INPLASY PROTOCOL

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Support: **None.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
None declared.

Efficacy, safety and optimum dosage of vericiguat in the treatment of heart failure: a network meta-analysis

Ma, J[1]; Li, B[2]; Guo, S[3]; Jiang, H[4].

Review question / Objective: **The aim of this meta-analysis is to evaluate the efficacy, safety and optimum dosage of vericiguat in the treatment of heart failure.**
Condition being studied: **Heart failure (HF) is a complex clinical syndrome and an advanced stage of various heart diseases. At present, guidelines for HF divide HF into three categories: heart failure with reduced ejection fraction (HFrEF), heart failure with intermediate ejection fraction (HFmEF) and heart failure with preserved ejection fraction (HFpEF). Studies have shown that nitric oxide (NO)- sGC (soluble guanylate cyclase)- cycle guanosine triphosphate (cGMP) pathway closely related to cardiovascular disease. Endothelial cells produce endogenous NO under the action of endothelial derived NO synthase. The combination of NO and sGC would promote the production of cGMP from guanosine triphosphate (GTP). Thus, increasing NO level, activation of sGC, as well as inhibition the degradation of GTP are three ways to improve the heart function. Vericiguat, a sGC activitor, could activiate sGC and independent of NO, has been approved for heart failure with preserved ejectin fraction, pulmonary hypertension, achalasia, sickle cell disease and diabetic nephropathy. Recently, more and more clinical trials on vericiguat for heart failure have been carried out to verify the function of vericiguat. So we conducted a meta-analysis to study the efficacy, safety and optimum dosage of vericiguat for heart failue.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 December 2021 and was last updated on 12 December 2021 (registration number INPLASY2021120057).

INTRODUCTION

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Condition being studied: Heart failure (HF) is a complex clinical syndrome and an advanced stage of various heart diseases. At present, guidelines for HF divide HF into three categories: heart failure with reduced ejection fraction (HFrEF), heart failure with intermediate ejection fraction (HFmEF) and heart failure with preserved ejection fraction (HFpEF). Studies have shown that nitric oxide (NO)- sGC (soluble guanylate cyclase)- cycle guanosine triphosphate (cGMP) pathway closely related to cardiovascular disease. Endothelial cells produce endogenous NO under the action of endothelial derived NO synthase. The combination of NO and sGC would promote the production of cGMP from guanosine triphosphate (GTP). Thus, increasing NO level, activation of sGC, as well as inhibition the degradation of GTP are three ways to improve the heart function. Vericiguat, a sGC activitor, could activiate sGC and independent of NO, has been approved for heart failure with preserved ejectin fraction, pulmonary hypertension, achalasia, sickle cell disease and diabetic nephropathy. Recently, more and more clinical trials on vericiguat for heart failure have been carried out to verify the function of vericiguat. So we conducted a meta-analysis to study the efficacy, safety and optimum dosage of vericiguat for heart failue.

METHODS

Participant or population: Patients with heart failure, regardless of ejection fraction level, will be included.Patients with heart failure

Intervention: Vericiguat is the main treatment. The treatment group was given varies dose of vericiguat.

Comparator: The control group was treated with basic treatment treatment, and the same doseof placebo.

Study designs to be included: Randomized controlled trials (RCT) of heart failure with preserved ejection fraction treated with vericiguat will be included.

Eligibility criteria: All included studies should be randomized controlled clinical trials, and at least two groups(vericiguat and control) were included.

Information sources: Literature retrieving was performed in three database, including PubMed, Cochrane Library, Embase.

Main outcome(s): The primary outcome indicators include mortality and rehospitalization. The secondary outcome include 6-minute walk test, left ventricular ejection fraction, brain natriuretic peptide, N-terminal B-type natriuretic peptide precursor and quality of life. The safety indicators include hypovolemia, hypoglycemia, kidney damage, etc.

Quality assessment / Risk of bias analysis: Two reviewers will assess the quality of included studies according to the Cochrane Collaborations's tool for randomized controlled trials. And another reviewer would join to assess the quality if there is any disagreement between the two reviewers. Five items, including random sequence generation, allocation concealment, blinding of participants and personnel, incomplete outcome data, selective reporting and other biases will be evaluated in three categoriese: low risk of bias, unclear bias and high risk of bias.

Strategy of data synthesis: The continuous variables will be analysed using the mean difference (MD) or standardized mean difference (SMD) and their CI, and the binary variables will be analysed using the odds ratio (or) or relative risk (RR) and their 95% confidence interval (CI).

Subgroup analysis: Subgroup analysis will be conducted to analyse the possible factors that may lead to heterogeneity(only if the results are heterogeneous).

Sensitivity analysis: Random-effects meta-analysis would be performed to assess the robustness of pooled results while heterogeneity displayed among included studies.

Language: English.

Country(ies) involved: China.

Keywords: heart failure, vericiguat.

Contributions of each author:
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Author 3 - Sheng Guo.
Author 4 - Huan Jiang.