Is hormone therapy really harmless in elderly people?

SIOG
INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

Matti S. Aapro
IMO
Genolier
Switzerland

COI

Dr Aapro is a consultant for

Amgen, BMS, Celgene, GSK, Helsinn, JnJ Novartis, Merck, Merck Serono, Pfizer, Pierre Fabre, Roche, Sandoz, Teva, Vifor

and has received honoraria for lectures at symposia of

Amgen, Bayer Schering, Cephalon, GSK, Helsinn, Hospira, Ipsen, JnJ OrthoBiotech, Merck, Merck Serono, Novartis, Pfizer, Pierre Fabre, Roche, Sandoz, Sanofi, Teva, Vifor

No responsibility accepted for involuntary errors or omissions.
The list may be incomplete, and does not reflect consultancy for NGOs, Universities, Governmental agencies, and others

WHOM TO THANK?

Laura Biganzoli
Robert Coleman
Diana Crivellari
Arti Hurria
Juan Morote
Hans Wildiers

And many others

BREAKFAST MENU

- Why the elderly and why should hormonal therapy be harmless?
- About breast cancer
- About prostate cancer
- A common topic: bone health
- To conclude

Median age of global population is increasing...

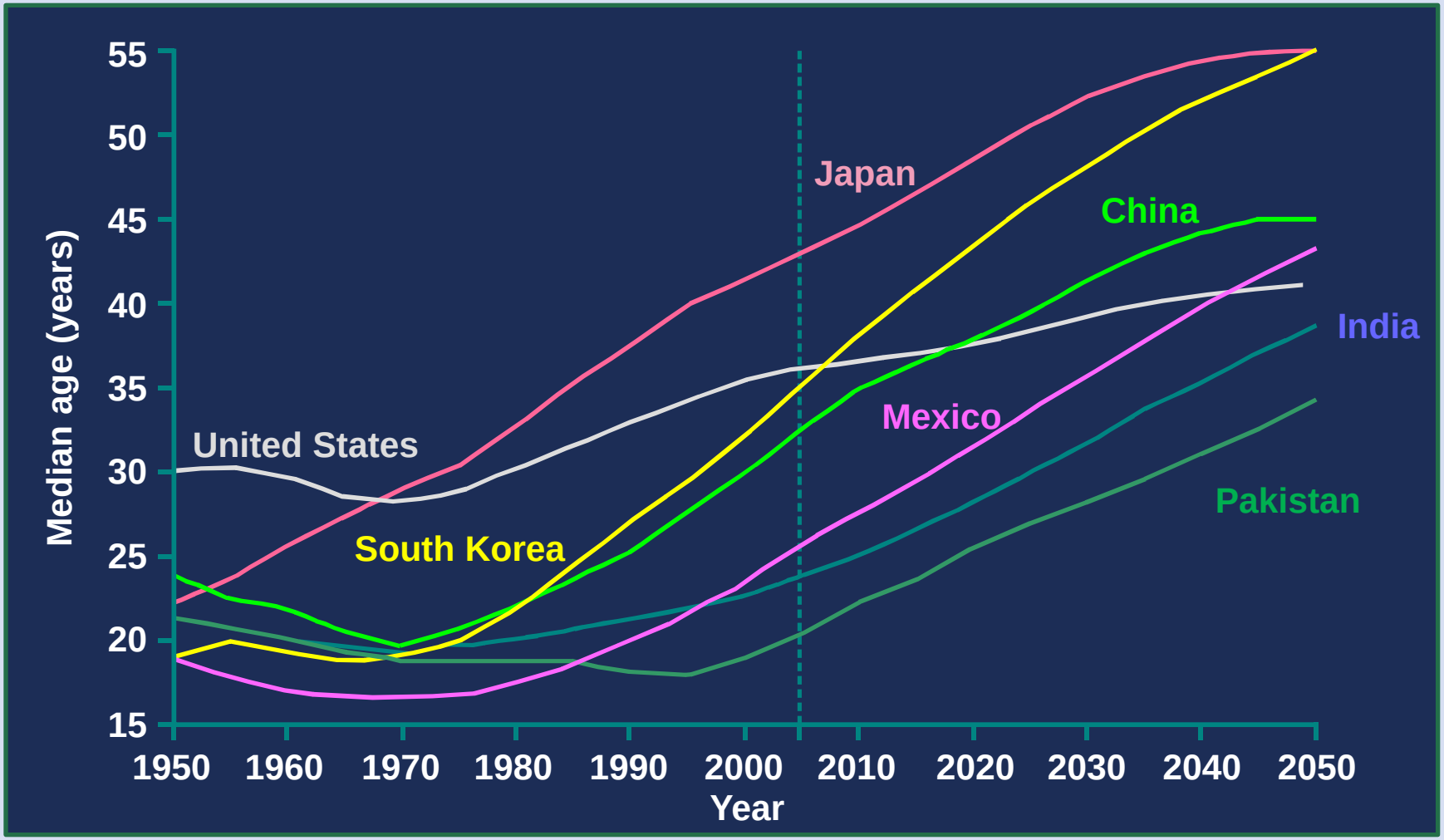
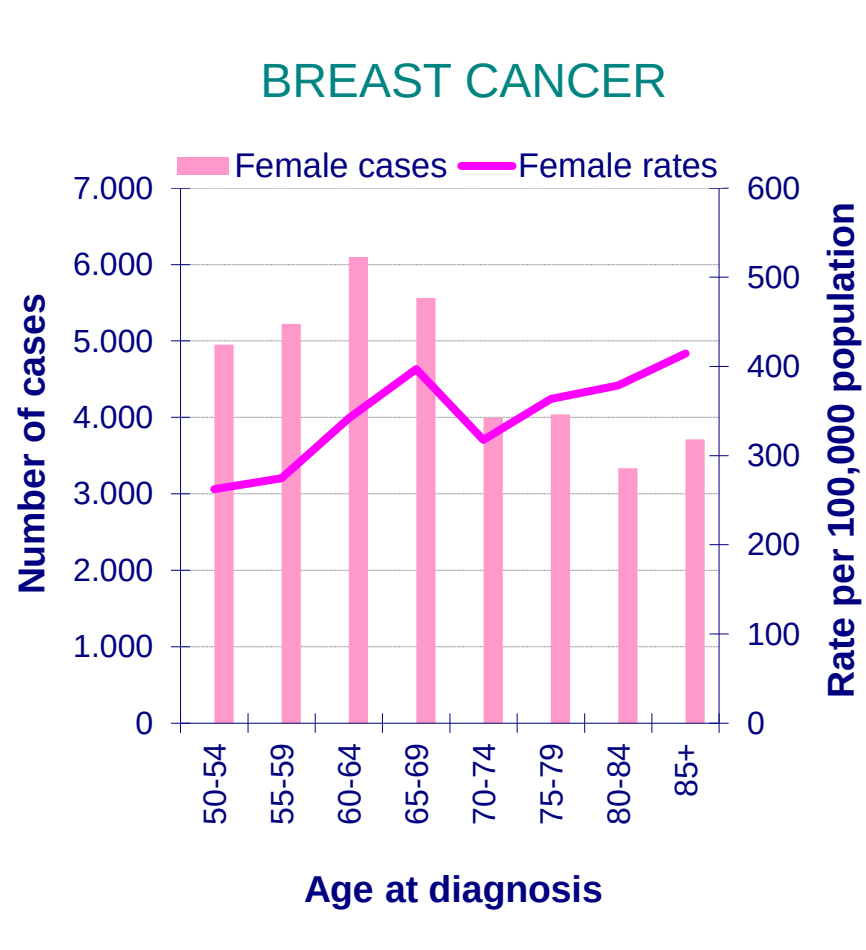


Figure taken from: United Nations World Population Prospects at http://esa.un.org/unpp/index.asp?panel=2

…with increased age cancer incidence also increases

- A peak occurrence rate can be identified in high age groups
- Therefore cancer is a disease that affects a lot of elderly patients
- Evidence suggests that these patients often do not receive standard treatment



N Hebert-Croteau et al. Cancer 1999;85:1104-1113
CA Townsley et al. J Clin Oncol 2005;23:3112-3124
Image adapted from: CancerResearchUK.org accessed August 2010

Société Internationale d'Oncologie Gériatrique

We cannot “simply” apply principles of clinical studies validated in younger patients

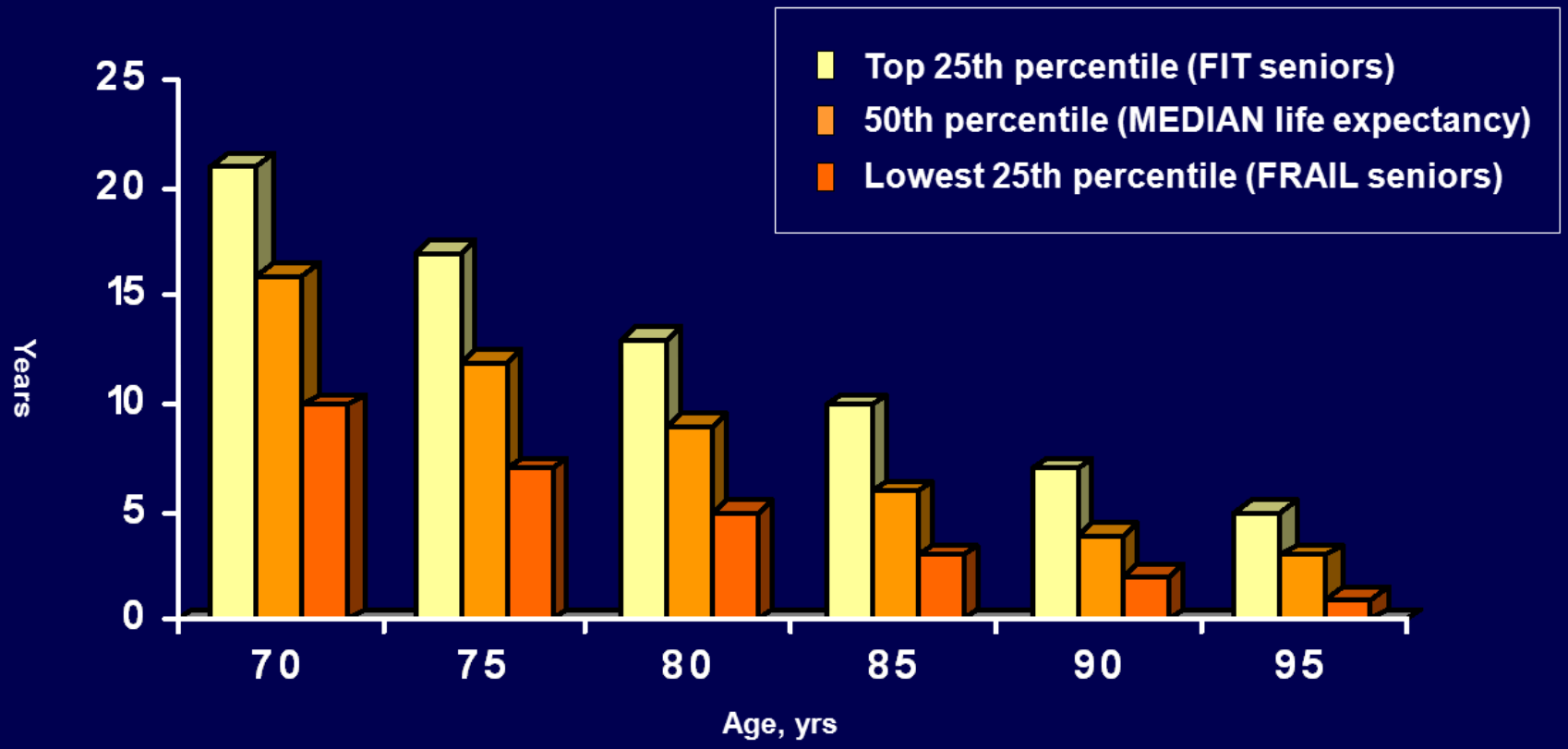
EORTC workshop on clinical trial methodology in older individuals with a diagnosis of solid tumors

A.G. Pallis, A. Ring, C. Fortpied, B. Penninckx, M.C. Van Nes, U. Wedding, G. von Minckwitz, C.D. Johnson, L. Wyld, A. Timmer, F. Bonnetain, L. Repetto, M. Aapro, A. Luciani, H.Wildiers

On behalf of the EORTC Elderly Task Force

Ann Oncol. 2011 Aug;22(8):1922-6

Life expectancy in senior adults: a large variability reflecting health status variability



Life expectancy for elderly women based on heath status

Walters et al. JAMA 2001

Management of elderly patients with breast cancer: updated recommendations of the International Society of Geriatric Oncology (SIOG) and European Society of Breast Cancer Specialists (EUSOMA)

