A New Therapeutic Era in the Management of Diabetic Kidney Disease

Diabetic kidney disease (DKD) is the most common cause of end-stage kidney disease (ESKD) worldwide. After 2 decades of negative trials, in the last few years there has been a major and welcome shift in the therapeutic options to treat DKD. Nephrologists will be in the forefront of implementation of these new therapies as well as in the education of their colleagues and patients on the benefits and possible side effects of these novel therapies.

In this issue of *Advances in Chronic Kidney Disease*, we are pleased to welcome an outstanding group of international DKD experts who have reviewed the rationale, mechanisms, and clinical benefits of these novel agents for DKD treatment as well as provided important insights into how to use these therapies. In addition, in this issue we include articles pertaining to special populations such as children, individuals with type 1 diabetes, and kidney transplant recipients.

We start this issue with an overview of DKD pathogenesis by Dr Merlin Thomas (pp 282-289). We then move on to the use of SGLT2 inhibitors in clinical practice by Drs Peter Rossing and Fred Persson (pp 290-297). Drs Brendon Neuen and Carol Pollock discuss the cardiovascular and kidney benefits of SGLT2 inhibitors (pp 298-308). Then Drs Lori Laffel and Rebecca Vitale (pp 309-317) discuss the rationale for SGLT2 inhibitors use in children or individuals with type 1 diabetes. Dr Joshua Neumiller and colleagues (pp 318-327) have written a comprehensive review about how we can overcome barriers to implement these novel therapies for DKD, using SGLT2 inhibitors as an example.

We then transition to GLP1 receptor agonist use in clinical practice by Drs Anna Solini and Domenico Tricò (pp 328-336). Dr Tommerdahl and colleagues (pp 337-346) then discuss the known and proposed mechanisms of cardiorenal protection by GLP1 receptor agonists. Dr Ofri Mosenzon and colleagues (pp 347-360) discuss the kidney and cardiovascular outcomes in published GLP1 receptor agonist clinical trials as well as what we will learn from ongoing efforts such as the FLOW trial.

Drs Nissaisorakarn and colleagues (pp 361-370) review glucose lowering therapies in the setting of solid organ transplantation, which remains an area with many unanswered questions and unmet clinical needs. Drs Al Dhaybi and Bakris (pp 371-377) provide a review of the evidence regarding the mineralocorticoid receptor antagonist finerenone as a kidney and cardiovascular protective therapy as well as ongoing trials with novel agents in this class. We then wrap up our tour de force reviews with Dr Susanne Nicholas (pp 378-390) who discusses novel anti-inflammatory agents for DKD including ongoing trials.

In order to slow CKD progression, we need to make sure to start these medications in eligible patients at an early stage. The use of SGLT2 inhibitor has increased over time from from 3.8% in 2015 to 11.9% in 2019, but remains low even among patients with heart failure, kidney disease, or cardiovascular disease, where these therapies exert clear and consistent benefits.[1] More alarming, use was less frequent in Blacks, Asians, females, and individuals of lower incomes, and sociodemographic disparities for these novel medications are seen around the world.[2,3] We therefore need to work together as a nephrology community to ensure that these medications are available for all patients, particularly those at increased risk of CKD.

We would like to thank again our outstanding group of authors for their contributions and Dr Charuhas Thakar for inviting us to be Guest Editors in this timely issue.

Sylvia E. Rosas, MD, MSCE
Kidney and Hypertension Unit
Joslin Diabetes Center
Boston, MA
Harvard Medical School
Boston, MA
David Z. I. Cherney, MD, PhD
Department of Medicine
Division of Nephrology
University of Toronto, Canada
Toronto General Hospital Research Institute
UHN, Toronto, Canada
Banting and Best Diabetes Centre Toronto, Canada Department of Physiology and Department of Pharmacology and Toxicology University of Toronto, Canada

Financial Disclosure: D.Z.I.C has received honoraria from Boehringer Ingelheim-Lilly, Merck, AstraZeneca, Sanofi, Mitsubishi-Tanabe, Abbvie, Janssen, Bayer, Prometic, BMS, Maze, and Novo-Nordisk and has received operational funding for clinical trials from Boehringer Ingelheim-Lilly, Merck, Janssen, Sanofi, AstraZeneca, and Novo-Nordisk. S.E.R.'s institution has received funding for clinical research from NIDDK, Bayer Healthcare, and AstraZeneca. Dr Rosas has participated in scientific advisory boards for Reata, Relypsa, Astra Zeneca, and Bayer Healthcare.
Support: D.Z.I.C. is supported by a Department of Medicine, University of Toronto Merit Award and receives support from the CIHR, Diabetes Canada and the Heart and Stroke Richard

1548-5595/$36.00
https://doi.org/10.1053/j.ackd.2021.11.002

Lewar Center of Excellence. S.E.R. is an employee of the Joslin Diabetes Center.

REFERENCES

1. Eberly LA, Yang L, Eneanya ND, et al. Association of race/ethnicity, gender, and socioeconomic status with sodium-glucose cotransporter 2 inhibitor use among patients with diabetes in the US. *JAMA Netw Open.* 2021;4(4):e216139.
2. Morton JI, Ilomki J, Magliano DJ, Shaw JE. The association of socioeconomic disadvantage and remoteness with receipt of type 2 diabetes medications in Australia: a nationwide registry study. *Diabetologia.* 2021;64(2):349-360.
3. Whyte MB, Hinton W, McGovern A, et al. Disparities in glycaemic control, monitoring, and treatment of type 2 diabetes in England: a retrospective cohort analysis. *PLoS Med.* 2019;16(10):e1002942.