International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Efficacy and safety of fibroblast growth factor 21 (FGF21) analogues for the treatment of nonalcoholic steatohepatitis (NASH) and NASH-associated fibrosis: a systematic review and meta-analysis

INPLASY2023110033

doi: 10.37766/inplasy2023.11.0033

Received: 07 November 2023

Published: 07 November 2023

Corresponding author:
Qin Feng

fengqin@shutcm.edu.cn

Author Affiliation:
Shanghai University of Traditional Chinese Medicine, Shuguang Hospital, Institute of Liver diseases.

Lin, RT[1]; Zheng, MH[2]; Feng, Q[3].

ADMINISTRATIVE INFORMATION

Support - Study for effect of Danggui Shaoyao Powder in the treatment of Non-alcoholic Fatty Liver Disease, No. SHDC2020CR4051.

Review Stage at time of this submission - Piloting of the study selection process.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2023110033

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 November 2023 and was last updated on 07 November 2023.

INTRODUCTION

Review question / Objective Several FGF21 analogs for the treatment of NASH and NASH-related fibrosis have been in clinical trials recently. We conducted a meta-analysis of the effects of FGF21 drugs on NASH and NASH-related fibrosis, as well as the effects on other relevant indicators and the safety of the drugs.

Condition being studied No drugs or therapies have been approved for the treatment of non-alcoholic steatohepatitis (NASH) and NASH-related fibrosis, several fibroblast growth factor 21 (FGF21) analogs for the treatment of NASH and NASH-related fibrosis are been in clinical trials recently. We performed a meta-analysis to evaluation of the efficacy and safety of the drugs.

METHODS

Participant or population Inclusion criteria for the studies: (1) RCT studies, (2) study examines effectiveness of FGF21 in ereating NASH and NASH-related fibrosis, (3) adult (age >18 years) individuals of any sex or ethnicity, and (4) patients must have a biopsy diagnosis of NASH combined with NASH CRN fibrosis staging f1-f4. Exclusion criteria for studies: (1) animal studies, (2) reviews, conference proceedings, letters, case reports, or comments, and (3) non-English language studies.

Intervention FGF21 analogs.

Comparator Placebo.

Study designs to be included RCT study.

Eligibility criteria Inclusion criteria for the studies: (1) RCT studies, (2) study examines effectiveness of FGF21 in ereating NASH and NASH-related fibrosis, (3) adult (age >18 years) individuals of any sex or ethnicity, and (4) patients must have a biopsy diagnosis of NASH combined with NASH CRN fibrosis staging f1-f4. Exclusion criteria for studies: (1) animal studies, (2) reviews, conference proceedings, letters, case reports, or comments, and (3) non-English language studies.

Information sources We systematically searched potential publications in five large electronic databases (PubMed, Embase and Cochrane Library), from database inception until October 3, 2023. Search terms were ("Fibroblast growth factor 21" OR "FGF21") AND ("NAFLD" OR "NASH" OR "Nonalcoholic fatty liver disease" OR "Nonalcoholic steatohepatitis" OR "NASH related-fibrosis").

Main outcome(s) The primary efficacy outcomes were defined as the proportion of patients with fibrosis improvement ≥1 stage without worsening of NASH, and the proportion of patients with NASH resolution without worsening of fibrosis. Secondary efficacy outcomes data included the proportion of patients with ≥30% relative reduction in hepatic fat fraction (HFF), changes in relative HFF, absolute HFF, alanine aminotransferase (ALT), aliquot transaminase (AST), liver stiffness, procollagen type III n-terminal propeptide (Pro-C3), enhanced liver fibrosis score (ELF score), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), hemoglobin A1c (HbA1c), body weight. And also includes treatment-related adverse events, such as nausea, vomiting, diarrhea, and injection site reactions. In addition, there were serious adverse events.

Quality assessment / Risk of bias analysis The quality of the included literature was evaluated using the Risk of Bias Assessment Tool for RCTs from the Cochrane Handbook. Two researchers evaluated independently.

Strategy of data synthesis Meta-analysis was performed using RevMan 5.3, Stata16 software. Effect sizes for dichotomous data were expressed using relative risk (RR); effect sizes for continuous variables were chosen to be expressed as mean difference (MD) or standardized mean difference (SMD), and absolute values of SMD greater than 0.2, 0.5, and 0.8 were used as the thresholds for small, medium, and large effect sizes, respectively. Heterogeneity was assessed using the chi-square test for Cochrane's Q statistic and calculating I2-statistics. The random-effects model was conducted when there was a significant heterogeneity with I2-statistic >50% or p-value 50%. When dichotomous variables are extracted and the number of specific event occurrences is unknown, the estimated number of event occurrences is calculated by multiplying the percentage of event occurrences by the total number of occurrences. When collecting data for continuous variables, if the mean and standard deviation (SD) were unavailable, the median and Least Squares (LS) mean were considered in place of the mean, in this instance, the SMD was utilized to indicate the effect size, while the interquartile range was converted to SD by dividing by 1.35. The standard error (SE) was converted using the formula "SD = SE*SQRT(n)". If only 95% confidence intervals were provided, SD was converted using the formula "SD=SQRT(n)*(Upper limit-Lower limit)/(TINV(1-0.95,n-1)*2)".

Subgroup analysis Subgroup analyses of primary efficacy outcomes based on drug structure, drug class, whether the drug was in development, and the stage of fibrosis in the patient were used to assess differences in efficacy within and between subgroups.

Sensitivity analysis Sensitivity analyses were performed by excluding changes in the observed results of the included literature one by one.

Country(ies) involved China.

Keywords FGF21 ; NASH ; NASH related fibrosis ; meta-analysis.

Contributions of each author

Author 1 - RuTao Lin.
Email: linrutao_2000@163.com
Author 2 - MingHua Zheng.
Email: zhengmh@wmu.edu.cn
Author 3 - Qin Feng.
Email: fengqin@shutcm.edu.cn