Dapagliflozin Does Not Impact Renal Function in Patients with Type 2 Diabetes

Written by ***Maria Vinall***

Treatment with dapagliflozin (DAPA) is not associated with an increased risk of acute renal toxicity or long-term deterioration of renal function in patients with type 2 diabetes mellitus (T2DM) according to the results of a pooled analysis of 12 studies [NCT00263276; NCT00972244; NCT00528372; NCT00736879; NCT00528879; NCT00855166; NCT00357370; NCT00680745; NCT00683878; NCT00673231; NCT00643851; NCT00859898]. The results were reported by Agata Ptaszynska, MD, Bristol-Myers Squibb, Princeton, New Jersey, USA.

The renal safety of DAPA is of special interest for 2 reasons: diabetic patients are at risk of nephropathy and urinary tract infections, and DAPA, a sodium-glucose cotransporter 2 inhibitor, decreases hyperglycemia by inhibiting renal glucose reabsorption. The purpose of this analysis was to assess the impact of DAPA on various aspect of renal function.

Adverse events (AEs) and laboratory test results were pooled from 12 Phase 2b/3 double-blind, placebo-controlled, randomized studies of T2DM patients receiving DAPA. Data were analyzed up to Week 24 (n=4545) for all 12 studies and beyond Week 24 (n=2854) for 6 of these 12 studies. DAPA 2.5-, 5-, and 10-mg/day doses were included in the analysis, but Dr. Ptaszynska focused on the more clinically significant 5- and 10-mg data. T2DM patients aged 18 to 79 years, body mass index ≤45 kg/m^2, and HbA1C from >6.5% to ≤12% were eligible for participation in the original studies.

Mean age of patients in the analysis was 55 years (56 years in the longer studies) and ~50% were women. Patients were Caucasian (~84%), African American (~3% total; ~10% of the US study population), Asian (~10%), and other (~3%). At baseline, mean duration of diabetes ranged from 3 to 4 years for patients in the short-term studies and slightly less than 6 years for those in long-term studies. Most patients (52.8% to 54.4%) had mild renal impairment and normal albuminuria values. Mean HbA1C was approximately 8.2% in both the short- and long-term studies.

At Week 1, estimated glomerular filtration rate (eGFR) decreased from baseline by –2.92 mL/min/1.73 m^2 (DAPA 5 mg) and –4.15 mL/min/1.73 m^2 (DAPA 10 mg) but returned to or above baseline by Week 24. There was no long-term effect on eGFR over 2 years. Modest decreases occurred in blood pressure, which were sustained over 102 weeks. Mean serum creatinine changed minimally from baseline to Week 24 and Week 102 in all groups. DAPA had no adverse effect on albuminuria through Week 102.

Renal AEs were similar between DAPA- and placebo-treated patients. Most events were transient changes in renal function measures. There were no reports of acute nephrotoxicity through 102 weeks and no AEs through impairment of other tubular functions (eg, regulation of electrolytes). Volume depletion events were uncommon and mild (mostly reported as nonserious AEs of hypotension). Urinary stones were reported more frequently among placebo patients. There were no changes in sodium potassium or calcium levels. Small increases were noted for magnesium and phosphorous.

In addition to not affecting renal function, DAPA was associated with improved glycemic control, reduced blood pressure, and reduced body weight; therefore, its use may support preservation of kidney function in patients with T2DM.

Population-Based Screening for Type 2 Diabetes: The ADDITION-Cambridge Trial

Written by ***Maria Vinall***

After completing a randomized controlled trial to examine the impact of a population-based diabetes screening program on mortality in England, Rebecca K. Simmons, PhD, Medical Research Council Epidemiology Unit, Cambridge, United Kingdom, concluded that screening for diabetes was not associated with a reduction in mortality and that the benefits of screening may be limited to those with detectable disease.

Although modeling studies suggest that screening might reduce diabetes-related mortality by 26% to 40% if conducted among middle-aged adults every 3 to 5 years, there was no evidence from randomized trials to confirm if these estimates are correct. The ADDITION-Cambridge cluster-randomized controlled trial was conducted to assess the impact of a population-based screening program on mortality among people at high risk of undiagnosed diabetes [Simmons RK et al. *Lancet* 2012].