The Role of Bone Modifying Agents in Metastatic Breast Cancer: An American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update
Introduction

• The American Society of Clinical Oncology (ASCO) has published a series of guidelines on the role of bone modifying agents (BMA) in metastatic breast cancer since in 2000.

• ASCO updates its guidelines at intervals determined by an Update Committee of the original expert panel.

• This focused update of the 2011 guideline, completed in collaboration with Cancer Care Ontario (CCO), provides recommendations for the intervals between dosing and the role of zoledronic acid in the control of bone pain.

• The guideline also provides a discussion of cost considerations in the use of available BMAs for this population.

• The remaining recommendations from the 2011 ASCO guideline are unchanged because there were no new data to support substantive revisions.
For this focused update, a set of three Phase III randomized non-inferiority trials addressing dosing interval of zoledronic acid provided a signal to update.

ASCO and CCO convened a joint Update Committee to review the evidence and to formulate updated recommendations for practice.

Final guideline approval by ASCO CPGC and Cancer Care Ontario Report Approval Panel.

The full Guideline methodology supplement can be found at:
www.asco.org/breast-cancer-guidelines
Clinical Questions

Question 1: What are the best intervals between dosing of zoledronic acid?

Question 2: What is the role of BMAs in control of pain secondary to bone metastases?
Target Audience

Medical oncologists, radiation oncologists, surgical oncologists, oncology nurses, advanced practice providers, patients, patient advocates, caregivers, oncology pharmacists
CLINICAL QUESTION 1

What are the best intervals between dosing of zoledronic acid?

*Updated recommendation.*

As recommended in the 2011 version of the ASCO bone modifying agents guideline, patients with breast cancer who have evidence of bone metastases should be treated with bone modifying agents.\(^1\) One BMA is not recommended over another. If patients are treated with zoledronic acid, 4 mg IV administered over no less than 15 minutes, dosing options are every 12 weeks or every 3-4 weeks (Type: Evidence based; benefits outweigh harms; Evidence quality: high; Strength of recommendation: Strong).
CLINICAL QUESTION 2
What is the role of bone-modifying agents in control of pain secondary to bone metastases?

Updated Recommendation.
The analgesic effects of bone-modifying agents (denosumab, pamidronate, or zoledronic acid) are modest and BMAs should not be used alone for bone pain. The Update Committee recommends that the current standard of care for supportive care and pain management be applied. This can include analgesia, adjunct therapies, radiotherapy, surgery, systemic anti-cancer therapy, and referral to supportive care and pain management. Evidence of a clinically meaningful benefit is insufficient to support the use of one BMA over another. Further research is needed on this clinical question (Type: Evidence based; benefits outweigh harms; Evidence quality: Low; Strength of recommendation: Weak)
Summary of Recommendations

Recommendations Unchanged From 2011 Guideline Update

• BMAs are recommended for patients with metastatic breast cancer with evidence of bone destruction.

• One BMA is not recommended over another.

• Mechanism of action, as well as the potential benefits and harms, should be taken into account when considering long-term use of BMA.

• In patients with creatinine clearance > 60 mL/min, no change in dosage, infusion time, or interval is required; monitor creatinine level with each intravenous bisphosphonate dose.

• In patients with creatinine clearance < 30 mL/min or on dialysis who may be treated with denosumab, close monitoring for hypocalcemia is recommended.

• All patients should have a dental examination and preventive dentistry before using a BMA.

• Use of biochemical markers to monitor BMA use is not recommended for routine care.
Cost Considerations

• Higher patient out-of-pocket costs have been shown to be a barrier to initiating and adhering to recommended cancer treatments.\textsuperscript{2,3}

• The search for published cost effectiveness analyses that might inform the clinical question of the relative value of available BMAs, provided no definitive evidence to inform cost considerations.

• Clinicians should exercise judgment, and, whenever it is practical and feasible, discuss with patients the use of less expensive alternatives when considering two or more treatment options that are comparable in terms of benefits and harms.\textsuperscript{4}

• Patients should be asked about their financial concerns by their caregivers and be offered financial counseling to address this complex and heterogeneous landscape.\textsuperscript{4}
Discussion and Directions for Future Research

• Until there is data to suggest otherwise, the Panel recommends that denosumab be prescribed as per packet insert labeling and clinical judgement.

• There are ongoing trials which will add to our understanding of dosing intervals for denosumab:
  – SAKK 96/12 (NCT02051218; REDUSE)
  – REaCT-BTA Study (NCT02721433)

• No known RCTs are currently investigating the optimal duration of therapy with a BMA.

• Since 2000, the ASCO guidelines have recommended the use of BMAs indefinitely. There are no new data to alter the 2000 duration of therapy recommendation.

• Data on the long-term dosing and long-term effects of BMAs are needed.
Additional Resources

More information, including a Data Supplement, a Methodology Supplement, slide sets, and clinical tools and resources, is available at www.asco.org/breast-cancer-guidelines

Patient information is available at www.cancer.net
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References


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