Geriatric assessment

- General health and functional status for older individuals may be captured by collaborative geriatric and oncology management
- Active intervention for CGA-identified reversible deficits in geriatric domains may reduce morbidity and mortality, and improve quality of life
- Serial geriatric assessment may identify incident deterioration, for which intervention may improve outcomes

Biganzoli et al. Lancet Oncol 2012

Comprehensive Geriatric Assessment (CGA)

- A well-established tool to assess the elderly patient for health status and risk of morbidity, mortality and toxicity[1]
- Data suggest that CGA can improve patient treatment and outcome[2]
- Breast cancer adj. chemotherapy can reduce relative death risk by 14–27%[3]
  - If CGA suggests patients should receive beta blockers, it is possible that survival data will be affected
  - Beta blockers have reduced myocardial infarction relative mortality by 23%[4]
  - Care is needed in balancing CGA assessments equally in arms of clinical studies
- Has limitations and is not always suitable for everyday use

1. Extermann M, et al. J Clin Oncol 2007;25:1824–31; 2. Monteserin R, et al. Fam Pract 2010;27:239–45
3. Early Breast Cancer Trialists Collaborative Group, Lancet 2008;371:29–40; 4. Colucci WS. Am J Cardiol 2004;93:13B–6B

General health status

Geriatric screening

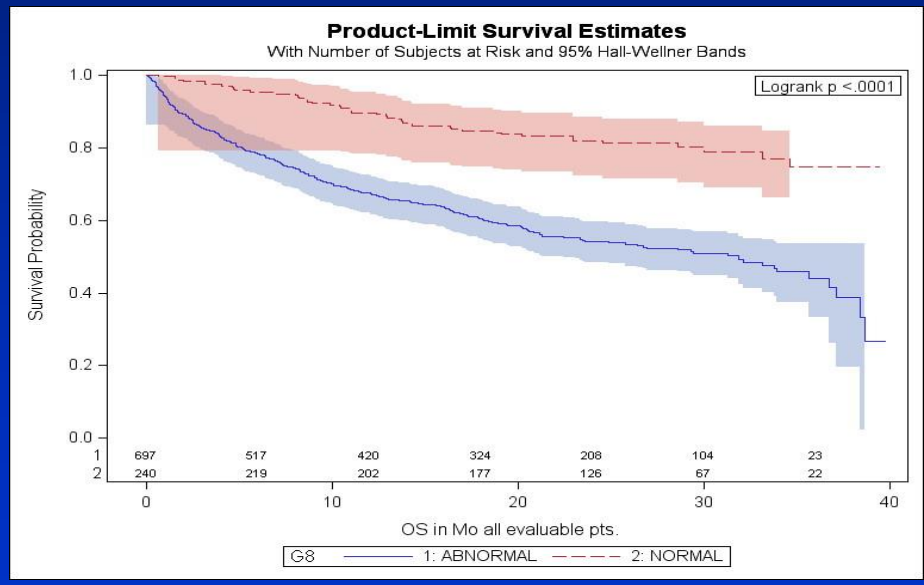
Results (4)

G8

(Soubeyran et al. 2008)

- Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?
- Weight loss during the last 3 months
- Mobility
- Neuropsychological problems
- Body Mass Index (weight in kg/height in m2)
- Takes more than 3 medications per day
- In comparison with other people of the same age, how does the patient consider his/her health status?
- Age

OS



Kenis, …, Wildiers, J Clin Oncol, 2013

BREAKFAST MENU

- Why the elderly and why should hormonal therapy be harmless?

- About breast cancer

- About prostate cancer

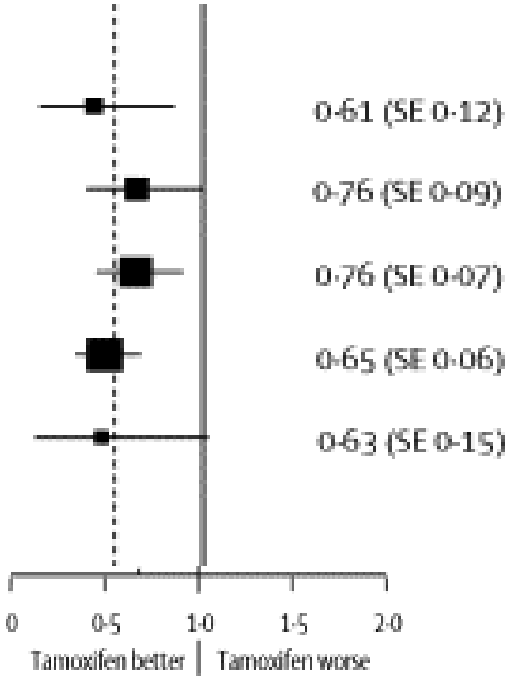
- A common topic: bone health

- To conclude

The benefit of adjuvant tamoxifen is independent from patient's age

Breast cancer mortality/women

Category	Deaths/women: Allocated tamoxifen	Deaths/women: Adjusted control	Tamoxifen deaths: Logrank O–E	Tamoxifen deaths: Variance of O–E	Ratio of annual death rates Tamoxifen : Control
(c) Entry age (trend χ^2_1=0·4; 2p>0·1; NS)					
Age <40	74/417 (17·7%)	119/398 (29·9%)	−21·9	44·0	0·61 (SE 0·12)
40–49	173/1119 (15·5%)	219/1139 (19·2%)	−24·8	90·3	0·76 (SE 0·09)
50–59	330/1591 (20·7%)	394/1535 (25·7%)	−45·2	161·7	0·76 (SE 0·07)
60–69	379/1822 (20·8%)	527/1789 (29·5%)	−87·3	200·4	0·65 (SE 0·06)
≥70	62/266 (23·3%)	89/286 (31·1%)	−13·6	29·9	0·63 (SE 0·15)
Age unknown	0/10	0/14			



EBCTCG. Lancet 2005

VOLUME 28 · NUMBER 3 · JANUARY 20 2010
JOURNAL OF CLINICAL ONCOLOGY
SPECIAL ARTICLE

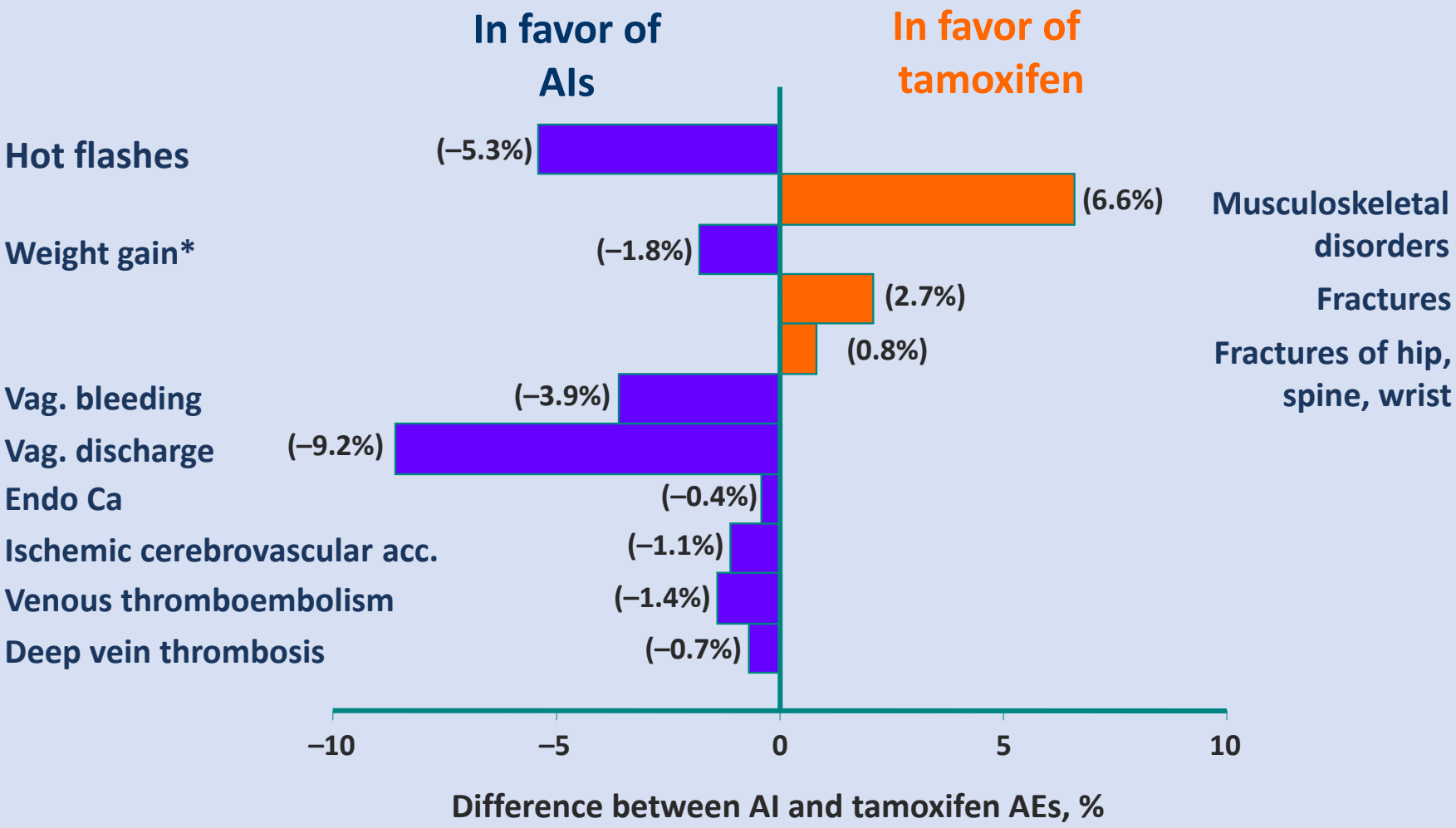
Meta-Analysis of Breast Cancer Outcomes in Adjuvant Trials of Aromatase Inhibitors Versus Tamoxifen

Mitch Dowsett, Jack Cuzick, Jim Ingle, Alan Coates, John Forbes, Judith Bliss, Marc Buyse, Michael Baum, Aman Buzdar, Marco Colleoni, Charles Coombes, Claire Snowdon, Michael Gnant, Raimund Jakesz, Manfred Kaufmann, Francesco Boccardo, Jon Godwin, Christina Davies, and Richard Peto

Strategy	No.	Mean follow-up	Absolute decrease in recurrence	Absolute decrease in BC mortality
Upfront	9.856	5.8 yrs	At 5 yrs	
ATAC BIG 1-98			2.9% (SE=0.7%) 2P<.00001	1.1% (SE=0.5%) 2P=.1
Sequential	9.015	3.9 yrs	At 3 yrs from treatment divergence	
ARNO ABCSG-8 IES ITA			3.1% (SE=0.6%) 2P<.00001	0.7% (SE=0.3%) 2P=.02

Which one to use?

(data not selected for the elderly)



The Trialists' Group. Cancer. 2003;98:1802-1810

M Baum , et al. Cancer. 2003;1802-1810.

*Proportion with ≥10% gain in body weight from baseline to year 2.

Safety profile

Tamoxifen	Aromatase inhibitors
Endometrial cancer Thromboembolic events	Musculoskeletal events Decreased bone mineral densitometry and bone fractures Cardiovascular events

Thromboembolism?

Osteoporosis?

Ischemic heart disease?

Arthralgia ?

