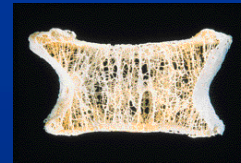
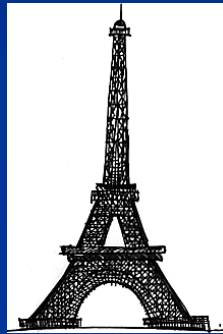


# Traitement de l'ostéoporose en 2020



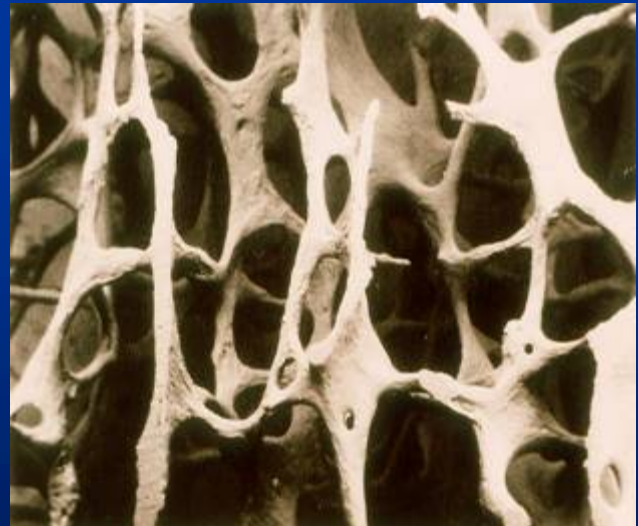
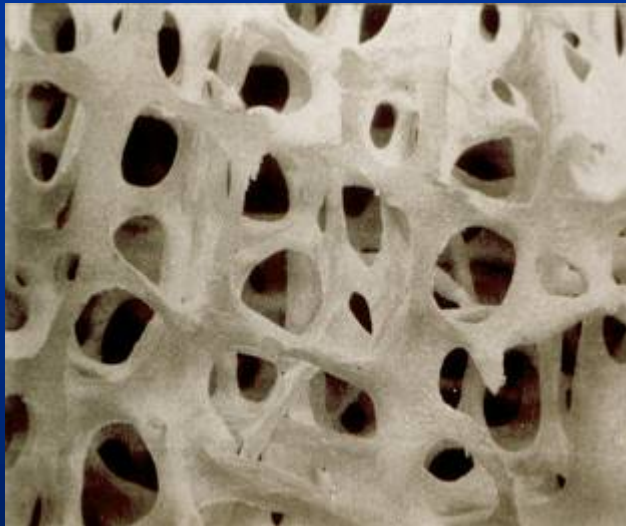
Luxembourg

07.12.2019

Y. Boutsen

# Ostéoporose: Définition

Maladie générale du squelette caractérisée par une **masse osseuse basse** et une **altération de la microarchitecture** du tissu osseux conduisant à une augmentation de la fragilité osseuse et un risque accru de **fractures**.



# Définition de l'ostéoporose chez la femme selon l'OMS (critères de remboursement)

Définition	Densité osseuse	Stratégie
Normal	T-score $\geq -1$ DS	Prévention
Ostéopénie	$-1 \text{ DS} > \text{T-score}$	
Ostéoporose	T-score $\leq -2.5$ DS	Traitement
Ostéoporose sévère	Ostéoporose avec fracture(s)	

**≠ Définition du risque absolu de fracture  
≠ Indication de traitement**



**ROULER MOINS VITE  
C'EST SAUVER PLUS DE VIES**

SÉCURITÉ ROUTIÈRE  
TOUS RESPONSABLES





---

 CARE OF THE AGING PATIENT:  
FROM EVIDENCE TO ACTION

---

# Hip Fracture Management

## Tailoring Care for the Older Patient

## **Box. Checklist of Important Care Elements Throughout Treatment Course of Patients With Hip Fracture**

### **Preoperative and Perioperative Care**

Surgical team (with support of geriatric consultant, medical consultant, and primary care physician)

- ☐ Consideration of operative vs nonoperative management

Emergency and surgical team (with support of geriatric and medical consultants)

- ☐ Adequate pain control: femoral nerve block, scheduled pain regimen, and as-needed pain regimen
- ☐ Correction of medical abnormalities prior to surgery
- ☐ Timing of surgery: early surgery, but treat medical problems first

Surgical team and anesthesia

- ☐ Regional vs general anesthesia

Surgical team and nursing

- ☐ Prophylaxis against venous thromboembolism
- ☐ Perioperative antibiotic prophylaxis
- ☐ Pressure ulcer prevention using pressure-redistributing support surfaces, and heel elevation device

### **Inpatient Postoperative Care**

Inpatient primary team (with support of geriatric and medical consultants)

- ☐ Adequate pain control: scheduled pain regimen, preemptive pain medications
- ☐ Delirium prevention: structured protocols
- ☐ Anemia management
- ☐ Oxygen support
- ☐ Multidisciplinary inpatient care

Rehabilitation services

- ☐ Early ambulation

Nutrition and primary team

- ☐ Consideration for nutrition support, particularly for patients with malnutrition

Nursing

- ☐ Urinary catheter management
- ☐ Pressure ulcer prevention

Discharging team

- ☐ Transitions management

### **Rehabilitation Postdischarge Care**

Rehabilitation services

- ☐ Rehabilitation exercises in facilities, home, and outpatient settings

Primary care clinicians and surgical team

- ☒ Secondary fracture prevention: bisphosphonates and fall prevention
- ☐ Monitor recovery of function
- ☐ Pain monitoring

Primary care

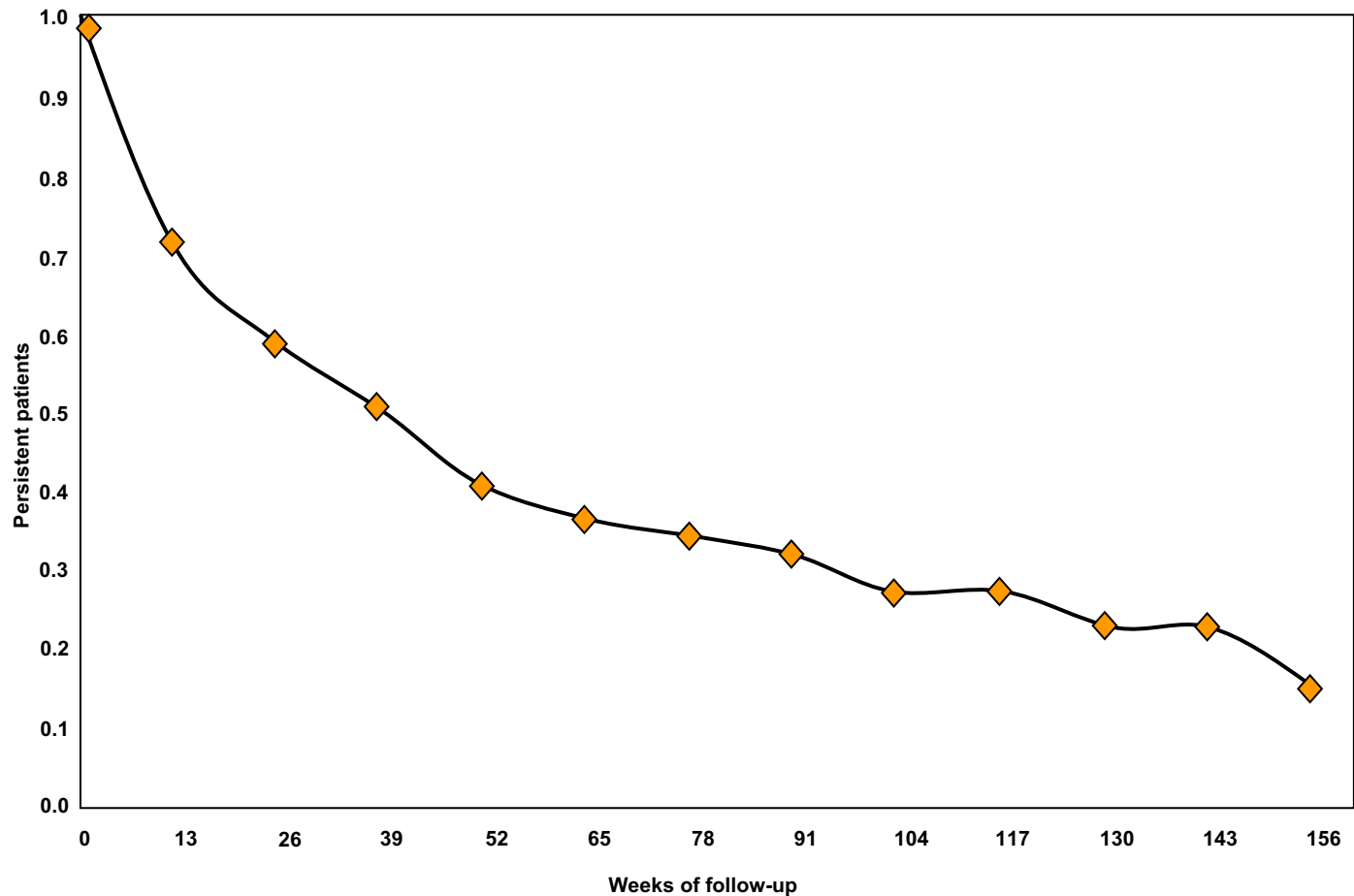
- ☐ Depression monitoring and treatment
- ☐ Consideration for other modalities of care eg, palliative care
- ☐ Communication: review trajectory of recovery and caregiver expectations

# Low Incidence of Anti-Osteoporosis Treatment After Hip Fracture

By Véronique Rabenda, MSc, Johan Vanoverloop, MSc, Valérie Fabri, MD, Raf Mertens, MD, François Sumkay, PhD, Carine Vannecke, MD, PhD, André Deswaef, PhD, Gert A. Verpooten, MD, PhD, and Jean-Yves Reginster, MD, PhD

## Cumulative Number of Patients with Hip Fracture According to Type of Treatment at Progressive Time Periods

	Month 3	Month 6	Month 9	Month 12	After Month 12
<b>Alendronate</b>	<b>311(1.34%)</b>	<b>534 (2.3%)</b>	<b>655(2.83%)</b>	<b>735 (3.18%)</b>	<b>1.053 (4.5%)</b>
<b>Risedronate</b>	<b>42 (0.18%)</b>	<b>64(0.28%)</b>	<b>79 (0.34%)</b>	<b>94 (0.41%)</b>	<b>163 (0.7%)</b>
<b>Raloxifene</b>	<b>30 (0.13%)</b>	<b>68 (0.29%)</b>	<b>88 (0.38%)</b>	<b>106 (0.46%)</b>	<b>160 (0.7%)</b>
<b>Total</b>	<b>383 (1.65%)</b>	<b>666 (2.88%)</b>	<b>822(3.55%)</b>	<b>935 (4.04%)</b>	<b>1.376 (6%)</b>

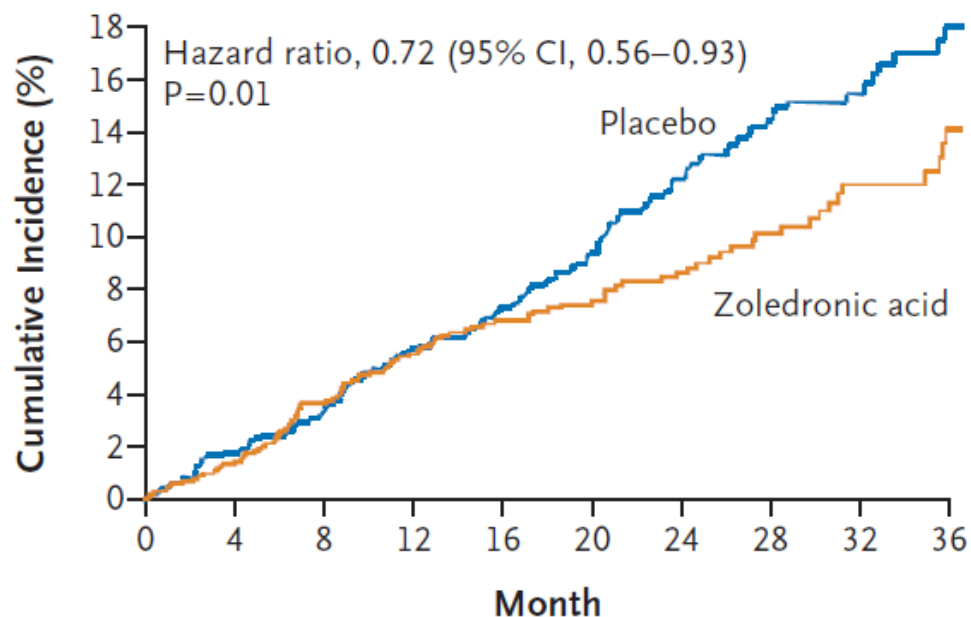


**Persistence with treatment in the total population of patients who began alendronate treatment (including the daily group, weekly group, and switch group) after the occurrence of a hip fracture**



# Zoledronic Acid and Clinical Fractures and Mortality after Hip Fracture

## E Death




### No. at Risk

Zoledronic acid	1054	1029	987	943	806	674	507	348	237	144
Placebo	1057	1028	993	945	804	681	511	364	236	149

FREQUENT ?



# European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J.A. Kanis<sup>1,2</sup>  • C. Cooper<sup>3,4</sup> • R. Rizzoli<sup>5</sup> • J.-Y. Reginster<sup>6,7</sup> • on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF)



Site	At 50 years		At 80 years	
	Men	Women	Men	Women
Forearm	4.6	20.8	1.6	8.9
Hip	10.7	22.9	9.1	49.3
Spine	8.3	15.1	4.7	8.7
Humerus	4.1	12.9	2.5	7.7
Any of these	22.4	46.4	15.3	31.7

Remaining lifetime probability of a major osteoporotic fracture at the age of 50 and 80 years in men and women from Sweden.



SEVERE ?





# Conséquences de la fracture de hanche

Dans l'année qui suit la fracture de hanche :

- 20% de mortalité chez les femmes
- 36% de mortalité chez les hommes
- 27% des personnes atteintes vont entrer pour la 1<sup>ère</sup> fois dans une maison de convalescence
- 40% ne peuvent plus marcher sans assistance
- 60% ont des difficultés dans des gestes essentiels de la vie courante  
(ex : faire sa toilette, cuisiner, s'habiller)
- 80% ont des difficultés dans d'autres activités quotidiennes (ex: courses, voiture)



# Identification des patients à risque

## Génétique :

- Anamnèse familiale (mère)
- Silhouette gracile (poids)

## Mode de vie :

- Abus de nicotine
- Abus d'alcool
- Malnutrition
- Sédentarité

## Médicaments :

- Glucocorticoïdes
- Hormones thyroïdiennes
- Anti-épileptiques

## Maladies :

- Affections rhumatismales inflammatoires
- Maladies intestinales inflammatoires
- Malabsorption
- Insuffisance rénale chronique


## Situation hormonale :

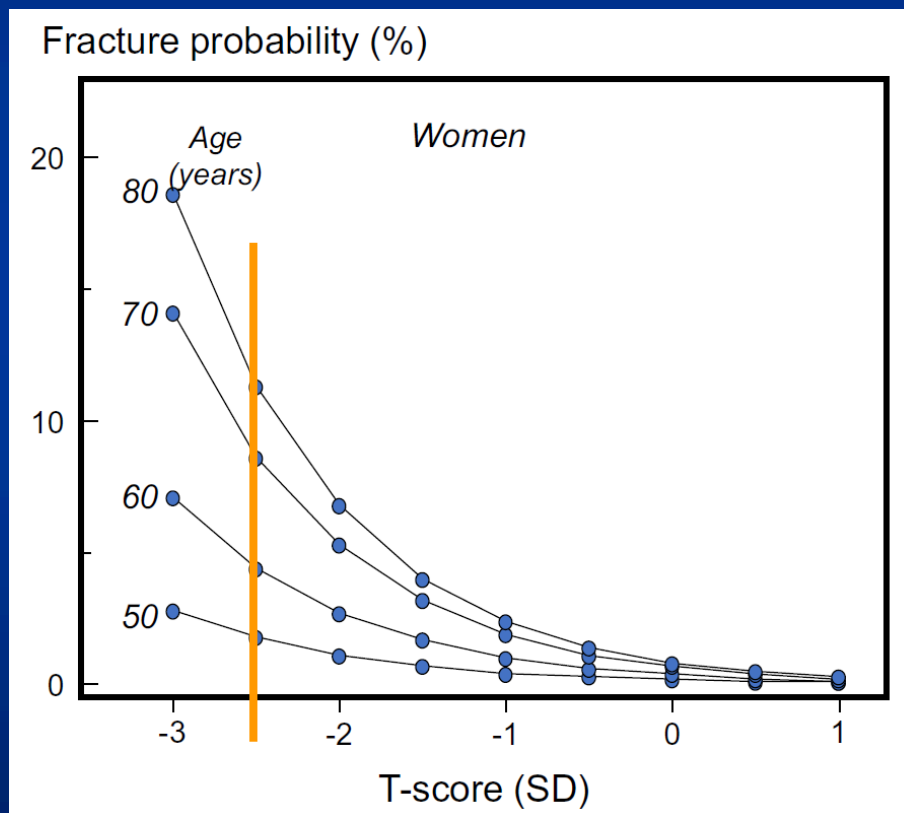
- Ménopause précoce (avant 45 ans)
- Hypogonadisme
- Hyperthyroïdie
- Hyperparathyroïdie
- Syndrome de Cushing

## RISQUE DE FRACTURE :

- Age
- Fracture à l'âge adulte
- Densité minérale osseuse basse

# European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J.A. Kanis<sup>1,2</sup>  • C. Cooper<sup>3,4</sup> • R. Rizzoli<sup>5</sup> • J.-Y. Reginster<sup>6,7</sup> • on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF)



Ten-year probability  
of hip fracture  
in women from Sweden  
according to age and T-score  
for femoral neck.

