58 CONGRESO NACIONAL DE LA SOCIEDAD ESPAÑOLA DE FARMACIA HOSPITALARIA

De la evidencia al beneficio de los pacientes con metástasis óseas

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AMGEN®

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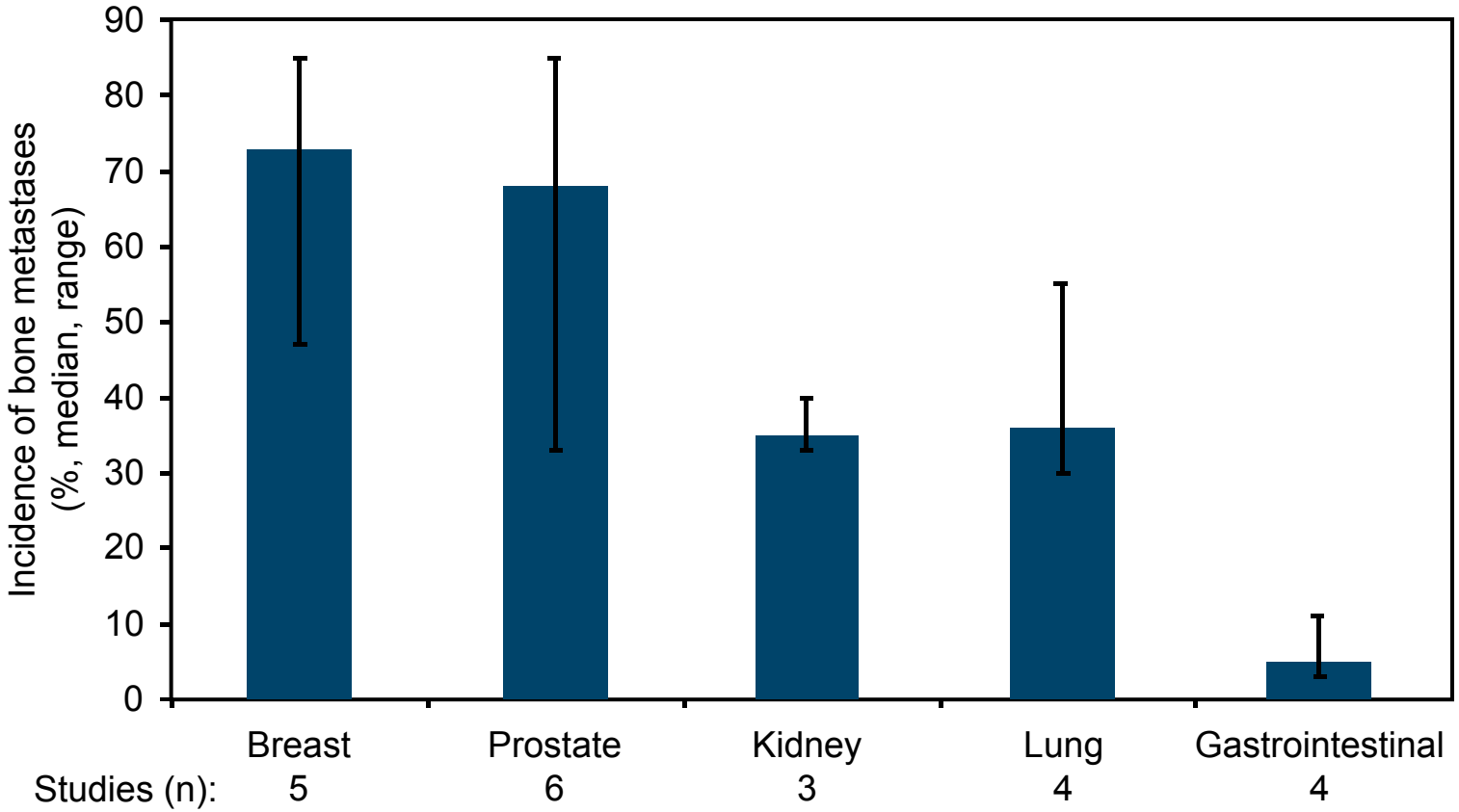
Many patients with advanced cancer develop bone metastases



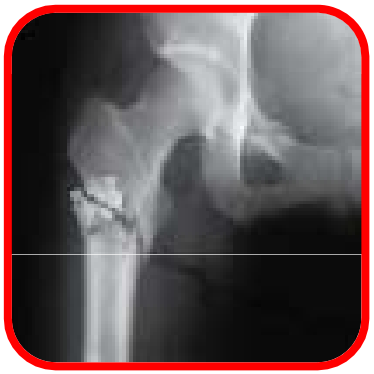
Data are median ± range;
Reported incidence may differ from clinical experience

Rubens RD, Coleman RE. Bone metastases. In: Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE, eds. Clinical oncology. New York: Churchill Livingstone, 1995:643–65.

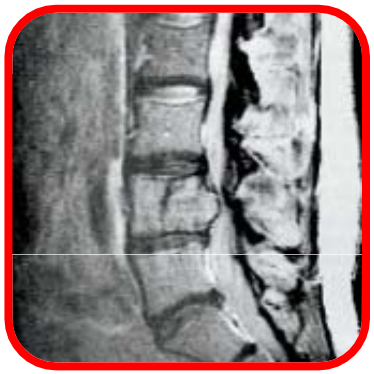
Bone metastases can result in serious and debilitating skeletal-related events (SREs)

- Since the late 1990s SREs have been defined as:[1,2]

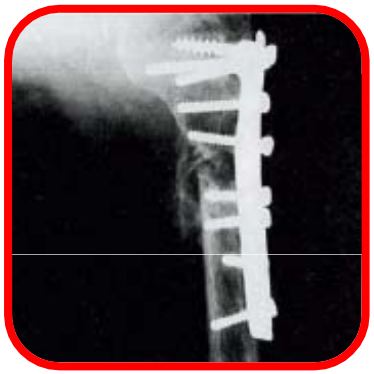
Radiation to bone



Pathological fracture



Spinal cord compression

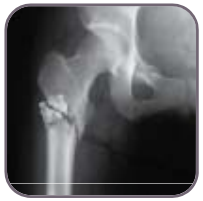


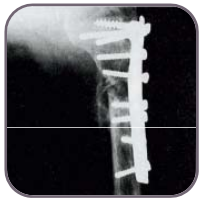
Surgery to bone

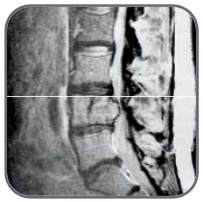
- A composite SRE endpoint is used to evaluate efficacy of bone-targeted agents for treatment of bone metastases[2]

1. Saad F et al. J Natl Cancer Inst 2004;96:879–82;
2.www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071590.pdf (Accessed 2 March 2011).

SREs have associated down-stream implications





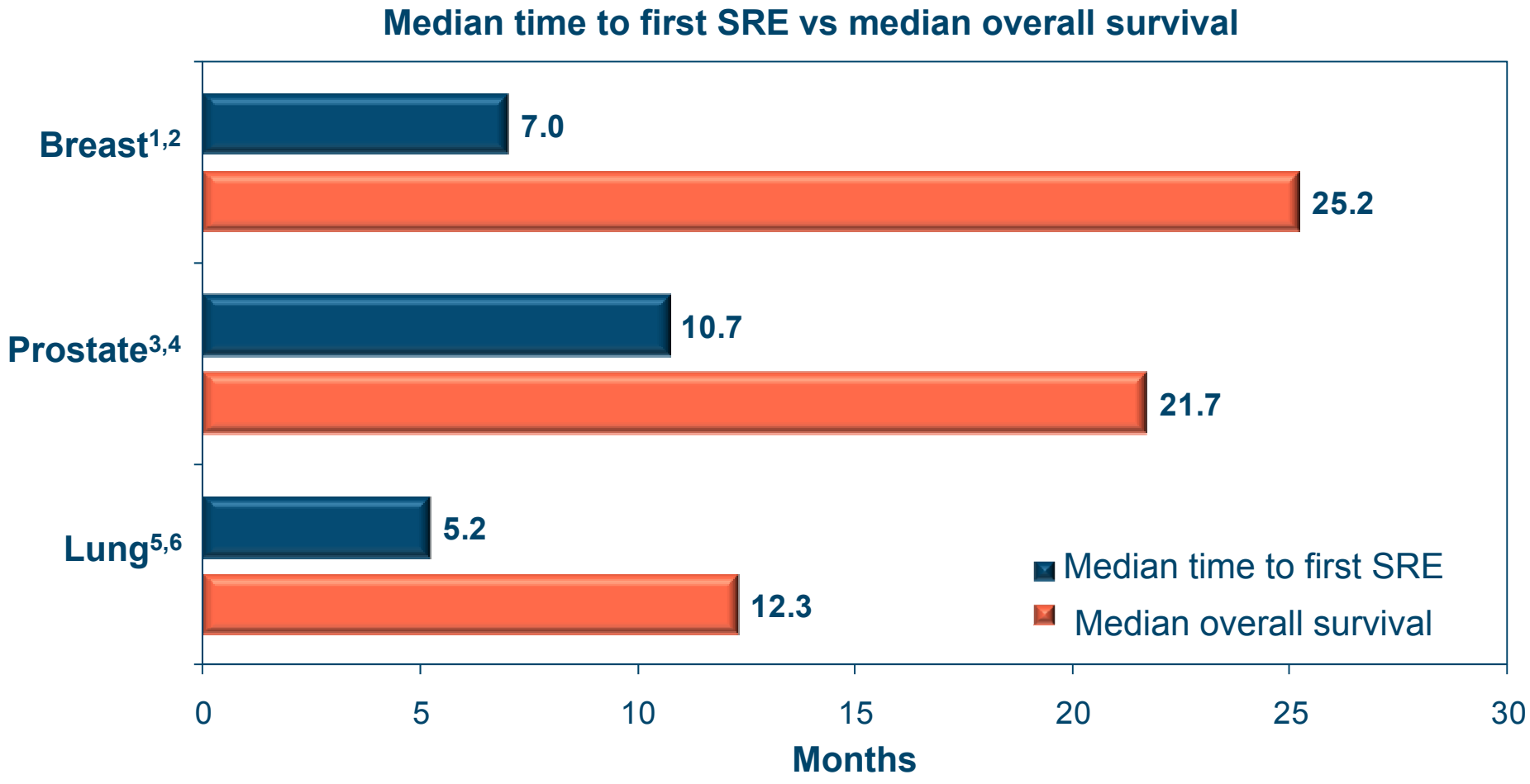


SRE	Potential complications
Pathological fracture	Extended healing time Reduced survival[1,2] Loss of mobility Need for care/ nursing home residence (especially hip fracture)[3]
Radiation to bone	Potential for 'pain flare' after therapy[4] Myelosuppression[5] Repeat visits for treating spinal cord compression[6]
Surgery to bone	Hospital stay In-hospital mortality rate ~8%[7] High rate of surgical complications[7,8] High failure rate; inability to restore function[7]
Spinal cord compression	Excruciating pain[8] Need for steroidal medications[8] Repeat visits for radiotherapy[6] Irreversible paraparesis or paraplegia[8] Loss of continence[8]

SRE: skeletal related event,

1. Gainor, Buchert. Clin Orthopaed Rel Res 1983;178:297–302; 2. Saad F et al. Cancer 2007;110:1860–7; 3. Poor et al. Osteoporos Int 1995;5:419–26; 4. Loblaw et al. Supp Care Cancer 2007;15:451–5; 5. Hellman, Krasnow. J Palliat Med 1998;1:277–83; 6. Maranzano et al. Tumori 2003;89:469–75; 7. Katzer et al. Arch Orthopaed Trauma Surg 2002;122:251–8; 8. Loblaw et al. J Clin Oncol 2005;23:2028–3.

