

Osteonecrosi mascellare e mandibolare (ONJ) Prevenzione

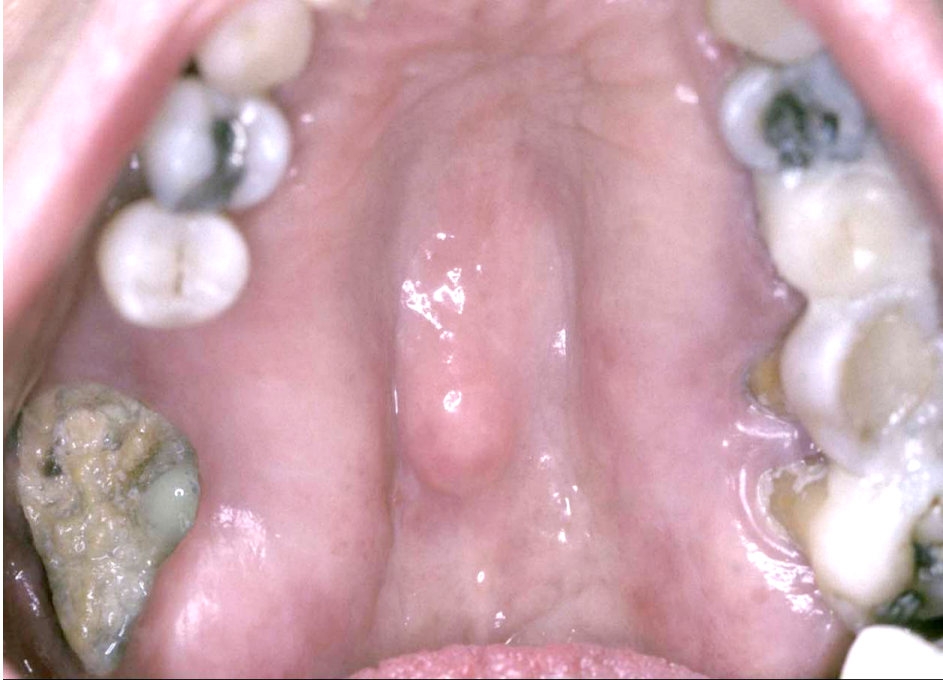
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Osteonecrosis of the Jaws



FIGURE 1. Exposed necrotic maxillary bone in a patient receiving zoledronic acid for 6 months. The patient had posterior maxillary extractions performed 4 months earlier. (Courtesy of Dr Jay Neugarten, New Hyde Park, NY.)



Osteonecrosis of the Jaw (ONJ): why jaw bones?

Risk factors specific to jaw bones may play a role:

- Unique challenges in terms of bone turnover and exposure to bacteria
 - constant stress from masticatory forces with consequent microdamage and microfractures
 - exposure to external environment through teeth
- Mandible bone > maxilla:
 - mandible bone: more compact and less vascularized
- Trauma from dental procedures
 - increased need for bone repair and remodeling

ONJ: Local risk factors

- Dental extractions
- Surgical bone manipulation
- Presence of oral infection
- Trauma from dentures
- Poor oral health

Referenze circa la prevenzione

- Expert panel recommendations for the prevention, diagnosis, and treatment of osteonecrosis of the jaws [No authors listed]. LDA J 64:21-24, 2004
- Marx RE, Sawatari Y, Fortin M, et al: Bisphosphonate-induced exposed bone (osteopetrosis) of the jaws: risk factors, recognition, prevention, and treatment. J Oral Maxillofac Surg 63:1567-1575, 2005
- Ruggiero S, Gralow J, Marx RE, et al: Practical Guidelines for the Prevention, Diagnosis, and Treatment of Osteonecrosis of the Jaw in Patients With Cancer. Journal of Oncology Practice 2:7-14, 2006
- Weitzman R, Sauter N, Eriksen EF, et al: Critical review: Updated recommendations for the prevention, diagnosis, and treatment of osteonecrosis of the jaw in cancer patients-May 2006. Crit Rev Oncol Hematol 62:148-152, 2007

Practical guidelines for the prevention

- Avoid elective jaw procedures
- Routine dental exams including panoramic radiograph
- Preventive dentistry prior to treatment
- Patient education regarding importance of good hygiene
- Perform visual inspection of oral cavity prior to BP therapy and at each follow-up visit

Bisphosphonate Treatment in Cancer Patients with Bone Metastases: Oral Health

Should a dental exam and preventive dentistry be performed before starting BP therapy?

