When bone metastases from breast cancer put her bones at risk[1]

Take on her risk of SREs. **Take action with XGEVA®.[1]**

XGEVA® demonstrated superiority vs. zoledronic acid (ZA) in reducing the risk of developing first and subsequent SREs* in patients with bone metastases from breast cancer:[†,1,2]

- **Risk of developing SREs reduced by 23% vs. ZA** (mean number of SREs per patient: 0.46 vs. 0.60; RR: 0.77; 95% CI: 0.66–0.89; superiority p-value:[‡] *p*=0.0012; secondary endpoint)

Indication and clinical use:

- XGEVA® (denosumab) is indicated for reducing the risk of developing SREs in patients with multiple myeloma and in patients with bone metastases from breast cancer, prostate cancer, non-small cell lung cancer, and other solid tumours.
- XGEVA is not indicated for use in pediatric patients other than skeletally mature adolescents (aged 13–17 years) with giant cell tumour of bone.

Contraindications:

XGEVA is contraindicated in patients with pre-existing hypocalcemia, which must be corrected prior to initiating therapy.

Most serious warnings and precautions:

Osteonecrosis of the jaw (ONJ): In clinical trials, the incidence of ONJ was higher with longer duration of exposure. In patients with risk factors for ONJ, an individual benefit-risk assessment should be performed before initiating therapy with XGEVA. An oral exam should be performed, and a dental exam with appropriate preventive dentistry is recommended prior to treatment with XGEVA, especially in patients with risk factors for ONJ. Avoid invasive dental procedures while receiving XGEVA. In patients who develop ONJ during treatment with XGEVA, a temporary interruption of treatment should be considered based on individual benefit-risk assessment until the condition resolves.

Other relevant warnings and precautions:

- Do not use concurrently with Prolia®.
- Do not use concurrently with bisphosphonates.
- Hypocalcemia has been reported (including severe symptomatic hypocalcemia and fatal cases).
- Caution on risk of hypocalcemia and accompanying increases in parathyroid hormone levels in patients with renal impairment.
- Clinically significant hypercalcemia has been reported in XGEVA-treated patients with giant cell tumour of bone and in patients with growing skeletons weeks to months following treatment discontinuation.
- Skin infections.
- Hypersensitivity reactions, including anaphylaxis.
- Atypical femoral fractures.
- Multiple vertebral fractures, not due to bone metastases, may occur following discontinuation of treatment with XGEVA, particularly in patients with risk factors such as osteoporosis or prior fracture.
- Avoid pregnancy and use highly effective contraception during treatment and for at least 5 months after the last dose of XGEVA.
- Breastfeeding.

For more information:

Please consult the Product Monograph at http://www.amgen.ca/Xgeva_PM.pdf for a full list of indications and information on conditions of clinical use, and important information relating to adverse reactions, drug interactions, and dosing information that has not been discussed here.

The Product Monograph can also be obtained by calling Amgen Medical Information at 1-866-502-6436.

SRE: skeletal-related event; RR: rate ratio; CI: confidence interval; SC: subcutaneous; IV: intravenous
*SREs were defined as pathological fracture, radiation therapy to bone, surgery to bone, and spinal cord compression.[1]
†Results of a Phase 3, randomized, double-blind, double-dummy, active-controlled study. Patients with breast cancer and bone metastases (n=2,046) received either 120 mg XGEVA SC Q4W (once every 4 weeks) (n=1,026) or 4 mg ZA IV Q4W (n=1,020). The primary outcome measure was to demonstrate non-inferiority of time to first on-study SRE as compared to ZA. The secondary outcome measures were superiority of time to first on-study SRE and superiority of time to first and subsequent SREs.[1,2]
‡p-value adjusted for multiplicity.[1]

References:
1. XGEVA Product Monograph. Amgen Canada Inc. June 14, 2019. **2.** Stopeck AT, et al. Denosumab compared with zoledronic acid for the treatment of bone metastases in patients with advanced breast cancer: a randomized, double-blind study. *J Clin Oncol*. 2010;28(35):5132–5139.

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Take on their risk of SREs. **Take action with XGEVA®.[1]**

XGEVA® demonstrated non-inferiority to zoledronic acid (ZA) in delaying time to first SRE* following randomization in newly diagnosed multiple myeloma patients:†,1,2

- **Median time to SRE was 22.83 months** (95% CI: 14.72, NE) for XGEVA vs. 23.98 months for ZA (95% CI: 16.56, 33.31) (HR:‡ 0.98; 95% CI: 0.85,1.14; non-inferiority p-value:‡ *p*=0.010)

Indication and clinical use:
- XGEVA (denosumab) is indicated for reducing the risk of developing SREs in patients with multiple myeloma and in patients with bone metastases from breast cancer, prostate cancer, non-small cell lung cancer, and other solid tumours.
- XGEVA is not indicated for use in pediatric patients other than skeletally mature adolescents (aged 13–17 years) with giant cell tumour of bone.

Contraindications:
XGEVA is contraindicated in patients with pre-existing hypocalcemia, which must be corrected prior to initiating therapy.

Most serious warnings and precautions:
Osteonecrosis of the jaw (ONJ): In clinical trials, the incidence of ONJ was higher with longer duration of exposure. In patients with risk factors for ONJ, an individual benefit-risk assessment should be performed before initiating therapy with XGEVA. An oral exam should be performed, and a dental exam with appropriate preventive dentistry is recommended prior to treatment with XGEVA, especially in patients with risk factors for ONJ. Avoid invasive dental procedures while receiving XGEVA. In patients who develop ONJ during treatment with XGEVA, a temporary interruption of treatment should be considered based on individual benefit-risk assessment until the condition resolves.

Other relevant warnings and precautions:
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- Do not use concurrently with bisphosphonates.
- Hypocalcemia has been reported (including severe symptomatic hypocalcemia and fatal cases).
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The Product Monograph can also be obtained by calling Amgen Medical Information at 1-866-502-6436.

SRE: skeletal-related event; CI: confidence interval; NE: non-estimable; HR: hazard ratio
*An SRE was defined as any of the following: pathologic fracture (vertebral or non-vertebral), radiation therapy to bone (including the use of radioisotopes), surgery to bone, or spinal cord compression.[1]
†Results of an international, randomized, double-blind, active-controlled study comparing XGEVA with ZA in 1,718 patients with newly diagnosed multiple myeloma. Patients with ≥ 1 bone lesion were randomized to receive either 120 mg XGEVA administered subcutaneously every 4 weeks (n=859) or 4 mg ZA administered intravenously every 4 weeks (n=859) (dose adjusted for renal impairment; patients with creatinine clearance ≤ 30 mL/min were excluded based on ZA prescribing information). The primary outcome measure was demonstration of non-inferiority of time to first SRE as compared to ZA.[1]
‡Based on a Cox proportional hazards model stratified by randomization stratification factors.[1]

References:
1. XGEVA Product Monograph. Amgen Canada Inc. June 14, 2019. **2.** Raje N, et al. Denosumab versus zoledronic acid in bone disease treatment of newly diagnosed multiple myeloma: an international, double-blind, double-dummy, randomised, controlled, Phase 3 study. *Lancet Oncol.* 2018;19(3):370–381.

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