Comorbidities

Toxicity of Adjuvant Endocrine Therapy in Postmenopausal Breast Cancer Patients: A Systematic Review and Meta-analysis

Eitan Amir, Bostjan Seruga, Saroj Niraula, Lindsay Carlsson, Alberto Ocaña

7 trials; 30.023 patients

Table 2. Absolute differences and number needed to harm associated with one adverse event of each type

	↑ Cardiovascular disease		= Cerebrovascular disease		↓ Venous thrombosis		↑ Bone fractures		↓ Endometrial Carcinoma	
Trial (reference)	Absolute difference, %	NNH	Absolute difference, %	NNH	Absolute difference, %	NNH	Absolute difference, %	NNH	Absolute difference, %	NNH
ATAC (5)	0.8	129	−0.8	−115	−1.8	−59	4.6	22	−0.6	−163
BIG01-98 (3)	0.9	107	0	∞	−1.8	−56	2.8	36	−0.5	−204
IES (13)	1.3	79	0	∞	−1.2	−84	2.1	48	−0.2	−479
ABCSG8/ARNO (4)	<0.1†	1643†	NS	NS	−0.6	−179	1.1	91	−0.3	−268
ITA (2)	1.3	72	NS	NS	−2.3	−40	NS	NS	−2.2	−46
N-SAS BC03 (14)	−0.3	−354	NS	NS	0.3	347	−1.2	−85	−0.3	−349
TEAM (15)	0.7	139	0.4	311	−1.1	−91	1.6	63	−0.2	−485
Pooled	0.8	132	−0.1	−974	−1.3	−79	2.2	46	−0.4	−258

Limitations:

- Literature rather than individual patient data meta-analysis
- Reports of trials with different durations of follow-up
- Information on the potentially confounding baseline host factors (eg, obesity, hypertension, diabetes, and family history of events of interest) or the use of concurrent medications was not reported

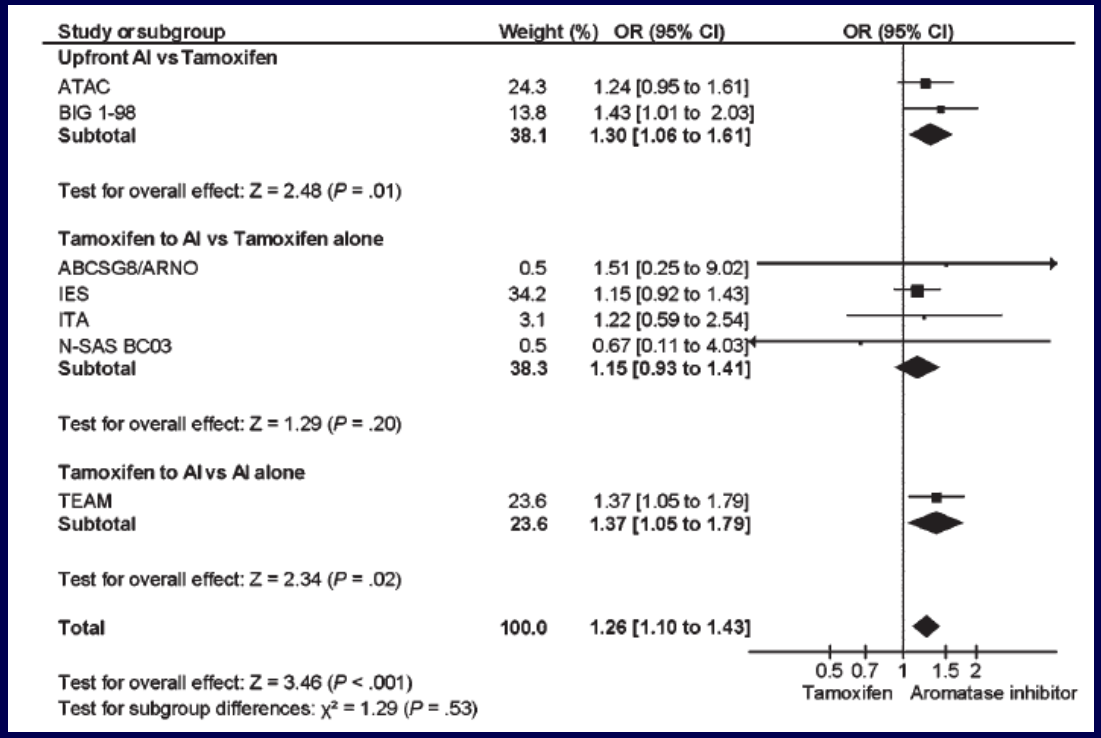
J Natl Cancer Inst 2011;103:1299–1309

Cardiovascular Considerations in Elderly Patients

- **Cardiovascular associated co-morbidities are common**
- **Tamoxifen is known to have a favorable effect on cholesterol but is associated with an increase in thromboembolic events**
- **Thromboembolic events are not associated with AI treatment**
  - Most trials have not linked hypercholesterolemia with the use of AIs and a sub-study of the TEAM trial actually reported a decrease in cholesterol levels associated with exemestane treatment

D Crivellari et al. Crit Rev Oncol Hematol 2010;73(1):92-8; Early Breast Cancer Trialists' Collaborative Group. Lancet 2005;365:1687-1717; B Thurlimann et al. N Engl J Med 2005;353:2747-2757; C Markopoulos et al. Ann Oncol 2009;209:49-55; PE Goss et al. J Natl Cancer Inst 2005;97:1262-1271

Cardiovascular events



Longer duration of AI use is associated with statistically significant increase in the odds of developing cardiovascular disease compared with TAM alone or shorter duration of AI use (OR 1.26; 95% CI 1.10-1.43, P<.001)

4.2% of patients in the AI group and 3.4% of patients in the TAM group suffered a cardiovascular event (difference in absolute risk=0.8%)

Amir et al. J Natl Cancer Inst 2011

Specific subpopulations might be at higher risk

- ATAC: in women with preexisting heart disease (7.5% of the total trial population) the incidence of cardiovascular events was 17% with anastrozole and 10% with tamoxifen [1]

- MA.17: In multivariable analyses, a treatment interaction was found with cardiovascular disease and a detrimental effect was observed with letrozole administration (*P* <.001) among patients who had cardiovascular disease at baseline [2]

[1] Food and Drug Administration.Anastrozole:FullPrescribingInformation.http://www.accessdata.fda.gov/drugsatfda_docs/label/2009/020541s024s025lbl.pdf. Accessed 18 November 2010

[2] Chapman et al. J Natl Cancer Inst 2008

Tamoxifen vs aromatase inhibitors in elderly patients: safety

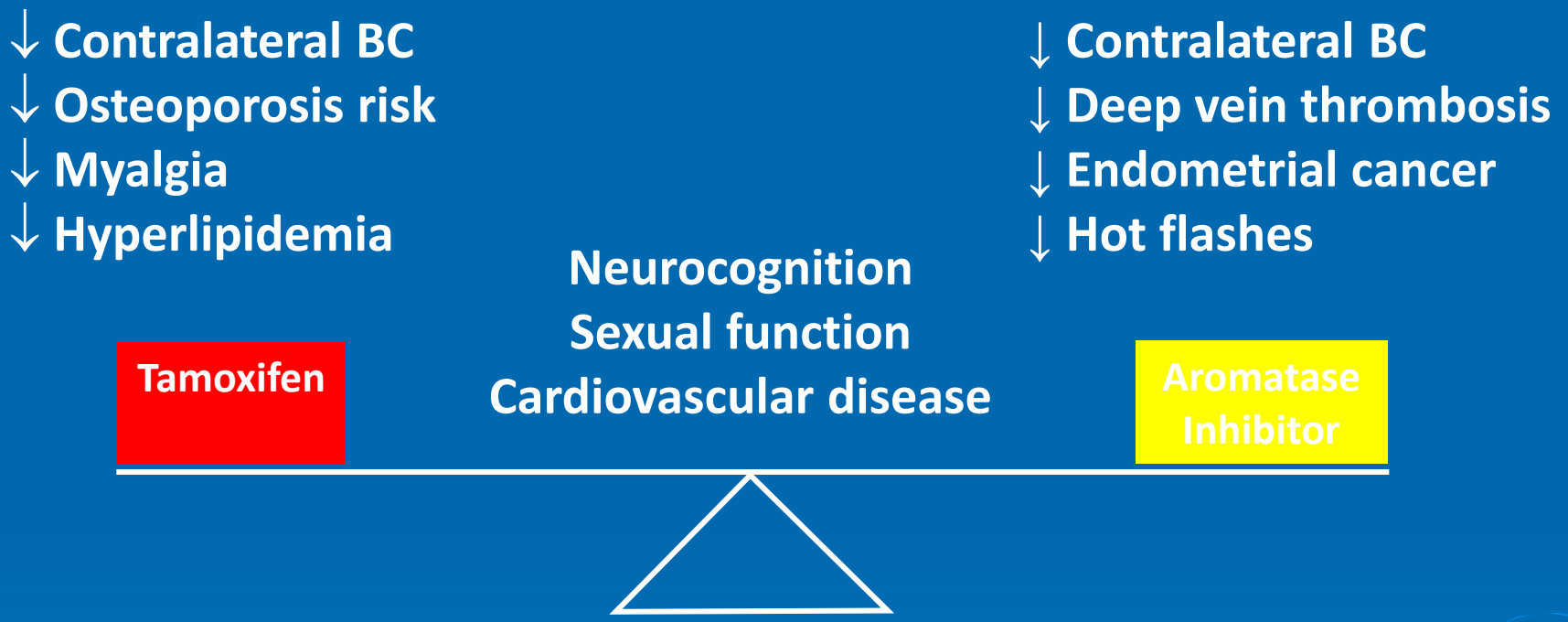
- Comorbidities present in older women might increase the risk of some AI's related side-effects
- Tamoxifen's side effects are correlated with age:

  - There is little uterine cancer risk or excess risk of fatal pulmonary embolus from administration of tamoxifen before age 45 years or at ages 45–54 years[1]

  - By contrast, for older women with an intact uterus the excess risk of death from endometrial cancer or pulmonary embolus could well be about 1%[2]

[1] Fisher B et al. J Natl Cancer Inst 2005; [2] EBCTCG. Lancet 2011

Aromatase Inhibitors and Tamoxifen: Potential Risks and Benefits



Cognitive functioning and HT

- Older age is often associated with cognitive decline and endocrine therapy may adversely affect cognitive functioning
- Tamoxifen has been shown to negatively impact cognitive functioning
- A sub-study of the TEAM trial and another of the BIG 1-98 trial show that letrozole or exemestane do not significantly impact cognitive functioning when compared to Tamoxifen or healthy control subjects
  - Tamoxifen users, on the other hand, performed significantly worse on verbal memory and executive functioning when compared to healthy controls.

A Paganini-Hill et al. Breast Cancer Res Treat. 2000;64:165–76
Schilder C et al. J Clin Oncol 2010; 28(8):1294-1300
Phillips KA, et al. Breast. 2010;19(5):388-95.

Tolerability profile of HT

- **Tamoxifen has a well defined adverse event profile**
  - Treatment is associated with increased gynecological events such as endometrial carcinoma and vaginal bleeding, thromboembolic events are also frequently reported
  - Tamoxifen has been shown to have a positive effect on bone and lipid profile
- **AIs have a different AE profile when compared to tamoxifen**
  - AI treatment is not associated with endometrial carcinoma or thromboembolic events
  - However, AIs are reported to cause more musculoskeletal AEs and are reported to cause more osteoporosis and a higher risk of fractures.

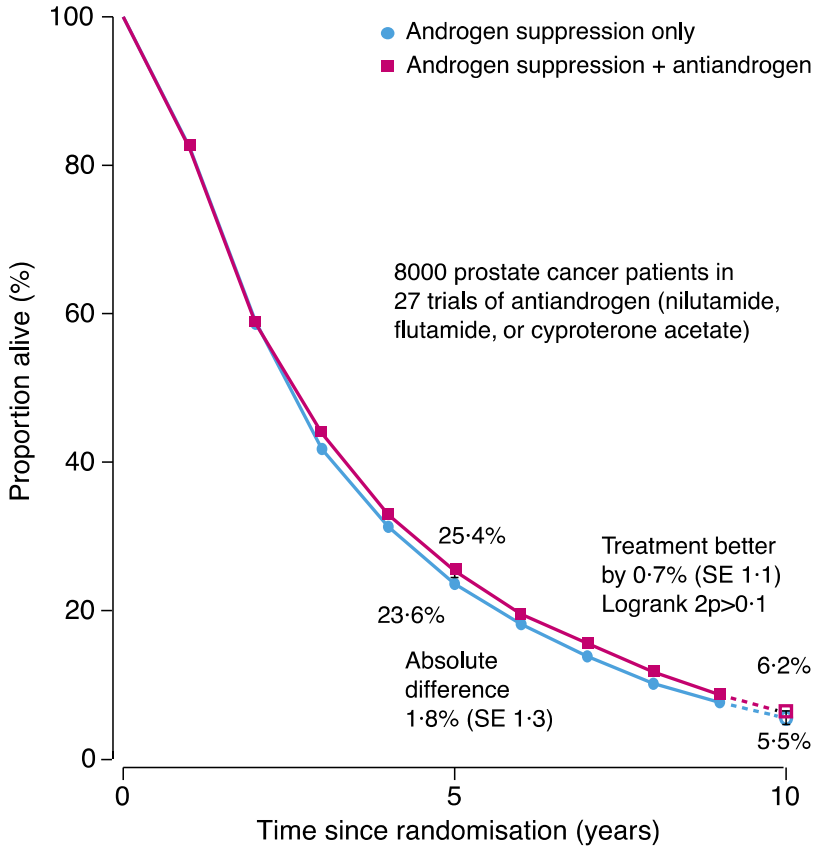
Early Breast Cancer Trialists' Collaborative Group. Lancet 2005;365:1687-1717; Ingle JN. Breast. 2013 Aug;22 Suppl 2:S180-3; RR Love et al. N Engl J Med 1992;326:852-856; RR Love et al. J Natl Cancer Inst 1994;86:1534-1539; RC Coombes et al. Lancet 2007;369:559-570; JF Forbes et al. Lancet Oncol 2008;9:45-53; Glück S, von Minckwitz G, Untch M.Breast. 2013 Apr;22(2):142-9. H Mouridsen et al. N Engl J Med 2009;20;361:766-776

