Cardiovascular risk assessment for osteoporosis patients considering Romosozumab

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Key messages:

Cardiovascular risk scoring tools are suitable for but not interchangeable within the osteoporosis clinic.

Dear Editor

Romosozumab is a novel agent approved for the management of osteoporosis in post-menopausal women. The drug is a sclerostin inhibitor and unique in its combined anabolic and antiresorptive mechanism of action. Impressively, when compared with Alendronic acid in the ARCH trial, it demonstrated a 48% lower risk of vertebral fractures over a 24-month period (1). However, concern exists regarding the cardiovascular risk profile of the drug, as the same trial showed an increased risk of serious cardiovascular events in the Romosozumab arm (1). This increased risk was not reproduced in trials which compared Romosozumab to a Placebo (2). However, a meta-analysis of key Romosozumab trials did find an increased risk of cardiovascular events in patients prescribed Romosozumab (3). Furthermore, studies using genetic proxies of sclerostin inhibition have also shown an increased risk of myocardial infarction, supporting the clinical trial data (4, 5). These findings highlight the need for clinicians to consider their patient's cardiovascular risk profile prior to starting Romosozumab.

Cardiovascular risk screening tools have been developed to highlight patients at increased risk of myocardial infarction or stroke and to guide primary prevention efforts. QRISK3 is such a tool and is

widely used within primary care in the UK for patients aged between 25-84 years (6). Alternatively, The European Society of Cardiology's HeartScore (ESC SCORE) is a newer cardiovascular risk screening tool that includes an older persons score for those aged over 70 years old, which has been validated in an older population (7). ESC SCORE requires fewer inputs than QRISK3. Both scoring systems provide a 10-year predicted risk that is shown numerically as a percentage. ESC SCORE also provides a colour; green, amber or red depending on the patient's risk adjusted for their age.

The Southwest bone group, a collective of osteoporosis clinicians based in the Southwest of England, developed local guidelines for the cardiovascular risk assessment of patients being considered for Romosozumab. To help in deciding the inclusion of one cardiovascular scoring system over another in this guidance, we compared 10-year cardiovascular risk scores using both QRISK3 and ESC SCORE in a real-world osteoporosis setting.

We prospectively gathered both the QRISK3 score and ESC SCORE on patients being considered for Romosozumab from four osteoporosis clinics in the Southwest of England. The project was approved by North Bristol NHS Trust in June 2023 and we collected data from September 2023 for a six-month period. Only individuals with complete data were included in the study. The continuous data are given as a mean and range. Differences in mean QRISK3 and ESC SCORE were examined using a paired t-test. Linear regression was used to examine the association between age and the respective scores.

41 patients had complete data. All patients were female, with an average age of 71 years old (range 54-87 years). We found the average 10-year cardiovascular risk was consistently higher when QRISK3 (mean 15.9%, range 3.5-48.0) was used compared with ESC SCORE (mean 8.2%, range 2.5-26.0). The mean difference between the two scores was 7.7% (95% CI 6.1-9.2, $P<0.0001$). Age showed a greater association with QRISK3 (β 0.9 [95%CI 0.6-1.2, $P<0.0001$]) than ESC Score (β 0.5 [95%CI 0.4-0.7, $P<0.0001$]) (Figure 1). The data also demonstrated progressive divergence; as the ESC SCORE increased so too did the difference between the scores. 39/41 (95%) of patients went on to be prescribed Romosozumab.

This small real-world study shows considerable differences in the predicted 10-year cardiovascular risk obtained from QRISK3 and ESC SCORE in an older osteoporosis population. QRISK3 produces markedly

higher risk estimates, especially in older adults. These results replicate a previous study that found QRISK3 overpredicts risk in an older population possibly due to the fact it does not take into account competing mortality (8). It is also possible that ESC SCORE underestimates risk as it does not currently evaluate the influence of diabetes on cardiovascular risk. Instead, the European Society of Cardiology advises that patients with diabetes are automatically labelled as high risk unless certain criteria are met. Anecdotal evidence from our study suggested that the ESC SCORE colour codes helped clinicians in discussions with patients about their cardiovascular risk. Despite the higher QRISK3 scores, the majority of patients went on to consent to Romosozumab, reflecting the relatively high fracture risk of such patients, which in most instances was felt to outweigh cardiovascular risk.

