

<b>DIABETES CORNER</b>
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**Diabetes News / Recent Literature Review / First Quarter 2018***Pinelopi Grigoropoulou, MD, PhD**Department of Internal Medicine and Diabetes Outpatient Department, General Hospital of Athens "ELPIS"***More Similarities Than Differences Testing Insulin Glargine 300 Units/mL Versus Insulin Degludec 100 units/mL in Insulin-Naïve Type 2 Diabetes: The Randomized Head-to-Head BRIGHT Trial**

The BRIGHT Study was a multicenter, open-label, 24 week study aiming to compare insulin glargine 300units/mL (Gla-300) versus insulin degludec 100 units/m: (IDeg-100) in insulin-naïve patients with uncontrolled type 2 diabetes. Participants were randomized 1:1 to evening dosing with Gla-300 (n=466) or IDeg-100 (N=463), titrated to a rather demanding target of fasting self-monitored plasma glucose of 80-100 mg/dl. At the end of the study (week 24) Gla-300 and Ideg-100 provided similar glycemic improvement with relatively low hypoglycemia risk. Both insulins demonstrated the same hypoglycemia incidence rate, although lower in favor of Gla-300 during the titration period (Rosenstock J et al, *Diabetes Care* 2018; doi.org/10.2337/dc18-0559).

**Management of Hyperglycemia in Type 2 Diabetes, 2018. A Consensus Report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD)**

The American Diabetes Association and the European Association for the Study of Diabetes updated the prior position statements, published in 2012 and 2015, on the management of type 2 diabetes in adults. The goals of treatment are to prevent or delay diabetes-related complications and maintain quality of life. The major change from prior consensus reports is based in new evidence that SGLT-2 inhibitors and GLP-1 receptor agonists improve cardiovascular outcomes, as well as heart failure and progression of renal disease. Among patients with type 2 diabetes and established atherosclerotic cardiovascular disease (ASCVD), SGLT-2 inhibitors or GLP-1 receptor agonists with proven cardiovascular benefit are recommended. Among patients with ASCVD in whom heart failure is of special concern, SGLT-2 are recommended. For patients with chronic kidney disease (CKD), with or without coronary vascular disease (CVD), it is proposed to consider the use of an SGLT-2 inhibitor to reduce CKD progression or, if contraindicated, a GLP-1 receptor agonist shown to

reduce CKD progression (Davies M, et al. *Diabetes Care* 2018;41:2669-2701).

**Empagliflozin as Adjunctive to Insulin Therapy in Type 1 Diabetes: The EASE Trials**

The EASE (Empagliflozin as Adjunctive to Insulin thErapy) program evaluated the safety and efficacy of empagliflozin 10- and 25-mg doses plus a unique dose of 2.5 mg as add-on therapy to intensified insulin treated patients with type 1 diabetes. Empagliflozin improved glycemic control (mean reduction of HbA1c 0.28-0.54,  $p < 0.0001$ ) at week 26 without increasing hypoglycemia. Total insulin dose was reduced by 12.7% (6.4 – 13.3 units). Ketoacidosis occurred more with empagliflozin 10 mg (4.3%) and 25 mg (3.3%) but was comparable between empagliflozin 2.5 mg (0.8%) and placebo (1.2%) (Rosenstock J et al, *Diabetes Care* 2018;41:2650-2569).

**Effects of n-3 Fatty Acid Supplements in Diabetes Mellitus**

The American Heart Association guidelines recommend n-3 fatty acid supplements for secondary prevention in coronary heart disease and fish consumption for primary prevention of cardiovascular disease (CVD). Randomized trials of supplementation with n-3 fatty acids have shown conflicting results regarding the effects on fatal or nonfatal outcomes. The ASCEND (A Study of Cardiovascular Events in Diabetes) aimed to assess the efficacy of daily supplements with n-3 fatty acids, compared to placebo, in patients with diabetes without evidence of CVD. The investigators randomly assigned 15,480 patients with diabetes to receive 1-g capsules containing either n-3 fatty acids or matching placebo (olive oil) daily. The primary outcome was a first serious vascular event. During a mean follow-up of 7.4 years a serious vascular event occurred in 8.9% in the fatty acid group and in 9.2% in the placebo group ( $P=0.55$ ). Thus there was no significant difference in the risk of serious vascular events between those who assigned to receive n-3 fatty supplements and those who receive placebo. These findings do not support the current recommendations for routine dietary supplementation of n-3 fatty acids to prevent vascular events (Bowman L et al, *NEJM* 2018;379:1540-1550).

### **Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus**

A total of 15,480 patients with type 2 diabetes and no evidence of cardiovascular disease were randomly assigned to receive aspirin 100 mg daily or placebo. The primary efficacy outcome was the first major vascular event (myocardial infarction, stroke or transient ischemic attack, or death from vascular event). The primary safety outcome was the first major bleeding event (intracranial hemorrhage, gastrointestinal bleeding, or other serious bleeding). During a median of 7.4 years follow-up, there was a significantly lower rate of serious vascular events in the aspirin group vs. placebo (8.51% vs 9.6%,  $P=0.01$ ). In contrast, major bleeding occurred in 314 (4.1%) in the aspirin group compared to 245 (3.2%) in the placebo group ( $P=0.003$ ). The use of low dose of aspirin led to a significantly lower risk of serious vascular events, yet with higher rates of major bleedings. The assessment of the balance between the benefit and harm of aspirin use in the content of primary prevention is complicated, and further follow-up is needed (Bowman L et al, *NEJM* 2018;379:1529-1539).

### **Association Between Bariatric Surgery and Macrovascular Disease Outcomes in Patients With Type 2 Diabetes and Severe Obesity**

In this retrospective study the relationship between bariatric surgery and incident macrovascular disease (coronary artery disease and cerebrovascular diseases) events was investigated among obese patients with type 2 diabetes. The study enrolled adults with type 2 diabetes and  $BMI \geq 35$  ( $n=5301$ ) who underwent bariatric surgical procedure between 2005 – 2011 in 4 intergraded health systems in the United States. These patients were matched with 14,934 control patients on age, sex, BMI, HbA1c, insulin use and diabetes duration. At the end of the study period (median of 4.7 years) bariatric surgery was associated with a lower composite incidence of macrovascular events (2.1% in the surgical vs 4.3% in the nonsurgical group) as well as a lower incidence of coronary artery disease (1.6% in the surgical vs. 2.8% in the nonsurgical group). The incidence of cerebrovascular disease was not significantly different between groups (0.7% in the surgical vs 1.7% in the nonsurgical group) (Fisher D et al, *JAMA* 2018;320:1570-1582).