Bifosfonatos ¿Un antineoplásico?

Dra. Mabel Arinoviche

Abril 2023

Cronología histórica de los Bisfosfonatos

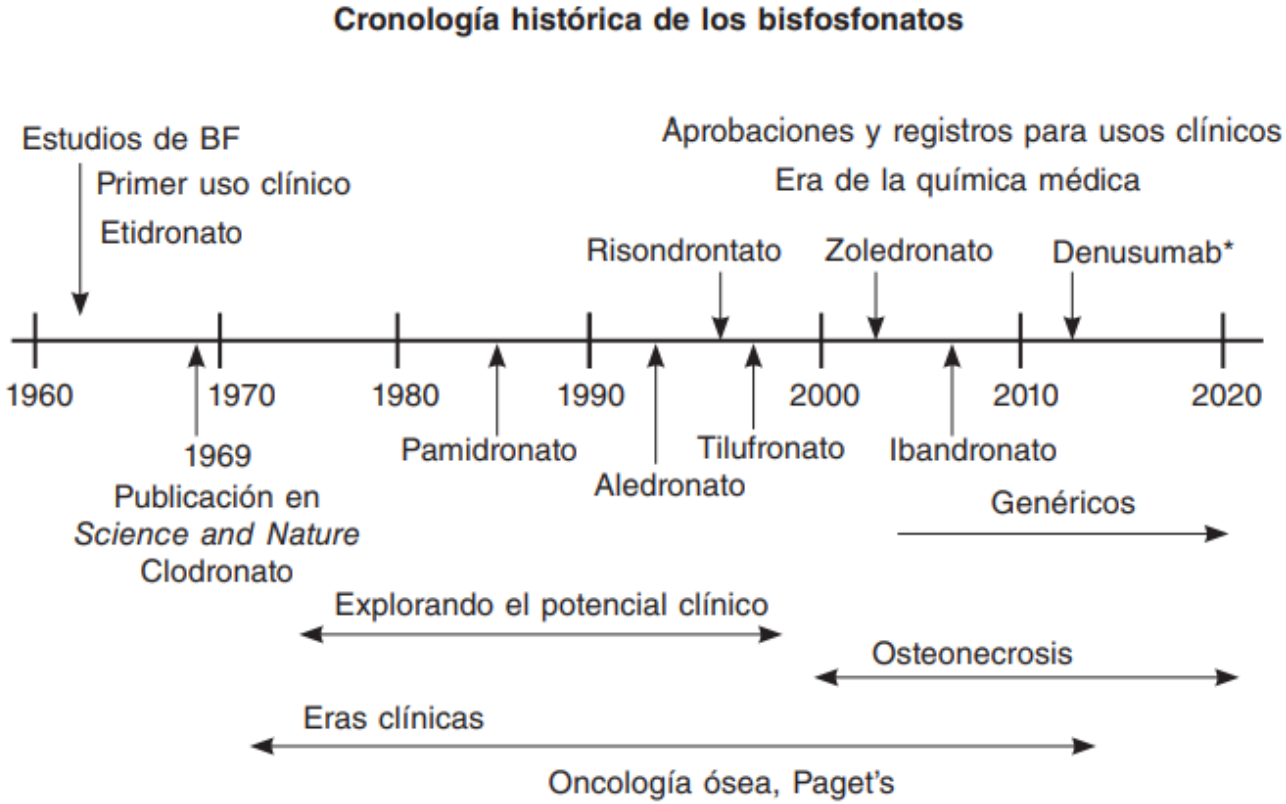
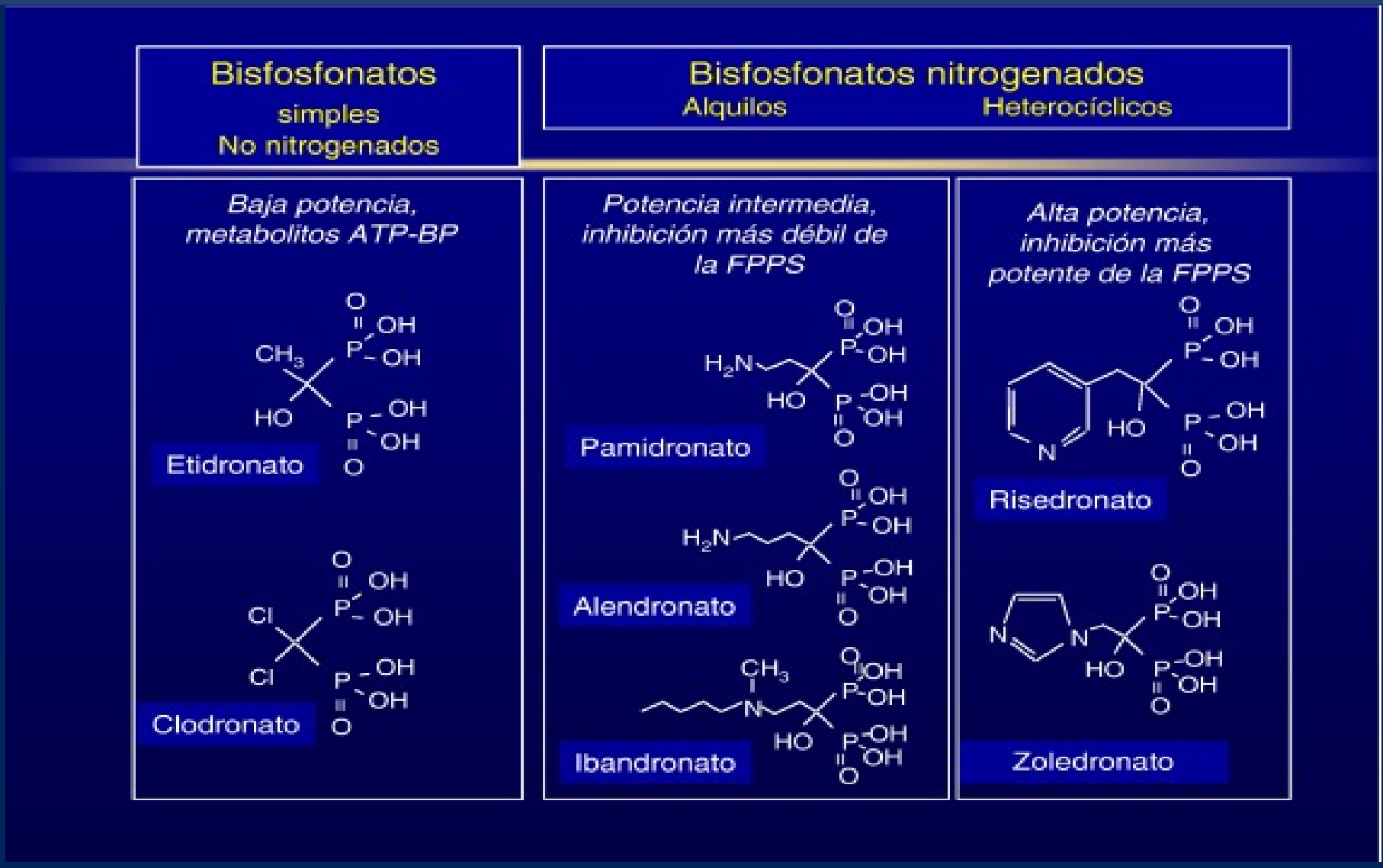
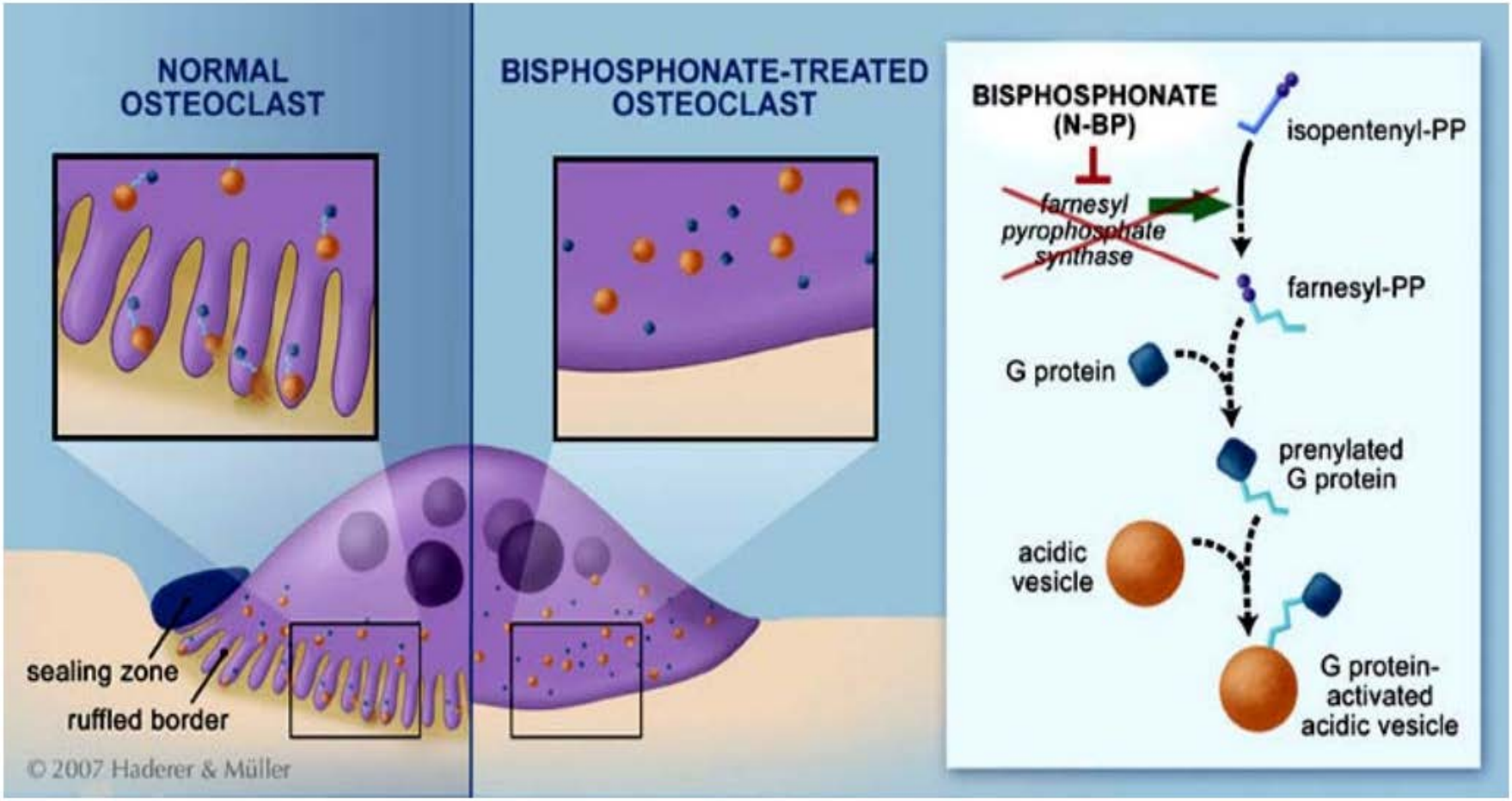


Figura 4. Cronología histórica de los BF.

Clasificación de Bifosfonatos:



Bisphosphonates Inhibit Bone Resorption by Preventing Formation of the Ruffled Border



Indicaciones de los Bifosfonatos

- Tratamiento de la osteoporosis postmenopáusica
- Tratamiento de la osteoporosis en hombres
- Tratamiento y prevención de la osteoporosis inducida por GC
- Tratamiento de la Enfermedad de Paget
- Tratamiento adyudante del cáncer de mama inicialcon RH en mujeres premenopáusicas asociado a hormonoterapia
- Prevención de complicaciones óseas(fx patológicas, compresión medular, radioterapia, cirugías, hipercalcemia) en pacientes con metástasis que afecten al hueso
- Prevención de fracturas y pérdida de masa ósea en mujeres postmenopáusicas con cáncer de mama en fase inicial tratadas con inhibidores de la aromatasa
- Tratamiento de la hipercalcemia tumoral

Metástasis óseas según tipo de tumor

	(Incidence of Bone Metastases)
Myeloma	(70–95%)
Renal	(20–25%)
Melanoma	(14–45%)
Bladder	(40%)
Thyroid	(60%)
Lung	(30–40%)
Breast	(65–75%)
Prostate	(65–75%)

