ISO
Padova 14-15 novembre 2017

Rischio osteonecrosi mascellare: il punto di vista dell'oncologo

Vittorio Fusco
ASO Alessandria

ONJ: QUANTO E' FREQUENTE?

Incidenza: ?
Prevalenza: ?
"Frequenza": ?

Numeri assoluti: ?
(epidemiologia)

Rischio individuale: ?
(rischio nel tempo…; costi-benefici….)

Oral Maxillofacial Surg Clin N Am ■ (2015) ■–■
http://dx.doi.org/10.1016/j.coms.2015.06.003

Abbreviations: BP, bisphosphonate; IV, intravenous; RCT, randomized controlled clinical trial.
[a] Sample size in parentheses.
[b] Zolendronate.
[c] Oral ibandronic acid.

Table 1
Risk for MRONJ among patients with cancer grouped by medication

		Medication					
Authors,[Ref.] Year	Study Design	Placebo[a]	IV BP[b]	Oral BP[c]	Denosumab	Bevacizumab	Bevacizumab and Zolendronate
Gnant et al,[6] 2015	RCT	0% (903)	0% (900)	—	—	—	—
Barrett-Lee et al,[10] 2014	RCT		1.3% (697)	0.7% (704)	—	—	—
Coleman et al,[7] 2014	RCT	0% (1678)	1.7% (1681)	—	—	—	—
Qi et al,[5] 2014	Systematic review	0% (1450)	1.1% (2928)	—	1.7% (4585)	—	—
Henry et al,[11] 2014	RCT	—	1.1% (792)	—	0.8% (786)	—	—
Jackson et al,[12] 2014	RCT	—	3.7% (981)	—	—	—	—
Chiang et al,[8] 2013	Prospective cohort study	—	0% (414)	—	—	—	—
Van den Wyngaert et al,[13] 2013	Prospective cohort study	—	6% (298)	—	—	—	—
Scagliotti et al,[15] 2012	RCT	—	0.8% (400)	—	0.7% (411)	—	—
Guarneri et al,[16] 2010	Systematic review	—		—	—	0.2% (1076)	0.9% (233)
Stopeck et al,[14] 2010	RCT	—	2.0% (1020)	—	1.4% (1013)	—	—
Vahtsevanos et al,[9] 2009	Prospective cohort study	—	6.7% (1163)	—	—	—	—
Mauri et al,[4] 2009	Systematic review	0.02% (5382)	0.3% (3987)	—	—	—	—

Per i pazienti **oncologici**, in trattamento con farmaci **anti-riassorbitivi** (BP, Denosumab) e/o **anti-angiogenetici** (Bevacizumab), il rischio totale di ONJ varia tra lo 0% e il 6.7%

EPIDEMIOLOGIA: ONJ DA BISFOSFONATI, DENOSUMAB E ALTRI FARMACI

Quali sono i farmaci che possono determinare la ONJ?

Quali sono le categorie di pazienti a maggior rischio di ONJ?

Esistono ad oggi "nuovi" sottogruppi di popolazione a più alto rischio?

FONTI DI DATI EPIDEMIOLOGICI

- ✓ **Studi randomizzati** (bracci con/senza farmaci in studio)
- ✓ **Studi osservazionali, case series** (bias di selezione…)
- ✓ **Studi sistematici di popolazione** (registro tumori, ecc)
- ✓ **Studi retrospettivi su database** (assicurazioni, dimissioni ospedaliere, utenti sistema sanitario)
- ✓ ***Surveys* di specialisti o unità specialistiche** (odonto/ maxillofacciali) **o di centri/gruppi oncologici** (es. Rete Oncologica Piemonte –VdA)

EPIDEMIOLOGIA: ONJ DA BISFOSFONATI E ALTRI FARMACI

Dati da trials :

SOTTOSTIMA !

Pazienti oncologici

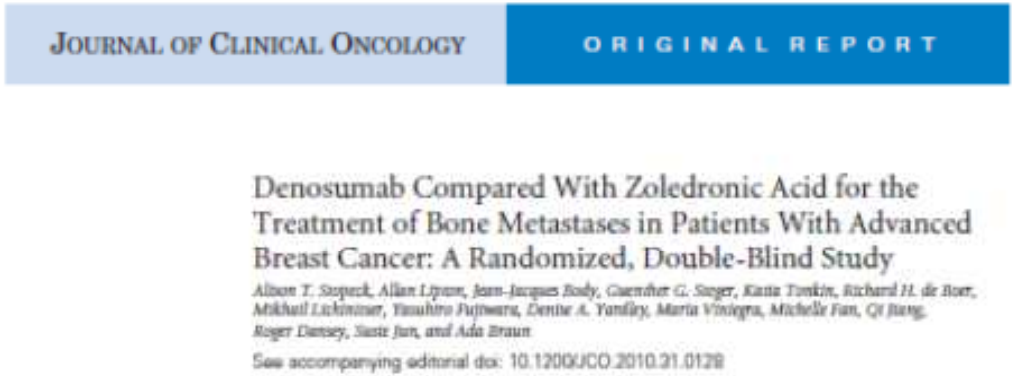
Zoledronato	0.3-1.1%
Denosumab	0.7-1.9%
Bevacizumab	0.2%
Beva+Zoled.	0.9%

Pazienti osteoporotici

BP orali	0.004-0.1%
Placebo	0-0.020%

da Ruggiero, JOMS 2014 - modif

ZOLEDRONATO *vs* DENOSUMAB: 3 TRIALS


JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Denosumab Compared With Zoledronic Acid for the Treatment of Bone Metastases in Patients With Advanced Breast Cancer: A Randomized, Double-Blind Study

