# PROGRAMA DE EDUCAÇÃO MÉDICA CONTINUADA 2017

Grupo ONCOCLÍNICAS
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INSTITUTO ONCOCLÍNICAS

SUSAN F. SMITH CENTER FOR WOMEN'S CANCERS

DANA-FARBER CANCER INSTITUTE

HARVARD MEDICAL SCHOOL

# Highlights from St. Gallen Conference

Otto Metzger, MD

Goiania

May 19, 2017

# EXPERT OPINION ON AREAS OF CONTROVERSY

- Escalation and de-escalation of treatment are major issues for management of early breast cancer
- Evidence from randomized clinical trials does not cover all controversies that arise in treating individuals
- The opinion of the panel members is used to implement guidance for controversial issues
- When data are lacking, expert opinion can be used
- This is the unique feature of the St. Gallen International Consensus

# International Consensus Panel 2017

**Chairpersons:** G. Curigliano (Italy), E. P. Winer (USA)

**Consensus Writing Committee:** G. Curigliano (Italy), H. Burstein (USA), M. Colleoni (Italy), P. Dubsky (Austria/Switzerland), M. Gnant (Austria), S. Loibl (Germany), M. Piccart (Belgium), M. Regan (USA), H.-J. Senn (Switzerland), B. Thuerlimann (Switzerland), E. P. Winer (USA)

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Zhiming Shao (PR China)
Ian Smith (UK)
Masakazu Toi (Japan)
Andrew Tutt (UK)
Toru Watanabe (Japan)
Timothy Whelan (Canada)
Binghe Xu (PR China)

# ST GALLEN CONFERENCE: EARLY-STAGE DISEASE

1. Surgical Margins
2. Management of axilla
3. The “clinical value” of neoadjuvant therapy
4. Statistical and methodological challenges while designing studies to de-escalate therapy
5. Adjuvant radiation
6. Adjuvant therapy
7. Adjuvant treatment  for ER+ disease
    1. Multi-gene signatures
    2. Extended endocrine therapy
8. Bone-modifying therapy in the early-stage setting

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# ADJUVANT ENDOCRINE THERAPY
# WHAT MATTERS IN OUR CLINICAL PRACTICE?

- What is the risk of recurrence after 5yrs of adjuvant therapy?
- Can we reduce the risk with extended endocrine therapy?
- Can we identify patients more likely to recur using classic clinico-pathologic characteristics?
- Can we refine our baseline assumptions using multi-gene signatures?

# EXTENDED ENDOCRINE THERAPY

1. Early-stage (I/II) ER+ patients have good overall prognosis, but >50% of recurrences occur after year 5
2. Previous studies have demonstrated benefit of extended endocrine therapy; however, without selection of patients, only a modest proportion of women benefited
3. NNT: ~25 to prevent any event; ~90-100 to prevent a distant recurrence

| Trial | Duration of Therapy (y) | | N | Median Follow-up (y) | Disease-free Survival[1] | Absolute Benefit | Hazard Ratio or Rate Ratio (95% CI) |
|---|---|---|---|---|---|---|---|
| MA.17 | TAM x 5y | → Placebo x 5y<br>→ AI x 5y | 2587<br>2583 | 2.5 | 89.8%<br>94.4% | 4.6% | HR 0.58 (0.45-0.76)<br>P<0.001 |
| NSABP B-33 | TAM x 5y | → Placebo x 5y<br>→ AI x 5y | 779<br>783 | 2.5 | 89%<br>91% | 2% | RR: 0.68<br>P=0.07 |
| ABCSG 6A | TAM x 5y | → Placebo x 3y<br>→ AI x 3y | 469<br>387 | 5.2 | 88.2%<br>92.9% | 4.7% | HR 0.62 (0.40-0.96)<br>P=0.031 |
| ATLAS | TAM x 5y | → No treatment<br>→ TAM x 5y | 3418<br>3428 | 7.6 | 74.9%<br>78.6% | 3.7% | RR 0.84 (0.76-0.94)<br>p=0.002 |
| aTTom | TAM x 5y | → No treatment<br>→ TAM x 5y | 3485<br>3468 | 10 | 68%<br>72% | 4% | RR 0.85 (0.76-0.95)<br>P=0.003 |
| MA.17R | TAM x 0-5y<br>→ AI x 5y | → Placebo<br>→ AI x 5y | 959<br>959 | 6.3 | 91%<br>95% | 4% | HR 0.66 (0.48-0.91)<br>P=0.01 |

1. Based on disease-free survival or cumulative risk of recurrence rates as reported in the primary publications (note that the definitions of disease-free were not identical across trials)

1. Goss PE et al, J Natl Cancer Inst 2005;97:1262–71. 2. Mamounas EP et al., J Clin Oncol 2008;26:1965-1971. 3. Jakesz et al., J Natl Cancer Inst. 2007 Dec 19;99(24):1845-53. 4. Davies C et al., Lancet. 2013 ;381(9869):805-16. 5. Gray et al., J Clin Oncol 31, 2013 (suppl; abstr 5). 6. Goss PE et al., N Engl J Med. 2016

# NEW DATA FROM SABCS 2016

1. Results from 3 extended AI randomized studies presented at SABCS 2016
2. In all 3 studies, primary analyses demonstrated no statistically significant benefit in DFS from extending AI therapy in post-menopausal patients.
3. Of note, results from B-42 and DATA were generally similar to previous extended endocrine therapy trials (~3-4% absolute benefit)

| | NSABP B-42 | DATA | IDEAL |
|---|---|---|---|
| Population | 3966 patients who completed 5 years of AI or up to 3 years TAM followed by AI (for a total of 5 years) | 1912 patients who completed 2-3 years of Tamoxifen | 1824 patients who completed 5 years of Tamoxifen |
| Treatment | 5y AI vs Placebo | 3y AI vs 6y AI | 2.5y AI vs 5y AI |
| HR | 0.85 (0.73 – 0.999) | 0.79 (0.62-1.02) | 0.96 (0.76-1.20) |
| DFS | 84.7% (5 years AI) vs 81.3% (Placebo) | 83.1% (6 years AI) vs 79.4% (3 years AI) | 87.9% (5 years AI) vs 88.4% (2.5 years AI) |
| P value | P=0.048 (n.s.) | P=0.07 (n.s.) | P=0.7 (n.s.) |

**Note, there was a statistically significant benefit in terms of prevention of distant recurrence (1.9% absolute benefit, P=0.03)**

