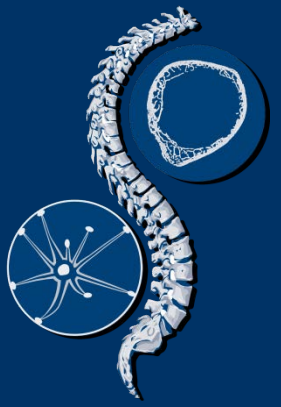

UniversitätsKlinikum Heidelberg

Osteoporosetherapie 2018

Wo ist der Fortschritt ?

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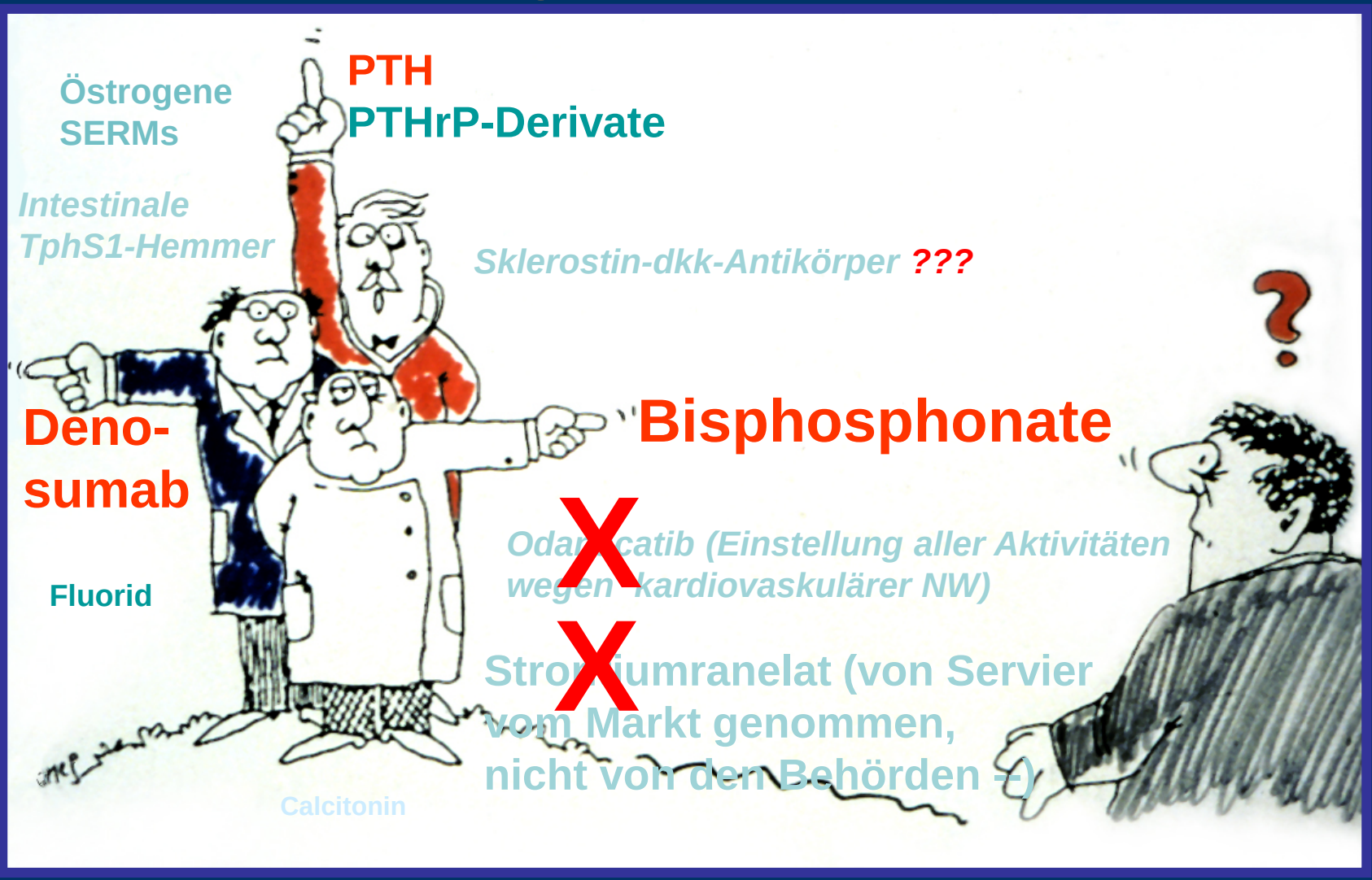
Verständnisbasierte Anwendung pharmakologischer Substanzen



Strontiumranelat

Roter Hand Briefe und EMA Indikationseinschränkung
Empfehlung, die Zulassung ruhen zu lassen, wurde aber nicht umgesetzt

Nicht bei AP, KHK, Myokardinfarkt, pAVK, Apoplex, schwerer Hypertonie, Thrombembolien, Hautreaktionen (DRESS, Stevens-Johnson-Syndrom)
Auch Bewußtseinsstörungen und Krämpfe sind unter Strontiumranelat aufgetreten.
Nur noch bei pm Frauen mit schwerer Osteoporose, hohem Frakturrisiko und Unverträglichkeit aller anderen Präparate

Pro 1000 Patientenjahre verhindert Strontiumranelat:

- **5 Radiusfrakturen**
- **15 WK Brüche**
- **6,4 Hüftfrakturen**

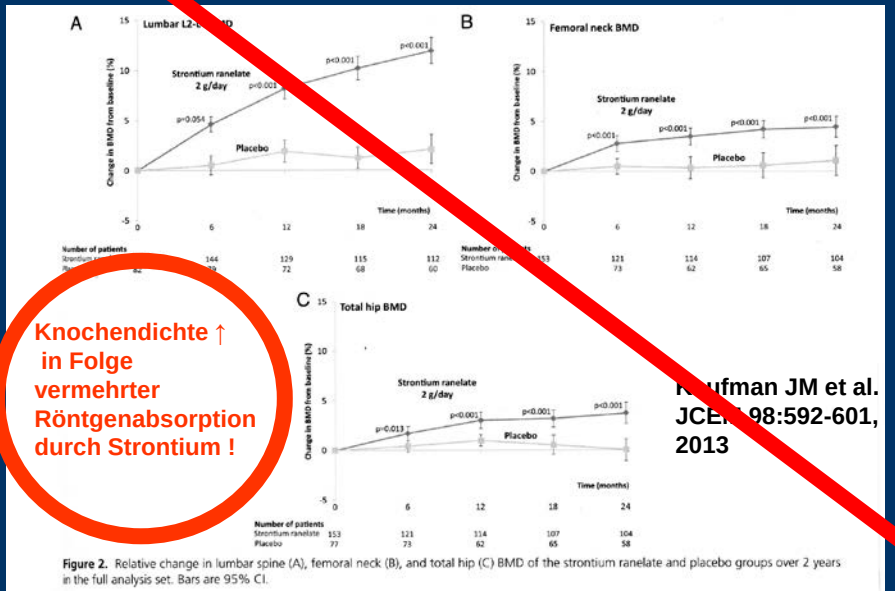


Figure 2. Relative change in lumbar spine (A), femoral neck (B), and total hip (C) BMD of the strontium ranelate and placebo groups over 2 years in the full analysis set. Bars are 95% CI.

Kaufman JM et al. JCEM 98:592-601, 2013

Drugs Approved by the FDA for the Treatment and Prevention of Osteoporosis.

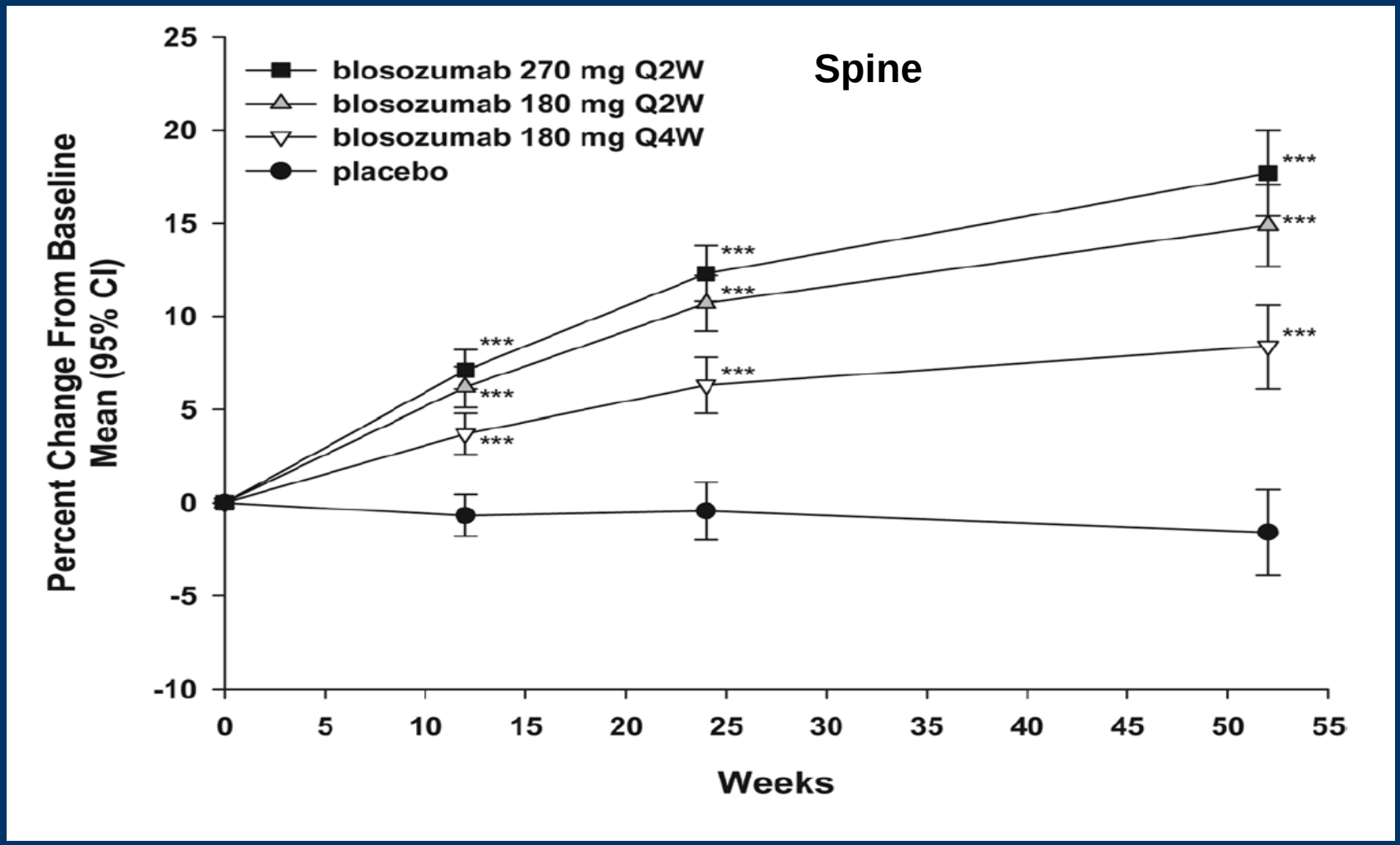
Table 2. Drugs Approved by the Food and Drug Administration for the Treatment and Prevention of Osteoporosis.*

Drug Class and Agent	Method and Frequency of Administration	Type of Fracture Risk Reduction	Side Effects	Approved Use for Osteoporosis
Bisphosphonates†				
Alendronate	Oral: 35–70 mg/wk	Vertebral, nonvertebral, hip	Common: esophagitis, musculoskeletal symptoms; rare: ONJ, atypical femur fractures	Treatment and prevention
Risedronate	Oral: 35 mg/wk or 150 mg/mo (in a single dose or in two 75-mg doses on consecutive days)	Vertebral, nonvertebral, hip	Common: esophagitis, musculoskeletal symptoms; rare: ONJ, atypical femur fractures	Treatment and prevention
Ibandronate	Oral: 150 mg/mo; intravenous: 3 mg every 3 mo	Vertebral	Common: first-dose (intravenous) reaction, esophagitis, musculoskeletal symptoms; rare: ONJ, atypical femur fractures	Treatment and prevention
Zoledronic acid	Intravenous: 5 mg/yr	Vertebral, nonvertebral, hip	Common: acute-phase response (most often after first dose),‡ musculoskeletal symptoms; rare: ONJ, atypical femur fractures	Treatment and prevention
Biologic: denosumab	Subcutaneous: 60 mg every 6 mo	Vertebral, nonvertebral, hip	Common: cellulitis or skin reactions; rare: ONJ, atypical femur fractures	Treatment
Anabolic: teriparatide	Subcutaneous: 20 μg/day	Vertebral, nonvertebral	Common: nausea, leg cramps; rare: hypercalcemia, osteosarcoma§	Treatment
Calcitonin¶	Intranasal: 200 IU/day	Vertebral	Nasal congestion	Treatment
SERM: raloxifene	Oral: 60 mg/day	Vertebral	Venous thromboembolism, hot flashes, leg cramps, nausea	Treatment and prevention
Estrogens‖			Venous thromboembolism, increased risk of breast cancer and cardiovascular disease	Prevention
Conjugated equine estrogen	Oral: 0.15–1.25 mg/day	Vertebral, nonvertebral, hip		
17β-estradiol	Oral: 0.5–1.0 mg/day; transdermal: 0.025–0.10 mg 2 times/wk	No data from randomized trials		
Ultra-low-dose 17β-estradiol	Oral: 0.014 mg/day	No data		

* ONJ denotes osteonecrosis of the jaw, and SERM selective estrogen-receptor modulator.
† Oral bisphosphonates are also approved in smaller doses for daily use to prevent osteoporosis, but currently those doses are seldom prescribed.
‡ Flulike symptoms including fever, arthralgia, or headache may occur after the first administration in up to one third of patients. Symptoms do not last more than 3 days after infusion.[8]
§ There is a black box warning about a risk of osteosarcoma, which has been reported with long-term teriparatide administration in rodents, but only one case in humans has been conclusively related to teriparatide administration.
¶ Calcitonin is no longer approved for the treatment of osteoporosis in Europe.
‖ Tibolone, which has estrogenic action, is approved for the treatment of postmenopausal osteoporosis in Europe.

