Medication-Related Osteonecrosis of the Jaw: MASCC/ISOO/ASCO Clinical Practice Guideline Summary

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INTRODUCTION

Medication-related osteonecrosis of the jaw (MRONJ) is defined as exposed bone or bone that can be probed through an intraoral or extraoral fistula (or fistulae) in the maxillofacial region and that does not heal within 8 weeks, occurring in a patient who has received a bone-modifying agent (BMA) or an angiogenic inhibitor agent and with no history of head and neck radiation.1,2 The condition may involve the mandible or the maxilla. BMAs that have been linked with MRONJ principally include bisphosphonates and denosumab. BMAs are a key component of the management of patients with cancer with skeletal metastases or multiple myeloma. These medications provide a number of clinical benefits, including a reduced incidence of skeletal-related events (eg, pathologic fractures and spinal cord compression) and reduced need for radiation or surgery to bone. Use of BMAs is associated with MRONJ, which can be challenging to treat and can cause significant pain and reduced quality of life. Many studies have established that preventive oral care methods alongside effective oral health practices are associated with a lower rate of MRONJ.3-16

The guideline focuses on the prevention and management of MRONJ in patients with cancer who receive BMAs for oncologic indications.17 The guideline does not address BMAs used for osteoporosis, which are administered at a lower dose and carry a lower risk for MRONJ.18 The guideline also does not address the prevention or management of MRONJ caused by medications other than BMAs. MRONJ has been reported in patients treated with other agents,19,20 and angiogenic inhibitors are included in a widely used definition of MRONJ,2 but evidence regarding the prevention and management of MRONJ caused by these other agents remains extremely limited. Throughout the guideline, the Expert Panel emphasizes the importance of collaboration among the cancer care team, dentists, and dental specialists. Dentists may be community based or hospital based and are the providers who typically complete the pre–cancer therapy dental evaluation and provide long-term preventive management. Dental specialists, as cited in this publication, are dentists with expertise in the clinical management of MRONJ. These individuals may be oral medicine specialists, oral maxillofacial surgeons, hospital dentists, clinical oral pathologists, and/or periodontists. Additional information is available at www.asco.org/supportive-care-guidelines. Patient information is available at www.cancer.net.
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Guideline Question

What are the recommended best practices for preventing and managing medication-related osteonecrosis of the jaw (MRONJ) in patients with cancer?

Target Population

Adult patients with cancer who are receiving bone-modifying agents (BMAs) for any oncologic indication.

Target Audience

Oncologists and other physicians, dentists, dental specialists, oncology nurses, clinical researchers, oncology pharmacists, advanced practitioners, and patients with cancer.

Methods

A systematic review of the medical literature was conducted, and a multidisciplinary Expert Panel was convened to evaluate the evidence and develop recommendations. Given the low volume of high-quality evidence, a majority of the recommendations are based on consensus using ASCO’s formal consensus process.

Recommendations

Clinical Question 1. What is the preferred terminology and definition for osteonecrosis of the jaw (maxilla and mandible) associated with pharmacologic therapies in oncology patients?

Recommendation 1.1. It is recommended that the term medication-related osteonecrosis of the jaw (MRONJ) be used when referring to bone necrosis associated with pharmacologic therapies (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

Recommendation 1.2. Clinicians should confirm the presence of all three of the following criteria to establish a diagnosis of MRONJ: current or previous treatment with a BMA or angiogenic inhibitor; exposed bone or bone that can be probed through an intraoral or extraoral fistula in the maxillofacial region and that has persisted for longer than 8 weeks; and no history of radiation therapy to the jaws or metastatic disease to the jaws (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

Clinical Question 2. What steps should be taken to reduce the risk of MRONJ?

Recommendation 2.1. (Coordination of care.) For patients with cancer who are scheduled to receive a BMA in a nonurgent setting, oral care assessment (including a comprehensive dental, periodontal, and oral radiographic exam when feasible to do so) should be undertaken before initiating therapy. On the basis of the assessment, a dental care plan should be developed and implemented. The care plan should be coordinated between the dentist and the oncologist to ensure that medically necessary dental procedures are undertaken before initiation of the BMA. Follow-up by the dentist should then be performed on a routine schedule (eg, every 6 months) once therapy with a BMA has commenced (Type: evidence based; Evidence quality: low/intermediate; Strength of recommendation: moderate).

