Treatment heterogeneity in comparative effectiveness of teriparatide vs bisphosphonates: multi-database cohort study

Alexandros Rekkas1, Annika M. Jödicke2, David van Klaveren1, Daniel Prieto-Alhambra1,2, Peter R. Rijnbeek1

1Erasmus University Medical Center, Rotterdam, The Netherlands, 2University of Oxford, Oxford, UK

Background

Bisphosphonates are first line treatments to prevent osteoporotic fractures. Teriparatide has been recently shown to be more effective in a head-to-head RCT, and is currently used for more severe cases.

Methods

Network new user cohort study using databases mapped to the OMOP common data model. We included subjects aged >50, registered for 1+ year, initiating treatment with bisphosphonate/s or teriparatide. The main outcome of interest is hip fracture.

We used large scale propensity scores for 1:4 matching to minimise confounding by indication. Models for the prediction of hip fracture risk were developed and validated in all databases. We conducted overall and risk-quartile stratified analyses.

We checked covariate imbalance (overall and for each risk stratum) excluding analyses with severe residual imbalance after matching. Finally, a total of 129 negative control outcomes were included to calibrate for residual confounding. Cox regression was used to estimate calibrated hazard ratios (HR) and Kaplan-Meier estimate differences on day 730 to estimate absolute effects. We provide meta-analytic estimates for the overall analysis and for the top quartile of risk.

Results

This is ongoing research. Early analyses were performed in IBM MarketScan® Medicare Supplemental Database (MDCR), Optum® De-Identified Clinformatics Data Mart Database – Date of Death (Optum-DOD) and Optum® de-identified Electronic Health Record Dataset (Optum-EHR). We included a total of 5,061 and 18,322 users of teriparatide and bisphosphonates from MDCR, 4,205 and 15,953 from Optum-DOD, and 5,301 and 18,872 from Optum-EHR. Overall HRs were 0.94 [0.76-1.18], 0.80 [0.65-0.99] and 0.92 [0.71-1.21] respectively, with meta-analytic HR of 0.88 [0.77-1.00]; I2=0%. We found evidence of residual confounding in quartiles 1-3 of predicted risk, but no identifiable imbalances in the top quartile of risk in all 3 databases. HRs for the top risk quartile were 0.83 [0.64-1.08], 0.74 [0.57-0.95] and 0.84 [0.62-1.14] (meta-analytic HR 0.80 [0.69-0.93]), with 2-year absolute risk reductions of 1.23% [-0.15% to 2.62%], 1.61% [0.30% to 2.93%], and 0.31% [-0.74% to 1.35%] respectively. Meta-analytic HR for top risk quartile 0.80 [0.68-0.93]; I2=0%.

Conclusion

Our findings are in line with previous trials and suggest a 12% relative risk reduction of hip fracture with teriparatide compared to bisphosphonates. A slightly stronger effect was seen amongst highest risk patients, where relative risk reduction was of 20%, with absolute risk reductions ranging from 0.3% to 1.6%. We intend to expand our analyses to include data from IBM MarketScan® Commercial Database, IBM MarketScan® Multi-State Medicaid Database and Phametrics Plus. Finally, we intend to consider 2 additional stratification schemes: a 25-75% split, focusing on the patients at the top quarter of baseline risk, and a stratification based on existing guidelines1.

References/Citations

1. Kanis JA, Harvey NC, McCloskey E, et al. Algorithm for the management of patients at low, high and