- It is recommended that patients be encouraged to have a dental exam before starting BP therapy or as soon as possible thereafter
- If the dental professional determines that the patient requires a surgical dental procedure, then it is recommended that it be completed before initiating BP therapy where possible

Bisphosphonate Treatment in Cancer Patients with Bone Metastases: Oral Health

How often should dental examination be recommended while on BP therapy?

- Patients are encouraged to seek appropriate dental maintenance care approximately every 6 months or more frequently if indicated
- Patients should maintain good oral hygiene
- Routine restorative treatments and dental hygiene procedures may be performed

Bisphosphonate Treatment in Cancer Patients with Bone Metastases: Oral Health

On BP therapy - Dental problem (other than ONJ)

Should dental treatment be modified?

- If possible, least invasive (non-surgical) dental treatment is recommended

Should BP be withheld before and after dental treatment? If so, for how long?

- No data exist. However, if tooth extractions or other dental surgery is required while on BP therapy, it is recommended that BP therapy be delayed until the site of the surgical procedure has healed
- For patients with high risk of HCM or SRE, it is recommended that BP therapy be maintained

Bisphosphonate Treatment in Cancer Patients with Bone Metastases: Oral Health

On BP therapy with working diagnosis of ONJ

Should BP be discontinued, temporarily withheld, or continued?

- Insufficient data exist, and potential risk-benefit should be discussed with the patient
- For Patients at high risk of SRE or HCM it is recommended that BP therapy be maintained. Patients not at high risk should be evaluated, and the discontinuation of BP be considered.
- Some factors that may correlate with increased risk of HCM or SRE include:
 - **Progression of underlying malignancy**
 - **Prior SRE (solid tumors)**
 - **≥ 4 bone lesions (solid tumors)**

Application of preventive measures minimizes the occurrence of the osteonecrosis of the jaw (ONJ) in solid tumors patients (pts) with bone metastases treated with bisphosphonates (BPs)

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pazienti e metodi

- Gruppo 1 (Pre-group)
- Revisione retrospettiva di 812 casi consecutivi di pazienti trattati con bisfosfonati da gennaio 1999 a febbraio 2007, che non sono stati sottoposti a prevenzione odontoiatrica prima dell'inizio del trattamento

pazienti e metodi

- Gruppo 2 (Post-group)
- 154 pz. consecutivi (dall'aprile 2005) trattati con bisfosfonati, sono stati sottoposti a visita odontoiatrica \pm OPT \pm terapie odontoiatriche prima dell' inizio del trattamento.
- Regolari ctr odontoiatrici durante il periodo di trattamento (circa ogni 6 mesi)

pazienti e metodi

L'incidenza di ONJ e' presentata come

$$\text{-IP} = \frac{\text{N}^\circ \text{ pts developing ONJ}}{\text{N}^\circ \text{ pts of study sample}} \times 100$$

$$\text{-IR} = \frac{\text{N}^\circ \text{ pts developing ONJ}}{\text{Total observation time of all pts of study sample}} \times 100$$

pazienti e metodi

- Confronto tra IPs prima e dopo il programma preventivo con Fisher's exact test ($p < 0.05$ era significativo)
- Confronto tra IRs valutando IR ratio (IRR) ed il 95% IC
- ITT analisi quando i pts, dopo la visita odontoiatrica, attuavano le terapie prescritte dagli odontoiatri
- PP analisi quando i pts, dopo la visita odontoiatrica, non attuavano le terapie prescritte dagli odontoiatri (es. terapia antibiotica)

	PRE- GROUP* n=812	POST- GROUP** n=154	TOTALE n=966
GENDER [N (%)]			
Female	672 (82.8)	115 (74.7)	787 (81.5)
Male	140 (17.2)	39 (25.3)	179 (18.5)
MEDIAN AGE (Range)	62.4 (21.4-	62.9 (29.8-84.3)	62.5 (21.4-90.4)
PRIMARY TUMOUR [N (%)]	90.4)		
Breast	590	112	702 (73%)
Lung	61	6	67 (7%)
Prostate	44	24	68 (7%)
TYPE OF ADMINISTERED BP [N (%)]			
Pamidronate	566 (69.7)	34 (22.1)	600 (62.2)
Zoledronic Acid	127 (15.6)	117 (76.0)	244 (25.3)
Pamidronate followed by Zoledronic Acid	79 (9.7)	0	79 (8.0)
Clodronate	40 (4.9)	3 (1.9)	43 (4.5)