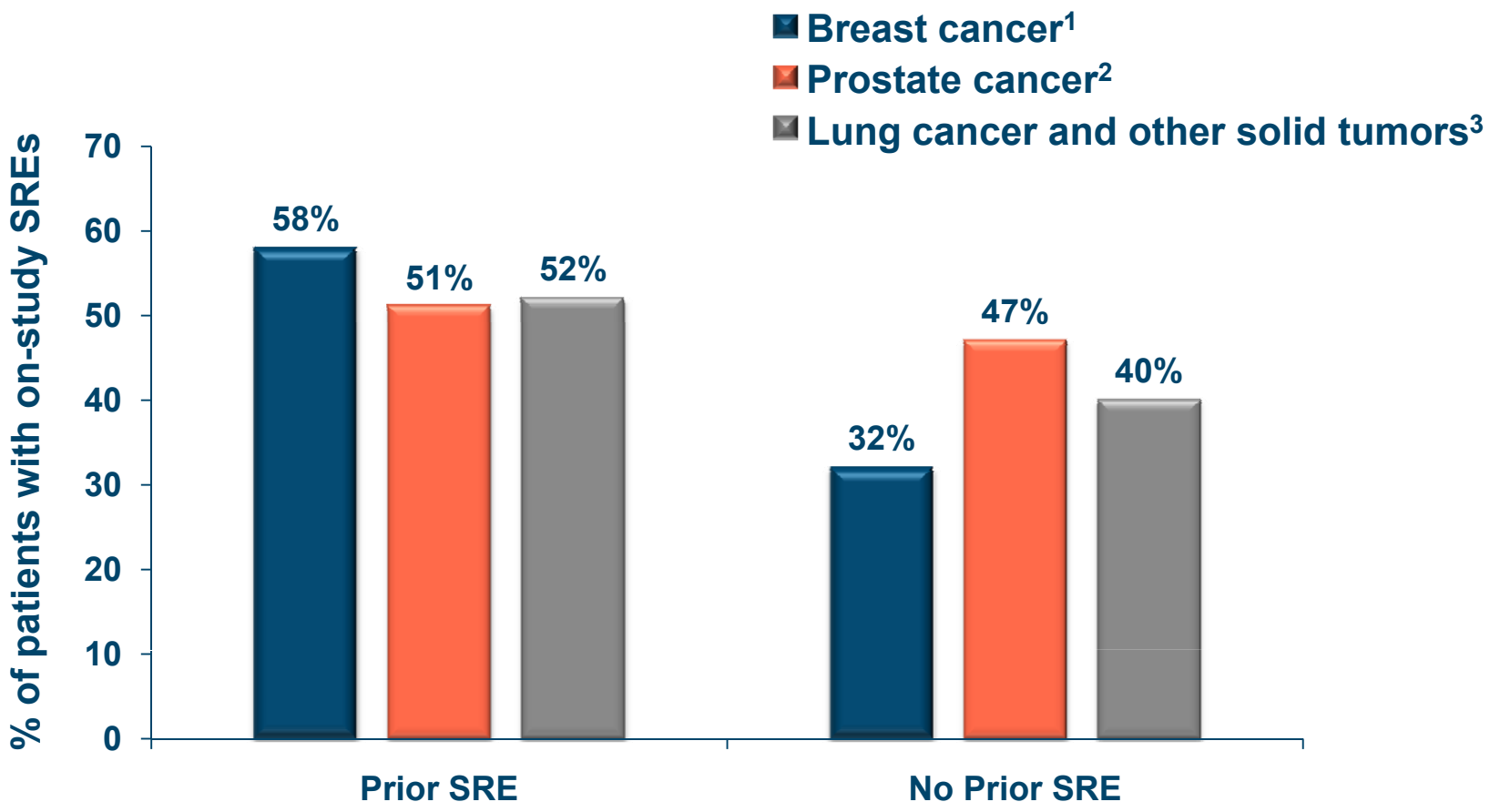
Patients have increased chances of developing SREs as survival times improve



SREs (Skeletal Related Events).

1. Lipton A, et al. Cancer 2000;88:1082–90; 2. Miller K, et al. N Engl J Med 2007;357:2666–76;
3. Saad F, et al. J Natl Cancer Inst 2002;94:1458–68; 4. Kantoff PW, et al. N Engl J Med 2010;363;411–22;
5. Rosen LS, et al. Cancer 2004;100:2613–21; 6. Sandler A, et al. N Engl J Med 2006;355:2542–50.

Prior SRE increases the risk for subsequent SREs



SRE: skeletal related event.

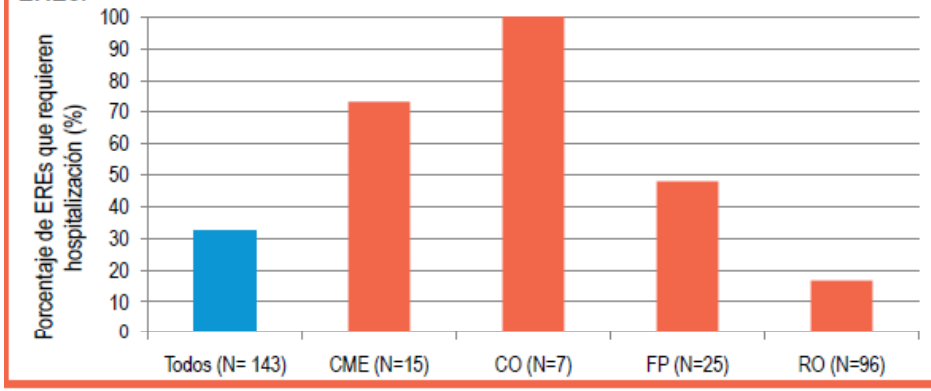
1. Kaminski M, et al. Poster presented at: ASCO Annual Meeting. June 5-8, 2004; New Orleans, LA. Abstract 857;
2. Saad F, et al. Clin Genitourin Cancer 2007;5:390–6;
3. Hirsh V, et al. Clin Lung Cancer 2004;6:170–4.

Hospitalisation rate and mean duration of inpatient stay per SRE type in Spain

A third of all SREs are associated with inpatient hospitalisation

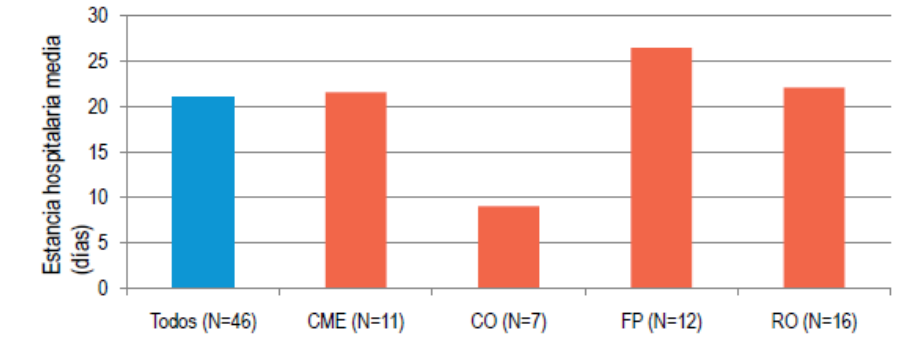
Mean duration of inpatient stays was 21 days

Figura 2. ***Porcentaje de EREs que requirieron hospitalizaciones por tipo de EREs.***



CME, compresión de la médula espinal; CO, cirugía ósea; FP, fractura patológica; RO, radioterapia ósea.

Figura 3. ***Estancia hospitalaria media por EREs****



* Excluye los EREs que no requieren hospitalización. CME, compresión de la médula espinal; CO, cirugía ósea; FP, fractura patológica; RO, radioterapia ósea.

Data from a prospective observational study to estimate costs of SREs.
SRE (skeletal related event)
Duran et al. XIII Congreso de la Sociedad Española de Oncología Médica, Málaga (España); Octubre 19-21, 2011. P-169.

SREs are associated with a considerable cost to Spanish healthcare systems

Mean costs per SRE type in solid tumours in Spain

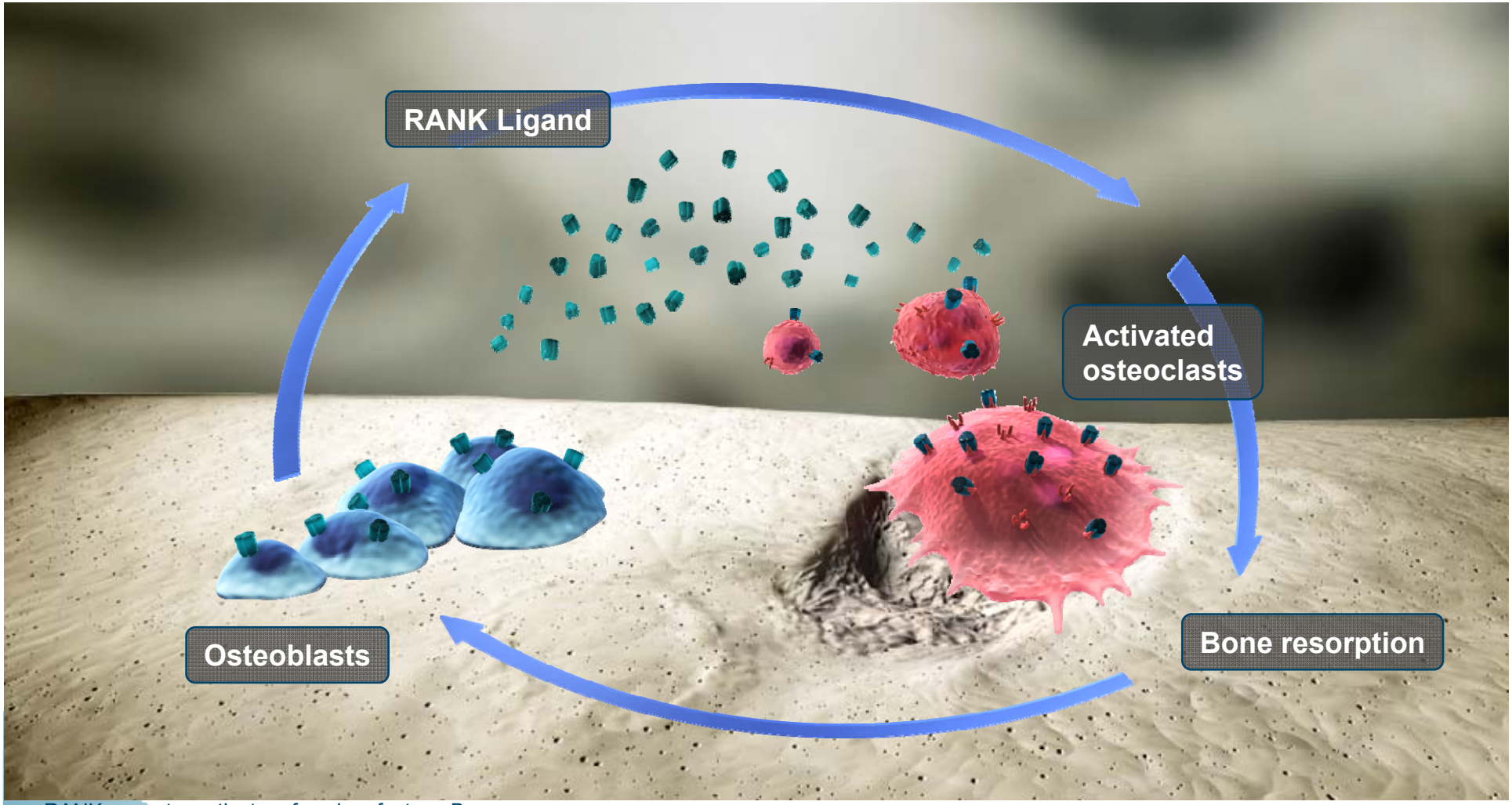
Type of SRE	Mean cost in Spain
Pathologic fracture	4.712,69 €
Radiation to bone	2.377,79 €
Spinal cord compression	7.902,62 €
Surgery to bone	4.262,67 €

Data from a prospective observational study to estimate costs of SREs.

SREs (skeletal related events)

Durán I, Garzón G, Sánchez A, et al. Clin Transl Oncol. Published online 13 August 2013. DOI 10.1007/s12094-013-1077-2.

