondary care, and the data was quite positive with regards to using canagliflozin earlier and giving more options (in preventing eGFR (estimated glomerular filtration rate) decline).

UA: So in this high-risk group, what they showed was an improvement in renal outcomes, and actually I think the take-home message from myself is that the most impressive bits of data were that there was actually an alteration in the slope of eGFR decline in this high-risk group. I think this is potentially a game-changer in the use of SGLT2i (sodium-glucose cotransporter 2 inhibitors) in the future.

SA: The other big trials with SGLT2i are those on heart failure outcomes, so there were a few sessions on dapagliflozin. There is the dapagliflozin heart failure (DAPA-HF) [ClinicalTrials.gov number NCT03036124] session coming up later today, but we went to the DEFINE heart failure (DEFINE-HF) [ClinicalTrials.gov number NCT02653482] and the dapagliflozin sessions yesterday. These sessions showed that there was an improvement in heart failure outcomes with dapagliflozin compared to placebo in both patients with diabetes and those without diabetes. This data again I think is a game-changer (in regards to patients), especially non-diabetic patients. And with trying to identify more patients with heart failure in our population and looking out for it, as well as doing more pro-BNPs (pro-hormone B-type natriuretic peptide) in our patients (for screening of silent/subclinical heart failure).

UA: I think it's interesting that, although the N-terminal (NT)-pro-BNP actually did not differ between the dapagliflozin and control group, what they found was an improvement in symptoms using the KANSAS (Kansas City Cardiomyopathy Questionnaire) score, which is a validated score (assessment) for heart failure (symptoms and quality of life), and I think it's important that the research was in a population, as stated by Dr. Azmi, who have diabetes and a population without diabetes, so there was a mixed population really, but with heart failure New York Heart Association (NYHA) class 2 or 3.

SA: So it is interesting that the actual pro-BNP did not change. They've got the DAPA heart failure (DAPA-HF) trial presenting later today which will have more information about this.

UA: So it will be really interesting to hear about that.

SA: Absolutely! The other sessions that I thought were really interesting to hear about were the type 1 technology sessions that we went to. The results from the COMISAIR study were presented, which looked at patients on self-monitoring of blood glucose versus CGMS (continuous glucose monitoring system). It basically showed that patients with CGM did better; they had improved and sustained time in range and improved hypoglycemia compared with those with self-monitoring, and this was independent of patients on insulin pump or MDI (multiple daily injections). So patients who were on MDI and CGMS actually did better than those who were on a pump and home monitoring, so adding more (evidence) for CGMS use.

UA: In terms of technology session, the presentation that I took quite a lot from was the clinical evaluation of the closed-loop insulin delivery system on glycemic control in adults with T1DM (type 1 diabetes). This showed really quite marked benefits and improvement in glycemic control with a modified closed-loop system and open Artificial Pancreas System (APS). Looking at the data there are real marked improvements in glycemic control, and I think this is really providing some food for thought for what kind of population we need to be using this in and do we need to spread this among more individuals with T1DM.

SA: Yes, absolutely, that was a very interesting talk. Another big thing I think that came up was the VERIFY study. This was presented yesterday, looking at duel metformin and vildagliptin at initiation versus monotherapy. What the study showed was that the time of failure to treatment was halved in the dual therapy group compared to the monotherapy group. In the monotherapy group, the next treatment was at 3 years, versus 5 years with the combination group, and so I think that was particularly interesting. There's a lot of debate on how we manage these patients initially, especially now that we do have more treatments. A lot of people ask the question of do we just go in strong with two agents or do we wait and add it as a step-wise approach, so I think this was promising (the former with two agents simultaneously).

UA: Yes, certainly, I mean clinical inertia within diabetes therapy is a major issue. There is this ongoing debate on when do we introduce the second therapy, and a lot of the guidelines don't give us a time to the next therapy. So actually starting with duel therapy early on would make sense. The one issue with this trial is the use of vildagliptin, which tends not to be used that often anymore, does it, Dr. Azmi?

SA: Yes, absolutely. I think this is a choice of medication (that we do not use often). We've got SGLT2i and GLP1s which we're pushing to use more second line, so I think it would be interesting to know about a metformin–SGLT2 inhibitor combination (or GLP-1 (glucagon-like peptide-1)) as first line as opposed to your DPP4i because then you might get the weight loss and cardiovascular benefits with the SGLT2i and the GLP-1, so I think that (again) will be interesting.