BREAKFAST MENU

- Why the elderly and why should hormonal therapy be harmless?
- About breast cancer
- About prostate cancer
- A common topic: bone health
- To conclude

Management of advanced prostate cancer: Specific considerations for senior adults

- First-line ADT **monotherapy** is the standard of care



Maximum androgen blockade results in a small advantage in OS, which is not clinically relevant

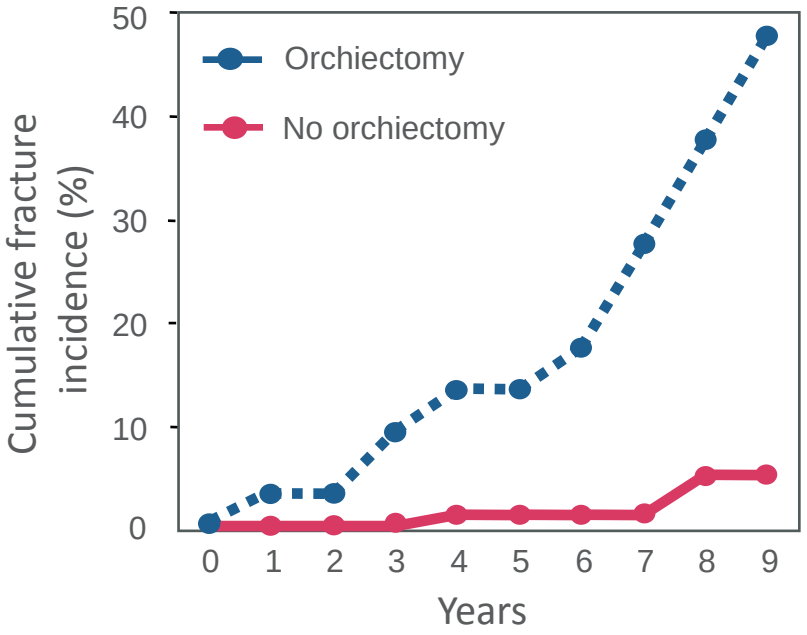
Maximum androgen blockade has significant effects on QoL

OS: Overall survival QoL: Quality of life.

Prostate Cancer Trialists Collaborative Group, *Lancet* 2000;355:1491–1498

Androgen deprivation therapy: Side effects

- Bone loss with increased risk of fracture[1,2]
  - Baseline bone density
  - Prevent risk of osteoporosis



- Increased risk of diabetes[3]
- Increased risk of fatal cardiac events[4–6]

Caution in patients with:

- History of stroke
- Chronic heart failure
- Myocardial infarction

LESS is BETTER ...

1. Daniell et al. *J Urol* 1997;157:439–444. 2. Shahinian VB et al. *N Engl J Med* 2005;352:154–164. 3. Keating NL et al. *JCO* 2006;27:4448–4456. 4. D'Amico et al. *JCO* 2007;25:2420–2425. 5. Hayes et al. *BJU Int* 2010;106:979–85. 6. Nguyen et al. *Int J Radiat Oncol Biol Phys* 2011 [Epub ahead of print]

Side effects of ADT

Visible		Non-visible	
Most common	**What you see**	**What you don't see**	**What you feel**
• Loss of libido • Erectile dysfunction • Hot flushes	• Weight gain • Gynaecomastia • Loss of muscle mass, strength • Decreased size – penis and testes • Hair changes	• Loss of BMD • Anaemia • Hypertension, diabetes, changes in lipid profile • (Metabolic syndrome)	• Fatigue • Lack of energy • Lack of initiative • Depression • Emotional distress • Alterations in cognitive function

Gacci et al. Int J Endocrinol. 2014; 2014:470-592 Quality of Life and Sexual Health in the Aging of PCa Survivors. Walsh JS, Eastell R. Osteoporosis in men Nat Rev Endocrinol. 2013 Nov;9(11):637-45

Higano CS, *Urology* 2003;61:32-8 (Suppl 2A)

BREAKFAST MENU

- Why the elderly and why should hormonal therapy be harmless?
- About breast cancer
- About prostate cancer
- A common topic: bone health
- To conclude

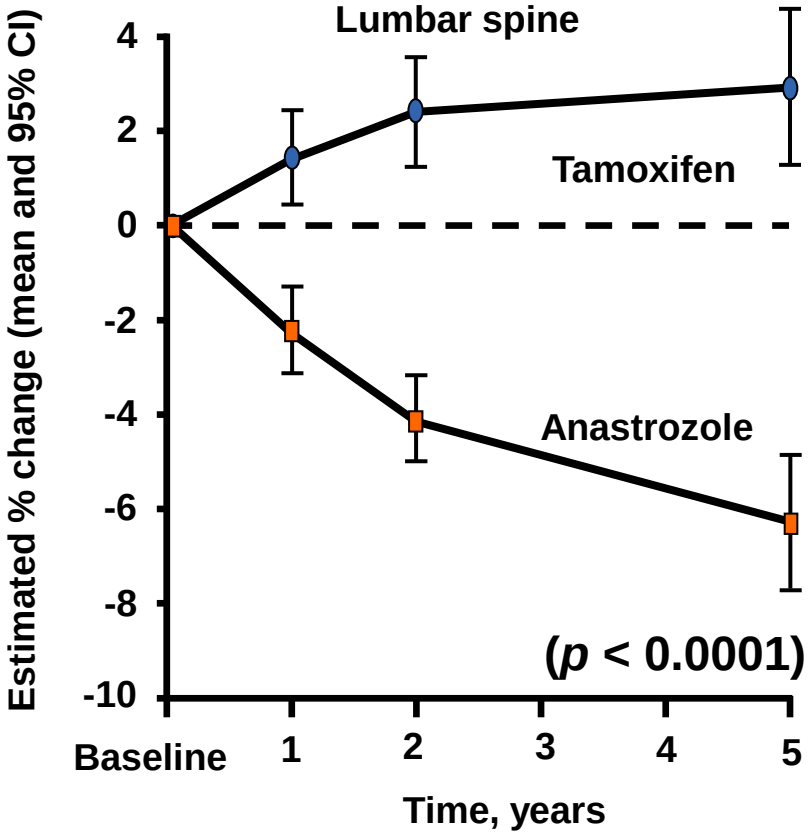
Osteoporosis in Elderly Patients

- Bone density decreases with age
- AI treatment and ADT are associated with an increased risk of osteoporosis. Tamoxifen is somewhat “protective”
- Treatment induced bone loss can be managed with additional medication such as vitamin D and calcium supplements and bisphosphonates/denosumab
- AI induced decrease in bone density reverses after treatment termination

D Crivellari et al. Crit Rev Oncol Hematol 2010;73(1):92-8
P Hadji et al. Ann Oncol 2008;19:1407-1416
RE Coleman et al. Breast Cancer Res Treat. 2010

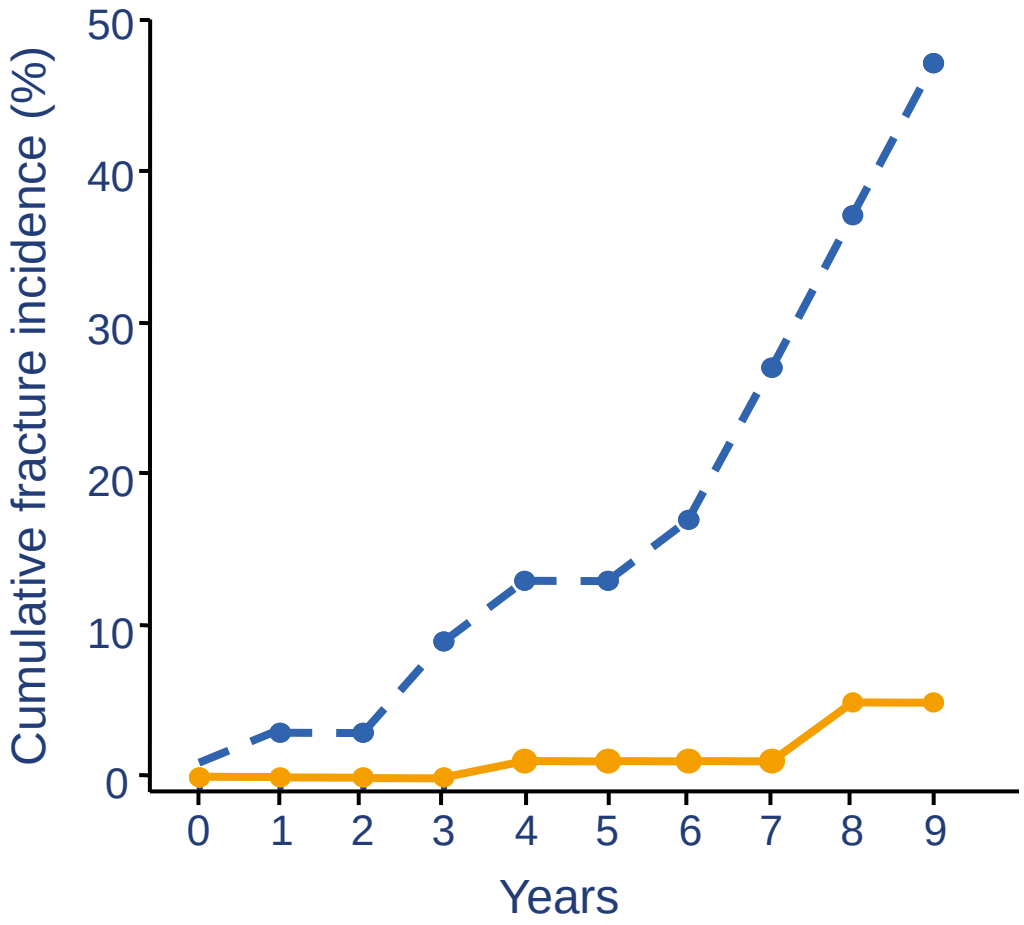
AI therapy is associated with rapid bone loss

Data from a substudy of ATAC (similar data with all AIs)



Based on Coleman *et al. J Clin Oncol* 2006;24:5S(abstract 511) / Eastell R, Adams JE, Coleman RE, et al. J Clin Oncol 2008;26: 051–8.

Iatrogenic effects of androgen deprivation on the skeleton in prostate cancer patients



