

Primary and secondary prevention to effectively reduce the risk of bisphosphonate-related osteonecrosis of the jaw in patients with bone metastases

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Background

- Bone is one of the most frequent site of metastasis in patients with advanced cancer. Nearly all patients with myeloma, 65–75% of patients with prostate or breast cancer, and 30–40% of patients with lung cancer or other solid tumors, eventually develop bone metastases.
- Bisphosphonates (BPs), particularly zoledronic acid and denosumab, were demonstrated to effectively reduce skeletal complications in patients with bone metastases.
- However, bisphosphonate-related osteonecrosis of the jaw (BRONJ) can occur spontaneously, favored by dental extraction, dental implant surgery, or denture wearing, in around 6% of patients.
- In order to reduce the risk of BRONJ, a Dental Prevention Service was created at Modena Cancer Center in 2010.
- Since 2010, all patients with bone metastases underwent a baseline mouth assessment (dental visit, Rx orthopantomography, and eventual tooth avulsion or dental care if necessary) prior to start BPs.

Aim

To underline the role of dental prevention as an effective tool to reduce the risk of BRONJ

Methods

- BRONJ was identified with the standardized query "osteonecrosis" among all data from patients treated at Modena Cancer Center from 2005 to 2016.
- For each case, demographic and medical information were analyzed, as well as data about BRONJ notification (year of occurrence, outcome), type and duration of BP exposure, and associated risk factors (dento-alveolar surgery, chemotherapy, antiangiogenics).
- Data were differently analyzed taking into account the implementation of a Dental Prevention Service in patients candidate for BP therapy.

Patients' characteristics

• Among 1663 patients treated with BP, 63 cases of BRONJ were identified (3.8%).

BRONJ cohort

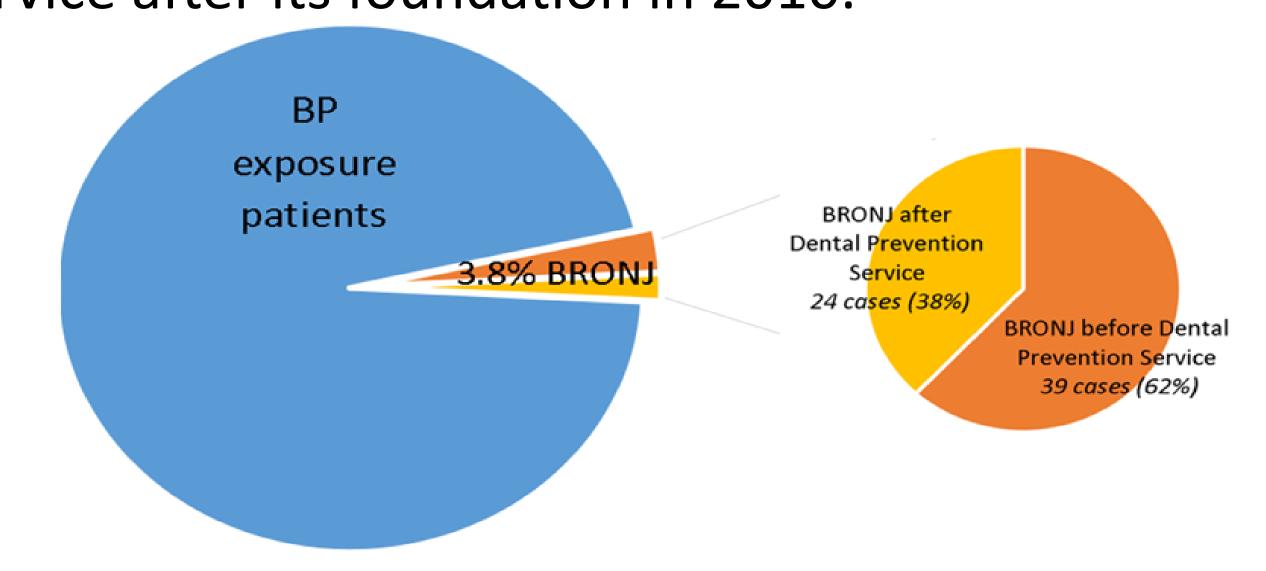
	(N=63)	
	N	
Age at BRONJ, median (years)	69	range 47-90
Sex:		
male	19	30%
female	44	70%
Cancer site:		
breast	34	54%
kidney	3	5%
lung	2	2%
Prostate	8	13%
hematologic malignancy	13	21%
other	3	5%
Comorbidity:		
rheumatoid arthritis	2	3%
cardiac ischemia	2	3%
diabetes	3	5%
cronic hematological disorders	2	3%

Associated factors and outcome

Median time to BRONJ	28 mos	1-89,1 mos
Mean n° of BP doses before BRONJ	25	1-90
Type of BP: Pamidronate->Zoledronate Zoledronate Zoledronate->Denosumab Densoumab	8 51 2 2	13% 81% 3% 3%
Site: maxilla mandible	15 48	24% 76%
Trigger event: dental extraction spontaneus	18 45	29% 71%
Concomitant medications: none chemo-therapy endocrine-therapy antiangiogenic-agents	11 17 21 9	17% 27% 33% 14%
Treatment: antibiotics surgery hyperbaric	30 29 4	48% 46% 6%
Outcome: not yet recovered recovered death unrelated to BRONJ unknown	3 13 37 10	5% 21% 59% 15%

Results

- Overall, in the period 2005-2016 only 14 patients (22%) with BRONJ received a baseline mouth assessment before starting BP.
- All but one of them, were evaluated by Dental Prevention Service after its foundation in 2010.



 After Dental Prevention Service institution, a drop of BRONJ incidence from 4.1 to 1.9% was observed.

Conclusions

- Prevention of BRONJ is critical in in bone metastatic patients.
- The incidence of BRONJ over time can drop to 1.9% when primary and secondary prevention measures are implemented in routine clinical practice.