Recommendation 2.2. (Modifiable risk factors.) Members of the multidisciplinary team should address modifiable risk factors for MRONJ with the patient as early as possible. These risk factors include poor oral health, invasive dental procedures, ill-fitting dentures, uncontrolled diabetes mellitus, and tobacco use (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: moderate).

Recommendation 2.3. (Elective dentoalveolar surgery.) Elective dentoalveolar surgical procedures (eg, non–medically necessary extractions, alveoplasties, and implants) should not be performed during active therapy with a BMA at an oncologic dose. Exceptions may be considered when a dental specialist with expertise in prevention and treatment of MRONJ has reviewed the benefits and risks of the proposed invasive procedure with the patient and the oncology team (Type: evidence based; Evidence quality: intermediate; Strength of recommendation: moderate).

Recommendation 2.4. (Dentoalveolar surgery follow-up.) If dentoalveolar surgery is performed, patients should be evaluated by the dental specialist on a systematic and frequently scheduled basis (eg, every 6 to 8 weeks) until full mucosal coverage of the surgical site has occurred. Communication with the oncologist regarding status of healing is encouraged, particularly when considering future use of BMA (see Table 2 of full guideline17) (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: moderate).

(continued on following page)
Recommendation 2.5. (Temporary discontinuation of BMAs before dentoalveolar surgery.) For patients with cancer who are receiving a BMA at an oncologic dose, there is insufficient evidence to support or refute the need for discontinuation of the BMA before dentoalveolar surgery. Administration of the BMA may be deferred at the discretion of the treating physician, in conjunction with discussion with the patient and the oral health provider (Type: informal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

Clinical Question 3. How should MRONJ be staged?

Recommendation 3.1. A well-established staging system should be used to quantify the severity and extent of MRONJ and to guide management decisions. Options include the 2014 American Association of Oral and Maxillofacial Surgeons staging system, the Common Terminology Criteria for Adverse Events version 5.0, and the 2017 International Task Force on Osteonecrosis of the Jaw staging system for MRONJ. The same system should be used throughout the patient’s MRONJ course of care. Diagnostic imaging may be used as an adjunct to these staging systems (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

Recommendation 3.2. Optimally, staging should be performed by a clinician experienced with the management of MRONJ (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

Clinical Question 4. How should MRONJ be managed?

Recommendation 4.1. (Initial treatment of MRONJ.) Conservative measures compose the initial approach to treatment of MRONJ. Conservative measures may include antimicrobial mouth rinses, antibiotics if clinically indicated, effective oral hygiene, and conservative surgical interventions (eg, removal of a superficial bone spicule) (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: moderate).

Recommendation 4.2. (Treatment of refractory MRONJ.) Aggressive surgical interventions (eg, mucosal flap elevation, block resection of necrotic bone, soft tissue closure) may be used if MRONJ results in persistent symptoms or affects function despite initial conservative treatment. Aggressive surgical intervention is not recommended for asymptomatic bone exposure. In advance of the aggressive surgical intervention, the multidisciplinary care team and the patient should thoroughly discuss the risks and benefits of the proposed intervention (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

Clinical Question 5. Should BMAs be temporarily discontinued after a diagnosis of MRONJ has been established?

Recommendation 5. For patients diagnosed with MRONJ while being treated with BMAs, there is insufficient evidence to support or refute the discontinuation of the BMAs. Administration of the BMA may be deferred at the discretion of the treating physician, in conjunction with discussion with the patient and the oral health provider (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

Clinical Question 6. What outcome measures should be used in clinical practice to describe the response of the MRONJ lesion to treatment?

Recommendation 6. During the course of MRONJ treatment, the dentist or dental specialist should communicate with the medical oncologist the objective and subjective status of the lesion (ie, resolved, improving, stable, or progressive). The clinical course of MRONJ may impact local and/or systemic treatment decisions with respect to cessation or recommencement of BMAs (Type: formal consensus; Evidence quality: insufficient; Strength of recommendation: weak).

The Multinational Association of Supportive Care in Cancer, International Society of Oral Oncology, and ASCO believe that cancer clinical trials are vital to inform medical decisions and improve cancer care, and that all patients should have the opportunity to participate.

Additional Resources

More information, including a Data Supplement with additional evidence tables, slide sets, and clinical tools and resources, is available at www.asco.org/supportive-care-guidelines. Patient information is available at www.cancer.net.
REFERENCES

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