Study Summary

Title
Fracture Risk in Women with Osteoporosis Initiated on Gastro-resistant Risedronate Versus Immediate Release Risedronate or Alendronate: A Claims Data Analysis in the USA.

Study Sponsor
The study was funded by Theramex Ltd, 5th Floor, 50 Broadway, London, SW1H 0BL.

Status
Completed.

Objectives
To compare in a real-world setting the risk of fractures between women with osteoporosis initiated on gastro-resistant (GR) risedronate and those initiated on:

- Immediate Release (IR) risedronate (a comparison in which the difference between cohorts is exclusively driven by the (GR vs. IR formulation)
- IR Alendronate (a comparison in which the difference between cohorts may be driven by either/both the GR vs IR formulation or/and the use of a different agent).

Study Type
Observational population-based retrospective study using claims data from the IBM® MarketScan® Commercial and Medicare (Q1 2009 to Q3 2019).

Study Population
- GR Risedronate cohort: Women whose first observed dispensing was for gastro-resistant (GR) risedronate. Total n = 1,080 (100%).
- IR Risedronate cohort: Women randomly selected to match the index year distribution of the GR risedronate cohort at a 1:1 ratio. Total n = 1,080 (17.0%).
- Alendronate cohort: Women randomly selected to match the GR risedronate index year distribution at a 1:13 ratio. Total n = 14,040 (32.8%).

Methodology
- Women aged ≥ 60 years with osteoporosis who had ≥ 2 oral bisphosphonate prescription fills were followed for ≥ 1 year after the first observed bisphosphonates dispensing (index date).
- Fracture risk was compared between the GR risedronate and IR risedronate/alendronate cohorts using adjusted incidence rate ratios (aIRRs), both overall and in subgroups with high fracture risk due to older age or comorbidity/medications.
- Site-specific fractures were identified based on diagnosis codes recorded on medical claims using a claims-based algorithm. Persistence on bisphosphonate therapy was evaluated for all groups.

Data Analysis
Incidence of fracture rates were compared using generalised linear models (log link/Poisson/negative binomial) to estimate unadjusted and adjusted IRRs with 95% CIs. Treatment persistence was assessed via Kaplan–Meier and Cox regression analyses for discontinuation and hazard ratio respectively.

Study Location
US Claims Databases.

Ethics approval
N/A.

Summary of Results
Adjusted incidence rate ratios (aIRRs) showed lower fracture risks with GR risedronate compared to IR risedronate and alendronate.

- GR vs IR risedronate: Statistically significant reductions were seen for pelvic fractures in the full cohort (aIRR = 0.37); for any fracture and pelvic fractures in women ≥ 65 years (aIRRs = 0.63 and 0.41); and for any fracture and pelvic fractures in women ≥ 70 years (aIRRs=0.69, 0.24); and for pelvic fractures in high-risk women due to comorbidity/medications (aIRRs=0.34)

- GR risedronate vs alendronate: Statistically significant reductions occurred for pelvic fractures in the full cohort (aIIRs=0.54); and any fracture and wrist/arm fractures in women ≥ 65 years (aIRRs=0.73, 0.63); and for any fracture, pelvic and wrist/arm fractures in women ≥ 70 years (aIRRs=0.72, 0.36, 0.58).

Across all cohorts, approximately 40% completely discontinued oral bisphosphonates within one year.

Conclusions

Discontinuation rates of oral bisphosphonate therapy were high. However, women initiated on GR risedronate had a significantly lower risk of fracture for several skeletal sites than women initiated on IR risedronate/alendronate, particularly those aged ≥ 70 years.

Limitations

- The retrospective study design allows only for association-level findings and does not establish causal relationships.
- The study population included only women with commercial or Medicare Supplemental health plans, which may not represent the broader osteoporosis population. Participants were relatively younger than the general population with osteoporosis.
- Fracture events were identified using claims-based algorithms that rely on diagnosis codes intended for billing, not clinical detail. This may have led to under- or overestimation of fractures, though sensitivity analyses showed consistent results.
- Claims data cannot confirm whether medications were taken as prescribed. To ensure treatment exposure, patients with fewer than two consecutive prescription fills were excluded—potentially underestimating true discontinuation rates.
- Although many confounders were adjusted for, unmeasured factors such as body mass index, family history of fractures, and over-the-counter supplement use (e.g., vitamin D) could still influence results.
- The small number of certain fracture types, particularly pelvic fractures, may have limited the ability to control for confounding in those comparisons.
- Use of other medications affecting bone density (e.g., estrogens) may have continued or begun after the index date, though this was unlikely to differ systematically by treatment group.

Reference

The study results published in peer-reviewed journal: Eisman, J.A., Cortet, B., Boolell, M. et al. Fracture risk in women with osteoporosis initiated on gastro-resistant risedronate versus immediate release risedronate or alendronate: a claims data analysis in the USA. *Osteoporos Int 34, 977–991 (2023). https://doi.org/10.1007/s00198-022-06627-0*