Black DM, Rosen CJ. N Engl J Med 2016;374:254-262

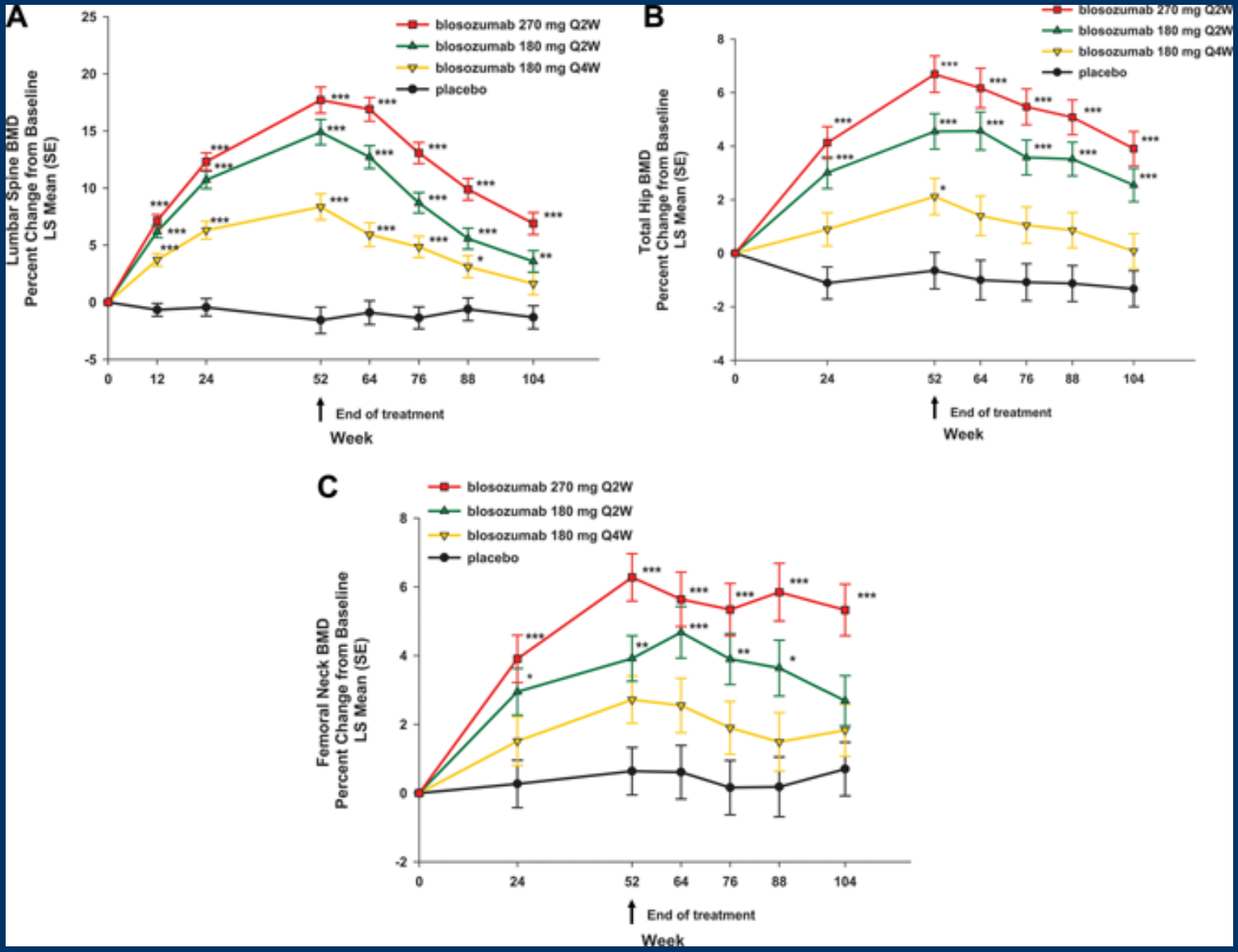
Sklerostin antibody blosozumab : BMD after 1 year in pm women



Percent change (mean, 95% CI) in bone mineral density of the lumbar spine from baseline to week 52 for all study patients according to study group. The least squares mean percent change (mean, 95% CI) in bone mineral density of the lumbar spine from baseline to week 52 is shown. Asterisks (*) indicate statistically significant differences ($p<0.050$, $p<0.010$, $p<0.001$) for each study group as compared with placebo.

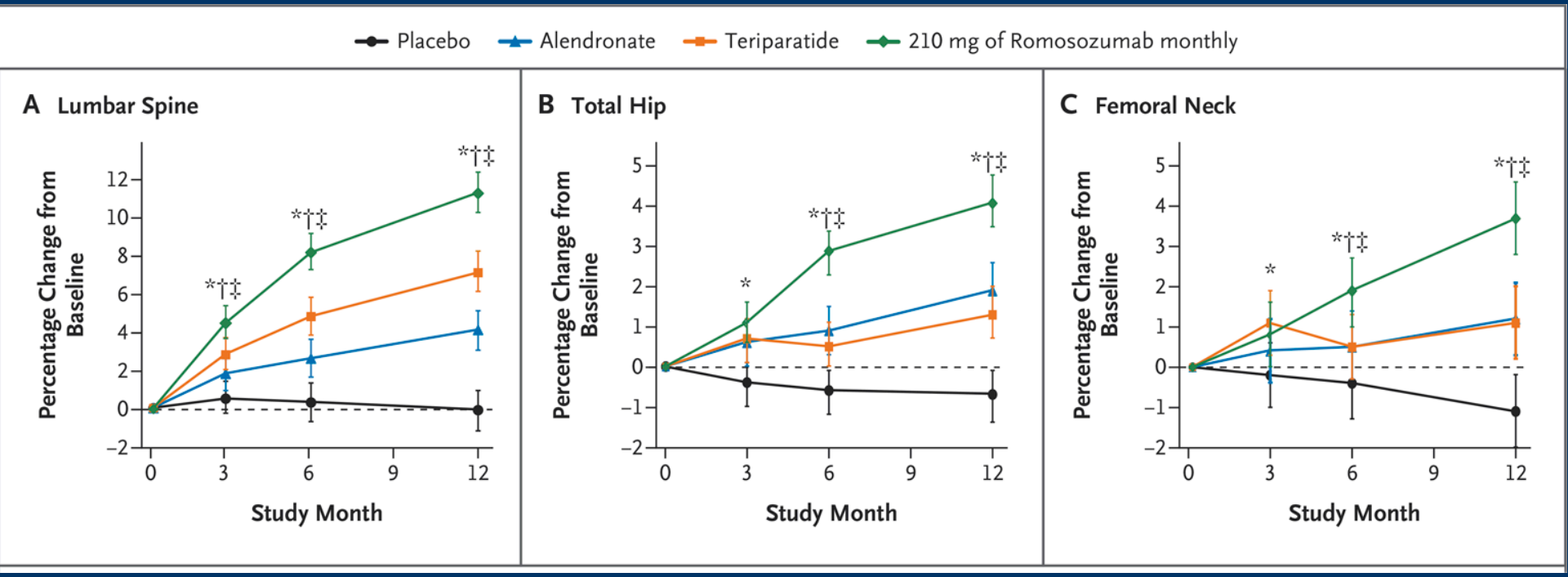
Recker RR et al. Journal of Bone and Mineral Research, Vol. 30, No. 2, February 2015, pp 216–224

The Effect of Discontinuing Treatment With Blosozumab: Follow-up Results of a Phase 2 Randomized Clinical Trial in Postmenopausal Women With Low Bone Mineral Density



Recknor CP et al. J Bone Miner Res. 2015 Sep;30(9):1717-25

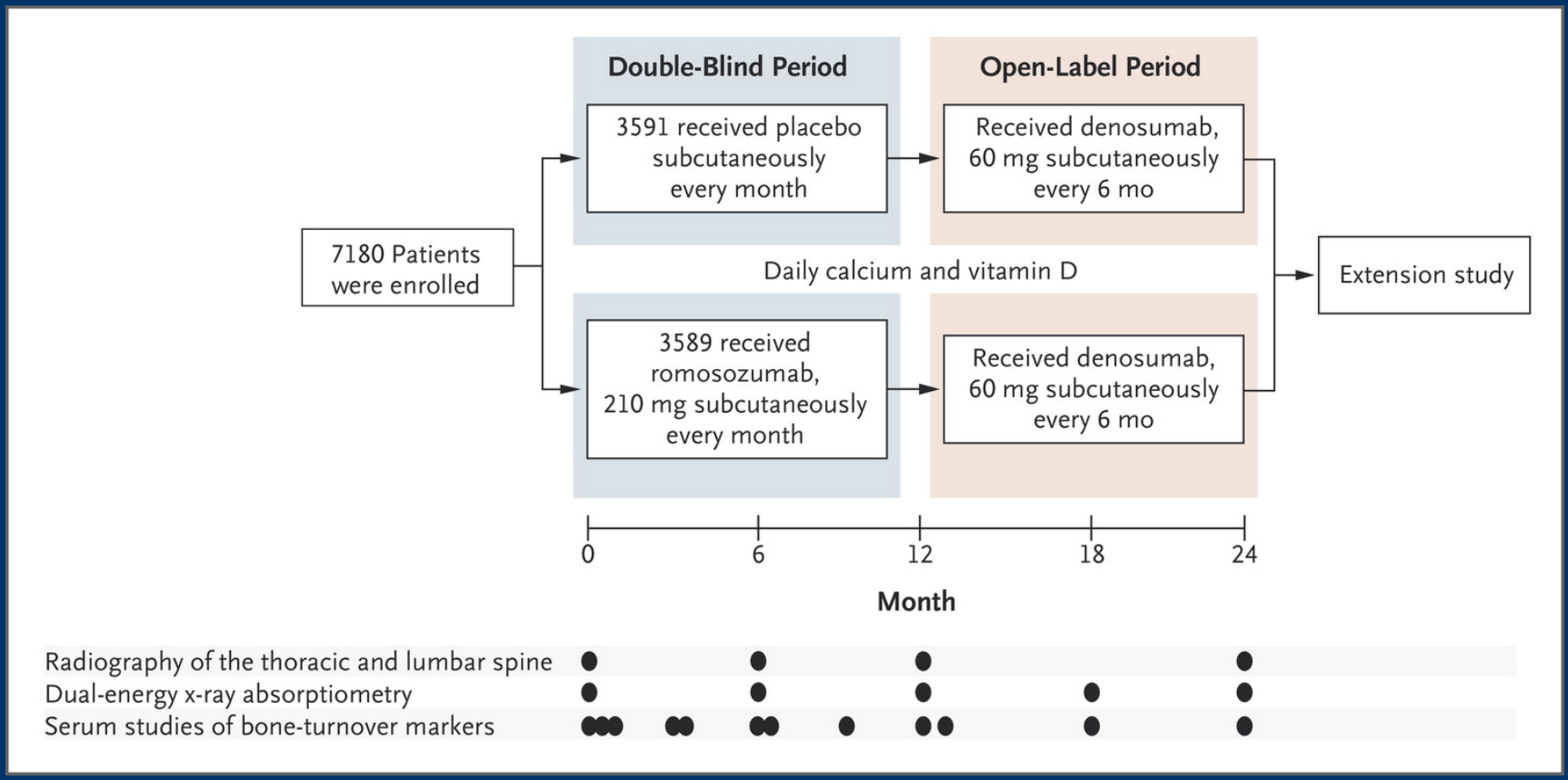
Romosozumab in postmenopausal women with low bone mineral density



Percentage Change from Baseline in Bone Mineral Density.

McClung MR et al. N Engl J Med 2014;370:412-420

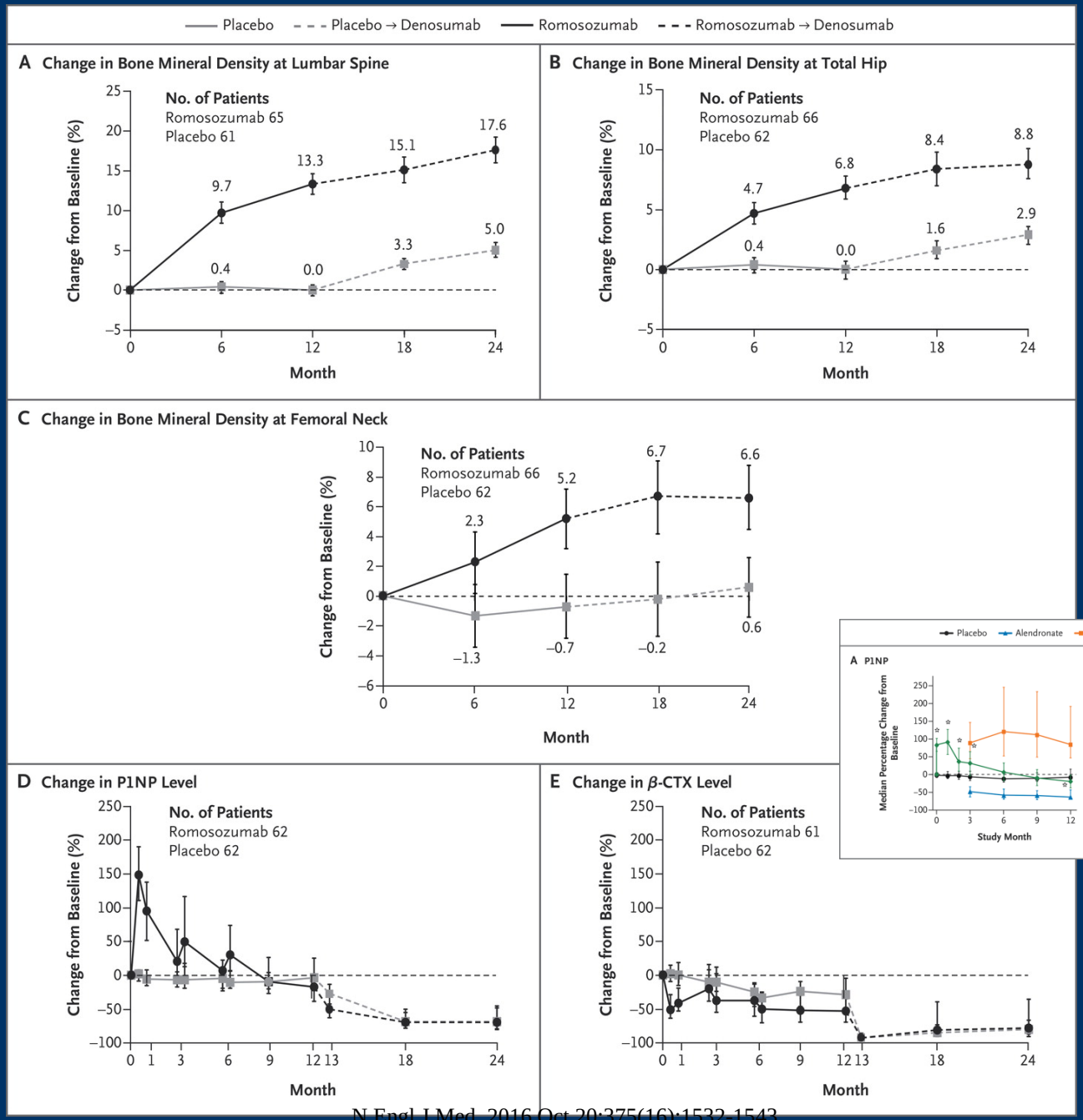
Romosozumab Treatment in Postmenopausal Women with Osteoporosis

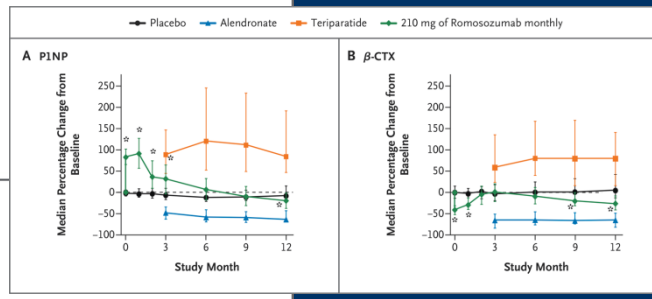


Trial Regimens and Assessments. Women were randomly assigned, in a 1:1 ratio, to receive subcutaneous injections of 210 mg of romosozumab or placebo once monthly for 12 months during the double-blind phase of the trial. Patients then received open-label denosumab, administered subcutaneously at a dose of 60 mg every 6 months for an additional 12 months; the initial group assignment was still blinded. Patients were stratified according to age (<75 years vs. ≥75 years) and prevalent vertebral fracture (yes vs. no). In a substudy of the overall population that involved 128 patients, bone mineral density was assessed at baseline and every 6 months. In a substudy of the overall population that involved 129 patients, the levels of bone-turnover markers were assessed at baseline, at day 14, and at months 1, 3, 3+14 days, 6, 6+14 days, 9, 12, 13, 18, and 24. After the 24-month trial period, patients continue to receive open-label denosumab in a 1-year extension study (data not shown).