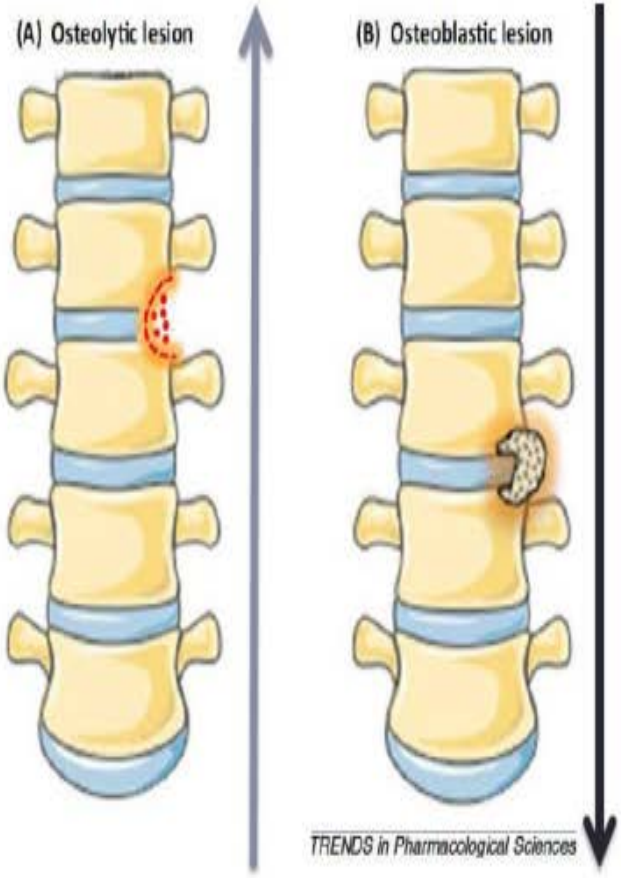
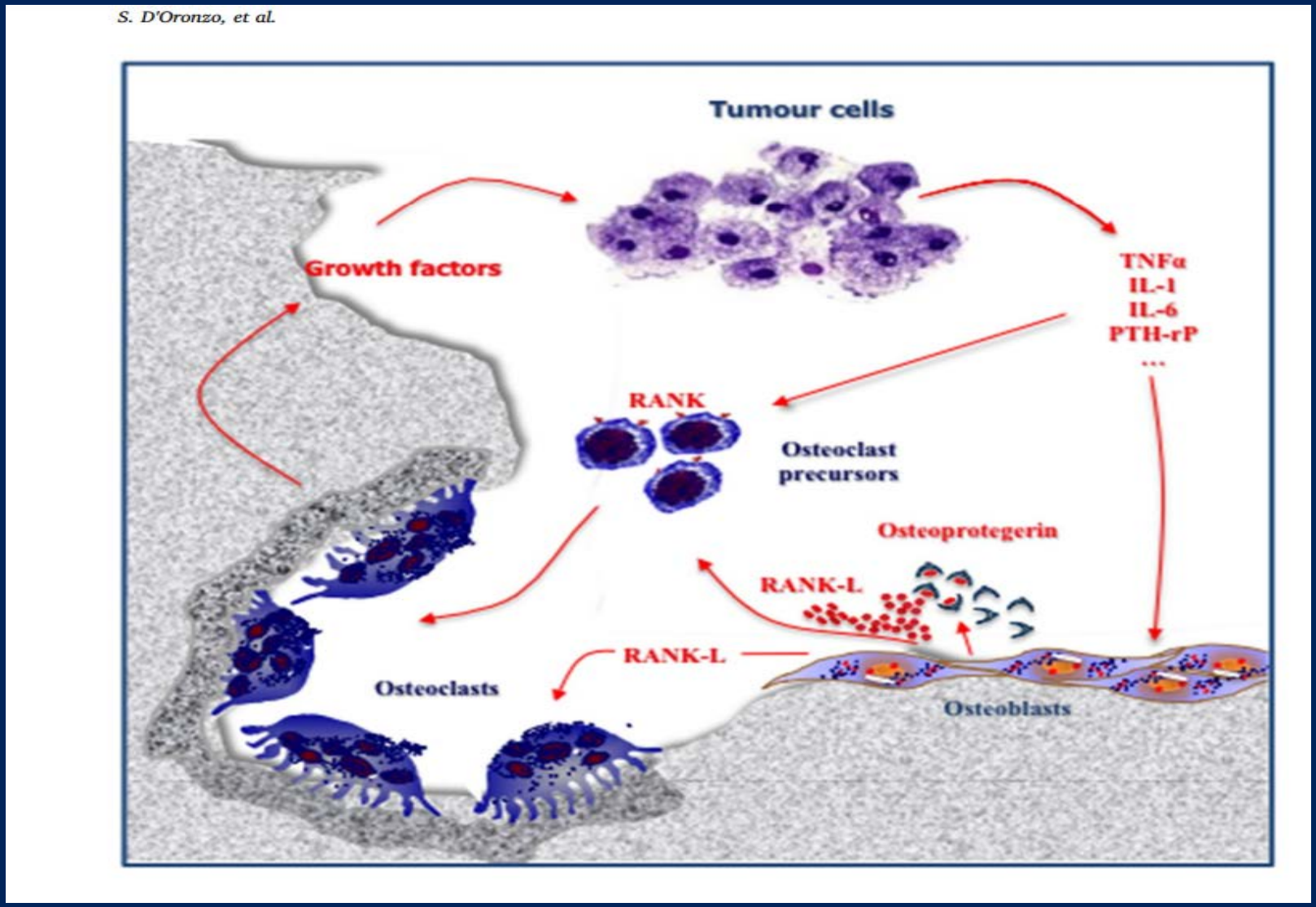


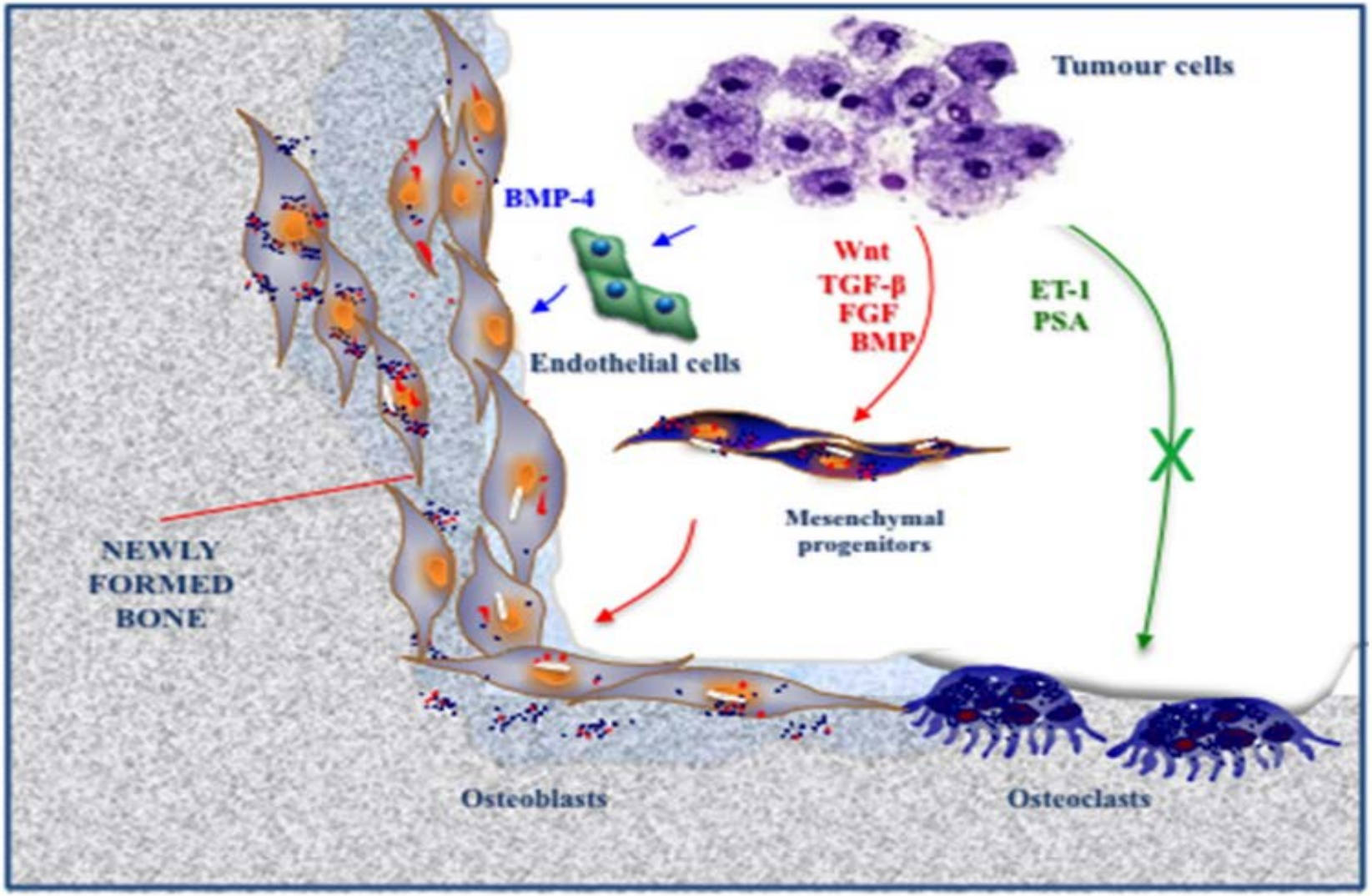
Figura 5. Naturaleza de las metástasis óseas según tipo tumor.


METASTASIS OSEAS
DOLOR
COMPRESION MEDULAR
HIPERCALCEMIA
FRACTURAS
PERDIDA DE ATONOMIA
INCREMENTO DE COSTO SANITARIO
CIRUGIA
RADIOTERAPIA
REDUCCION DE SUPERVIVENCIA

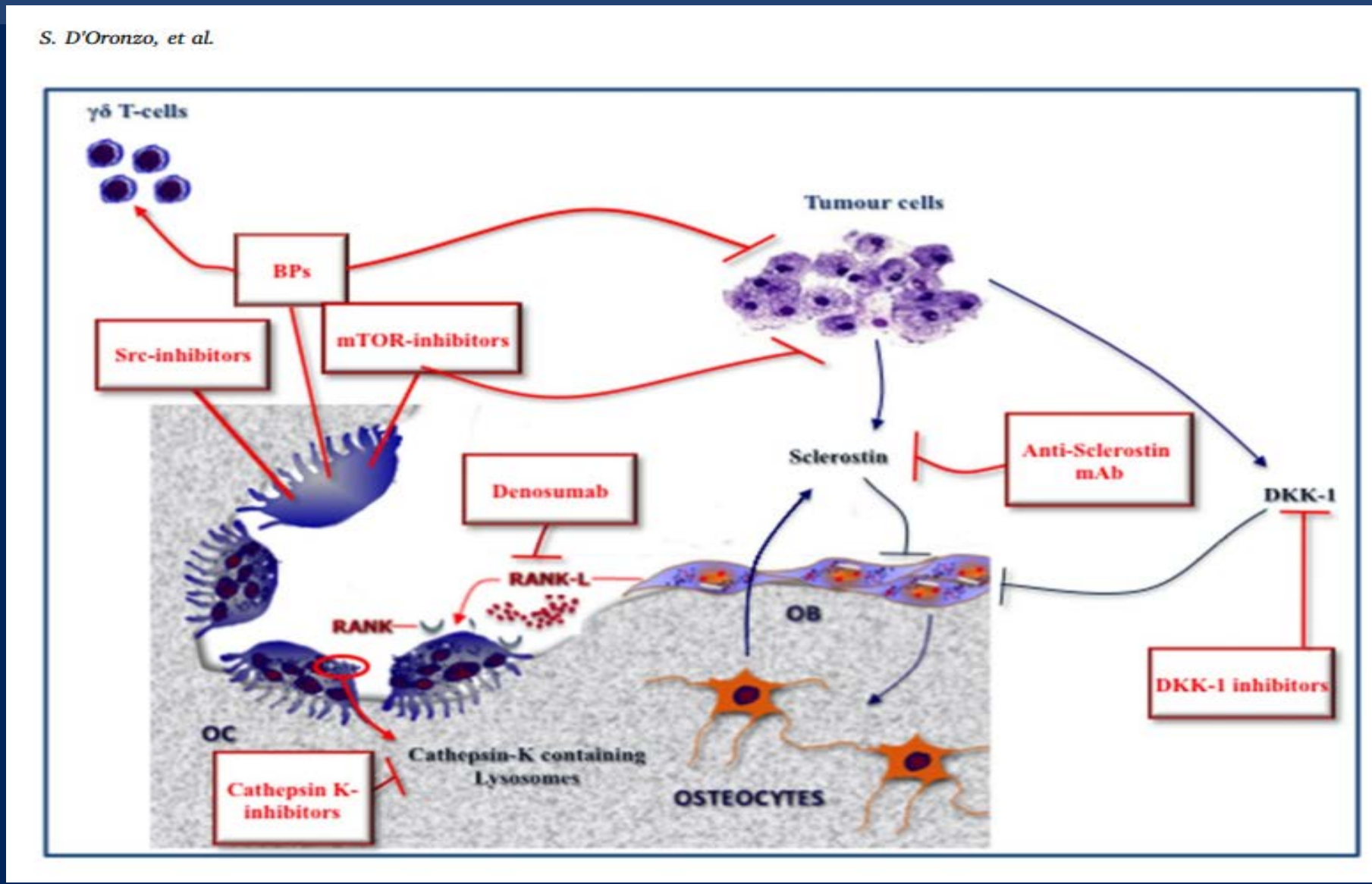
El círculo vicioso de metástasis osteolíticas en tumores sólidos



Mecanismo de formación de metástasis osteoblásticas



Mecanismo de acción de agentes terapéuticos para el manejo de MO



Annals of Oncology

Annals of Oncology 24: 398–405, 2013
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Published online 9 October 2012

Zoledronic acid (zoledronate) for postmenopausal women with early breast cancer receiving adjuvant letrozole (ZO-FAST study): final 60-month results

R. Coleman[1*], R. de Boer[2], H. Eidtmann[3], A. Llombart[4], N. Davidson[5], P. Neven[6], G. von Minckwitz[7], H. P. Sleeboom[8], J. Forbes[9], C. Barrios[10], A. Frassoldati[11], I. Campbell[12], O. Paija[13], N. Martin[14], A. Modi[14] & N. Bundred[15]

[1]Academic Unit of Clinical Oncology, CR-UK/YCR Sheffield Cancer Research Centre, Sheffield, UK; [2]Department of Medical Oncology, Royal Melbourne and Western Hospitals, Melbourne, Australia; [3]Clinic for Gynecology and Obstetrics, Universitäts-Frauenklinik Kiel, Kiel, Germany; [4]Medical Oncology Service, Institute Oncologica, Valencia, Spain; [5]Cancer Services Directorate, Broomfield Hospital, Chelmsford, Essex, UK; [6]Department of Gynecological Oncology, Breast Clinic, UZ Gasthuisberg, Leuven, Belgium; [7]German Breast Group, Frankfurt, Germany; [8]Department of Internal Medicine, Haga Hospital, Den Haag, The Netherlands; [9]Faculty of Health, School of Medical Practice and Population Health, University of Newcastle, Newcastle, NSW, Australia; [10]Faculty of Medicine, PUCRS School of Medicine, Porto Alegre, Brazil; [11]Clinical Oncology Unit, St. Anna University Hospital, Ferrara, Italy; [12]Department of General Surgery, Waikato Hospital, Breast Care Center, Hamilton, New Zealand; [13]Department of Medical Oncology, Turku University Central Hospital, Turku, Finland; [14]Novartis Oncology, East Hanover, New Jersey, USA; [15]Department of Academic Surgery, South Manchester University Hospital, Education and Research Center, Manchester, UK

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- Estudio randomizado, multicéntrico, fase III
- Mujeres postmenopáusicas con cáncer de mama inicial en estados I,II,o IIIA con receptor + a estrógeno y/o progesterona
- T score col < -2 T score cadera total >-2
- Resección quirúrgica,quimio y radioterapia terminadas 12 semanas antes del enrolamiento, sin evidencia de enfermedad residual
- **Criterios de exclusión**
- Evidencia radiológica o clínica de metástasis
- Preexistencia de fracturas de cadera o columna
- Otras patologías que afecten la DMO
- Insuficiencia renal
- Uso previo de Letrozol u otra terapia endocrina adyudante, TRH, BP ev

- Todas las pacientes recibieron letrozol 2.5 mgs al día durante 5 años
- Calcio y vitamina D

