Letter to the Editor

Long-term cardiorenal efficacy of finerenone in patients with chronic kidney disease and type 2 diabetes

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We read with great interest Fu *et al.*'s meta-analysis (1) recently published in the journal *Annals of Palliative Medicine*. In that meta-analysis (1) Fu and colleagues assessed the effects of finerenone on the short-term intermediate indicators such as urine albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) in patients with chronic kidney disease (CKD), as well as its safety. However, the authors (1) failed to assess the efficacy of finerenone on long-term renal and cardiovascular endpoints in CKD patients. Moreover, they (1) also failed to include the latest cardiorenal outcome trial (CROT) of finerenone, namely, the FIGARO-DKD trial (2) assessing cardiorenal outcomes with finerenone in patients with CKD and type 2 diabetes (T2D). Thus, we conducted a further meta-analysis by incorporating these two CROTs (2,3) of finerenone [i.e., FIGARO-DKD (2) and FIDELIO-DKD (3)] to evaluate the long-term cardiorenal endpoints of finerenone in patients with T2D and CKD.

Both FIGARO-DKD (2) and FIDELIO-DKD (3) focused on comparing the cardiorenal outcomes of finerenone with those of placebo in patients with T2D and CKD. The former (2) involved 3,686 patients in the finerenone group and 3,666 patients in the placebo group, while the later (3) involved 2,833 patients in the finerenone group and 2,841 patients in the placebo group. Outcomes of interest for this meta-analysis were cardiovascular composite outcome (i.e., a composite of death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, or hospitalization for heart failure) and its components, kidney composite outcome (1) (i.e., a composite of kidney failure, a sustained decrease of at least 40% in the eGFR from baseline, or death from renal causes) and its components, kidney composite outcome (2) (i.e., a composite of kidney failure, a sustained decrease of at least 57% in the eGFR from baseline, or death from renal causes) and its components, death from any cause, and hospitalization for any cause. We extracted the study-level binary data (i.e., the numbers of events of interest and those of total subjects in each study group), and performed fixed-effects meta-analysis due to the lack of heterogeneity or low heterogeneity. Pooled effect size was presented as risk ratio (RR) and 95% confidence interval (CI). A P value of <0.05 denoted statistically significant difference. Meta-analyses were conducted in Stata/MP 16.0 (StataCorp LLC., College Station, TX, USA).

Figure 1 shows the results of meta-analysis on 14 long-term cardiorenal outcomes. Compared with placebo, finerenone reduced cardiovascular composite outcome (RR: 0.86, 95% CI: 0.78–0.95, P<0.01; *Figure 1A*) by 14%, hospitalization for heart failure (RR: 0.78, 95% CI: 0.66–0.92, P<0.01; *Figure 1E*) by 22%, kidney composite outcome (1) (RR: 0.83, 95% CI: 0.75–0.92, P<0.01; *Figure 1F*) by 17%, end-stage kidney disease (RR: 0.80, 95% CI: 0.64–0.99, P=0.04; *Figure 1H*) by 20%, sustained decrease in eGFR of <15 mL/min/1.73 m^2 (RR: 0.81, 95% CI: 0.67–0.99, P=0.04; *Figure 1I*) by 19%, sustained ≥40%

