

INPLASY

INPLASY2023100085

doi: 10.37766/inplasy2023.10.0085

Received: 26 October 2023

Published: 26 October 2023

Corresponding author:

Guo Ma

mg0328@fudan.edu.cn

Author Affiliation:

The entire systematic review was completed in Fudan University.

Evaluation and comparison of efficacy and safety of tirzepatide and semaglutide in patients with type 2 diabetes mellitus: A Bayesian network meta-analysis

Ding, Y¹; Guan, R²; Liu, H³; Wang, Z⁴; Cao, X⁵; Li, J⁶; Cai, W⁷; Ma, G⁸.

ADMINISTRATIVE INFORMATION

Support - This work was supported by the National Natural Science Foundation of China (grant numbers 82374133, 82074109, 81873078 and 81374051).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

INPLASY registration number: INPLASY2023100085

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 October 2023 and was last updated on 26 October 2023.

INTRODUCTION

Review question / Objective As new antidiabetic drugs, tirzepatide (Tir) and semaglutide (Sem) are increasingly applied in clinical practice, but their efficacy, safety have hardly been systematically evaluated. Therefore, a Bayesian network meta-analysis aimed to evaluate and compare efficacy and safety of Tir and Sem in treating type 2 diabetes mellitus (T2DM) was conducted. In patients with Type 2 diabetes, how is the blood glucose and body weight control efficacy and safety of semaglutide and tirzepatide compared to other antidiabetic drugs and placebo? And which one of semaglutide and tirzepatide have better efficacy and safety?

Condition being studied This meta-analysis will focus on glucose-lowering, body weight control efficacy and safety of semaglutide and tirzepatide.

METHODS

Search strategy

PubMed

(((((Tirzepatide[Title/Abstract]) OR (LY-3298176[Title/Abstract]) OR (Mounjaro[Title/Abstract]) OR (oral semaglutide[Title/Abstract]) OR (semaglutide tablet[Title/Abstract]) OR (Rybelsus[Title/Abstract]) OR (((semaglutide[Title/Abstract]) OR (NN-9535[Title/Abstract]) OR (Nn-9536[Title/Abstract]) OR (Nn-9931[Title/Abstract]) OR (NN9924[Title/Abstract]) OR (NNC-0113-0217[Title/Abstract])))) AND

((((((((diabetes mellitus, type 2[MeSH Terms]) OR (Diabetes Mellitus, Noninsulin-Dependent[Title/Abstract])) OR (Diabetes Mellitus, Ketosis-Resistant[Title/Abstract])) OR (Diabetes Mellitus, Non-Insulin Dependent[Title/Abstract])) OR (Diabetes Mellitus, Stable[Title/Abstract])) OR (Diabetes Mellitus, Type II[Title/Abstract])) OR (NIDDM[Title/Abstract])) OR (Diabetes Mellitus, Maturity-Onset[Title/Abstract])) OR (MODY[Title/Abstract])) OR (Diabetes Mellitus, Slow-Onset[Title/Abstract])) OR (Type 2 Diabetes Mellitus[Title/Abstract])) OR (Noninsulin-Dependent Diabetes Mellitus[Title/Abstract])) OR (Diabetes, Maturity-Onset[Title/Abstract])) OR (Type 2 Diabetes[Title/Abstract])) OR (Diabetes Mellitus, Adult-Onset[Title/Abstract]))

Web of Science

#1 (((((TS=(semaglutide)) OR TS=(NN-9535)) OR TS=(Nn-9536)) OR TS=(Nn-9931)) OR TS=(NN9924)) OR TS=(NNC-0113-0217)

#2 (((((TS=(oral semaglutide)) OR TS=(semaglutide tablet)) OR TS=(Rybelsus)) OR TS=(tirzepatide)) OR TS=(LY-3298176)) OR TS=(Mounjaro)

