

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## PPAR-alpha/gamma agonists, glucagon-like peptide-1 receptor agonists and metformin for non-alcoholic fatty liver disease: A network meta-analysis

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**Review question / Objective:** This network meta-analysis is performed to evaluate the efficacy of these drugs on the progression of nonalcoholic fatty liver disease.

**Condition being studied:** Saroglitazar, belonging to peroxisome proliferator-activated receptor- $\alpha/\gamma$  agonist, is the first drug for non-alcoholic fatty liver disease. Glucagon-like peptide 1 receptor agonists may also be used to improve symptoms of nonalcoholic fatty liver disease. Metformin has also been used to improve nonalcoholic fatty liver disease. The direct comparison of the effects of these drugs on nonalcoholic fatty liver disease are still lack.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 April 2023 and was last updated on 19 April 2023 (registration number INPLASY202340066).

### INTRODUCTION

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activated receptor- $\alpha/\gamma$  agonist, is the first drug for non-alcoholic fatty liver disease. Glucagon-like peptide 1 receptor agonists may also be used to improve symptoms of nonalcoholic fatty liver disease. Metformin has also been used to improve nonalcoholic fatty liver disease. The direct comparison of the effects of these drugs

on nonalcoholic fatty liver disease are still lack.

## METHODS

**Participant or population:** Patients with NAFLD were confirmed by biopsy or other testing, including adults and adolescents.

**Intervention:** Interventions include PPAR alpha / $\gamma$  agonists (saroglitazar) or GLP-1 receptor agonists (including semaglutide, liraglutide and dulaglutide) or metformin.

**Comparator:** The target population received saroglitazar, a GLP-1 agonist, metformin, and a placebo as a control. The minimum duration of action is 4 months. Finally, ALT and AST were taken as the main outcome and TG as the secondary outcome.

**Study designs to be included:** Placebo controlled; single blinded; non-blinded; double-blinded; single center; multi center.

**Eligibility criteria:** The improvement effects of different drugs on ALT and AST levels in patients with NAFLD were analyzed, and corresponding 95% confidence intervals (CI) were provided.

**Information sources:** Databases such as EMBASE, PubMed, Cochrane Library databases serve as the intended sources of information.

**Main outcome(s):** We reported the main outcome of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels.

**Additional outcome(s):** The addition outcome was whether different drugs improved TG levels in patients with NAFLD.

**Quality assessment / Risk of bias analysis:** The Cochrane Risk of Bias Tool (Higgins et al., 2011) was used to evaluate the Risk of Bias of each study over the course of the study, including the random generation of sequence, concealment of assignments, subject and investigator blinding, outcome assessment blinding, incomplete outcome

data, selective results reporting, or other sources of bias. Risk of bias was classified as low, high, or unclear risk.

**Strategy of data synthesis:** The required outcome measures were included from selected clinical studies and examined independently by two authors to ensure the accuracy of the data. Review Manager Version 5.3 was developed by the Review Manager, which was developed by the Review Manager. Resolve the differences involved through discussion.

**Subgroup analysis:** Subgroup analysis was performed when heterogeneity was too large, which was not performed in this study.

**Sensitivity analysis:** Sensitivity analysis was performed according to random assignment, subject blind method and therapist blind method.

**Language restriction:** English.

**Country(ies) involved:** China.

**Keywords:** NAFLD; saroglitazar; GLP-1 receptor agonists Saroglitazar.

### Contributions of each author:

Author 1 - Zhuoya ZHANG - designed research, wrote the paper and data collection.

Author 2 - Qi YAN - conducted research and data collection.

Author 3 - Wenhao WU - analyzed data.

Author 4 - Yuan ZHAO - modified the paper.

Author 5 - Hua ZHANG - modified the paper.

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