# Perte Osseuse et Traitements Oncologiques

## Réduction DMO Lombaire à 1 an

Homme normal	0.5 %
Ménopause installée	1.0 %
Ménopause récente	2.0 %
Aromatase Inhibiteurs (AI)	2.6 %
Grefe moëlle	3.3 %
Antiandrogènes	4.6 %
AI + GNRH agoniste	7.0 %
Castration post chimio	7.6 %
Glucocorticoïdes	> 10 %



# Evaluer le risque de fracture ???



# Evaluer le risque de fracture ???



# FRAX™ and the assessment of fracture probability in men and women from the UK


**Table 1** Ten-year probability (%) of a major osteoporotic fracture or hip fracture in men and women aged 65 years according to the presence of a single clinical risk factor

	Without BMD				T-score $-2.5$ SD			
	Men		Women		Men		Women	
	Osteoporotic <sup>a</sup>	Hip	Osteoporotic <sup>a</sup>	Hip	Osteoporotic <sup>a</sup>	Hip	Osteoporotic <sup>a</sup>	Hip
No clinical risk factors	4.9	0.8	8.6	1.3	9.8	3.6	12.4	3.0
Parental history of hip fracture	9.3	1.0	16.0	1.7	16.5	3.7	22.1	3.2
Current cigarette smoking	5.1	1.1	9.2	1.9	11.0	5.6	13.7	5.1
Alcohol intake >2 units daily	6.0	1.2	10.4	2.0	12.5	5.4	15.4	4.6
Rheumatoid arthritis	6.8	1.4	11.7	2.3	12.8	5.0	16.1	4.3
Oral glucocorticoids	7.5	1.5	13.7	2.7	15.0	6.1	19.7	5.5
Previous fragility fracture	9.6	1.9	16.4	3.2	16.0	5.9	20.2	5.0

# FRAX® Outil d'Evaluation des Risques de Fractures

## Bienvenue à FRAX

L'outil FRAX® a été développé à partir de données basées sur des modèles individuels de risque de fracture, combinant des facteurs de risques cliniques aussi bien que la Densité Minérale Osseuse (DMO).



Dr. John A Kanis  
Professor Emeritus,  
University of Sheffield

Les modèles FRAX® ont été développés à partir de données de populations étudiées en Europe, en Asie, en Australie. Dans sa forme la plus récente, l'outil est informatisé et est disponible en plusieurs langues simplifiées, basées sur le nombre de données disponibles, et peuvent être utilisées en bureau.

Les algorithmes du FRAX® sont basés sur des données de 20 ans. Les données obtenues sont basées sur la fracture de la hanche ou de la colonne (fracture clinique de la colonne ou de l'épaule).

Asie

Europe

Amérique du Nord

Amérique latine

Océanie

Autriche

**Belgique**

Danemark

Finlande

France

Allemagne

Hongrie

Pays-Bas

Italie

Espagne

Suède

Suisse


Turquie


Royaume-Uni


### Web Version 3.1


[View Release Notes](#)

### Links

[www.iofbonehealth.org](http://www.iofbonehealth.org)

[www.nof.org](http://www.nof.org)

[www.jpof.or.jp](http://www.jpof.or.jp)

[www.esceo.org](http://www.esceo.org)



## Outil de Calcul

Veuillez répondre aux questions ci-dessous pour calculer la probabilité de fracture sur 10 ans sans ou avec DMO



Pays: **Belgique** Nom/Identité: Dupont T. [A propos des facteurs de risques](#) ⓘ

### Questionnaire :

1. Âge (entre 40 et 90 ans) ou Date de Naissance

Âge :  Date de Naissance :  
A  M  J

2. Sexe ☐ Masculin ☐ Féminin

3. Poids (kg)

4. taille (cm)

5. Fracture Précédente ☒ Non ☐ Oui

6. Parent fracture de la hanche ☒ Non ☐ Oui

7. Actuellement Fumeur ☒ Non ☐ Oui

8. Glucocorticoïdes ☒ Non ☐ Oui

9. Polyarthrite rhumatoïde ☒ Non ☐ Oui

10. Ostéoporose secondaire ☒ Non ☐ Oui

11. Alcool 3 unités ou plus par jour ☒ Non ☐ Oui

12. DMO du Col Fémoral (g/cm<sup>2</sup>)

Choisissez DXA

Effacer

Calculer


### Weight Conversion

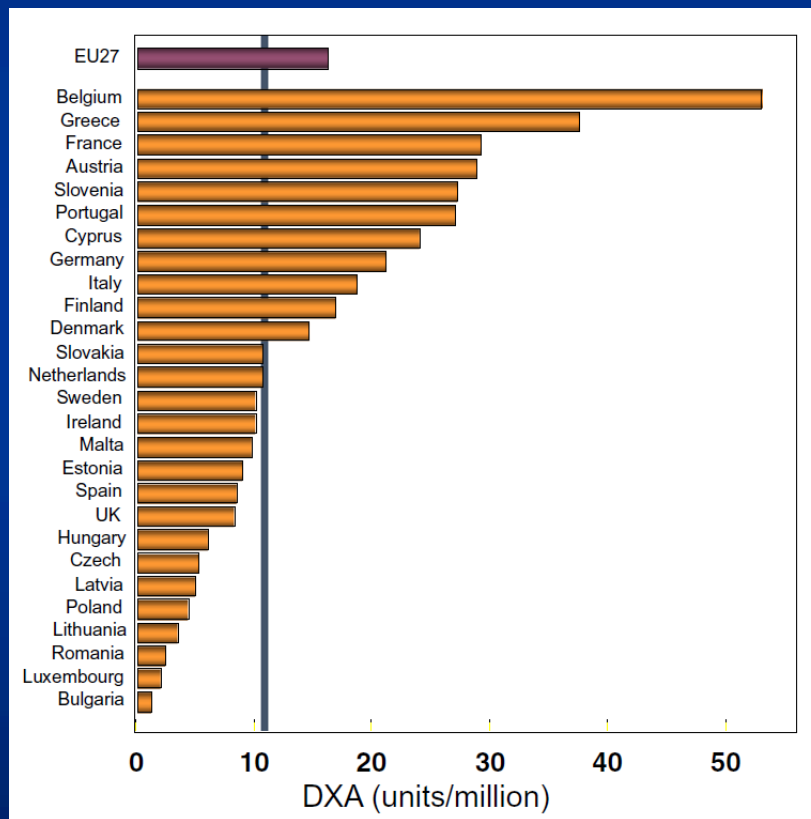
Pounds ➔ Kgs

### Height Conversion

Inches ➔ Cms

# European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J.A. Kanis<sup>1,2</sup>  • C. Cooper<sup>3,4</sup> • R. Rizzoli<sup>5</sup> • J.-Y. Reginster<sup>6,7</sup> • on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF)



The density of central DXA equipment (units/million of the general population) in the EU countries in 2010.

## Outil de Calcul

Veuillez répondre aux questions ci-dessous pour calculer la probabilité de fracture sur 10 ans sans ou avec DMO



Pays: **Belgique**

Nom/Identité: Dupont T

[A propos des facteurs de risques](#)



### Questionnaire :

1. Âge (entre 40 et 90 ans) ou Date de Naissance

Âge : 51  
Date de Naissance : 1958 M 11 J 22

2. Sexe ☐ Masculin ☒ Féminin

3. Poids (kg) 65

4. taille (cm) 158

5. Fracture Précédente ☒ Non ☐ Oui

6. Parent fracture de la hanche ☒ Non ☐ Oui

7. Actuellement Fumeur ☒ Non ☐ Oui

8. Glucocorticoïdes ☒ Non ☐ Oui

9. Polyarthrite rhumatoïde ☒ Non ☐ Oui

10. Ostéoporose secondaire ☒ Non ☐ Oui

11. Alcool 3 unités ou plus par jour ☒ Non ☐ Oui

12. DMO du Col Fémoral (g/cm<sup>2</sup>)

T-Score -1.6

Effacer

Calculer

BMI 26.0

The ten year probability of fracture (%)



avec DMO

Major osteoporotic	4.9
Hip fracture	0.7

### Weight Conversion

Pounds → Kgs

Convert

### Height Conversion

Inches → Cms

Convert

## Outil de Calcul

Veuillez répondre aux questions ci-dessous pour calculer la probabilité de fracture sur 10 ans sans ou avec DMO



Pays: **Belgique**

Nom/Identité: Dupont T.

[A propos des facteurs de risques](#)



### Questionnaire :

1. Âge (entre 40 et 90 ans) ou Date de Naissance

Âge :

81

Date de Naissance :

A

1928

M

11

J

22

2. Sexe

☐ Masculin ☒ Féminin

3. Poids (kg)

65

4. taille (cm)

158

5. Fracture Précédente

☐ Non ☒ Oui

6. Parent fracture de la hanche

☐ Non ☒ Oui

7. Actuellement Fumeur

☒ Non ☐ Oui

8. Glucocorticoïdes

☒ Non ☐ Oui

9. Polyarthrite rhumatoïde

☒ Non ☐ Oui

10. Ostéoporose secondaire ☒ Non ☐ Oui

11. Alcool 3 unités ou plus par jour ☒ Non ☐ Oui

12. DMO du Col Fémoral (g/cm<sup>2</sup>)

T-Score

-2.6

Effacer

Calculer

**BMI 26.0**

**The ten year probability of fracture (%)**



**avec DMO**

☒ Major osteoporotic

**44**

☒ Hip fracture

**34**

### Weight Conversion

Pounds ➔ Kgs


Convert

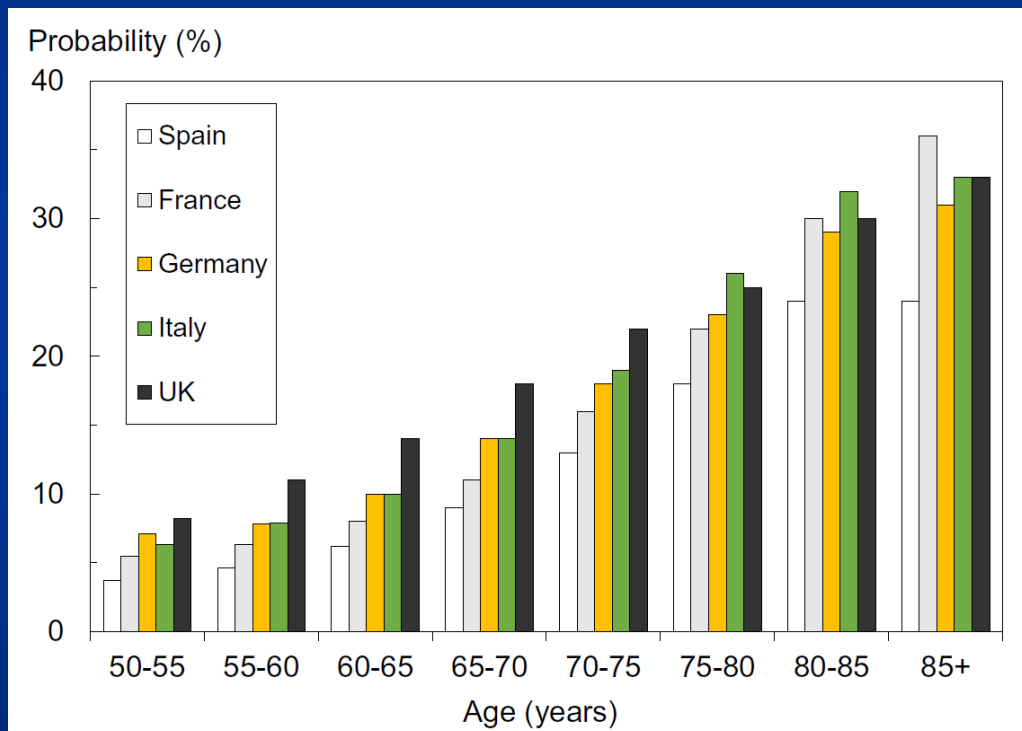
### Height Conversion

Inches ➔ Cms

Convert


# European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J.A. Kanis<sup>1,2</sup>  • C. Cooper<sup>3,4</sup> • R. Rizzoli<sup>5</sup> • J.-Y. Reginster<sup>6,7</sup> • on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF)



The 10-year probability of a major osteoporotic fracture by age in women with a prior fracture and no other clinical risk factors in five major EU countries as determined with FRAX (version 3,5).

# European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J.A. Kanis<sup>1,2</sup>  • C. Cooper<sup>3,4</sup> • R. Rizzoli<sup>5</sup> • J.-Y. Reginster<sup>6,7</sup> • on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF)


Age range (years)	Ten-year fracture probability (%)		
	Intervention threshold	Lower assessment threshold	Upper assessment threshold
40–44	5.2	2.3	6.2
45–49	5.4	2.4	6.5
50–54	6.3	2.9	7.6
55–59	7.6	3.6	9.1
60–64	9.9	4.9	11.9
65–69	13.4	6.9	16.1
70–74	17.6	9.7	21.5
75–79	23.0	13.7	27.6
80–84	29.1	18.7	34.9
85–89	31.8	20.9	38.2
90–94	31.7	20.8	38.0
95–99	32.2	21.1	38.6
100+	32.5	21.3	39.0

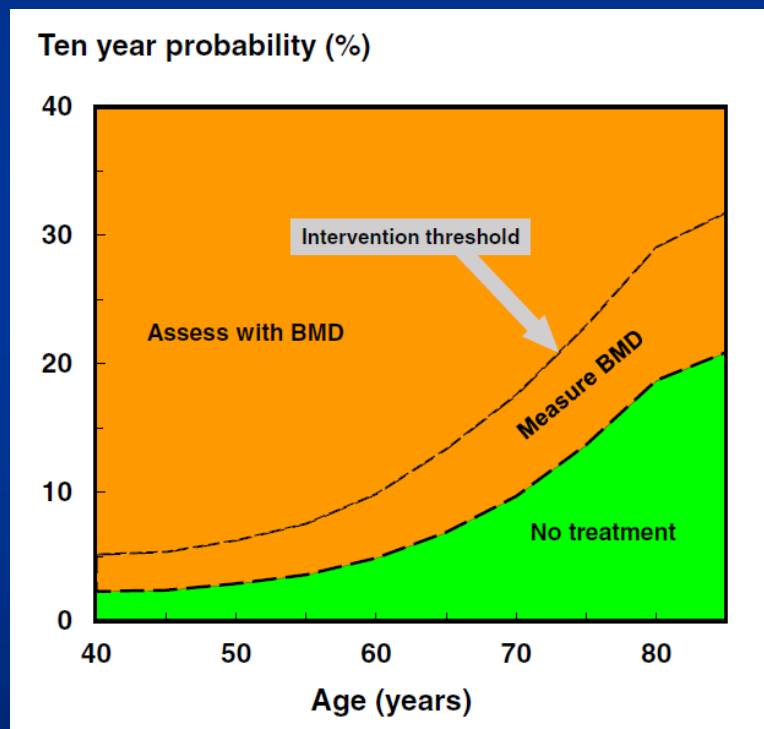
**Intervention thresholds** as set by FRAX-based 10-year probability (%) of a major osteoporotic fracture equivalent to women with a previous fracture (no other clinical risk factors, a body mass index of 24 kg/m<sup>2</sup> and without BMD).

The **lower assessment thresholds** set by FRAX is based on the 10-year probability (%) of a major osteoporotic fracture equivalent to women without clinical risk factors (a body mass index of 24 kg/m<sup>2</sup> and without BMD).

The **upper assessment threshold** is set at 1.2 times the intervention threshold. Population weighted mean values for the five major EU countries.

# European guidance for the diagnosis and management of osteoporosis in postmenopausal women

J.A. Kanis<sup>1,2</sup>  • C. Cooper<sup>3,4</sup> • R. Rizzoli<sup>5</sup> • J.-Y. Reginster<sup>6,7</sup> • on behalf of the Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF)



Assessment of major osteoporotic fracture risk in countries with high access to DXA.

