INPLASY PROTOCOL

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Corresponding author:
Kun Zhao
zhaokun0428@zju.edu.cn

Author Affiliation:
School of Medicine, Zhejiang University

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The authors declare no conflicts of interest.

Effectiveness of tanezumab for the treatment of pain in knee and hip osteoarthritis: a dose-response network meta-analysis

Zhao, K[1]; Nie, L[2];

ABSTRACT

Objective: **To determine the effectiveness of different preparations and doses of tanezumab for osteoarthritis.**

Condition being studied: **Hip or knee osteoarthritis(OA) is a chronic degenerative disease mostly treated with analgesics and non-steroidal anti-inflammatory drugs(NSAIDs), but these drugs can cause well-described hepatotoxicity, gastrointestinal and cardiovascular side effects, especially if taken chronically and the response to them is not satisfactory in some patients. Effective analgesic with acceptable side-effect profiles may help avoid or delay surgical intervention. Prior meta-analysis have established the superiority of tanezumab over placebo in the treatment of OA knee and hip pain, but considered only direct evidence and did not address the comparison for different injection method (intravenous or subcutaneous), doses or multiple time points.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 March 2020 and was last updated on 31 March 2020 (registration number INPLASY202030019.

INTRODUCTION

Objectives / Review question: **o determine the effectiveness of different preparations and doses of tanezumab for osteoarthritis.**

Condition being studied: **Hip or knee osteoarthritis(OA) is a chronic degenerative disease mostly treated with analgesics and non-steroidal anti-inflammatory drugs(NSAIDs), but these drugs can cause well-described hepatotoxicity, gastrointestinal and cardiovascular side effects, especially if taken chronically and the response to them is not satisfactory in some patients. Effective analgesic with acceptable side-effect profiles may help avoid or delay surgical intervention. Prior**

meta-analysis have established the superiority of tanezumab over placebo in the treatment of OA knee and hip pain, but considered only direct evidence and did not address the comparison for different injection method (intravenous or subcutaneous), doses or multiple time points.

METHODS

Participant or population: Adult patients who were clinically diagnosed with OA based on the criteria described by the American College of Rheumatology or clinical and radiological information.

Intervention: Tanezumab at any a fixed-dose regimen.

Comparator: Placebo.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: We included all randomized controlled trials involving adult patients who were clinically diagnosed with OA based on the criteria described by the American College of Rheumatology or clinical and radiological information that investigated the effect of tanezumab at any a fixed-dose regimen and any phase and reported extractable data for at least one or both outcome measures, pain and physical function, measured with standard medical instruments. Data recorded in studies with participants receiving NSAIDs, other analgesics, or a dosing regimen adjusted for body weight were excluded.

Information sources: We searched the PubMed, Cochrane library, EMBASE and clinicaltrial.gov databases from the inception dates to November 9, 2019, using the keywords tanezumab, fasinumab, fulranumab, osteoarthritis. All searches were limited to randomized controlled trials in humans. No limits were applied for language, publication date, or publication status.

Main outcome(s): The mean change from baseline to various administration or follow-up timepoints of Western Ontario and McMaster Universities OA Index (WOMAC) pain subscale or WOMAC physical function subscale.

Quality assessment / Risk of bias analysis: Two reviewers will independently assesses the quality of the selected studies according to the Cochrane Collaboration's tool for randomized controlled trials. Items will be evaluated in three categories: Low risk of bias, unclear bias and high risk of bias. The following characteristics will be evaluated: Random sequence generation (selection Bias) Allocation concealment (selection bias) Blinding of participants and personnel (performance bias) Incomplete outcome data (attrition bias) Selective reporting (reporting bias) Other biases. Results from these questions will be graphed and assessed using Review Manager 5.3.

Strategy of data synthesis: First, we will perform pairwise meta-analyses and mean difference (MD) will be calculated as the effect size for continuous outcomes with 95% CI. Statistical heterogeneity will be tested in each pairwise comparison with the I^2 statistic and p value. Second, we will peform a network meta-analysis within a Bayesian framework with R software and gemtc package. We will summay the results of network meta-analysis with effect sizes (MD) and their credible intervals (CrI). We will estimate the ranking probabilities and surface under the cumulative ranking curve (SUCRA) for all treatments of being at each possible rank for each intervention.

Subgroup analysis: None.

Sensibility analysis: We will perform sensitivity network meta-analyses for pain relief and function improvement by differentiating placebos into intravenous and subcutaneous injections.

Countries involved: China.

Keywords: tanezumab; osteoarthritis; network meta-analysis.