Discontinuation of AIs in all these trials was ~40% in the extended period

1. Mamounas E et al, 2016 SABCS. 2. Tjan-Heijnen VC et al, 2016 SABCS. 3. Block EJ et al, 2016 SABCS

# WHAT IS THE ACTUAL RISK OF RECURRENCE AFTER 5 YEARS OF ENDOCRINE THERAPY?

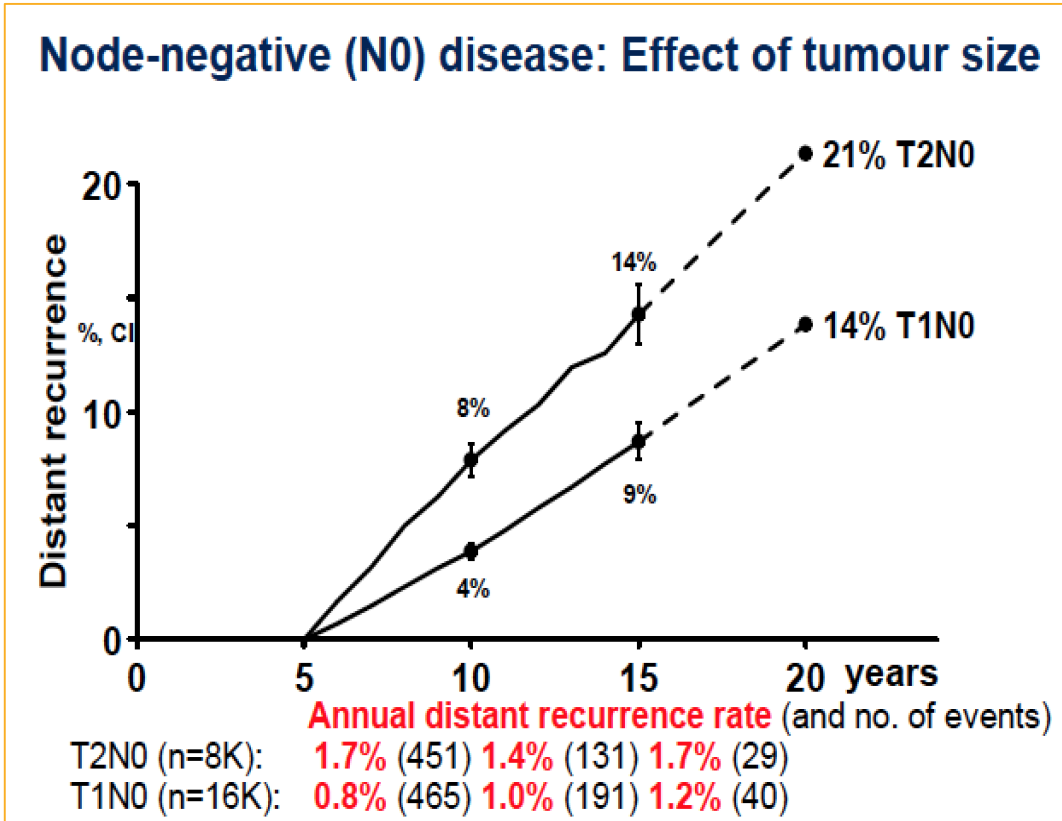
## Methods: Study of prognostic factors

- Data from 91 trials on each individual with ER+ disease allocated only 5 years of ET*
- Analyse just the 46,000 women (n=46K) who were still alive and disease-free at year 5

* ET was 3/4 Tam and 1/4 AI (or partly AI); analyses are only of T1 or T2 tumours (diameter ≤20 or 21-50 mm) with <10 nodes (N0-N9) & age <80 after 5 years ET

H.Pan for EBCTCG, ASCO 2106

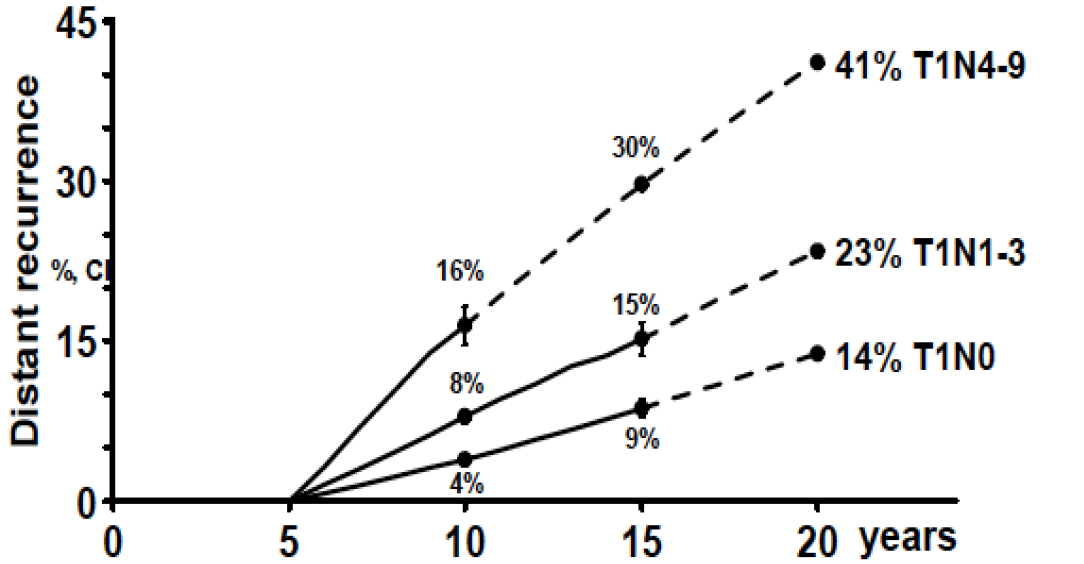
# WHAT IS THE RISK OF DISTANT RECURRENCE FOR T1 N0 AND T2 N0 ?




H.Pan for EBCTCG, ASCO 2106

## Small tumours (T1 disease): Effect of nodal status

(Half got chemotherapy if N+, 1/6 if T1N0)



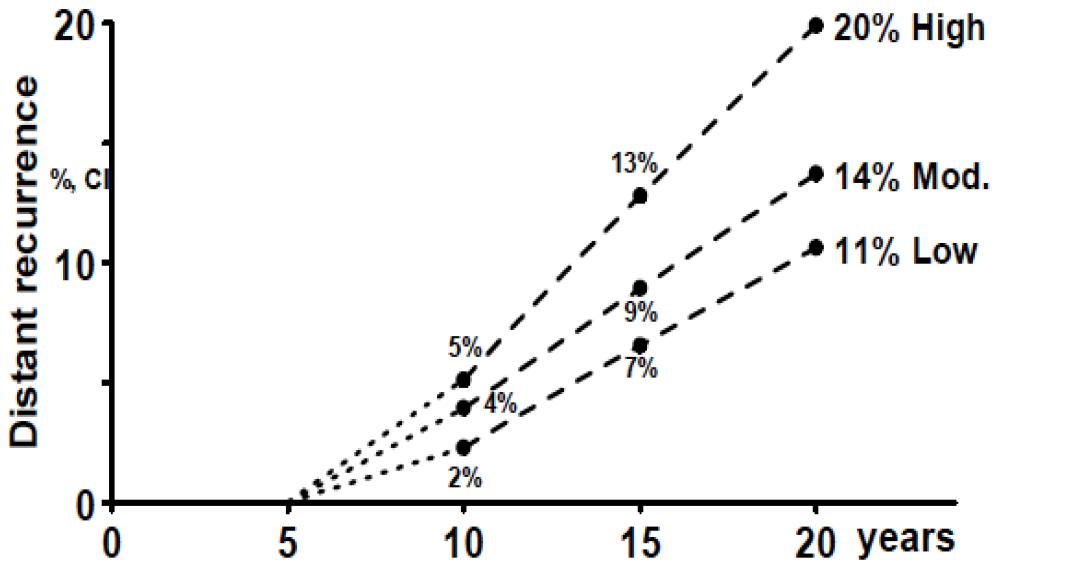

Annual distant recurrence rate (and no. of events)