- 1065 pacientes fueron enroladas en 2 grupos:
- 1-TRATAMIENTO INMEDIATO recibieron 4 mgs ácido zoledrónico cada 6 meses desde el primer mes del enrrolamiento.
- 2-TRATAMIENTO RETARDADO recibieron 4 mgs de ácido zoledrónico cada 6 meses si el Tscore disminuía de -2 o si tenían una fractura clínica no traumática o una fractura asintomática detectada en la evaluación a los 36 meses

La DMO fue evaluada en ambos grupos anualmente

Variables de eficacia y seguridad

- La variable principal:

El % de cambio de la DMO de columna lumbar en las ramas con A.Zoledrónico inmediato y con A. Zoledrónico retardado

- Variables secundarias:

El % de cambio de la DMO en columna y cadera total a los 2,3,4 y 5 años

Incidencia de fracturas a los 36 meses

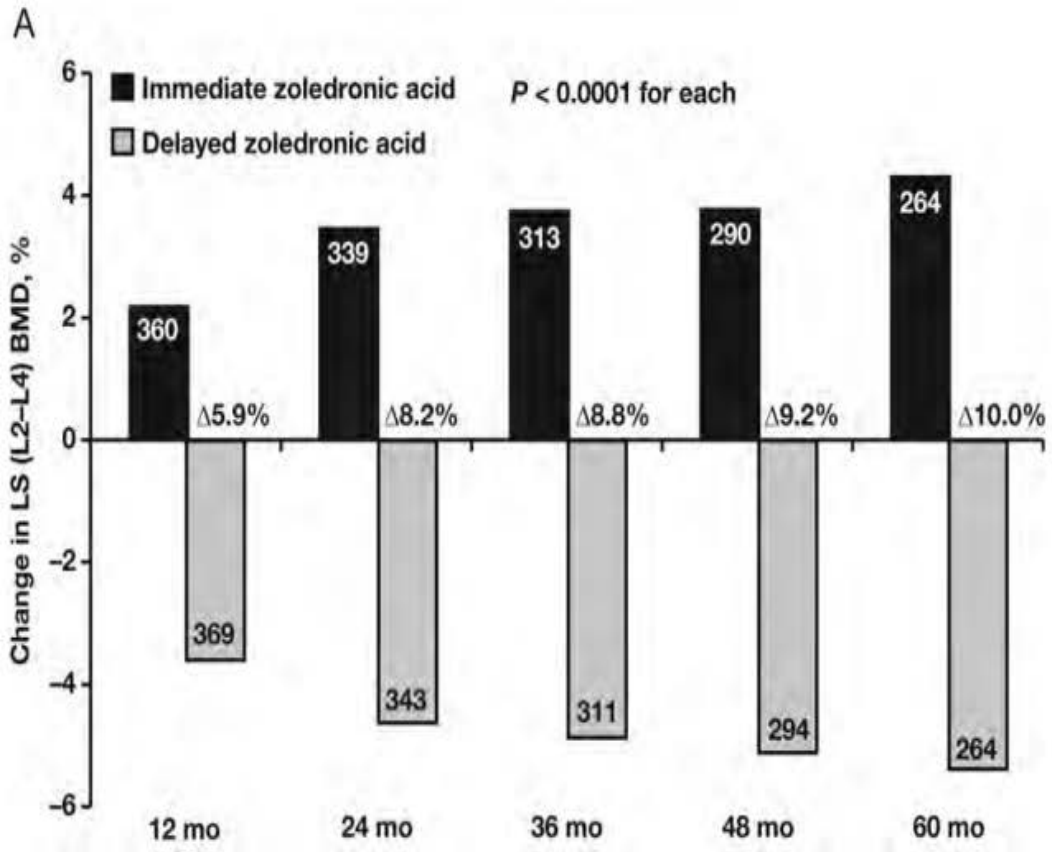
Tiempo de recurrencia de enfermedad (DFS)

Sobrevida General (OS)

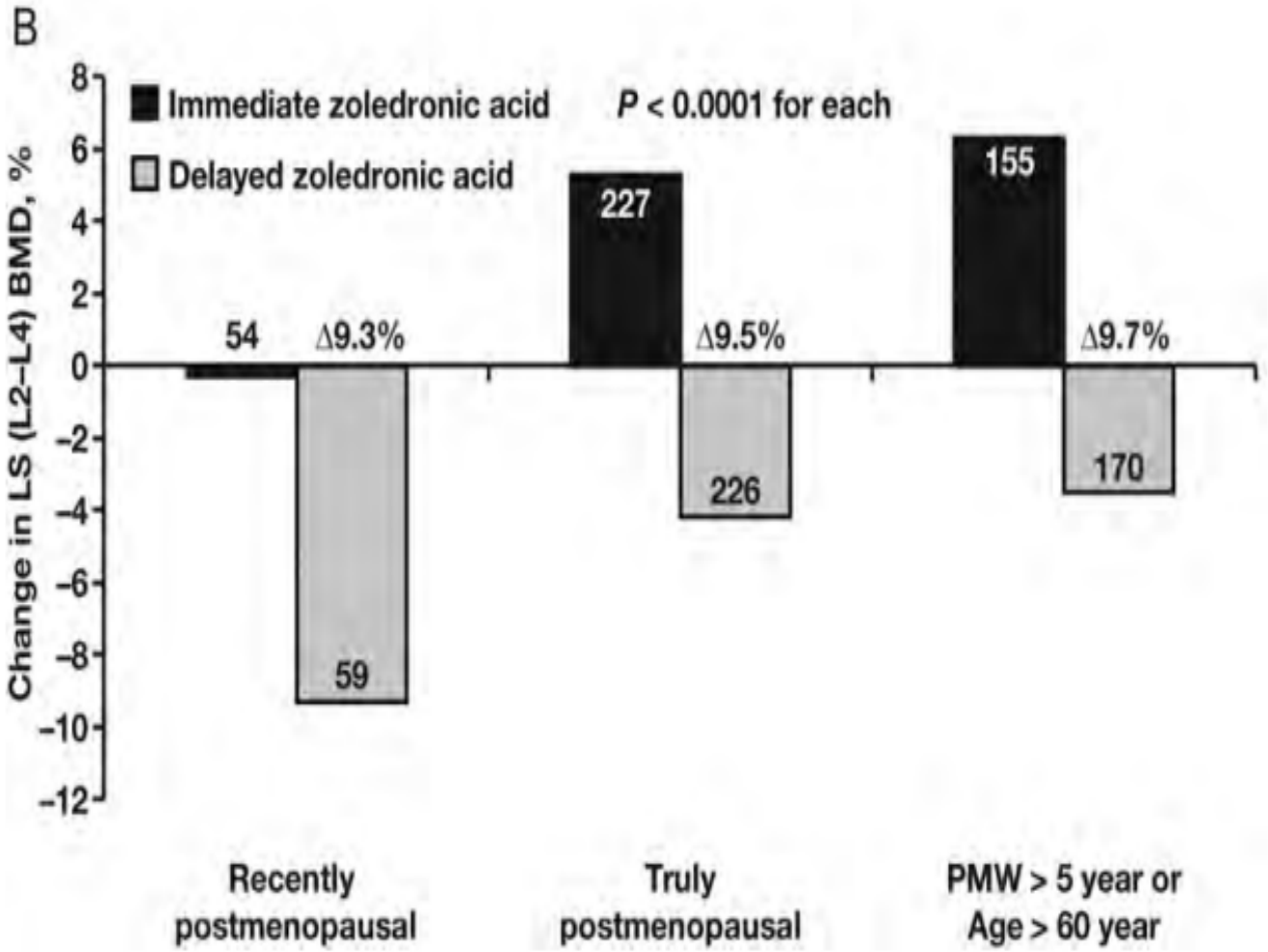
Seguridad

Cambios de la DMO durante 60 meses

Annals of Oncology



Cambio de la DMO a 60 meses según status de menopausia



Recurrencia de enfermedad

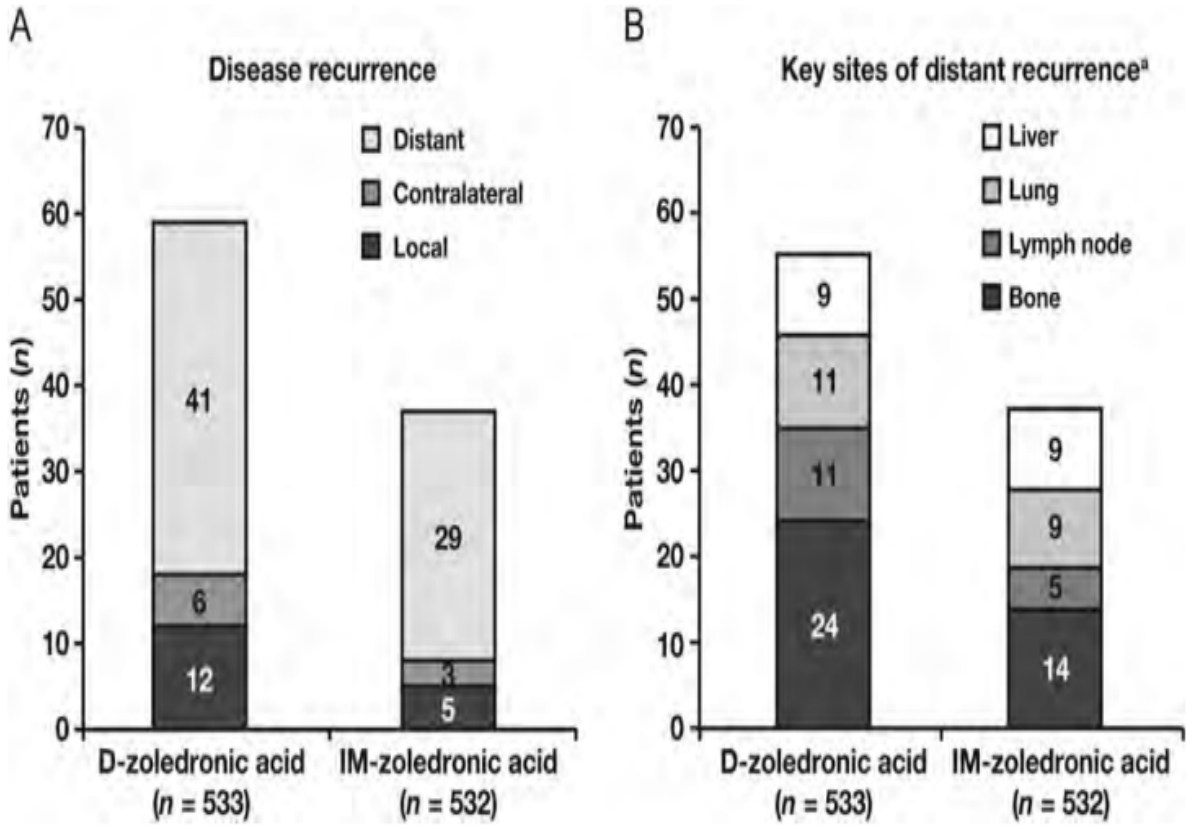
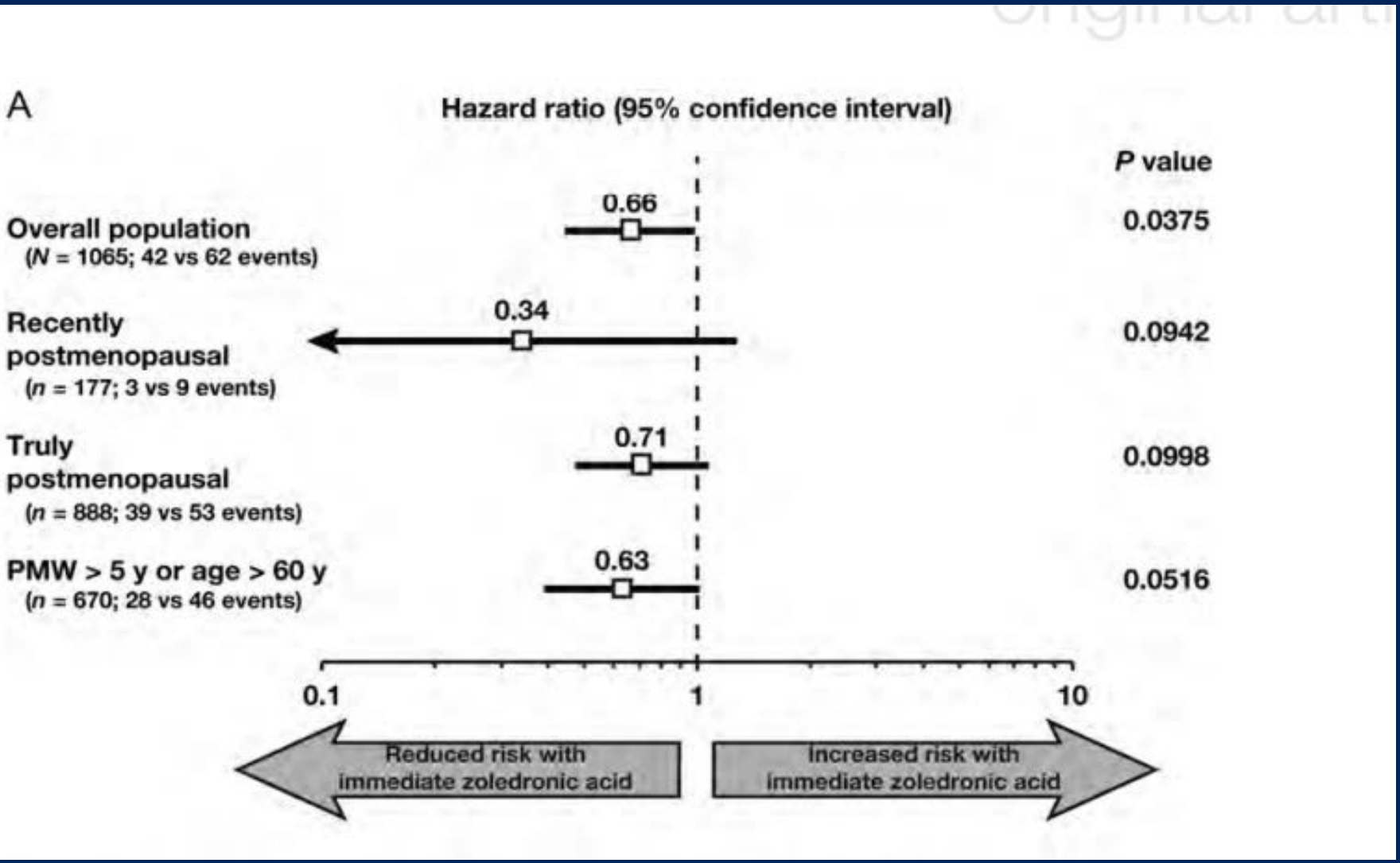


Figure 3. Disease recurrence events by the treatment arm. (A) Grouped as distant, contralateral and local recurrence; (B) breakdown by the site of distant recurrences. D-ZOL, delayed zoledronate; IM-ZOL, immediate zoledronic acid. [a]Multiple sites may be reported for the same patient. Distant metastases include bone, brain, liver, lung, skin, lymph node, and other.