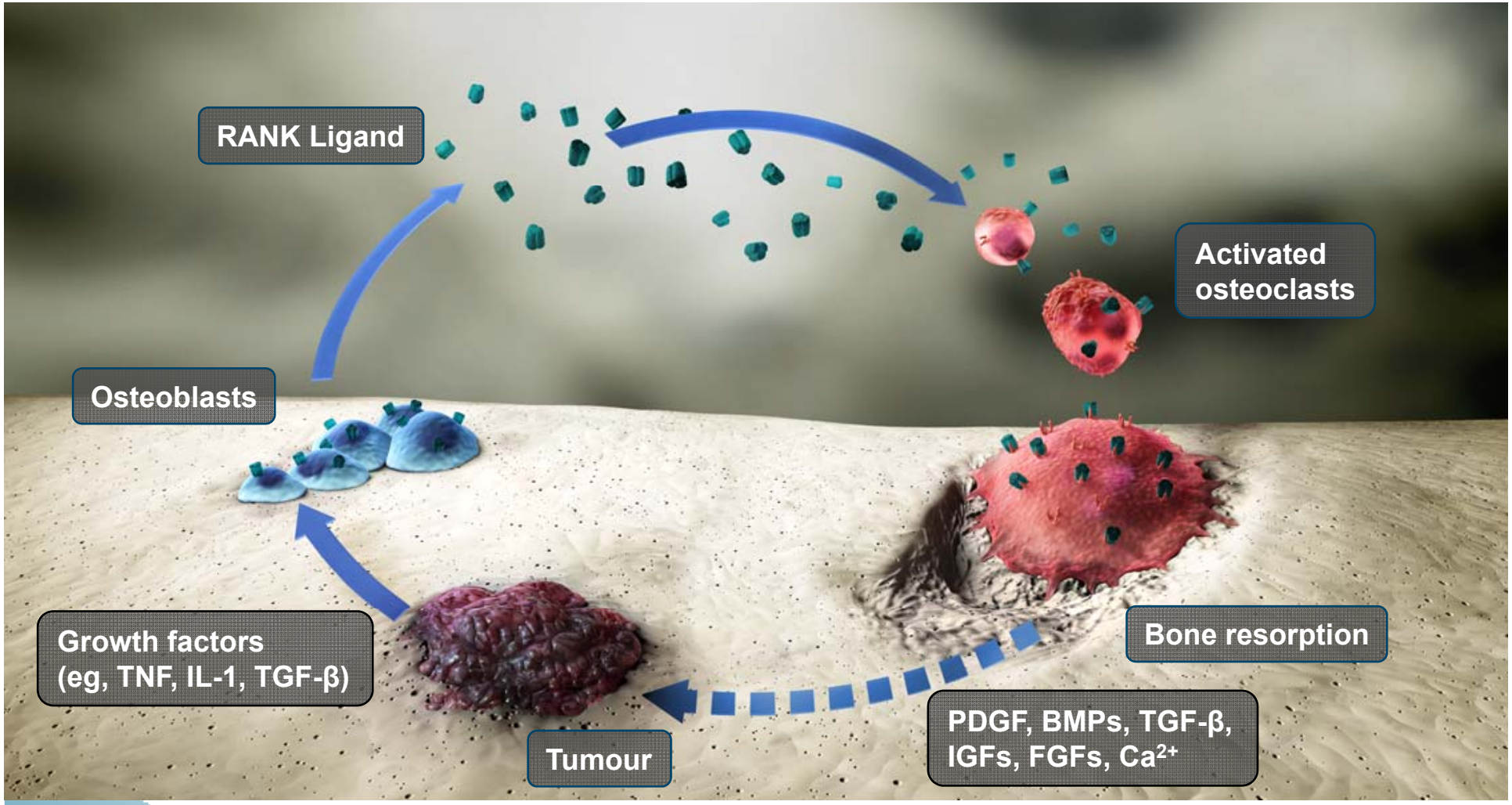
RANK Ligand is an essential mediator of osteoclast formation, function, and survival



RANK, receptor activator of nuclear factor κ B.

1. Boyle WJ, et al. Nature 2003;423:337–42;
2. Roodman GD. N Engl J Med 2004;350:1655–64.

RANK Ligand is an essential mediator of the vicious cycle of bone destruction

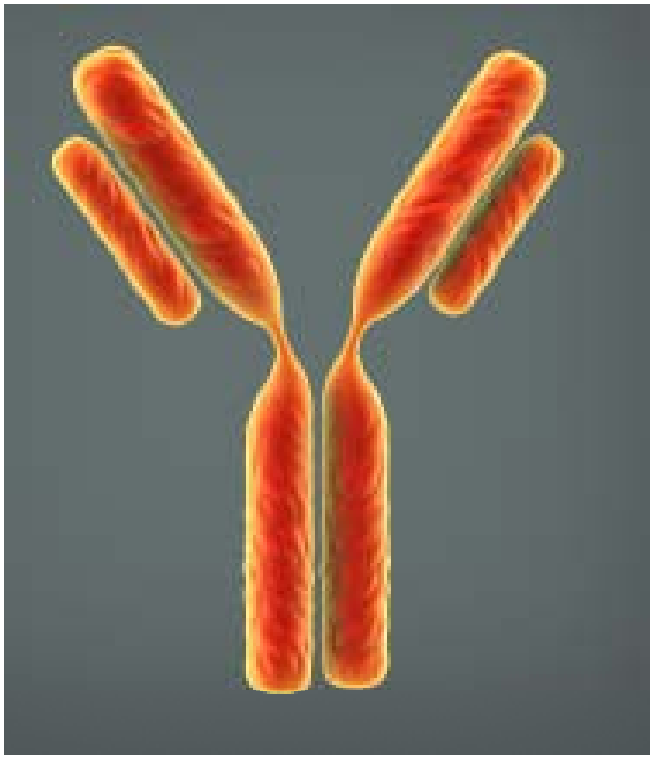


1. Boyle WJ, et al. Nature 2003;423:337–42;
2. Roodman GD. N Engl J Med 2004;350:1655–64.

BMPs=bone morphogenetic proteins; Ca^{2+}= calcium; FGF=fibroblast growth factor; IGF=insulin-like growth factor; IL=interleukin; PDGF=platelet-derived growth factor; TGF-β = transforming growth factor-beta; TNF=tumour necrosis factor .

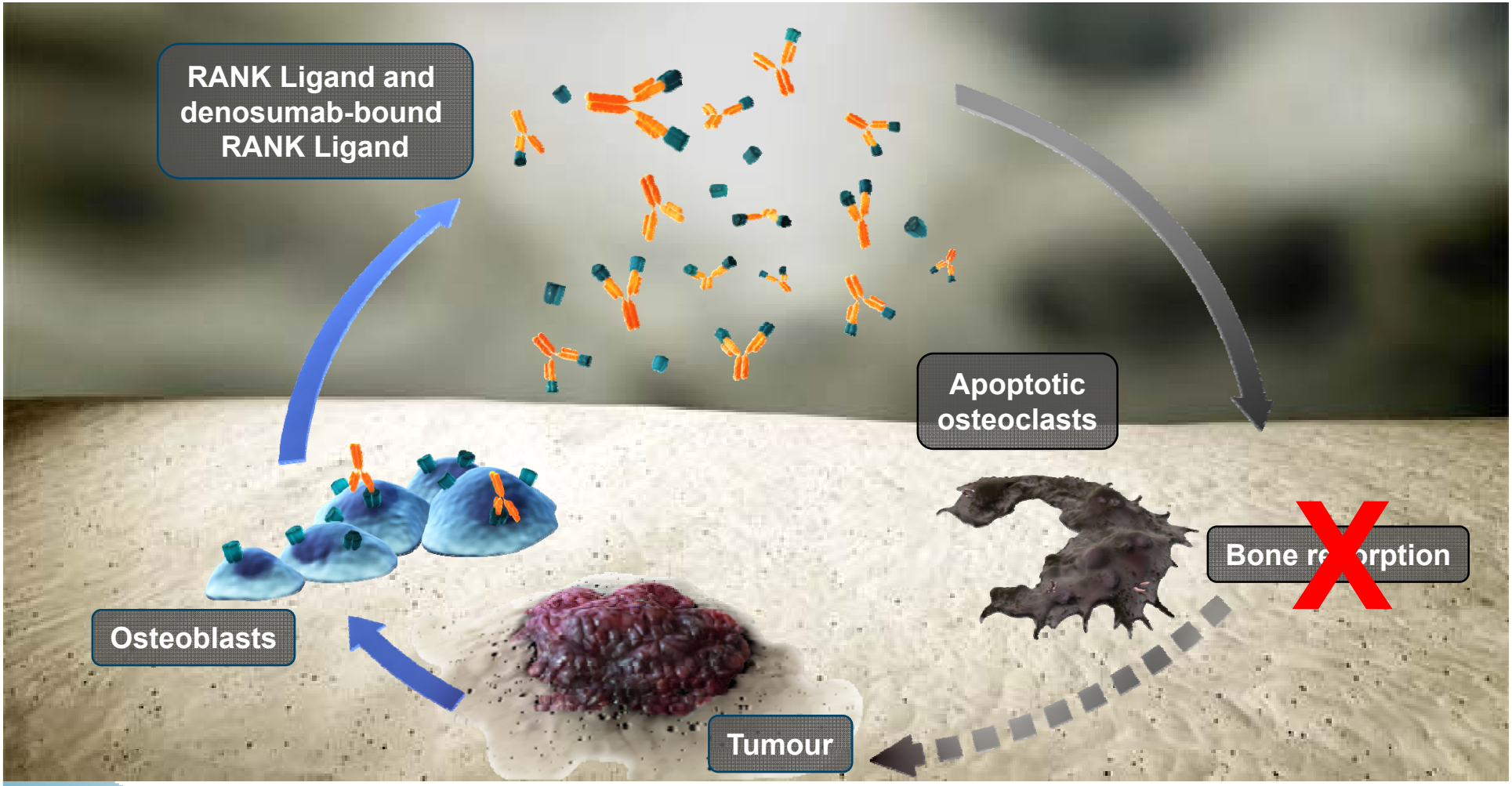
Denosumab inhibits RANK Ligand

- Denosumab is a fully human monoclonal antibody that binds human RANK Ligand with high affinity and specificity[1]
- By binding to RANK Ligand, denosumab prevents RANK Ligand from activating its receptor, RANK, on the surface of osteoclasts and their precursors[1]
- In clinical trials, no neutralising antibodies were detected[2–4]
  - As with all therapeutic proteins, there is potential for immunogenicity



1. McClung MR et al. New Engl J Med 2006;354:821–31;
2. Stopeck AT et al. J Clin Oncol 2010;28:5132–9;
3. Fizazi K et al. Lancet 2011; Lancet 2011;377:813–22;
4. Henry DH et al. J Clin Oncol 2011;29:1125–32.

Denosumab inhibits RANK Ligand to interrupt the vicious cycle of bone destruction



RANK, receptor activator of nuclear factor κ B.

1. Boyle WJ, et al. Nature 2003;423:337–42;
2. McClung MR, et al. New Engl J Med 2006;354:821–31.

Overall Denosumab Clinical Registration
12 phase III studies (> 20,000 patients to enroll) - cont

120 mg Q4W

Prevention or Delay of Bone Metastasis* ~ 6.000 patients	Prevention or Delay of SREs ~ 7.000 patients	Giant Cell Tumour of Bone (GCTB)~	Treatment of Hypercalcemia of malignancy (HCM)†
Prostate cancer[1] (n = 1.432)	**Prostate cancer[3] (n = 1.904)**	**20040215 study[6] (n=37)**	**20070315 study [2] (n ~ 33) *Active, not enroling**
Breast cancer - D-CARE[2] (n ~ 4.500) *Active, not enrolling	**Breast cancer[4] (n = 2046)**	**20062004 study[2] (n ~ 375) *Enrolling**	
	Solid tumor and MM[5] (n = 1.776)**		
	Multiple Myeloma[2*] (n ~ 1.520) *Enrolling**		

1.- Smith MR, et al. Lancet 2012;379:39-46. 2.- www.clinicaltrials.gov Accessed 14 May 2012. 3.- Fizazi K et al. The Lancet 2011;377;813-822. ***4***.- Stopeck AT et al. J Clin Oncol *2010;28:5132-5139* 5.- Henry DH et al. J Clin Oncol 2011;29(9):1125-32. 6.-Thomas et al. Lancet Oncol 2010;11:275-80.

SREs = Skeletal Related Events; PMO = postmenopausal osteoporosis; FREEDOM = Fracture REduction Evaluation of Denosumab in Osteoporosis Every 6 Months; DEFEND = DEnosumab Evaluation For PrEserving BoNe Density; DECIDE = Determining Efficacy: Comparison of Initiating Denosumab vs. AlEndronate; STAND = Study of Transitioning from AleNdronate to Denosumab; ABCSG = Austrian Breast and Colorectal Cancer Study Group; D-CARE= Denosumab as adjuvant Treatment for Women with early-stage breast CAncer at high risk of Recurrence; MM = multiple myeloma.

*Denosumab is currently not approved in EU for the prevention or delay of the development of bone metastases. Denosumab is investigational in that setting.

**Denosumab is not indicated for use in patients with multiple myeloma (MM). Denosumab is investigational in that setting.

~Denosumab is not indicated for the treatment of giant cell tumor of the bone (GCTB). Denosumab is investigational in this setting.