Alison T. Stopeck, Allan Lipton, Jean-Jacques Body, Guenther G. Steger, Kasia Tonkin, Richard H. de Boer, Mikhail Lichinitser, Yasuhiro Fujiwara, Denise A. Yardley, Maria Viniegra, Michelle Fan, Qi Jiang, Roger Dansey, Susie Jun, and Ada Braun

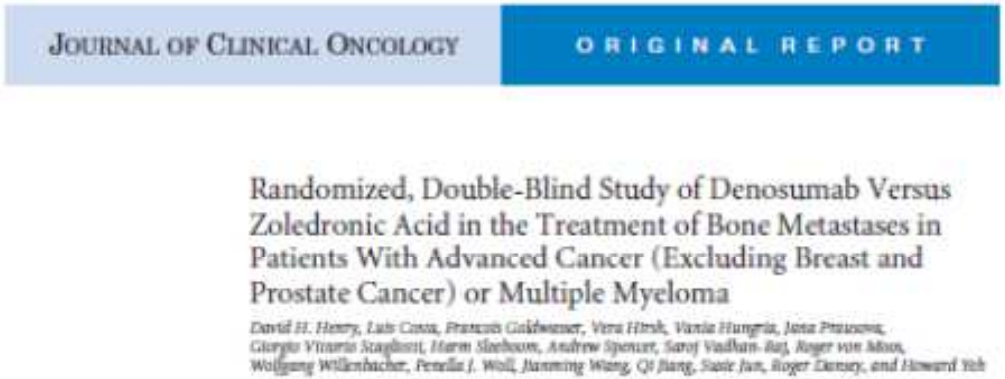
See accompanying editorial doi: 10.1200/JCO.2010.31.0129

Stopeck, JCO 2010
2046 pts
First on-study SRE: HR 0.82
(26.4 months *vs* not reached)

Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study

Karim Fizazi, Michael Carducci, Matthew Smith, Ronaldo Damião, Janet Brown, Lawrence Karsh, Piotr Milecki, Neal Shore, Michael Rader, Huei Wang, Qi Jiang, Sylvia Tadros, Roger Dansey, Carsten Goessl

Fizazi, Lancet 2011
1904 pts
First on-study SRE: HR 0.82
(17.1 *vs* 20.7 months)


JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Randomized, Double-Blind Study of Denosumab Versus Zoledronic Acid in the Treatment of Bone Metastases in Patients With Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma

David H. Henry, Luis Costa, François Goldwasser, Vera Hirsh, Vania Hungria, Jana Prausova, Giorgio Vittorio Scagliotti, Harm Slatkoun, Andrew Spencer, Saroj Vadhan-Raj, Roger von Moos, Wolfgang Willenbacher, Pernilla J. Wolf, Jianming Wang, Qi Jiang, Susie Jun, Roger Dansey, and Howard Yeh

Henry, JCO 2011
1776 pts
First on-study SRE: HR 0.8 (non inferiority)
(16.3 *vs* 20.6 months)

ONJ NEI TRIALS CON DENOSUMB

Denosumab Compared With Zoledronic Acid for the Treatment of Bone Metastases in Patients With Advanced Breast Cancer: A Randomized, Double-Blind Study

Allison T. Stopeck, Allan Lipton, Jean-Jacques Body, Guenther G. Steger, Kuna Tonkin, Richard H. de Boer, Mikhail Lichinitser, Yasuhiro Fujiwara, Denise A. Yardley, Maria Viniegra, Michelle Fan, Qi Jiang, Roger Dansey, Susie Jun, and Ada Braun

See accompanying editorial doi: 10.1200/JCO.2010.31.0129

Stopeck, JCO 2010

ONJ 2% (DEN) *vs* 1.4% (ZA)

Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study

Karim Fizazi, Michael Carducci, Matthew Smith, Ronaldo Damião, Janet Brown, Lawrence Karsh, Piotr Milecki, Neal Shore, Michael Rader, Huei Wang, Qi Jiang, Sylvia Todros, Roger Dansey, Carsten Goessl

Fizazi, Lancet 2011

ONJ 2% (DEN) *vs* 1% (ZA)

Randomized, Double-Blind Study of Denosumab Versus Zoledronic Acid in the Treatment of Bone Metastases in Patients With Advanced Cancer (Excluding Breast and Prostate Cancer) or Multiple Myeloma

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Henry, JCO 2011

ONJ 1.1% (DEN) *vs* 1.3% (ZA)

Frequenza di ONJ dopo Zoledronato o Denosumab

JOURNAL OF CLINICAL ONCOLOGY | CORRESPONDENCE

Osteonecrosis of the Jaw After Zoledronic Acid and Denosumab Treatment

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Giovannino Ciccone
Centro di Prevenzione Oncologica, Azienda Ospedaliera San Giovanni Battista, Torino, Italy

POSSIBILI CAUSE DI SOTTOSTIMA DELLA FREQUENZA DI ONJ

- ✓ ***Case Adjudication* (AAOMS)**
- ✓ **Selezione dei pazienti**
- ✓ **Breve *follow-up***
- ✓ **Incidenza non cumulativa**

Fusco V et al (letter) – J Clin Oncol 2011

DEFINIZIONE (E STAGING) DI ONJ

American Association of Oral and Maxillofacial Surgeons (AAOMS) medication-related ONJ (MRONJ) staging

Stadio ONJ	caratteristiche
A rischio	Nessun apparente osso necrotico in pazienti trattati con terapie che agiscono sul riassorbimeto osseo
Stadio 0	Non evidenza clinica di osso necrotico, ma aspecifici risultati, cambiamenti radiologici e sintomi
Stadio 1	Osso necrotico esposto, o presenza di fistola collegata all'osso , in pazienti asintomatici senza evidenza di infezione
Stadio 2	Osso necrotico esposto o presenza di fistola collegata all'osso associata ad infezione come evidenziato da dolore ed eritema nella regione esposta dell'osso ± drenaggio purulento
Stadio 3	Osso necrotico esposto o presenza di fistola collegata all'osso in pazienti con dolore, infezione ed 1 o piu' complicazioni*

*osso esposto e necrotico che si estende oltre la regionedell'osso alveolare risultante in frattura patologica, fistola extra orale, comunicazione oroantrale/oronasale o osteolisi che si estende al bordo inferiore della mandibola o al pavimento dei seni nasali

Ruggiero SL, et al. J Oral Maxillofac Surg 2014;72:1938–56.