| | | | |
|---|---|---|---|
| T1N4-9 (n=2K): | 3.6% (293) | 2.9% (54) | 2.5% (5) |
| T1N1-3 (n=9K): | 1.6% (504) | 1.7% (123) | 1.8% (16) |
| T1N0 (n=16K): | 0.8% (465) | 1.0% (191) | 1.2% (40) |

H.Pan for EBCTCG, ASCO 2106

## Lowest-stage (T1N0) disease: Effect of tumour grade

Plot of smoothed rates for years 5-10, and for years 10-20



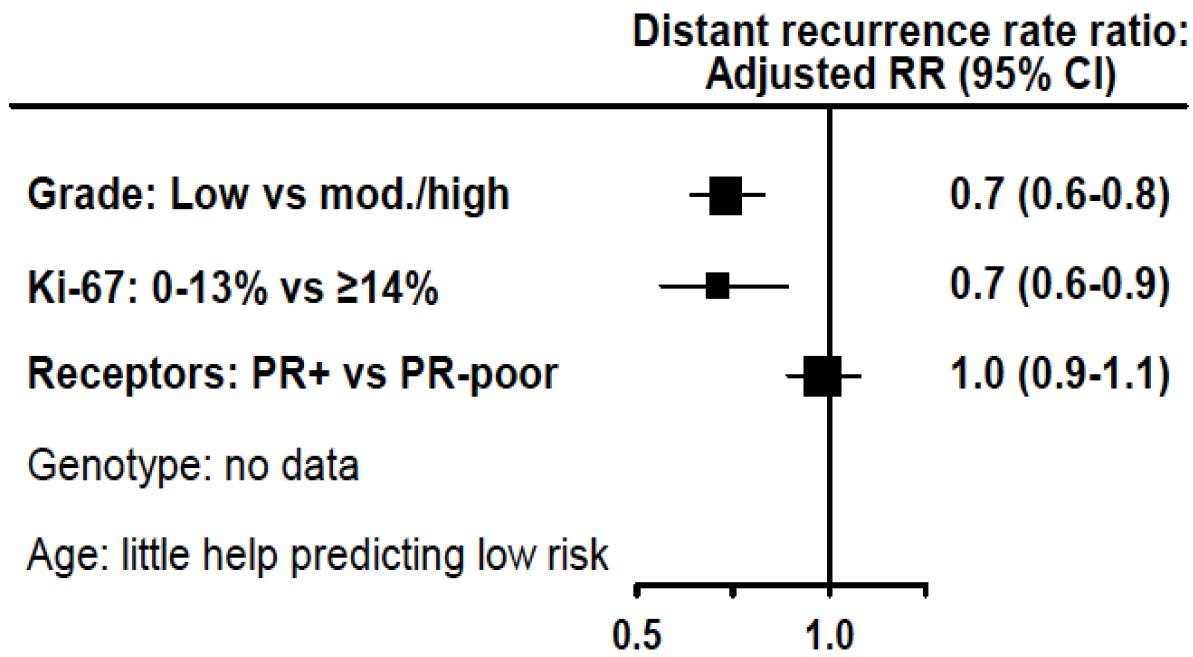

**Annual distant recurrence rate** (and no. of events)

| | | | |
|---|---|---|---|
| High (n=2K): | 1.1% (75) | 1.5% (30) | 2.7% (6) |
| Mod. (n=6K): | 0.8% (168) | 1.0% (57) | 1.1% (6) |
| Low (n=3K): | 0.5% (47) | 0.9% (23) | 0.6% (2) |

H.Pan for EBCTCG, ASCO 2106

## All women: Additional predictors of lower risk in years 5-20

Any (T1/2, N0-9) ER+ disease, adjusted for T and N status




H.Pan for EBCTCG, ASCO 2106

# LIMITATIONS OF OXFORD OVERVIEW DATA

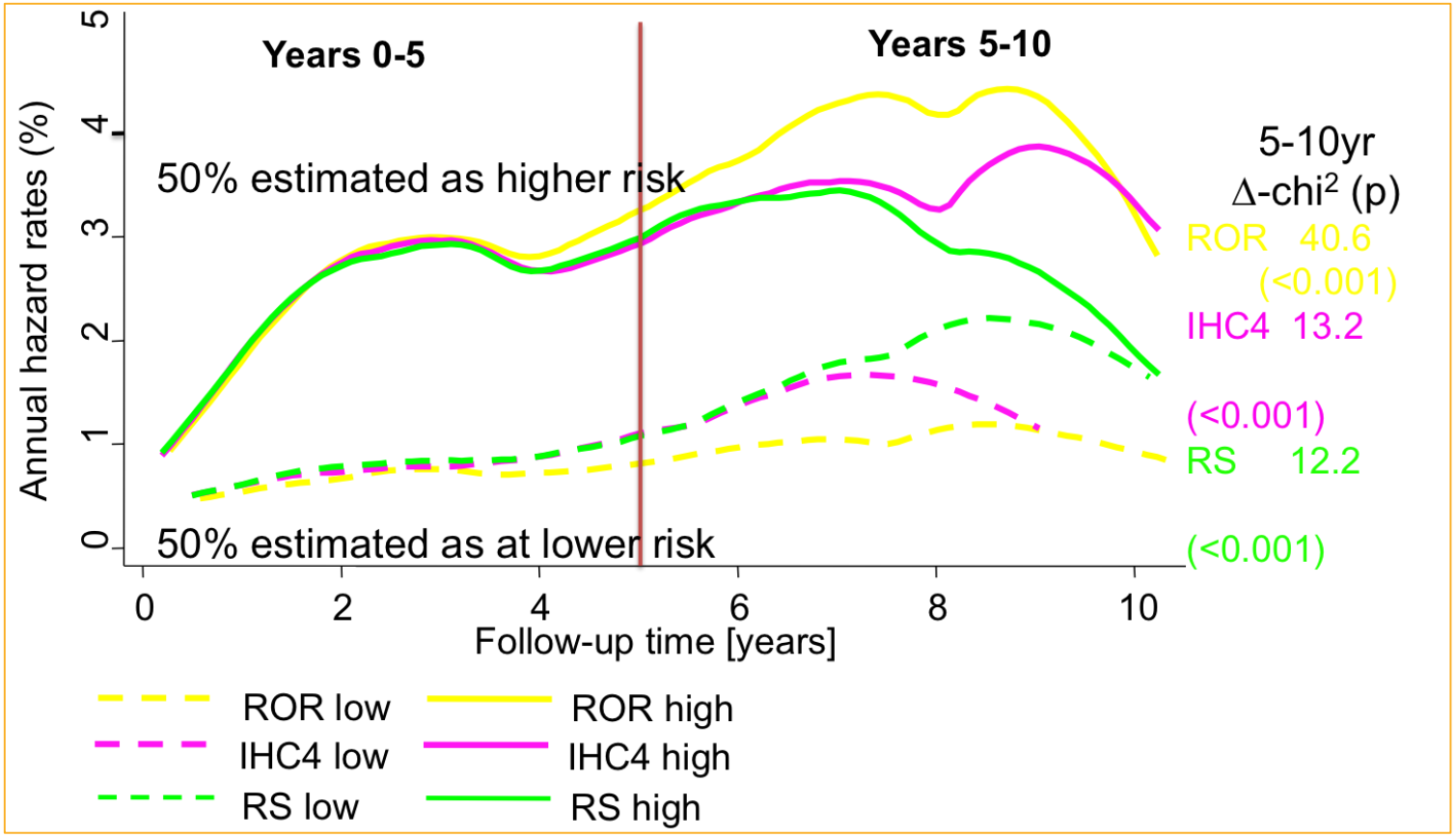
- Old studies
- Lack of detailed information on biomarker data
- Larger clinico-pathologic variables (?)