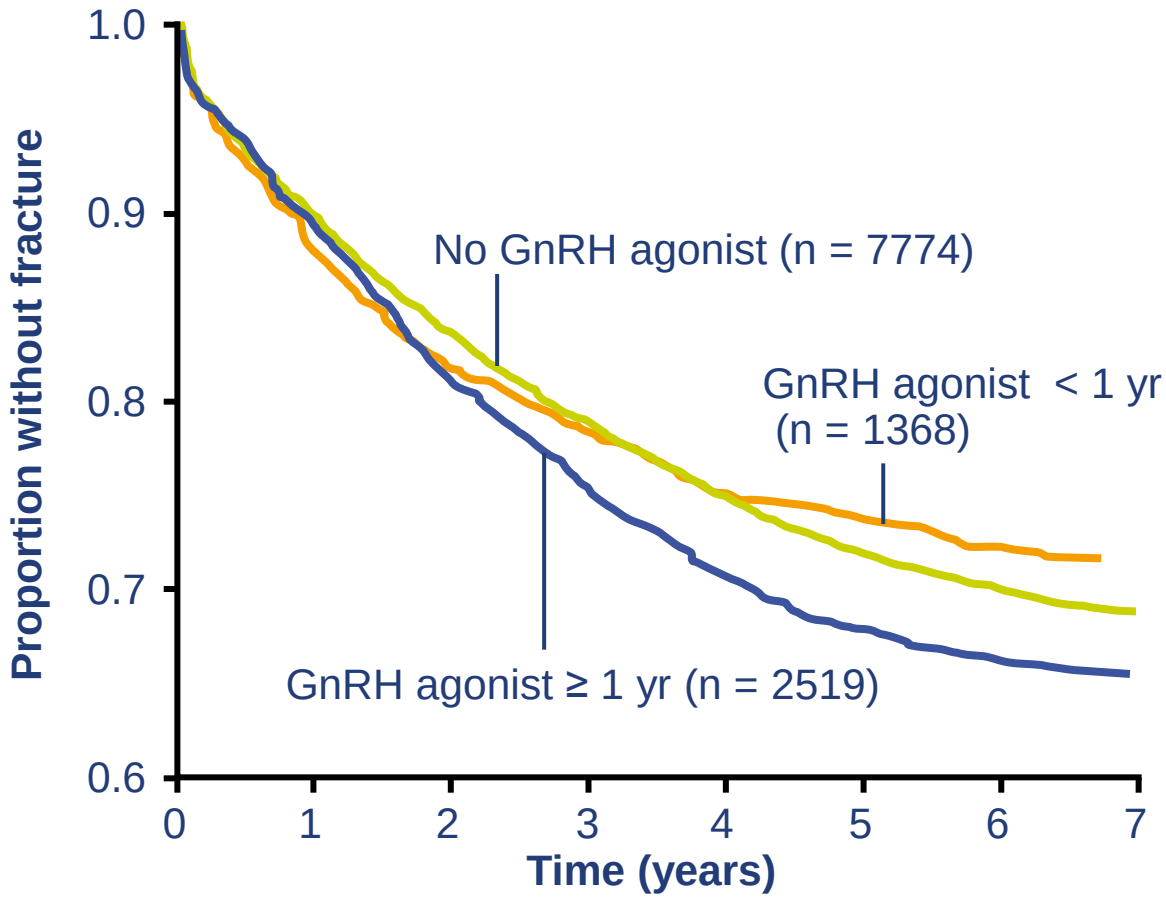
Orchidectomy

No orchidectomy

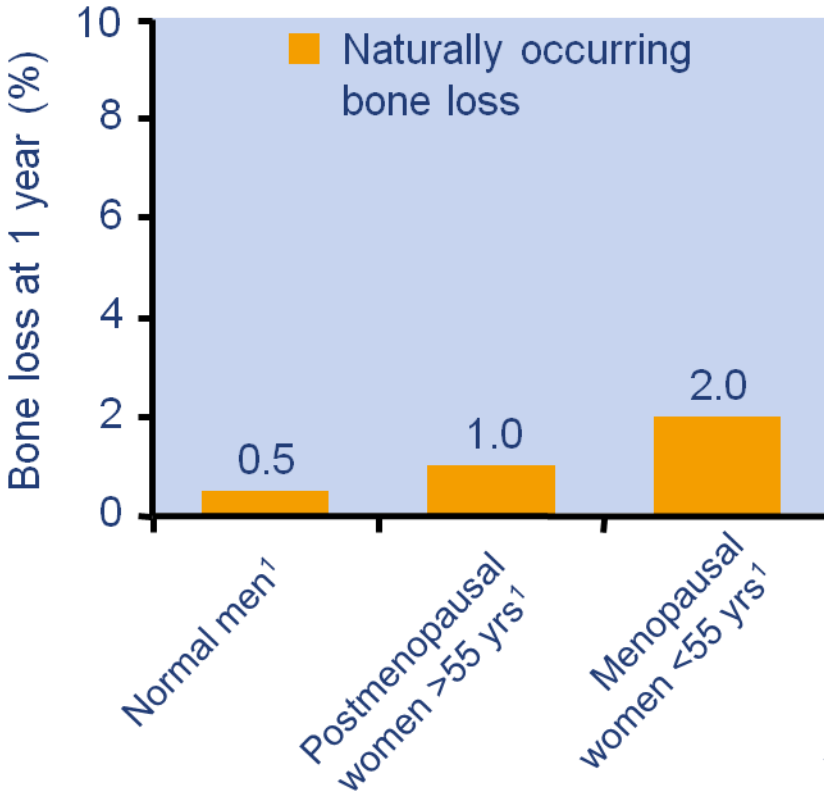
- Approximately 2000 osteoporosis-induced fractures in the US every year

Daniell HW, et al. *J Urol* 1997;157:439–44.

GnRH agonists and time to first fracture

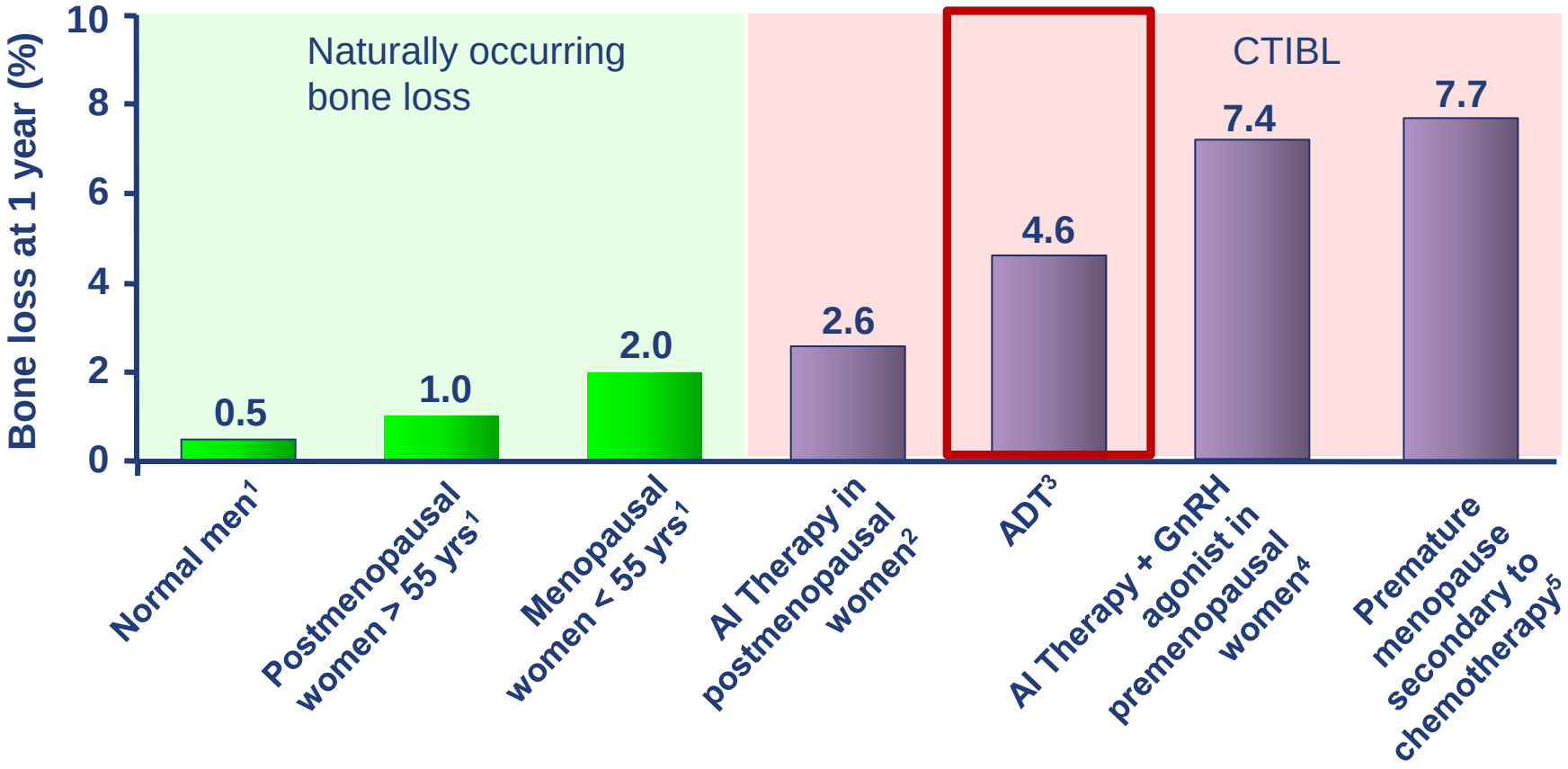


CTIBL is more rapid than naturally occurring bone loss



1. Higano CS. *Nat Clin Pract Urol*. 2008; 5:24-34;
2. Eastell R, *et al*. *J Bone Miner Res* 2006; 21:1215-23;
3. Maillefert JF, *et al*. *J Urol* 1999; 161:1219-22;
4. Gnant MF, *et al*. *Lancet Oncol* 2008; 9:840-9;
5. Shapiro CL, *et al*. *J Clin Oncol* 2001; 19:3306-11.

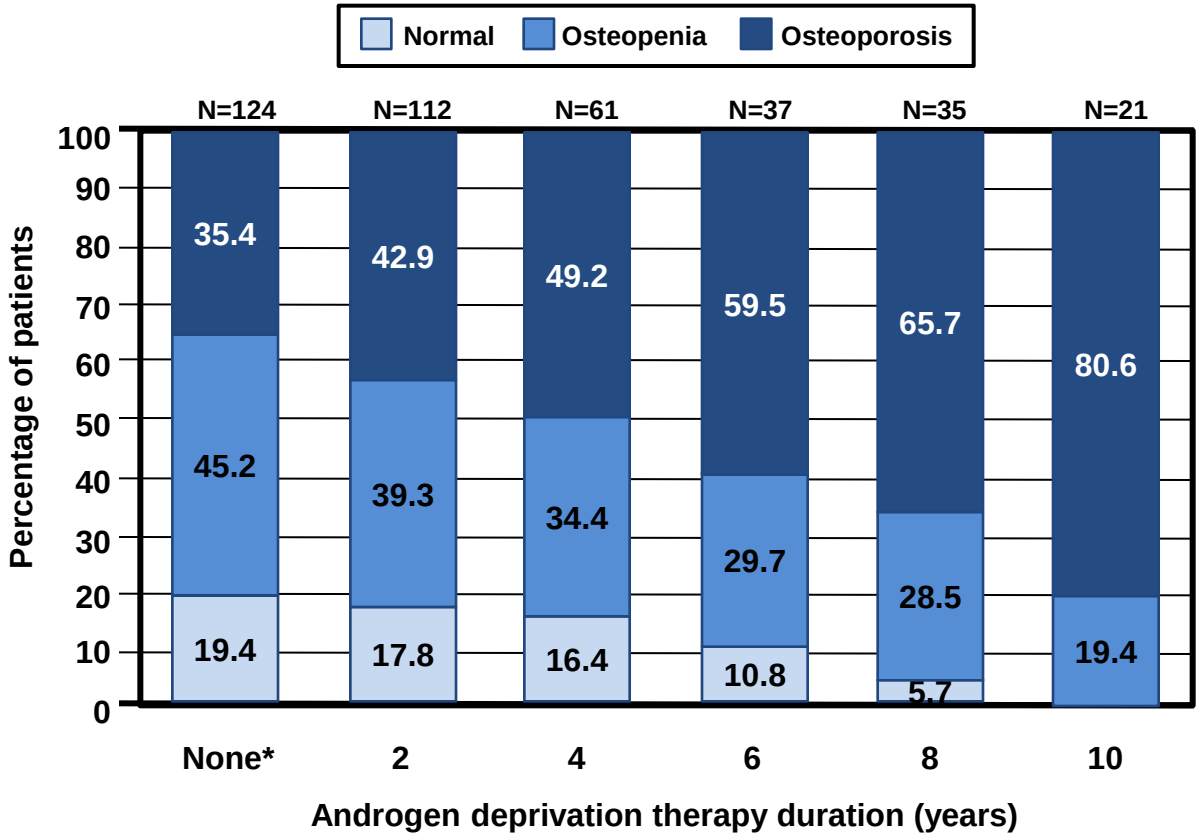
Bone loss induced by ADT for prostate cancer is rapid and clinically significant



1. Higano CS. *Nat Clin Pract Urol* 2008;5:24-4; 2. Eastell R, *et al*. *J Bone Miner Res* 2006;21:1215-23;
3. Maillefert JF, et al. *J Urol* 1999;161:1219-22; 4. Gnant MF, et al. *Lancet Oncol* 2008;9:840-9;
5. Shapiro CL, et al. *J Clin Oncol* 2001;19:3306-11

Prevalence of Osteoporosis During Long-Term Androgen Deprivation Therapy in Patients with Prostate Cancer

Juan Morote, Jacques Planas Morin, Anna Orsola, Jose M. Abascal, Carles Salvador, Enrique Trilla, Carles X. Raventos, Lluis Cecchini, Gloria Encabo, and Jaume Reventos



Morote J, et al. *Urology* 2007;69:500-4

Characteristics of bone mass loss in prostate cancer patients on ADT

- Intense during the first year
- Slows after the second year
- Continuous over 10 years

