Opinion

Type 2 diabetes – 2019 hot topics

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This year is being an incredible year for type 2 diabetes treatment. In these last months, several novelties popped out and the hot topics are about the glucagon-like peptide-1 receptor agonists (GLP-1a), the sodium-glucose cotransporter 2 inhibitors (SGLT2i) and the new guidelines for cardiovascular disease prevention in people with diabetes or prediabetes, from the European Society of Cardiology (ESC) in collaboration with European Association for the Study of Diabetes (EASD), released at the European Society of Cardiology (ESC) Congress in Paris, this August and early September. Actually, the focus of the treatment of type 2 diabetes is strongly directed to the prevention and management of comorbid cardiovascular and renal diseases. The recent released trials are stronger and more consistent on these hard outcomes, adding body to the evidence on these novel therapies and helping the clinicians to tailor the best treatment for each individual patient

The REWIND (researching cardiovascular events with a weekly incretin in diabetes) trial was a cardiovascular outcome trial involving the once-weekly dulaglutide, administered via subcutaneous injection, and placebo. The results were notable: a significant reduction in cardiovascular risk, irrespective of whether participants had established cardiovascular disease and also regardless of sex, age and HbA1c level. These findings suggest that dulaglutide may be cardioprotective even in patients without clinical events, and besides the documented slight increase in pulse rate. Similar results have been noted with other GLP-1a (LEADER, SUSTAIN-6, HARMONY trials), suggesting that this might be a class effect. In addition, there was also found a significant risk reduction for renal outcomes (new macroalbuminuria, sustained decline in estimated glomerular filtration rate and chronic renal replacement therapy), in an exploratory analysis. Severe hypoglycemic event, acute pancreatitis and pancreatic cancer were not statically significant, reinforcing the safety of the medication.

The DAPA-HF (Study to evaluate the effect of dapagliflozin on the incidence of worsening heart failure or cardiovascular death in patients with chronic heart failure) trial showed that dapagliflozin (a sodium-glucose co-transporter 2 inhibitor) was associated with a reduction in cardiovascular death and heart failure events compared to placebo, among patients with heart failure with reduced ejection fraction, regardless of the presence or absence of type 2 diabetes. There was also no sign of adverse safety events. The DEFINE-HF (Dapagliflozin effects on symptoms and biomarkers in patients with heart failure with reduced ejection fraction) trial suggested a favorable effect on improving disease-specific health status in patients with optimal medical therapy for heart failure with reduced ejection fraction, with our without type 2 diabetes, with no imbalance in adverse outcomes.

These findings come along and in accordance to EMPA-REG OUTCOME (Empagliflozin cardiovascular outcome event trial in type 2 diabetes mellitus patients), trial that already demonstrated that empagliflozin (a sodim-glucose cotransporter 2 inhibitor) was superior to placebo in improving glycemic control and reducing cardiovascular events, including mortality and established cardiovascular disease, as well as renal outcomes, namely nephropathy, creatinine values, progression to macroalbuminuria and initiation of renal replacement therapy. All these "new" drugs reduce hyperglycemia in patients with type 2 diabetes and are also known to cause slight reductions in blood pressure and weight. The renal benefits noted in REWIND trial are similar to those noted with SGLT-2i, and may be due to a combination of reduced weight and better glycemic and blood pressure control, although other undefined pathways and mechanisms may also likely to play a role. This September is also remarkable for other breaking news, namely the approval by The Committee for Medicinal Products for Human Use (CHMP) from the European Medicines Agency's (EMA) committee responsible for human medicines, of the fixed-dose three-drug combination (*Qternmet XR*) extended released tablets of metformin hydrochloride/saxagliptin/dapagliflozin (850/2.5/5mg and 1000/2.5/5mg, respectively) for the treatment of type 2 diabetes and the U.S. Food and Drug Administration (FDA) approval of the first oral GLP-1a treatment for type 2 diabetes (semaglutide oral tables – *Rybelsus*).

Regarding the new ESC/EASD 2019 guidelines for cardiovascular disease prevention in people with diabetes or prediabetes, the changes in recommendations are about the individualized blood pressure targets according to age and risk of cerebrovascular events or diabetic kidney disease, tighter control on LDL-cholesterol targets according to cardiovascular risks (lower cutoffs than back in 2013), antiplatelet therapy just for type 2 diabetes high/very high cardiovascular risk in the absence of clear contraindications, new revascularization recommendations according to the 2018 ESC/EACTS myocardial revascularization guidelines, the preference of non-vitamin K antagonists oral anticoagulants in the management of arrhythmias, the cardiovascular risk assessment in accordance to the 2016 ESC guidelines on cardiovascular prevention, the paradigm shift on glucose-lowering treatment based on management and prevention of cardiovascular and renal diseases, the treatment recommendations for heart failure following positive results from the recent cardiovascular outcome trials and the new evidence on diagnostic methods and management of peripheral arterial disease. So, still in September 2019 but what a quite a year.

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Conflicts of interest

The author declares that there is no conflict of interest.

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