- Can we do better in identifying those less likely to recur using classic clinico-pathologic variables alone?

# PROGNOSTIC VALUE OF GENOMIC SIGNATURES

# SMOOTHED HAZARD RATES FOR RS, IHC4 AND ROR IN TRANSATAC OVER 10 YEARS

**(Node negative and positive combined)**



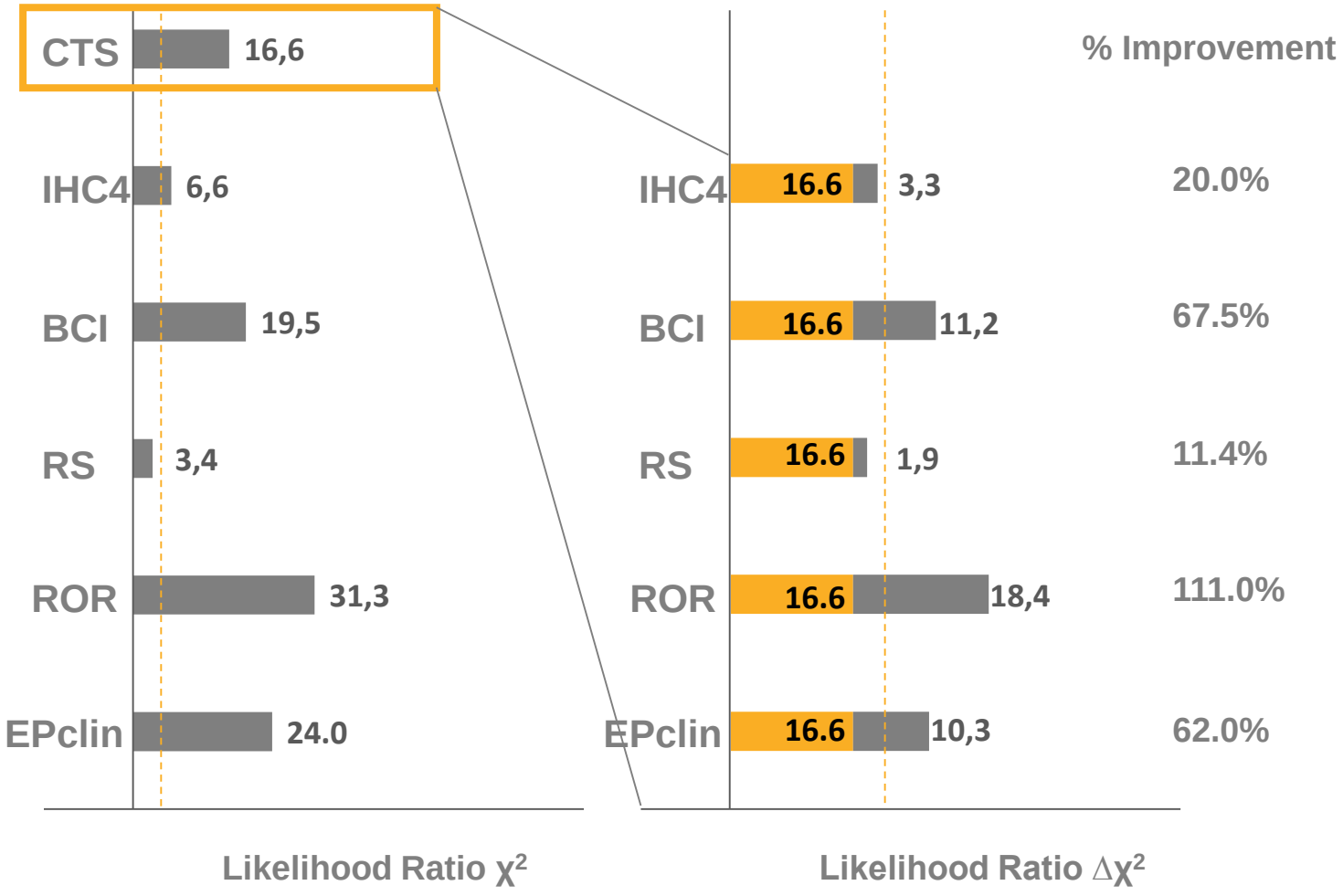

Sestak et al 2013, JNCI, 105, 1504-11

# WHAT IS THE ADDITIONAL PROGNOSTIC VALUE OF SIGNATURES TO CLINICAL VARIABLES?

| Signature | Information included |
|---|---|
| Clinical Treatment Score (CTS) | Nodal status, grade, tumour size, age, treatment |
| Immunohistochemical markers (IHC4) | ER, PgR, Ki67, HER2 |
| Oncotype Recurrence Score (RS) | 21 genes (oestrogen, proliferation, invasion, HER2 genes) |
| Breast Cancer Index (BCI) | H/I and 5 proliferation genes (Molecular Grade Index) |
| Prosigna (ROR) | 46 genes, proliferation score, tumour size (EU cut-offs from transATAC for N- and N+) |
| EndoPredict (EPclin) | 12 genes (proliferation, differentiation, oestrogen); nodal status and tumour size |