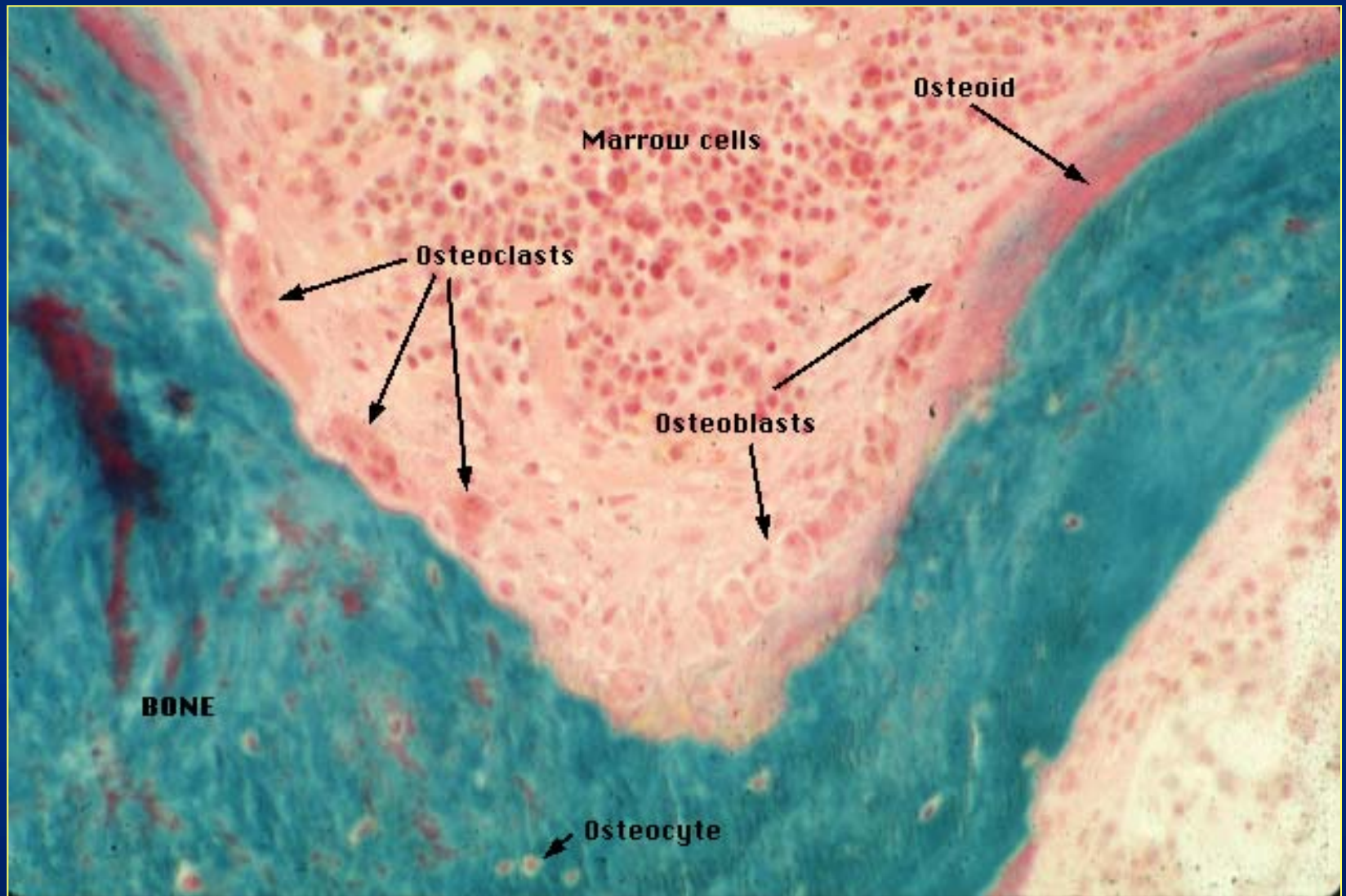
DXA is undertaken in women with a clinical risk factor.

Assessment with DXA and/or treatment is not recommended where the FRAX probability is lower than the lower assessment threshold (green area).

BMD is recommended in other women and treatment recommended where the fracture probability exceeds the intervention threshold (dotted line).



# Traitements de l'ostéoporose



# Traitements de l'ostéoporose

- Antirésorbeurs

Calcium

Œstrogènes ± progestatifs

Modulateurs récepteurs oestrogénique: Raloxifène, ...

Tibolone

Calcitonines

Bisphosphonates: Etidronate, Pamidronate, Alendronate,  
Risédronate, Ibandronate, Zolédronate....

- Denosumab

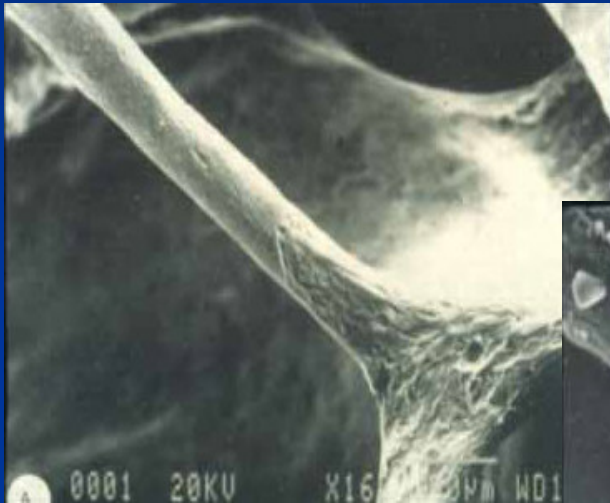
- Ostéoformateurs

Tériparatide ; Romosozumab

- Divers

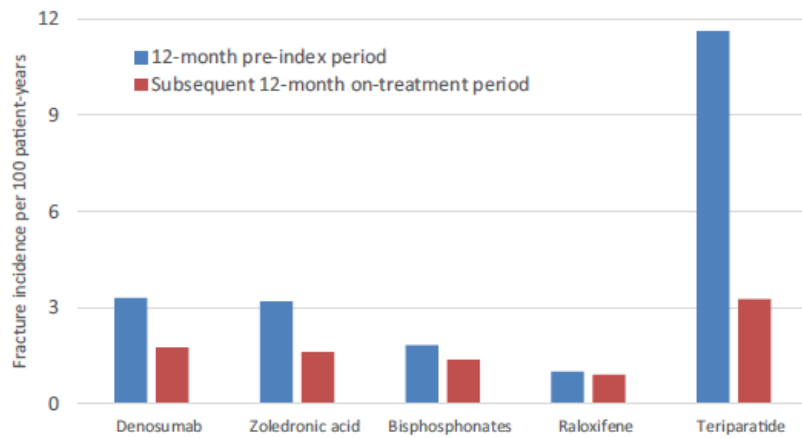
Anabolisants, Vitamine D et dérivés, Diurétiques, Ipriflavone, ...

# Importance de la Microarchitecture

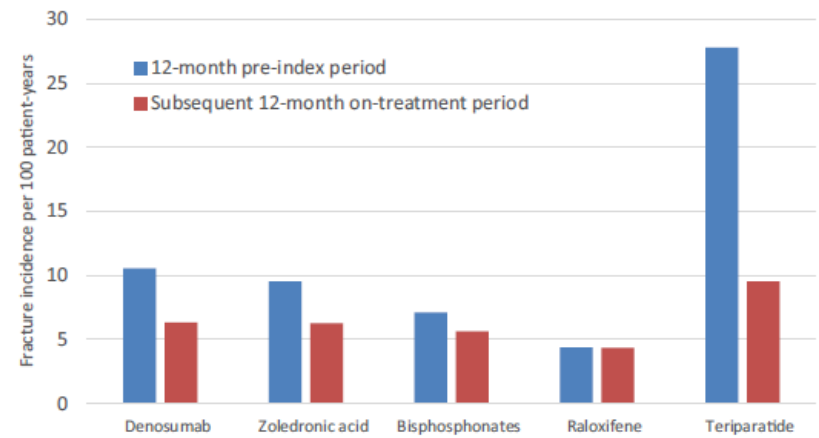


# Real-world effectiveness of osteoporosis therapies for fracture reduction in post-menopausal women

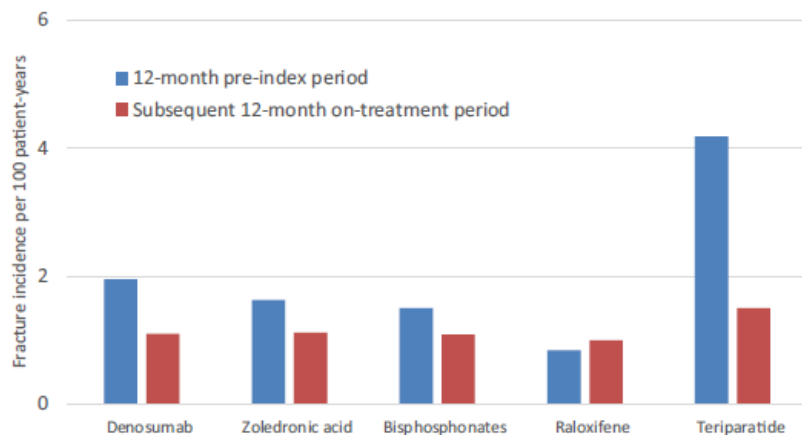
Clinical vertebral fracture



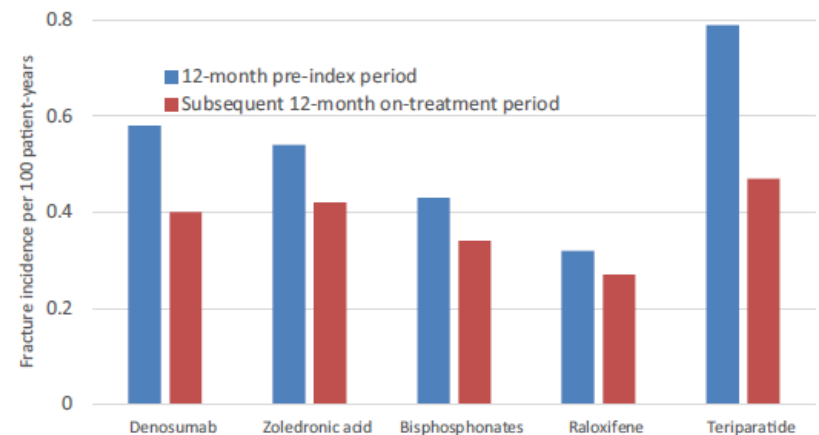
Any fracture



Hip fracture



Wrist fracture

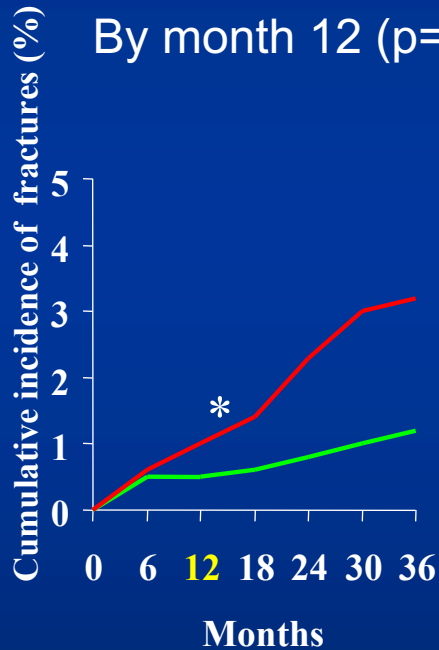


# Alendronate (FIT study)

## Réduction rapide du risque de fracture

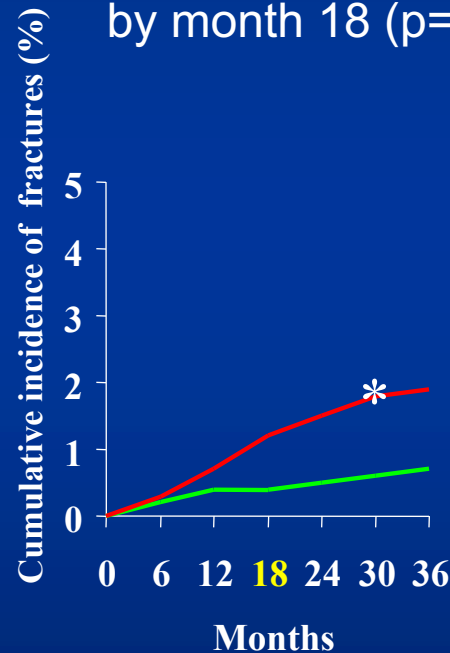
### Clinical vertebral Fracture <sup>1</sup>

Risk reduction: **59%**  
By month 12 (p=0.03)



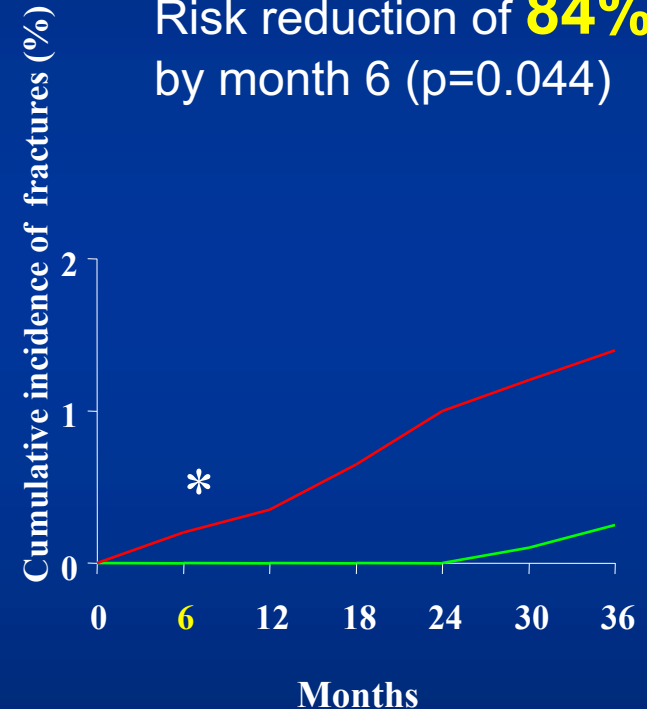
### Hip Fracture <sup>1</sup>

Risk reduction of **63%**  
by month 18 (p=0.014)



### Multiple Symptomatic Vertebral Fractures <sup>2</sup>

Risk reduction of **84%**  
by month 6 (p=0.044)



— Alendronate 10 mg  
(n= 1841)

— Placebo  
(n= 1817)