Cosman F et al. N Engl J Med 2016;375:1532-1543

Romosozumab treatment in pm women with osteoporosis



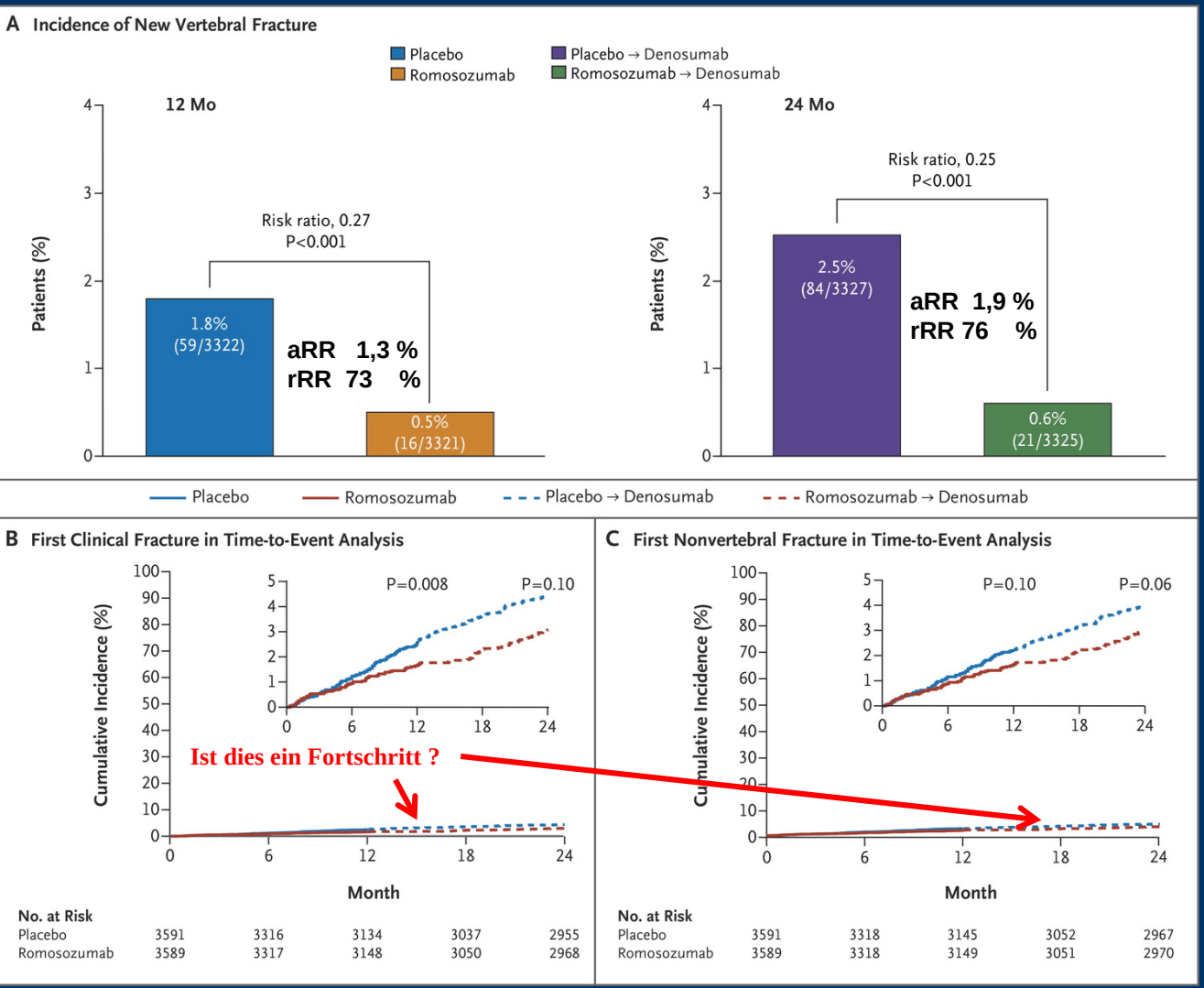


McClung MR et al. N Engl J Med 370: 412-420, 2014

N Engl J Med. 2016 Oct 20;375(16):1532-1543

Cosman F et al. Romosozumab treatment in postmenopausal women with osteoporosis. N Engl J Med 375:1532-1543, 2016

Incidence of New Vertebral, Clinical, and Nonvertebral Fractures



Vertebral fracture 12 mo
16 of 3321 on r.
59 of 3322 on p.

Clinical fracture 12 mo
58 of 3589 on r.
90 of 3591 on p.

Non vertebral fracture 12
56 of 3589 on r.
75 of 3591 on p.

Vertebral fracture 24 mo
21 of 3325 on r./d.
84 of 3327 on p./d.

Every patient daily
500-1000 mg Ca
600-800 IE Vit D

Cosman F et al. Romosozumab treatment in postmenopausal women with osteoporosis.
N Engl J Med 375:1532-1543, 2016

Romosozumab Treatment in Postmenopausal Women with Osteoporosis

Table 2. Adverse Events.*

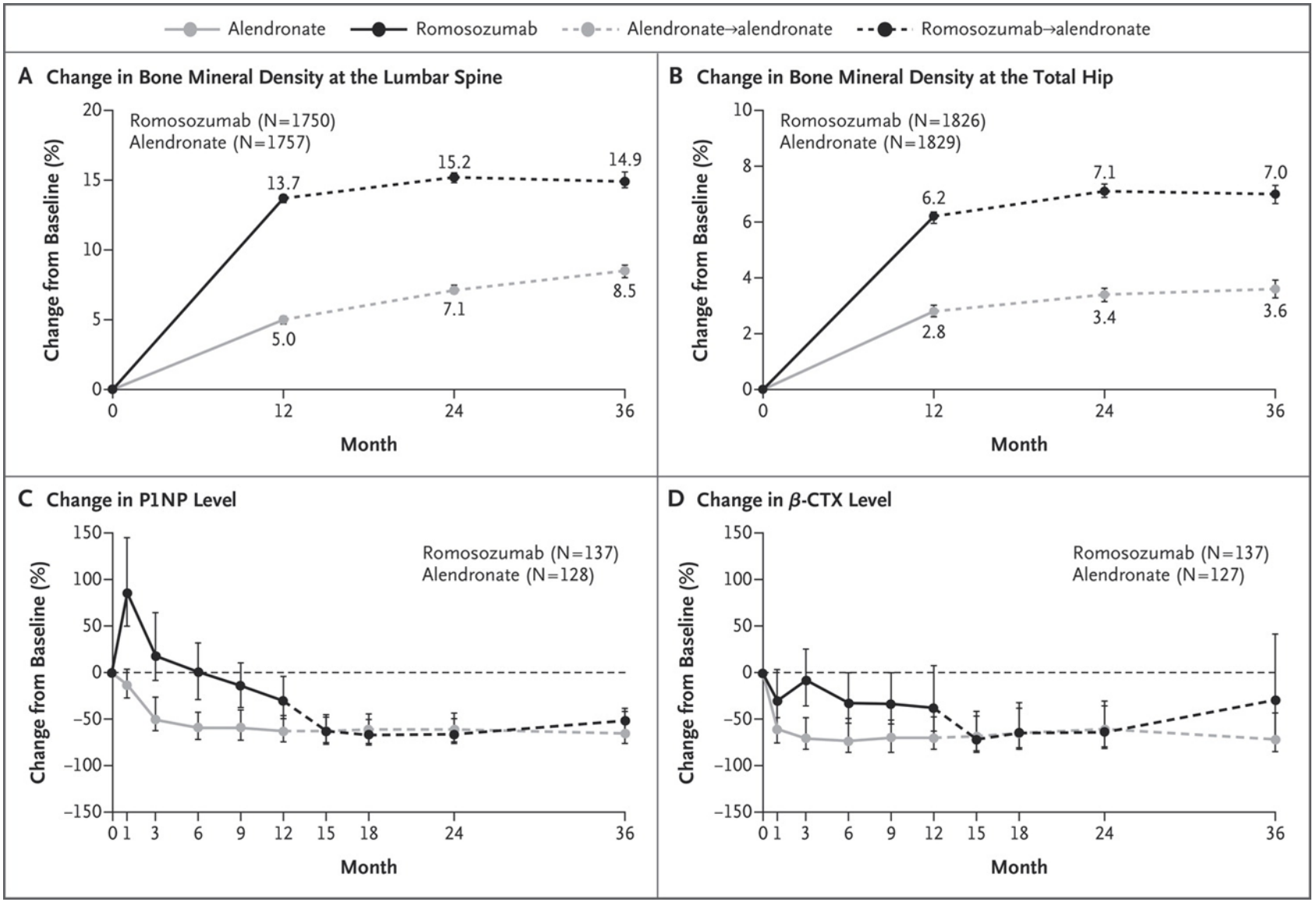
Event	12 Months		24 Months	
	Placebo (N=3576)	Romosozumab (N=3581)	Placebo to Denosumab (N=3576)	Romosozumab to Denosumab (N=3581)
	number of patients (percent)			
Adverse event during treatment†	2850 (79.7)	2806 (78.4)	3069 (85.8)	3053 (85.3)
Arthralgia	429 (12.0)	467 (13.0)	565 (15.8)	585 (16.3)
Nasopharyngitis	438 (12.2)	459 (12.8)	546 (15.3)	557 (15.6)
Back pain	378 (10.6)	375 (10.5)	516 (14.4)	463 (12.9)
Serious adverse event	312 (8.7)	344 (9.6)	540 (15.1)	565 (15.8)
Adjudicated serious cardiovascular event‡	41 (1.1)	44 (1.2)	79 (2.2)	82 (2.3)
Death	23 (0.6)	29 (0.8)	47 (1.3)	52 (1.5)
Adjudicated cardiovascular death‡	15 (0.4)	17 (0.5)	29 (0.8)	31 (0.9)
Event leading to discontinuation of trial regimen	94 (2.6)	103 (2.9)	110 (3.1)	122 (3.4)
Event leading to discontinuation of trial participation	50 (1.4)	44 (1.2)	56 (1.6)	52 (1.5)
Event of interest§				
Hypocalcemia	0	1 (<0.1)	3 (0.1)	6 (0.2)
Hypersensitivity¶	245 (6.9)	242 (6.8)	331 (9.3)	314 (8.8)
Injection-site reaction‖	104 (2.9)	187 (5.2)	106 (3.0)	188 (5.2)
Hyperostosis	27 (0.8)	19 (0.5)	40 (1.1)	35 (1.0)
Cancer	69 (1.9)	59 (1.6)	100 (2.8)	105 (2.9)
Osteoarthritis	315 (8.8)	281 (7.8)	431 (12.1)	396 (11.1)
Osteonecrosis of the jaw‡	0	1 (<0.1)	0	2 (<0.1)
Atypical femoral fracture‡	0	1 (<0.1)	0	1 (<0.1)

Was ist relevant für den Patienten ?

* The population for this analysis included all the patients who underwent randomization and received at least one dose of placebo or romosozumab in the 12-month double-blind period. At month 12, patients made the transition to denosumab for the second year of the trial.
† The events listed are the most frequent adverse events in the double-blind period that occurred in 10% or more of the patients in either group.
‡ The events listed include adverse events that were adjudicated as positive by an independent adjudication committee. Cardiovascular deaths include fatal events that were adjudicated as being cardiovascular-related or undetermined (presumed to be cardiac-related).
§ Events of interest were those that were identified by prespecified *Medical Dictionary for Regulatory Activities* search strategies.
¶ Seven patients in the romosozumab group had serious adverse events during the 12-month double-blind period. Events that were reported by the investigator as being related to romosozumab included dermatitis, allergic dermatitis, and macular rash, all of which resolved; the drug was withdrawn or withheld in these cases.
‖ The most frequent adverse events of injection-site reactions (occurring in >0.1% of the patients) in the romosozumab group during the 12-month double-blind period included injection-site pain (in 1.7% of the patients), erythema (1.5%), bruising (0.8%), pruritus (0.7%), swelling (0.4%), hemorrhage (0.4%), rash (0.3%), and hematoma (0.2%).

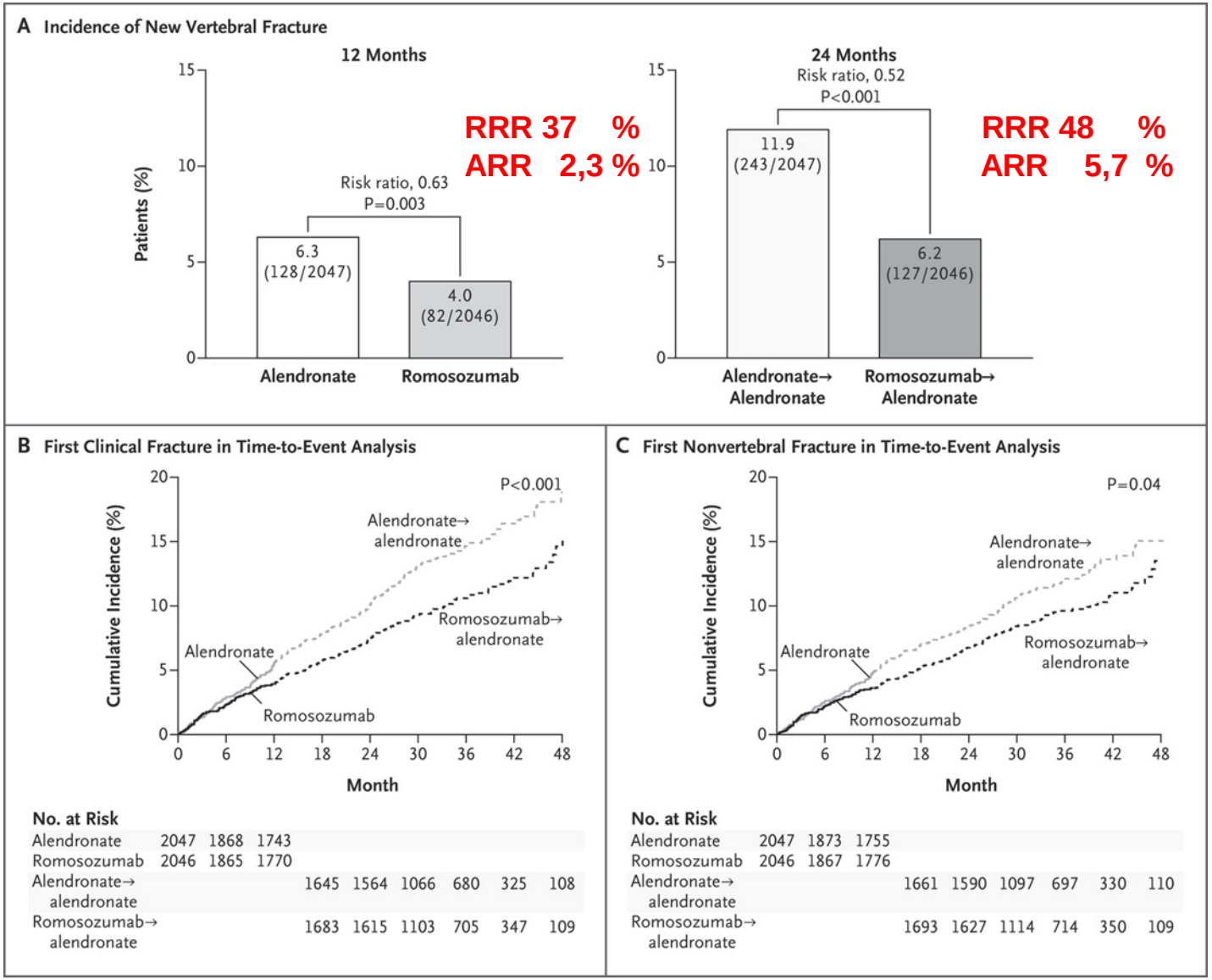
Cosman F et al. N Engl J Med 2016;375:1532-1543

Percentage Change from Baseline in Bone Mineral Density and Levels of Bone-Turnover Markers.



Saag KG et al. N Engl J Med 2017. DOI: 10.1056/NEJMoa1708322

Incidence of New Vertebral, Clinical, and Nonvertebral Fracture.



Saag KG et al. N Engl J Med 2017. DOI: 10.1056/NEJMoa1708322

Adverse Events.