Sestak et al SABCS 2016

# PROGNOSTIC VALUE YEARS 5-10 – NODE-NEGATIVE (N=591; 34 EVENTS)

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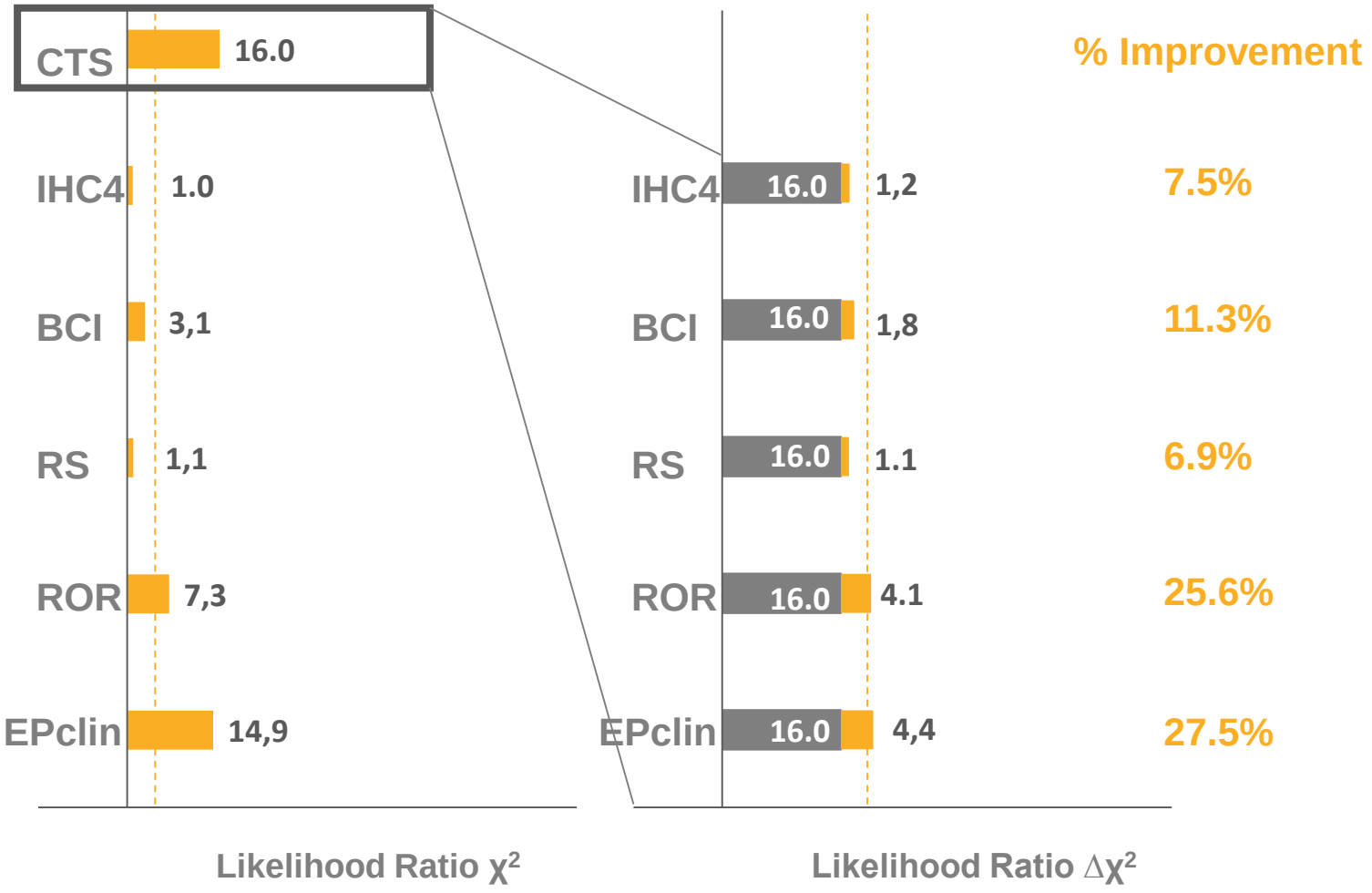
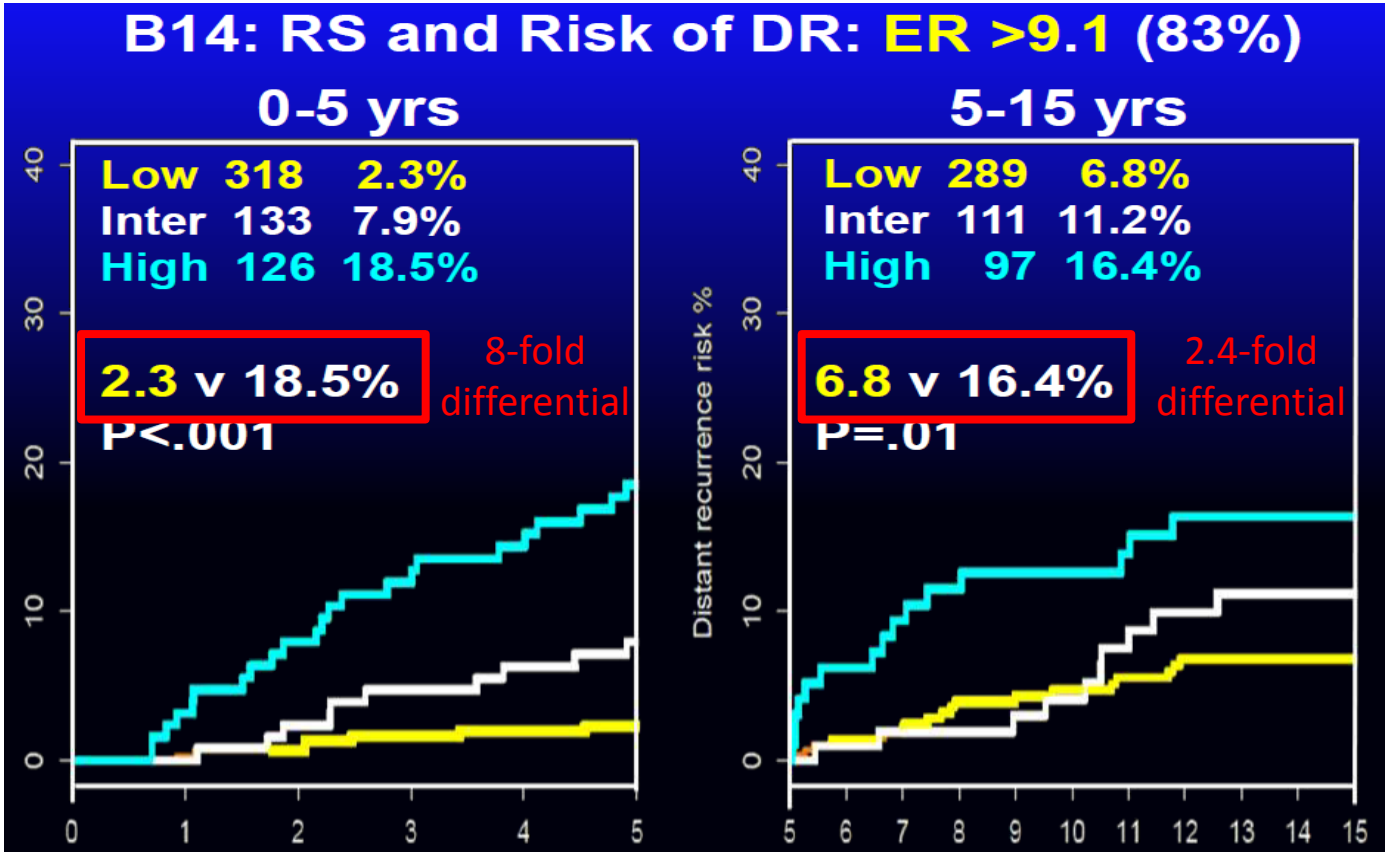
# PROGNOSTIC VALUE YEARS 5-10 - NODE-POSITIVE (N=227; 31 EVENTS)