†Denosumab is not indicated for the treatment of hypercalcemia of malignancy (HCM). Denosumab is investigational in this setting.

Phase 3 SRE Studies
All pivotal studies published in key journals


VOLUME 28 · NUMBER 35 · DECEMBER 10 2010

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

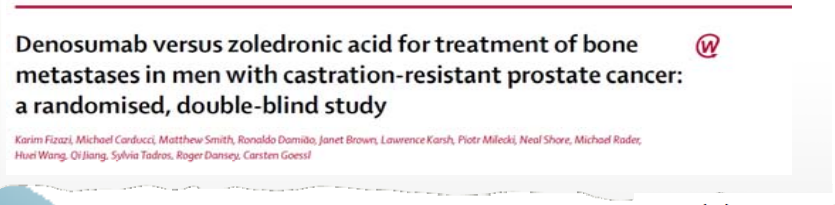
Alison T. Stopeck, Allan Lipton, Jean-Jacques Body, Guenther G. Steger, Katia Tonkin, Richard H. de Boer, Mikhail Lichinitser, Yasuhiro Fujiwara, Denise A. Yardley, Maria Viniegra, Michelle Fan, Qi Jiang, Roger Dansey, Susie Jun, and Ada Braun


VOLUME 29 · NUMBER 9 · MARCH 20 2011

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, Francois Goldwasser, Vera Hirsh, Vania Hungria, Jana Prausova, Giorgio Vittorio Scagliotti, Harm Sleeboom, Andrew Spencer, Saroj Vadhan-Raj, Roger von Moos, Wolfgang Willenbacher, Penella J. Woll, Jianming Wang, Qi Jiang, Susie Jun, Roger Dansey, and Howard Yeh


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

www.thelancet.com Vol 377 March 5, 2011

Combined analysis
Lipton A, et al.


European Journal of Cancer (2012) **48**, 3082–3092

ELSEVIER

Available at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.ejcancer.info

EJC

Superiority of denosumab to zoledronic acid for prevention of skeletal-related events: A combined analysis of 3 pivotal, randomised, phase 3 trials ☆

Allan Lipton [a,*], Karim Fizazi [b], Alison T. Stopeck [c], David H. Henry [d], Janet E. Brown [e], Denise A. Yardley [f], Gary E. Richardson [g], Salvatore Siena [h], Pablo Maroto [i], Michael Clemens [j], Boris Bilynskyy [k], Veena Charu [l], Philippe Beuzeboc [m], Michael Rader [n], Maria Viniegra [o], Fred Saad [p], Chunlei Ke [q], Ada Braun [q], Susie Jun [q]

Stopeck AT et al. J Clin Oncol *2010;28:5132-5139;* Henry DH et al. J Clin Oncol 2011;29(9):1125-32; Fizazi K et al. The Lancet 2011;377;813-822; Lipton A et al. Eur J Cancer 2012;48:3082-3092.

MM, multiple myeloma, SRE, skeletal related event.

XGEVA®(denosumab) is not approved for the prevention of SREs in patients with multiple myeloma. Denosumab is investigational in that setting.

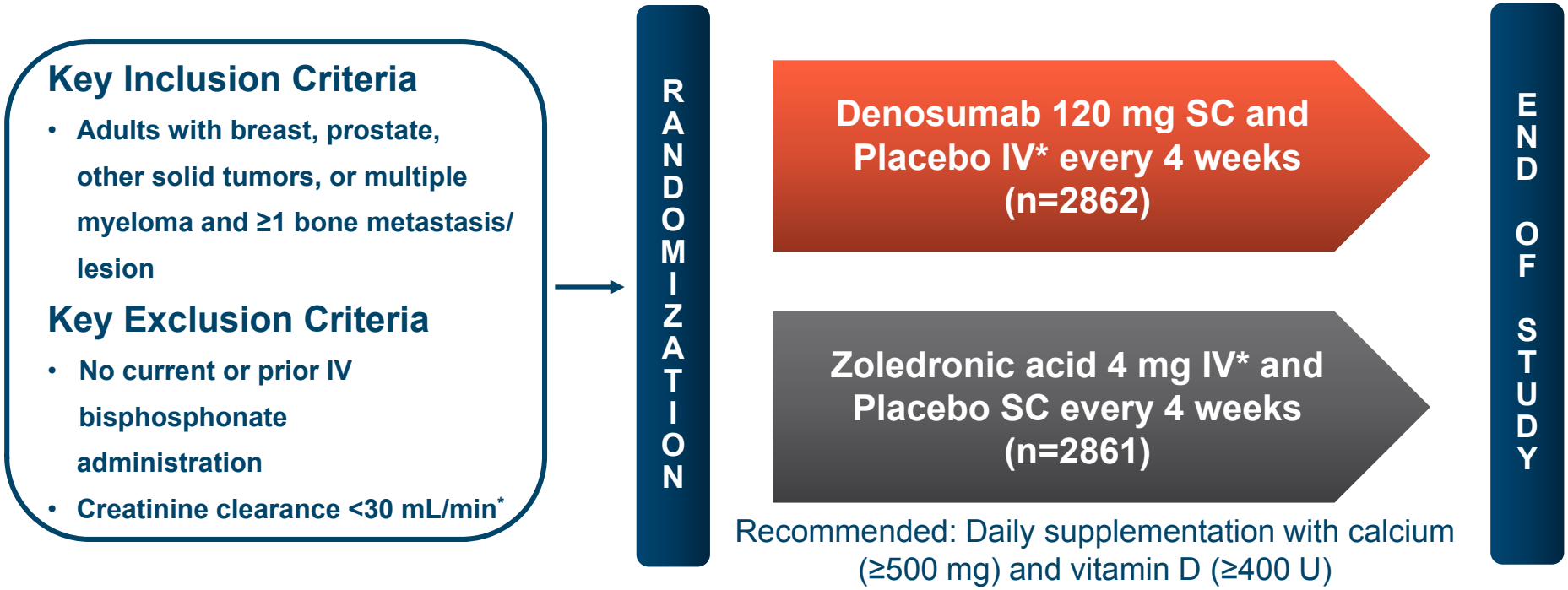
Data from three Phase III denosumab trials have been combined in a pre-planned integrated analysis

- Trials of identical design in different patient populations
  - Breast cancer[1]
  - Prostate cancer[2]
  - Other solid tumours or multiple myeloma[3]

- Benefits of integrated analysis
  - Improves precision of estimates for study endpoints by providing larger patient data samples for sub-group analyses
    - Pain analysis
    - Osteonecrosis of the jaw (ONJ)

1. Stopeck AT et al. J Clin Oncol 2010;28:5132–9;
2. Fizazi K et al. Lancet 2011; Lancet 2011;377:813–22;
3. Henry DH et al. J Clin Oncol 2011;29:1125–32.

Three Identical International, Randomized, Double-Blind, Active-Controlled Trials



Primary Endpoint: Time to first on-study skeletal-related event (SRE) (Non-inferiority)

Secondary : Time to first on-study SRE (Superiority), time to first and subsequent on-study SRE(s) (Superiority)

*Per protocol and Zometa® label, IV product dose adjusted for baseline creatinine clearance and subsequent dose intervals determined by serum creatinine. No SC dose adjustments made due to increased serum creatinine.

Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.

Baseline Characteristics (1)

Characteristics, n (%) or Median (Q1, Q3)	Denosumab (n=2862)	Zoledronic Acid (n=2861)
Sex, n (%)		
Male	1546 (54)	1512 (53)
Female	1316 (46)	1349 (47)
Age (years), median	63	63
ECOG PS of 0 or 1, n (%)	2585 (90)	2546 (89)
Presence of visceral metastases, n (%)	1187 (42)	1154 (40)
Lung	481 (17)	404 (14)
Liver	398 (14)	369 (13)
Other	829 (29)	862 (30)
Previous SRE*	1112 (39)	1157 (40)
Time from initial cancer diagnosis to first bone metastasis, months	16.6 (0.9, 54.7)	16.5 (1.0, 57.3)
Time from first metastasis to randomization, months	2.2 (1.0, 7.1)	2.3 (1.0, 7.6)

*Based on stratification group at randomization

Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.

Baseline Characteristics (2)

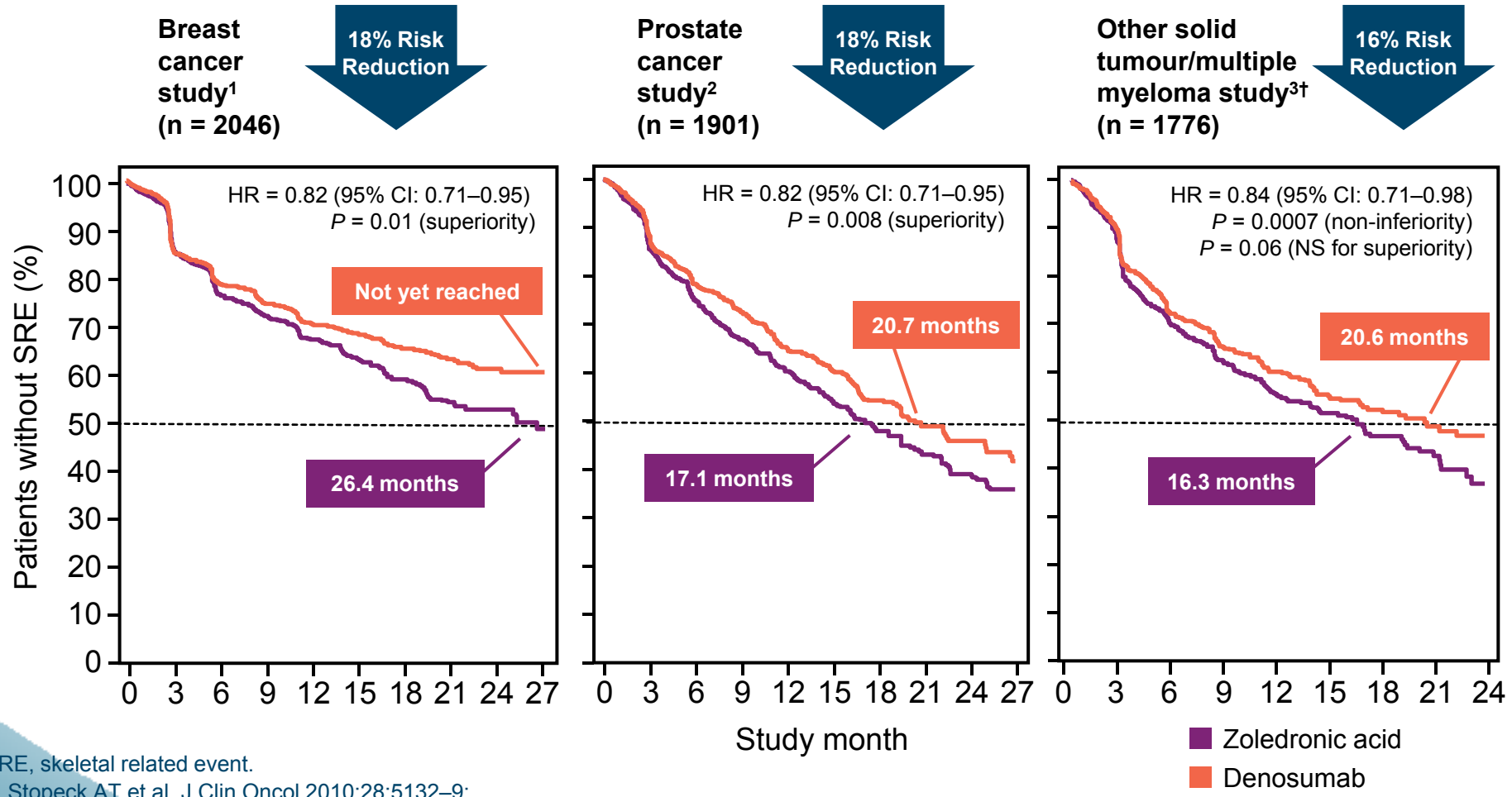
Characteristics, n (%) or Median (Q1, Q3)	Denosumab (n=2862)	Zoledronic Acid (n=2861)
Tumor type*		
Breast	1026 (36)	1020 (36)
Prostate	950 (33)	951 (33)
Non-small cell lung	350 (12)	352 (12)
Multiple myeloma	87 (3)	93 (3)
Renal	70 (2)	85 (3)
Small cell lung	61 (2)	48 (2)
Bladder	28 (1)	35 (1)
Rectal	25 (1)	35 (1)
Colon	30 (1)	29 (1)
Other#	235 (8)	213 (7)

*Based on randomization; total number may equal 100% due to rounding; #Includes >50 other tumor types each representing 1% or less of total sample
SRE=skeletal-related event

Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.