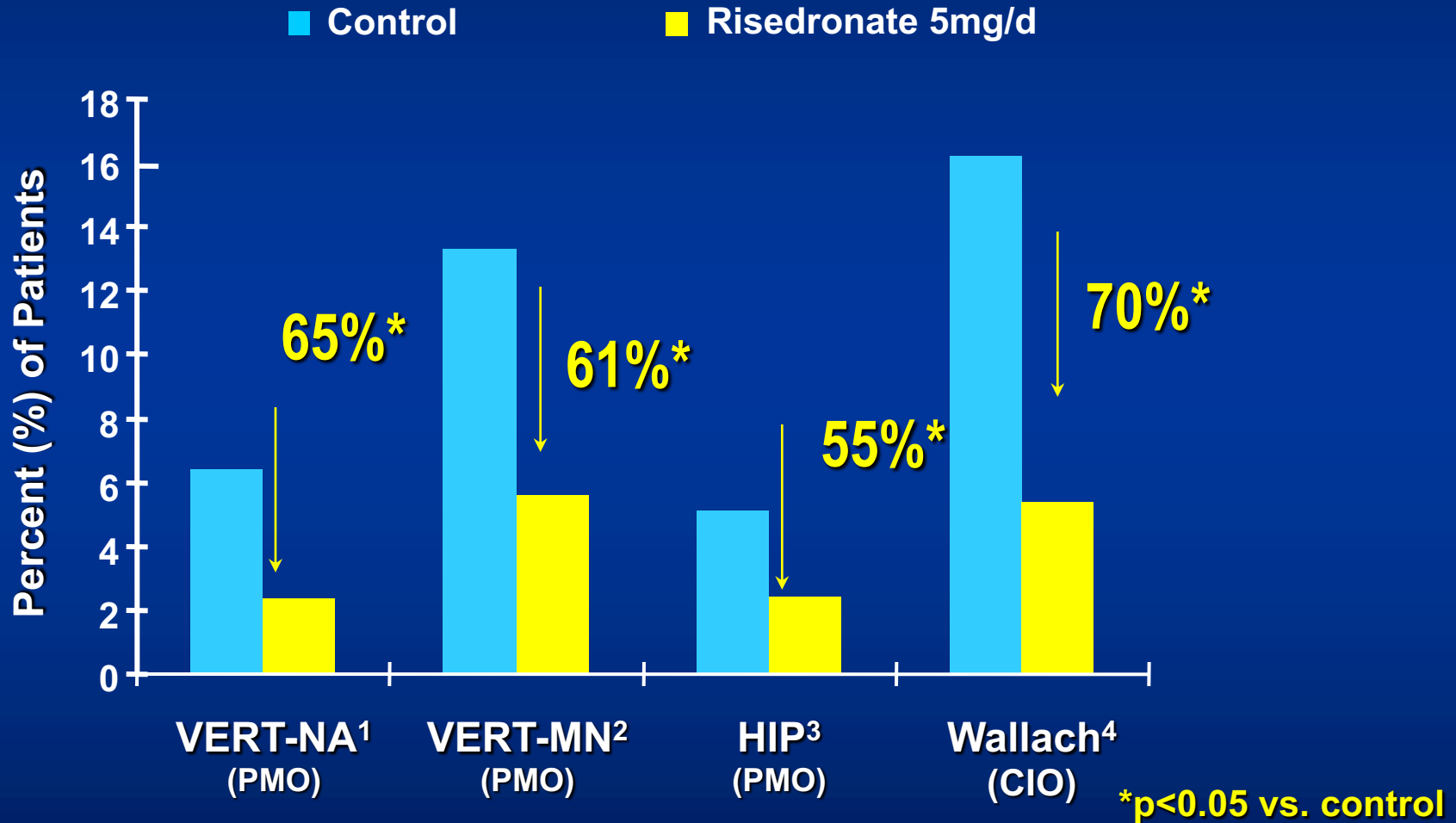
\* p<0.05 vs placebo

\* p=0.044 vs placebo

<sup>1</sup> Black, JCEM, 2000, 4118

<sup>2</sup> Levis et al. J Am Geriatr Soc. 2002;50: 409-415

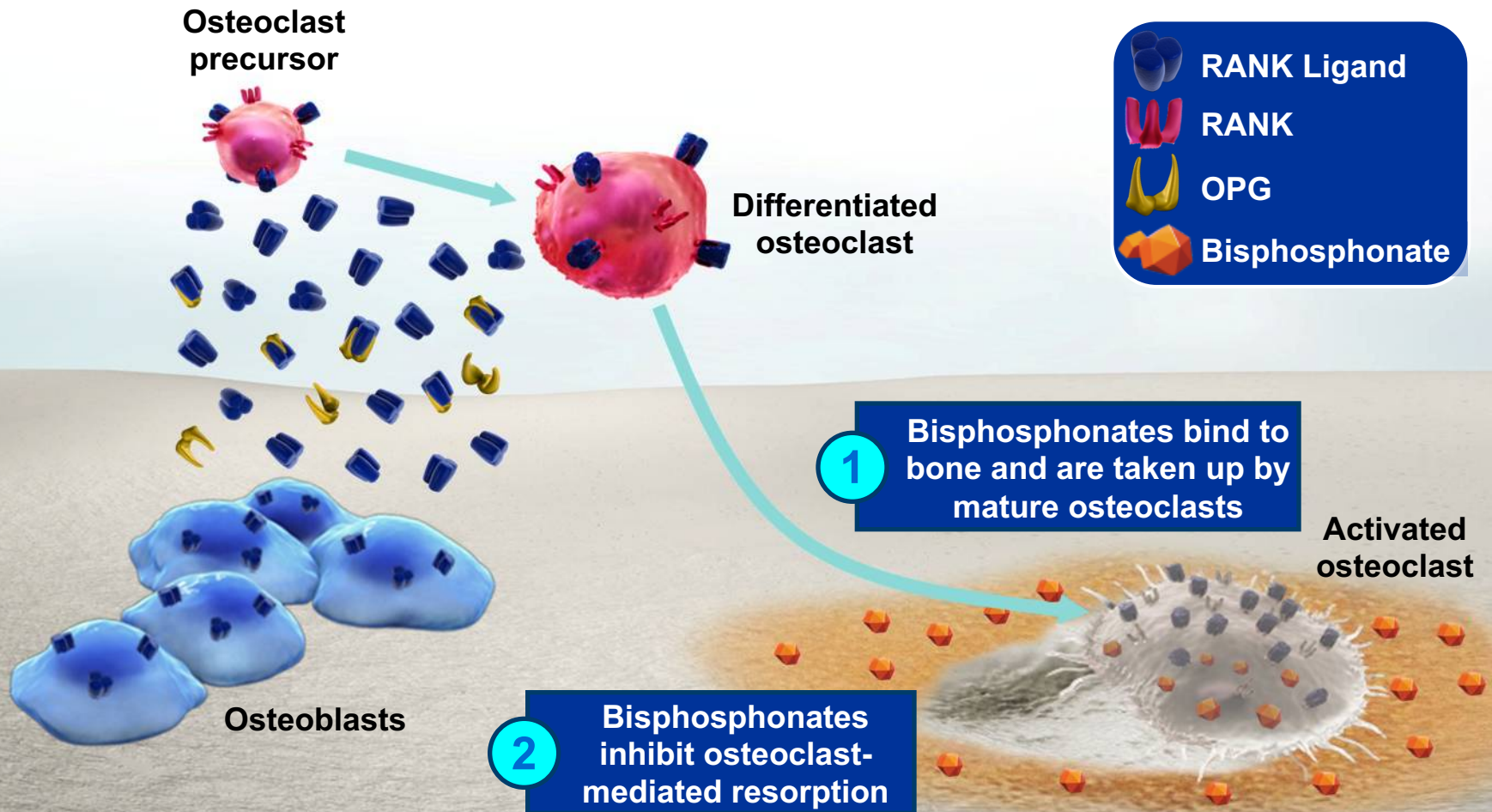
# Le Risedronate Réduit Systématiquement le Risque de Fractures Vertébrales déjà après 1 an



Adapted from: 1.Harris et al. JAMA 1999; 282(14): 1344-52; 2. Reginster et al. OI 2000; 11: 83-91;  
3. Greenwald et al. JBMR 2000; 15 (Suppl 1): S226; 4. Wallach, et al. Cal Tiss Int 2000; 67: 277-85,



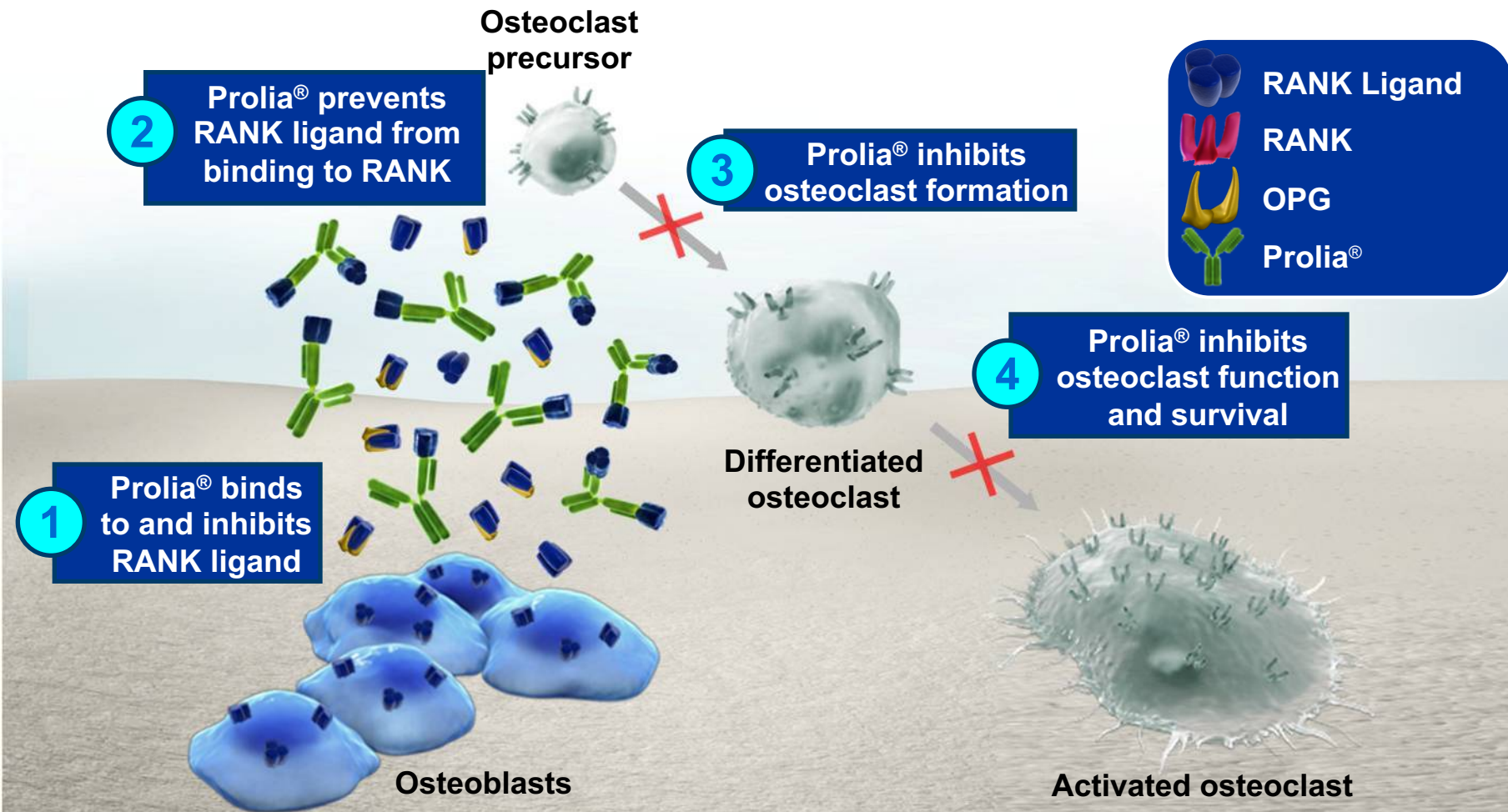
# Bisphosphonates Bind to Bone and Inhibit Osteoclasts at the Bone Surface



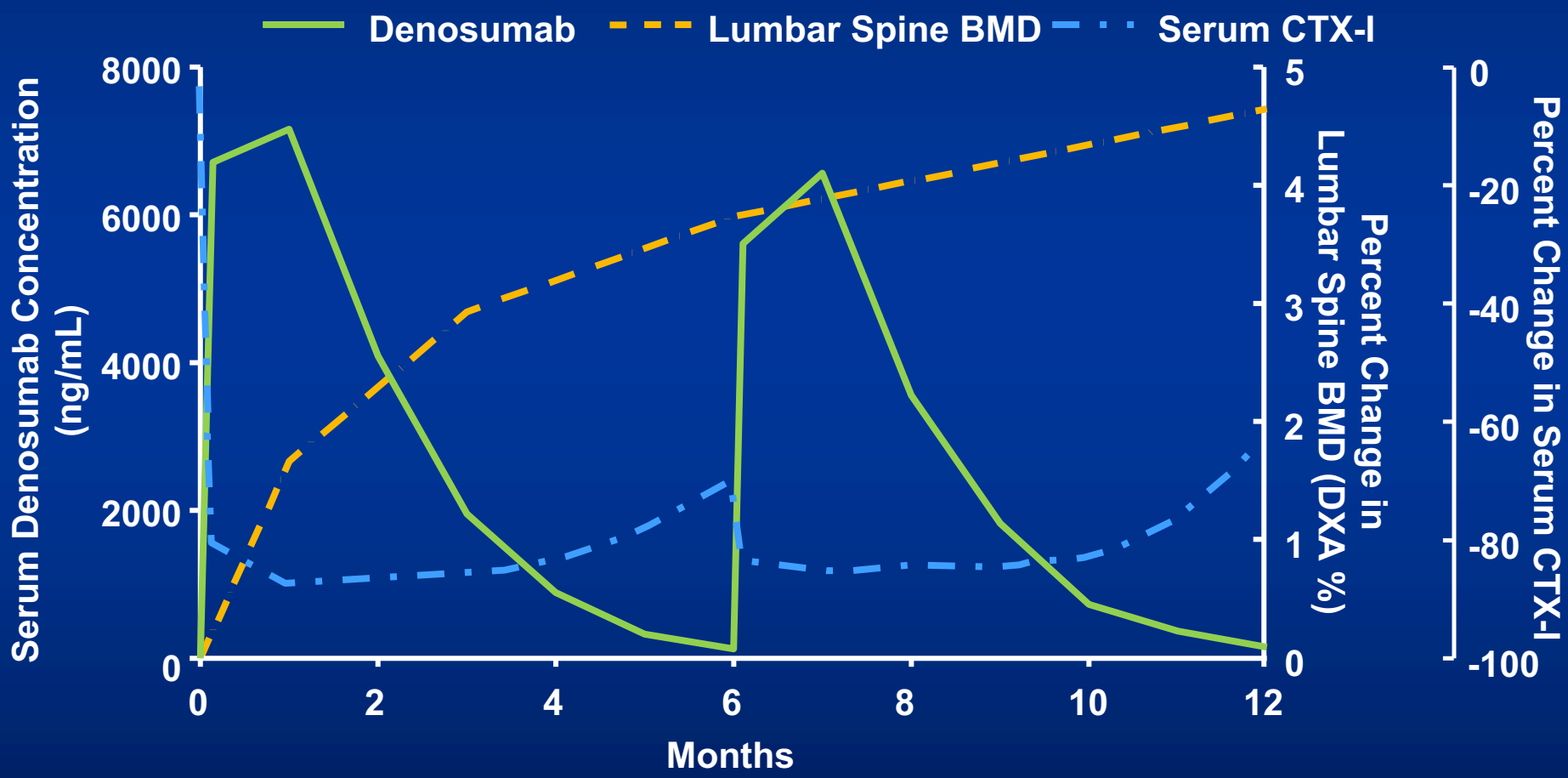
Mechanism of action representations are for illustrative purposes only and are not meant to imply any clinical efficacy



# Denosumab, a RANK Ligand Inhibitor, Inhibits Osteoclast Formation, Function, and Survival

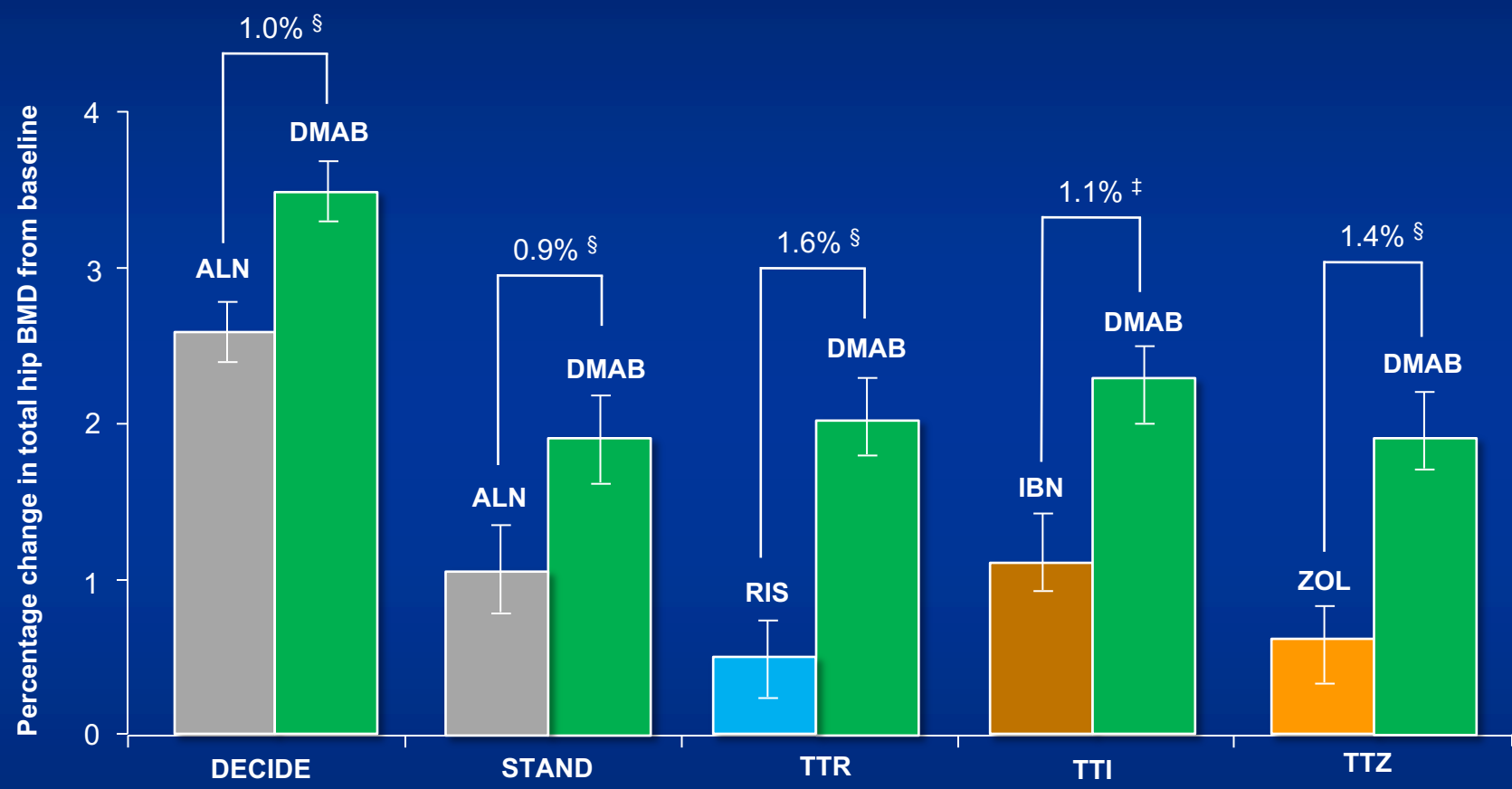


# Pharmacokinetic and Pharmacodynamic Properties of Denosumab Support the 60 mg SC Q6M Dosing Regimen



Q6M = once every 6 months; BMD = bone mineral density; CTX-I = type I C-telopeptide; DXA = dual-energy x-ray absorptiometry  
McClung MR, et al. N Engl J Med. 2006;23:821-831  
Peterson MC, et al. J Bone Miner Res. 2005;20(Suppl 1):S293;Abstract SU446 and poster  
CHMP public assessment report (EMA/21672/2010)