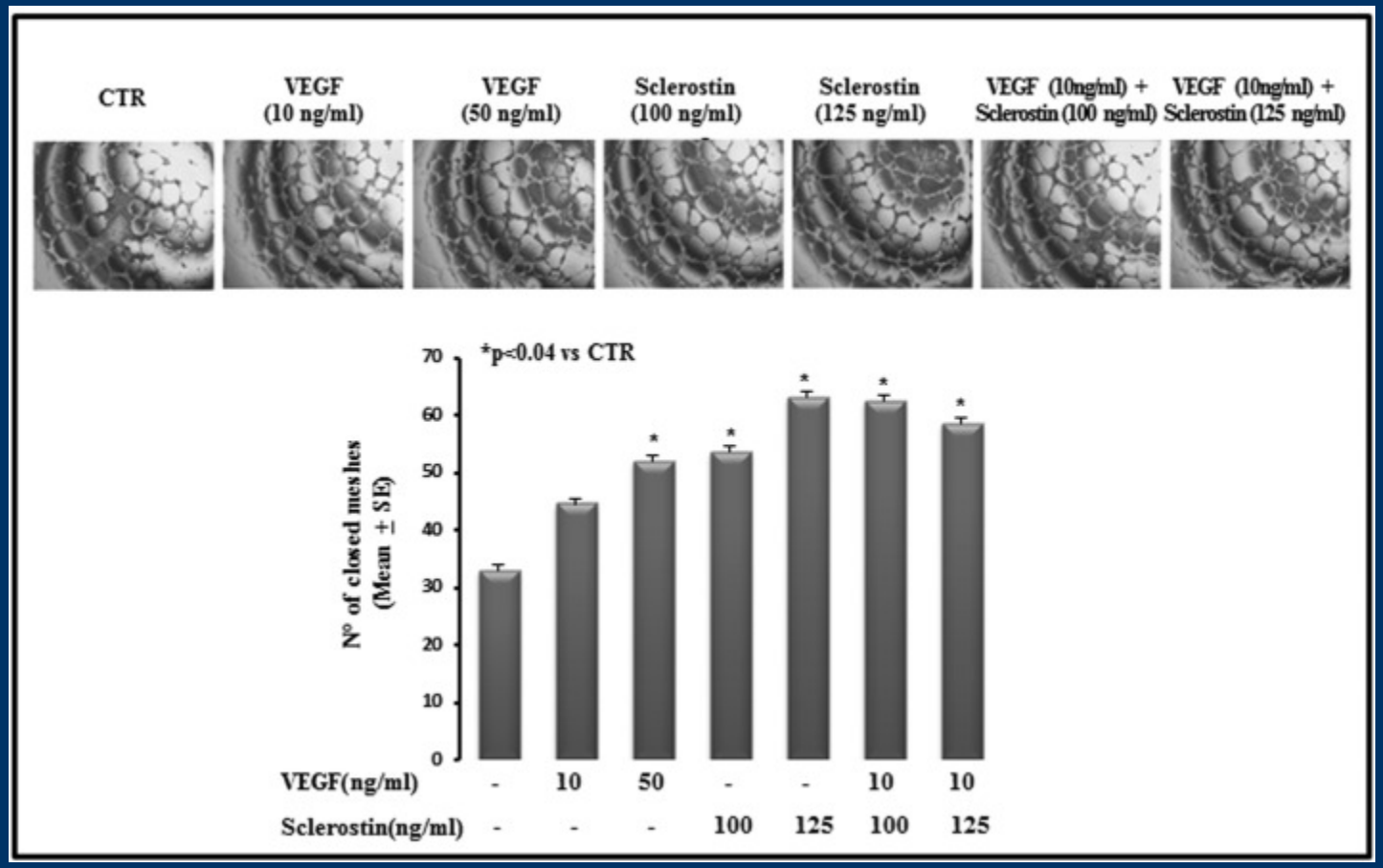
Table 2. Adverse Events.

Event	Month 12: Double-Blind Period		Primary Analysis: Double-Blind and Open-Label Period*	
	Alendronate (N=2014)	Romosozumab (N=2040)	Alendronate to Alendronate (N=2014)	Romosozumab to Alendronate (N=2040)
	number of patients (percent)			
Adverse event during treatment	1584 (78.6)	1544 (75.7)	1784 (88.6)	1766 (86.6)
Back pain†	228 (11.3)	186 (9.1)	393 (19.5)	329 (16.1)
Nasopharyngitis†	218 (10.8)	213 (10.4)	373 (18.5)	363 (17.8)
Serious adverse event	278 (13.8)	262 (12.8)	605 (30.0)	586 (28.7)
Adjudicated serious cardiovascular event‡	38 (1.9)	50 (2.5)	122 (6.1)	133 (6.5)
Cardiac ischemic event	6 (0.3)	16 (0.8)	20 (1.0)	30 (1.5)
Cerebrovascular event	7 (0.3)	16 (0.8)	27 (1.3)	45 (2.2)
Heart failure	8 (0.4)	4 (0.2)	23 (1.1)	12 (0.6)
Death	12 (0.6)	17 (0.8)	55 (2.7)	58 (2.8)
Noncoronary revascularization	5 (0.2)	3 (0.1)	10 (0.5)	6 (0.3)
Peripheral vascular ischemic event not requiring revascularization	2 (<0.1)	0	5 (0.2)	2 (<0.1)
Death	21 (1.0)§	30 (1.5)	90 (4.5)§	90 (4.4)
Event leading to discontinuation of trial regimen	64 (3.2)	70 (3.4)	146 (7.2)	133 (6.5)
Event leading to discontinuation of trial participation	27 (1.3)	30 (1.5)	43 (2.1)	47 (2.3)
Event of interest¶				
Osteoarthritis‖	146 (7.2)	138 (6.8)	268 (13.3)	247 (12.1)
Hypersensitivity	118 (5.9)	122 (6.0)	185 (9.2)	205 (10.0)
Injection-site reaction**	53 (2.6)	90 (4.4)	53 (2.6)	90 (4.4)
Cancer	28 (1.4)	31 (1.5)	85 (4.2)	84 (4.1)
Hyperostosis††	12 (0.6)	2 (<0.1)	27 (1.3)	23 (1.1)
Hypocalcemia	1 (<0.1)	1 (<0.1)	1 (<0.1)	4 (0.2)
Atypical femoral fracture‡	0	0	4 (0.2)	2 (<0.1)
Osteonecrosis of the jaw‡	0	0	1 (<0.1)	1 (<0.1)

Was ist relevant für den Patienten ?

Saag KG et al. N Engl J Med 2017. DOI: 10.1056/NEJMoa1708322

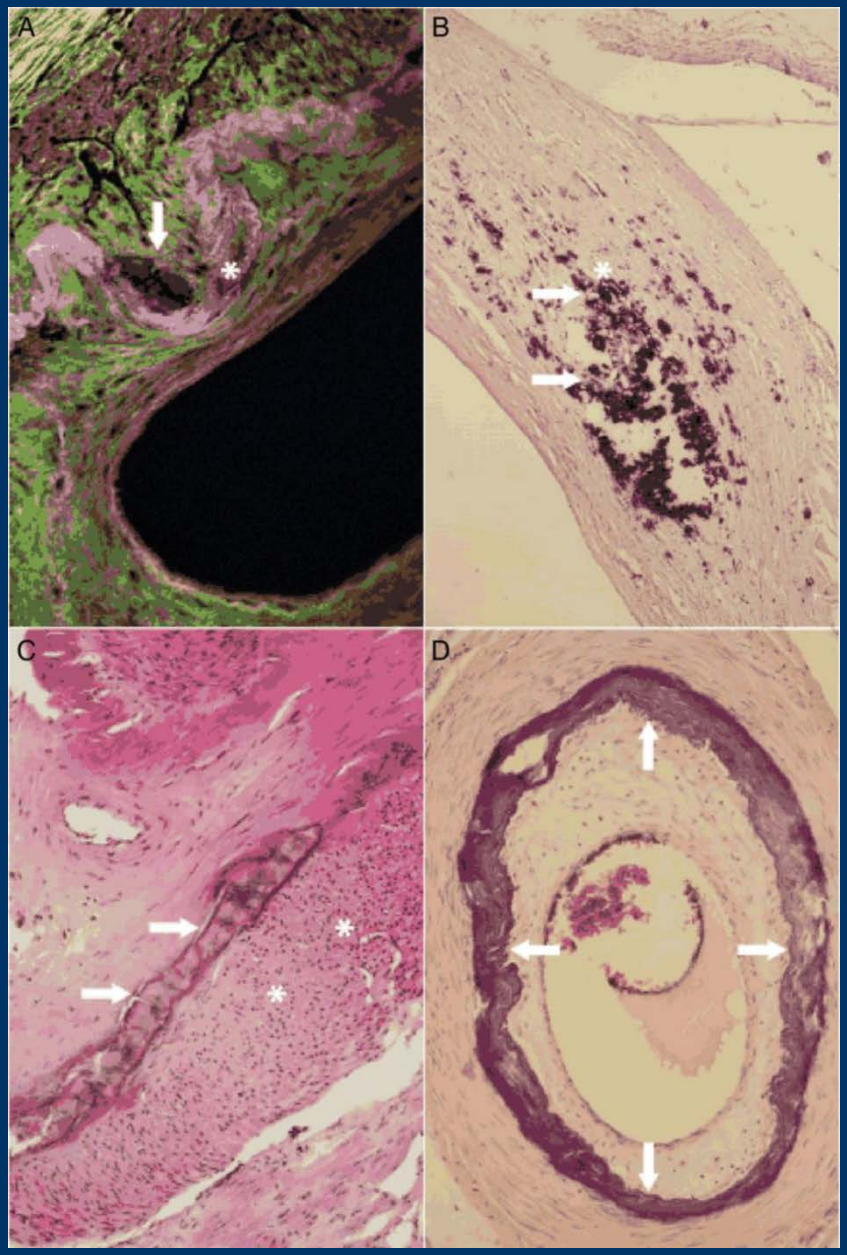
Sclerostin stimulates angiogenesis in human endothelial cells



Sclerostin increases tubulogenesis *in vitro*.

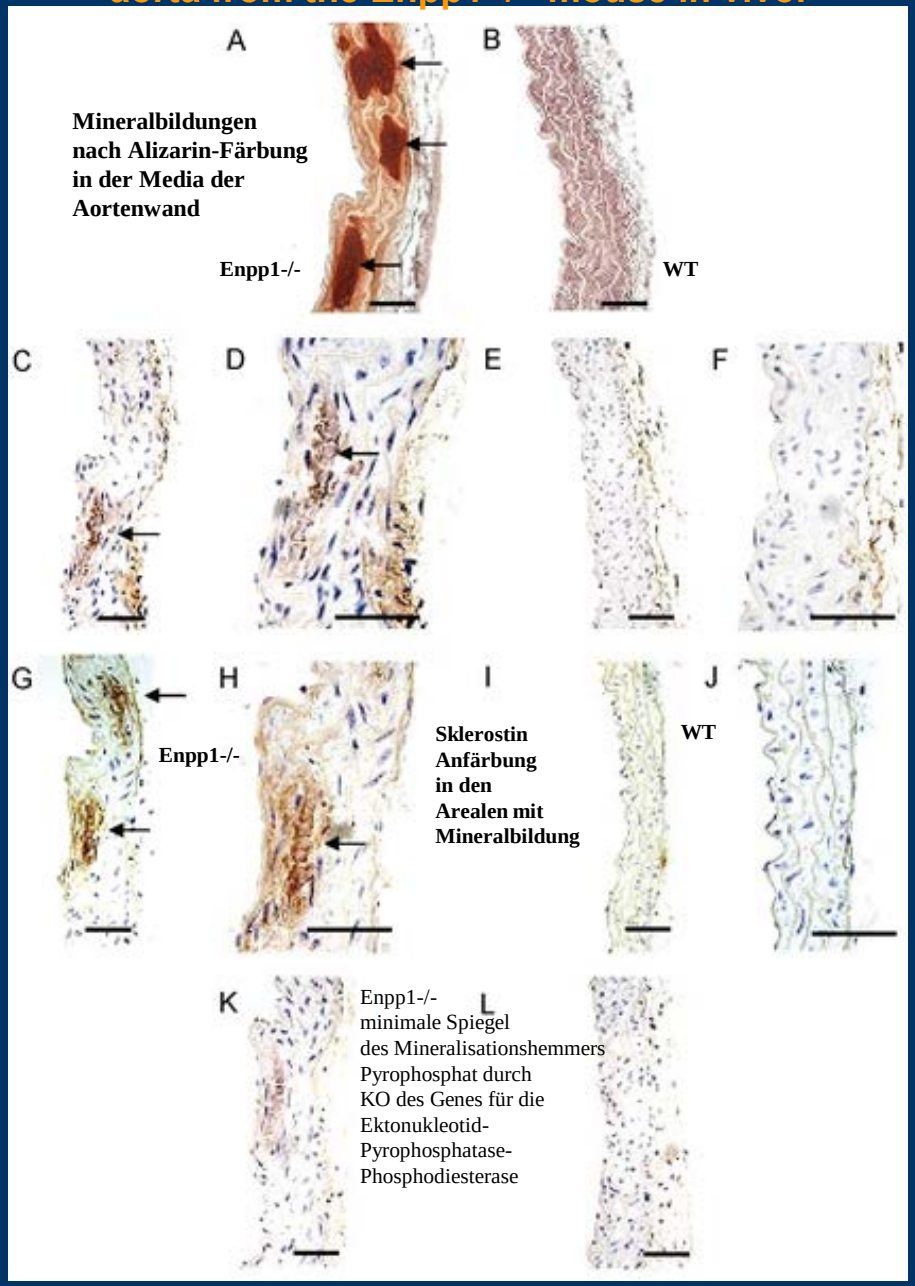
Bone, Volume 101, 2017, 26–36

Microscopical images of medial calcifications in human arteries.



Lanzer P et al. Medial vascular calcification revisited. Eur Heart J. 2014;35(23):1515-1525

Emergence of osteocytic markers in the calcified aorta from the Enpp1−/− mouse in vivo.