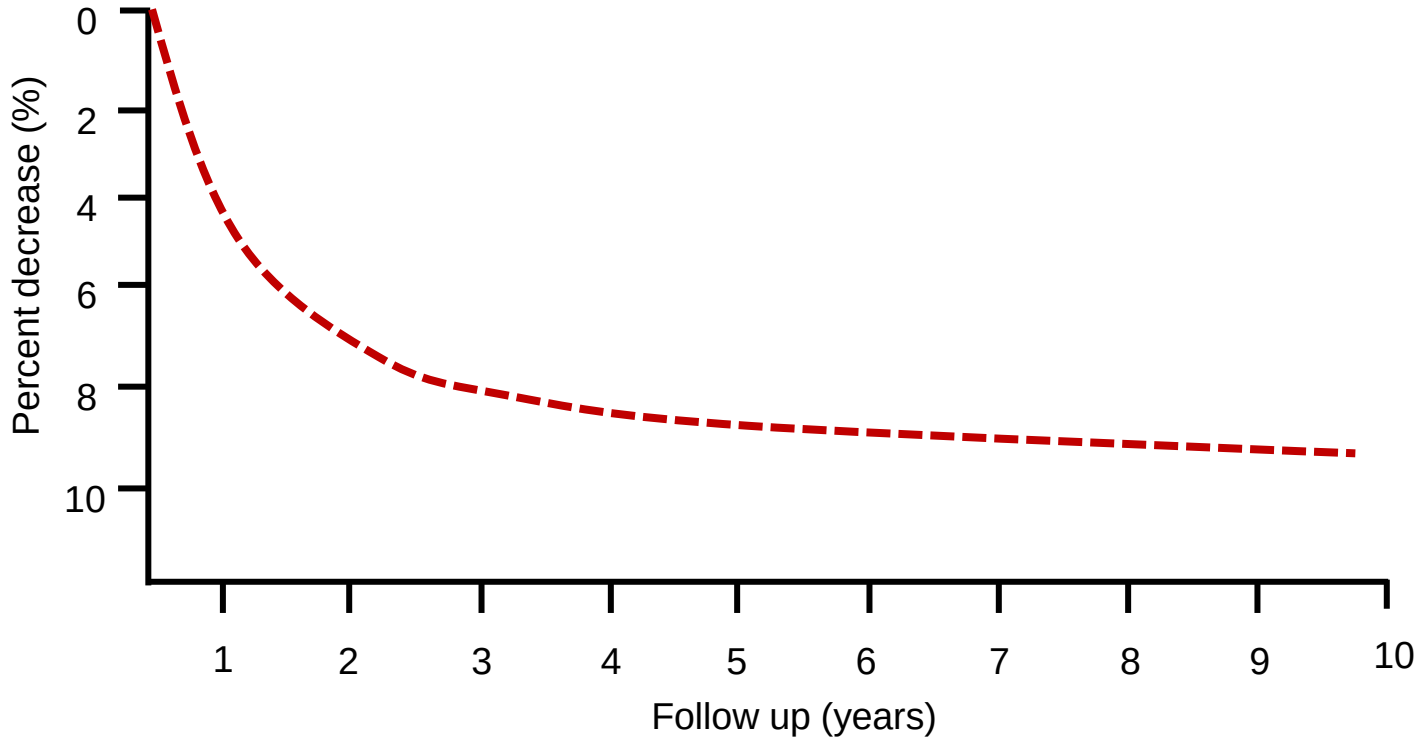


Image provided by J. Morote, Autonoma University of Barcelona, Spain

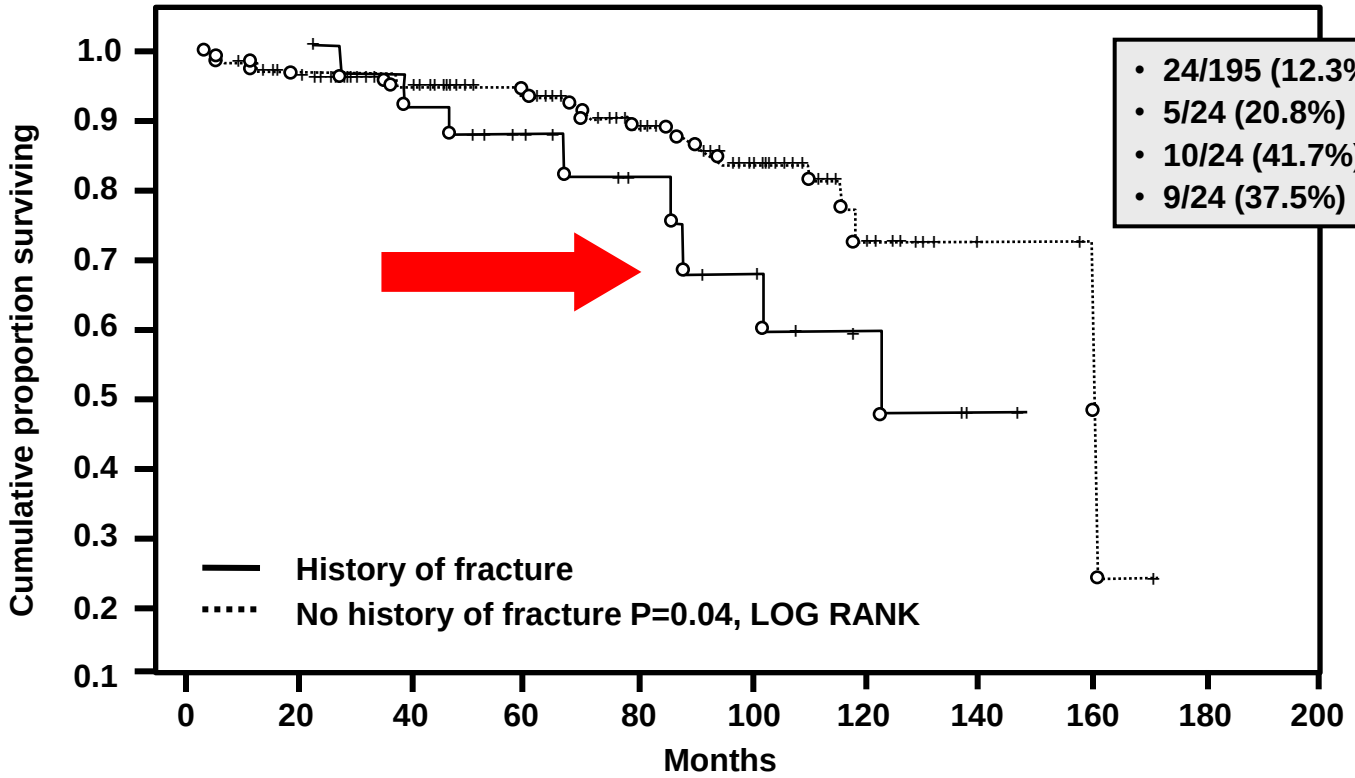
0022-5347/02/1683-1005/0
THE JOURNAL OF UROLOGY®
Copyright © 2002 by AMERICAN UROLOGICAL ASSOCIATION, INC.®

Vol. 168, 1005–1007, September 2002
Printed in U.S.A.
DOI: 10.1097/01.ju.0000024395.86788.cc

SKELETAL FRACTURES NEGATIVELY CORRELATE WITH OVERALL SURVIVAL IN MEN WITH PROSTATE CANCER.

MICHAEL G. OEFELEIN, VINCENT RICCHIUTI, WILLIAM CONRAD AND MARTIN I. RESNICK*

From the Department of Urology, University Hospitals of Cleveland, Case Western Reserve School of Medicine, Cleveland, Ohio



- 24/195 (12.3%)
- 5/24 (20.8%) pathologic
- 10/24 (41.7%) osteoporotic
- 9/24 (37.5%) bedore ADT ??

Multivariate Forward Stepwise Regression Analysis

Variable	p Value	Relative Death Risk (95% CI)
Skeletal metastasis	0.002	9.5 (8.5–10.5)
Skeletal fracture history	0.007	7.4 (6.1–8.7)
Nadir PSA	0.09	2.8 (0.8–4.8)

Oefelein MG, et al.*J Urol* 2002;168:1005-7

Fractures and post-fracture mortality in prostate cancer patients receiving ADT

- Analysis from SEER database, N = 72,400 pts with PCa diagnosed 1996–2003

	Orchidectomy	LHRH-agonist during first 6 mo after diagnosis	No ADT during FU
N (%)	2.2%	47.2%	50.6%
Fracture risk (HR, 95% CI)	1.7 (1.5–1.9)	1.3 (1.3–1.4)	1
Fractures resulting in hospitalisation (HR, 95%CI)	1.9 (1.6–2.3)	1.4 (1.3–1.5)	1

- Fractures resulting in hospitalisation were associated with increased mortality (HR: 1.2, 95% CI: 1.2–1.3)

PCa pts receiving ADT are at increased risk of fractures; fractures resulting in hospitalisation are associated with a 20% increase in risk of mortality

Cetin K. *J Clin Oncol* 2010:28(15S):356s(abs.4559)

Consequences of CTIBL

- Reduced overall strength of the bone and loss of BMD leads to bone fragility and increased susceptibility to fractures
- Common sites
  - Femoral neck
  - Radius
  - Vertebral spine
  - Lumbar spine
- Fractures are associated with increased mortality
- Because natural restoration of bone is limited, prevention, early diagnosis and treatment of CTIBL are essential to improve patient outcome and quality of life

Pfeilschifter J, Diel IJ. *J Clin Oncol* 2000; 18:1570-93.

Pharmacological prevention of bone mass loss during ADT

Reference	Design	Duration	No pts	Endpoints	Results
Smith, et al *J Urol* 2003	Zoledronate (IV 4 mg Q3M) vs placebo	One year	106	% change BMD lumbar spine	+5.6 zoledronate vs -2.2 placebo
Michelson, et al *J Clin Oncol* 2007	Zolodronate (IV 4 mg on day one) vs placebo	One year	40	% change BMD lumbar spine	+4.0% zoledronate vs -3.1 placebo
Greenspan, et al *Ann Int Med* 2007	Alendronate oral (70 mg Q1W) vs placebo	One year	112	% change BMD lumbar spine	+3.7 alendronate vs -1.4 placebo
Smith, et al *N Eng J Med* 2009	Denosumab (SC 60 mg Q6M) vs placebo	Three years	1468	% change BMD lumbar spine and vertebral fractures*	+5.5 denosumab vs -1 placebo (24m) 1.5% denosumab vs 3.9% denosumab (36m)

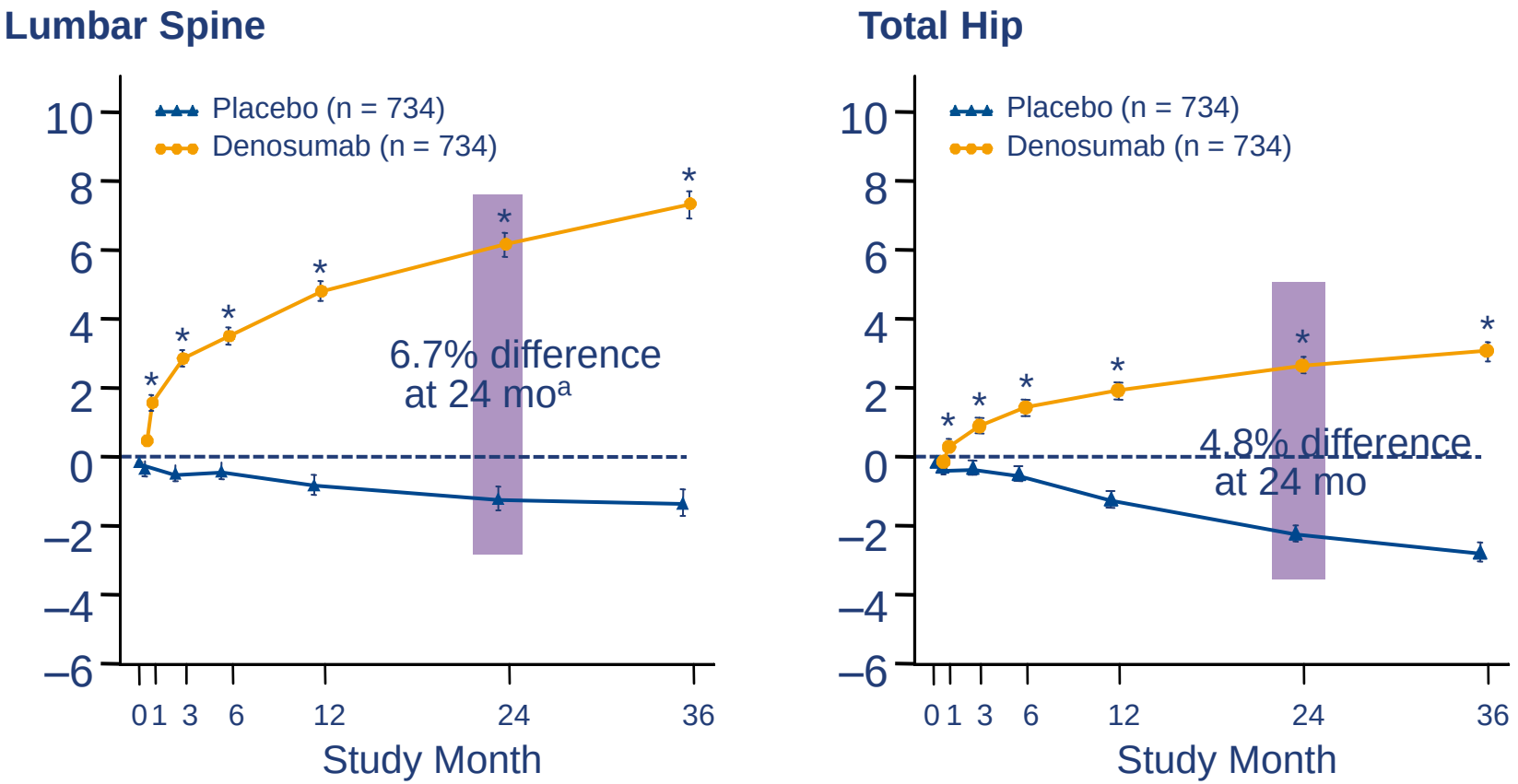
*FDA Good Guidance Practice guidelines for preclinical and clinical evaluation of agents used in the prevention or treatment of postmenopausal osteoporosis 1997

*EMEA guideline on the evaluation of new medicinal products in the treatment of primary osteoporosis 2005.