# Prognostic performance of Oncotype Dx in tamoxifen arm of NSABP B14 (node negative): ER >9.1 by rt-PCR




Wolmark et al J Clin Oncol 34 (2016) 2350

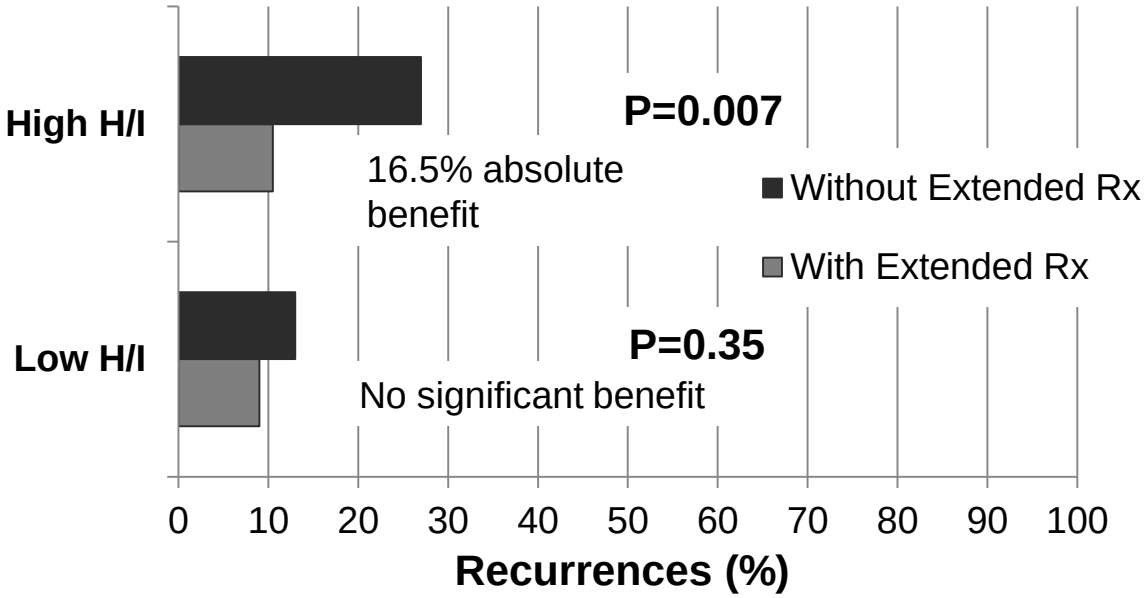
# Do we have a Genomic Tool able to Predict the benefit of Endocrine Therapy?

# OVERVIEW OF BCI PREDICTIVE

1. BCI Predictive (HoxB13/IL17BR ratio; H/I) has been evaluated as an endocrine response biomarker in 3 randomized control trial cohorts, including >1500 patients
2. Validated in the extended endocrine setting in the MA.17 study
3. Investigations in 2 additional RCT cohorts (Stockholm and TransATAC) provide further support that H/I is a generalizable biomarker of endocrine therapy response

# BCI Predictive (H/I) Results: MA.17 RCT Cohort

1. In patients with High H/I, extended letrozole reduced recurrence rate significantly from 27% to 10.5% (P=0.007)
2. No significant reduction in patients with Low H/I (P=0.35)




Sgroi et al, J Natl Cancer Inst. 2013;105:1036-1042

# SUMMARY OF BCI PREDICTIVE (H/I) VALIDATION DATA

1. H/I shown to be a significant predictor of endocrine benefit in 3 randomized trial cohorts

| Study Cohort | Treatment | Predictive analysis | Interaction P value |
|---|---|---|---|
| **Stockholm (n=600)[1]** | Adjuvant tamoxifen vs untreated | H/I High HR: 0.35 (0.19-0.65); p=0.0005<br>H/I Low HR: 0.67 (0.36-1.24), p=0.2 | 0.003 |
| **TransATAC (n=665)[2]** | Adjuvant anastrozole vs tamoxifen | H/I High HR: 0.51 (0.27-0.97); p=0.04<br>H/I Low HR: 1.33 (0.65-2.71), p=0.4 | 0.004 |
| **MA.17 (n=249)[3]** | Extended letrozole vs placebo | H/I High OR: 0.33 (0.15-0.73); p=0.006<br>H/I Low OR: 0.58 (0.25-1.36), p=0.21 | 0.03 |

- Results suggest generalizability as an endocrine response biomarker

1. Zhang Y, et al. Clin Cancer Res. 2013;19(15):4196-205. 2. Sgroi D, et al. Lancet Oncol. 2013 Oct;14(11):1067-76. 3. Sgroi et al, J Natl Cancer Inst. 2013;105:1036-1042

# TAKE HOME MESSAGES

1. Tumor size, nodal status and histological grade are important predictors for early and late-recurrence
2. Genomic tools add prognostic value to clinical variables but are not routinely used to define who should be treated with extended endocrine therapy
3. Data from TransATACT points to a differential prognostic value among available genomic tests. Results are intriguing and deserve validation.
4. BCI provides predictive information as an endocrine response biomarker