Tabella 2. Stadiazione clinico-radiologica della ONJ (da "Raccomandazioni clinico-terapeutiche su osteonecrosi delle ossa mascellari associata a bisfosfonati e sua prevenzione". Bedogni A, Campisi G, Fusco V, Agrillo A. Ed. CLEUP, Marzo 2013).

Stadiazione clinico-radiologica BRONJ	
Stadio 1	**BRONJ FOCALE:** in presenza di almeno 1 segno clinico minore e con un *addensamento osseo alla TC limitato al solo processo dento-alveolare** della mandibola o del mascellare, con o senza altri segni radiologici precoci. **Segni clinici minori e sintomi**: alitosi, ascesso odontogeno, asimmetria mandibolare, dolore di origine dentale e osseo, esposizione ossea, fistola mucosa, mancata riparazione mucosa alveolare post-estrattiva, mobilità dentale a rapida insorgenza, parestesia/disestesia delle labbra, secrezione purulenta, sequestro spontaneo di frammenti ossei, trisma, tumefazione dei tessuti molli. **Segni TC**: *ispessimento trabecolare, osteosclerosi midollare focale*, con o senza ispessimento cresta alveolare e lamina dura, persistenza alveolo post-estrattivo, slargamento spazio parodontale. a. **asintomatica;** b. **sintomatica** (presenza di dolore e/o suppurazione).
Stadio 2	**BRONJ DIFFUSA:** in presenza di almeno 1 segno clinico minore e con un *addensamento osseo alla TC esteso anche al processo basale* della mandibola o del mascellare, con o senza segni radiologici tardivi. **Segni clinici minori e sintomi:** come per stadio 1. **Segni TC**: *osteosclerosi diffusa*, con o senza fistola oro-antrale e oro-nasale, ispessimento del canale alveolare, reazione periostale, sequestro, sinusite. a. **asintomatica;** b. **sintomatica** (presenza di dolore e/o suppurazione).
Stadio 3	**BRONJ COMPLICATA:** come in stadio 2, in presenza di uno o più dei seguenti: **Segni clinici minori:** fistola extra-orale, fuoriuscita di liquidi dal naso, mobilità pretematurale della mandibola con o senza occlusione conservata; **Segni TC**: fistola muco-cutanea, frattura patologica, osteolisi estesa al seno mascellare, osteosclerosi di zigomo e/o palato duro.

NB. si intende per regione dento-alveolare quella struttura ossea anatomica che costituisce il supporto scheletrico agli elementi dentari. Per definizione, il processo dento-alveolare termina in senso cranio-caudale subito al di sotto della radice degli elementi dentari

Frequenza di ONJ dopo Zoledronato o Denosumab

Incidence, risk factors, and outcomes of osteonecrosis of the jaw: integrated analysis from three blinded active-controlled phase III trials in cancer patients with bone metastases

Results: Of 5723 patients enrolled, 89 (1.6%) patients were determined to have ONJ: 37 (1.3%) received zoledronic acid and 52 (1.8%) received denosumab ($P = 0.13$). Tooth extraction was reported for 61.8% of patients with ONJ. ONJ treatment was conservative in >95% of patients. As of October 2010, ONJ resolved in 36.0% of patients (29.7% for zoledronic acid and 40.4% for denosumab).

5723 pts

Event as ***potential*** **ONJ** ***276 (4.8%)***

Adjudicated ONJ cases ***89 (1.5%)***

(according to AAOMS definition)

ONJ resolved in 36.0%
(29% zoledronic acid, 40% denosumab)

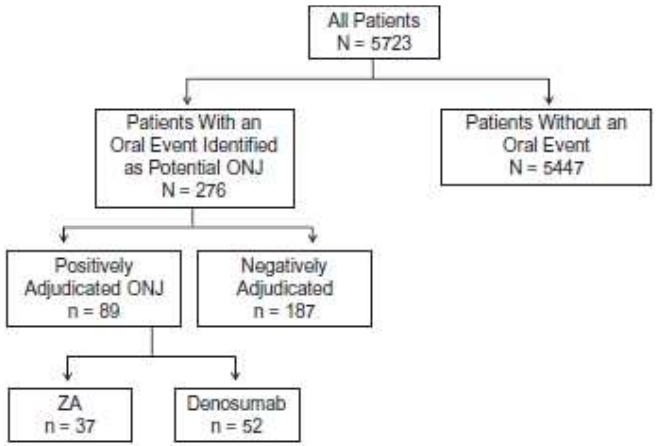


Figure 1. CONSORT diagram. Outcome of ONJ adjudication process. CONSORT, Consolidated Standards of Reporting Trials; ONJ, osteonecrosis of the jaw.

Saad et al – Ann Oncol 2012

Stopeck et al- Supp Care Cancer 2015

Safety of long-term denosumab therapy: results from the open label extension phase of two phase 3 studies in patients with metastatic breast and prostate cancer

Alis
Ing
Nea
Hu

Purpose Zoledronic acid (ZA) or denosumab treatment reduces skeletal-related events; however, the safety of prolonged therapy has not been adequately studied. Here, we describe safety results of extended denosumab therapy in patients with bone metastases from the open-label extension phase of two phase 3 trials.