Zhu D et al. 2011 The Appearance and Modulation of Osteocyte Marker Expression during Calcification of Vascular Smooth Muscle Cells. PLOS ONE 6(5): e19595

Sclerostin Serum Levels and Vascular Calcification Progression in Renal Transplant Recipients

Table 3. Linear Regression Analysis With Absolute Annualized CAC Change (log) as Dependent Variable

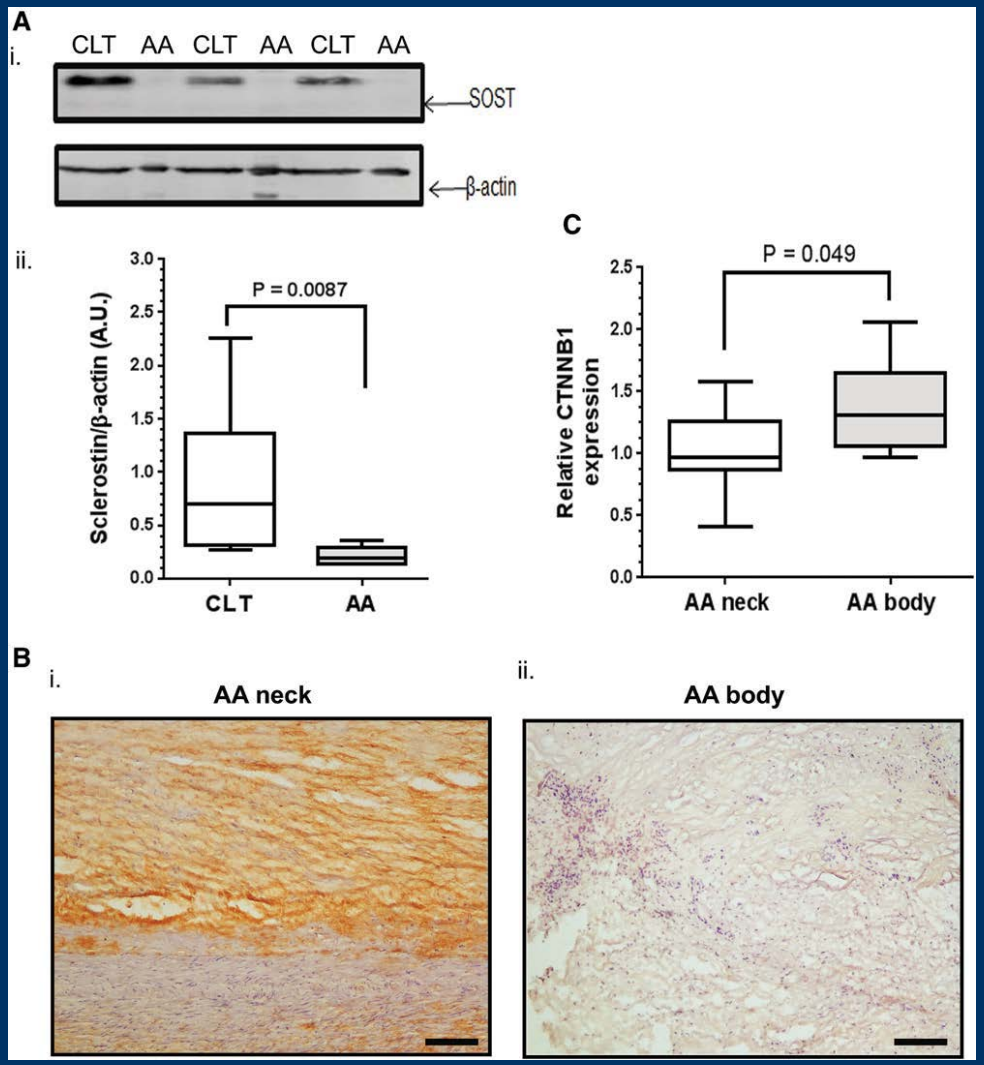
		Univariate			Multivariable Model 1 (R^2 = 0.45)			Multivariable Model 2 (R^2 = 0.69)		
Parameter	**Unit**	**β**	***t***	***P***	**β**	***t***	***P***	**β**	***t***	***P***
Age	y	0.04	7.67	<.0001	0.04	6.41	<.0001			
Dialysis vintage	y	0.12	3.7	.0003	0.08	3.24	.002			
Pulse pressure	mmHg	0.01	3.72	.0003						
Gender	M 0, F 1	−0.47	−3.46	.0007	−0.45	−4.01	<.0001			
Diabetes	No, 0; Yes, 1	0.04	2	<.05						
CV history	No, 0; Yes, 1	0.65	4.28	<.0001				0.22	2.37	.02
Aspirin	No, 0; Yes, 1	0.41	1.75	.08						
Statin	No, 0; Yes, 1	0.54	3.94	.0001	0.30	2.55	.01			
Phosphate	mg/dL	0.06	0.64	.5						
OPG (log)	log, pg/mL	0.47	1.73	.08						
PTH (log)	log, ng/L	0.75	2.99	.003						
CRP (log)	log, mg/dL	0.47	1.73	.09						
Sclerostin (log)	log, ng/mL	1	2.84	.005	−0.94	−2.68	.008			
Calcidiol (log)	log, μg/L	−0.93	−2.97	.05	−0.56	−2.26	.03			
Calcitriol (log)	log, ng/L	−0.03	−0.09	.9						
Baseline CAC (log)	log, U	0.0005	8.2	<.0001				0.59	17.8	<.0001

Model 1, all parameters with $P < .2$ in univariate analysis, except baseline CAC. Model 2, all parameters with $P < .2$ in univariate analysis.

Hohe Serum-Sklerostinspiegel sind assoziiert mit geringerer Gefäßverkalkung und verminderter Progression der vaskulären Mineralbildung in nierentransplantierten Patienten

Evenepoel P et al., J Clin Endocrinol Metab. 2015 Dec;100(12):4669-76

Wnt Signaling Pathway Inhibitor Sclerostin inhibits Aortic Aneurysm and Atherosclerosis



Aortic SOST protein level was downregulated in human AA.

Arterioscler Thromb Vasc Biol. 2017;37:553-566

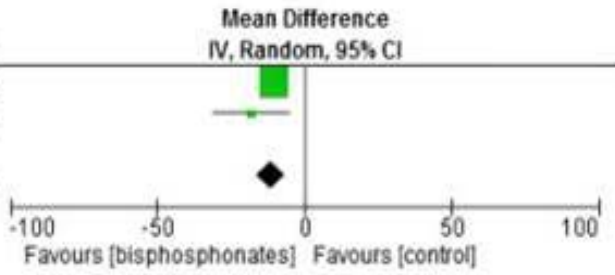
Bisphosphonates for cardiovascular risk reduction

Kranenburg G et al. Bisphosphonates for cardiovascular risk reduction. Atherosclerosis. 2016 Sep;252:106-15

Percentage change in aortic arterial calcification

Study or Subgroup	Bisphosphonates Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Kawahara 2013	-11.4	8.5159	37	-0.9	8.2825	35	86.3%	-10.50 [-14.38, -6.62]
Toussaint 2010	20.3	18	25	38.2	27.7	25	13.7%	-17.90 [-30.85, -4.95]
Total (95% CI)			62			60	100.0%	-11.52 [-16.51, -6.52]

Heterogeneity: Tau² = 3.59; Chi² = 1.15, df = 1 (P = 0.28); I² = 13%
Test for overall effect: Z = 4.52 (P < 0.00001)

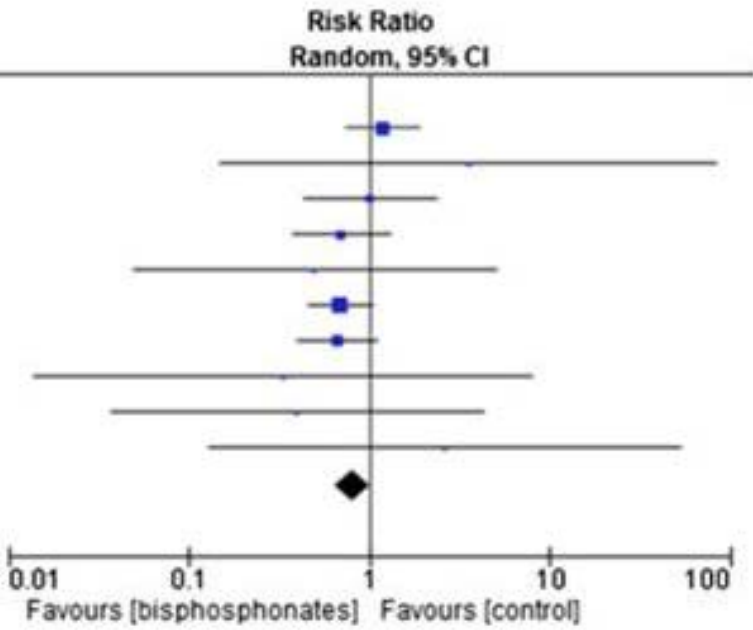


The mean difference in percentage change of aortic arterial calcification progression and the 95% confidence interval are depicted. To assess aortic arterial calcification the percentage change in maximum aortic vessel wall thickness from Kawahara et al. were used and Hounsfield units from Toussaint et al. were used.

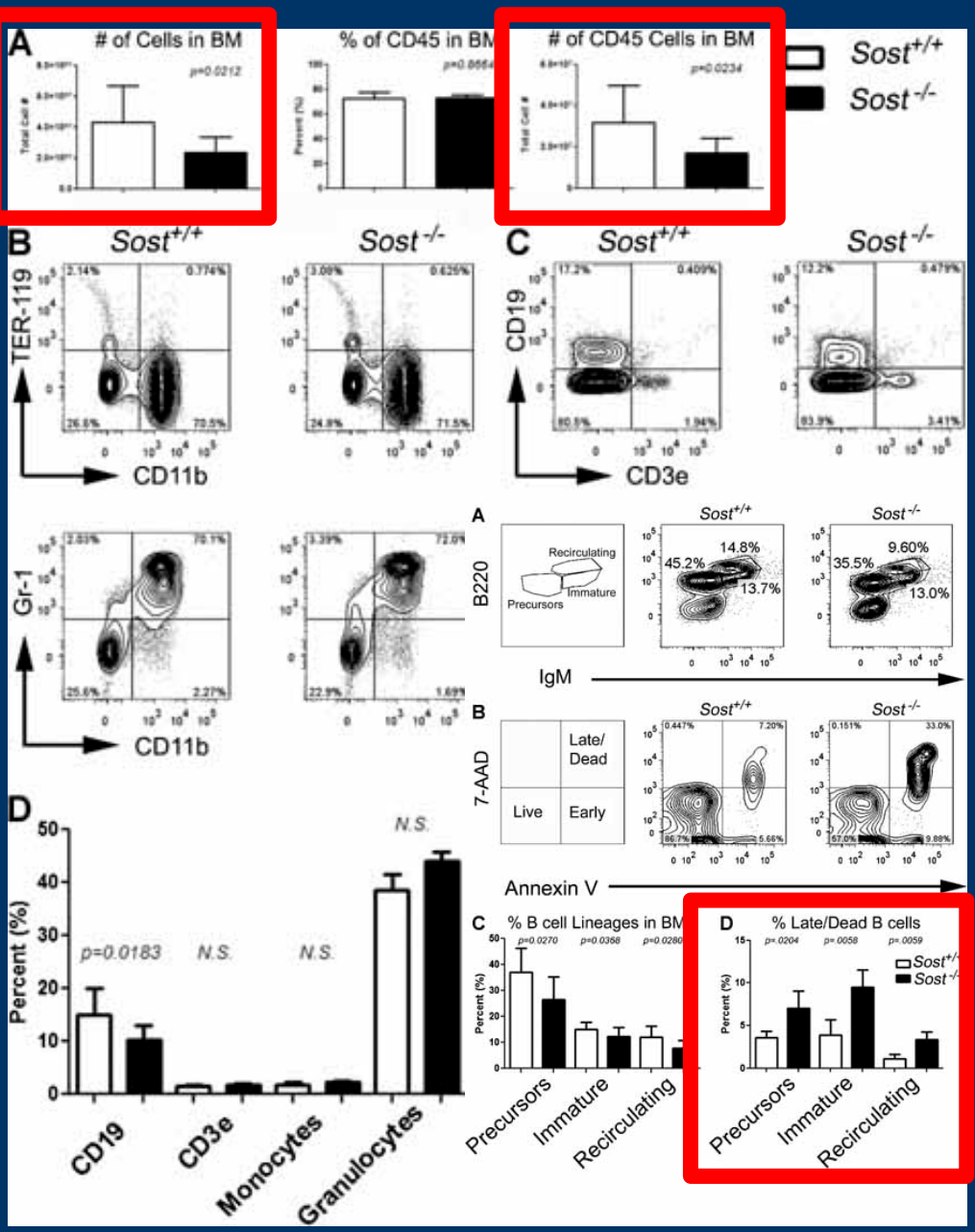
Cardiovascular mortality

	Bisphosphonates Events	Total	Control Events	Total	Weight	Risk Ratio Random, 95% CI
Cardiovascular mortality						
Black 2007	39	3862	33	3852	24.8%	1.18 [0.74, 1.87]
Chailurkit 2003	1	32	0	38	0.5%	3.55 [0.15, 84.14]
Dearnaley 2003	10	155	10	156	7.4%	1.01 [0.43, 2.35]
Denham 2014	16	536	23	537	13.5%	0.70 [0.37, 1.30]
Kraj 2004	1	23	2	23	1.0%	0.50 [0.05, 5.14]
Lyles 2007	36	1054	52	1057	30.5%	0.69 [0.46, 1.05]
Mason 2007	22	254	33	254	20.3%	0.67 [0.40, 1.11]
Palomba 2008	0	45	1	45	0.5%	0.33 [0.01, 7.97]
Ravn 1996	2	150	1	30	0.9%	0.40 [0.04, 4.27]
Stoch 2009	2	114	0	59	0.6%	2.61 [0.13, 53.47]
Total (95% CI)		6225		6051	100.0%	0.81 [0.64, 1.02]
Total events	129		155			

Heterogeneity: Tau² = 0.00; Chi² = 6.32, df = 9 (P = 0.71); I² = 0%
Test for overall effect: Z = 1.79 (P = 0.07)
Test for subgroup differences: Not applicable



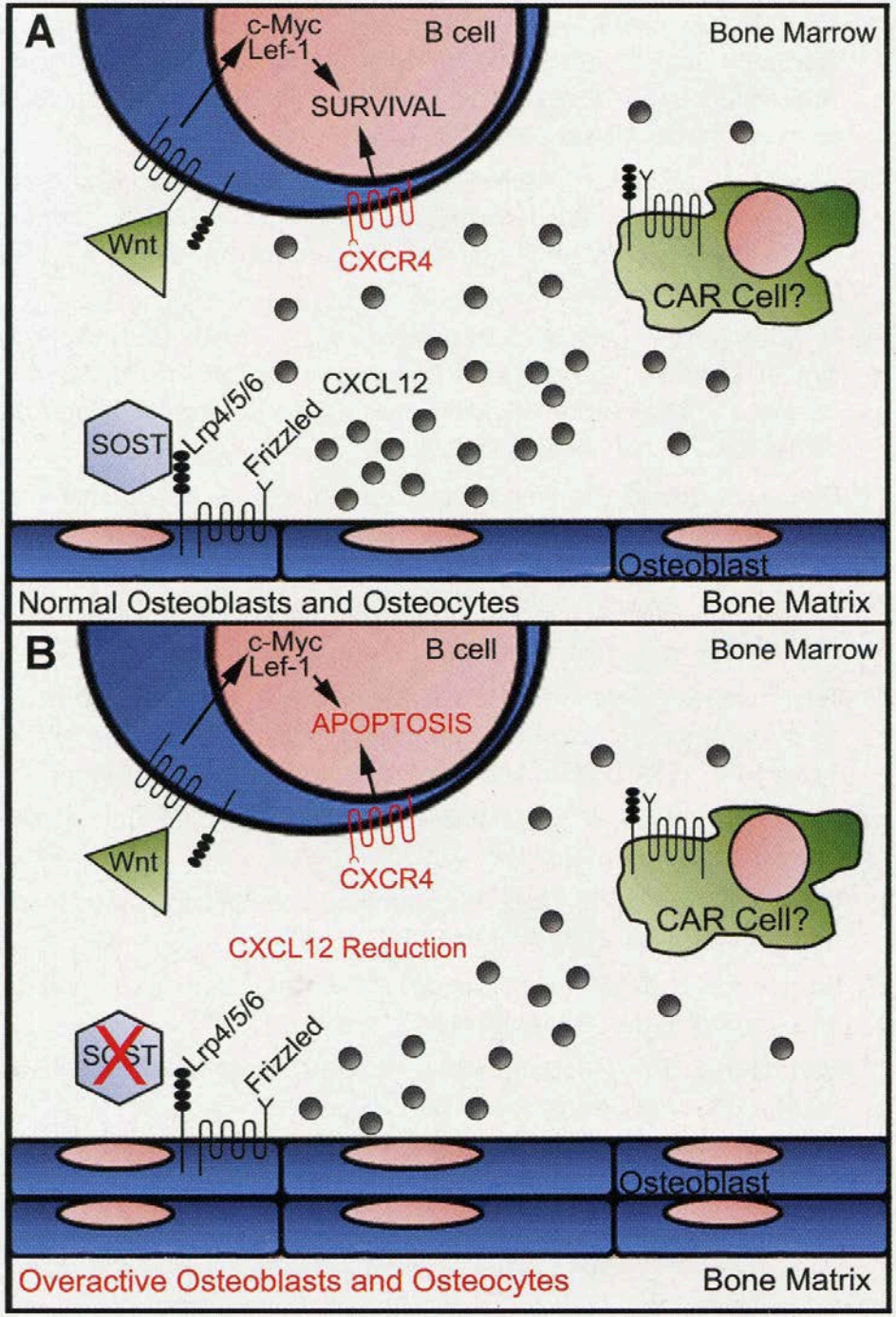
Absence of sclerostin adversely affects B-cell survival



CD19pos B-cell populations in the bone marrow are reduced in Sost−/− mice.