# Denosumab transition studies – overall results at the hip

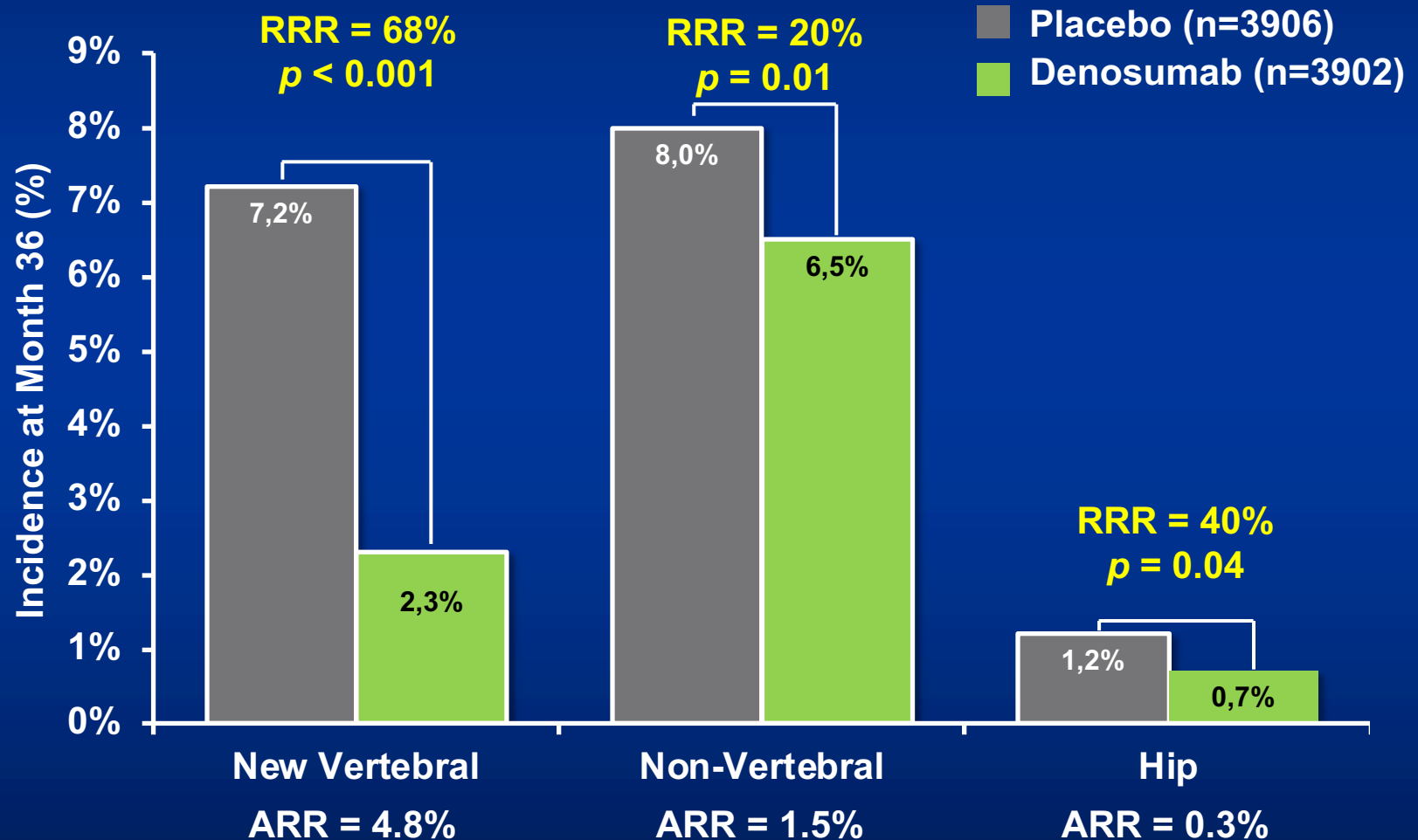


GRAPH IS SHOWN FOR ILLUSTRATIVE PURPOSES ONLY. RESULTS FROM DIFFERENT STUDIES SHOULD NOT BE DIRECTLY COMPARED

ALN – alendronate; DMAB – denosumab; RIS – risedronate; IBN – ibandronate; ZOL – zoledronate  
TTR – transition to risedronate, TTI – transition to ibandronate, TTZ – transition to zoledronate; Data are least-squares means and 95% confidence intervals.  
§ -  $p < 0.0001$ ; ‡ -  $p < 0.001$ . Miller PD, et al. ASBMR 2015 poster SU0340 (Data adapted from Roux C, et al. *Bone*. 2014; 58: 48-54. Recknor C, et al. *Obstet Gynecol*. 2013; 121: 1291-9.. Kendler DL, et al. *J Bone Miner Res*. 2010; 25: 72-81. Brown JP, et al. *J Bone Miner Res*. 2009; 24: 153-161. Miller PD, et al. *J Clin Endocrinol Metab*. 2016; 101: 3163-3170)

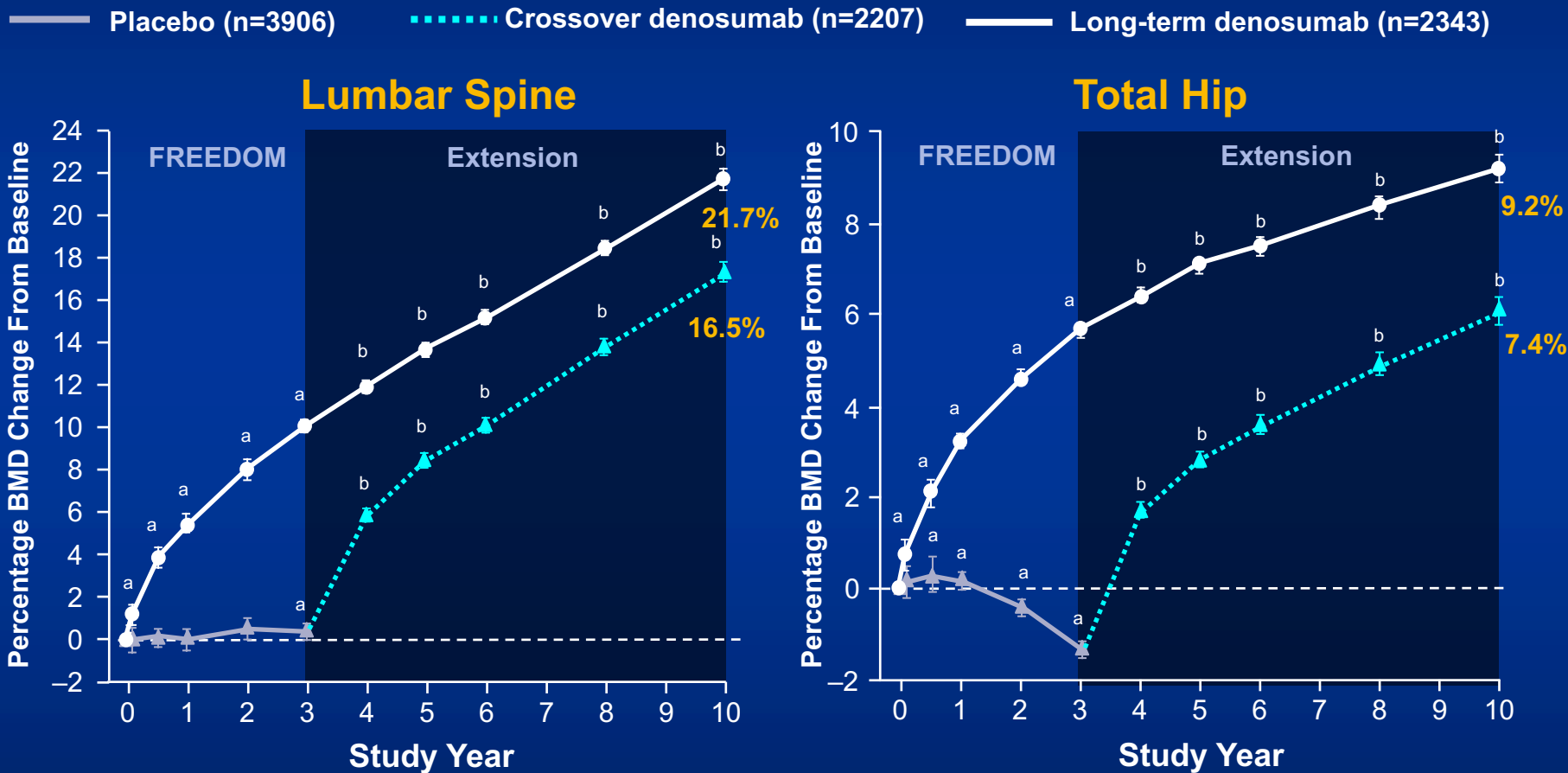
# Denosumab significantly lowers relative risk of fractures at 36 months

*Phase 3: The FREEDOM Trial*



# Change in Lumbar Spine and Total Hip BMD Through 10 Years With Denosumab Treatment

## *FREEDOM and the Open-Label FREEDOM Extension*



Data represent least-squares means and 95% CI.

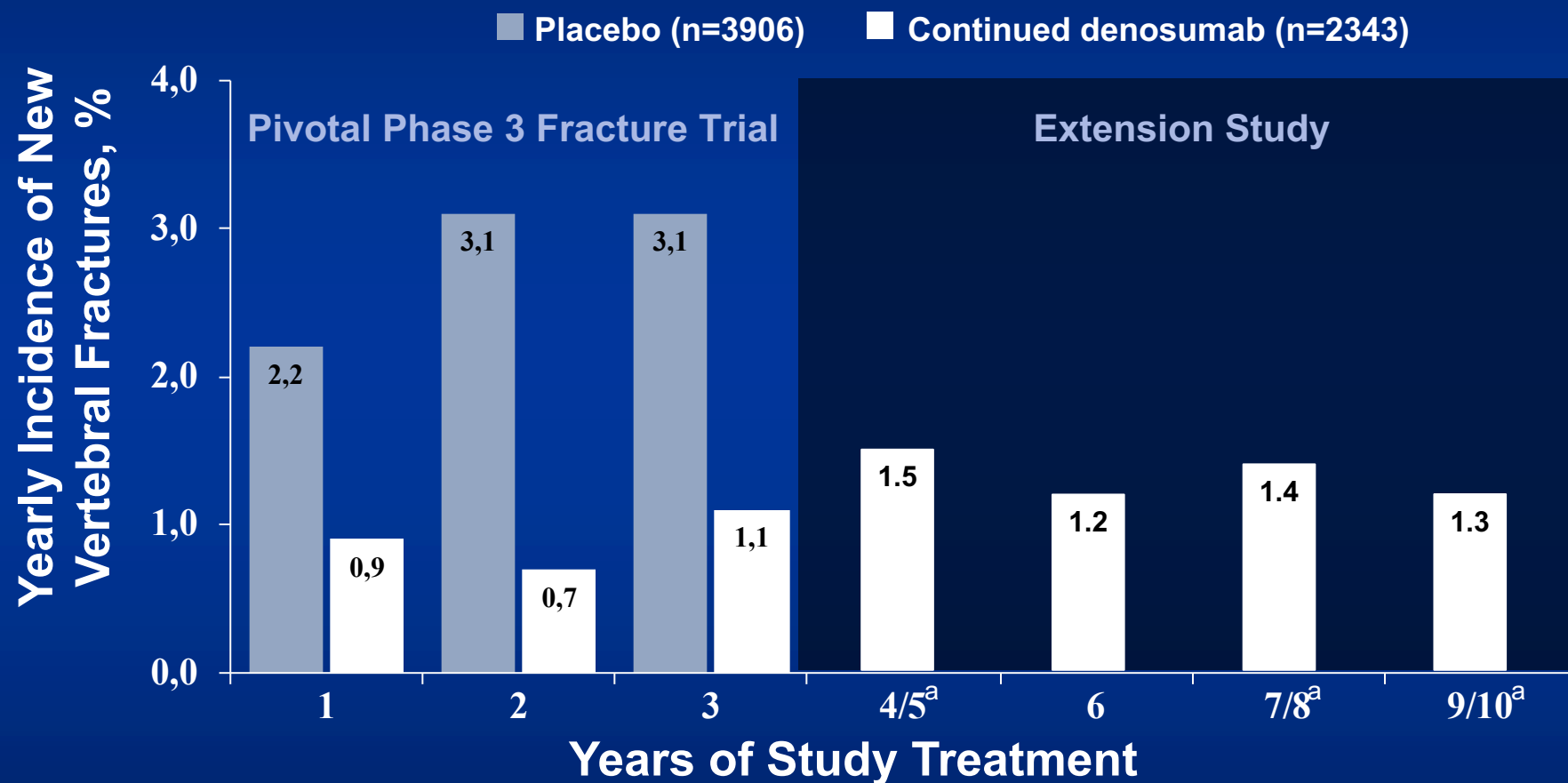
<sup>a</sup>p<0.05 compared with FREEDOM baseline. <sup>b</sup>p<0.05 compared with FREEDOM and extension baselines.

BMD = bone mineral density. Adapted from: Bone HG, et al. *Lancet Diabetes Endocrinol.* 2017; 5: 513-523.



# Yearly Incidence of New Vertebral Fractures Through 10 Years

*Pivotal Phase 3 Study – Extension*



The primary endpoint of the open-label extension study was safety and tolerability of denosumab for up to 10 yrs. Fractures were collected as AEs in this study.

<sup>a</sup>Annualized incidence: (2-year incidence) / 2.

Adapted from: Bone HG, et al. *Lancet Diabetes Endocrinol.* 2017; 5: 513-523..

# Yearly Exposure-adjusted Participant Incidence of Adverse Events per 100 Participant-years of Follow-up

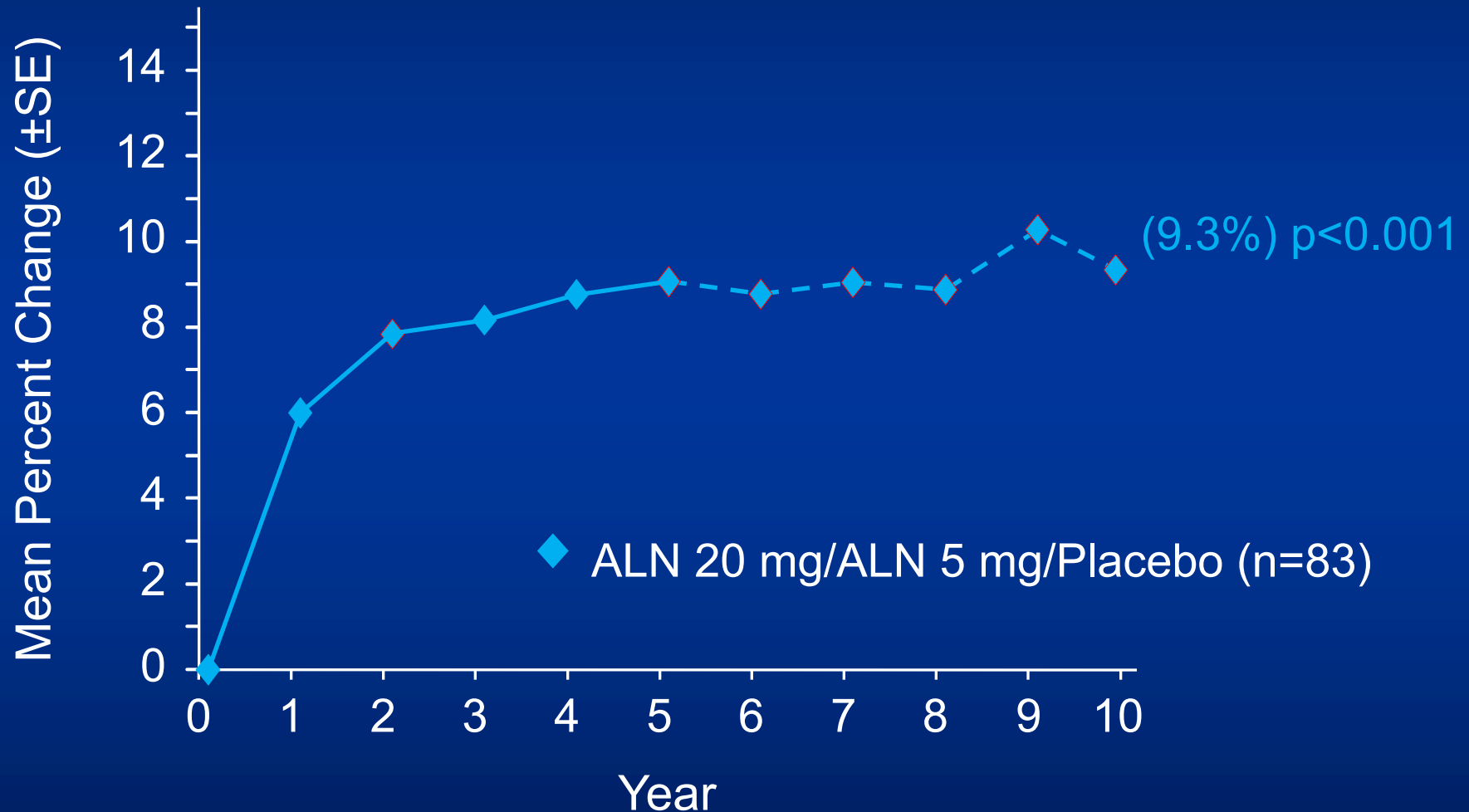
## *FREEDOM and the Open-Label FREEDOM Extension*

Years of treatment	Placebo				Long-term and crossover denosumab groups combined									
	1	2	3		1	2	3	4	5	6	7	8	9	10
N =	3,883	3,687	3,454		6085	5787	5452	4099	3890	3582	3261	1743	1585	1451
<b>All adverse events</b>	189.5	156.3	132.8		165.3	137.8	124.6	129.9	110.9	110.0	108.4	107.6	109.5	95.9
<b>Infections</b>	38.6	33.9	31.7		35.1	30.3	29.5	29.1	26.0	27.2	26.5	27.0	27.0	23.0
<b>Malignancies</b>	1.8	1.6	1.5		1.9	1.5	2.2	2.3	2.4	2.2	2.7	1.7	2.6	1.6
<b>Eczema</b>	0.8	0.5	0.6		1.4	1.1	1.0	1.1	1.2	0.9	0.7	0.8	0.9	1.3
<b>Hypocalcemia</b>	<0.1	0	<0.1		<0.1	<0.1	0	<0.1	0.1	0	<0.1	<0.1	0	0.1
<b>Pancreatitis</b>	<0.1	<0.1	0		<0.1	<0.1	<0.1	0	<0.1	0.1	<0.1	0.1	<0.1	0
<b>Serious adverse events</b>	11.7	11.9	10.8		12.0	11.5	12.3	11.5	12.9	12.6	14.4	11.5	13.1	12.3
<b>Infections</b>	1.1	1.4	1.4		1.5	1.6	1.4	1.4	1.3	1.9	2.3	1.2	1.5	2.6
<b>Cellulitis or erysipelas</b>	0	0	<0.1		<0.1	<0.1	0.2	<0.1	<0.1	0.1	<0.1	0.2	<0.1	0.1
<b>Atypical femoral fracture</b>	0	0	0		0	0	<0.1	0	0	0	<0.1	0	0	0
<b>Osteonecrosis of the jaw</b>	0	0	0		0	<0.1	0	<0.1	0	0.2	<0.1	0	<0.1	<0.1
<b>Fatal adverse events</b>	0.8	0.8	1.0		0.7	0.6	0.7	0.5	0.8	0.9	1.5	0.7	1.0	0.9

Analyses were based on the original randomized treatments in FREEDOM. All adverse and serious adverse events were coded using MedDRA v13.0. N = number of women who received ≥1 dose of investigational product in FREEDOM or the Extension. All subjects treated with denosumab during FREEDOM are included in the first 3 years. Years 1-7 of denosumab exposure include the first 7 years for the long-term group, and the 7 years of the active treatment extension for the cross-over group. Years 8-10 are the last 3 years for the long-term group only.