#3 #1 OR #2

#4 ((((((((((TS=(diabetes mellitus, type 2)) OR TS=(Diabetes Mellitus, Noninsulin-Dependent)) OR TS=(Diabetes Mellitus, Ketosis-Resistant)) OR TS=(Diabetes Mellitus, Non-Insulin Dependent)) OR TS=(Diabetes Mellitus, Stable)) OR TS=(Diabetes Mellitus, Type II)) OR TS=(NIDDM)) OR TS=(Diabetes Mellitus, Maturity-Onset)) OR TS=(MODY)) OR TS=(Diabetes Mellitus, Slow-Onset)) OR TS=(Type 2 Diabetes Mellitus)) OR TS=(Noninsulin-Dependent Diabetes Mellitus)) OR TS=(Diabetes, Maturity-Onset)) OR TS=(Type 2 Diabetes)

#5 #3 AND #4

EMBASE

(semaglutide:ab,ti OR 'nn 9535':ab,ti OR 'nn 9536':ab,ti OR 'nn 9931':ab,ti OR nn9924:ab,ti OR 'nnc 0113 0217':ab,ti OR 'oral semaglutide':ab,ti OR 'semaglutide tablet':ab,ti OR rybelsus:ab,ti OR tirzepatide:ab,ti OR 'ly 3298176':ab,ti OR mounjaro:ab,ti) AND ('non-insulin dependent diabetes mellitus'/exp OR 'diabetes mellitus, type 2':ab,ti OR 'diabetes mellitus, noninsulin-dependent':ab,ti OR 'diabetes mellitus, ketosis-resistant':ab,ti OR 'diabetes mellitus, non-insulin dependent':ab,ti OR 'diabetes mellitus, stable':ab,ti OR 'diabetes mellitus, type ii':ab,ti OR niddm:ab,ti OR 'diabetes mellitus, maturity-onset':ab,ti OR mody:ab,ti OR 'diabetes mellitus, slow-onset':ab,ti OR 'type 2 diabetes mellitus':ab,ti OR 'noninsulin-dependent diabetes mellitus':ab,ti OR 'diabetes, maturity-onset':ab,ti OR 'type 2 diabetes':ab,ti OR 'diabetes mellitus, adult-onset':ab,ti)

Cochrane Library

#1 (Tirzepatide):ti,ab,kw OR (LY-3298176):ti,ab,kw OR (Mounjaro):ti,ab,kw

#2 (oral semaglutide):ti,ab,kw OR (semaglutide tablet):ti,ab,kw OR (Rybelsus):ti,ab,kw OR (semaglutide):ti,ab,kw OR (NN-9535[Title/Abstract]))

#3 (Nn-9536):ti,ab,kw OR (Nn-9931):ti,ab,kw OR (NN9924):ti,ab,kw OR (NNC-0113-0217):ti,ab,kw

#4 (diabetes mellitus, type 2):ti,ab,kw OR (Diabetes Mellitus, Noninsulin-Dependent):ti,ab,kw OR (Diabetes Mellitus, Ketosis-Resistant):ti,ab,kw OR (Diabetes Mellitus, Non-Insulin Dependent):ti,ab,kw OR (Diabetes Mellitus, Stable):ti,ab,kw

#5 (Diabetes Mellitus, Type II):ti,ab,kw OR (NIDDM):ti,ab,kw OR (Diabetes Mellitus, Maturity-Onset):ti,ab,kw OR (MODY):ti,ab,kw OR (Diabetes Mellitus, Slow-Onset):ti,ab,kw

#6 (Type 2 Diabetes Mellitus):ti,ab,kw OR (Noninsulin-Dependent Diabetes Mellitus):ti,ab,kw OR (Diabetes, Maturity-Onset):ti,ab,kw OR (Type 2 Diabetes):ti,ab,kw OR (Diabetes Mellitus, Adult-Onset):ti,ab,kw

#7 #2 OR #3

#8 #1 OR #2

#9 #4 OR #5

#10 #9 OR #6

#11 #8 AND #10

ClinicalTrail.gov

"oral semaglutide" OR "semaglutide tablet" OR "Rybelsus" OR "semaglutide" OR "NN-9535" OR "Nn-9536" OR "Nn-9931" OR "NN9924" OR "NNC-0113-0217" OR "Tirzepatide" OR "LY-3298176" OR "Mounjaro" | Type 2 Diabetes Mellitus

Terms and electronic databases included in the review.

