中文題目：比較 Denosumab 及 Alendronate 對於骨鬆病患之心血管及腎預後的影響

英文題目：The Effects of Denosumab and Alendronate on Cardiovascular and Renal Outcomes in Osteoporotic Patients

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***Background:*** Evidence has revealed the correlation between osteoporosis, chronic kidney disease (CKD) and cardiovascular diseases (CVD). Vascular calcification, a characteristic change in the vessels of CKD patients, may share common pathogenetic mechanisms with osteoporosis via the osteoprotegerin (OPG)/receptor activator of nuclear factor-kB (RANK)/RANK Ligand (RANKL) pathway. Denosumab, a human monoclonal antibody and acts as RANKL inhibitor, prevents fractures in patients with osteoporosis. However, limited information is available regarding the effects of denosumab on CVD risks and renal function progression. This study aims to compare the effects of denosumab to alendronate, a widely used bisphosphonate agent, on cardiovascular and renal outcomes in osteoporotic patients.

***Methods:*** We retrospectively analyzed the all patients undergone denosumab and alendronate from Jan 2005 to Dec 2017 at Chang Gung Memorial Hospitals (CGMH) in Taiwan. Propensity score matching (PCM) was used to adjust for significant covariates. The incidence of the composite of major CVD, including myocardial infarction, congestive heart failure, and ischemic stroke. Renal outcomes were assessed by the mean changes in eGFR from baseline and by the incident of eGFR decline ≥30% of baseline. Time to CVD endpoint was analyzed using Kaplan–Meier with log-rank tests. Multivariate regression models and stratified analysis were used to assess the CV and renal outcomes in these two groups.

***Results:*** After PCM, there were 5046 patients in total, with 2523 in each group. The overall incidence of composite CVD was similar between patients in the denosumab and alendronate groups after the 5-year follow-up. However, in patients with medication possession ratio (MPR) ≥60%, incidence of CVD disease was significantly lower in the denosumab group than in the alendronate group. For the renal outcomes, there was no significant difference in cumulative of eGFR decline ≥30% of baseline. Nevertheless, denosumab treatment had a trend toward poor renal outcome compared with alendronate therapy in male, patients with poor renal function (baseline eGFR < 60mL/min/1.73 $m^2$) and acute kidney injury (AKI) episodes.

***Conclusion:*** Denosumab and alendronate treatments revealed no difference in CVD incidence in the 5-year period. However, in patients with MPR ≥60%, denosumab treatment was associated with lower risk of CVD development. On the contrary, denosumab treatment, compared with alendronate therapy, had a trend toward poorer renal outcome in males and in patients with poor renal function at baseline and AKI episodes.