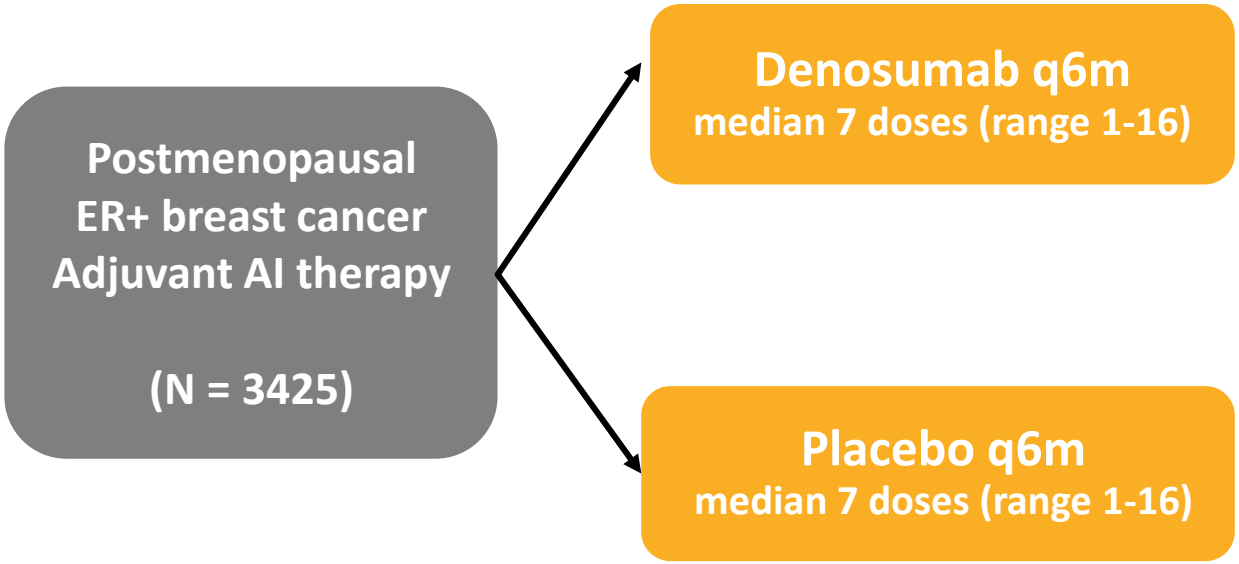
# Role of Adjuvant Bisphosphonates in Early-Stage Breast Cancer?

# ROLE OF ADJUVANT BISPHOSPHONATES IN EARLY BREAST CANCER

1. Prevent and treat cancer therapy induced bone loss
    1. Improve bone mineral density
        1. Achieved reliably with bisphosphonates[1]
    2. Reduce fractures
        1. Previous bisphosphonate trials underpowered
        2. Secondary or exploratory endpoint only in previous trials
2. Prevent metastasis and improve survival
    1. Variable individual trial results
    2. Recent EBCTCG meta-analysis demonstrated clear benefit in postmenopausal women
        1. 33% reduction in risk of bone metastases[2]
        2. 18% reduction in risk of death[2]

[1] Hadji P et al Ann Oncol 2011; 22:2546; [2] EBCTCG, Lancet 2015

# ABCSG 18 – STUDY DESIGN



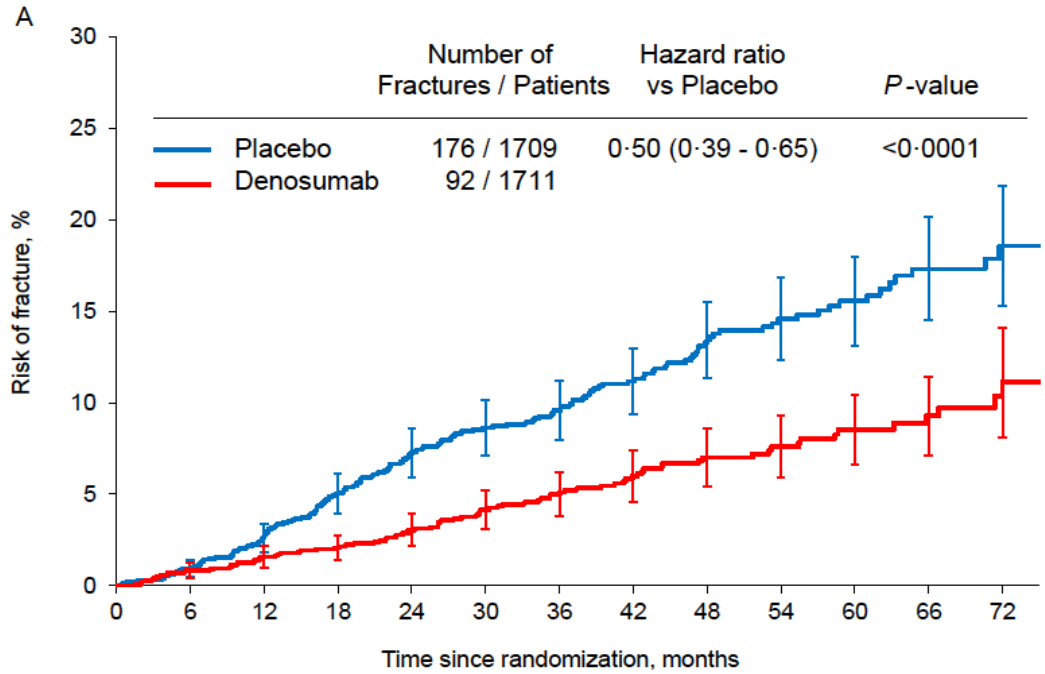

Primary endpoint: Time to first clinical fracture *

Secondary endpoints: Change in BMD at 36 months
Vertebral fractures (new/worsening)