Cain CJ et al. Journal of Bone and Mineral Research 27 (7):1451-1461, 2012

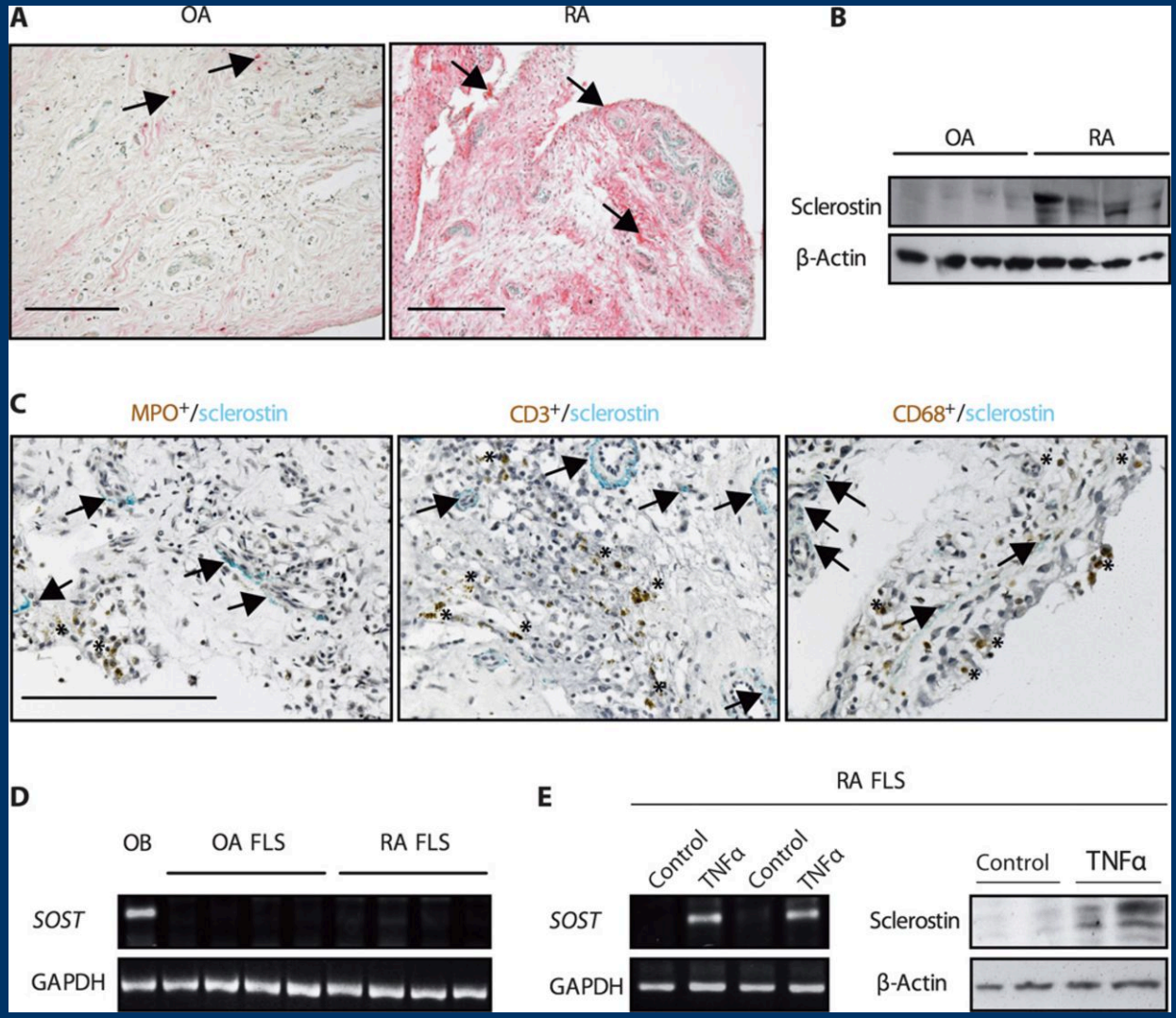
Sklerostin ermöglicht B-Zell Überleben im Knochenmark



Sklerostin hemmt im Knochenmark die Osteoblastenreifung, was eine höhere Sekretion von CXCL12 ins Knochenmark bewirkt. CXCL12 ist ein Überlebensfaktor für B Zellen und deren Vorläufer.

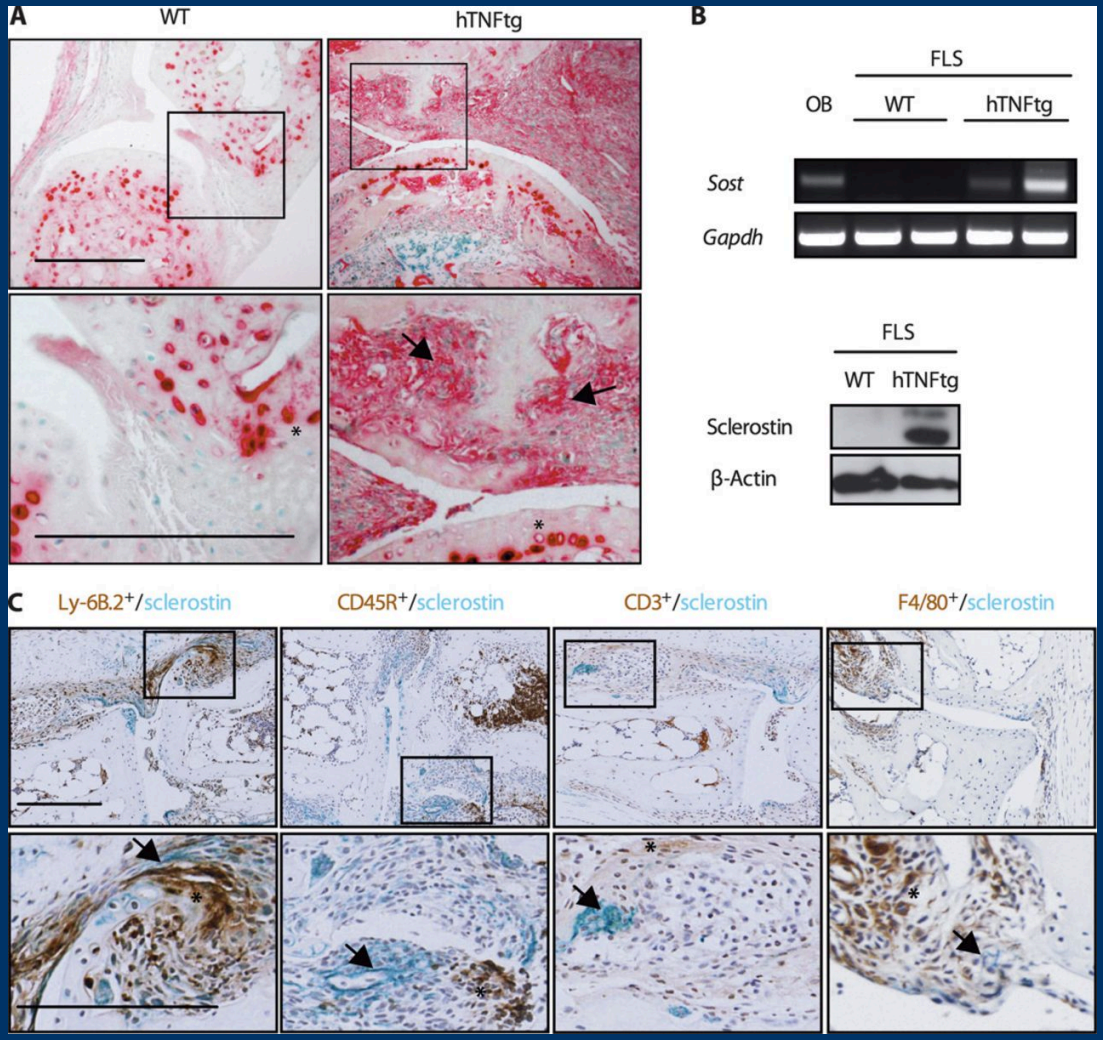
Cain CJ et al. JBMR 27:1451-1461, 2012

Increased sclerostin expression in synovial tissues of RA patients



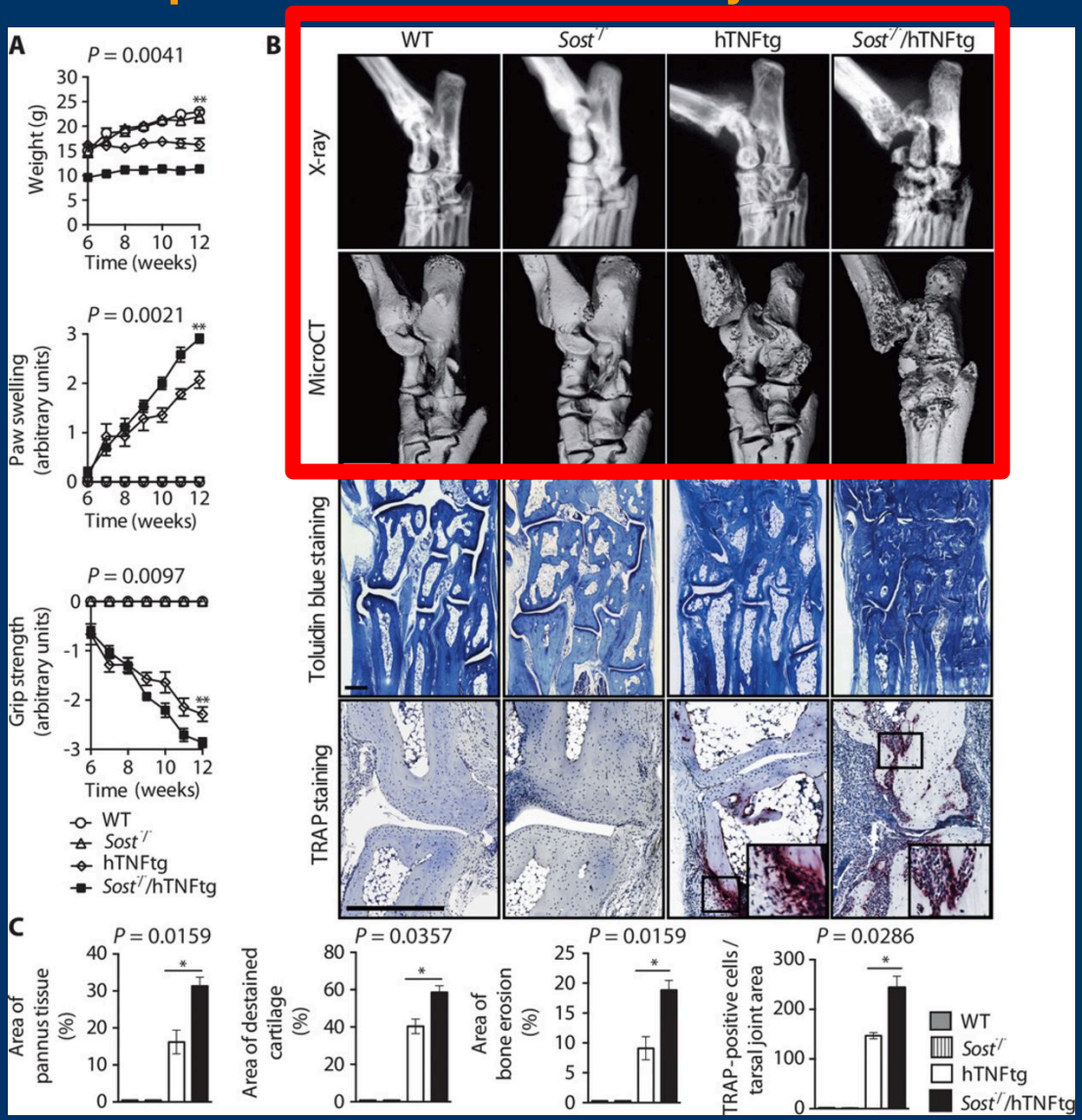
Wehmeyer C et al. Sclerostin inhibition promotes TNF-dependent inflammatory joint destruction. Sci Transl Med 8:330ra35, 2016

Increased sclerostin expression in synovial tissues of hTNFtg mice



Wehmeyer C et al. Sclerostin inhibition promotes TNF TNF dependent inflammatory joint destruction. Sci Transl Med 2016;8:330ra35

Sclerostin deficiency worsens experimental arthritis and promotes pannus formation and joint destruction in hTNFtg mice



(A) Disease progression indicated by weight, paw swelling, and grip strength was assessed in WT, Sost−/−, hTNFtg, and Sost−/−/hTNFtg mice from week 6 to 12. Data are averages ± SEM (n = 7 for hTNFtg mice and n = 11 for Sost−/−/hTNFtg). P value determined by Mann-Whitney U test, two-tailed test.

(B) Representative x-ray images, three-dimensional surface microCT images (scale bar, 1 mm), toluidine blue staining (scale bar, 400 μm), and tartrate resistant acid phosphatase (TRAP) staining of tarsal joint sections from the hind paws of 12-week-old WT, Sost−/−, hTNFtg, and Sost−/−/hTNFtg mice. TRAP-positive osteoclasts labeled as purple spots (scale bar, 400 μm).

(C) Quantitative histomorphometric analysis of synovial pannus formation, destained cartilage, bone erosion, and number of osteoclasts in tarsal joints.

Wehmeyer C et al. Sclerostin inhibition promotes TNF dependent inflammatory joint destruction. Sci Transl Med 2016;8:330ra35

Zusammenfassung
Sklerostin-Antikörper Therapie

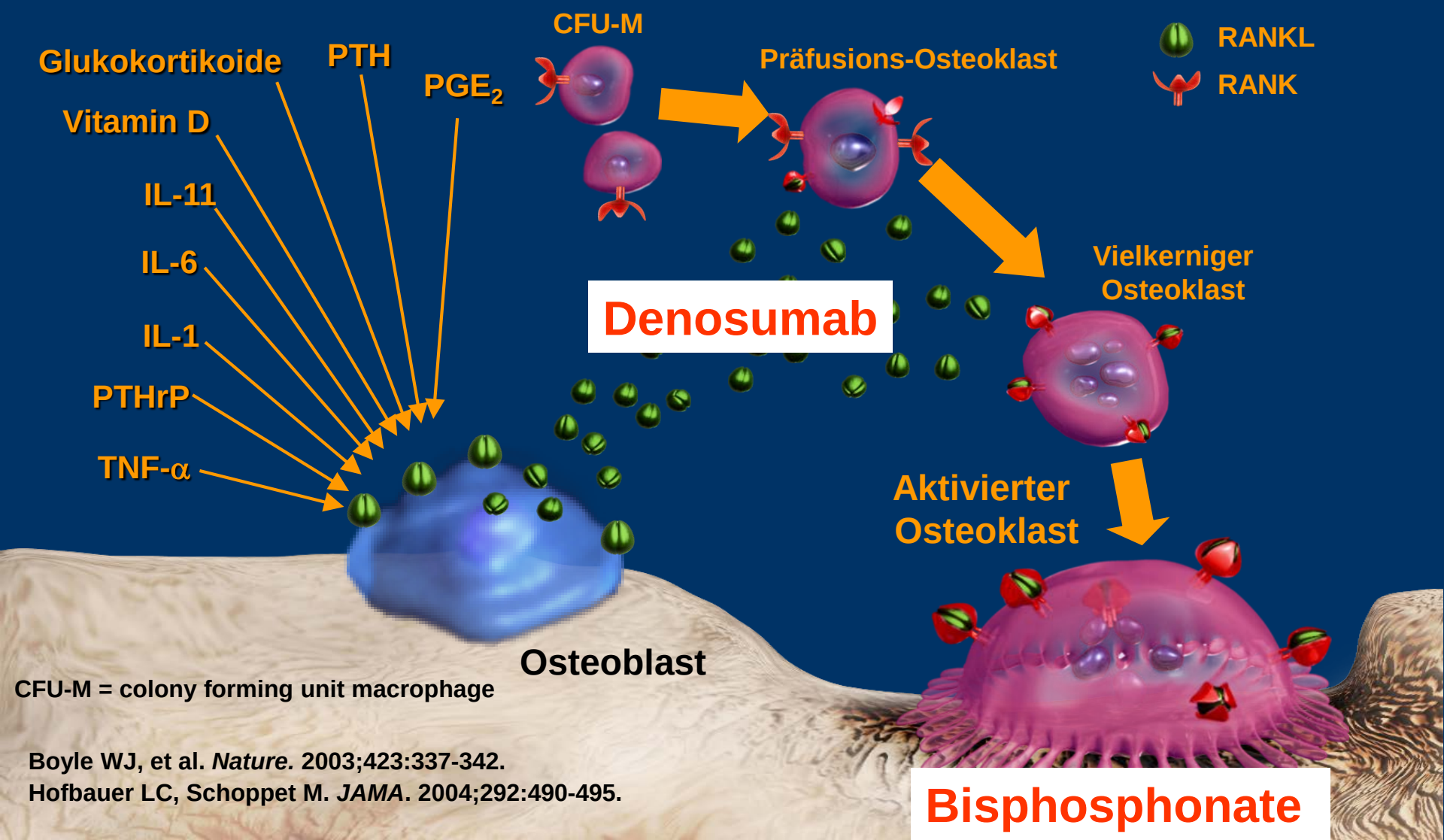
Schnell wirksames osteoanaboles Therapieprinzip innerhalb eines Jahres bei pm Frauen mit Osteoporose, Anbaumarker aber bereits nach 6 Monaten auf Ausgangsniveau

Bisphosphonattherapie im Anschluß vermutlich sinnvoll zum vollen Erhalt der Knochenmasse nach Therapieende (Vermeidung Anschlußfrakturen nach Absetzen von Denosumab: Popp AW et al. OI 2016; Lamy O et al. JCEM 102.354, 2017) ?