Adapted from: Bone HG, et al. *Lancet Diabetes Endocrinol.* 2017; 5: 513-523.

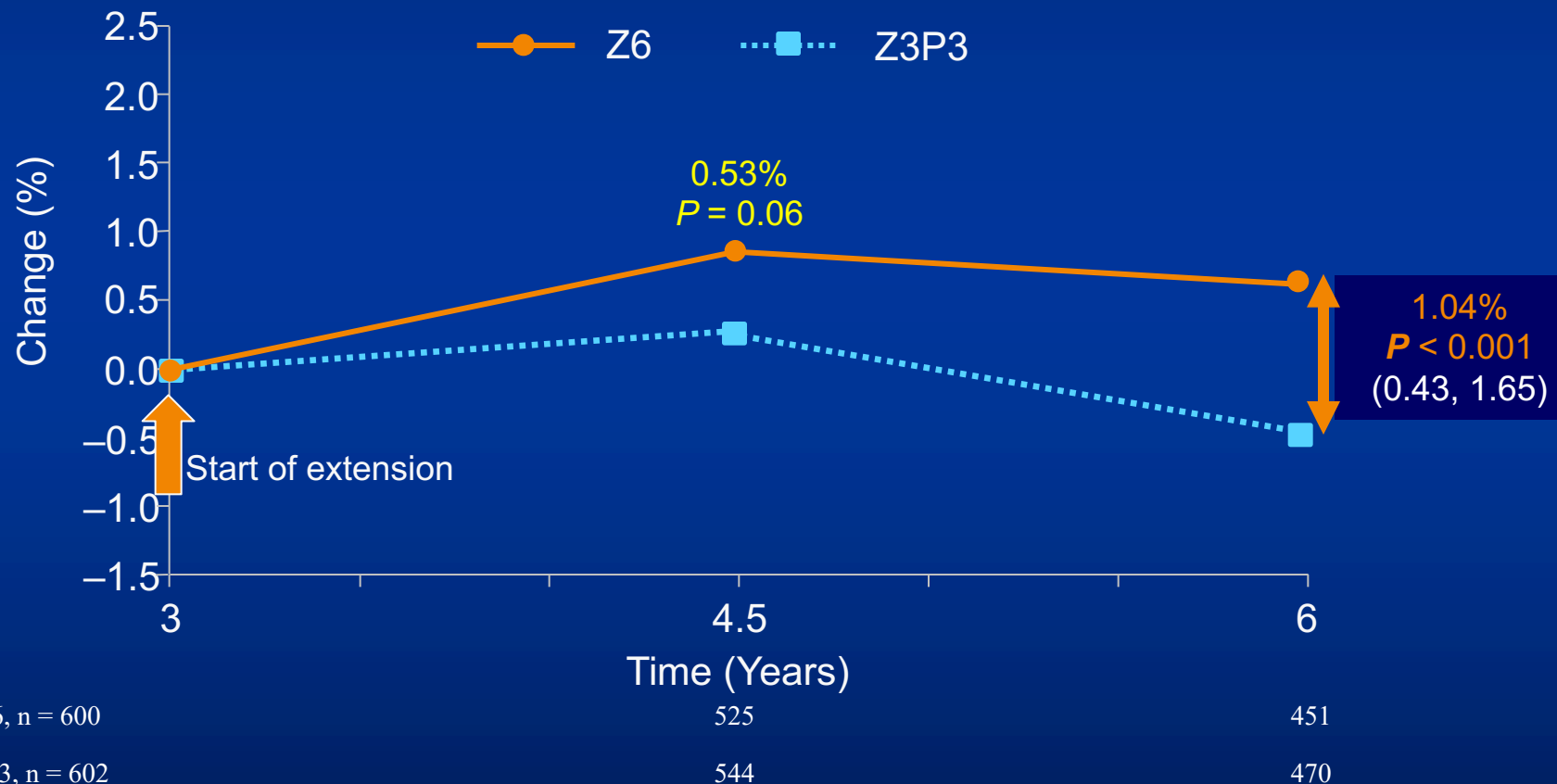
## 10 ans Alendronate: DMO (lombaire)



The mean percent change from baseline to year 10 appears in parentheses following each treatment group.

# Femoral Neck BMD: Primary Endpoint

Between-treatment Comparison in % Change in Femoral Neck BMD at Year 6 Relative to Year 3



The numbers in parenthesis are 95% confidence interval calculated based on a t-distribution for BMD. *P* value is obtained from ANOVA with treatment and region as explanatory variables.

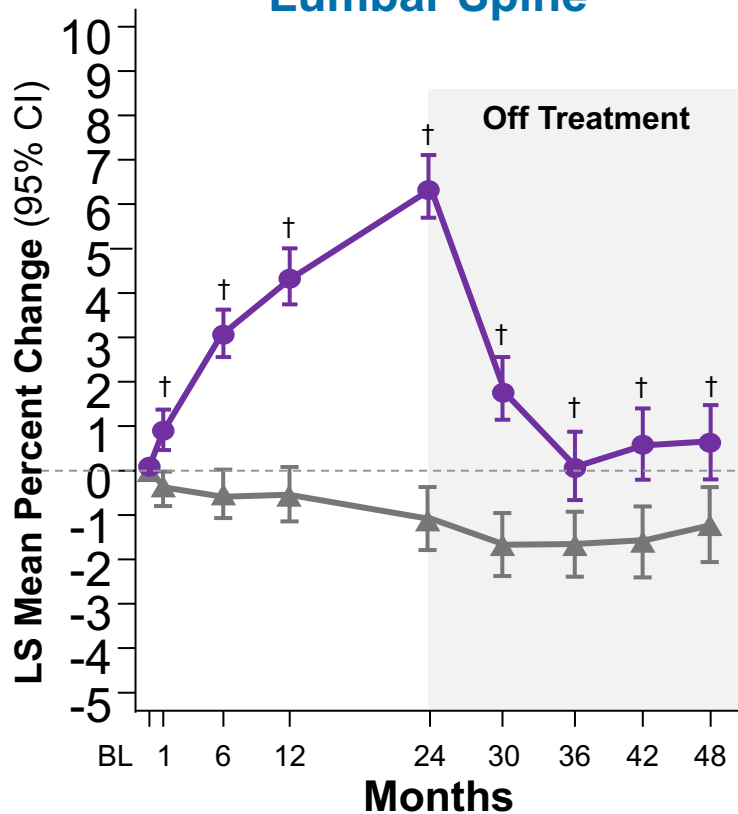
Adapted from Black DM, et al. *J Bone Miner Res.* 2012; 27:243-254 and available upon request

# After Denosumab Discontinuation, BMD Returns Toward Baseline Levels Within 1–2 Years But Remains Higher Than For Subjects Who Received Placebo<sup>1</sup>

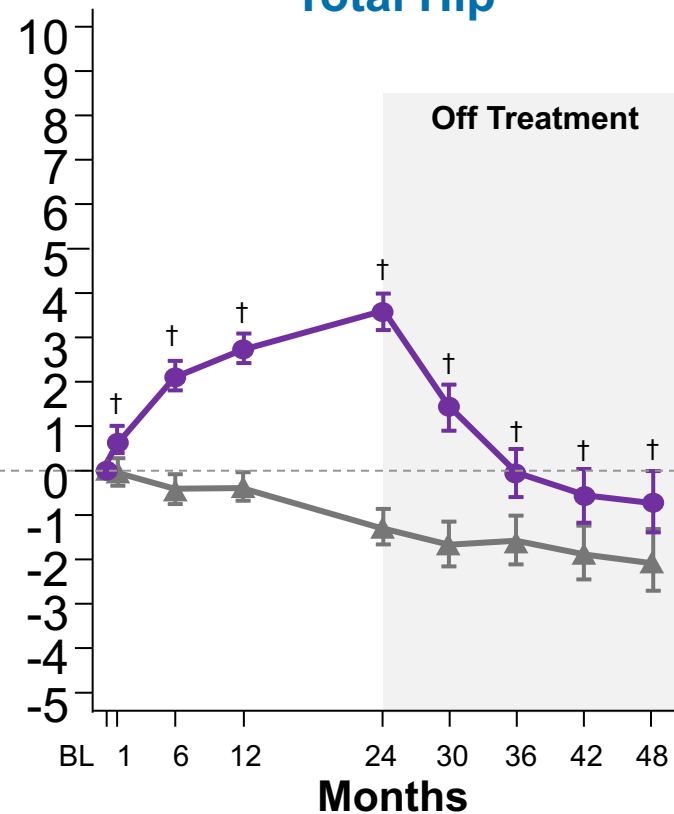
## Phase 3 Prevention Trial – Extension Study

▲ Placebo (n = 110–128\*) ● Denosumab 60 mg Q6M (n = 109–128\*)

### Lumbar Spine



### Total Hip



\*Includes subjects enrolled in the off-treatment phase with observed values at Month 0 and time point of interest. BL=baseline; BMD=bone mineral density; CI=confidence interval; LS=least-squares; Q6M=once every 6 months

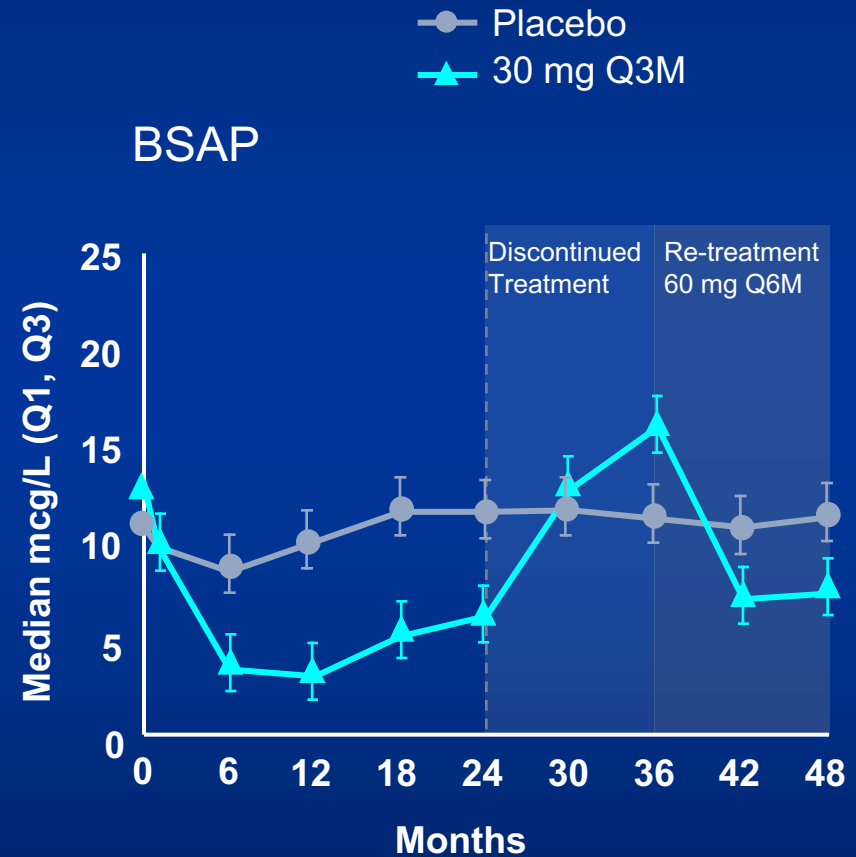
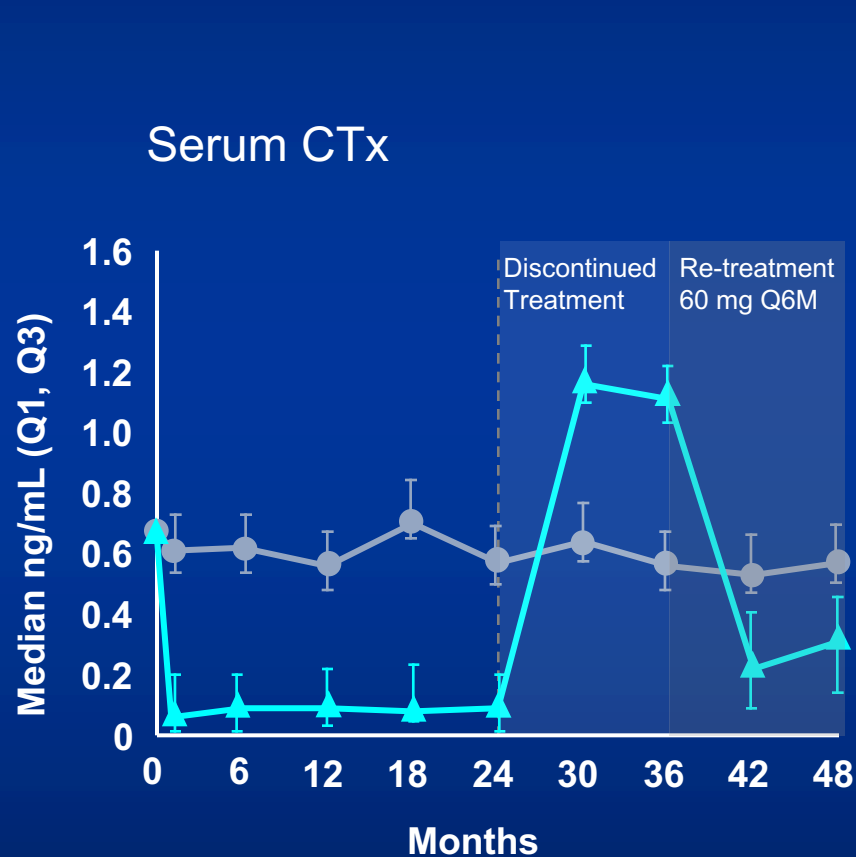
<sup>†</sup> $P \leq 0.0071$  vs placebo.