UA: Yes absolutely, there is a lot of data coming out, there is a lot of renal data, cardiovascular data, so watch this space; it's really an exciting time.

UA: In terms of my own speciality, which is diabetic neuropathy and complications, there's a number of talks which I think are really excellent talks and will have a change in management in the future. There were the two talks by Dinesh Selvarajah, who along with the other members of the team, including Solomon Tesfaye, have presented some work on central mechanisms of pain and painful neuropathy. As you're all aware, painful neuropathy is a major complication of diabetes, with around one-third of patients experiencing this, and it's really difficult to manage. They presented their data in two separate talks. In one session, they showed that there were actually differences in the way the pain is perceived in the brain, and they measured this through functional magnetic imaging scans (fMRI), showing alterations in irritable nociceptive (phenotype) painful neuropathy within the insula (cortex). The other thing they've noted is there are actual changes in the response to therapies. For example, regarding intravenous lignocaine (lidocaine) therapy, there are actually alterations in the brain (determined through resting state fMRI) which can be suggestive of those who may respond versus those who don't really respond. As you are aware, only about one-third of people actually benefit from any kind of painful neuropathy treatment.

SA: Both our interests are in neuropathy, so for me also this was a really good session. The work that they're doing is fantastic because painful neuropathy is such a big problem that we see day-in/day-out in the clinic, and absolutely more work needs to be done in this area. The brain imaging techniques that they're using to look and identify the causes of pain and trying to figure out what else we can do to try and manage this is really interesting. It gives us an idea of the mechanism(s) behind the complexity of pain in diabetic neuropathy.

UA: Regarding the complexity of pain, there was a talk which was actually in the same neuropathy session, where the authors were trying to delineate more clinical factors in relationship to pain. They did find an increase in BMI in those with painful neuropathy, but this was actually shown in diabetic patients neuropathy without pain as well. It is really difficult to try to delineate neuropathy based on clinical characteristics, but I think this is where the work in painful neuropathy will be going in the future—trying to delineate central mechanisms for pain (in relation to clinical/neuropathy phenotyping).

SA: I think pain, especially pain with neuropathy, is something that hasn't attracted as

much interest and been highlighted because there hasn't been much that we can do about it. We're at a place where things (seem to be progressing), both research-wise and in terms of data being presented at meetings, and there is quite a lot going on, but this is just not crossing the border into the clinical world. The next step for neuropathy (should be) looking at these changes and determining how we can implement these so that they actually make a change to practice.

UA: We both attended the Camillo Golgi lecture, which was awarded to Professor Rayaz Malik who is now based in Qatar. It is always a pleasure to hear this lecturer who has spent a life-time of work on painful neuropathy and who is really trying to break the dogma of actual diabetic neuropathy in terms of how it's perceived. It has traditionally been perceived as a large-fiber disease, in some ways because we used to use large fiber tests in the clinical trials (as a FDA endpoint); well, we are moving away to more of a small fiber test. It's the small fibers that are initially affected. With Rayaz Malik being my previous PhD supervisor, it was a real pleasure to attend this lecture. I'm sure Dr. Azmi can talk more about this as well.

SA: Absolutely, Professor Malik was my PhD supervisor as well, and this was probably one of my favourite lectures of the whole EASD, although I am a bit biased. I think he did a fantastic overview of the issues that we have with diabetic neuropathy. I think for young researchers as well, he gave an insight into his story and how he went from one thing to another and challenged what was there previously and the issues that he'd faced when a lot of people would say 'no actually that's not a good idea'. However, he would go on to think that despite this, if you have an idea you should try and see if it will work. I think not only was it inspiring with regards to neuropathy, but also for young researchers, I think it really promoted the concept that if you believe in something then go out and do it. I spoke to a few people afterwards about it. Neuropathy is (still) a specialist area, especially with confocal microscopy and small fibers, it is quite a niche; however, a lot of people in general practice and general diabetology found it really useful and a really good overview. They followed it quite well, and they enjoyed the story and the work, and they feel that they gained (knowledge) from it. I found that that was one of my favorite presentations. Congratulations Professor Malik.

Yeah absolutely!