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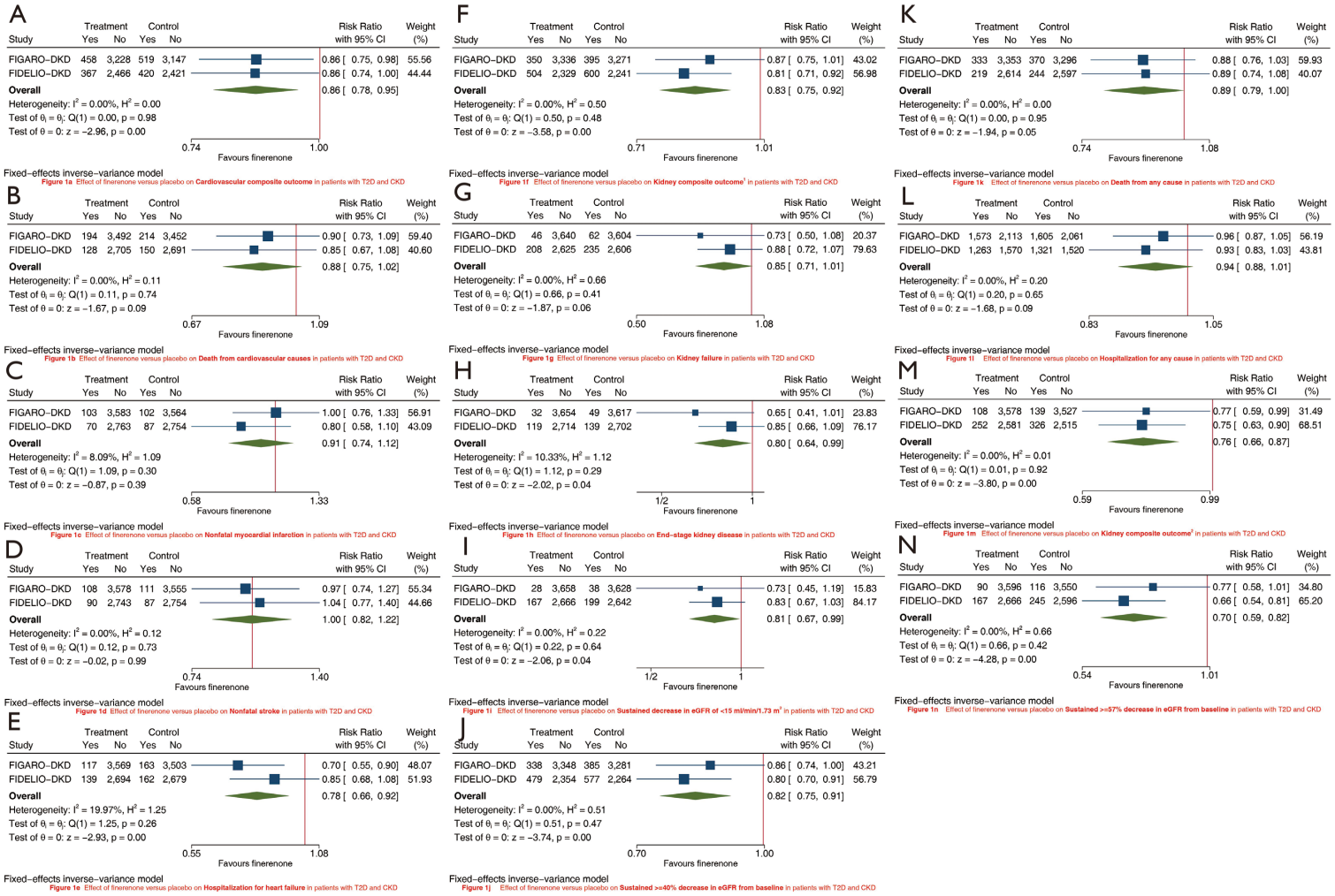

Figure 1 Forest plots showing the effects of finerenone versus placebo on 14 long-term cardiorenal outcomes in patients with T2D and CKD. CI, confidence interval; T2D, type 2 diabetes; CKD, chronic kidney disease.

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decrease in eGFR from baseline (RR: 0.82, 95% CI: 0.75–0.91, P<0.01; *Figure 1J*) by 18%, kidney composite outcome (2) (RR: 0.76, 95% CI: 0.66–0.87, P<0.01; *Figure 1M*) by 24%, and sustained ≥57% decrease in eGFR from baseline (RR: 0.70, 95% CI: 0.59–0.82, P<0.01; *Figure 1N*) by 30%. Finerenone versus placebo showed the reduced trends in the risks of death from cardiovascular causes (RR: 0.88, 95% CI: 0.75–1.02, P=0.09; *Figure 1B*), kidney failure (RR: 0.85, 95% CI: 0.71–1.01, P=0.06; *Figure 1G*), death from any cause (RR: 0.89, 95% CI: 0.79–1.00, P=0.05; *Figure 1K*), and hospitalization for any cause (RR: 0.94, 95% CI: 0.88–1.01, P=0.09; *Figure 1L*). Finerenone versus placebo did not have significant effects on nonfatal myocardial infarction (RR: 0.91, 95% CI: 0.74–1.12, P=0.39; *Figure 1C*) and nonfatal stroke (RR: 1.00, 95% CI: 0.82–1.22, P=0.99; *Figure 1D*).

Fu *et al.*'s meta-analysis (1) mainly revealed that finerenone versus placebo significantly reduced the UACR in patients with CKD. This suggests the benefits of finerenone on short-term renal indicators, but does not mean that finerenone can provide long-term renal protective effects for CKD patients. Moreover, that meta-analysis (1) also failed to evaluate the long-term cardiovascular efficacy of finerenone versus placebo. On the contrary, our meta-analysis revealed that in CKD patients with T2D compared to placebo finerenone significantly reduced not only cardiovascular and renal composite outcomes but also individual cardiorenal outcomes including hospitalization for heart failure, end-stage kidney disease, and sustained decrease in eGFR. Moreover, in this meta-analysis finerenone versus placebo was also observed with the reduced trends in the risks of cardiovascular death and all-cause death in patients with T2D and CKD. Our findings suggest that finerenone should be recommended in patients with T2D and CKD to improve long-term cardiovascular and renal prognosis.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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