Challenging the Restrictive Approach: Reconsidering Sodium-Glucose Transport Protein 2 Inhibitor Use in CKD

To the Editor: We have read with interest the review by Tarun *et al.*[1] titled "updates on new therapies for patients with chronic kidney disease (CKD)," which provides a comprehensive discussion of new treatment options for CKD. Although we appreciate the thoroughness of the authors' work, we wish to raise some concerns regarding their proposed treatment algorithms.

The authors suggest that sodium-glucose transport protein 2 inhibitors should not be used for patients not on a renin-angiotensin-aldosterone system (RAAS) inhibitor, depending on several landmark trials. However, we believe this approach may be overly restrictive. The EMPA-KIDNEY trial is one of the most recent and largest studies on sodium-glucose transport protein 2 inhibitors in CKD.[2] The authors state that the EMPA-KIDNEY trial excluded subjects not receiving RAAS blockade. However, this statement is only partially true. The trial's protocol allowed for the inclusion of such patients if the investigator judged that a RAAS inhibitor was not indicated or would not be tolerated. In the end, approximately 15% of all subjects (18% for estimated glomerular filtration rate <30 ml/min population) were not on any RAAS blocking agent.

Recently, the EMPA-KIDNEY consortium published "effects of empagliflozin on progression of CKD: a prespecified secondary analysis from the EMPA-KIDNEY trial," which shows that estimated glomerular filtration rate slopes of patients with or without RAAS inhibitors were both better than placebo.[3] We believe that until new data is available, there is enough evidence to prescribe sodium-glucose transport protein 2 inhibitors (at least empagliflozin) without a RAAS blocker.

The same prespecified analysis suggests that estimated glomerular filtration rate slopes of nonalbuminuric subjects are ameliorated by empagliflozin. The failure to improve CKD results of nonalbuminuria subjects in the EMPA-KIDNEY trial could therefore be a consequence of a shorter follow-up time rather than an absolute failure. Although we agree with Tarun *et al.*[1] on the limited data of gliflozins on nonalbuminuric subjects, we must notice that the results of EMPA-KIDNEY still bear some promise.

The language used in a review in a prestigious journal such as KI reports can influence the practice of physicians. Several studies have repeatedly shown that gliflozins are underprescribed as of now.[4] Such limitations of sodium-glucose transport protein 2 inhibitors would obviously not benefit the current situation.

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