risultati

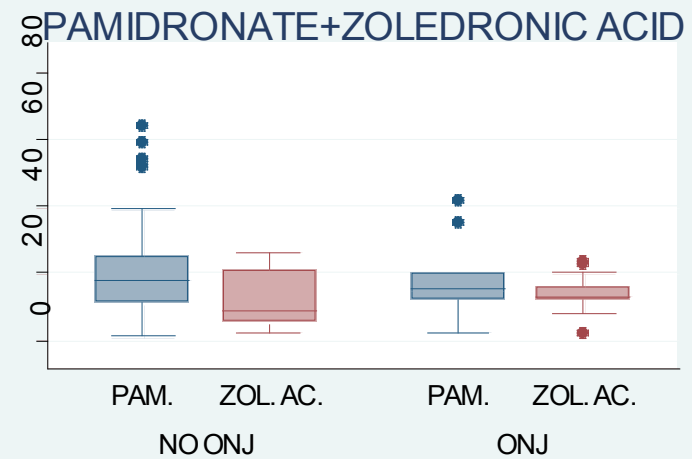
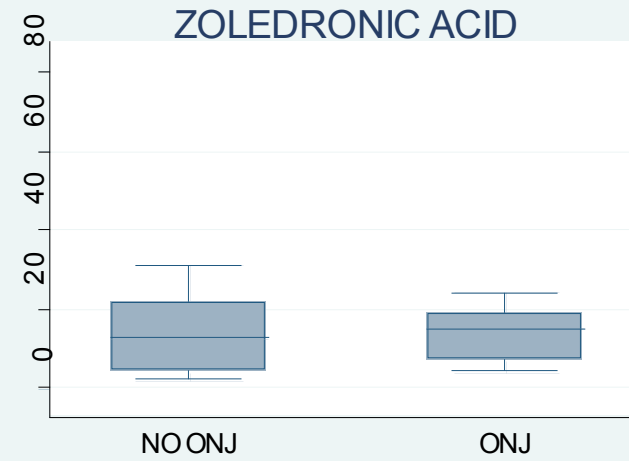
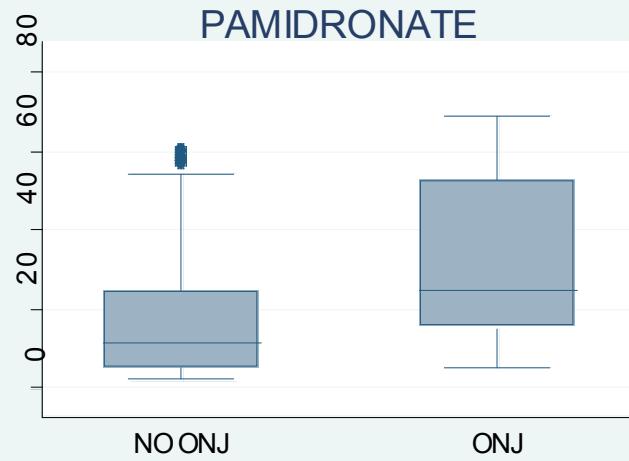
- Il 2.9% dei pazienti studiati ha avuto ONJ
- ZOL/PAM+ZOL = 19 casi ONJ, PAM = 9.
- Nel PRE Group, i casi di ONJ osservati erano 27 (3.3%)
- Nel POST Group e' stato osservato 1 caso di ONJ (0.6%)(p =0.048)
considerando l'analisi PP