Methods Patients with metastatic breast or prostate cancer received subcutaneous denosumab 120 mg Q4W or intravenous ZA 4 mg Q4W in a double-blinded fashion. Denosumab demonstrated superior efficacy in the blinded treatment phase; thus, patients were offered open-label denosumab for up to an additional 2 years.

Stopeck et al- Supp Care Cancer 2015

Support Care Cancer

Table 3 Adverse events during the open-label treatment phase

Event, *n* (%)	Breast cancer study		Prostate cancer study	
	Denosumab/Denosumab ($N = 318$)[a]	Zoledronic Acid/Denosumab ($N = 334$)[a]	Denosumab/Denosumab ($N = 147$)[a]	Zoledronic Acid/Denosumab ($N = 118$)[a]
All adverse events	283 (89.0)	303 (90.7)	138 (93.9)	105 (89.0)
Serious adverse events	126 (39.6)	133 (39.8)	78 (53.1)	63 (53.4)
Most common adverse events				
Nausea	72 (22.6)	77 (23.1)	20 (13.6)	16 (13.6)
Anemia	3 (16.7)	50 (15.0)	34 (23.1)	26 (22.0)
Fatigue	70 (22.0)	74 (22.2)	23 (15.6)	15 (12.7)
Back pain	66 (20.8)	56 (16.8)	29 (19.7)	19 (16.1)
Asthenia	40 (12.6)	48 (14.4)	29 (19.7)	11 (9.3)
Arthralgia	57 (17.9)	61 (18.3)	25 (17.0)	17 (14.4)
Adverse events of infection[b]	135 (42.5)	135 (40.4)	58 (39.5)	33 (28.0)
Osteonecrosis of the jaw (ONJ)[c, d]	20 (6.3)	18 (5.4)	12 (8.2)	7 (5.9)
CTCAE, v 3 grade 3	2 (0.6)	6 (1.8)	3 (2.0)	1 (0.8)
CTCAE, v 3 grade 4	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.8)
Adverse events of new primary malignancy[e]	2 (0.6)[f]	1 (0.3)[g]	1 (0.7)[h]	0 (0.0)
Adverse events of hypocalcemia[i]	12 (3.8)	9 (2.7)	8 (5.4)	5 (4.2)
Serious	3 (0.9)	0 (0.0)	1 (0.7)	1 (0.8)

ONJ : 20/318 (6.3 %) 18/334 (5.4 %) 12/147 (8.2 %) 7/118 (5.9 %)

Fusco et al- Supp Care Cancer 2016

Definition and estimation of osteonecrosis of jaw (ONJ), and optimal duration of antiresorptive treatment in bone metastatic cancer patients: supplementary data from the denosumab extension study?

Vittorio Fusco[1] · Alberto Bedogni[2] · Alfredo Addeo[3] · Giuseppina Campisi[4]

We collected data from the text and the tables of the paper published by Stopeck et al. [1] and summarized them in a new table (Table 1).

Fusco et al- Supp Care Cancer 2016

Interestingly, the frequency of ONJ cases in the open label extension study appears substantially higher than what is found in the initial blinded phase (ONJ frequency ranging from 1 to 2 %) [2, 3] despite median denosumab exposure was not significantly longer in the former. The crude ONJ figures increased both in denosumab/denosumab groups and in ZA/denosumab populations: ONJ cases were respectively 20/318 (6.3 %) in breast patients and 12/147 (8.2 %) in prostate patients in the denosumab/denosumab group, whereas they were 18/334 (5.4 %) breast patients and 7/118 (5.9 %) prostate patients in the ZA/denosumab group.

Such an increase in ONJ frequency highlights the need for longer patients' monitoring and the adoption of nonparametric actuarial estimation (Kaplan-Meier), as done in other studies [4–9], to obtain the projected individual ONJ risk at 2, 3, and 4 years of treatment. Separate analysis should be performed by Stopeck et al. [1] for breast and prostate cancer patients, showing these latter ones a similar ONJ rate increase even after shorter median drug exposure.

Più alta incidenza di ONJ, nonostante lieve incremento di esposizione mediana.

Necessità di valutazione attuariale.

Necessità di più lunghi follow-up per valutare l'incidenza di Adverse Events.

Fusco et al- Supp Care Cancer 2016

There are two burning aspects that we would like to address: the definition of ONJ and the optimal duration of antiresorptive (bisphosphonates or denosumab) treatment.

1. **The definition of ONJ is highly debated and controversial, with evident consequences on clinical practice, trials and epidemiological studied… (TOO MUCH RESTRICTED !!!)**

2. **The optimal duration of bone metastases treatment with antiresorptive drugs (ie BPs, denosumab) is yet to be defined.**

Supp Care Cancer 2016

Response to letter to the Editors—Safety of long-term denosumab therapy

Alison T. Stopeck & Douglas J. Warner

i numeri assoluti di ONJ in pazienti con tumore della mammella o della prostata salivano a valori tra il 5.4% e l'8.2%

i casi "adjudcated" erano una minoranza dei casi sospetti (140 casi su 341)

Continuano a mancare dati attuariali

Incidence of osteonecrosis of the jaw in patients with bone metastases treated sequentially with bisphosphonates and denosumab

Acta Clin Belg 2017

Tine Loyson , Thomas Van Cann, Patrick Schöffski, Paul M. Clement, Oliver Bechter, Isabel Spriet, Ruxandra Coropciuc , Constantinus Politis , Raf O. Vandeweyer, Joseph Schoenaers, Herlinde Dumez, Patrick Berteloot, Patrick Neven, Kristiaan Nackaerts, Feng J. S. H. Woei-A-Jin, Kevin Punie, Hans Wildiers & Benoit Beuselinck

