INPLASY PROTOCOL

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None declared.

Evaluation of the Efficacy and Safety of Romosozumab (Evenity) for the Intervention of Osteoporotic Vertebral Compression Fracture in Postmenopausal Women: a Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Review question / Objective: **We performed this Comprehensiveness systematic review and meta-analysis of the efficacy of Romosozuma (Evenity) versus placebo through primary outcomes (vertebral, nonvertebral and clinical fractures.), secondary outcomes (BMD determined by dual-energy X-ray absorptiometry at the total hip, lumbar spine, and femoral neck) and incidence of adverse effects (AEs) including cardiovascular events, death, hypersensitivity, osteoarthritis, injection-site reaction, etc for the intervention of osteoporotic vertebral compression fracture in postmenopausal women.**

Information sources: **Databases such as PubMed, Cochrane library, NIPH Clinical Trials, International Clinical Trials Registry Platform and Clinical Trials.gov.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 June 2021 and was last updated on 20 June 2021 (registration number INPLASY202160068).

INTRODUCTION

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secondary outcomes (BMD determined by dual-energy X-ray absorptiometry at the total hip, lumbar spine, and femoral neck) and incidence of adverse effects (AEs) including cardiovascular events, death, hypersensitivity, osteoarthritis, injection-site reaction, etc for the intervention of osteoporotic vertebral compression fracture in postmenopausal women.

Condition being studied: Osteoporotic vertebral compression fracture (OVCF), is a common fragile fracture resulting from osteoporosis, has caused a huge decline in quality of life (QOL) and increased the risk of morbidity and mortality especially in postmenopausal women , osteoporosis in postmenopausal women is a type of primary osteoporosis which patients will show low back or whole-body bone pain, severe cases will show spinal deformation, and the most serious consequence is a fracture, there were RCTs and systematic reviews comparing the efficacy and safety of Romosozumab with placebo for treating OVCT and low bone density but the final outcomes differed from each other, we performed this comprehensiveness systematic review and meta-analysis of the efficacy of Romosozuma (Evenity) versus placebo through primary outcomes (vertebral, nonvertebral and clinical fractures.), secondary outcomes (BMD determined by dual energy X-ray absorptiometry at the total hip, lumbar spine, and femoral neck) and incidence of adverse effects (AEs) including cardiovascular events, death, hypersensitivity, osteoarthritis, injection-site reaction, etc for the intervention of osteoporotic vertebral compression fracture in postmenopausal women on epidemiologic studies.

METHODS

Search strategy: We searched the relevant literature from databases such as PubMed, Cochrane library, NIPH Clinical Trials, International Clinical Trials Registry Platform and Clinical Trials.gov to December 2020 was performed, the following search terms were used: ("Osteoporotic Vertebral Compression Fracture" OR "fracture" OR "Osteoporosis") AND ("Romosozumab" OR "Evenity" OR "AMG 785") AND ("RCT" OR "Randomized Controlled Trial"). The detail terms and searching results are tabled in Supplement 1. All articles in English were selected and reviewed for meta-analysis by their titles and abstracts and the search process is outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Participant or population: Postmenopausal women who suffering from osteoporotic vertebral compression fracture.

Intervention: Romosozumab subcutaneous injection monthly with a dose of 210, 140, or 70 mg.

Comparator: Matching placebo, teriparatide and alendronate subcutaneous injection monthly.

Study designs to be included: Randomized controlled trials on efficacy and safety of romosozumab compared with control group on osteoporotic vertebral compression fracture in postmenopausal women.

Eligibility criteria: Randomized controlled trials were included in the analysis if they: 1) investigated the efficacy of Romosozuma for OVCT in patients (women) with Romosozuma groups and placebo groups of once-monthly subcutaneous (6 months, 12 months, 24 months) Romosozumab injection with a dose of 210, 140, or 70 mg. 2) reported estimates of RR (pooled relative risks, ORs, WMD, MD, SMD, and corresponding 95%CI for estimating the outcomes.

Information sources: Databases such as PubMed, Cochrane library , NIPH Clinical

Trials, International Clinical Trials Registry Platform and Clinical Trials.gov.

Main outcome(s): Incidence of vertebral, non-vertebral, clinical fractures, BMD changes from baseline of total hip, lumbar spine, femoral neck, number and percentage of adverse events in each group.

Quality assessment / Risk of bias analysis: The Cochrane Collaboration Risk of Bias Tool.

Strategy of data synthesis: The extracted data were calculated for the MD (mean difference) and RR (risk ratio) with 95% confidence intervals (CIs), MD was calculated for percentage changes of BMD in total hip, lumbar spine, and femoral neck, RR was calculated for the risk of incident of vertebral fractures, nonvertebral fractures, clinical fractures, and adverse event in Review Manager 5.3 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark) was used to create the forest plot and assess the heterogeneity with Cochrane Q and I2 statistics using fix/random-effect models, if I2>50%, random effect models were applied, and P-value ≤0.05 were considered significant, if I2 ≦50%, then fixed model was applied, We still performed subgroup analysis: control, dose, and duration , the meta-regression was used to analyze the source of heterogeneity if more than 50% (STATA, version 16.0; StataCorp, College Station, Tex).

Subgroup analysis: We still performed subgroup analysis: control, dose, and duration to explore the source of heterogeneity.

Sensitivity analysis: Eliminate each selected research one by one, and use the likelihood ratio test to determine whether the combined effect of scale is the sensitivity of individual clinical trials. The stability of the valence effect scale to the two statistical models.

Language: English.

Country(ies) involved: Japan.

Keywords: Romosozumab; osteoporosis; osteoporotic vertebral compression fracture (OVCT); fractures; meta-analysis; systematic review.

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