Sobrevida libre de enfermedad



Sobrevida general

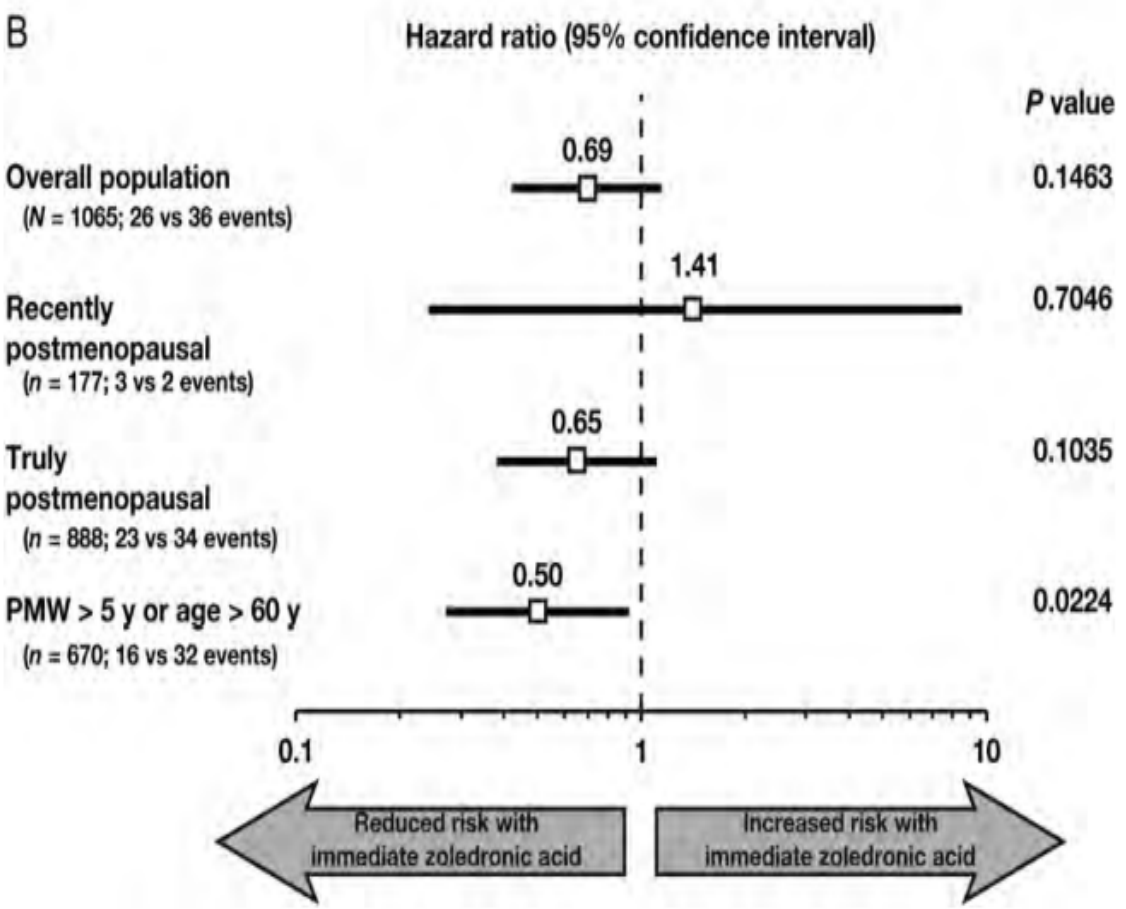


Figure 4. Forest plots for the overall population and by menopausal status of (A) disease-free survival (risk of disease recurrence or death) and (B) overall survival (risk of death). *P*-values were based on the log-rank test. PMW, postmenopausal women; ZOL, zoledronate.

Conclusiones

- Se evidenció mejoría en la DMO a los 12 meses en el grupo con Acido Zol.inmediato vs el grupo con Acido Zol. retardado.El cambio medio fue +4,3% en el grupo de Zol. Inmediato vs -5,4% en el grupo con Zol. retardado a los 60 meses.
- Hubo un 34% de reducción relativa del riesgo de recurrencia de enfermedad o muerte en el grupo con Zol inmediato vs Zol retardado a los 60 meses.
- El Acido Zoledrónico mejoró en mayor medida la SLE(sobrevida libre de enfermedad) y la ST(sobrevida total) en mujeres mayores de 60 años o que tenían más de 5 años de menopausia
- Esto sugiere que el potencial antineoplásico del Acido Zoledrónico podría ser más eficaz en un ambiente con menor nivel de hormonas reproductivas

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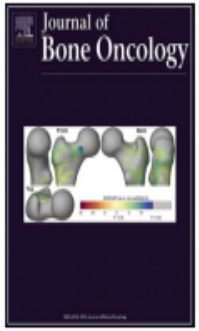


Research Paper

Management of bone metastasis with zoledronic acid: A systematic review and Bayesian network meta-analysis

Justin-Pierre Lorange [a], Jose Ramirez Garcia Luna [b], Frédéric Grou-Boileau [a], Derek Rosenzweig [b], Michael H. Weber [b], Elie Akoury [b,*]

[a] *Faculty of Medicine, McGill University, Montreal, Quebec, Canada*

[b] *Department of Surgery, Division of Orthopaedics, McGill University and The Research Institute of the McGill University Health Centre, Injury Repair Recovery Program, Montreal, Quebec, Canada*

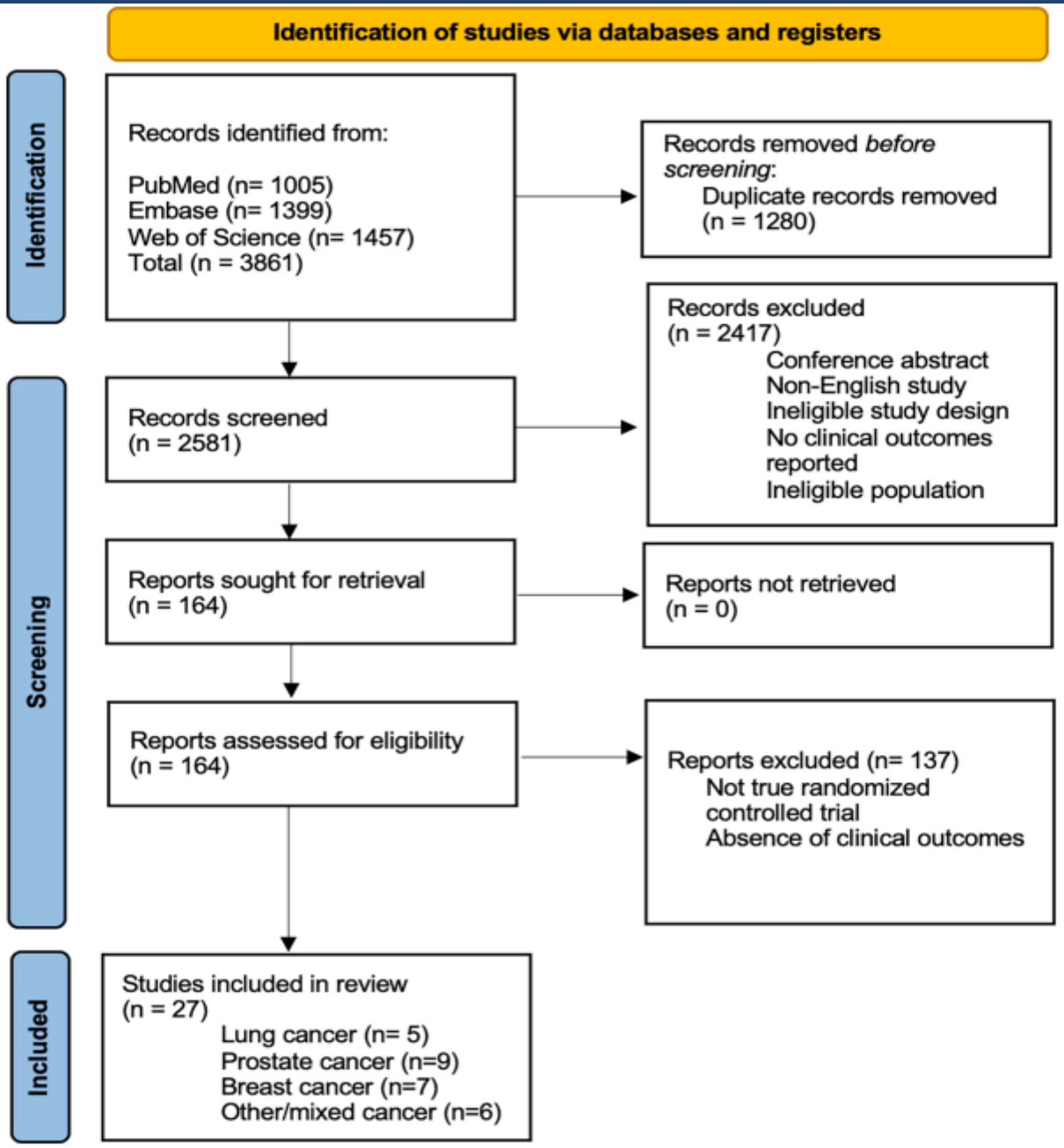
- La revisión sistemática se realizó de acuerdo a las guías PRISMA
- Población adulta, independiente de edad y sexo con metástasis óseas secundarias a cualquier tumor sólido
- Uso de Acido Zoledrónico con cualquier comparador incluido placebo

Se comparó el Acido zoledrónico con otras opciones terapéuticas

- Capacidad de mejorar la sobrevida general
- Disminuir incidencia de ERE
- Disminuir el dolor en pacientes con metástasis óseas secundarias a cualquier tumor sólido

- Variables Principales:
- Desarrollo de un nuevo EREsea éste una nueva metástasis, fractura patológia, compresión médula espinal o dolor incapacitante.
- Tiempo en desarrollar un nuevo ERE durante el estudio
- Sobrevida libre de progresión de enfermedad

- Variable Secundaria:
- Dolor a los 3,6 y 12 meses


Identification of studies via databases and registers
Identification
Records identified from:
PubMed (n= 1005)
Embase (n= 1399)
Web of Science (n= 1457)
Total (n = 3861)
Records removed *before screening*:
Duplicate records removed (n = 1280)
Screening
Records screened (n = 2581)
Records excluded (n = 2417)
Conference abstract
Non-English study
Ineligible study design
No clinical outcomes reported
Ineligible population
Reports sought for retrieval (n = 164)
Reports not retrieved (n = 0)
Reports assessed for eligibility (n = 164)
Reports excluded (n= 137)
Not true randomized controlled trial
Absence of clinical outcomes
Included
Studies included in review (n = 27)
Lung cancer (n= 5)
Prostate cancer (n=9)
Breast cancer (n=7)
Other/mixed cancer (n=6)

Estudios incluidos

Table 1
List of included studies. The data of each randomized controlled trial is represented in the columns. NSCLC = Non-small cell lung cancer, ZA = Zoledronic Acid, SR-89 = Strontium-89, SC = Subcutaneous, IV = Intravenous, MBq = Megabecquerel.

Authors	Year	Primary cancer	Time of treatment compared to the main therapy	Treatment	Population size for treatment (n)	Comparator	Population size for comparator (n)
Barrett-Lee, P [33]	2014	Breast cancer	During	ZA- 4 mg/ 4 weeks	699	Ibandronic acid- 50 mg daily	705
Broom, R. J [34]	2015	Renal cell carcinoma	Before	Everolimus and ZA - 4 mg/ 4 weeks	15	Everolimus- 10 mg daily	15
Choudhury, K. B [31]	2011	NSCLC + others	During	ZA – 4 mg/ 4 weeks	60	1. Ibandronate- 6 mg/ 4 weeks 2. Pamidronate- 90 mg/ 4 weeks	1. 65 2. 62
Cleeland, C. S [76]	2013	Breast cancer	Before	ZA – 4mg/ 4 weeks + SC placebo	1020	Denosumab- 120 mg/ 4 weeks + IV placebo	1026
Fizazi, K [35]	2011	Prostate cancer	After	ZA – 4 mg/ 4 weeks + SC placebo	951	Denosumab- 120 mg/ 4 weeks + IV placebo	950
Francini, F [36]	2011	NSCLC	During	ZA – 4mg/ 4 weeks	28	Ibandronic acid- 50 mg/day	27
Henry, D [37]	2014	NSCLC	Before	ZA - 4 mg/ 4 weeks + SC placebo	797	Denosumab SC- 120 mg/ 4 weeks with placebo IV	800
Hilton, J. F [38]	2018	Breast cancer	After	ZA – 4 mg/ 4 weeks	38	Pamidronate	35
Jacobs, C [39]	2016	Breast cancer	During	ZA – 4 mg/ 4 weeks	35	Pamidronate	38
James, N [40]	2016	Prostate cancer	Before	Docetaxel, ZA – 4 mg/ 4 weeks	188	1. Docetaxel- 75 mg/m2/ 3 weeks, 2. Docetaxel and ZA 3. Docetaxel + Sr-89.	1. 191 2. 188 3. 190
Kamba, T [41]	2016	Prostate cancer	Before	ZA – 4 mg/ 4 weeks with combined androgen blockade	115	80 mg of bicalutamide orally once a day and subcutaneous luteinizing hormone-releasing hormone agonist every 4 or 12 weeks	112
Kohno, N [42]	2005	Breast cancer	During	ZA – 4 mg/ 4 weeks	114	Placebo	114
Martin, M [43]	2012	Breast cancer	Before	ZA – 4 mg/ 4 weeks + SC placebo	1020	Denosumab- 120 mg/ 4 weeks + IV placebo	1026
Murakami, H [44]	2014	NSCLC	After	ZA – 4 mg/ 4 weeks with Docetaxel	50	Docetaxel- 60 mg/m2	50
Pan, Y [45]	2014	Prostate cancer	After	Docetaxel-based chemotherapy + ZA - 4 mg/ 3 weeks	53	Docetaxel-based chemotherapy- 75 mg/ m2 of docetaxel for 21 days and placebo	52
Pandya, K. J [56]	2010	NSCLC	After	Docetaxel, Carboplatin and ZA – 4 mg/ 4 weeks	64	Docetaxel- 75 mg/m2 for 1 h and carboplatin- IV for 15 min	64
Price, N [32]	1999	NSCLC + others	Before	ZA - A. 4 mg / 3 weeks B. 8 mg/ 3 weeks; reduced to 4 mg/ 3 weeks	A. 254 B. 265	Placebo	247
Rosen, L. S [46]	2003	Multiple myeloma and breast cancer	During	ZA - A. 4 mg/ 4 weeks B. 8 mg/ 4 weeks; later switched to 4 mg/ 4 weeks	A. 564 B. 526	Pamidronate- 90 mg/ 3 or 4 weeks	558
Rosen, L. S [47]	2004	NSCLC + others	During	ZA - A. 4 mg/ 4 weeks B. 8 mg/ 4 weeks; later switched to 4 mg/ 4 weeks	A. 257 B. 266	Placebo	250
Saad, F [48]	2002	Prostate cancer	During	ZA - A. 4 mg / 4 weeks B. 8 mg/ 4 weeks;later switched to 4 mg/ 4 weeks	A. 214 B. 221	Placebo	208
Smith, M. R [50]	2014	Prostate cancer	Before	ZA – 4 mg/ 4 weeks	323	Placebo	322
Smith, M. R. [49]	2015	Prostate cancer	After	ZA – 4 mg/ 4 weeks	951	Denosumab- 120 mg/ 4 weeks	950
Stopeck, A.T [51]	2010	Breast cancer	During	ZA – 4 mg/ 4 weeks + SC placebo	1020	Denosumab- 120 mg/ 4 weeks + IV placebo	1026
Ueno, S [52]	2013	Prostate cancer	Before	ZA – 4 mg/ 4 weeks with combined androgen blockade	29	Combined androgen blockade – 80 mg/ day	31
Wang, F [53]	2013	Prostate cancer	Before	ZA – 4 mg/ 4 weeks	69	Clodronate- 1600 mg / day	68
Wang, Y [55]	2013	NSCLC	Before		45	1. ZA – 4 mg every 3/4 weeks	1. 45

