Evaluation of medication-related osteonecrosis of the jaw in patients receiving bone-modifying agents for bone metastases and multiple myeloma

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BACKGROUND

- Bone-modifying agents (BMAs), such as parenteral bisphosphonates and denosumab, play a crucial role in the management of patients with bone metastases [1]
- Medication-related osteonecrosis of the jaw (MRONJ) is a rare but serious complication of BMAs[1,2]
- The incidence of MRONJ in patients on bone-modifying therapies occurs in approximately 1% to 9% of patients with advanced cancer[1]
- The pathophysiology of MRONJ is unclear, but it may be related to multiple mechanisms such as the inhibition of bone resorption and remodeling, inflammation and infection, inhibition of angiogenesis, direct soft tissue toxicity, and immune dysfunction[2,3]
- Risk factors for MRONJ include duration of BMA therapy, history of diabetes mellitus, tobacco use, chronic corticosteroid use, and poor oral health[3,4]
- The National Comprehensive Cancer Network (NCCN) and the American Society of Clinical Oncology (ASCO) recommend that all patients receive a comprehensive dental examination and appropriate preventative dentistry before initiating bone-modifying therapies and also have routine follow up throughout treatment[1,4]
- Pharmacologic treatment for the management of MRONJ is unclear and reinitiating the BMA is controversial[3]

OBJECTIVE

- To identify and evaluate patients with MRONJ or dental-related complications who are receiving a parenteral BMA and their subsequent management

METHODS

- Study design: Single-center, retrospective chart review of patients receiving BMAs between August 1, 2020 and February 28, 2021
- Inclusion Criteria:
  - Age ≥ 18 years old
  - Received at least 1 dose of a parenteral BMA (denosumab, pamidronate, or zoledronic acid)
  - Indicated for bone lesions from metastatic solid tumors or multiple myeloma
- Exclusion Criteria:
  - Pregnant women
  - Patients receiving oral bisphosphonates
- Primary Outcome: Incidence of MRONJ or dental-related complications, defined as either the presence of the ICD-10 code or mentioned in provider documentation
- Secondary Outcomes:
  - Number of patients who required emergency room (ER) visits or hospitalization
  - Length of hospitalization
  - Number of BMA doses received prior to identification of MRONJ or dental-related complication
  - Number of internal dental consults
  - Documentation rate of BMA education
- Exploratory Outcomes:
  - Frequency of MRONJ on concomitant angiogenesis inhibitors
  - Initiation of pharmacotherapy for management of MRONJ
  - Number of patients reinitiated on BMA after diagnosis
- Statistical analysis: Descriptive statistics (median, mode, range)

RESULTS

Figure 1. Patient Eligibility

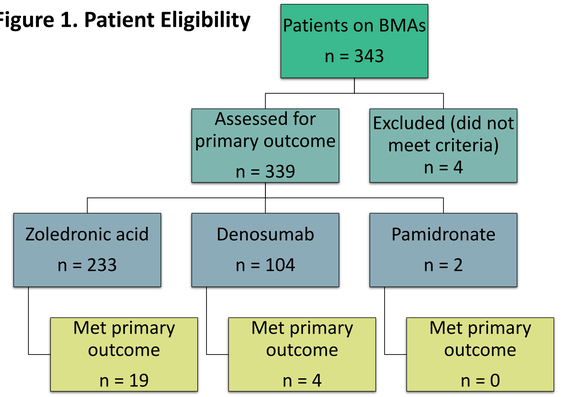


Figure 2. Indication and Treatment Regimen

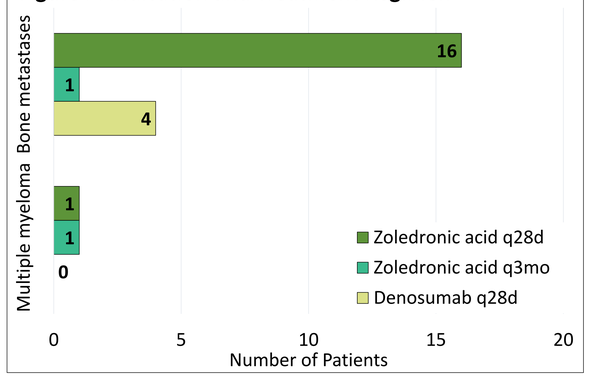


Table 2. Secondary and Exploratory Outcome Results

Secondary Outcomes	N = 23
Number of doses received – median (range)	16.5 (1 – 32)
Internal dental provider seen – no. (%)	14 (61)
ER visit – no. (%)	6 (26)
Hospitalized – no. (%)	5 (22)
Length of stay – median days (range)	3 (2 – 4)
Documented education – no. (%)	
BMA side effects	7 (30)
Dental monitoring	1 (4)
Exploratory Outcomes	**n = 9**
Reinitiated on BMA after MRONJ diagnosis – no. (%)	4 (44)
Initiated on pharmacotherapy for MRONJ – no. (%)	
Chlorhexidine gluconate rinse	4 (44)
Antibiotics	2 (22)
Pentoxifylline and tocopherol	0
MRONJ and concomitant antiangiogenic use – no. (%)	1* (11)

