KSN SEOUL, KOREA 2023
April 27(Thu) - 30(Sun), 2023
Coex, Seoul, Korea

Submission No.: PL01-0001
Session Title: Plenary Lecture 1
Date & Time, Place: April 27 (Thu), 17:10 - 18:00, Auditorium

New Therapies for the Treatment of CKD: Are We Ready to Move from a One-size-fits-all Approach to a One-fit for Everyone?

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Patients with type 2 diabetes and chronic kidney disease face a high risk of kidney failure, cardiovascular complications and premature death. The current mainstay of therapy for the management of diabetic kidney disease are ACE-inhibitors and Angiotensin Receptor Blockers. Despite the use of these agents, the risk of kidney failure and cardiovascular complications remains very high in a large proportion of patients which at least in part can be attributed to suboptimal treatment response to these therapies. Novel therapies are thus desired to augment kidney and cardiovascular protection.

In the last years various new drugs have emerged that slow the progressive loss of kidney function in patients with diabetes and CKD. SGLT-2 inhibitors have been shown to reduce the risk of heart failure and kidney failure in patients with CKD with and without type 2 diabetes. The mineralo-corticoid receptor antagonist finerenone has also been shown to reduce the risk of kidney and cardiovascular outcomes in patients with type 2 diabetes and CKD. Moreover, both in patients with type 2 diabetes and IgA nephropathy, endothelin receptor antagonist (ERA) reduce albuminuria and in patients with type 2 diabetes and CKD the ERA atrasentan also reduces the risk of kidney failure. Finally, GLP-1 RA reduce cardiovascular events and this clinical benefit is apparent in both patients with and without CKD.

Although these drugs are effective at a population level, not every patient will benefit to the same degree. For example, dedicated studies with SGLT2 inhibitors have shown that about 20% of patients do not show a satisfactory albuminuria response and similar findings were observed for GLP-1 receptor agonists and finerenone. Because of the large variation in drug response and because multiple agents with different modes of action have been shown to slow the progression of CKD, we are transitioning to an era where existing and novel therapies could be individualized based on a patient specific characteristics. The unprecedented progress in molecular, genetic, bio-informatic and imaging technologies has resulted in a better insight in the pathophysiology of diabetes and response to treatment. These improved insights may help in guiding optimal treatment decisions for individual patients