Risk reduction in time to first SRE consistently favoured denosumab across tumour types

Time to first SRE



SRE, skeletal related event.

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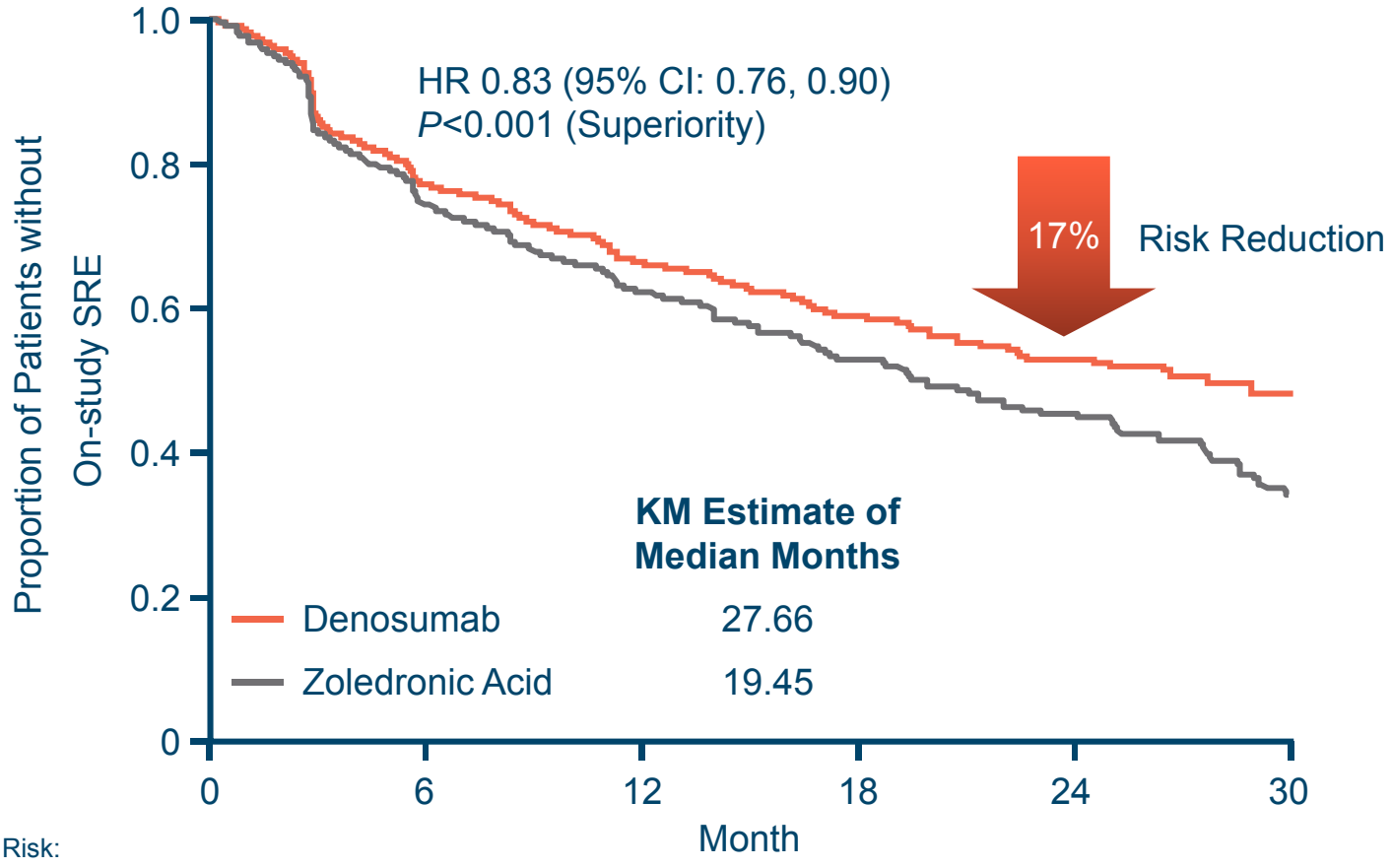
2. Fizazi K et al. Lancet 2011;377:813–22;
3. Henry DH et al. J Clin Oncol 2011;29:1125–32.

†Excluding breast and prostate. All data from primary analyses

Primary Endpoint: Time to First On-Study SRE

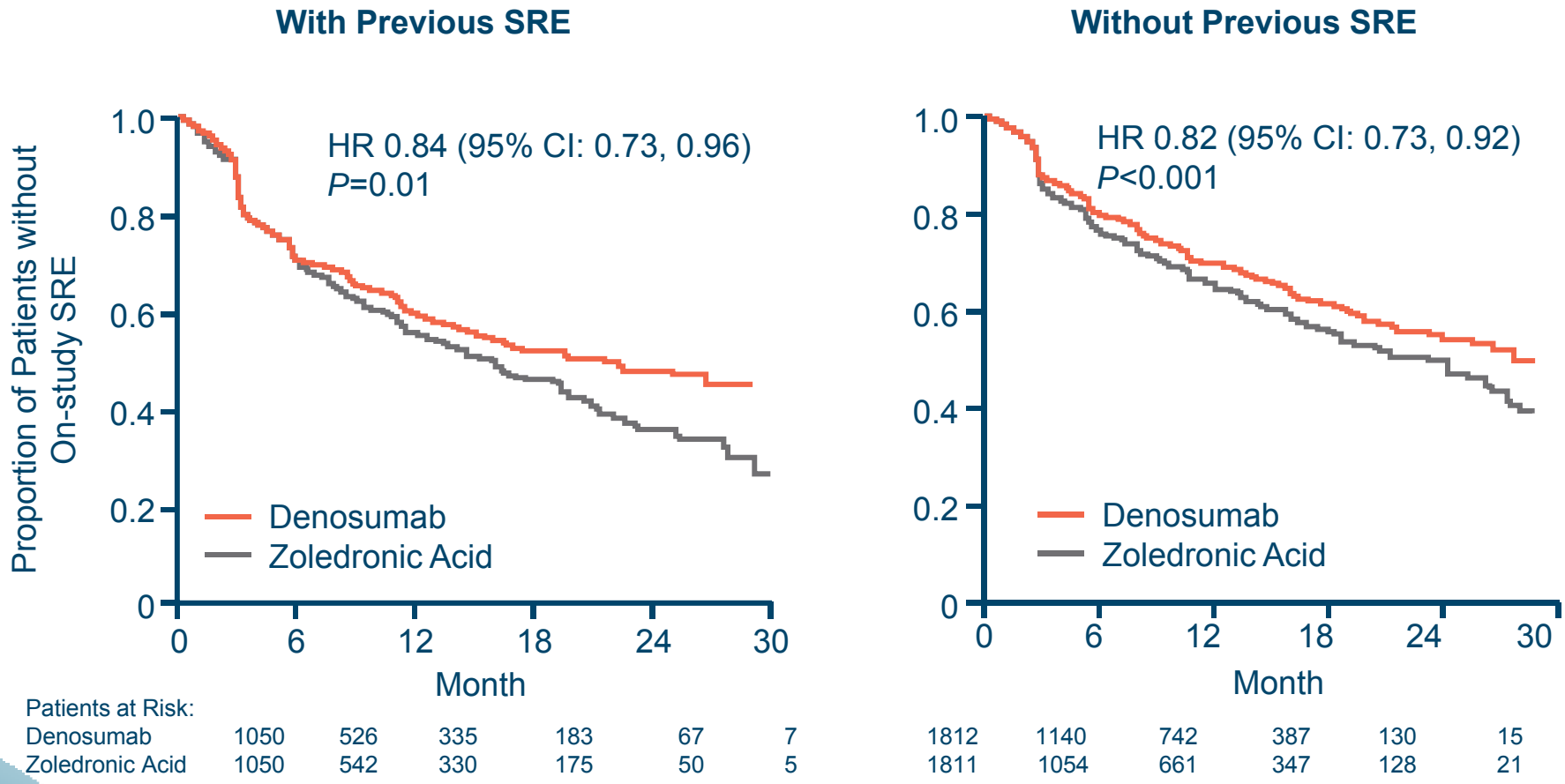


Patients at Risk:

Denosumab	2862	1666	1077	570	197	22
Zoledronic Acid	2861	1596	991	522	178	26

Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.

Time to First On-Study SRE by Previous SRE History



Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.

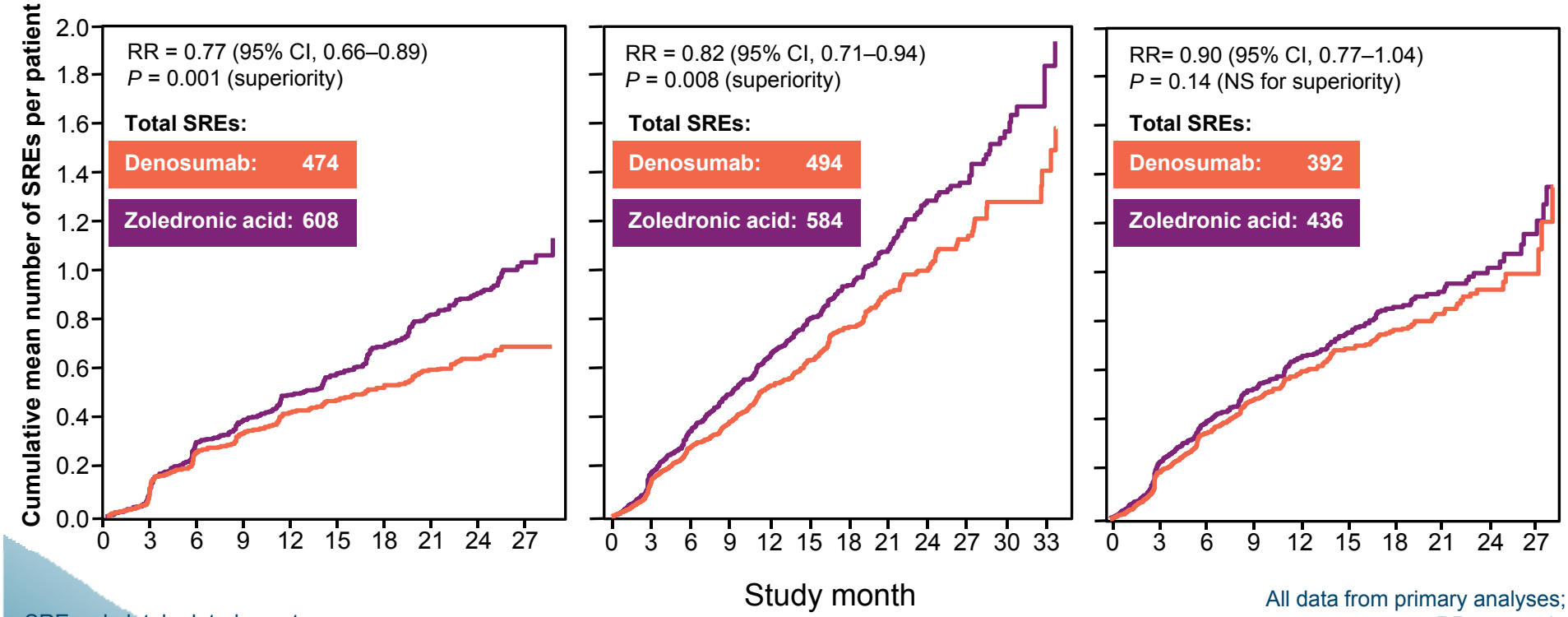
Significantly fewer SREs with denosumab across different tumour types