Results: We identified 110 patients sequentially treated with bisphosphonates and denosumab with a median total BRI exposure of 36 months (sequential group). Median bisphosphonates exposure was 16 months and median denosumab exposure was 13 months. About 299 patients were included in the bisphosphonates control group with a median bisphosphonate exposure 19 months. About 6.7% (20/299) of patients developed ONJ. About 240 patients were included in the denosumab control group with a median denosumab exposure 17.5 months. About 10.0% of patients (24/240) developed ONJ. In the sequential group, 15.5% of patients (17/110) developed ONJ. The incidence of ONJ was 1.8% (2/110), 6.3% (6/99), 4.9% (4/82), 5.6% (3/54), and 3.4% (1/29), respectively in the first, second, third, fourth, and fifth year of BRI exposure, an ONJ-incidence similar to ONJ-incidence in the denosumab control group. In a time-to-ONJ-analysis,

ONJ INCIDENCE : sequential 17/110 (15.5%)

BP only 20/299 (6.7%)

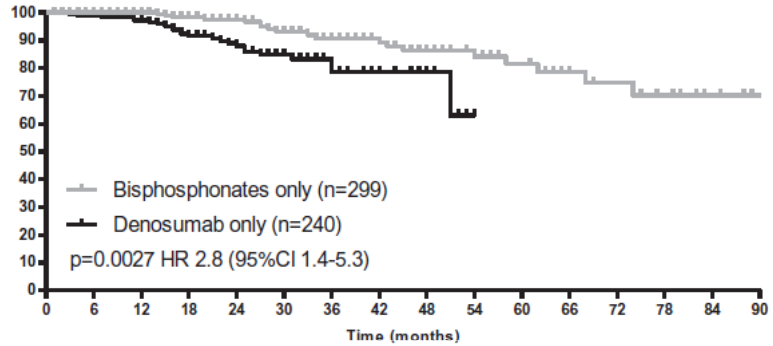
denosumab only 24/240 (10.0%)

Incidence of osteonecrosis of the jaw in patients with bone metastases treated sequentially with bisphosphonates and denosumab

Tine Loyson , Thomas Van Cann, Patrick Schöffski, Paul M. Clement, Oliver Bechter, Isabel Spriet, Ruxandra Coropciuc , Constantinus Politis , Raf O. Vandewever, Joseph Schoepaers, Herlinde Dumez, Patrick Berteloot, Patrick e, Hans

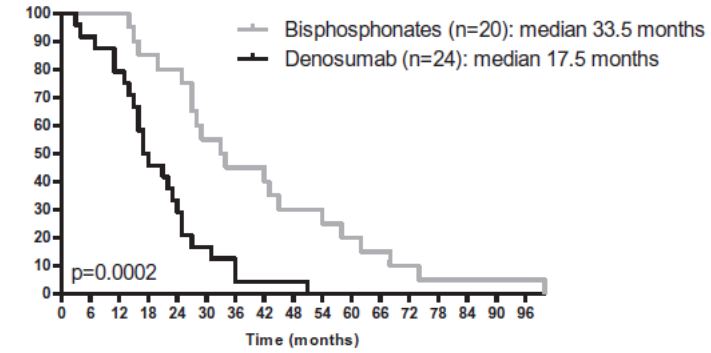
Curve attuariali !

(B) Time-to-ONJ (%):



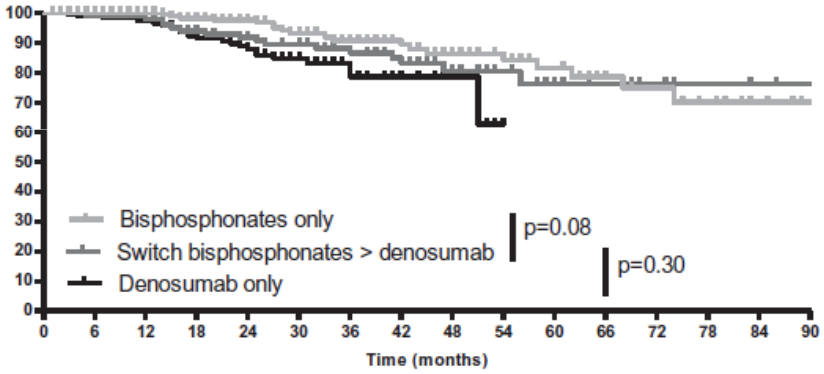
Months	0	12	24	36	48	60	72	84
Bisphosphonates	299	185	126	75	51	31	16	8
Denosumab	240	153	94	36	7	0	0	0

(C) Time-to-ONJ (%) in patients who developed ONJ:



Months	0	6	12	18	24	30	36	42
Bisphosphonates	20	20	20	17	16	11	9	6
Denosumab	24	22	19	12	8	4	3	1

(B) Time-to-ONJ (%):



Months	0	12	24	36	48	60	72	84
Bisphosphonates	299	185	126	75	51	31	16	8
Switch	110	103	83	56	30	16	8	5
Denosumab	240	153	94	36	7	0	0	0

Loyson et al, Acta Clin Belgica 2017

Denosumab-related osteonecrosis of the jaw: A retrospective study

A total of 141 patients treated at the ICL (cancer Institute of Lorraine) between January 2010 and December 2015 were included.
All patients were treated with XGEVA®.
Of the 141 patients included in the study, 10 developed DRONJ.
The incidence of DRONJ increases with the duration of follow-up as follows: 3% at 1 year, 7% at 2 years, and 8% from 30 months on.