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Desarrollo de un ERE

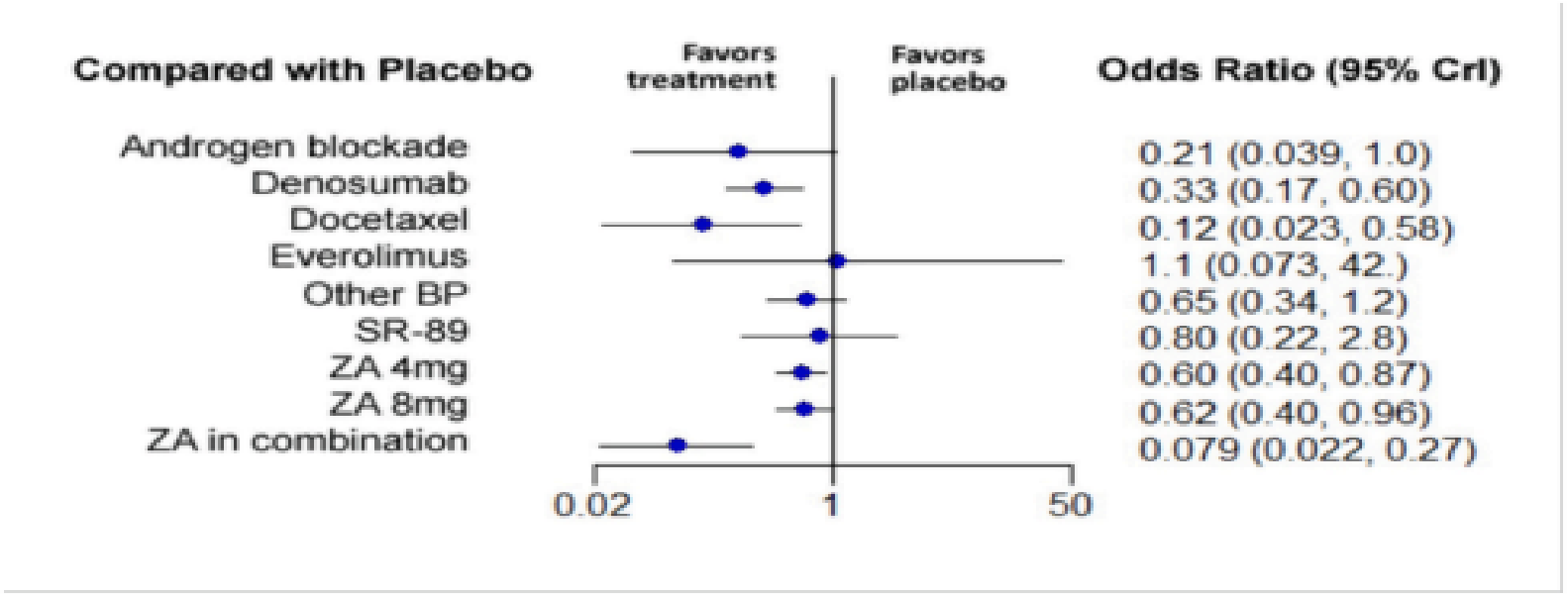

Fig. 3. Forest plot of the impact of the different therapies in preventing the development of a SRE when compared to placebo. On the left, the different therapies are labelled. On the right, the odds ration corresponding to each therapy when compared to placebo are represented. In parenthesis, the 95 % credible intervals are shown. BP = Bisphosphonate, ZA = Zoledronic Acid, SR-89 = Strontium-89, CrI = Credible Intervals.

Tiempo en desarrollar el primer ERE

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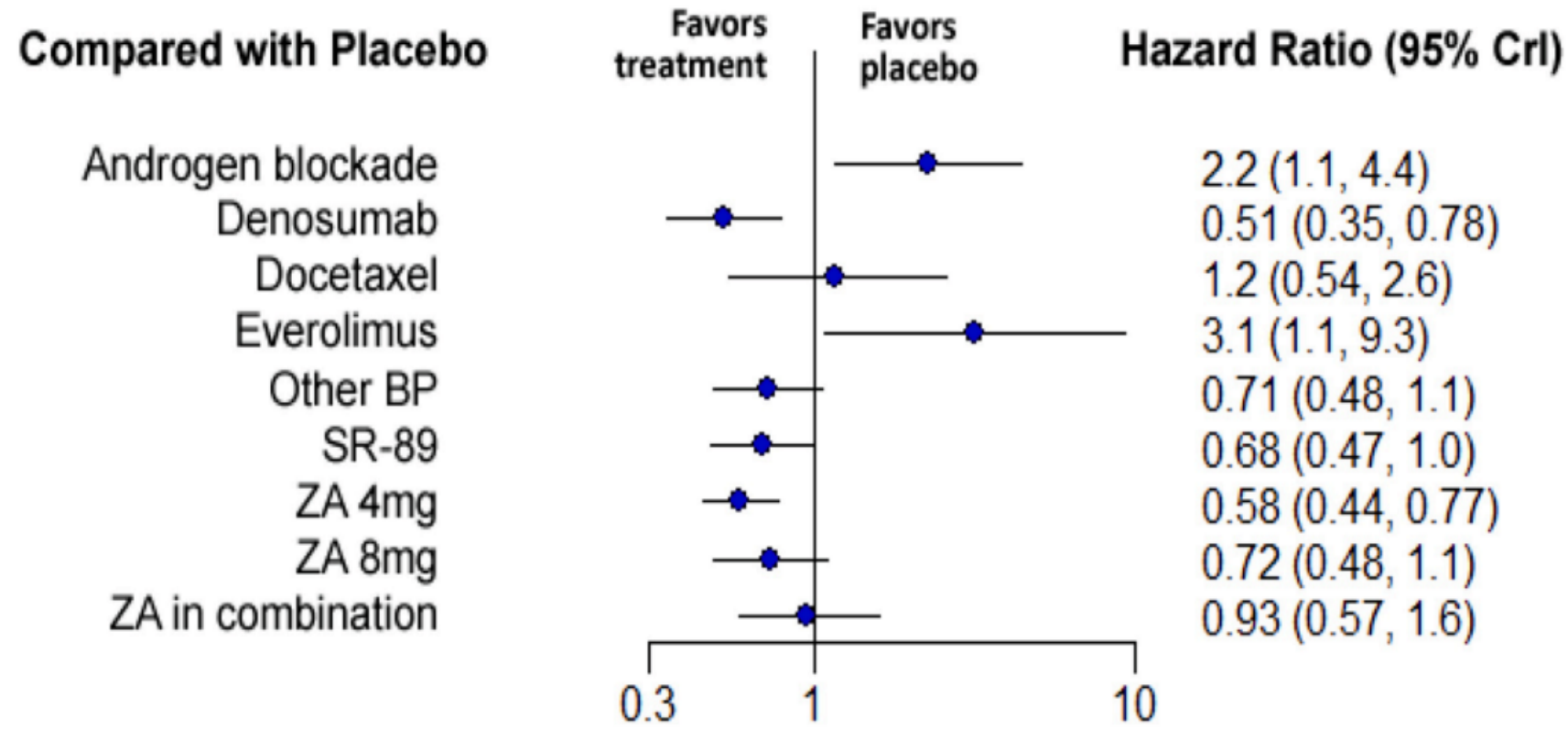

Fig. 4. Forest plot of the relative effectiveness of the different therapies to modify the time to develop a first SRE when compared to placebo. On the left, the different therapies are labelled. On the right, the hazard ratios corresponding to each therapy when compared to placebo are represented. In parenthesis, the 95 % credible intervals are shown. BP = Bisphosphonate, ZA = Zoledronic Acid, SR-89 = Strontium-89, CrI = Credible Intervals.

Sobrevida libre de progresión

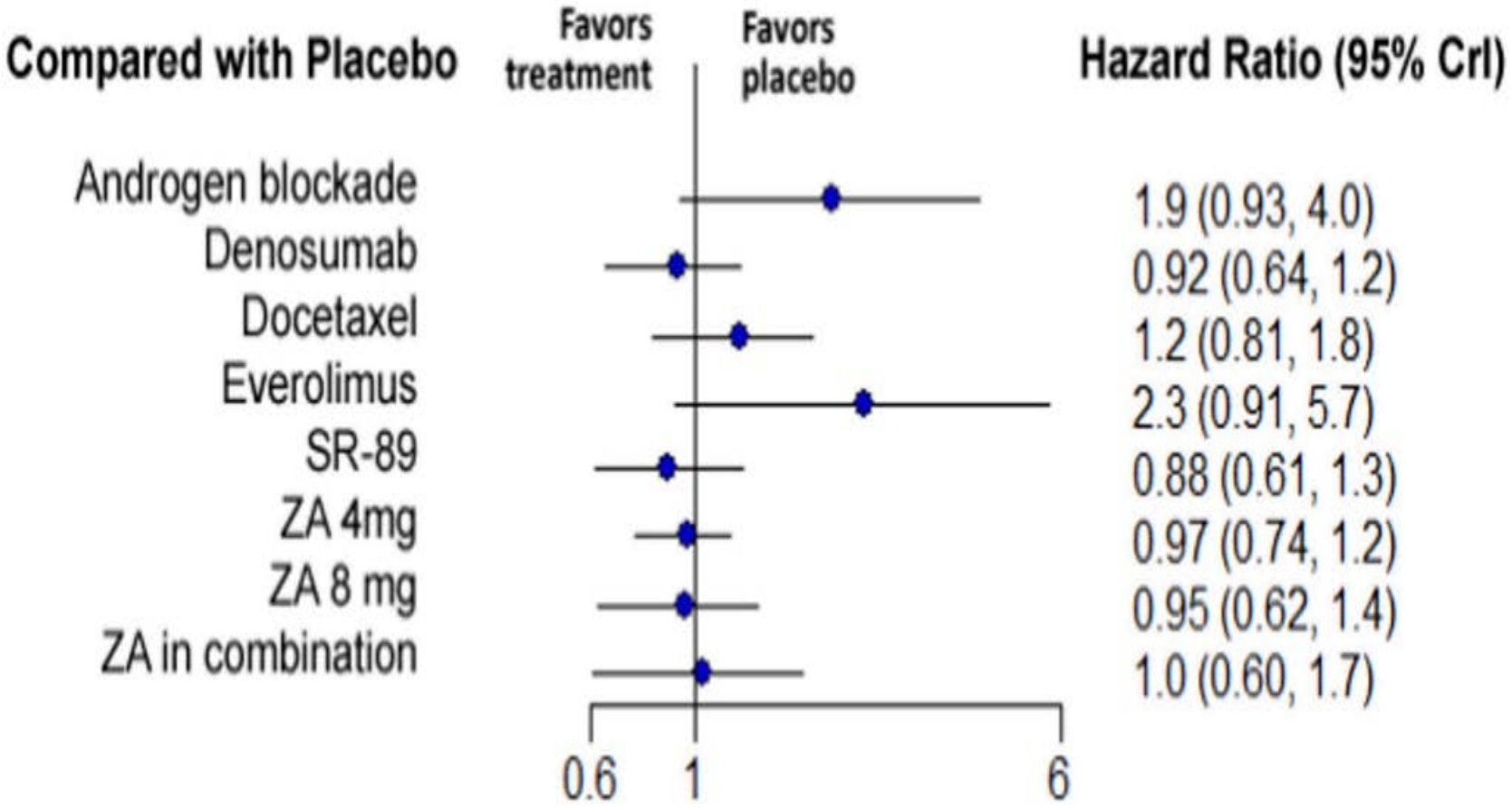

Fig. 5. Forest plot of the relative effectiveness of the different therapies for progression-free survival when compared to placebo. On the left, the different therapies are labelled. On the right, the hazard ratios corresponding to each therapy when compared to placebo are represented. In parenthesis, the 95 % credible intervals are shown. ZA = Zoledronic Acid, SR-89 = Strontium-89, CrI = Credible Intervals.