Time to first and subsequent SREs

Breast cancer[1] (n = 2046) — 23% Risk Reduction

Prostate cancer[2] (n = 1901) — 18% Risk Reduction

Other solid tumour/ multiple myeloma[3] (n = 1776) — 10% Risk Reduction

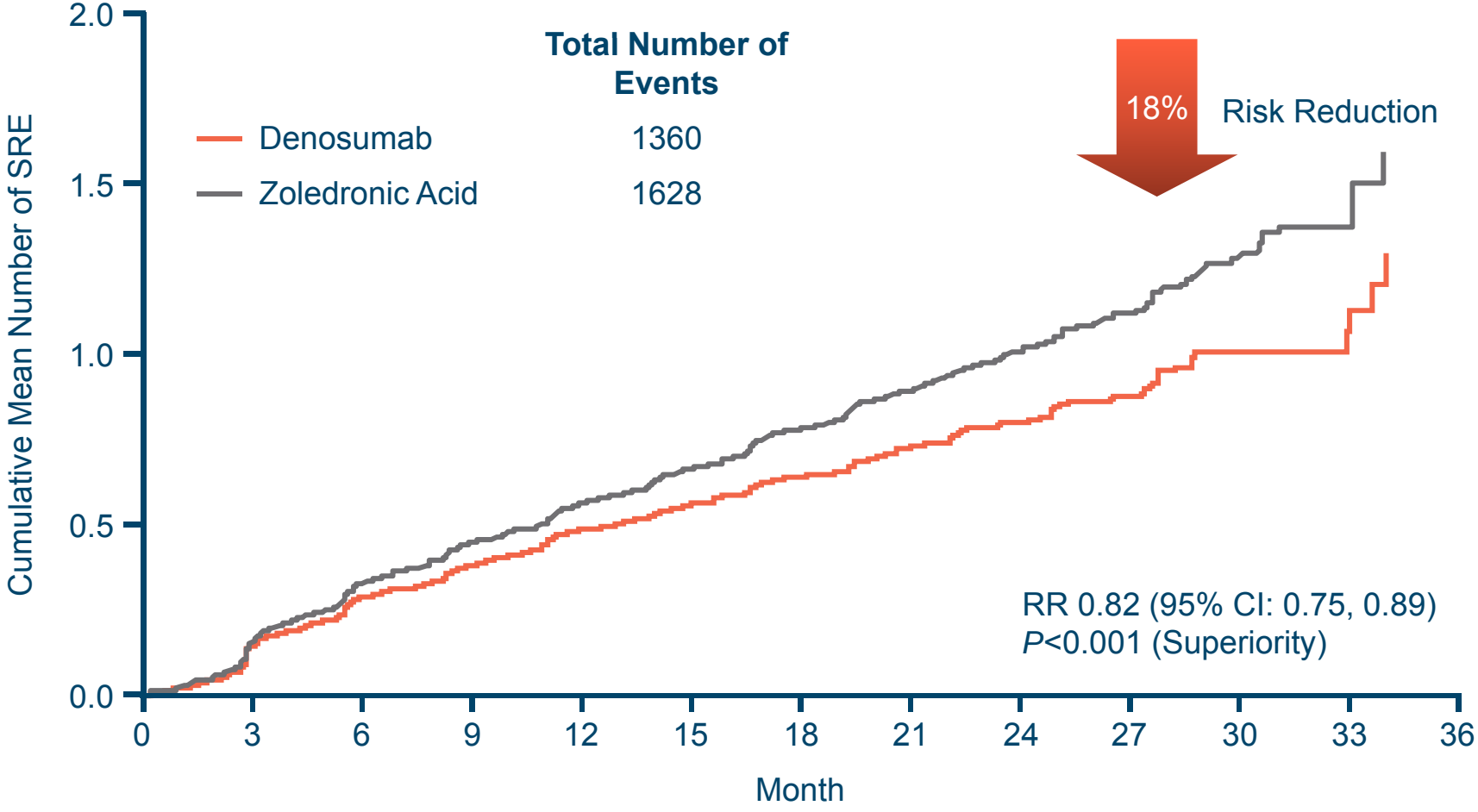


All data from primary analyses;
RR, rate ratio

SREs, skeletal related events.

1. Stopeck AT et al. J Clin Oncol 2010;28:5132–9; 2. Fizazi K et al. Lancet 2011;377:813–22; 3. Henry DH et al. J Clin Oncol 2011;29:1125–32.

Time to First and Subsequent On-Study SRE*

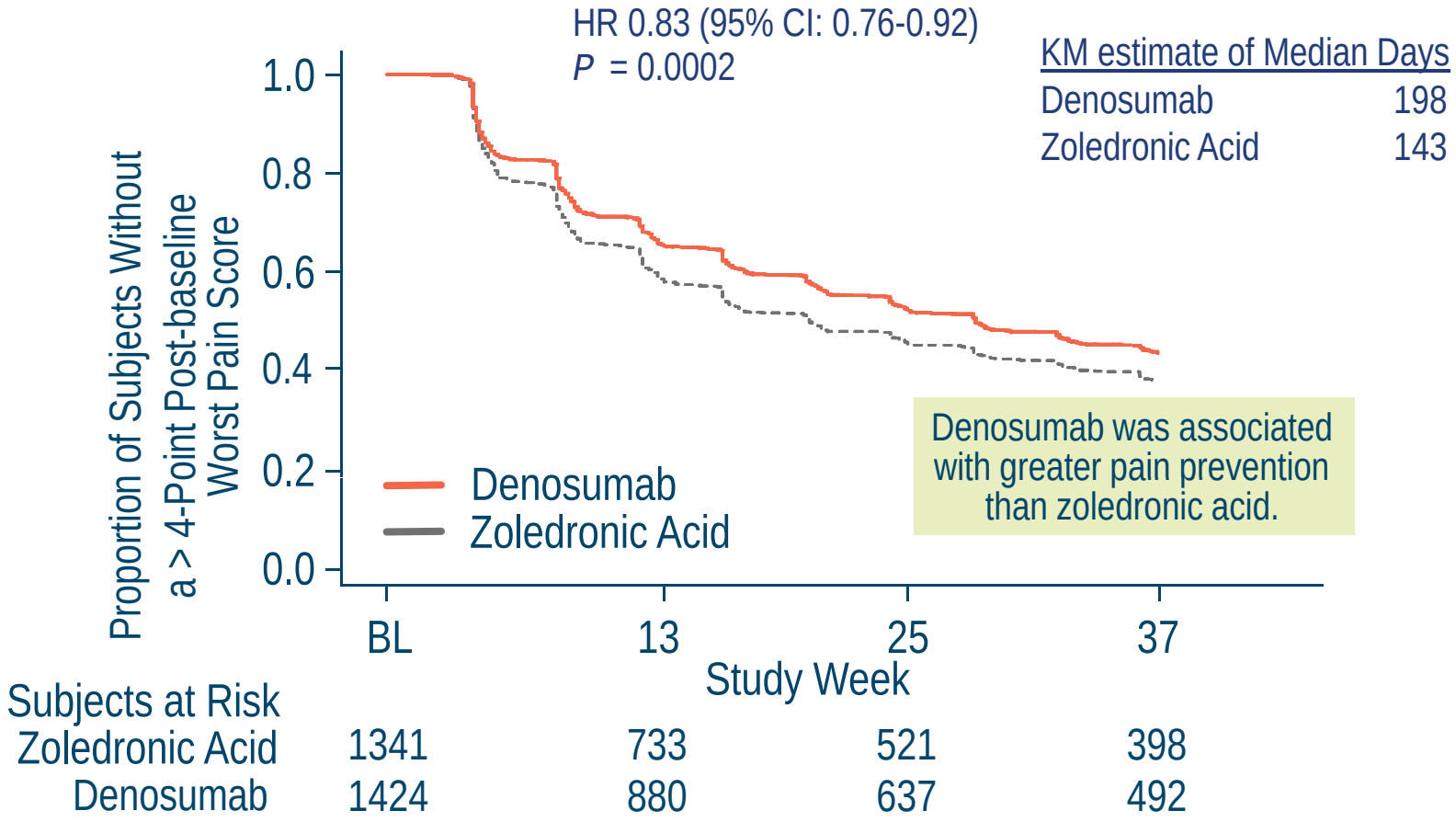


*Events that occurred at least 21 days apart; *P*-value adjusted for multiplicity.

Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.

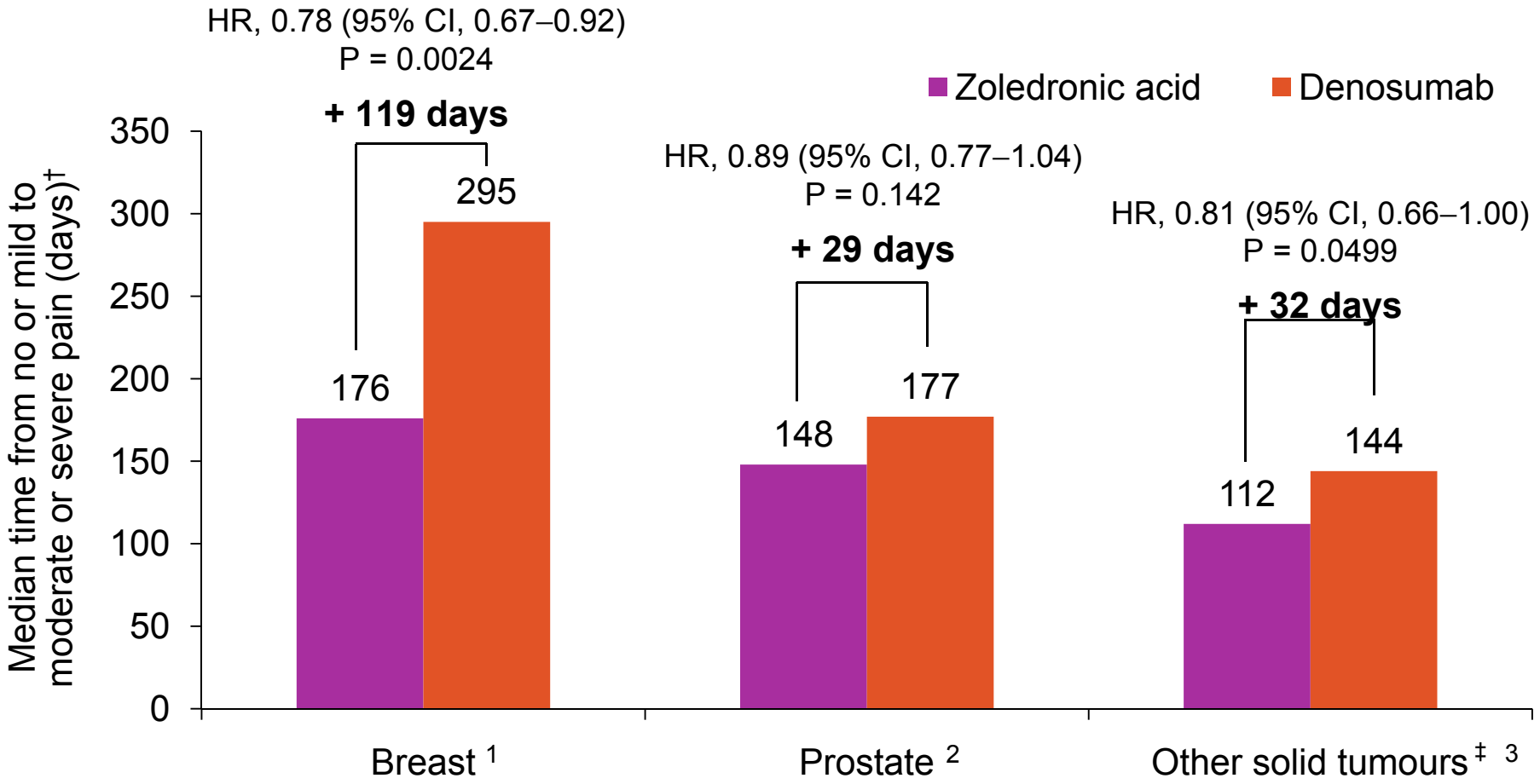
Results – Pain Prevention

Time to Moderate or Severe Pain (> 4 Points) In Patients With No or Mild Pain (0–4) at Baseline



Cleeland CS, Patrick DL, Fallowfield L, et al. ESMO 2010: abstract 1248P and poster presentation.