1. Adapted from: Bone HG, et al. *J Clin Endocrinol Metab*. 2011;96:972-980.



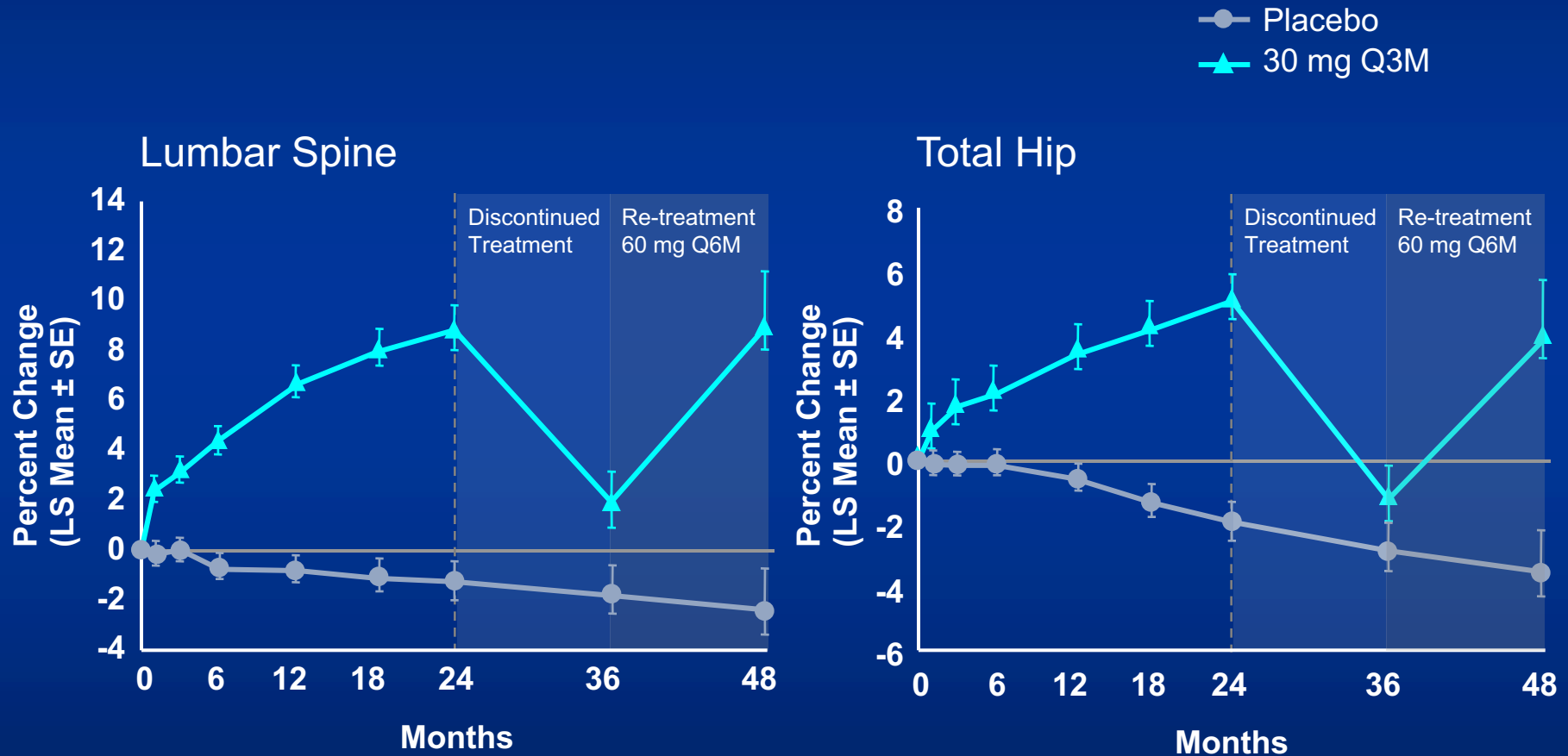
# Denosumab Re-treatment and Changes to Serum CTx and BSAP Levels

## Phase 2: Postmenopausal Women With Low BMD

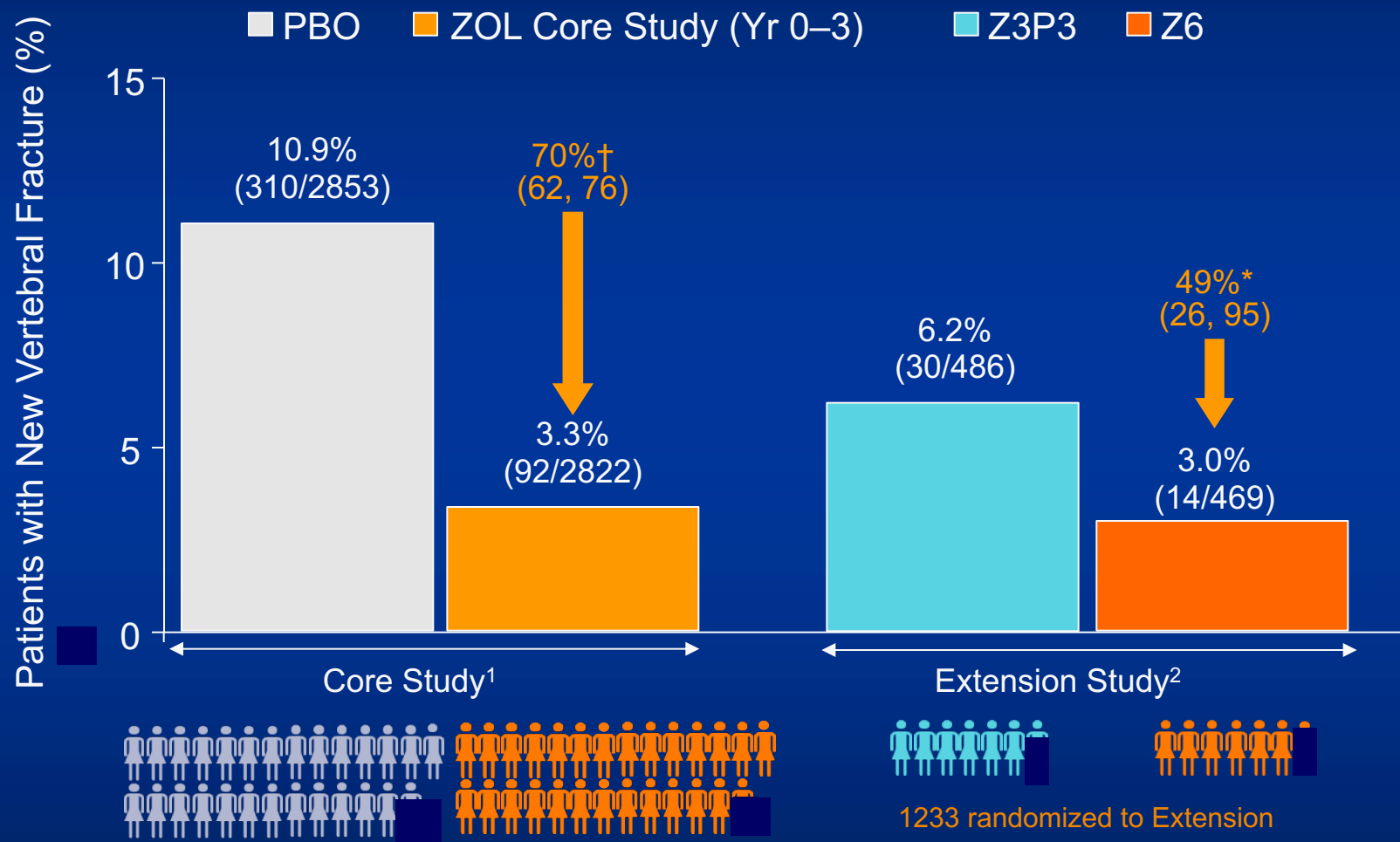


# Denosumab Re-treatment and Changes in Lumbar Spine and Total Hip BMD

## Phase 2: Postmenopausal Women With Low BMD



# Risque fracturaire à l'arrêt du traitement par acide zoledronique



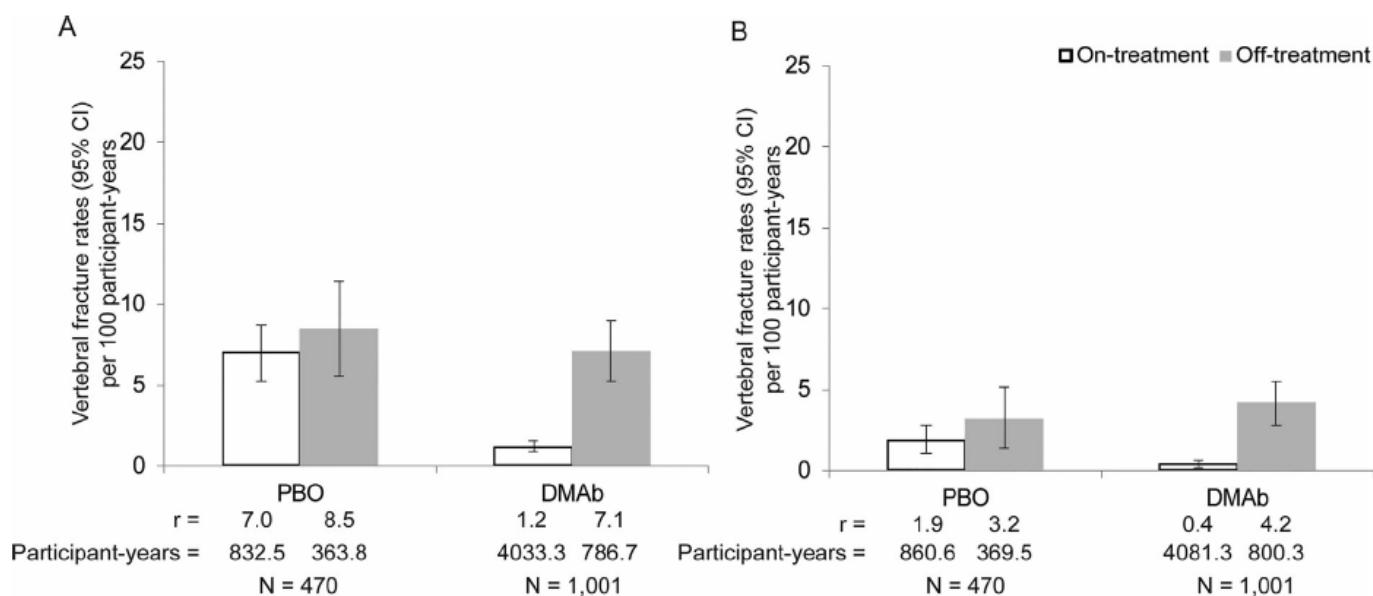
Core study: † $P < 0.001$  relative risk reduction vs. placebo (PBO).

\* $P = 0.0348$ , relative risk reduction vs Z3P3; n = the number of patients in the analysis population with X-rays at Year 3 and Year 6  
ITT = intention to treat, Z3P3 = ZOL for 3 years and placebo for 3 years, Z6 = ZOL for 6 years.

1. Adapted from Black DM, et al. *N Engl J Med*. 2007;356:1809–1822 and available upon request 2. Adapted from Black DM, et al. *J Bone Miner Res*. 2012; 27:243-254 and available upon request

## Vertebral Fractures After Discontinuation of Denosumab: A Post Hoc Analysis of the Randomized Placebo-Controlled FREEDOM Trial and Its Extension

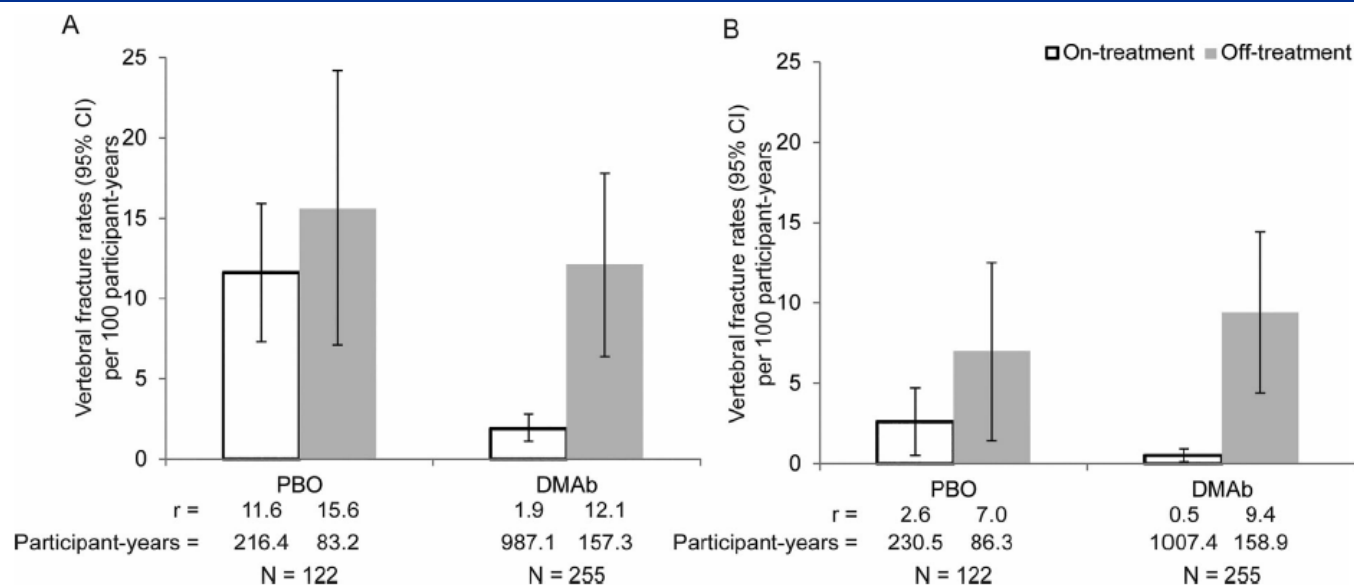
Steven R Cummings,<sup>1</sup> Serge Ferrari,<sup>2</sup> Richard Eastell,<sup>3</sup> Nigel Gilchrist,<sup>4</sup> Jens-Erik Beck Jensen,<sup>5</sup> Michael McClung,<sup>6</sup> Christian Roux,<sup>7</sup> Ove Törring,<sup>8</sup> Ivo Valter,<sup>9</sup> Andrea T Wang,<sup>10</sup> and Jacques P Brown<sup>11</sup>



**Fig. 2.** Exposure-adjusted rates of (A) any and (B) multiple vertebral fractures in participants who received placebo or denosumab in the FREEDOM study and denosumab in the Extension before (white bar) and after (gray bar) discontinuing treatment. DMAb = denosumab; PBO = placebo; r = rate per 100 participant-years.

## Vertebral Fractures After Discontinuation of Denosumab: A Post Hoc Analysis of the Randomized Placebo-Controlled FREEDOM Trial and Its Extension

Steven R Cummings,<sup>1</sup> Serge Ferrari,<sup>2</sup> Richard Eastell,<sup>3</sup> Nigel Gilchrist,<sup>4</sup> Jens-Erik Beck Jensen,<sup>5</sup> Michael McClung,<sup>6</sup> Christian Roux,<sup>7</sup> Ove Törring,<sup>8</sup> Ivo Valter,<sup>9</sup> Andrea T Wang,<sup>10</sup> and Jacques P Brown<sup>11</sup>

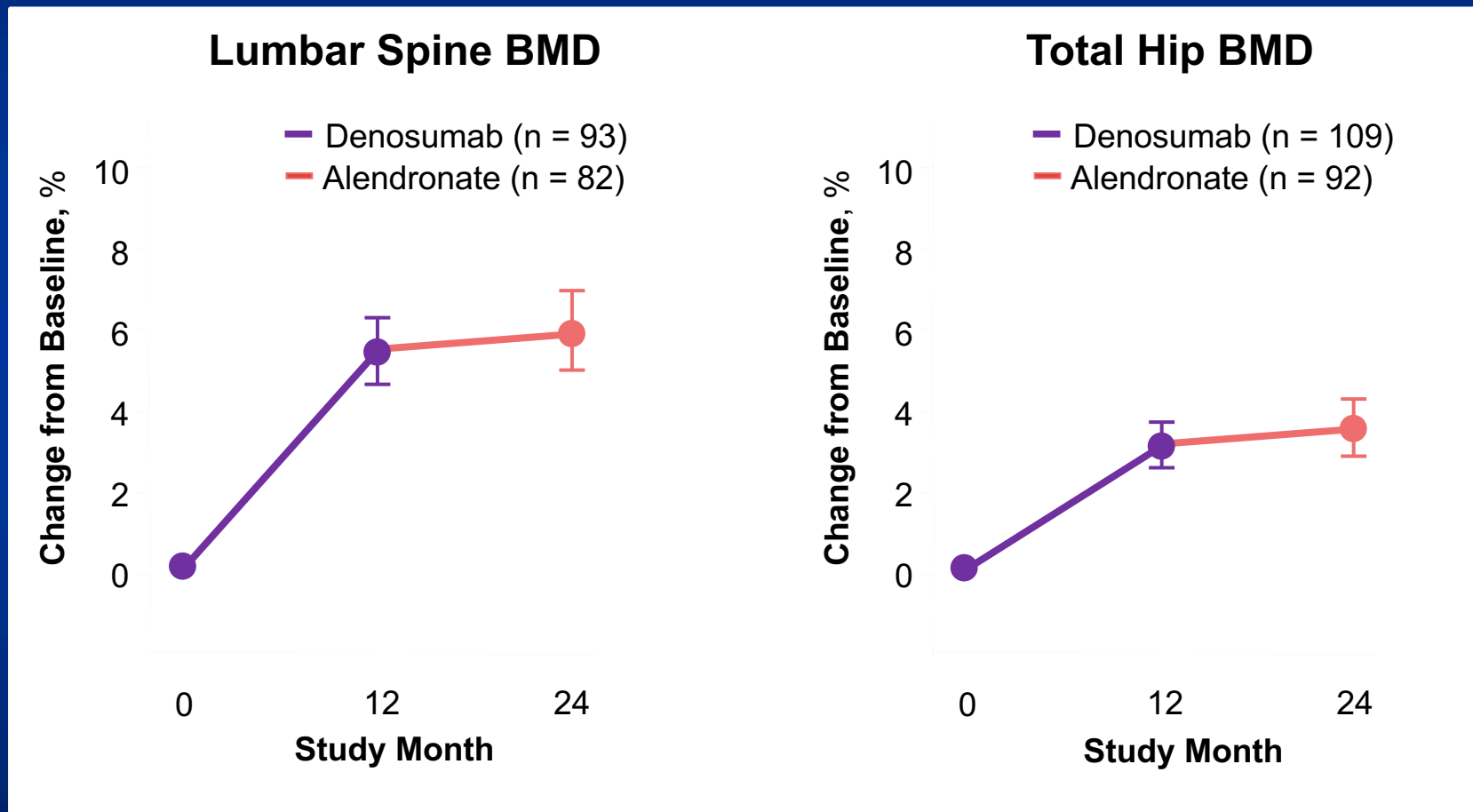


**Fig. 3.** Exposure-adjusted rates of (A) any and (B) multiple vertebral fractures in participants with prevalent vertebral fractures who received placebo or denosumab in the FREEDOM study and denosumab in the Extension before (white bar) and after (gray bar) discontinuing treatment. DMAb = denosumab; PBO = placebo; r = rate per 100 participant-years.