Denosumab is the only agent licensed for this indication.

Denosumab in men receiving ADT for prostate cancer

Mean percent changes in BMD from baseline

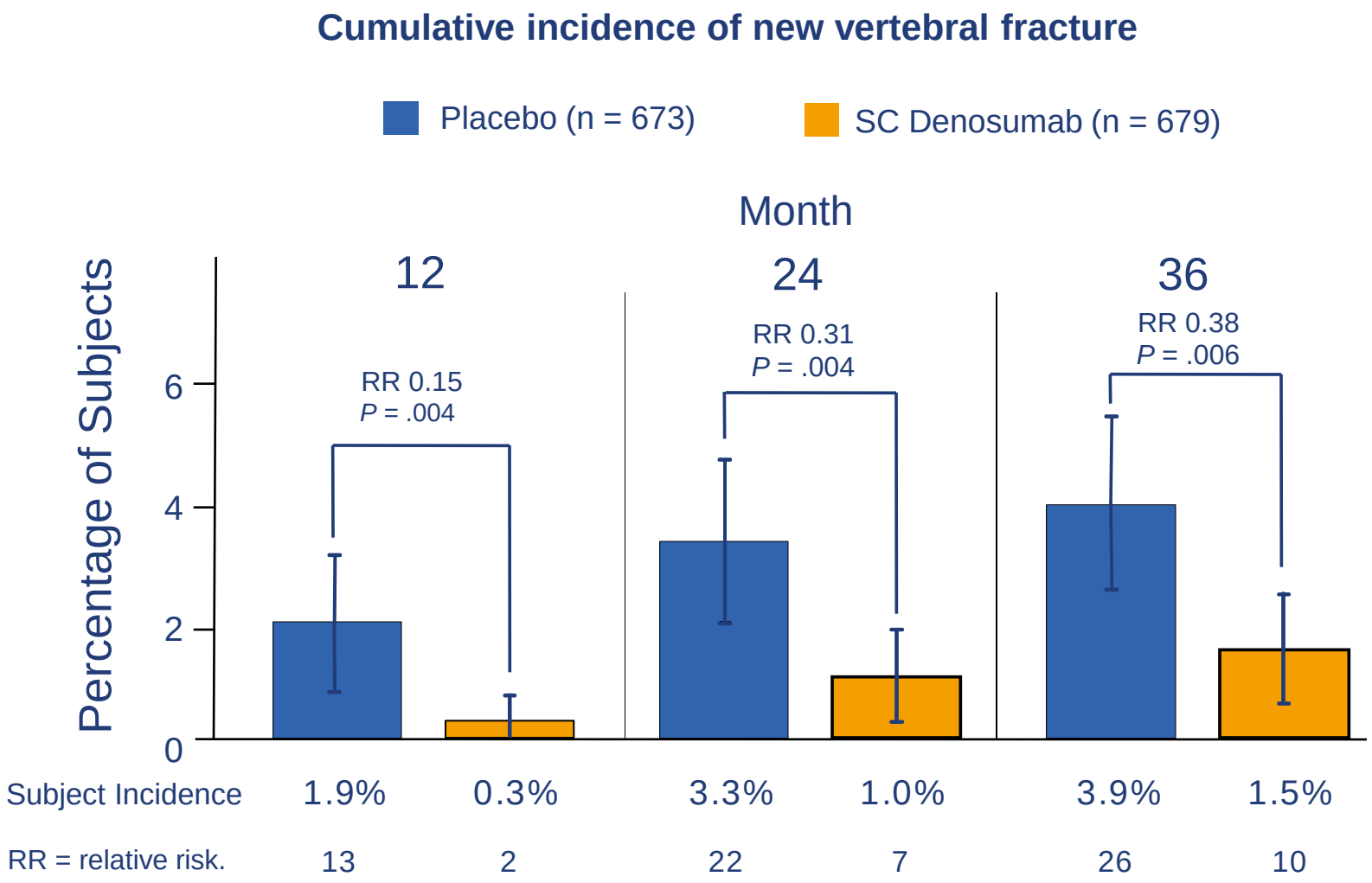


*$P \leq .001$ at all measured sites

[a]Primary end point

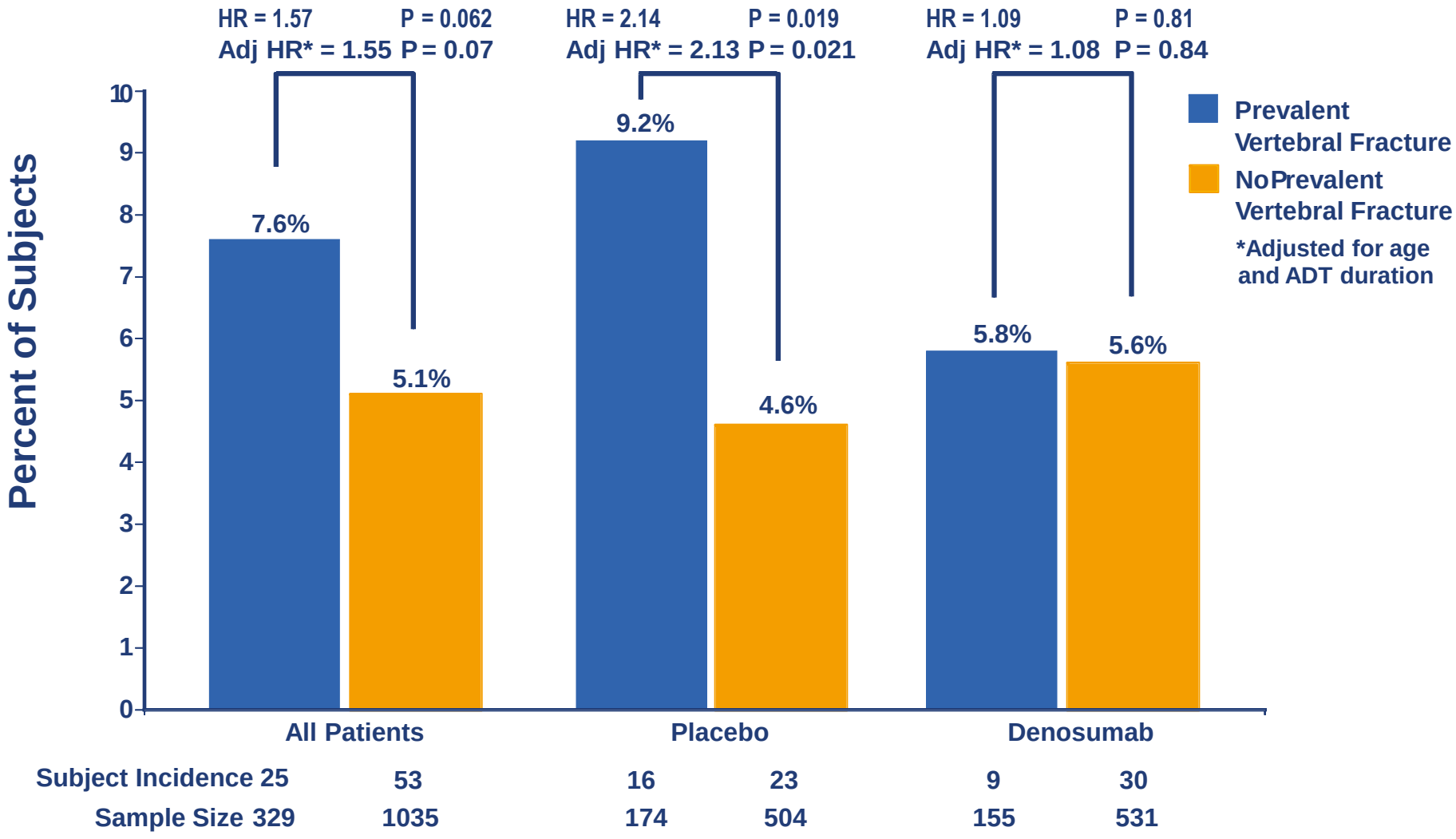
Smith MR, et al. *N Engl J Med* 2009;361:745-55. Reprinted with permission from the *New England Journal of Medicine*.

Denosumab in men receiving ADT for prostate cancer



Smith MR, et al. *N Engl J Med* 2009;361:745-55. Reprinted with permission from the *New England Journal of Medicine*.

Post-hoc analysis: Higher death rate in patients with vertebral fracture



Adapted from Smith MR, et al. ECCO-ESMO 2009; Abstract 7005

Specific considerations for senior adults

Abiraterone

- Hypokalaemia, hypertension & fluid retention due to mineralocorticoid excess

Use with caution in patients with cardiovascular diseases

- Adrenocortical insufficiency

Caution after interruption of daily steroids and/or concurrent infection or stress

- Hepatotoxicity

Monitor liver function

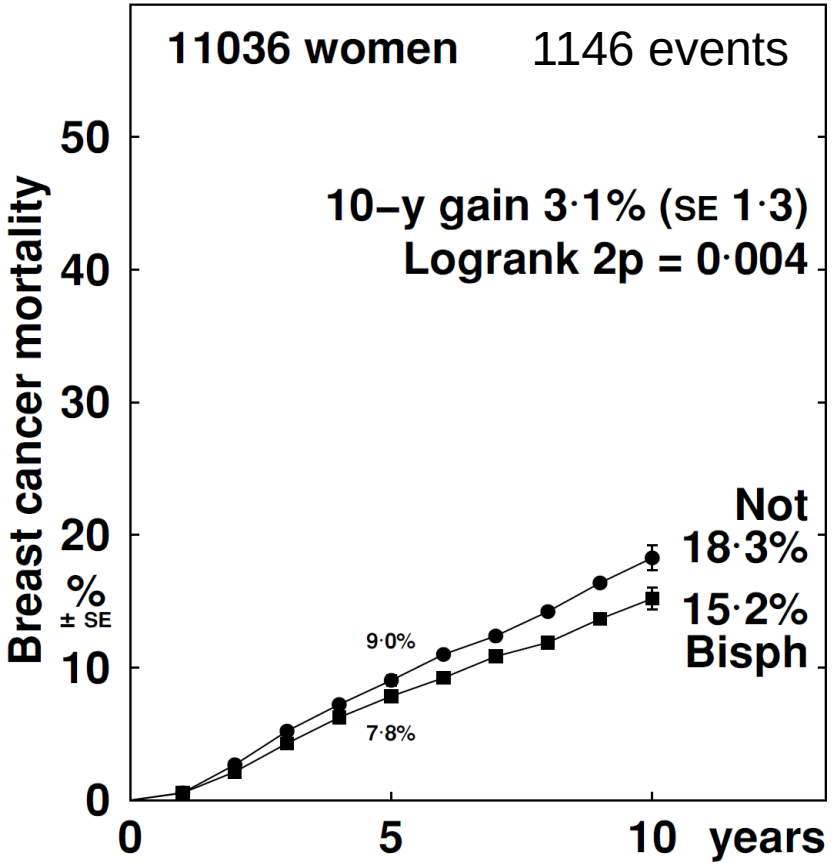
Effects Of Bisphosphonate Treatment On Recurrence And Cause-specific Mortality In Women With Early Breast Cancer: A Meta-analysis Of Individual Patient Data From Randomised Trials

R Coleman, M Gnant, A Paterson, T Powles, G von Minckwitz, K Pritchard, J Bergh, J Bliss, J Gralow, S Anderson, D Cameron, V Evans, H Pan, R Bradley, C Davies, R Gray.