Sobrevida general

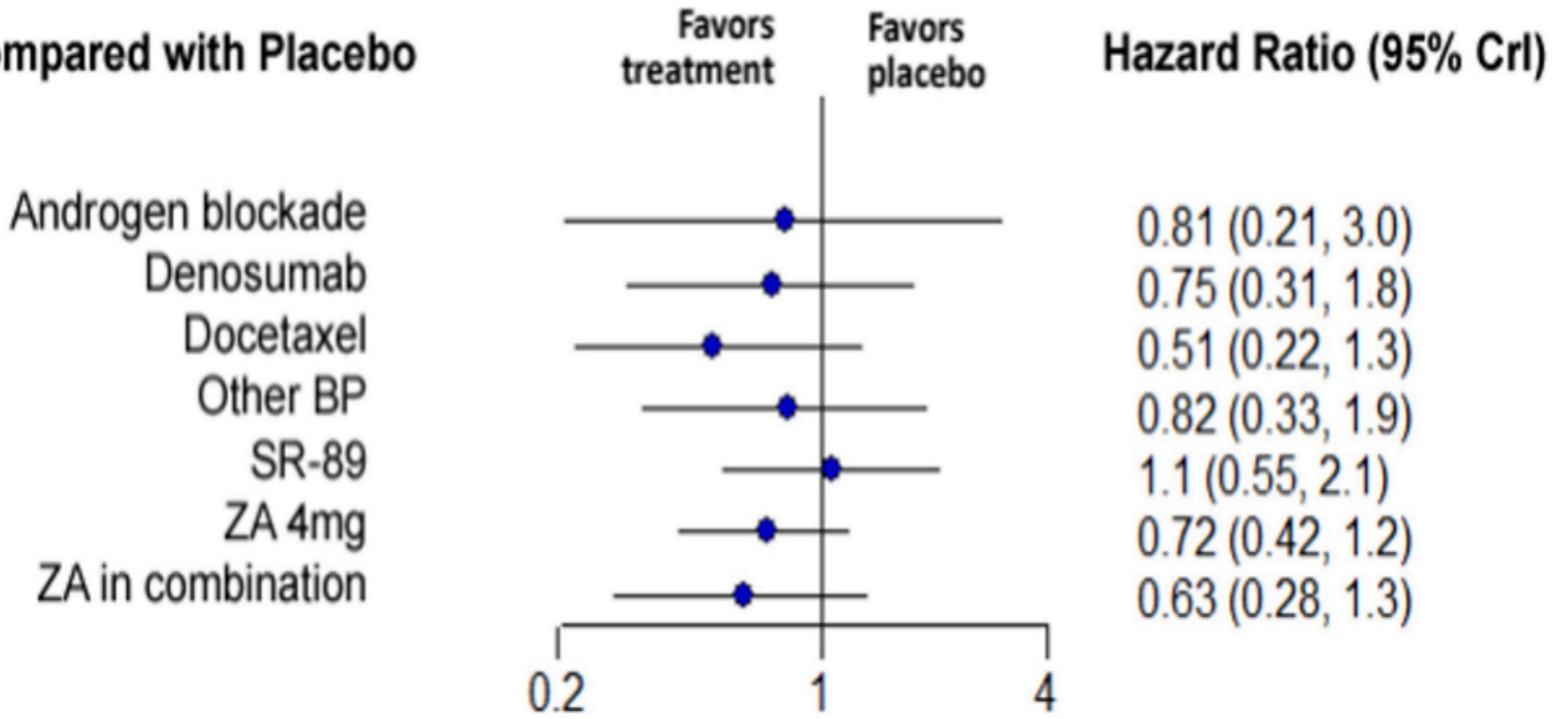

Fig. 6. Forest plot of the relative effectiveness of the different therapies for overall survival when compared to placebo. On the left, the different therapies are labelled. On the right, the hazard ratios corresponding to each therapy when compared to placebo are represented. In parenthesis, the 95 % credible intervals are shown. BP = Bisphosphonate, ZA = Zoledronic Acid, SR-89 = Strontium-89, CrI = Credible Intervals .

Modificación del Dolor

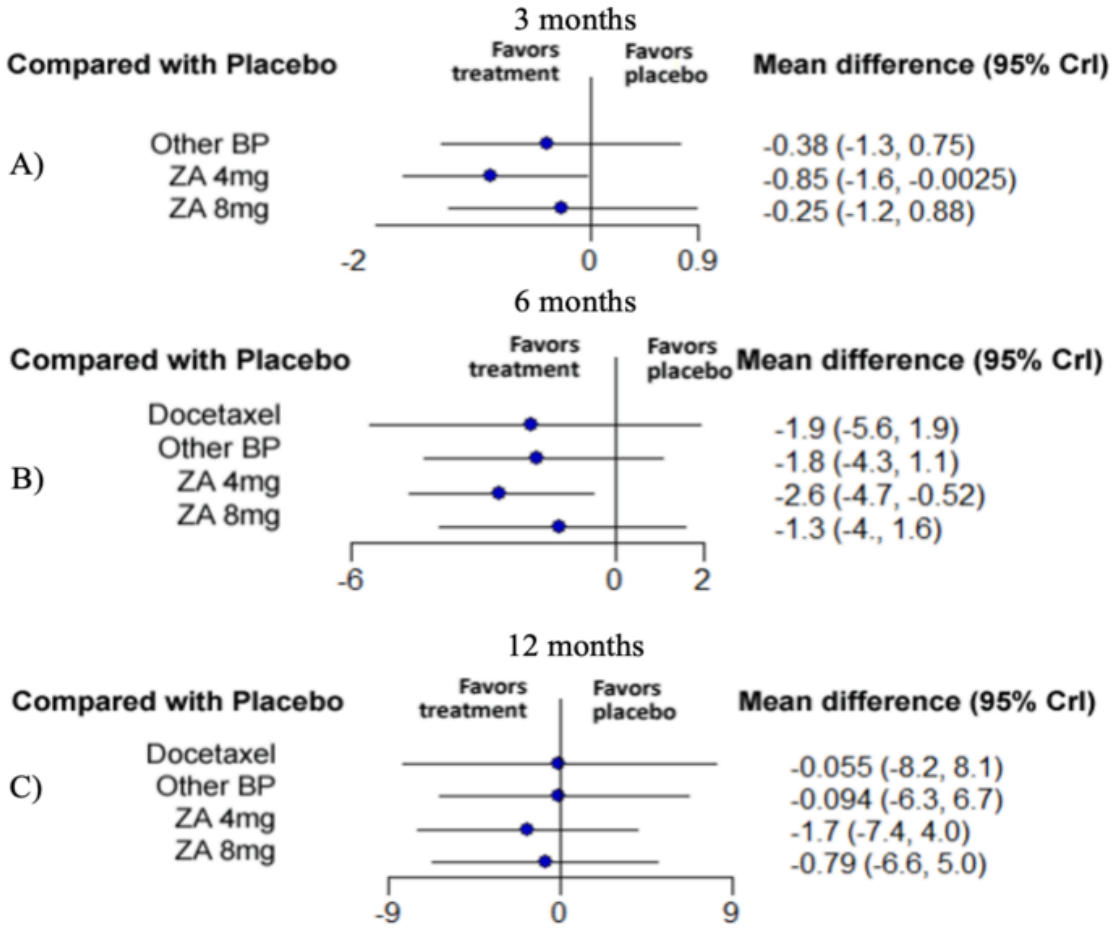

Fig. 7. Forest plot of the relative effectiveness of the different therapies to modify pain BPI/VAS scores when compared to placebo at A) 3 months, B) 6 months and C) 12 months. On the left, the different therapies are labelled. On the right, the standardized mean difference corresponding to each therapy when compared to placebo is represented. In parenthesis, the 95 % credible intervals are shown. BP = Bisphosphonate, ZA = Zoledronic Acid, CrI = Credible Intervals.

Conclusiones

- El uso de 4 mgs de acido zoledrónico cada 3-4 meses:

- Redujo la incidencia de nuevos ERE
- Aumentó el tiempo de aparición de un ERE
- Produjo disminución del dolor a corto y mediano plazo
- La mayor efectividad en reducir la incidencia de ERE fue en combinación con quimioterapia o terapia hormonal
- Desafortunadamente ningún tratamiento mostró un aumento estadísticamente significativo de la sobrevida en general ni de la sobrevida libre de progresión de la enfermedad comparado con placebo..

Wilson *et al. BMC Cancer* (2015) 15:55
DOI 10.1186/s12885-015-1066-7

BMC Cancer

RESEARCH ARTICLE Open Access

The differential anti-tumour effects of zoledronic acid in breast cancer – evidence for a role of the activin signaling pathway

Caroline Wilson[1*], Penelope Ottewell[2], Robert E Coleman[1] and Ingunn Holen[1]

- Estudios in vitro han mostrado efectos antitumorales del Acido zoledrónico: reduce la adherencia, migración e invasión de células tumorales además de inducir la apoptosis
- La Activina A es una proteína producida por las células del cáncer de mama e inhibe su proliferación
- La folistatina es un antagonista paracrino de la Activina, al unirse a la Activina previene la unión de ésta a su receptor y de esta manera se promueve la proliferación celular.

Vía de la señalización de la Activina

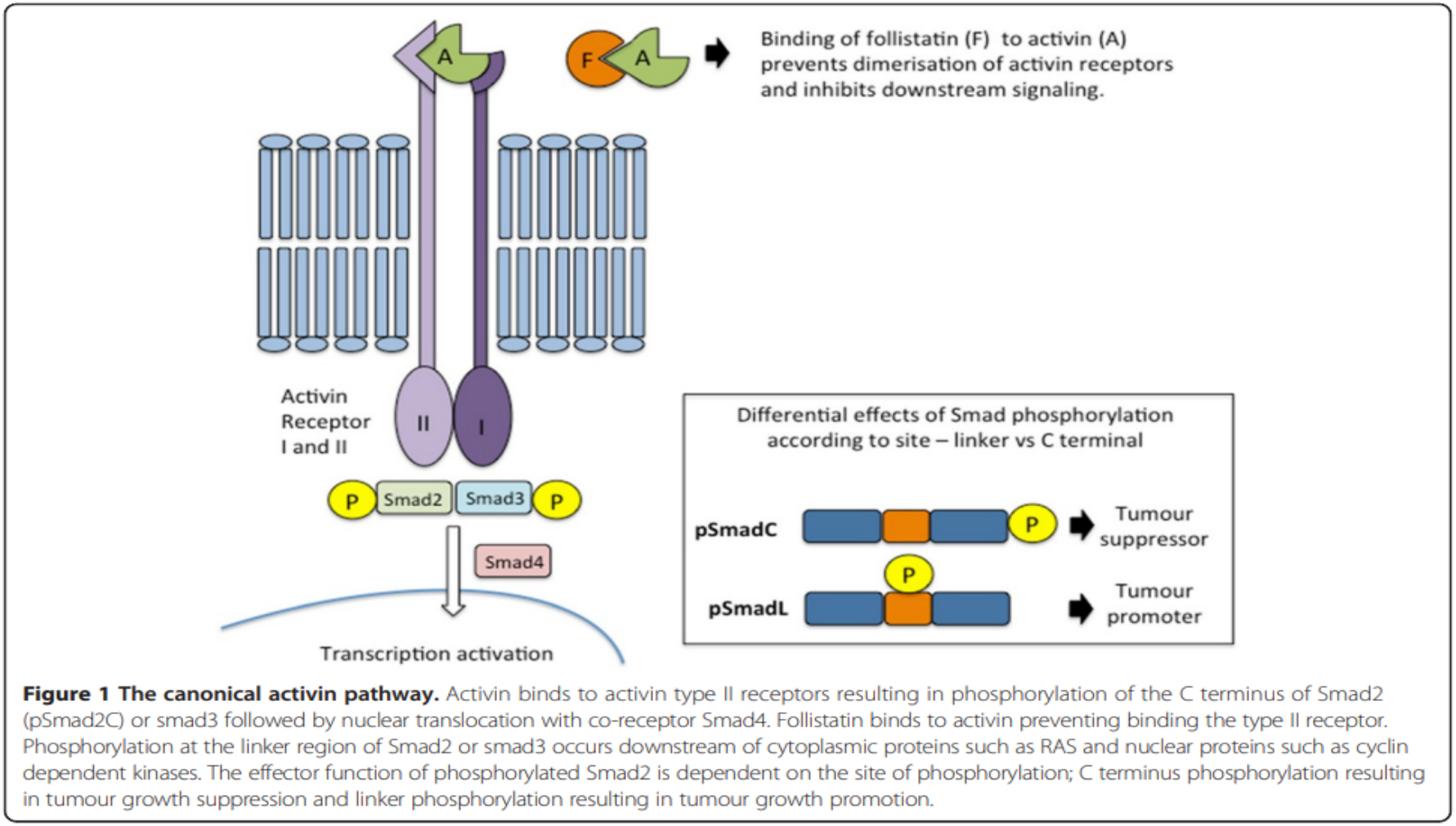

Figure 1 The canonical activin pathway. Activin binds to activin type II receptors resulting in phosphorylation of the C terminus of Smad2 (pSmad2C) or smad3 followed by nuclear translocation with co-receptor Smad4. Follistatin binds to activin preventing binding the type II receptor. Phosphorylation at the linker region of Smad2 or smad3 occurs downstream of cytoplasmic proteins such as RAS and nuclear proteins such as cyclin dependent kinases. The effector function of phosphorylated Smad2 is dependent on the site of phosphorylation; C terminus phosphorylation resulting in tumour growth suppression and linker phosphorylation resulting in tumour growth promotion.