UA: The other really exciting bit of data is from the ISDR study [2] [ISRCTN registry number ISRCTN87561257] which is the individualized screening for diabetic retinopathy. This was a two-arm parallel design equivalent randomized controlled trial in people with diabetes. They were either randomized to 1–2–1 individualized screening, compared to annual screening. Over 4000 participants entered the study, around 2200 of whom were in the individualized arm. The authors concluded that actually varying the interval between screening episodes based on each person's own risk of progression to site-threatening retinopathy was really quite safe and that there were also some improvements of quality of life and cost-effectiveness. Really looking at it quite enviously from the point of view of a specialist in diabetic neuropathy, this is the kind of screening program that we really should be integrating nationwide; it has really been shown to be effective in diabetic retinopathy.

SA: There were quite a few other pharma trials, one of which was CONCLUDE [ClinicalTrials.gov number NCT03078478] which looked at glargine U300 versus degludec U200. I think this is quite an interesting one because these are the two major second-generation low-volume insulins, and in clinical practice you are always debating which one do you use and what differentiates them. This trial showed that there was no actual difference in the hypoglycemia between both these medications and that was the primary endpoint. However, lower doses of degludec were needed compared to glargine, and the other points were that the degludec U200 group had lower HbA1c and that there was less weight gain for the glargine U300 group. The conclusion that I take from this trial is that these insulins are actually really good, and there's not much that differentiates them both. There are minor points on each so it is very much having a look at the patient in front of you and seeing what is important with

regards to that particular patient (management). This is the kind of stuff we need with regards to head-to-head comparisons between different medications.

SA: On a similar line there was SUSTAIN 8 [ClinicalTrials.gov number NCT03136484] which looked at semaglutide versus canagliflozin. The authors found a greater HbA1c and weight reduction in patients with semaglutide; however, there was better blood pressure reduction with canagliflozin, and better lipid reduction with semaglutide. So again, a really good trial comparing two drugs, which I suppose are both very different. However, it's good to see well actually (there is data on this to use) when you're deciding, do you need your GLP analogue next or your SGLT2 after metformin…how do we pick? And we've seen the cardiovascular data and are quite excited to see the numbers with regards to HbA1c, blood pressure and lipids as well.

SA: Similarly, PIONEER 2 [ClinicalTrials.gov number NCT02863328] looked at oral semaglutide versus empagliflozin, and they saw a better HbA1c reduction with semaglutide.

VG: Does this suggest that we need to really be looking at personalized medicine?

SA: I think this is what these last couple of trials we have mentioned have shown, because at the end of the day there is not a lot (of difference) between most of these. There are a few small differences, and in particular we will talk about the DECLARE (-TMI 58) trial in a second [ClinicalTrials.gov number NCT01730534]. (When) you are looking at cardiovascular (outcomes), is it heart failure, is it cardiovascular disease, and what are the actual important issues for the patient and what are the goals—is it weight, how much HbA1c reduction is needed, what is the cholesterol? And I think we need to look at these questions as a focus before deciding the second line. I think it gives us more work to do; it won't be as easy to determine which is first line, which is second line, because within a class we then have a lot of options to choose from.

UA: I need to probably discuss the DECLARE study which has of course been previously presented as well at the American Heart Association, but there is some additional data here. I think it's really important that we take on board in terms of what SGLT2i are really providing and there's been a new call for guidance with SGLT2i, particularly within that session that was chaired on the Wednesday. The authors presented some new renal data and some efficacy and safety in elderly populations, but I think this is really an exciting time for SGLT2i.

Please note, (parentheses) represent additional information not mentioned in the podcast that has been added into the transcript by the authors for transparency.

ACKNOWLEDGEMENTS

This commentary is authored by Editorial Board Members of the journal and, contrary to the journal's standard single-blind peer-review process, has not been peer-reviewed.

Funding. No funding or sponsorship was received for this study or publication of this article.

Authorship. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Disclosures. Uazman Alam has received honoraria for educational meetings from Pfizer, Eli Lilly, Sanofi, Astra Zeneca, Boehringer Ingelheim and Napp, is currently a local investigator for BIIB074 (Biogen: NCT03339336) and is a member of the journal's Editorial Board. Shazli Azmi has received honoraria for educational meetings from Eli Lilly and is a member of the journal's Editorial Board.

Compliance with Ethics Guidelines. This article does not contain any studies with human participants or animals performed by any of the authors.

REFERENCES

1. 55th EASD annual meeting of the European Association for the Study of Diabetes. Diabetologia. 2019;62[Suppl 1]:1–600.
2. Broadbent DM, Sampson CJ, Wang A, et al. Individualised screening for diabetic retinopathy: the ISDR study—rationale, design and methodology for a randomised controlled trial comparing annual and individualised risk-based variable-interval screening. BMJ Open. 2019;9(6):e025788.