Denosumab consistently delayed pain progression vs zoledronic acid across tumour types



HR, Hazard Ratio, MM, Multiple Myeloma

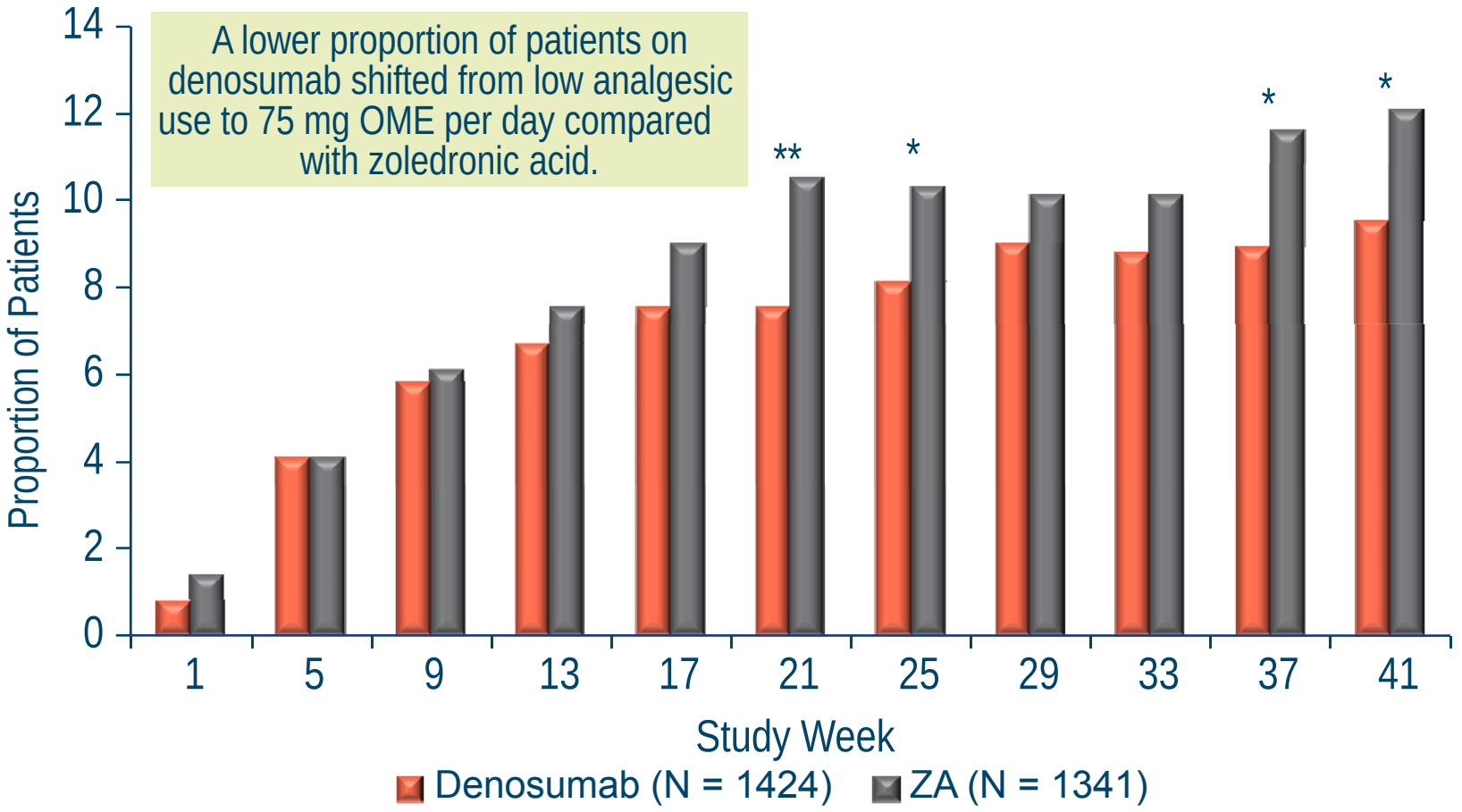
Denosumab is not indicated for use in patients with multiple myeloma (MM). Denosumab is investigational in that setting.

1. Stopeck A, et al. J Clin Oncol 2010;28(Suppl 15): [Abstract 1024];
2. Brown JE, et al. Eur Urol Suppl 2011;10:336 [Abstract 1091];
3. Fallowfield L, et al. Oral presentation at EMCC 2011 [Abstract 7004].

†Patients with pain worsening (≥ 2-point increase) among patients with no or mild pain (0–4) at baseline. ‡Excluding breast and prostate. MM, multiple myeloma.

Results – Analgesic Use

Proportion of Patients Who Shifted From Low Analgesic Use (No Analgesics, Non-Narcotic Analgesics, and Weak Analgesics) to ≥ 75 mg OME per day



*P<0.05; **P<0.01; Not adjusted for multiplicity

Cleeland CS, Patrick DL, Fallowfield L, et al. ESMO 2010: abstract 1248P and poster presentation.

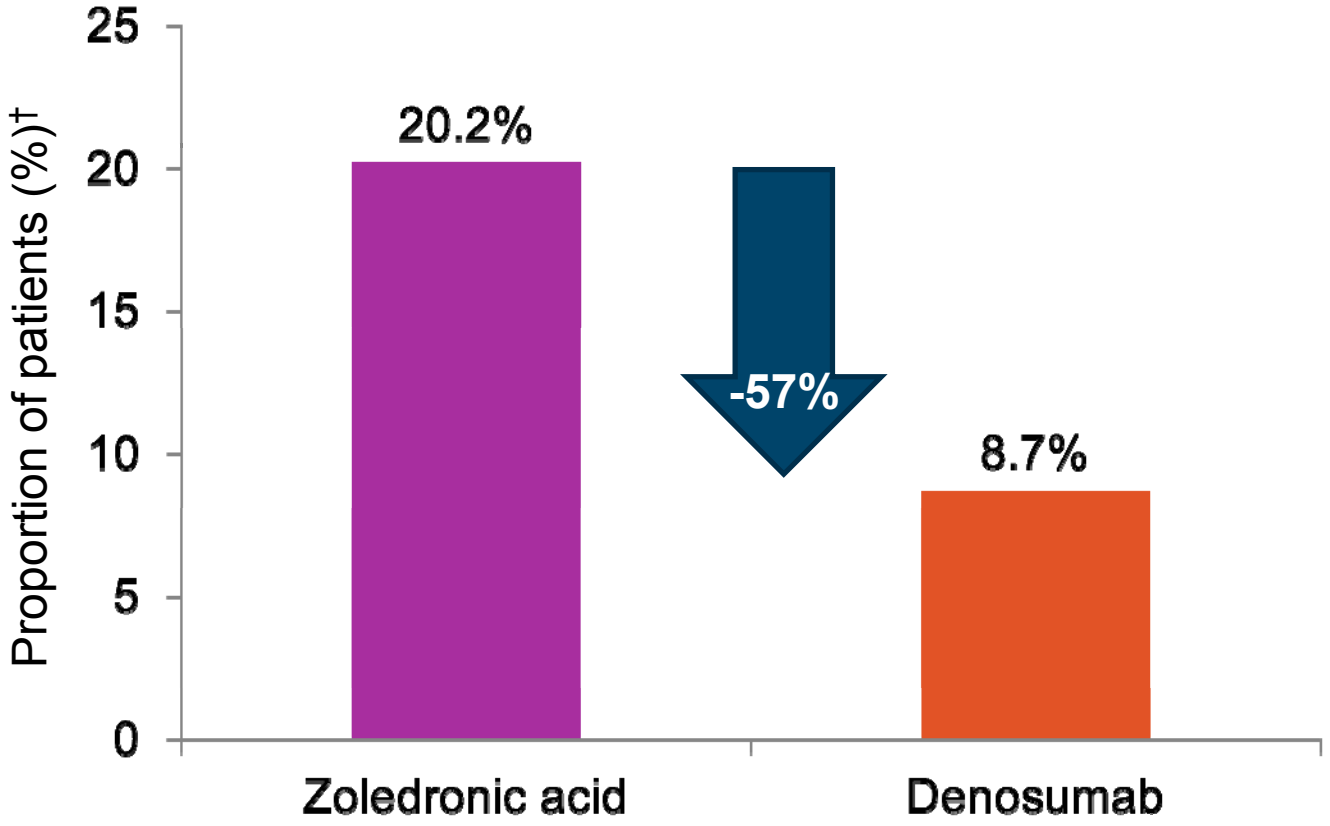
Adverse Events in the Presence of Denosumab or Zoledronic Acid

Adverse events (AEs), n (%)	Denosumab (n=2841)	Zoledronic Acid (n=2836)
Experienced at least one AE	**2734 (96.2)**	**2745 (96.8)**
Most common AEs		
Nausea	876 (30.8)	895 (31.6)
Anemia	771 (27.1)	859 (30.3)
Fatigue	769 (27.1)	766 (27.0)
Back pain	718 (25.3)	747 (26.3)
Decreased appetite	656 (23.1)	694 (24.5)
CTCAE Grade 3, 4, or 5 AEs	2000 (70.4)	2009 (70.8)
Serious AEs	1599 (56.3)	1620 (57.1)
AEs leading to study discontinuation	270 (9.5)	280 (9.9)
Infectious AEs	1233 (43.4)	1218 (42.9)
Infectious serious AEs	329 (11.6)	309 (10.9)
Acute phase reactions (first 3 days)	246 (8.7)	572 (20.2)
Cardiac AEs	381 (13.4)	380 (13.4)
Renal AEs*	262 (9.2)	335 (11.8)
Hypocalcemia[$]	273 (9.6)	141 (5.0)
Received IV calcium supplementation	104 (3.6)	47 (1.7)
Grade 3 or 4 hypocalcemia	105 (3.7)	48 (1.7)
Hypophosphatemia	61 (2.1)	32 (1.1)
ONJ	52 (1.8)	37 (1.3)
New primary malignancy[&]	28 (1.0)	18 (0.6)
Infection site reactions	10 (0.4)	5 (0.2)

*Includes increased blood creatinine, renal failure, acute renal failure, proteinuria, renal impairment, oliguria, increased blood urea, hypercreatininemia, decreased urine output, anuria, decreased creatinine renal clearance, azotemia, chronic renal failure, abnormal renal function test and abnormal blood creatinine; [$]Includes adverse event preferred terms of hypocalcemia, blood calcium decreased, calcium deficiency, and calcium ionized decreased; [&]New primary malignancies reported: acute lymphocytic leukemia, acute myeloid leukemia, bile duct cancer, bladder cancer, chronic myeloid leukemia, colon cancer, gastric cancer, lung cancer, lymphoma, malignant melanoma, multiple myeloma, mycosis fungoides, nasal sinus cancer, pancreatic carcinoma, rectal cancer, renal cell cancer, squamous cell carcinoma, squamous cell carcinoma of skin, uterine cancer, Waldenstrom's macroglobulinemia

Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.

Fewer acute phase reactions with denosumab vs zoledronic acid



Lipton A, et al. Ann Oncol 2010;21(Suppl 8):viii379 [Abstract 1249P].

†Patients experiencing acute phase reactions associated with a flu-like syndrome (within first 3 days).

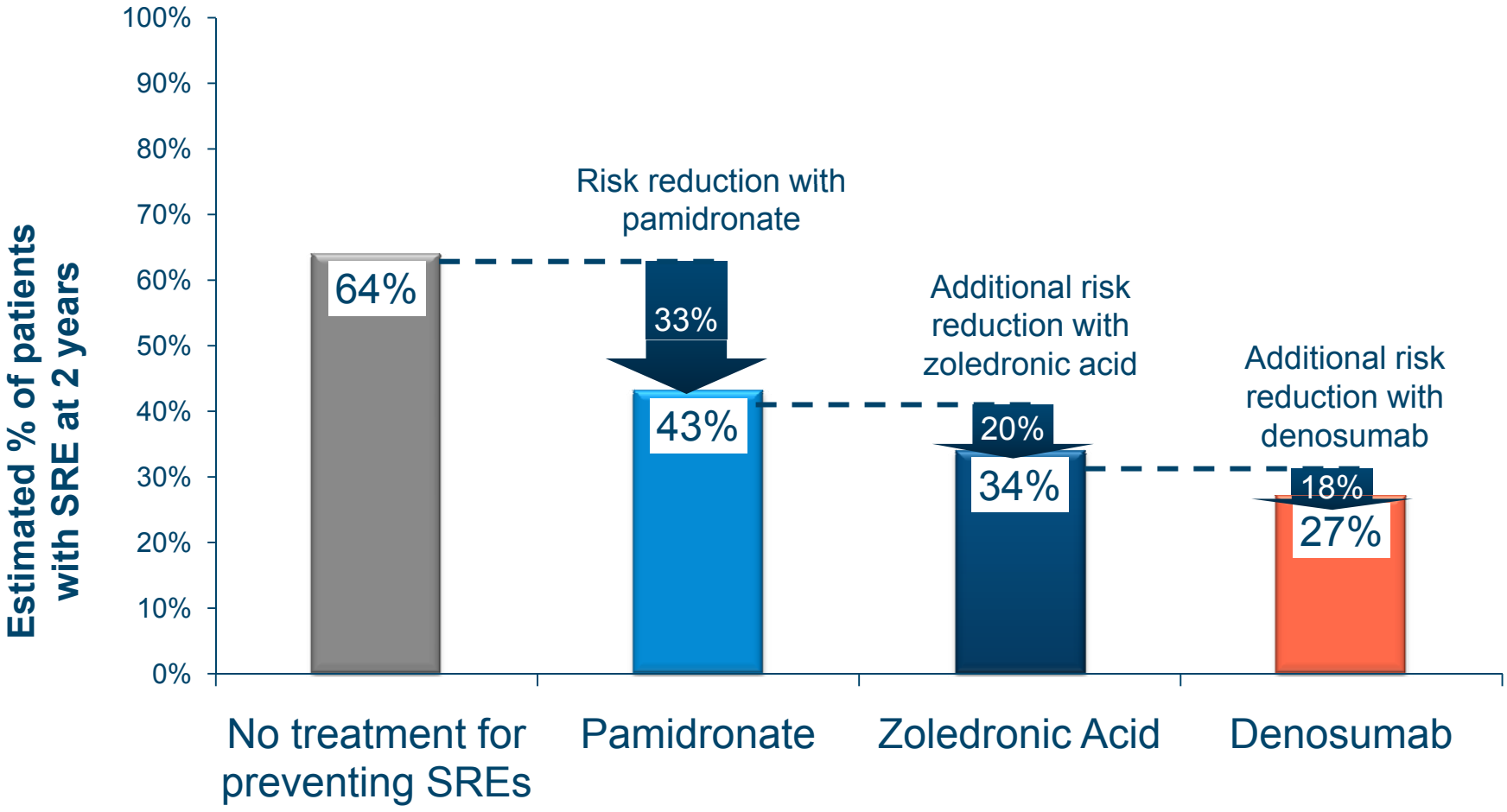
Drug Exposure and Adjustments for Renal Function

