Comparative Cardiovascular Safety of Romosozumab and Denosumab in Osteoporosis Treatment: A Multi-national Real-World Cohort Study

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Introduction

Romosozumab and denosumab have recently become two highly effective and widely used osteoporosis treatments.[1] There is no study has directly compared the efficacy of romosozumab and denosumab in a clinical setting using large-scale, real-world data.[2,3]

Objectives

In this study, we evaluated the cardiovascular risk associated with romosozumab compared to denosumab in osteoporosis treatment.

Methods

Data were sourced from TriNetX, including patients aged >60 years who received either romosozumab (n=3,898) or denosumab (n=49,067) between January 2019 and December 2024. After 1:1 propensity score matching (PSM) for baseline characteristics, 3,892 patients remained in each group. Kaplan-Meier analysis was applied to estimate 1-year cumulative incidence of cardiovascular outcomes, including three-point major adverse cardiovascular events (3P-MACE), heart failure, hypertension, cardiomyopathy, and peripheral arterial disease (PAD). The primary analysis focused on patients without prior cardiovascular disease. Sensitivity analyses explored (1) 5-year outcomes in patients without cardiovascular history and (2) both 1- and 5-year outcomes in those with prior cardiovascular disease.

Results

No significant differences were found in 1-year cardiovascular outcomes between romosozumab and denosumab, including 3P-MACE (HR: 0.460; 95% CI: 0.421–1.044; p=0.074), heart failure (HR: 0.501; p=0.129), hypertension (HR: 1.165; p=0.562), cardiomyopathy (HR: 1.134; p=0.796), and PAD (HR: 0.669; p=0.835). However, a potential long-term risk of PAD associated with romosozumab was observed in patients with a history of cardiovascular disease (HR: 1.548; 95% CI: 1.143-2.098; p-value 0.004).

Conclusions

Romosozumab may be a feasible and safe treatment option for osteoporosis, as it was not significantly associated with increased cardiovascular risk or mortality. However, in patients with a history of cardiovascular disease, the use of romosozumab should be approached with caution due to the potential long-term risk of PAD.

