Renal News

CREDENCE Trial

Lowered risk of chronic kidney disease leads to early halting of a diabetes drug trial. Janssen Pharmaceutical partnered with George Clinical to facilitate sites for this trial which enrolled 4,400 patients.

Janssen Pharmaceuticals, Inc. of Johnson & Johnson ended the phase III *Canagliflozin and Renal Events in Diabetes with Established Nephropathy Clinical Evaluation*, also known by the acronym CREDENCE, early due to achieving pre-specified efficacy criteria.

The goal of the study was to assess whether INVOKANA (canagliflozin, Janssen) has a renal and vascular protective effect in reducing the progression of renal impairment relative to placebo in patients with type 2 diabetes mellitus, stage 2 or 3 CKD and macroalbuminuria.

INVOKANA, a prescription medicine targeted for adults with type 2 diabetes, can be used along with diet and exercise to lower blood sugar in adults with type 2 diabetes.

This medication "has the potential to be the first new therapy in more than 15 years for slowing the progression of chronic kidney disease in patients with type 2 diabetes," according to Janssen.

The impact of the successful trial could be significant for the renal field since across the world, approximately 160 million patients with type 2 diabetes are at risk for developing chronic kidney disease. The CREDENCE phase III trial assessed INVOKANA for renal protection by evaluating the risk reduction of the composite endpoint of time to dialysis or kidney transplantation, doubling of serum creatinine, and renal or cardiovascular death, when used in addition to standard care.

"Nearly half of all people with type 2 diabetes will develop chronic kidney disease, causing a high risk of kidney failure and cardiovascular disease, and impacting their quality and length of life, even with the current best available care," said Vlado Perkovic, MBBS, PhD, FACN, FRACP, CREDENCE steering committee co-chair, professor of medicine at the University of New South Wales Sydney and executive director of The George Institute for Global Health Australia. "We have accepted the advice of the independent data monitoring committee to stop

the CREDENCE trial early due to demonstration of efficacy and look forward to sharing the findings as soon as possible."

The trial enrolled approximately 4,400 patients with type 2 diabetes and an estimated glomerular filtration (eGFR) rate between 30 mL/min/1.73 m2 and 90 mL/min/1.73 m2, and albuminuria, defined as a urinary albumin to creatinine ratio between 300 mg/g and 5,000 mg/g. Patients were required to be on the maximum labeled or tolerated dose of an angiotensin-converting enzyme inhibitor or angiotensin 2 receptor blocker for more than four weeks prior to randomization.

According to *Healio Nephrology News & Issues*, "It has been well established that patients with type 2 diabetes have an increased risk of renal disease and cardiovascular mortality. SGLT-2 Inhibitors, a relatively new class of oral anti-diabetic medication, has shown promising results on the potential cardiovascular and renal benefits in previous studies. Canagliflozin, FDA approved in 2013, is the primary therapy studied in the CANVAS Program, the largest SGLT-2 Inhibitor study evaluating cardiovascular outcomes." This previous study provided significant news for both patients and health care providers in regards to the use of canagliflozin in patients with type 2 diabetes.

Endocrine Today previously reported the CREDENCE trial which was originally estimated to be completed by 2020, "was designed to assess whether canagliflozin has a renal and vascular protective effect in reducing the progression of renal impairment relative to placebo in participants with type 2 diabetes, stage 2 or 3 CKD and macroalbuminuria."

"Chronic kidney disease is a progressive condition that impacts a person's overall health and well-being, and with millions of people worldwide suffering from the disease, we know that there is a clear need for new treatment options," stated James List, MD, PhD, global therapeutic area head for cardiovascular and metabolism at Janssen Research and Development.

"We are excited about the possibility of bringing forth INVOKANA as the first therapy to treat patients with chronic kidney disease and type 2 diabetes in more than 15 years," said List.

Canagliflozin is currently contraindicated for patients with severe renal impairment, defined as eGFR of less than 30 mL/min/1.73 m2, ESRD or patients on dialysis. Additionally, canagliflozin is not recommended in patients with an eGFR that is persistently lower than 45 mL/min/1.73 m2.

George Clinical's Role

- Project management, site management, site monitoring (regional coordination in selected countries)
- Development strategy advice
- Academic and medical leadership
- Study design and protocol development
- Lead and support committees and national leaders
- Global endpoint adjudication coordination

Contact our business development team to explore how George Clinical can utilize our scientific leadership, responsive service and results-focused clinical research solutions for your company today.

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