Egloff-Juras C. et al J Oral Pathology 2017

Incidence of medication-related osteonecrosis of the jaw in patients treated with both bone resorption inhibitors and vascular endothelial growth factor receptor tyrosine kinase inhibitors

T. van Cann[1] · T. Loyson[1] · A. Verbiest[1] · P. M. Clement[1] · O. Bechter[1] · L. Willems[2] · I. Spriet[2] · R. Coropciuc[3] · C. Politis[3] · R. O. Vandeweyer[1] · J. Schoenaers[3] · P. R. Debruyne[4] · H. Dumez[1] · P. Berteloot[5] · P. Neven[5] · K. Nackaerts[6] · F. J. S. H. Woei-A-Jin[1,7] · K. Punie[1] · H. Wildiers[1] · B. Beuselinck[1]

Results Ninety patients were treated concomitantly with BRIs and VEGFR-TKIs with a median BRI-exposure of 5.0 months. Total MRONJ-incidence was 11.1%. During the first year of BRI-exposure (with a median concomitant exposure of 4.0 months), 6 out of 90 patients (6.7%) developed a MRONJ, compared to 1.1% in the control group (odds ratio 5.9; 95%CI 2.0–18.0; $p = 0.0035$). In Kaplan-Meier estimates, time-to-ONJ-incidence was significantly shorter in patients treated with BRIs and VEGFR-TKIs compared to BRIs alone (hazard ratio 9.5; 95%CI 3.1–29.6; $p < 0.0001$). MRONJs occurred earlier in patients treated concomitantly compared to patients treated with BRIs only (after a median exposure of 4.5 and 25.0 months, respectively; $p = 0.0033$).

Conclusion With a global MRONJ-incidence of 11%, patients receiving concomitant treatment with VEGFR-TKIs and BRIs have a five to ten times higher risk for development of MRONJ compared to patients treated with BRIs alone.

Aumento di incidenza di ONJ di 5-10 volte

JAMA 2017 : due studi

Research

JAMA Oncology | Original Investigation

Continued Treatment Effect of Zoledronic Acid Dosing Every 12 vs 4 Weeks in Women With Breast Cancer Metastatic to Bone
The OPTIMIZE-2 Randomized Clinical Trial

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Research

JAMA | Original Investigation

Effect of Longer-Interval vs Standard Dosing of Zoledronic Acid on Skeletal Events in Patients With Bone Metastases
A Randomized Clinical Trial

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Cosa è la osteonecrosi di mascellari e mandibola (ONJ) e come si manifesta? Esistono una definizione ed uno staging system della ONJ universalmente condivisi ?

Esiste un rischio di sottostima del fenomeno ONJ nei pazienti trattati con BP e denosumab ?

E' possibile integrare la diagnosi clinica di ONJ con un adeguato imaging ?

E' possibile prevenire la ONJ ?

Come si tratta la ONJ ?

Sono possibili interventi odontoiatrici in corso di terapia con BP o denosumab ?

LG AIOM 2017 Metastasi ossee

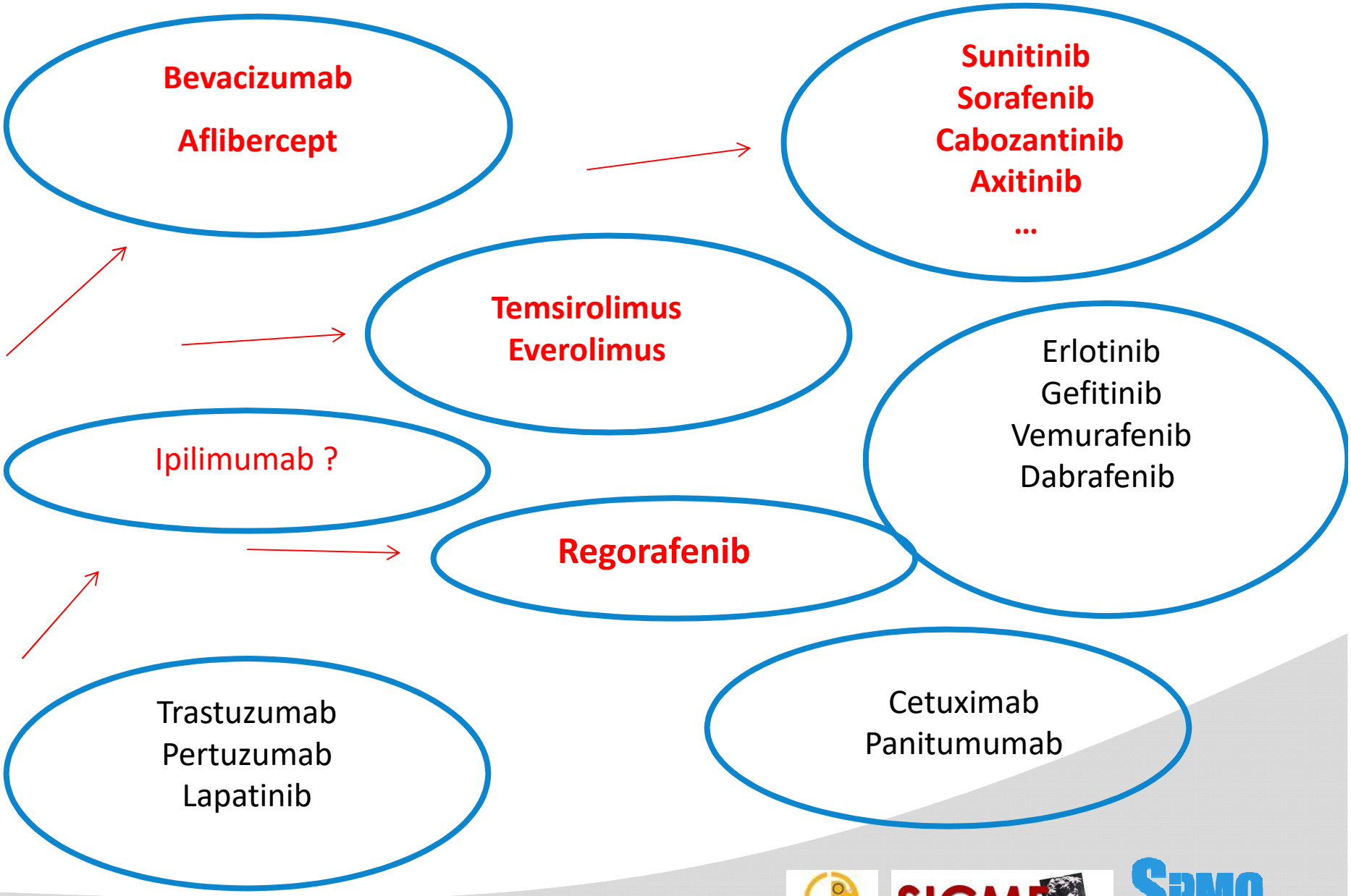
Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
D	La definizione correntemente adottata (AAOMS 2014) di ONJ (Osteonecrosi di mandibola e/o mascella), basata su osso esposto o fistola di durata superiore a 8 settimane, è restrittiva. Ogni paziente trattato con antiriassorbitivi o altri farmaci a rischio di ONJ con sintomatologia aspecifica (dolore, ascesso, difficoltà masticatoria, parestesia, mobilità dentaria, ecc) necessita di adeguata anamnesi e dovrebbe essere sottoposto a gruppi multidisciplinari includenti specialisti esperti (odontoiatri, chirurghi maxillofacciali, radiologi, ecc).	Positiva forte

