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

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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 guidelines[1].

References/Citations

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

very high risk of osteoporotic fractures [published correction appears in Osteoporos Int. 2020 Apr;31(4):797-798]. *Osteoporos Int.* 2020;31(1):1-12. doi:10.1007/s00198-019-05176-3