INPLASY PROTOCOL

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None declared.

Efficacy and safety of Aldafermin (NGM282) in reducing liver fibrosis in patients with NASH: a systematic evaluation and meta-analysis

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Review question / Objective: **P:patients with NASH, I:Aldafermin（NGM282), C:Placebo，O：reducing liver fibrosis in patients with NASH，S：meta-analysis.**

Condition being studied: **NAFLD is now considered to be the most common chronic liver disease, afflicting approximately 25% of the adult population worldwide [19]. Non-alcoholic steatohepatitis (NASH) is the clinically progressive inflammatory subtype of non-alcoholic fatty liver disease (NAFLD), and the pathology of NASH is characterized by excessive accumulation of triglycerides (steatosis) in hepatocytes, inflammation, injury and apoptosis, leading to a significant increase in the incidence of cirrhosis and hepatocellular carcinoma in the context of negative disease progression.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 November 2022 and was last updated on 13 November 2022 (registration number INPLASY2022110062).

INTRODUCTION

Review question / Objective: **P:patients with NASH, I:Aldafermin（NGM282), C:Placebo，O：reducing liver fibrosis in patients with NASH，S：meta-analysis.**

Rationale: **NASH is currently the leading cause of chronic liver disease worldwide with no well-established effective pharmacological treatment options,The clinically applicable drug Aldafermin (an engineered FGF19 analogue NGM282) presented here is still in clinical trials,There**

are now some experimental proofs It has the ability to inhibit bile acid synthesis, and it has a significant effect on the reduction of liver fat content.

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METHODS

Search strategy: Pubmed: # 1 ((((((((((((Non alcoholic Fatty Liver Disease) OR (NAFLD)) OR (Nonalcoholic Fatty Liver Disease)) OR (Fatty Liver, Nonalcoholic)) OR (Fatty Livers, Nonalcoholic)) OR (Liver, Nonalcoholic Fatty)) OR (Livers, Nonalcoholic Fatty)) OR (Nonalcoholic Fatty Liver)) OR (Nonalcoholic Fatty Livers)) OR (Nonalcoholic Steatohepatitis)) OR (Nonalcoholic Steatohepatitides)) OR (Steatohepatitides, Nonalcoholic)) OR (Steatohepatitis, Nonalcoholic) (38143)
2 Non-alcoholic Fatty Liver Disease[MeSH Terms] (20834)
#3 NGM282 (33)
#4 aldafermin (18)
(#1 OR #2) AND (#3 OR #4) (22)
Embase:
#1 'nonalcoholic fatty liver'/exp (61015)
#2 'ngm282'/exp OR ngm282 (227)
#1 AND #2 (148)
Cochrane:
#1Non-alcoholic Fatty Liver Disease (2706)
#2 NGM282 (53)
#1 AND #2 (4)
others:
Non-alcoholic Fatty Liver Disease AND NGM282 (13).

Participant or population: Phase 2b study (ALPINE 2/3) in patients with biopsy-confirmed NASH and stage 2 or 3 fibrosis.

Intervention: The experimental group used different doses of NGM283.

Comparator: NGM282 (a drug) as an intervention.

Study designs to be included: Randomised controlled trial.

Eligibility criteria: (1) randomized controlled trials (RCTs) or clinical trials; (2) interventions using aledafermin where the control group was placebo; (3) studies involving liver histology or fibrosis measurements such as LFC by MRI-PDFF imaging, Pro-C3,ELF, C4 ALT, NAS activity score, etc. The Data were used to calculate the corresponding statistics. Animal studies, review articles and conference abstracts were not included.

Information sources: Cochrane Library, PubMed database, Embase database, and the ClinicalTrials.gov.

Main outcome(s): It has a Significant decreases in liver fibrosis markers such as pro-c3 (N-terminal type III collagen pro-peptide) and ELF (enhanced-liver-fibrosis) scores were measured in NASH patients after 12 to 24 weeks.

Additional outcome(s): After 12 to 24 weeks There are significant changes in the serological parameters of the liver,such as ALT (alanine aminotransferase)、C4 (7α-hydroxy-4-cholesten-3-one) and LFC (Liver fat content).

Quality assessment / Risk of bias analysis: The quality of the studies involved in this meta-analysis was assessed using Cochrane criteria to determine selection bias, implementation bias, measurement bias, and reporting bias for each trial. Individual articles were next assessed to determine the level of bias in the defined domains.

Strategy of data synthesis: Statistical analyses were performed using RevMan software (version 5.4, Cochrane, Oxford, UK). Outcomes were assessed quantitatively using the Higgins index (I2) using either a fixed-effects model or a combination of random-effects models, depending on the level of heterogeneity between studies.

Subgroup analysis: No.

Sensitivity analysis: No.

Language restriction: Only English.

Country(ies) involved: China.

Keywords: Aldafermin; Non-alcoholic Fatty Liver Disease; Systematic evaluation; Meta-analysis.

Contributions of each author:

Author 1 - Tongxi Li - Ideas; formulation or evolution of overarching research goals and aims.
Author 2 - Dan Tan - Preparation, creation and presentation of the published work, specifically writing the initial draft (including substantive translation).
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Author 3 - YongLang Cheng - Preparation, creation and presentation of the published work by those from the original research group, specifically critical review, commentary or revision – including pre-or postpublication stages.
Author 4 - Peng Tan - Preparation, creation and presentation of the published work, specifically data presentation.
Author 5 - Yichao Du - Preparation, creation and presentation of the published work, specifically data presentation.
Author 6 - Yifan Chen - searched articles and reviewed them for quality.
Author 7 - Tianying Cai - searched articles and reviewed them forquality.
Author 8 - Ziming Wu - Application of statistical, mathematical.
Author 9 - Wenguang Fu - Management and coordination responsibility for the research activity planning and execution, Reviewing and Editing.