Activina inhibe proliferación celular

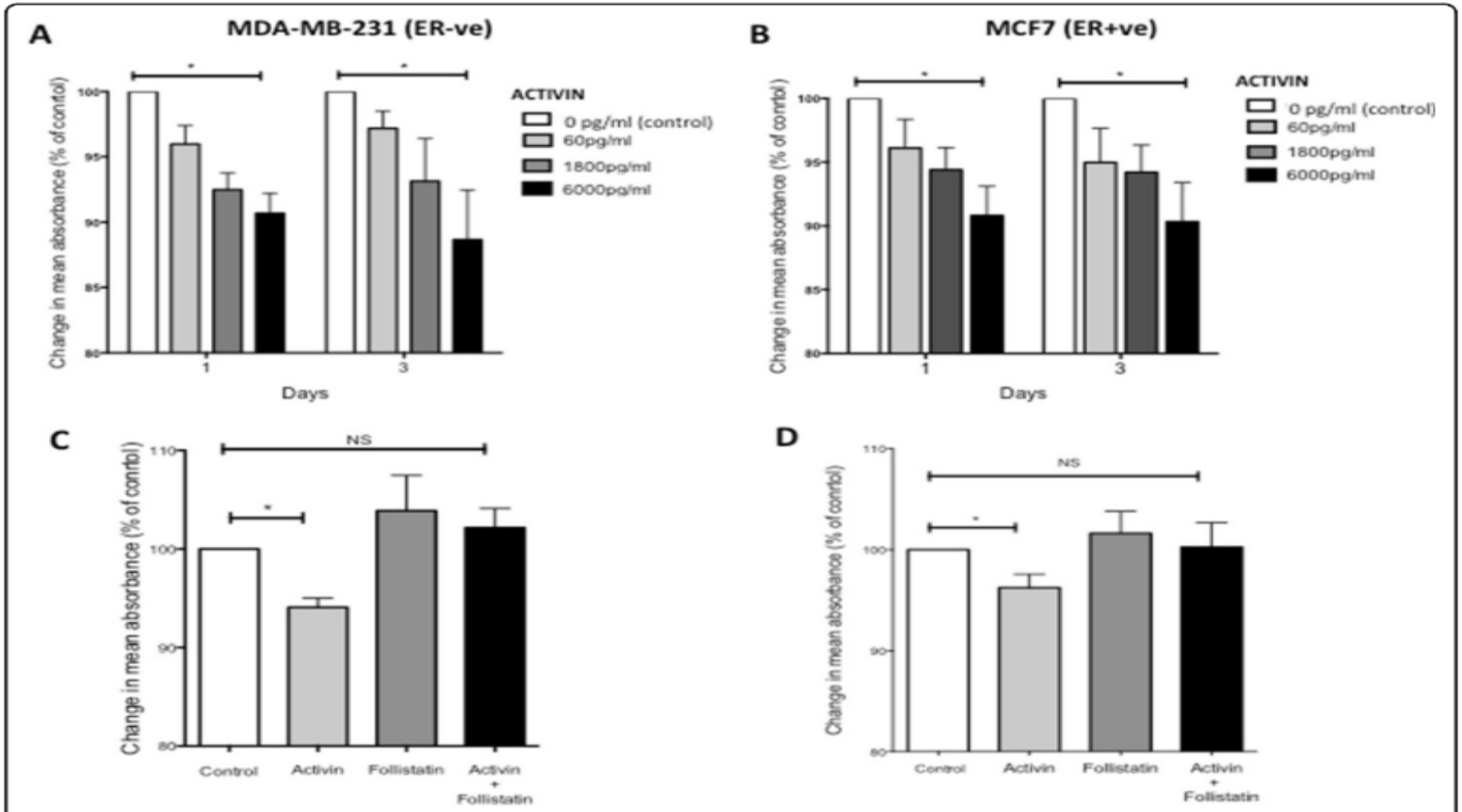

Figure 2 Activin inhibits breast cancer cell proliferation. MDA-MB −231 **(A + C)** and MCF7 **(B + D)** cells were treated with increasing doses of activin in a timecourse experiment **(A + B)**, or with recombinant activin (6000 pg/ml) +/− follistatin (64,000 pg/ml) for 72 hours **(C + D)**. 20 μl of MTS solution was added 4 hours prior to the final time points to evaluate absorbance of treated cells relative to control untreated cells. Data represents mean + SEM of 8 replicates and 5 repeats. Wilcoxon Signed-Rank test for significance, *p value <0.05, NS not significant.

Secreción de Activina y Folistatina

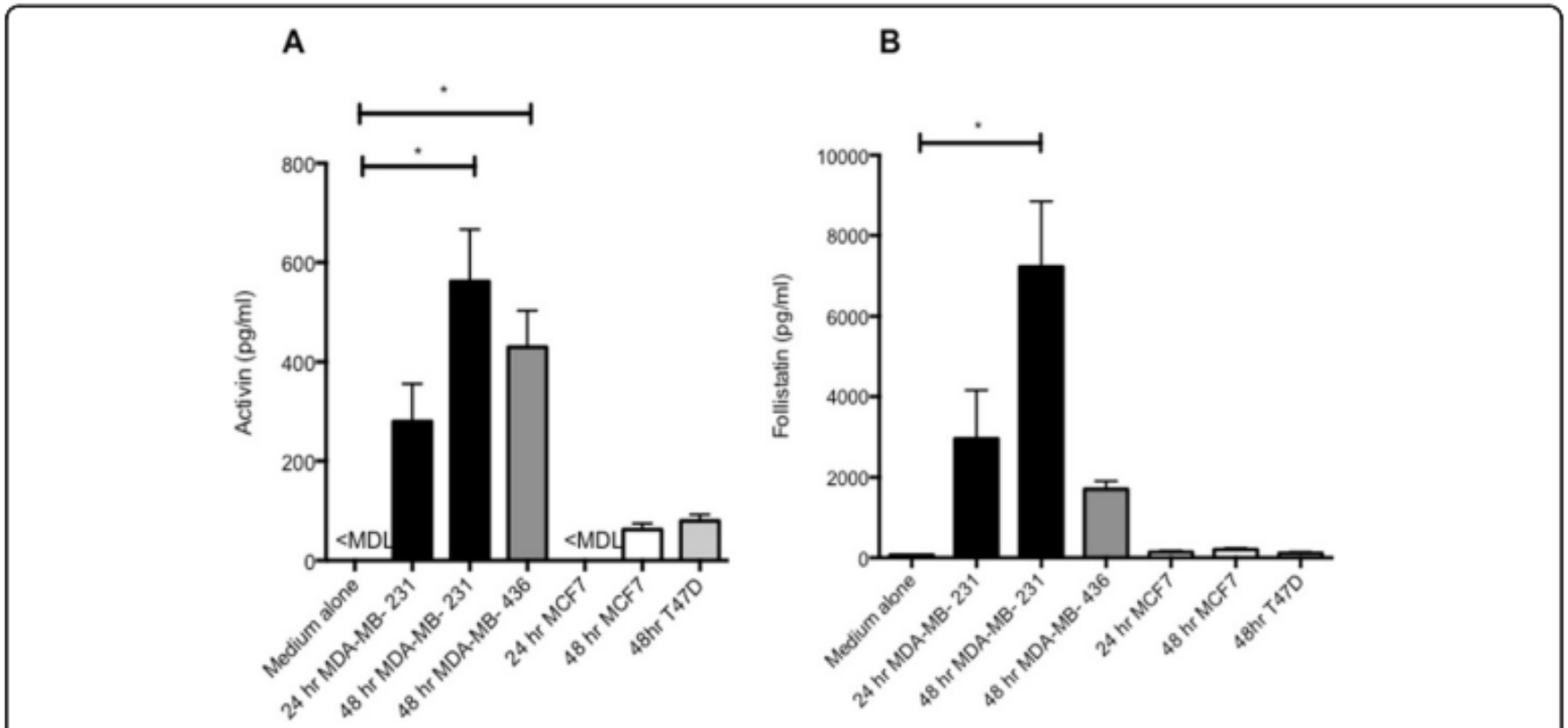

Figure 3 Activin and follistatin secretion from ER- breast cancer cell lines and ER + ve breast cancer cell lines. $1x10^5$ MDA-MB-231 or MDA-MB-436 (ER-ve) and $4x10^5$ MCF7 or T47D (ER + ve) cell lines were plated in 6 well plates and levels of Activin **(A)** and follistatin **(B)** in the medium determined by ELISA at 24 and 48 hours. Data represents 3 replicates and 3 repeats. Mann Whitney test for significance comparing wells with cells to media alone (no cells), *p value <0.05. <MDL = below assay minimum detection limit.

Efectos del Acido Zoledrónico en proliferación celular

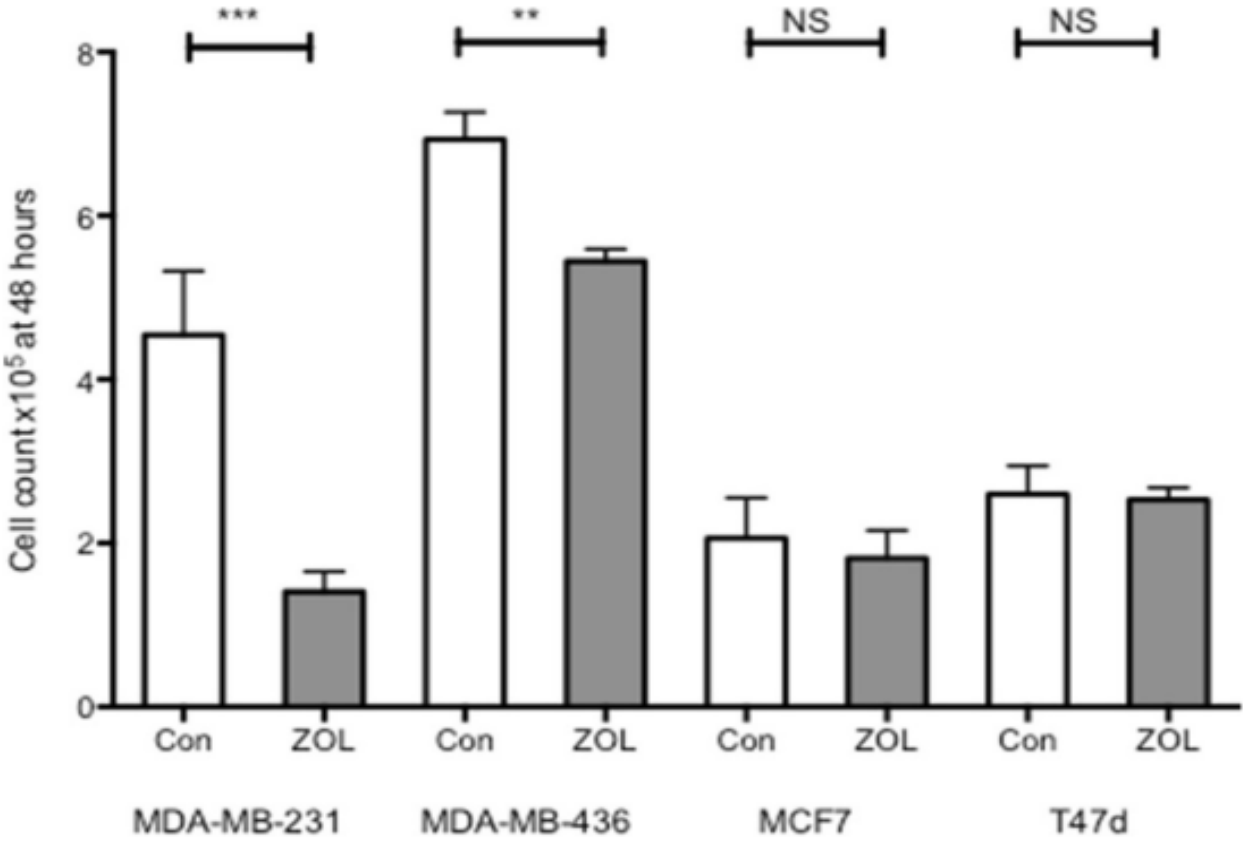

Figure 4 Effects of zoledronic acid on proliferation of ER + ve and ER-ve cell lines. $1x10^5$ MDA-MB-231, MDA-MB-436 (ER-ve),MCF7 or T47D (ER + ve) cell lines were plated in 6 well plates. Cell were treated for 48 hours with medium +/− 50 μM ZOL. At 48 hours viable cell count was performed using trypan blue. Data represents 3 replicates and 3 repeats. Mann Whitney test for significance comparing control with ZOL treated, NS not significant, **p value < 0.005, ***p value <0.0005.

Efectos del Acido Zoledrónico en la secreción de folistatina

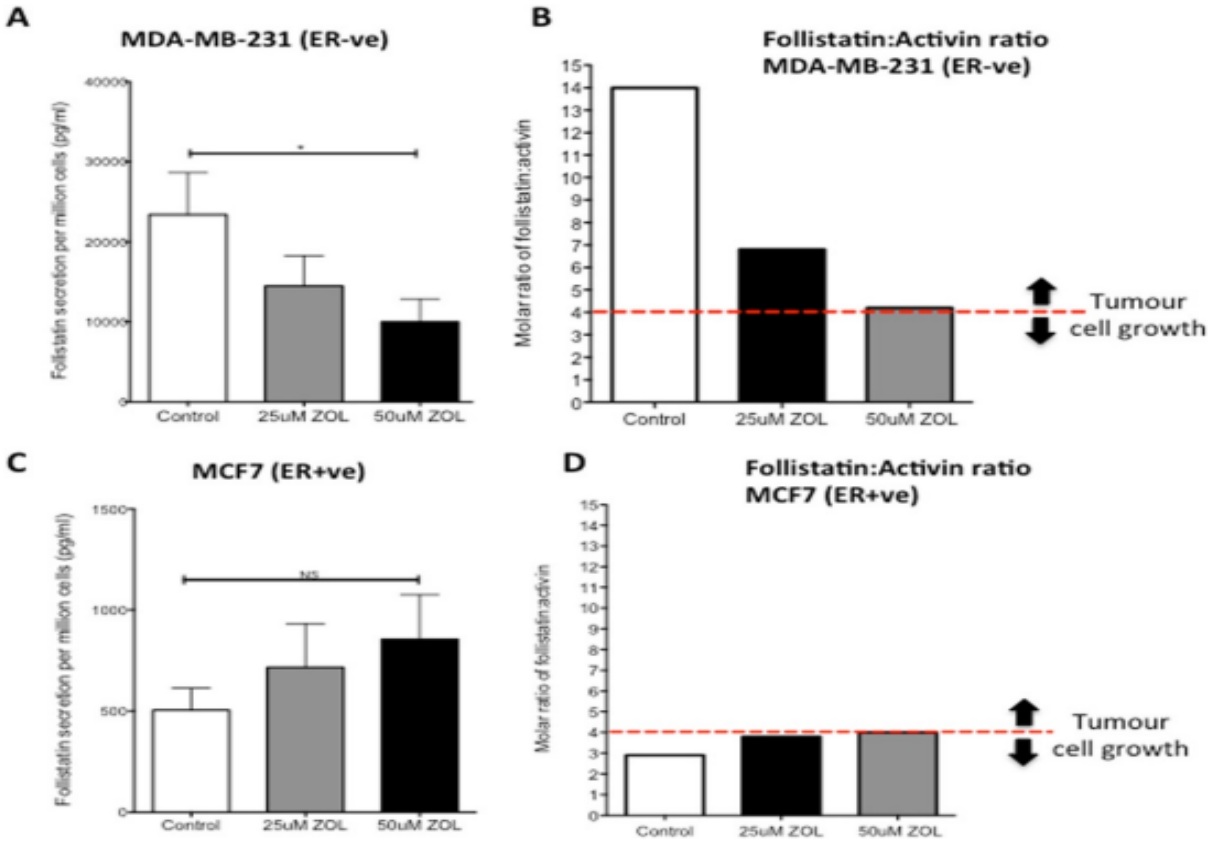

Figure 5 Effects of zoledronic acid on follistatin secretion and follistatin:activin ratio. MDA-MB-231 **(A)** and MCF7 **(C)** cells were treated with medium alone, 25 μM or 50 μM ZOL for 48 hours and levels of secreted activin and follistatin measured by ELISA. Molar ratio of follistatin: activin **(B + D)** was calculated by converting mean quantity of secreted protein per million cells (pg/ml) to pmol/l by dividing by the molecular weight of each protein, and then expressed as a ratio. A molar ratio of 4 (dashed line) represents the level at which activin is neutralised by follistatin: an excess of follistatin:activin increases tumour growth (above dashed line). Data represents mean + SEM of 3 replicates and 3 repeats, *= p value <0.05, NS not significant.