risultati

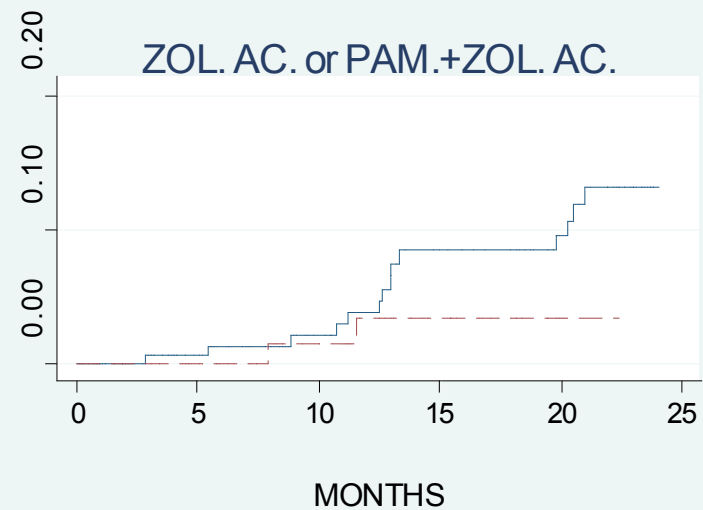
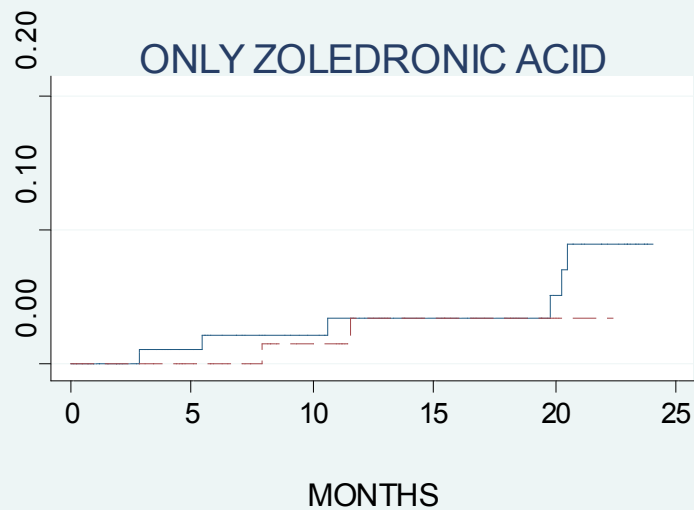
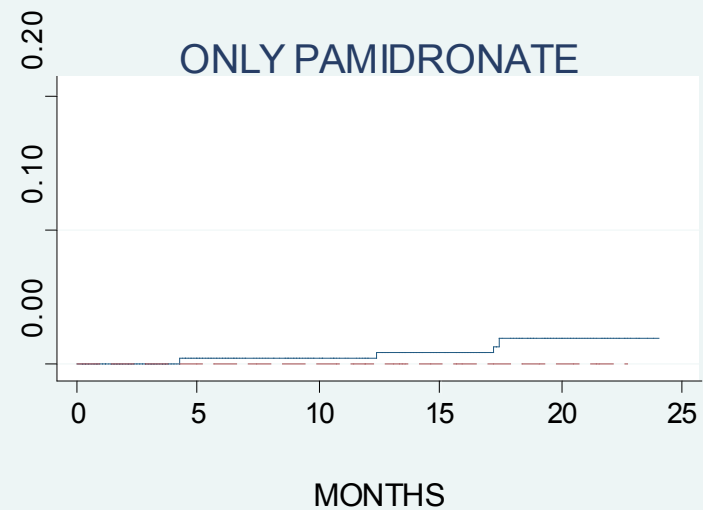
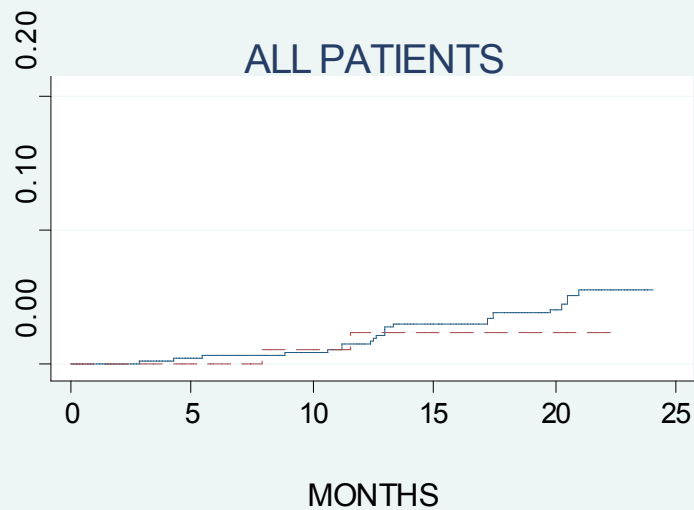
- Considerando i pts esposti a ZOL/PAM+ZOL, l'applicazione di misure preventive ha portato ad una consistente riduzione di frequenza di ONJ (Group PRE 8.7% vs group POST 0.9%, $p = 0.002$)
- La IR della ONJ in tutti i 966 pazienti trattati con BPs era 0.03/yr per il gruppo PRE e 0.007/yr per il gruppo POST (IRD=0.023, 95% CI from 0.0045 to 0.041).

conclusioni

- L'applicazione di routine di misure preventive prima e durante il trattamento con BPs riduce del 75% l'incidenza di ONJ.
- Questa evidenza supporta la rilevanza nella applicazione di misure preventive in tutti i pts che ricevono un trattamento con BPs



Box plots of the number of infusions by ONJ development and BP administered. For patients taking pamidronate and then zoledronate, numbers of infusions of each drug are separated



Time to onset of ONJ by prevention programme implementation and BP administered. Data are censored at 24 months. ITT analysis*