Qualità dell'evidenza SIGN	Raccomandazione clinica	Forza della raccomandazione clinica
D	I valori di frequenza di ONJ nei pazienti trattati con antiriassorbitivi (BP, denosumab), basati su una definizione restrittiva (AAOMS 2009) di ONJ e su studi con follow-up breve, sono ampiamente sottostimati. Tale sottostima deve essere presa in considerazione nella valutazione rischio-beneficio del prolungamento del trattamento oltre i 2 anni (standard secondo letteratura).	Positiva forte

ONJ DA BISFOSFONATI : PERCHE'?

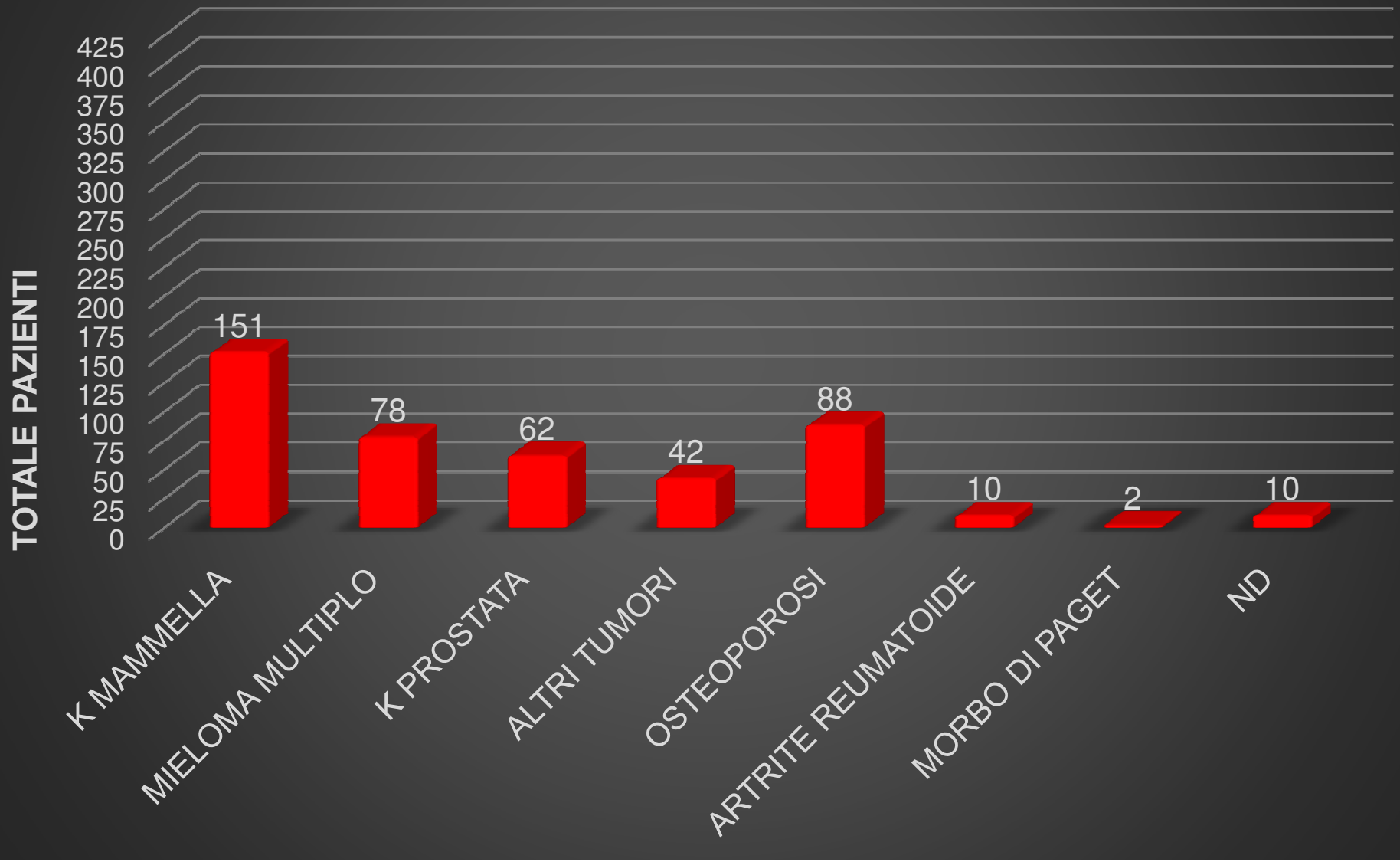
V. Fusco
(da Allen modificata)

