

INPLASY PROTOCOL

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None declared.

Impact of baseline heart failure status on glucagon-like peptide-1 receptor agonists heart failure-related outcomes in type 2 diabetes: a systematic review and meta-analysis of seven cardiovascular outcome trials

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Review question / Objective: The primary aim was to evaluate whether prevalent heart failure (HF) modifies the effects of glucagon-like peptide-1 receptor agonists (GLP1-RAs) on heart failure-related outcomes in type 2 diabetes?

Condition being studied: In 2022, American Diabetes Association (ADA) Consensus Report challenging the concept that heart failure (HF) may also be the first presentation of cardiovascular disease in many individuals with diabetes. This recognition stems in part from trials focused on cardiovascular safety of newer drugs to treat diabetes, or large cohort study of individuals with type 2 diabetes without prior cardiovascular disease. When onset of heart failure, the mortality rates of approximately 50% at 5 years. It is also the case that the presence of diabetes per se adversely affects long-term survival and risk of hospitalization in patients with HF. Given a strong, bidirectional association between HF and diabetes, it is highly important to provide the patients with treatment options with a favourable impact on both conditions. In recent years, the concept that hypoglycemic agents prevent HF has attracted extensive attention in the field of cardiovascular diseases. The update meta-analysis showed that GLP-1 RAs significantly reduced hospital admission for heart failure by 11%. However, this analysis was fail to differentiate between the prevention of heart failure in those at risk versus the treatment of individuals with manifest HF. Therefore, it is important to evaluate whether prevalent heart failure alters the effects of GLP 1-RAs on heart failure-related outcomes.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 June 2023 and was last updated on 05 June 2023 (registration number INPLASY202360016).

INTRODUCTION

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glucagon-like peptide-1 receptor agonists (GLP1-RAs) on heart failure-related outcomes in type 2 diabetes?

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METHODS

Participant or population: T2D with or without heart failure.

Intervention: glucagon-like peptide-1 receptor agonists (GLP-1RAs) .

Comparator: Placebo.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: Inclusion criteria: (1) GLP-1RAs cardiovascular outcome trials or post hoc analysis ;(2) trials that reported at least one of the following outcomes:

including primary composite outcome (PCO) cardiovascular death or hospitalization for heart failure (CV death or HHF), each component of composite endpoint, major adverse cardiovascular events (MACE) and all-cause mortality (ACM) by baseline heart failure status (with or without HF).

Information sources: Three electronic databases, including PubMed, Embase, Cochrane Central Register of Controlled Trials.

Main outcome(s): The primary endpoints included primary composite outcome (PCO) cardiovascular death or hospitalization for heart failure and single hospitalization for heart failure (HHF).

Additional outcome(s): Secondary outcomes were cardiovascular death (CV death), major adverse cardiovascular events (MACE) and all-cause mortality (ACM).

Quality assessment / Risk of bias analysis: Cochrane's bias risk Assessment tool.

Strategy of data synthesis: We extract point estimates reported as HRs and 95% CIs from Cox proportional hazards models, point estimates from each study were combined by use of inverse variance-weighted averages of logarithmic HRs in random-effects analysis. Stata will be used for meta-analysis.

Subgroup analysis:

- 1、 By the GLP-1RAs structure
- 2、 By the GLP-1RAs steady-state concentration
- 3、 By the GLP-1RAs molecular weight.

Sensitivity analysis: In sensitivity analyses, REWIND or ELIXA trials were excluded . The ELIXA trial was excluded because lixisenatide is a short-acting agent (estimated plasma half-life 3 h) and was administered only once daily, raising the concern that patients did not have sustained inhibition of GLP-1, as compared with the other drugs studied. In addition,

the REWIND trial expanded the definition of outcome for heart failure hospitalization.

Country(ies) involved: China.

Keywords: glucagon-like peptide-1 receptor agonists ; Heart failure ; cardiovascular outcome trials ; Meta-analysis.

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