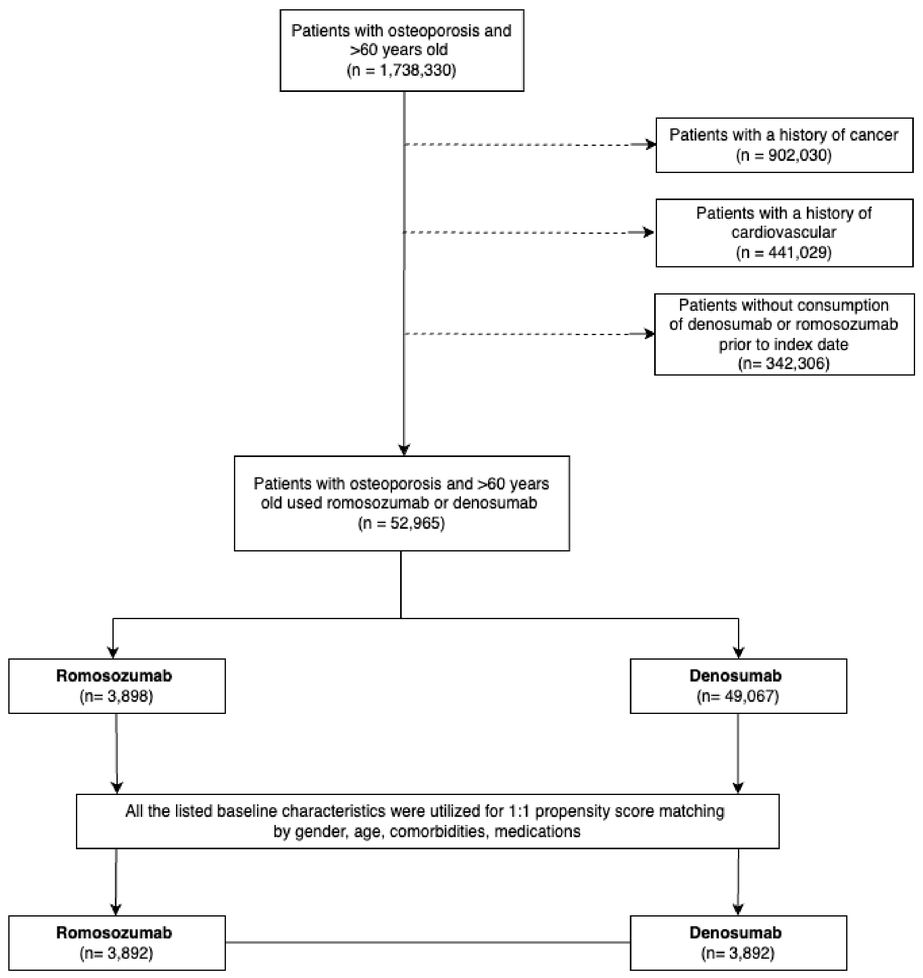

Figure 1. Flowchart of the cohort selection process

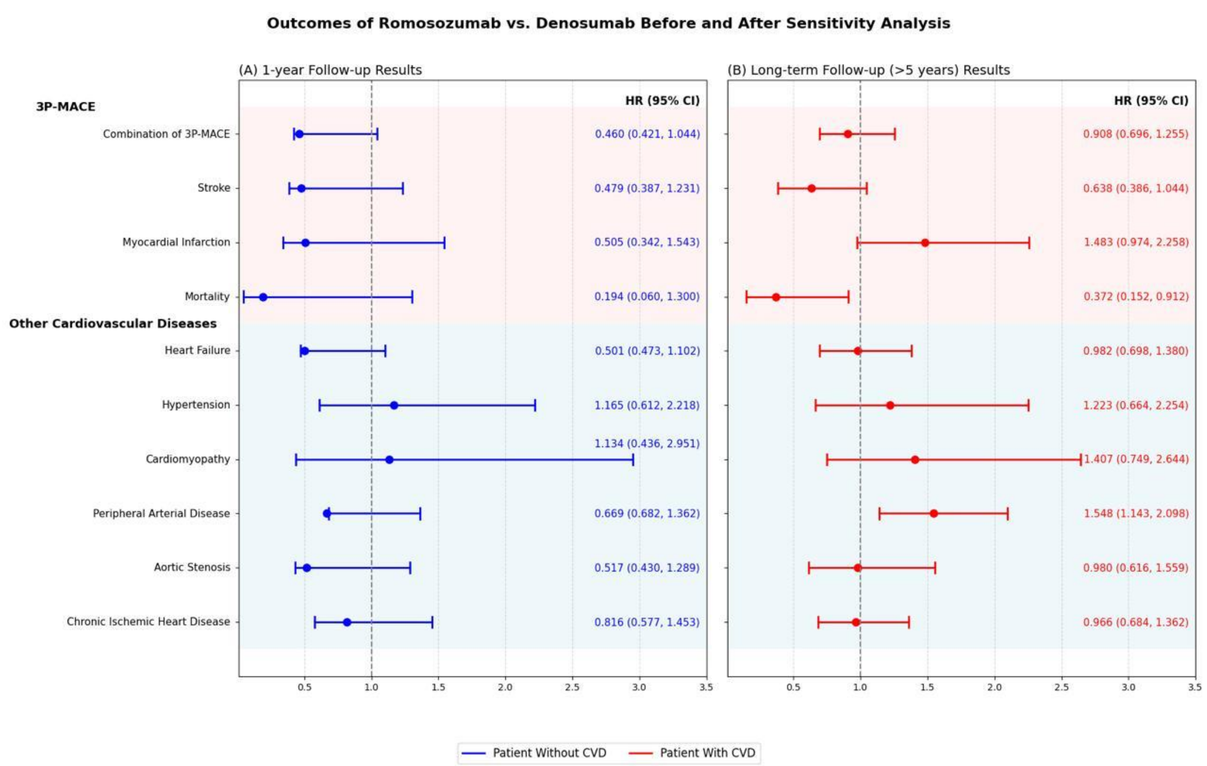

Figure 2. Outcomes of romosozumab vs. denosumab before and after sensitivity analysis

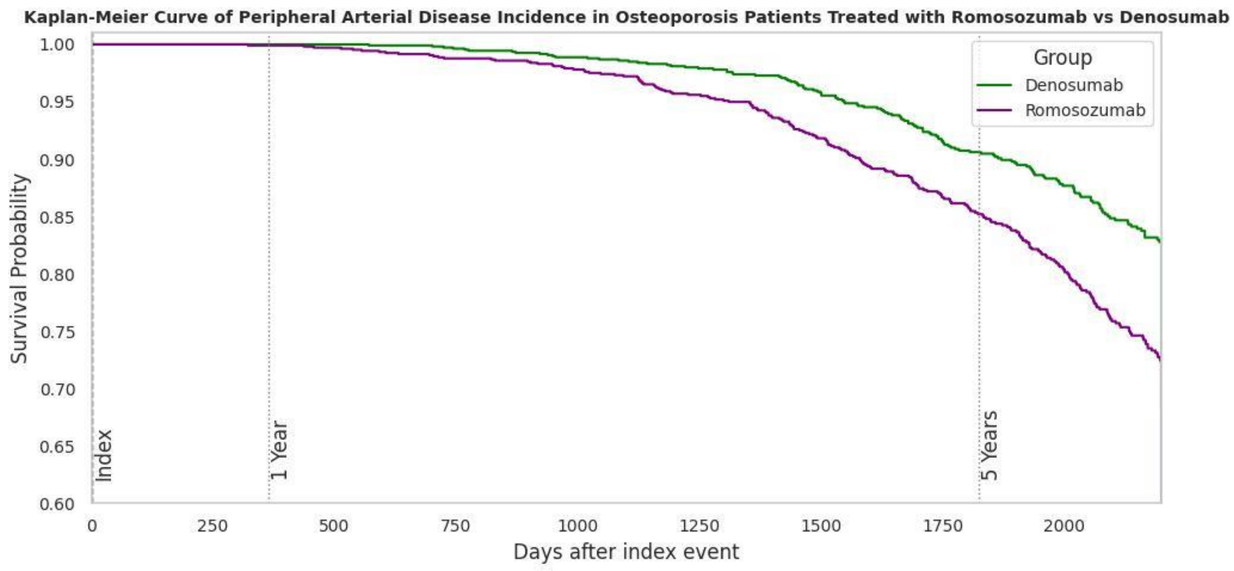

Figure 3. Kaplan-meier curve of peripheral arterial disease incidence in osteoporosis patients with history of cardiovascular

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Keywords

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