*Patient was taking lenalidomide

Table 1. Baseline Characteristics

	N = 23
Patient Demographics	
Median age – years (range)	60.5 (32 – 89)
Gender – no. (%)	
Female	18 (78)
Male	5 (22)
Risk Factors	
Comorbidities – no. (%)	
Hypertension	12 (52)
Diabetes	4 (17)
Hyperlipidemia	3 (13)
Current smoker at time of infusion – no. (%)	4* (17)
History of radiation to the jaw – no. (%)	1 (4)
Chronic systemic corticosteroid use** – no. (%)	2 (9)

*One patient was vaping at the time of infusion
**Defined as ≥ 20 mg oral prednisone equivalent for ≥ 4 weeks

Figure 3. Primary Outcome Results

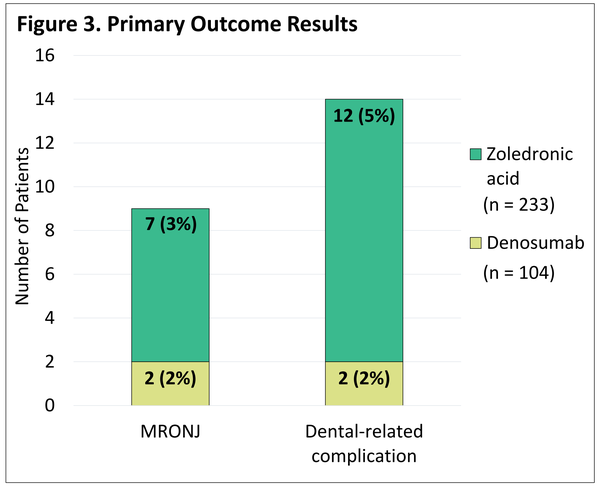
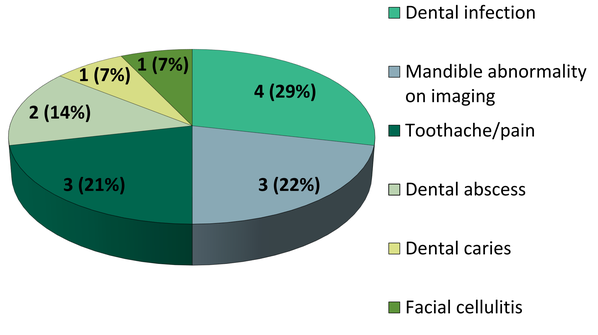


Figure 4. Dental-related Complications



DISCUSSION

- The primary outcome occurred in 23 patients (9 with MRONJ and 14 with dental-related complications) out of the total 339 patients that were assessed
- Patients on zoledronic acid experienced MRONJ more frequently compared to denosumab (3% vs. 2%, respectively)
- Only 1 of the 14 patients with dental-related complications, had documented recommendations for dental monitoring and had a documented baseline dental examination prior to initiation of the BMA
- Six patients required an ER visit and 5 of those patients were subsequently hospitalized
  - Four of the 5 hospitalized patients were diagnosed with MRONJ
- Patients with a diagnosis of MRONJ were further reviewed for the exploratory outcomes
  - Four of the 9 patients (44%) with MRONJ were reinitiated on the same BMA that they were previously on (zoledronic acid)
  - For pharmacologic management, 4 patients received chlorhexidine gluconate rinse and 2 patients received oral antibiotics (doxycycline ± metronidazole)
  - No patients were initiated on pentoxifylline and tocopherol, despite its known role in osteoradionecrosis
  - One patient who developed MRONJ was concomitantly taking lenalidomide

CONCLUSION

- In this retrospective, single-center study, the overall incidence of MRONJ was 2.7% (9 cases out of 339 patients on BMAs), which aligns with the overall incidence reported in literature
- Limitations:
  - Provider documentation
  - Small sample size
  - Narrow patient demographics
- Future directions:
  - Implement medication education prior to BMA initiation
  - Utilize the on-site dentist to schedule routine dental monitoring while on therapy
  - Establish a pharmacy-driven protocol that requires documented baseline dental examination prior to BMA initiation

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4. Gralow JR, Biermann JS, Farooki A, et al. NCCN task force report: Bone health in cancer care. *J Natl Compr Canc Netw* 2013;11(3):S1-50.

DISCLOSURES

- All authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have direct or indirect interest in the subject matter of this presentation
- Primary investigator's email: EOsmon@baptisthealth.net