Ohne weitere Langzeitstudien (üblich 3 Jahre) Zurückhaltung bei Ost.Pat. mit

- **KHK oder AVK oder Aneurysma**
- **renaler Osteopathie**
- **TNF vermittelten Erkrankungen wie Arthritis, Crohn, Colitis etc.**
- **immun-kompromitierten Patienten (z.B. Transplantierte oder Patienten unter dauerhafter Glukokortikoidbehandlung)**

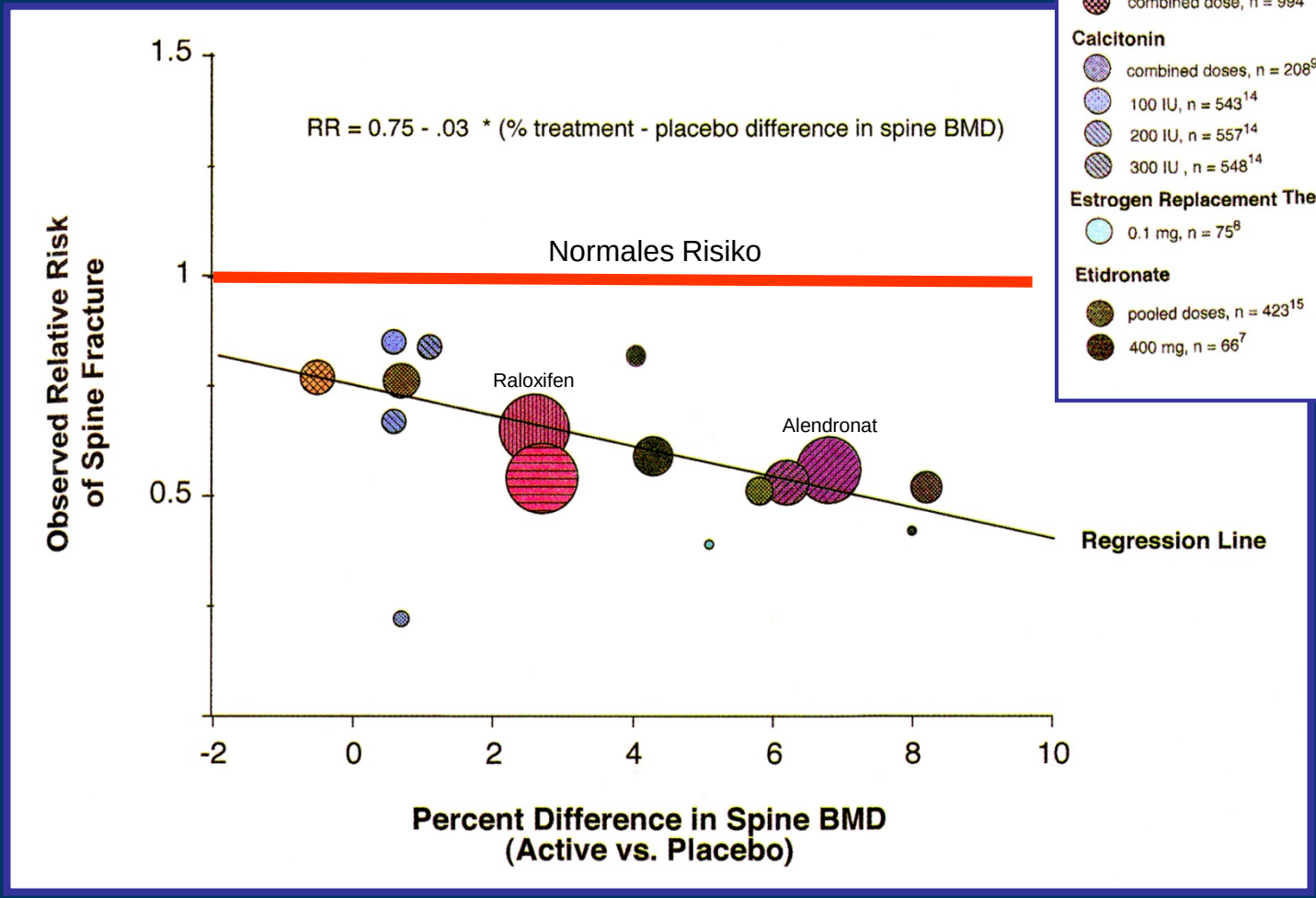
Antiresorptive Standardtherapie der Osteoporose



CFU-M = colony forming unit macrophage

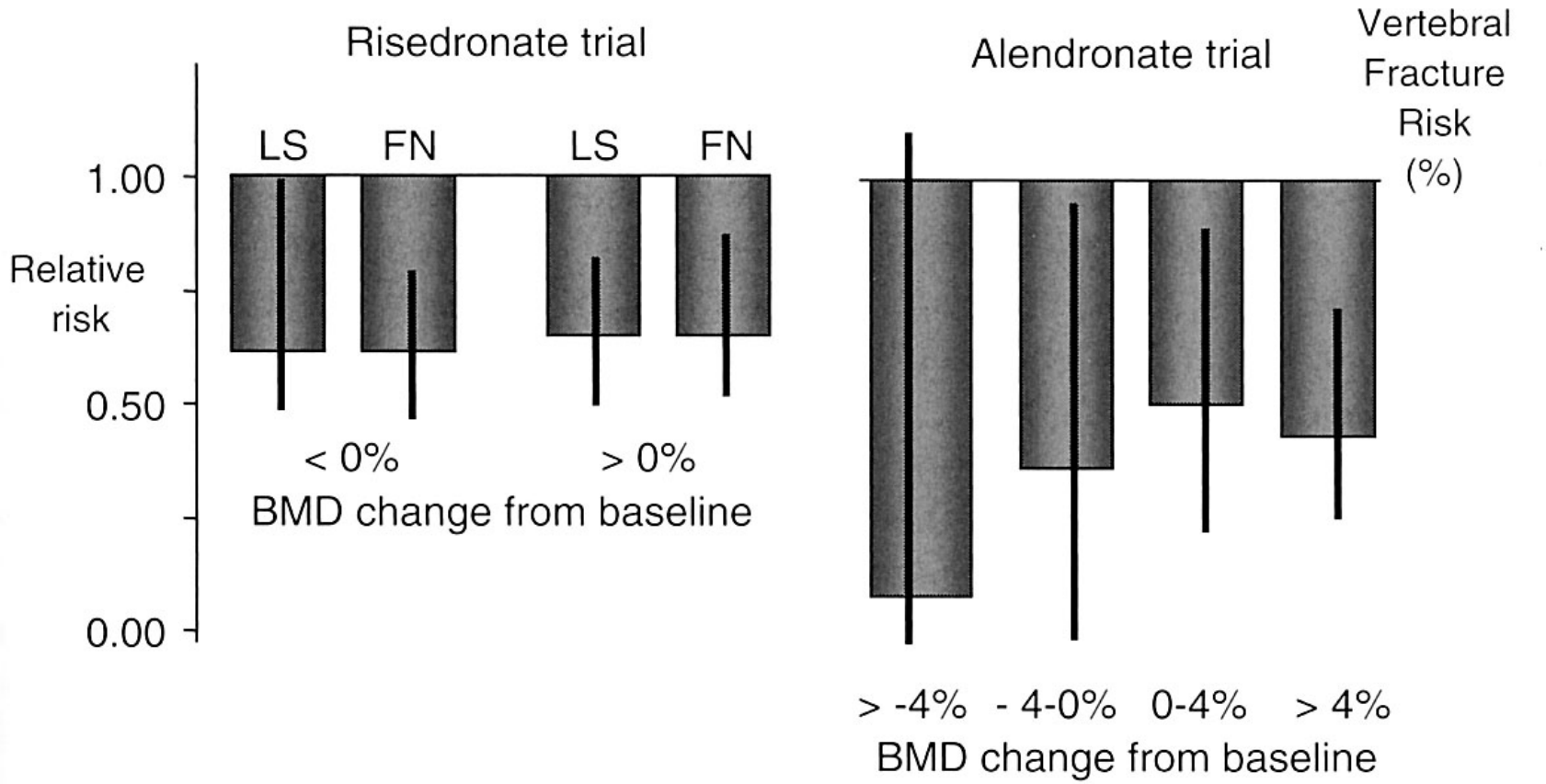
Boyle WJ, et al. *Nature.* 2003;423:337-342.
Hofbauer LC, Schoppet M. *JAMA*. 2004;292:490-495.

Frakturrisiko und Dichteänderung unter Therapie

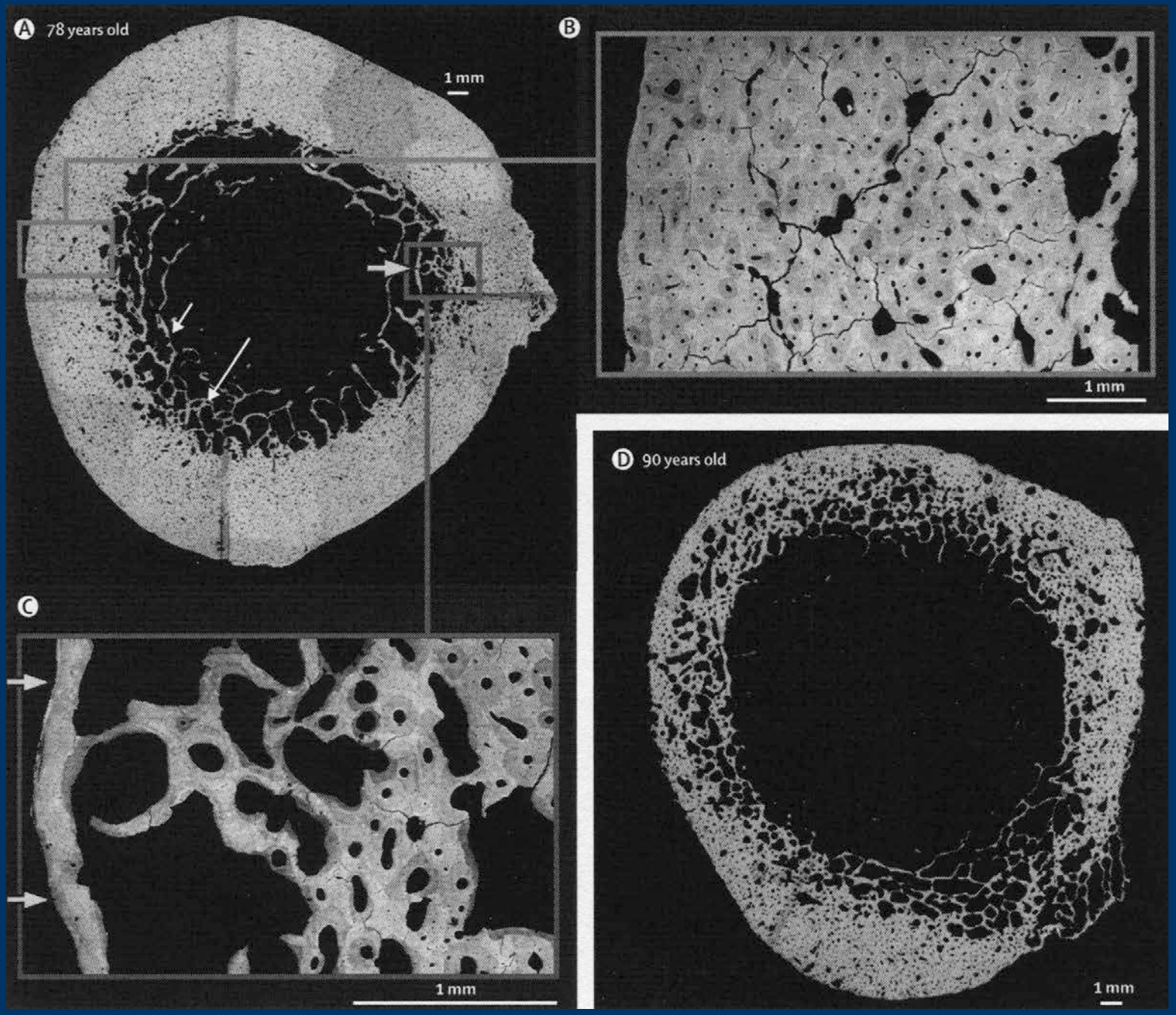


Cummings et. al, Amer. J. Med. 112; 9332-9343, 2002

Frakturrisiko und Dichteänderung (bei sichergestellter Compliance !)



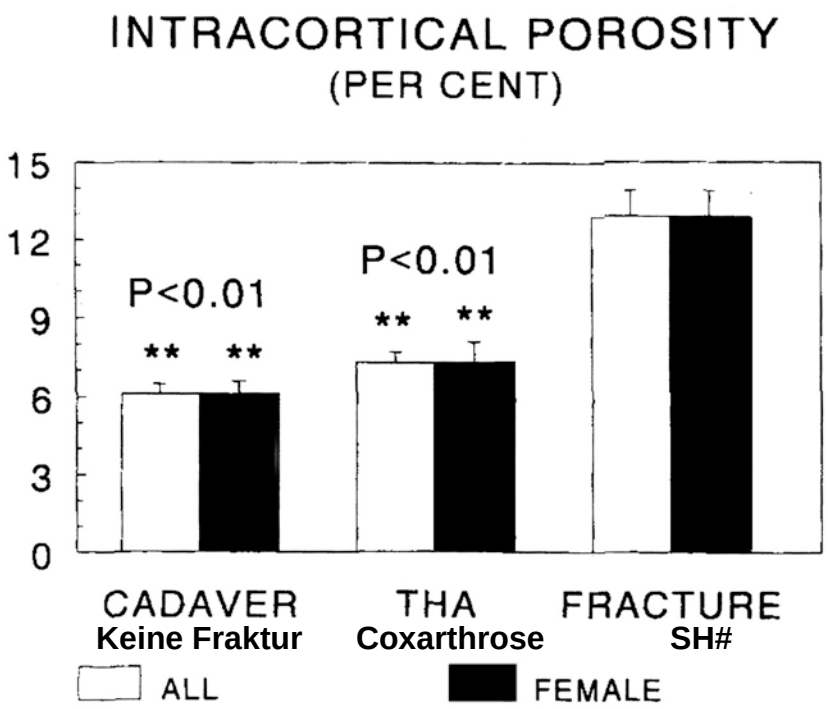
Seemann E Bone 41:308-317,2007



Kortikale Porosität 78 J. vs. 90 J.

