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Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

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CKD Treatment and Prevention Heralding a Sea Change in Nephrology

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Half of all chronic kidney disease (CKD) worldwide is now attributable to diabetes, making it by far the most common cause. Treatment strategies must address the high mortality and cardiovascular risks, as well as prevention of kidney failure, because most patients with diabetes and CKD will die primarily due to cardiovascular causes. The mechanisms underpinning CKD in diabetes fall into three main categories: metabolic, hemodynamic, and inflammation and fibrosis. Importantly, these are final common pathways to kidney damage from multiple inciting factors, which provides biological rationale to extend therapeutic targets from diabetic to non-diabetic CKD. Sodium glucose cotransporter 2 (SGLT2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists were originally developed as glucose-lowering agents but were subsequently discovered to have broad benefits to preserve kidney function and reduce major cardiovascular events. Agents in SGLT2 inhibitor and GLP-1 receptor agonist classes also may reduce risks of cardiovascular death, and in some cases all-cause mortality, for both diabetic and non-diabetic patients with and without CKD. Notably, in patients without CKD from the glycemic lowering and cardiovascular outcome trials, SGLT2 inhibitors and GLP-1 receptor agonists also have been shown to prevent CKD onset. These agents target complementary mechanisms that may be additive, paving the way for combination therapeutic regimens. Newer agents under study include dual and triple agonists directed at GLP-1 combined with other incretins that show promise of greater efficacy for kidney protection. Anti-inflammatory agents targeting signal transduction, innate immune responses, and cell therapy are currently under investigation for CKD with or without diabetes. CKD may improve or be prevented by SGLT2 inhibitors, GLP-1 receptor agonists, and possibly investigational anti-inflammatory therapies. The field of nephrology is now set for a sea change focused on CKD prevention and treatment rather than simply “slowing progression.”

Keywords: Inflammation, GLP-1 receptor agonists, SGLT2 inhibitors, diabetes, cardiovascular disease