Zol afecta fosforilación de Smad en terminal C y región Linker según RE

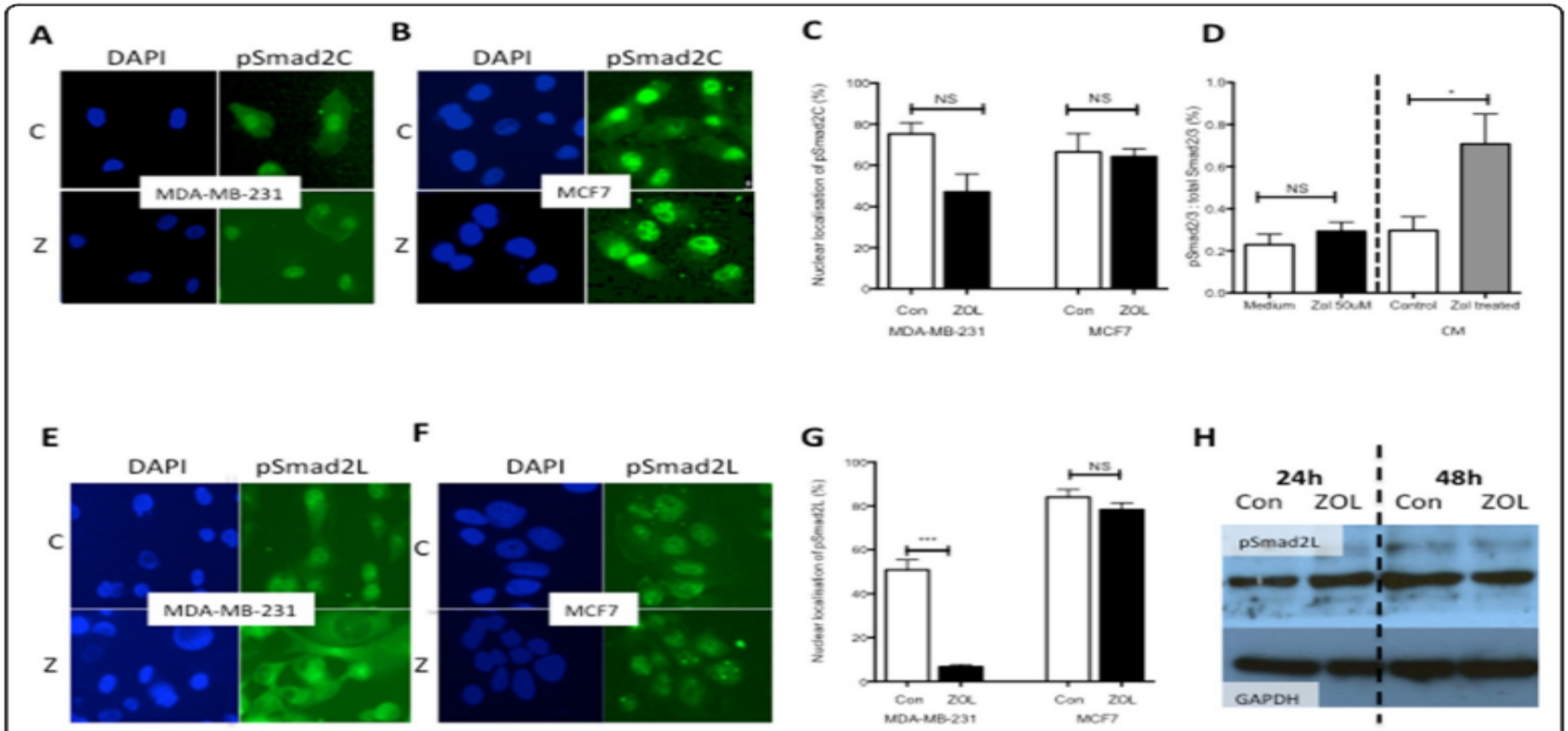

Figure 7 Smad2 phosphorylation at both c terminus and linker region is differentially affected by zoledronic acid according to ER status of breast cancer cells. A + B Representative immunofluorescent images of pSmad2C (green) and dapi staining (blue) in MDA-MB-231 cells **(A)** and MCF7 cells **(B)** treated with medium alone (C) or ZOL (Z) for 48 hours. **C**. Quantification of nuclear localisation of pSmad2C in MDA-MB-231 and MCF7 cells treated for 48 hours with medium alone (con) or ZOL (50 μM). Data represents minimum 100 cells per group, Mann Whitney U test for significance, NS = not significant **D**. Ratio of total cellular quantity of total Smad2/3 to pSmad2/3 in MDA-MB-231 cells treated for 1 hour with medium alone, ZOL (50 μM) or conditioned medium (CM) from MDA-MB-231 cells previously treated with ZOL (50 μM) or medium (control). Data represents 3 replicates and 3 repeats, Mann Whitney U test for significance, NS = not significant, *p = <0.05 **E + F** Representative immunofluorescent images of pSmad2L (green) and dapi staining (blue) in MDA-MB-231 cells **(E)** and MCF7 cells **(F)** treated with medium alone (C) or ZOL (Z) for 48 hours. **G**. Quantification of nuclear localisation of pSmad2L in MDA-MB-231 and MCF7 cells treated for 48 hours with medium alone (con) or ZOL (50 μM). Data represents minimum 100 cells per group, Mann Whitney U test for significance, NS = not significant, ***p value <0.001. **H**. Representative western blots for cellular quantity of pSmad2L and gapdh in MDA-MB-231 cells treated with medium alone (con) or ZOL (50 μm).

Cambios en la expresión de folistatina y pSmad2L in vivo

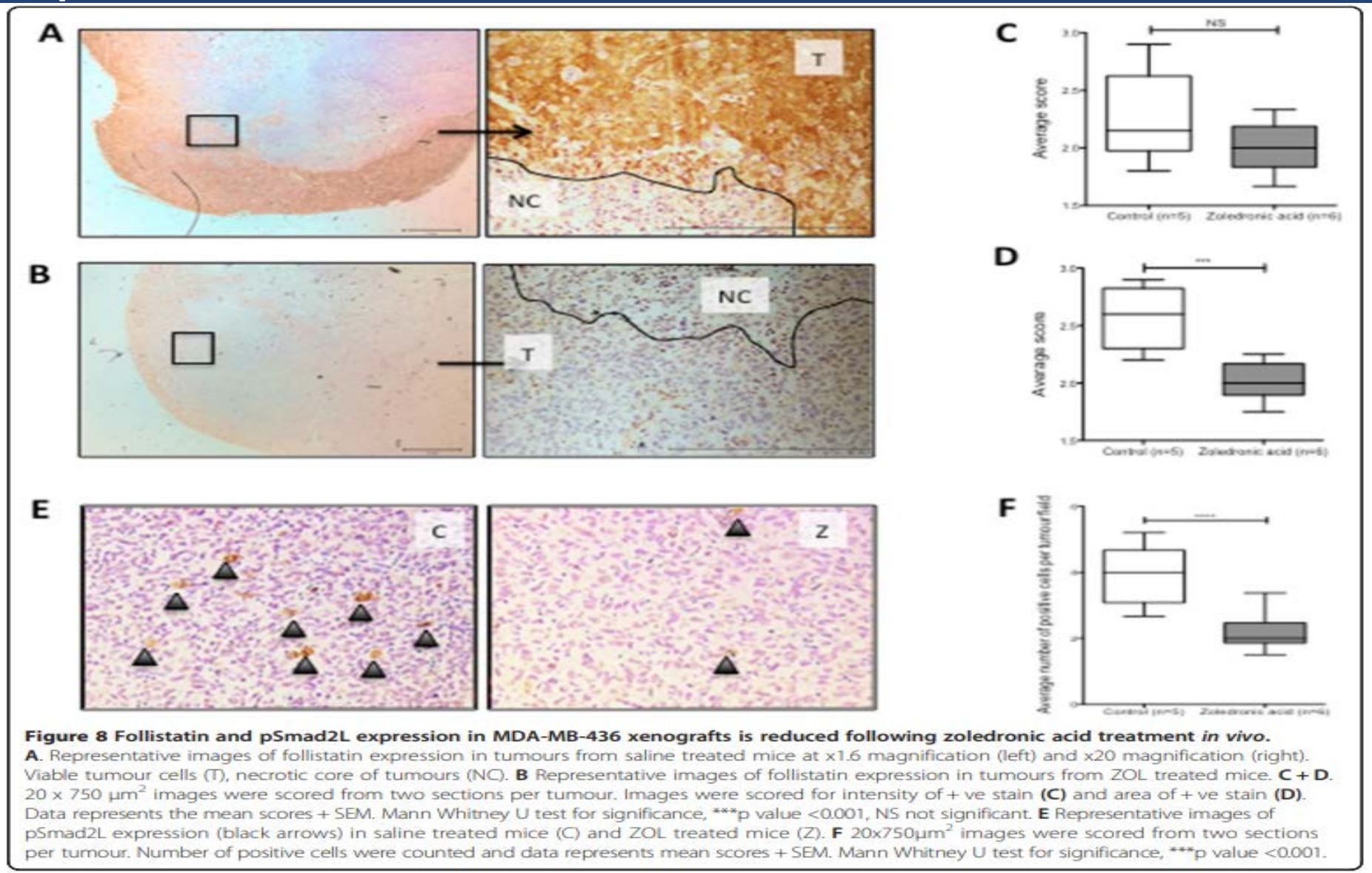

Figure 8 Follistatin and pSmad2L expression in MDA-MB-436 xenografts is reduced following zoledronic acid treatment *in vivo*. **A**. Representative images of follistatin expression in tumours from saline treated mice at x1.6 magnification (left) and x20 magnification (right). Viable tumour cells (T), necrotic core of tumours (NC). **B** Representative images of follistatin expression in tumours from ZOL treated mice. **C + D**. 20 x 750 μm^2 images were scored from two sections per tumour. Images were scored for intensity of + ve stain **(C)** and area of + ve stain **(D)**. Data represents the mean scores + SEM. Mann Whitney U test for significance, ***p value <0.001, NS not significant. **E** Representative images of pSmad2L expression (black arrows) in saline treated mice (C) and ZOL treated mice (Z). **F** 20x750μm^2 images were scored from two sections per tumour. Number of positive cells were counted and data represents mean scores + SEM. Mann Whitney U test for significance, ***p value <0.001.

Conclusiones

- Los datos respaldan un mecanismo de acción dual del ácido zoledrónico en la vía de señalización de la Activina en células de cáncer de mama RE –
- Principalmente a través de la disminución de la secreción de folistatina dando lugar a un aumento en el supresor de tumor pSmad2C y secundariamente vía la disminución de la localización nuclear del promotor tumoral pSmad2L
- Esta data entrega un posible nuevo mecanismo directo antiproliferativo de acción del Acido Zoledrónico en células de cáncer de mama involucrando la señalización de la activina

ASCO special articles

Use of Adjuvant Bisphosphonates and Other Bone-Modifying Agents in Breast Cancer: ASCO-OH (CCO) Guideline Update

Andrea Eisen, MD[1]; Mark R. Somerfield, PhD[2]; Melissa K. Accordino, MD[3]; Phillip S. Blanchette, MD[4]; Mark J. Clemons, MD[5]; Sukhbinder Dhesy-Thind, MD[6]; Melissa S. Dillmon, MD[7]; Stella D'Oronzo, MD, PhD[8]; Glenn G. Fletcher, MSc[9]; Elizabeth S. Frank, EdM[10]; Sigrun Hallmeyer, MD[11]; Issam Makhoul, MD[12]; Beverly Moy, MD[13]; Alia Thawer, MD[1]; Joy Y. Wu, MD, PhD[14]; and Catherine H. Van Poznak, MD[15]

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Philip J. Saylor, MD[1]; R. Bryan Rumble, MSc[2]; Scott Tagawa, MD, MS[3]; James A. Eastham, MD[4]; Antonio Finelli, MD, MSc[5]; Pavan S. Reddy, MD[6]; Terry M. Kungel, MBA[7]; Merel G. Nissenberg, JD[8]; and Jeff M. Michalski, MBA, MD[9]

reviews

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Adjuvant bisphosphonates in early breast cancer: consensus guidance for clinical practice from a European Panel

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Treating Prostate Cancer

Last Revised: June 10, 2020

Treatments for Prostate Cancer Spread to Bones

If prostate cancer spreads to other parts of the body, it nearly always goes to the bones first. Bone metastasis[1] can be painful and can cause other problems, such as fractures (breaks), spinal cord compression (an area of cancer is pressing on the spinal cord), or high blood calcium levels, which can be dangerous or even life threatening.

If the cancer has grown outside the prostate, preventing or slowing the spread of the cancer to the bones is a major goal of treatment. If the cancer has already reached the bones, controlling or relieving pain and other complications is also a very important part of treatment.

Treatments such as hormone therapy, chemotherapy, and vaccines may help with this, but other treatments specifically target bone metastasis and the problems it may cause.

Conclusiones

- Las metástasis óseas son una complicación importante de los tumores
- Pueden causar dolor, fracturas y déficit neurológico y pueden deteriorar gravemente la autonomía y calidad de vida de los pacientes
- El diagnóstico precoz y el tratamiento adecuado son primordiales
- Hay tratamientos muy eficaces para reducir las complicaciones de las metástasis óseas como son los Bifosfonatos

Gracias