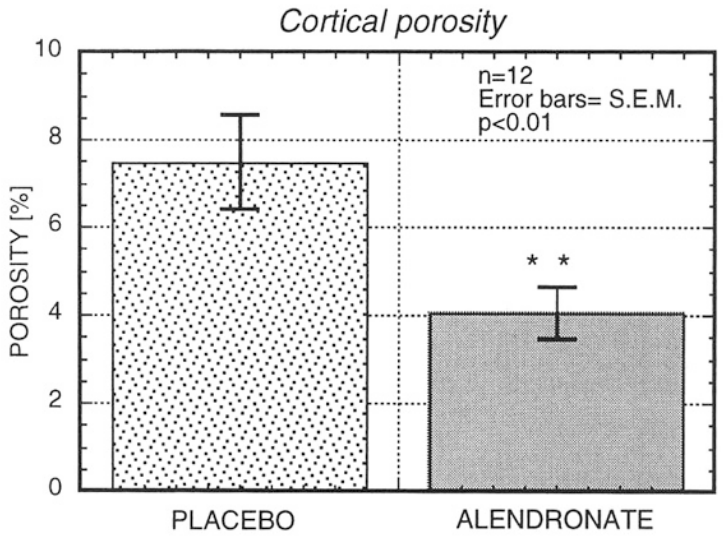
Zebaze RMD et al. Lancet 375:1729-1736, 2010

Kortikale Porosität bei Frauen mit SH-Fraktur



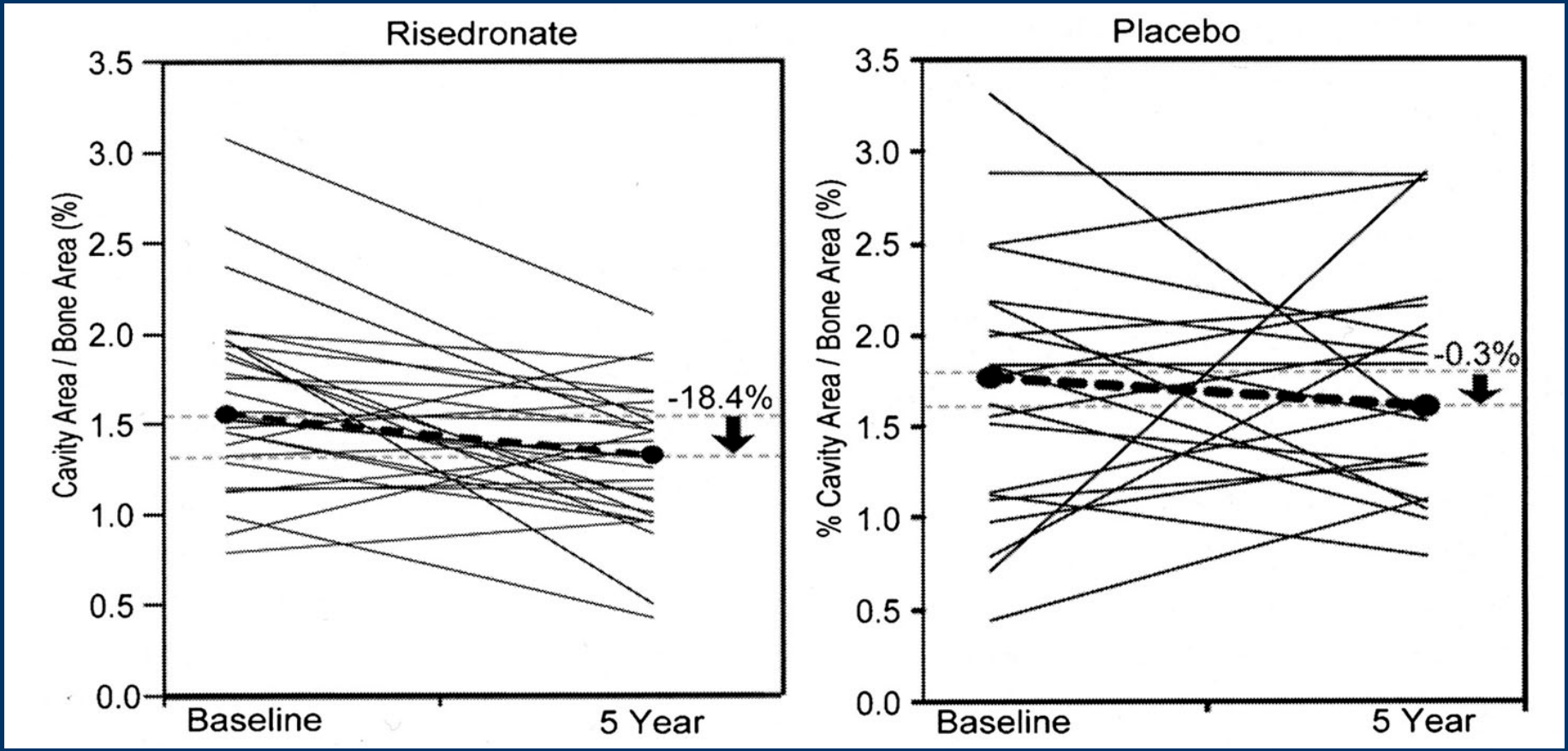
Barth RW et al. Clin Orthopaedics Rel Res 283:178-186, 1992

Kortikale Porosität unter BP Therapie



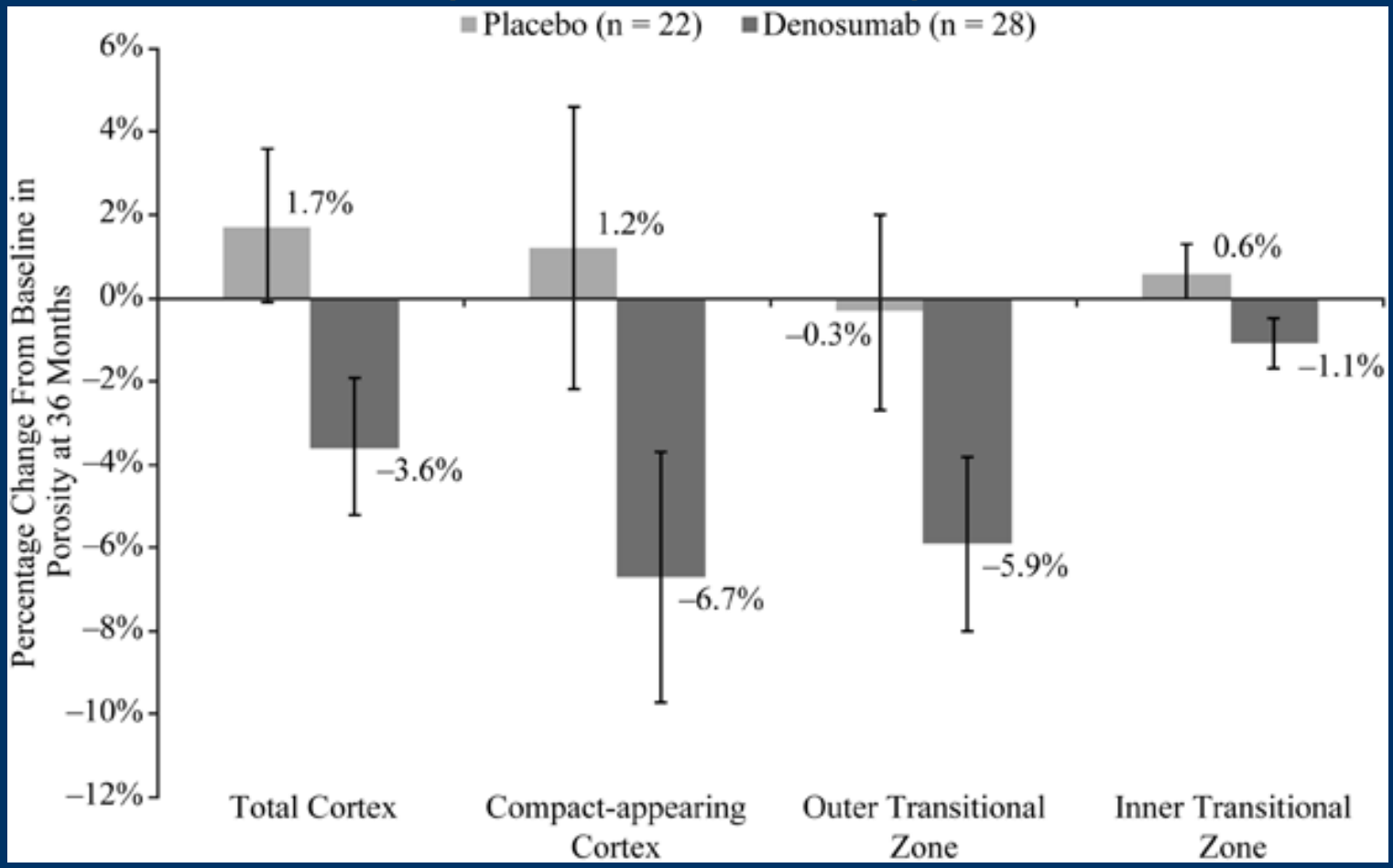
Roschger P et al. Bone 29:185-191, 2001

Risedronat reduziert kortikale Porosität



Borah B et al. JBMR 25:41-47, 2010

Denosumab Reduces Cortical Porosity of the Proximal Femoral Shaft in Postmenopausal Women With Osteoporosis



Percentage change from baseline at 36 months in proximal femoral total cortical porosity assessed distal to the lesser trochanter in response to denosumab or placebo treatment. In the denosumab group, porosity decreased in all regions relative to baseline at 36 months. The reduction in porosity of the total cortex was mainly attributable to decreases in porosity of the compact-appearing cortex and outer transitional zone. Porosity remained unchanged relative to baseline in the placebo group. The differences in porosity in the denosumab group relative to placebo at 36 months were significant in all regions (all $p < 0.01$).

Zebaze R et al. Journal of Bone and Mineral Research. 31:1827-1834, 2016

Raloxifen

Raloxifene Use for The Heart trial (RUTH Studie)

Welchen Fortschritt bringt diese Substanz ?

Ergebnisse

- **Reduziert das Risiko klinisch relevanter WK-Frakturen um 35%**
- **Reduziert das allgemeine Brustkrebs-Risiko um 33%**
- Keinen signifikanten Effekt auf das Risiko prim. CV-Ereignisse (HR 0,95)
- Keinen signifikanten Unterschied bezügl. des allgemeinen Stroke-Risikos

ABER: **Raloxifen assoziiert mit einem erhöhten Risiko für letalen Stroke (um 49% höher)**

Risiko für venöse Thrombembolien um 44% erhöht

Nutzen abwägen

Geringe Frakturprävention

Verstärkung postmenopausaler Beschwerden

Thrombembolie Risiko erhöht wie bei Östrogenen

Barrett-Connor et al., N Engl J Med 2006; 355:125-137

Zusammenfassung

Standardtherapie der Osteoporose sind die Bisphosphonate.

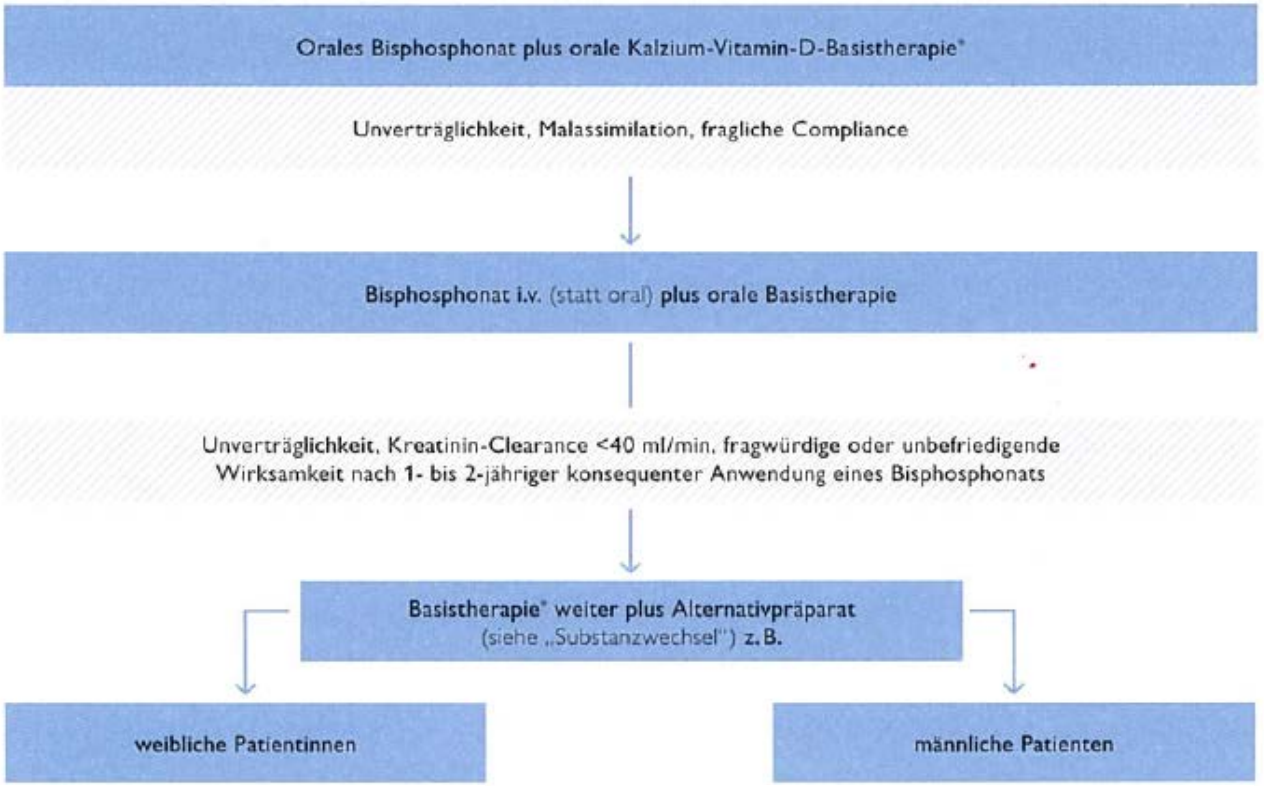
Bei sichergestellter Compliance gibt es keine „beste“ Substanz.

Neue Frakturen (Ursache !) oder Dichteverluste < 4 %/a (g/cm2 Werte) in den ersten 2 Jahren einer BP Therapie sind keine absolute Indikation zum Präparatewechsel,
eher für einen längeren Therapiezeitraum.

Alternativen müssen entsprechend der individuellen Krankheitssituation des Patienten und der bekannten Nebenwirkungsprofile geprüft werden.

Experten Rat: Nach Absetzen/Pausieren von Nicht-Bisphosphonaten (z.B. Denosumab, Teriparatid) 1-jährige BP-Nachbehandlung oder zumindest Dichtekontrolle schon nach 6-12 Monaten und dann jährlich erscheint zweckmäßig.

Zweckmäßiger Osteoporose-Therapie-Algorithmus



Konsens für Baden-Württemberg Uniklinik HD, KV, MDKs
Verordnungsforum 25 und KVBW Internet-Seite


Vielen Dank