Participant or population Adults with type 2 diabetes.

Intervention Semaglutide (including subcutaneous semaglutide and oral semaglutide) or tirzepatide.

Comparator Placebo and other antidiabetic drugs.

Study designs to be included This meta-analysis will include randomized clinical trials (RCTs) which lasted for over 12 weeks.

Eligibility criteria All criteria were detailed in above PICOS sections.

Information sources RCTs will be detected in electronic databases including PubMed, EMBASE, Web of Science, Cochrane library and ClinicalTrials.

Main outcome(s) Efficacy outcomes: change of glycated hemoglobin (HbA1c), body weight, body mass index (BMI), and number of participants with HbA1c < 7%.

Safety outcome: number of participants with gastrointestinal adverse events.

Data management Two authors will individually finish data extraction using standardized Excel data sheet. Following information of each study will be extracted to describe characteristics of included RCTs: basic information of RCTs, participant characteristics, intervention, baseline mean of the measured outcomes. Any controversy will be resolved by discussions among all authors. Change of HbA1c, BW and BMI from baseline to the end of intervention, number of participants with HbA1c < 7 % and number of participants with gastrointestinal adverse events will be extracted. If change of HbA1c, BW and BMI is not available in the original research, then baseline mean and mean at the end of intervention will be extracted to calculate the change of mean. Change of HbA1c, BW and BMI from baseline to the end of intervention will be converted to the form of mean and SD, number of participants with HbA1c < 7 % and number of participants with gastrointestinal adverse events will be converted to the form of number of responders and sample size.

Quality assessment / Risk of bias analysis Risk of bias will be assessed with Cochrane ROB_2 by two authors. Any controversy will be resolved by discussions among all authors.

Strategy of data synthesis Results of the analysis of the change of HbA1c, BW and BMI will be measured by mean differences (MDs) and 95% confidence intervals (CIs), results of proportion of participants with HbA1c < 7 % and participants with gastrointestinal adverse events will be measured by odd ratios (ORs) and 95 % CIs. The surface under the cumulative ranking curve (SUCRA) will be used to estimate the ranking probabilities for different interventions. Interventions with higher SUCRA value will be considered as have higher possibility to be the best treatment. Heterogeneity levels will be detected with I² test. Inconsistency will be detected using node split approaches. Deviation information criterion (DIC) will be calculated for the outcomes with obvious inconsistency. If difference of DIC between consistency and inconsistency model is below 5, then the difference of model-fitting degree of consistency and inconsistency model will be considered as inconspicuous, a consistency model will be used for analysis, otherwise the model with lower DIC

would be considered as having better fitting degree and chosen for analysis.

Publication bias will be presented using funnel plot. Bayesian network meta-analysis will be conducted using R 4.2.3 ("R & R" of the Statistics Department of the University of Auckland). Analysis of publication bias will be carried out using Stata 16.0 (Stata Corp, College Station, TX, United States).

Subgroup analysis No subgroup analysis will be carried out in this meta-analysis.

Sensitivity analysis Two sensitivity analyses will be conducted to assess robustness of the results. One only included double-blind RCTs, and the other only included RCT with intervention duration between 26 weeks and 56 weeks.

Language restriction There is no language restriction in this meta-analysis.

Country(ies) involved China.

Keywords semaglutide; tirzepatide; type 2 diabetes mellitus; Bayesian network meta-analysis.

Contributions of each author

Author 1 - Yanan Ding.

Email: 23211030059@m.fudan.edu.cn

Author 2 - Ruifang Guan.

Email: 19111030079@fudan.edu.cn

Author 3 - Haiyang Liu.

Email: 23211030015@m.fudan.edu.cn

Author 4 - Zihan Wang.

Email: 1169448284@qq.com

Author 5 - Xinyue Cao.

Email: 20301030060@fudan.edu.cn

Author 6 - Jiyifan Li.

Email: 20301030046@fudan.edu.cn

Author 7 - Weimin Cai.

Email: weimincai@fudan.edu.cn

Author 8 - Guo Ma.

Email: mg0328@fudan.edu.cn