Real-world outcomes comparing zoledronic acid and denosumab in patients with metastatic breast cancer with bone metastases: A propensity score matched analysis from a global federated health research network

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INTRODUCTION

- Patients with metastatic breast cancer commonly encounter bony metastatic disease and other skeletal related events (SREs).
- These significantly affect their quality of life and may also adversely affect their outcomes.
- Bisphosphonates and denosumab are the most widely used agents in this setting.
- We aim to study the real world comparative data between bisphosphonates and denosumab in breast cancer patients with bony metastatic disease along with evaluation of their toxicity profiles.

METHODS

- A retrospective cohort study was conducted using the US Collaborative Network TriNetX, covering January 2000 to December 2023, and encompassing data from 105 global healthcare organizations.
- Female patients aged 18 and above with breast cancer metastatic to the bone were identified and then stratified into two groups based on treatment with zoledronic acid or denosumab.
- The two groups were then propensity-matched based on age, sex, race, and comorbidities.
- We followed these patients for 5 years to assess outcomes, including mortality, osteoporotic fracture, hypercalcemia, pathological fracture, fall, and osteonecrosis.

RESULTS

- We identified 7887 patients in the zoledronic acid cohort and 8910 patients in the pamidronate cohort.
- After propensity matching, each cohort consisted of 7887 patients with similar baseline characteristics.
- The average age was 66.4 years in zoledronic acid cohort and 68.5 in the denosumab cohort.
- In the zoledronic acid cohort, the ethnicity distribution was 74.68 % White, 11.55% African American, and 6.36% Hispanic. In comparison, the denosumab group had an ethnicity distribution of 74.49% White, 10.31% African American, and 5.68% Hispanic.
- Our analysis found that within 5 years, patients with breast cancer metastatic to the bone who received **zoledronic acid had a significantly lower risk of mortality.**
- However, patients in the zoledronic acid arm were noted to have a higher risk of:
  - Osteoporotic fracture
  - Hypercalcemia
  - Pathological fracture
- There was no significant difference in the occurrence of falls and osteonecrosis between the two subgroups.

TABLE 1: Outcomes among patients with breast cancer metastatic to the bone who received zoledronic acid

Outcomes	HR; RD	95% CI	p-value
Mortality	RD -3.49%	-5.063% to -1.916%	<0.001
Osteoporotic fracture	RD 0.817%	0.232% to 1.402%	0.006
Hypercalcemia	HR 1.524	1.407 to 1.65	<0.001
Pathological fracture	HR 1.501	1.349 to 1.671	0.03

HR Hazard Ratio; RD* Risk Difference*

CONCLUSIONS

- Our study revealed that patients with breast cancer with metastatic disease to the bone who received zoledronic acid had significantly lower rates of mortality but higher occurrence of osteoporotic fracture, hypercalcemia, and pathological fracture compared to those receiving denosumab.
- Additional longitudinal cohort studies are imperative to explore the outcomes between these agents and inform clinical practice guidelines in these patients.

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