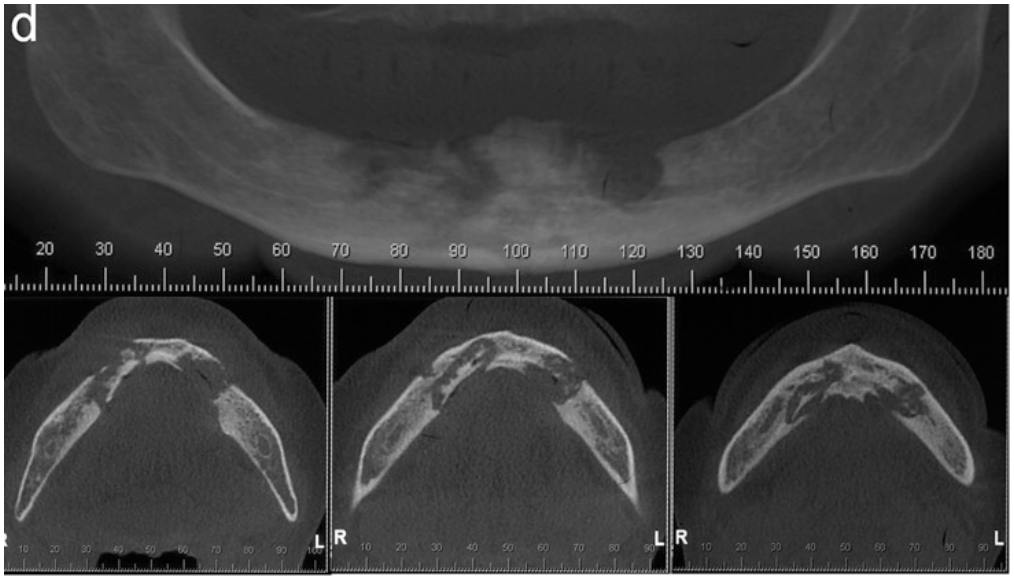
Ad oggi quali farmaci sembrano determinare rischio di ONJ?



UNITO

DISTRIBUZIONE IN VALORI ASSOLUTI PER PATOLOGIA NEL CAMPIONE DI 438 PAZIENTI

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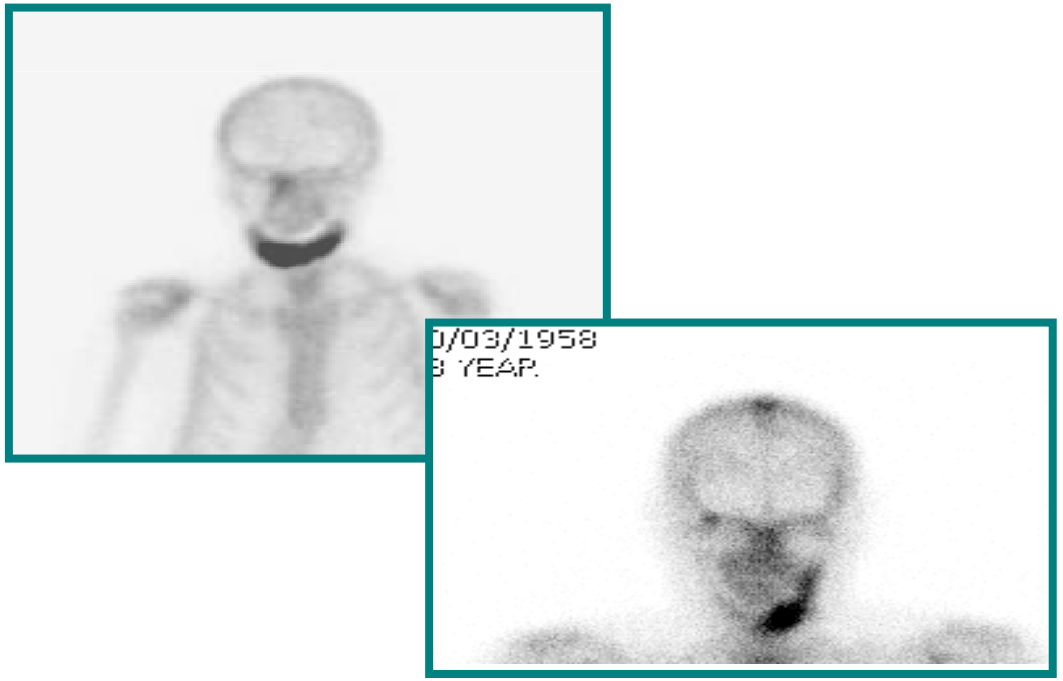
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3 YEAR

ONJ in ONCOLOGIA: CONCLUSIONI

✓ **I Bisfosfonati e il Denosumab hanno un ruolo centrale nel trattamento dei pazienti con metastasi ossee**

✓ **ONJ è *uncommon* (non "rare") e potenzialmente severa**

✓ **ONJ può essere "prevenuta" (riduzione del rischio)**

✓ **Alert per i pazienti trattati con agenti biologici (*target*)**

✓ **Aggiornare e seguire Raccomandazioni e Linee Guida**

Grazie per l’attenzione !