In conclusion, there remains uncertainty around how best to risk stratify an older, female population when considering the use of Romosozumab. Both QRISK3 and ESC SCORE are feasible options to do this in clinic. Our results highlight the need for clinicians to be aware that the risk estimates generated by these tools are not interchangeable. The Southwest bone group has opted to use ESC SCORE in their local guidance. Further work is justified to come up with a consensus guidance for cardiovascular risk assessment in the osteoporosis clinic.

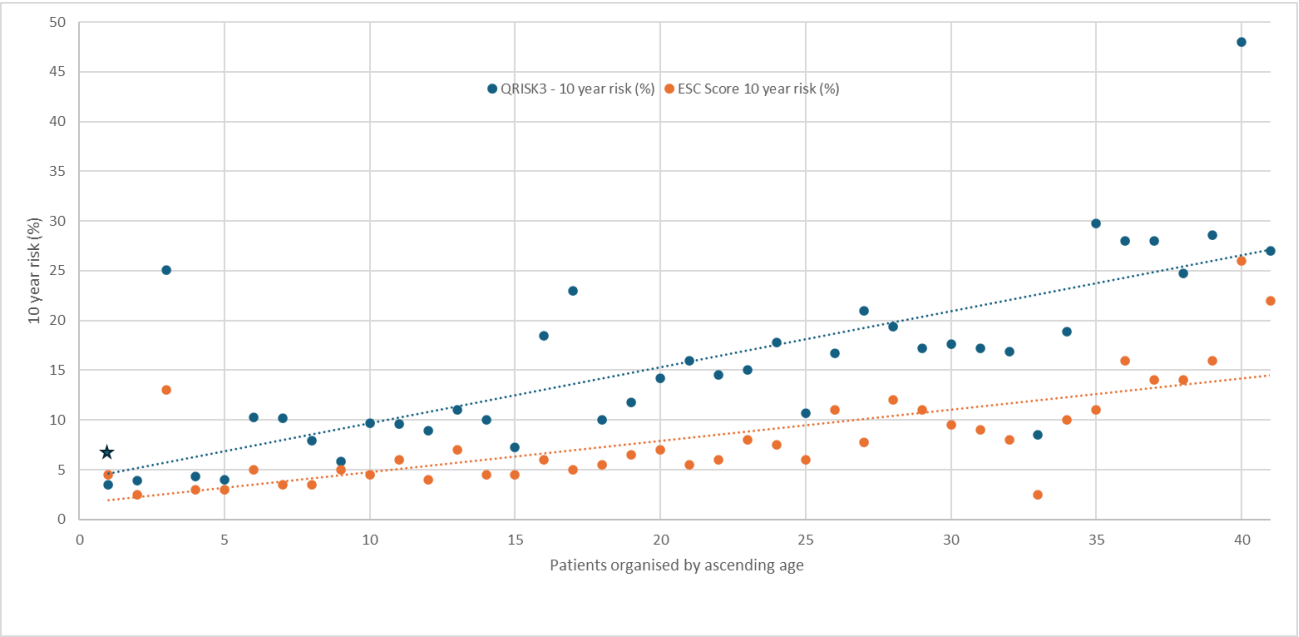

Figure 1. A Graph to show how the QRISK3 and ESC SCORE 10-year risk changes as patient age increases. The patients are ordered by age ascending age left to right. A line of best fit is drawn for each scoring system (QRISK3 – blue & ESC Score – orange). The star represents the only patient whose QRISK3 score was lower than their ESC SCORE.

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