Early Breast Cancer Trialists' Collaborative Group (EBCTCG)'s Bisphosphonate Working Group.

BPs Decrease Mortality In Post-menopausal Women

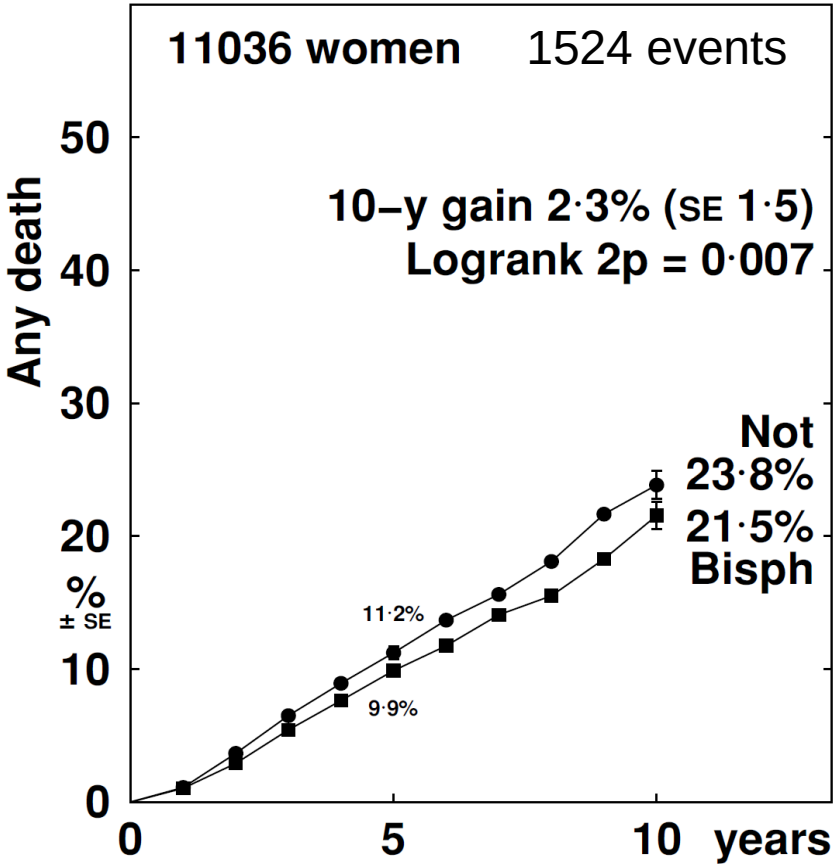
Breast cancer mortality



Death rates (% / year: total rate – rate in women without recurrence) & logrank analyses

Allocation	Years 0 – 4	Years 5 – 9	Year 10+
Bisph	1·64 SE 0·08	1·60 SE 0·14	1·30 SE 0·49
Not	1·83 SE 0·09	2·04 SE 0·16	2·73 SE 0·73
Rate ratio, from	0·86 SE 0·07	0·78 SE 0·11	0·52 SE 0·38
(O–E) / V	–26·4 / 173·1	–16·3 / 65·0	–2·4 / 3·6

All cause mortality



Death rates (% / year) and logrank analyses

Allocation	Years 0 – 4	Years 5 – 9	Year 10+
Bisph	2·07 (510 / 24627)	2·40 (201 / 8380)	3·71 (20 / 539)
Not	2·32 (534 / 23006)	2·88 (236 / 8189)	4·48 (23 / 513)
Rate ratio, from	0·87 SE 0·06	0·84 SE 0·09	0·94 SE 0·34
(O–E) / V	–31·3 / 224·4	–17·2 / 95·6	–0·5 / 8·0

ESMO clinical practice guideline: Bone health in cancer patients


Annals of Oncology Advance Access published April 29, 2014

clinical practice guidelines

Bone health in cancer patients: ESMO Clinical Practice Guidelines†

- Clinicians treating cancer patients need to be aware of:
  - Treatments to reduce skeletal morbidity in metastatic disease
  - Strategies to minimise cancer treatment-induced skeletal damage
- ESMO guidelines “provide a framework for maintaining bone health in patients with cancer”

Coleman R et al. *Ann Oncol* 2014;00:1–14.

Prevention of bone loss in patients with treatments known to increase the risk of fractures

Baseline fracture risk factor assessment

- e.g. age >65 years, smoking, oral corticosteroid use >6 months, low BMI (<20), family history of hip-fracture, personal history of fragility fracture after age 50

Bone mineral density (BMD) measurement

Lifestyle changes

- Take more weight-bearing exercise
- Stop smoking
- Reduce alcohol consumption

Dietary measures and supplements

- Adequate calcium (1000 mg/day) intake
- Supplementary vitamin D (to total intake of 1000–2000 units/day)

In selected cases – bone directed anti-resorptive therapy to manage low BMD or rapid bone loss

Coleman R et al. *Ann Oncol* 2014;00:1–14.

Diagnosis: Recommended techniques

Isotope bone scan

- Sensitive test used to detect presence of skeletal pathology
- Gives little information about nature of damage/metastatic disease

CT and MRI

- Recommended for obtaining structural information on skeletal damage from metastatic bone disease

PET

- Provides functional information that may aid in diagnosis

DXA scan

- Recommended for patients at risk of fracture or cancer treatment-induced bone loss

Plain radiographs

- *An insensitive test for metastasis – lesions need to be >1cm with bone mineral loss of ~50% to be recognized*

Coleman R et al. *Ann Oncol* 2014;00:1–14.

Patient evaluation

Patient examination	• Assessment of symptoms and activity status is essential
Skeletal radiography	• Used to assess response to treatment, and fractures • But structural changes are slow to evolve and the method is insensitive
Isotopic bone scanning	• Not useful for monitoring treatment response
Biochemical markers	• e.g. amino (N) and carboxy (C) cross-linked telopeptides of type I collagen (NTC, CTX) • May provide information on prognosis and response to treatments but are not recommended for routine clinical use

Coleman R et al. *Ann Oncol* 2014;00:1–14.

Regulatory approval for anti-resorptive agents in cancer patients

Indication	Regulatory approval
Prevention of skeletal-related events	
Zoledronic acid 4 mg i.v. every 3–4 weeks	All solid tumours and multiple myeloma
Denosumab 120 mg s.c. every 4 weeks	All solid tumours
Pamidronate 90 mg i.v. every 3–4 weeks	Breast cancer and multiple myeloma
Clodronate 1600 mg p.o. daily	Osteolytic lesions*
Ibandronate 50 mg p.o. daily	Breast cancer*
Ibandronate 6 mg i.v. monthly	Breast cancer*
Prevention of breast cancer metastases	
Zoledronic acid 4 mg i.v. 6 monthly	None
Zoledronic acid 4 mg i.v. monthly x 6, then 3–6 monthly	None
Clodronate 1600 mg daily	None
Prevention of prostate cancer metastases	
Denosumab 120 mg s.c. monthly	None
Prevention of treatment-induced bone loss	
Denosumab 60 mg s.c. 6 monthly	Prostate and breast cancer
Zoledronic acid 4 mg i.v. 6 monthly	None
Alendronate 70 mg p.o. weekly	None
Risedronate 35 mg p.o. weekly	None
Ibandronate 150 mg p.o. monthly	None
Pamidronate 90 mg i.v. every 3 months	None

*European approval only (not US)
i.v. – intravenous; s.c. subcutaneous; p.o. per oral

Coleman R et al. *Ann Oncol* 2014;00:1–14.

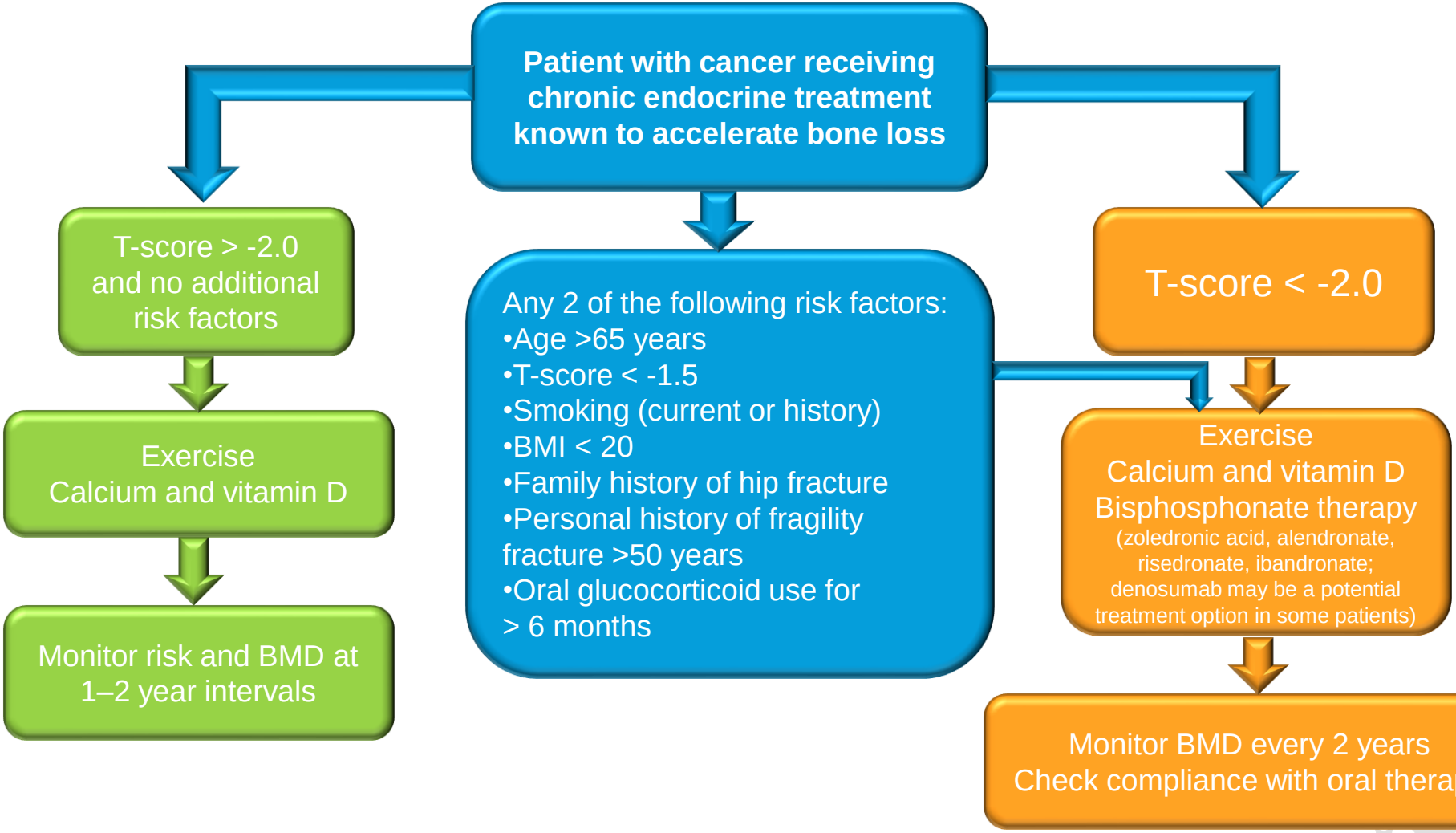
Treatment recommendations

Prevention of treatment-induced bone loss

- **Bisphosphonates** and **denosumab** prevent bone loss associated with ovarian suppression/aromatase inhibitors in **early breast cancer** and androgen deprivation therapy in **prostate cancer**

Coleman R et al. *Ann Oncol* 2014;00:1–14.

ESMO recommended algorithm for managing bone health during cancer treatment



Coleman R et al. *Ann Oncol* 2014;00:1–14.

BREAKFAST MENU

- Why the elderly and why should hormonal therapy be harmless?
- About breast cancer
- About prostate cancer
- A common topic: bone health
- To conclude

Hormone therapy is not harmless but one can decrease its toxicity

SIOG
INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

SEE YOU IN LISBON

SIOG

INTERNATIONAL SOCIETY OF GERIATRIC ONCOLOGY

2014

LISBON
PORTUGAL
23 - 25 OCT.

14th SIOG Meeting, Lisbon - Portugal




SAVE THE DATE - 23 to 25 October 2014

THANK YOU
to all the patients
and their
physicians, nurses and carers