INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Efficacy and safety of finerenone in chronic kidney disease associated with type 2 diabetes: meta-analysis of randomized clinical trials

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Review question / Objective: **To assess the beneficial effect and safety of finerenone for patients with chronic kidney disease associated with type 2 diabetes.**
Condition being studied: **Chronic kidney disease (CKD) is a major contributor to morbidity and mortality from non-communicable diseases, affecting almost 700 million people worldwide. Approximately 40% of patients with diabetes have CKD, which exposes them to a 3-fold higher risk of cardiovascular death versus those with T2D alone. Strategies to protect the kidneys of patients with CKD and T2D may reduce their risk of cardiovascular events. Finerenone, a nonsteroidal, selective mineralocorticoid receptor antagonist, reduced composite kidney and cardiovascular outcome in trials involving patients with chronic kidney disease. Recently, quite a few clinical studies have been conducted to compare finerenone and placebo. Our meta-analysis aimed to investigate the efficacy and safety of finerenone in chronic kidney disease associated with T2D.**

1st author* - Mingzhu Zhang and Wujisiguleng Bao contributed equally to this study.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 March 2022 and was last updated on 05 March 2022 (registration number INPLASY202230020).

INTRODUCTION

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Condition being studied: **Chronic kidney disease (CKD) is a major contributor to morbidity and mortality from non-communicable diseases, affecting almost 700 million people worldwide.**

Approximately 40% of patients with diabetes have CKD, which exposes them to a 3-fold higher risk of cardiovascular death versus those with T2D alone. Strategies to protect the kidneys of patients with CKD and T2D may reduce their risk of cardiovascular events. Finerenone, a nonsteroidal, selective mineralocorticoid receptor antagonist, reduced composite kidney and cardiovascular outcome in trials involving patients with chronic kidney disease. Recently, quite a few clinical studies have been conducted to compare finerenone and placebo. Our meta-analysis aimed to investigate the efficacy and safety of finerenone in chronic kidney disease associated with T2D.

METHODS

Search strategy: Electronic databases: PubMed; Embase; The Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library; China National Knowledge Infrastructure (CNKI); Wanfang Data; Chinese Biomedical Literature Database (SinoMed) and China Science and Technology Journal database (VIP).

Participant or population: Patients were adults (≥18 years old) with chronic kidney disease, regardless of race, gender or economic status will be included.

Intervention: Experimental intervention is finerenone, administered orally, taken either alone or in combination with other active treatment. Control intervention is placebo.

Comparator: Control intervention is placebo.

Study designs to be included: Randomized clinical trials (RCTs).

Eligibility criteria: Randomized clinical trials (RCTs) comparing finerenone with placebo or other active interventions will be included, regardless of language and publication status.

Information sources: Electronic databases: PubMed; Embase; The Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library; China National Knowledge Infrastructure (CNKI); Wanfang Data; Chinese Biomedical Literature Database (SinoMed) and China Science and Technology Journal database (VIP). If necessary, we will contact with authors.

Main outcome(s): 1) decrease in eGFR; 2) change in urinary albumin-to-creatinine ratio (UACR).

Additional outcome(s): 1) eGFR decreasing by more than 40% ; 2) cardiovascular outcomes; 3)hyperkalemia; 4)Serum potassium;5) Adverse events.

Data management: Retrieved citations from the various search engines will be imported into EndNote and checked for duplicates. Two review authors will use a pre-piloted data extraction form to extract data on general information (study ID, study author and title); methodological information (study design, the number of groups, sequence generation, allocation sequence concealment, blinding, selective outcome reporting, baseline comparability); participant characteristics (diagnostic criteria, inclusion criteria, exclusion criteria, total number of intervention groups, number lost during follow-up, age, sex, country, setting and disease duration); intervention (the name of therapeutic drug, dosage and regimen, other treatments given, drug combination, duration of treatment), and outcome measures. We will record relevant data using a pre-defined data extraction form. We will resolve disagreements through discussion, and contact the corresponding trial author in case of unclear and missing data.

Quality assessment / Risk of bias analysis: We will use the Cochrane "Risk of bias"tool of Cochrane Handbook for Systematic Reviews of Interventions to evaluate each trial's methodological quality, and then recorded in the table. The key components in the tool were: sequence generation, allocation concealment, blinding of participants, personnel and outcomes assessors, incomplete outcome data, selective outcome reporting and other

possible sources of bias. Any disagreements will resolve through discussion with a third author.

Strategy of data synthesis: We will use RevMan to analyze the data. We will use RR with 95% CIs and a random-effects model to pool their results in the meta-analyses if there are sufficient clinically similar studies available. For dichotomous outcomes, we will calculate the RR for each study and then aggregate the data. For continuous outcomes, if all the trials measured results on the same scale, we will pool MDs between the treatment arms at the end of the follow-up, otherwise we will pool SMDs. Where a meta-analysis is inappropriate, we will summarize data in tables.

Subgroup analysis: We will perform the following subgroup analyses for people with CKD to investigate heterogeneity: dosage regimen; stages of CKD; whether or not patients had diabetes.

Sensitivity analysis: We will conduct sensitivity analyses to explore the impact of losses to follow-up on the effect estimates for the primary outcomes and to exclude studies considered to be high risk of bias. For dichotomous outcomes, we will vary the event rate within the missing patients from intervention and control groups within plausible limits. For continuous data, we will perform sensitivity analyses using methods described by Ebrahim 2013 and Ebrahim 2014.

Language: No restriction.

Country(ies) involved: China.

Other relevant information: There are two contributions - Author 1, Mingzhu Zhang and Wujisiguleng Bao.

Keywords: Finerenone; chronic kidney disease; T2DM; meta-analysis; randomized clinical trials.

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