Overall Exposure	SC Denosumab	IV Zoledronic Acid
Median number of active doses, n (Q1, Q3)	13 (6, 20)	11 (5, 19)
Cumulative exposure (patient-years)	2969	2852
Adjustments for Renal Function		
Patients with dose adjustments for creatinine clearance at baseline, n (%)	NA	502 (18)
Patients with doses withheld for serum creatinine increases on study, n (%)	NA	277 (10)
Patients with prostate cancer	NA	143 (52)
Patients with solid tumors	NA	78 (28)
Patients with multiple myeloma	NA	56 (20)
Total number of doses withheld due to serum creatinine increases on study	NA	1181

NA=Not applicable per protocol

Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.

Incremental benefits in risk reduction of SREs in breast cancer patients[1]



SRE: skeletal related event.

1. Casas A, Llombart A, Martín M. Denosumab for the treatment of bone metastases in advanced breast cancer. Breast. 2013 Jun 4. doi:pii: S0960-9776(13)00110-0. 10.1016/j.breast.2013.05.007. [Epub ahead of print]

Summary: integrated analysis adds to results of three pivotal phase III trials

- The combined analysis with over 5700 patients confirms results from the individual studies
  - Denosumab provided superior efficacy for prevention of SREs
  - Denosumab extended the time to a first SRE by over 8 months and maintained superiority in preventing multiple SREs
  - Efficacy of denosumab was consistent among SRE low- and high-risk patient subgroups showing that the treatment effect was independent of prior SRE status
- Rates of adverse events were similar between the treatment groups:
  - Increased incidence of acute-phase reactions in zoledronic acid group
  - Increased incidence of hypocalcemia in denosumab group
  - ONJ occurred at a similar rate in both groups.
- Denosumab delayed worsening of pain compared with zoledronic acid. A lower proportion of patients receiving denosumab experienced increasing analgesic use over time

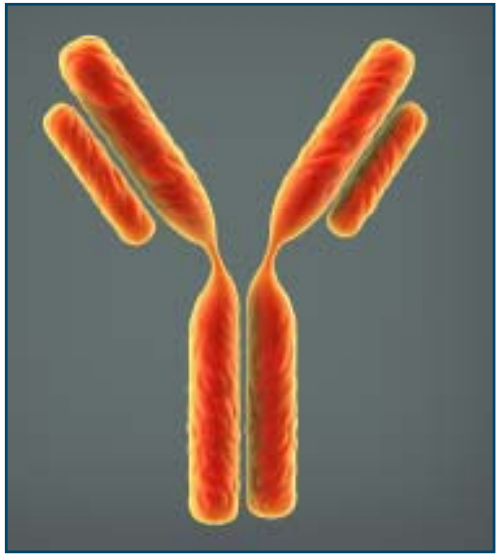
SRE, skeletal related event; ONJ, osteonecrosis of the jaw.

Lipton A et al. Eur J Cancer 2012;48:3082-3092; Cleeland CS, Patrick DL, Fallowfield L, et al. ESMO 2010: abstract 1248P and poster presentation.
Cassinello Espinosa J et a. Clin Transl Oncol. 2012 Jul;14(7):505-11.

Denosumab (XGEVA®) – Therapeutic indication approved by EMA

- Denosumab is a fully human monoclonal antibody that binds human RANK Ligand with high affinity and specificity[1]

	XGEVA® (denosumab)[2]
Dose	**120 mg SC**
Regimen	**Every 4 weeks**
Indication(s)	**Prevention of skeletal related events** (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with **bone metastases from solid tumours**



EMA: European Medicines Agency; SC, subcutaneous.

1. McClung MR et al. New Engl J Med 2006;354:821–31.
2. XGEVA® (Denosumab) Summary of product characteristics, Amgen. Available at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/medicines/human/medicines/002173/human_med_001463.jsp&murl=menus/medicines/medicines.jsp&mid=WC0b01ac058001d124 Accessed 14 June 2012.

Guidelines on bone-targeted agents for the prevention of SREs

Overview of international guideline recommendations for denosumab

	ASCO	NCCN	ESMO	EAU
Breast cancer	●	●	●	**N/A**
CRPC	**N/A**	●	●	●
NSCLC		●	●	**N/A**
Renal cell carcinoma	**N/A**	●		
Bladder cancer	**N/A**			●
Cancer pain			●	**N/A**

● Denosumab use recommended

N/A No guidelines exist

ASCO, American Society of Clinical Oncology; CRPC, castration-resistant prostate cancer; EAU, European Association of Urology; ESMO, European Society for Medical Oncology; NCCN, National Comprehensive Cancer Network; NSCLC, non-small cell lung cancer.

Van Poznak CH, et al. J Clin Oncol 2011;29:1221−7; NCCN Clinical Practice Guidelines Oncology. www.nccn.org (Accessed January 2013); Cardoso F, et al. Ann Oncol 2012;23(Suppl 7):vi11–9; Heidenreich A, et al. Guidelines on Prostate Cancer. EAU 2012, available at: http://www.uroweb.org/fileadmin/guidelines/2012_Guidelines_large_text_print_total_file.pdf (Accessed October 2012); ESMO Pocket Guidelines Urogenital Cancer smartphone app, available at: http://www.esmo.org/education-research/esmo-clinical-practice-guidelines/esmo-pocket-guidelines.html (Accessed October 2012); Peters S, et al. Ann Oncol 2012;23 (Suppl 7):vii56–64; Escudier B, et al. Ann Oncol 2012;23(Suppl 7):vii65–71. Stenzl A, et al. EAU 2012. http://www.uroweb.org/guidelines (Accessed October 2012); Ripamonti CI, et al. Ann Oncol 2012;23(Suppl 7):vii139–54.

SEOM guidelines for the treatment of bone metastases from solid tumours

Clin Transl Oncol (2012) 14:505-511
DOI 10.1007/s12094-012-0832-0

CLINICAL GUIDES IN ONCOLOGY

SEOM guidelines for the treatment of bone metastases from solid tumours

Javier Cassinello Espinosa · Aránzazu González del Alba Baamonde · Fernando Rivera Herrero · Esther Holgado Martín

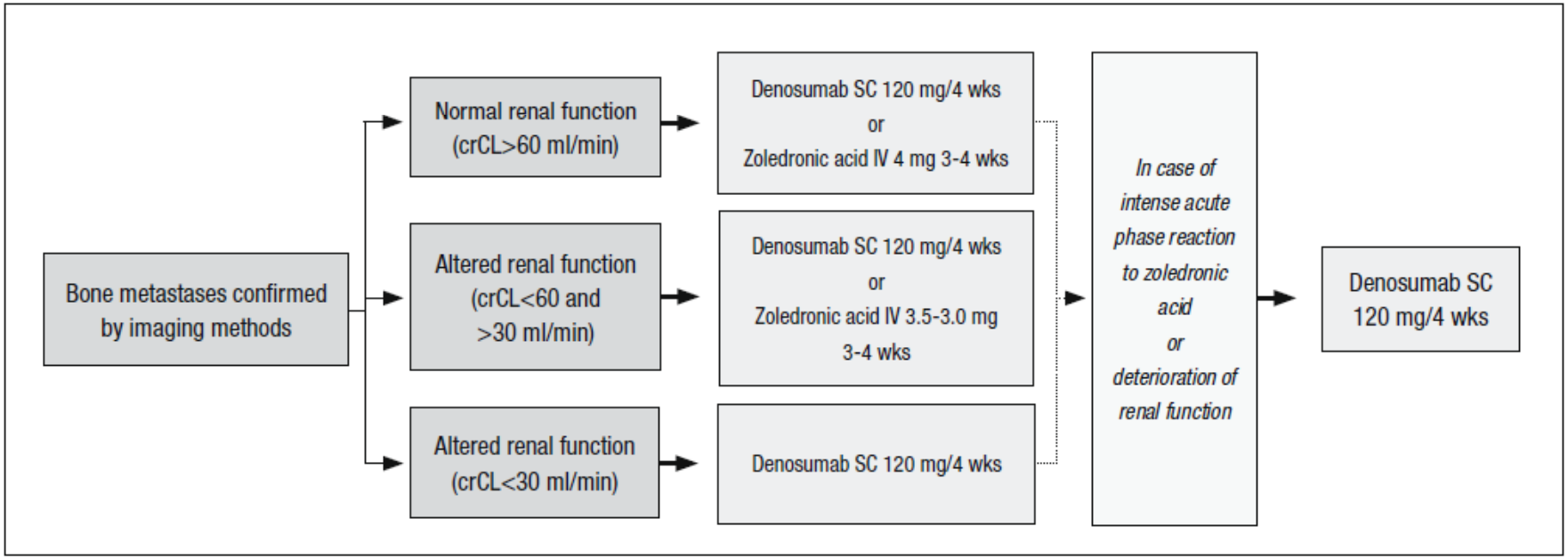
"…**denosumab**, a fully human antibody that specifically targets the RANK-L, has been demonstrated in two phase III studies to be superior to zoledronic acid in preventing or delaying SREs in breast and prostate cancer and non-inferior in other solid tumours and myeloma. Moreover, the convenient subcutaneous administration of denosumab and the fact that no dose adjustment is required in patients with renal impairment make this agent an attractive new therapeutic option in patients with bone metastases. Nonetheless, it should be pointed out that osteonecrosis of the jaw (ONJ) appears with a similar frequency with both bisphosphonates and denosumab and that the cost-effectiveness of the two drugs needs to be considered when making therapeutic decisions in the clinical context of these patients."

SEOM, Sociedad Española de Oncología Médica; wks, weeks; SC, subcutaneous; IV, intravenous; crCL; creatinine clearance.

Cassinello Espinosa J, González Del Alba Baamonde A, Rivera Herrero F, Holgado Martín E. SEOM guidelines for the treatment of bone metastases from solid tumours. Clin Transl Oncol. 2012 Jul;14(7):505-11.

SEOM guidelines for the treatment of bone metastases from solid tumours

Algorithm for treatment with bone-modifying agents in patients with bone metastases



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Cassinello Espinosa J, González Del Alba Baamonde A, Rivera Herrero F, Holgado Martín E. SEOM guidelines for the treatment of bone metastases from solid tumours. Clin Transl Oncol. 2012 Jul;14(7):505-11.

CONCLUSIONES

1. Denosumab es superior a AZ en la prevención de los EREs.
2. Denosumab evita reacciones de fase aguda y problemas renales.
3. La ONM ocurre con una tasa similar a AZ.
4. La Hipocalcemia fue más frecuente con Denosumab que con AZ.
5. Adecuación, conveniencia, calidad de vida y ¿costes?.

Lipton A, Fizazi K, Stopeck A, et al. *Eur J Cancer* 2012;48:3082-3092.
Hechmati G, Cure S, Goupéo A, et al. *Journal of Medical Economics* 2013;5:691-700.

¡Gracias!