# Follow-on Alendronate Therapy Prevented Reductions in Spine and Hip BMD in Subjects Who Discontinued Denosumab



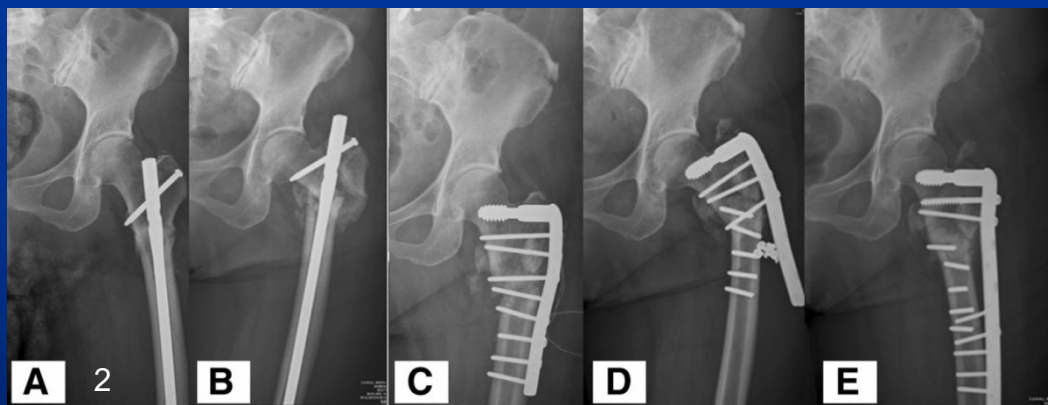
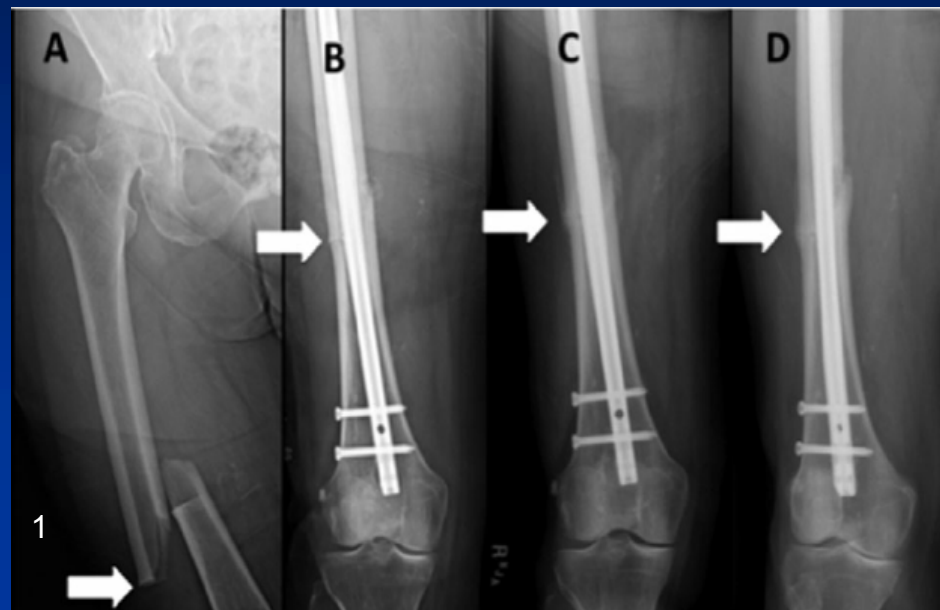
BMD=bone mineral density

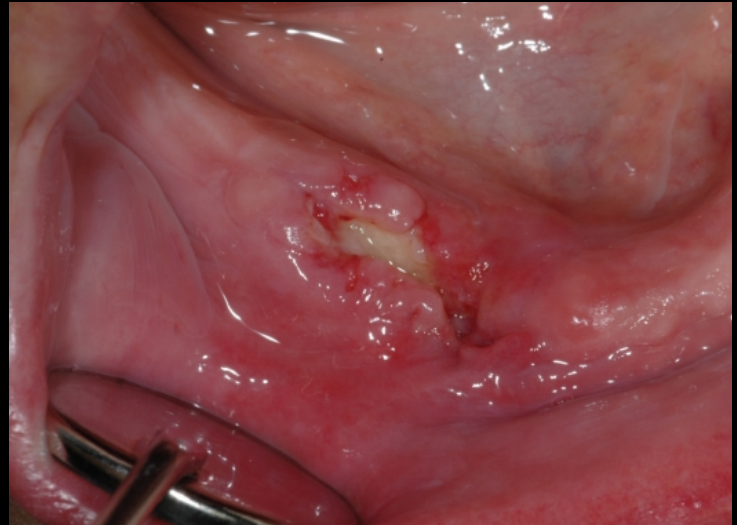
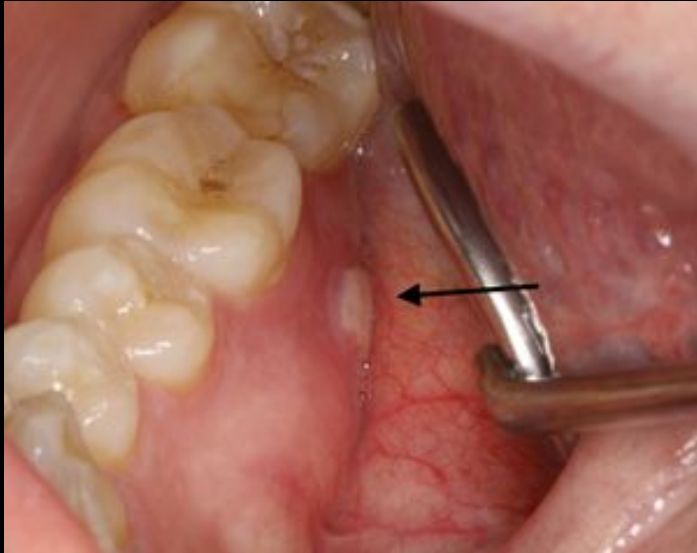
1. Freemantle N, et al. *Osteoporos Int* 2012;23:317-326. DAPS = Denosumab Adherence Preference Satisfaction

# Inflammatory ocular adverse events with the use of oral bisphosphonates: a retrospective cohort study

Mahyar Etminan PharmD MSc, Farzin Forooghian MD MSc, David Maberley MD MSc

<b>Bisphosphonates</b>	<b>users 10.827</b>	<b>non users 923.320</b>
<b>Uveitis incidence</b>	<b>29/10.000</b>	<b>20/10.000</b>
<b>Scleritis incidence</b>	<b>63/10.000</b>	<b>36/10.000</b>
<b>Number needed to harm</b>	<b>1.100</b>	<b>370</b>





# The Dental Management of Patients at Risk of Medication-Related Osteonecrosis of the Jaw: New Paradigm of Primary Prevention

Olga Di Fede <sup>1</sup>, Vera Panzarella <sup>1</sup>, Rodolfo Mauceri <sup>1</sup>, Vittorio Fusco,<sup>2</sup>  
Alberto Bedogni,<sup>3</sup> Lorenzo Lo Muzio <sup>4</sup>, SIPMO ONJ Board,<sup>5</sup> and Giuseppina Campisi <sup>1</sup>

TABLE 2: Main dental treatments with respect to patients' categories in the pre-treatment phase with drugs related to ONJ.

Dental procedures on patients in the pre-treatment phase	Cancer patients	Non-cancer patients
Non-Surgical Procedures		
Restorative dentistry	Indicated	Indicated
Endodontic treatment	Indicated	Indicated
Orthodontic treatment	Possible	Possible
Periodontal treatments: oral hygiene and non-surgical treatments	Indicated	Indicated
Prosthesis	Possible	Possible
Surgical Procedures		
Dentoalveolar surgery	Indicated*	Indicated
Preimplant bone surgery	Contraindicated	Possible*
Dental implant surgery	Contraindicated	Possible*
Periodontal/endodontic surgery	Indicated <sup>§</sup>	Indicated <sup>§</sup>

\* Advisable to wait for wound healing (4–6 weeks) before initiating antiresorptive or antiangiogenic treatment for cancer therapy. When treatment with ONJ-related drugs cannot be deferred, dentoalveolar surgery is indicated; in this case, the surgical protocol and medical treatment of oncological patients already in-treatment with MRONJ-related drugs will also be performed. <sup>§</sup>To Perform only if any infective processes cannot be treated via periodontal/endodontic, non-invasive treatment. \* Advise the patient that the risk of MRONJ is indefinable in the long term.

# The Dental Management of Patients at Risk of Medication-Related Osteonecrosis of the Jaw: New Paradigm of Primary Prevention

Olga Di Fede <sup>1</sup>, Vera Panzarella <sup>1</sup>, Rodolfo Mauceri <sup>1</sup>, Vittorio Fusco,<sup>2</sup>  
Alberto Bedogni,<sup>3</sup> Lorenzo Lo Muzio <sup>4</sup>, SIPMO ONJ Board,<sup>5</sup> and Giuseppina Campisi <sup>1</sup>

TABLE 3: Main dental treatments in patients in-treatment phase with drugs related to ONJ.

Dental procedures on patients in-treatment phase	Cancer patients	Non-cancer patients	
		Category A	Category B
Non-Surgical Procedures			
Restorative dentistry	Indicated	Indicated	Indicated
Endodontic treatment	Indicated	Indicated	Indicated
Orthodontic treatment	Possible	Possible	Possible
Periodontal treatments: oral hygiene and non-surgical treatments	Indicated (every 4 months)	Indicated	Indicated
Prosthesis	Possible	Possible	Possible
Surgical Procedures			
Dentoalveolar surgery	Indicated	Indicated	Indicated
Preimplant bone surgery	Contraindicated	Possible <sup>*</sup>	Possible <sup>**</sup>
Dental implant surgery	Contraindicated	Possible <sup>*</sup>	Possible <sup>**</sup>
Periodontal/endodontic surgery	Indicated <sup>§</sup>	Indicated	Indicated <sup>§</sup>

<sup>°</sup>Follow the surgical protocol + adapt the flaps, avoid of tension and suture in order to prioritize healing of the wound. <sup>§</sup>Perform only if any infective processes cannot be treated with non-invasive periodontal/endodontic procedures. <sup>\*</sup> Advise the patient of an indefinable risk of MRONJ in the long term. <sup>\*\*</sup> Advise the patient of an indefinable risk of MRONJ in the short term.



# The Dental Management of Patients at Risk of Medication-Related Osteonecrosis of the Jaw: New Paradigm of Primary Prevention

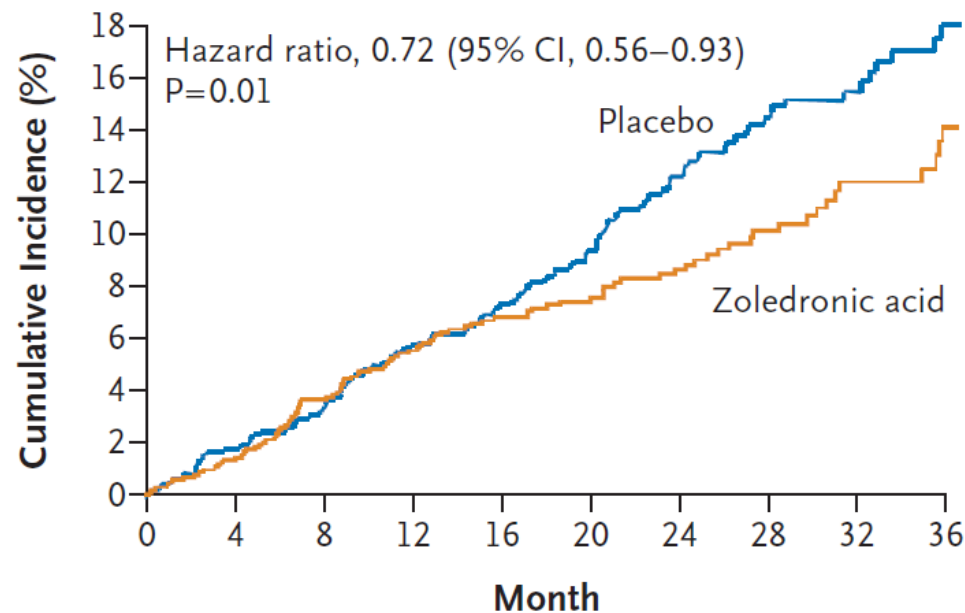
Olga Di Fede <sup>1</sup>, Vera Panzarella <sup>1</sup>, Rodolfo Mauceri <sup>1</sup>, Vittorio Fusco,<sup>2</sup>  
Alberto Bedogni,<sup>3</sup> Lorenzo Lo Muzio <sup>4</sup>, SIPMO ONJ Board,<sup>5</sup> and Giuseppina Campisi <sup>1</sup>

TABLE 6: Drug suspension for non-cancer patients; it must be agreed upon with the prescriber and performed according to the table.

Drug holiday in <u>non-cancer patients</u>		
Active pharmaceutical ingredient	Last administration	Therapy resumption
Bisphosphonate* (AR)	1 week before	4–6 weeks after
Denosumab (AR)	No suspension**	

\* Administered by more than three years or for less than three years and in the presence of other systemic risk factors; \*\* suspension is not needed thanks to the latency between drug administrations. It is useful to perform invasive procedures between the first and the third month from the last administration, so as to ensure an adequate period for healing before the next dose.


# Zoledronic Acid and Clinical Fractures and Mortality after Hip Fracture

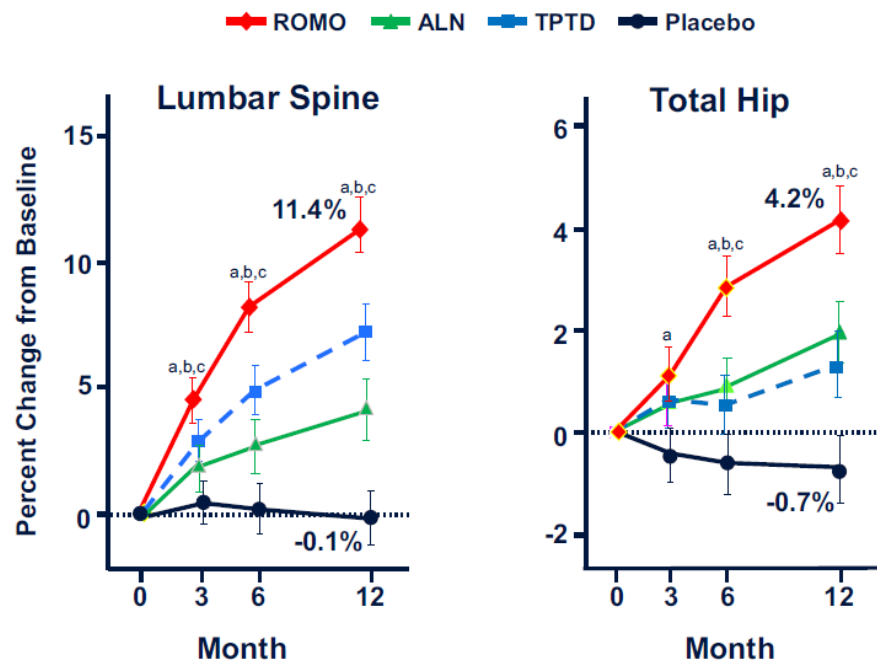


## No. at Risk

Zoledronic acid	1054	1029	987	943	806	674	507	348	237	144
Placebo	1057	1028	993	945	804	681	511	364	236	149

# Sclerostin Inhibition in the Management of Osteoporosis

Natasha M. Appelman-Dijkstra<sup>1</sup> · Socrates E. Papapoulos<sup>1</sup> 



Percent changes of lumbar spine and total hip BMD during treatment of postmenopausal women with low bone mass with

- Romosozumab (ROMO) 210 mg once-monthly sc
- Teriparatide (TPTD) 20  $\mu$ g daily sc
- Alendronate (ALN) 70 mg once-weekly orally
- Placebo.

a =  $p < 0.05$  between ROMO and placebo,  
 b =  $p < 0.02$  between ROMO and ALN,  
 c =  $p < 0.02$  between ROMO and TPTD (2)

# Romosozumab Treatment in Postmenopausal Women with Osteoporosis

F. Cosman, D.B. Crittenden, J.D. Adachi, N. Binkley, E. Czerwinski, S. Ferrari, L.C. Hofbauer, E. Lau, E.M. Lewiecki, A. Miyauchi, C.A.F. Zerbini, C.E. Milmont, L. Chen, J. Maddox, P.D. Meisner, C. Libanati, and A. Grauer

**A** Incidence of New Vertebral Fracture