Gnant M. et al. ASCO 2015, abs

* Clinically evident fracture with associated symptoms

# ABCSG 18 – RISK OF FRACTURES

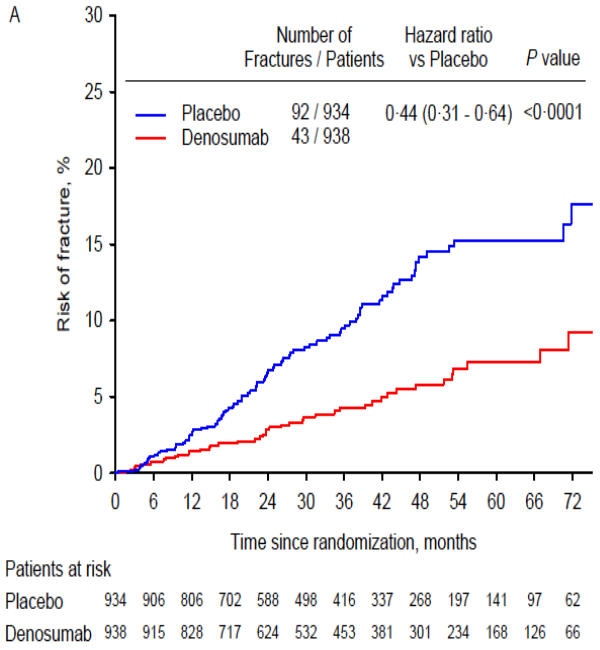



Fracture rate higher than expected (15%) at 5 years

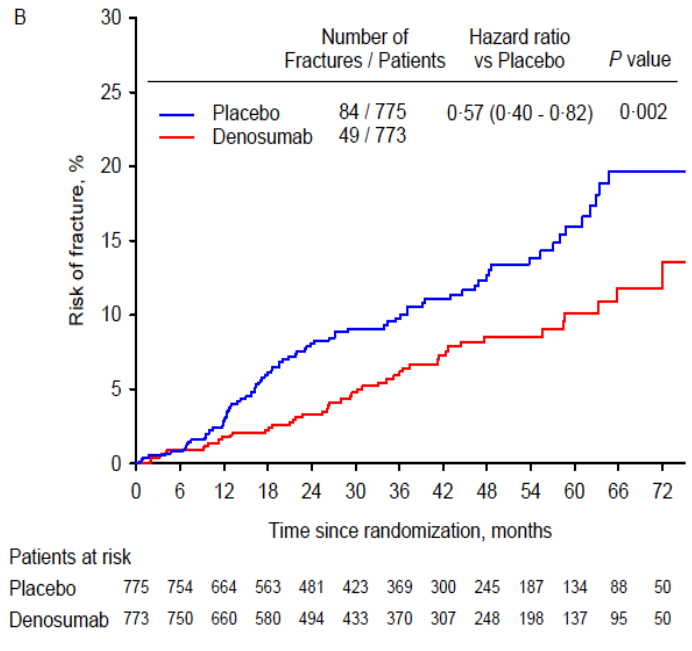
Gnant M. et al. ASCO 2015, abs

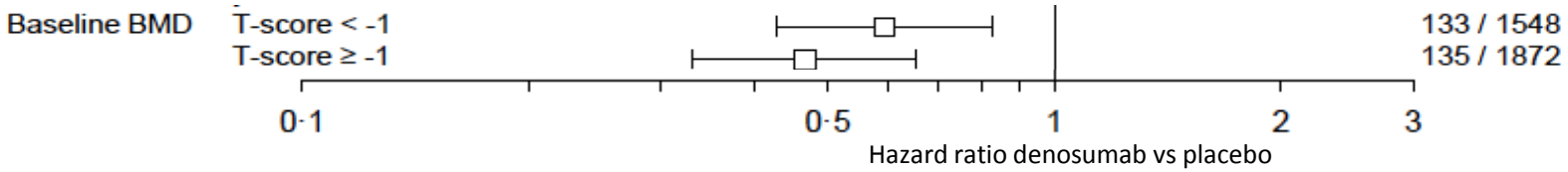
# RISK OF FRACTURES BY BASELINE BMD

## Normal BMD at Baseline



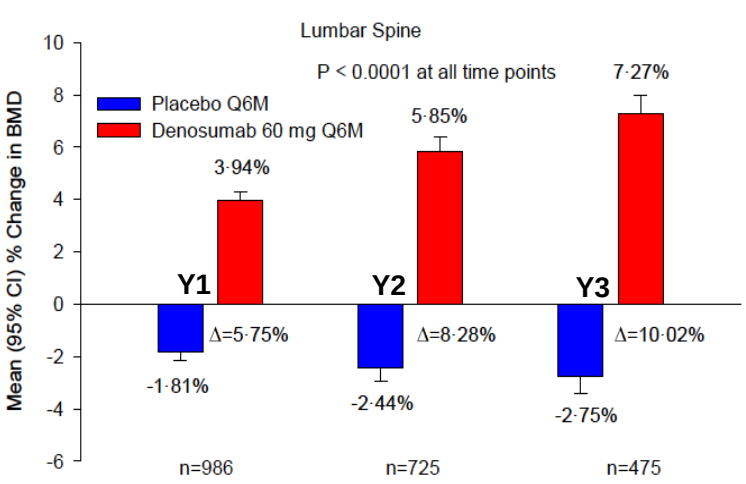

## Osteopenia at Baseline

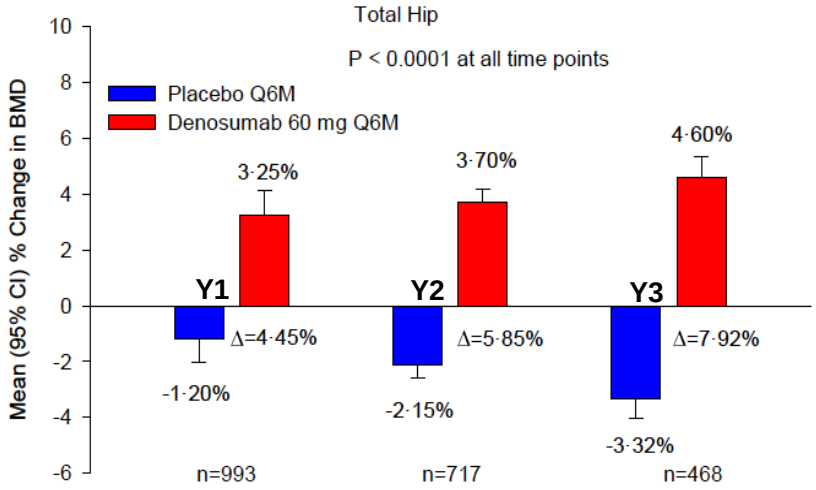



Gnant M. et al. ASCO 2015, abs

# ABCSG 18 – BONE MINERAL DENSITY CHANGES

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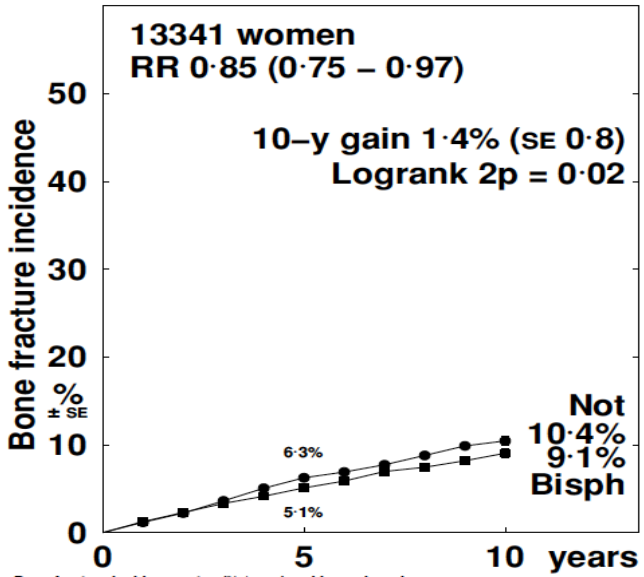
# EBCTCG META-ANALYSIS – FRACTURE DATA

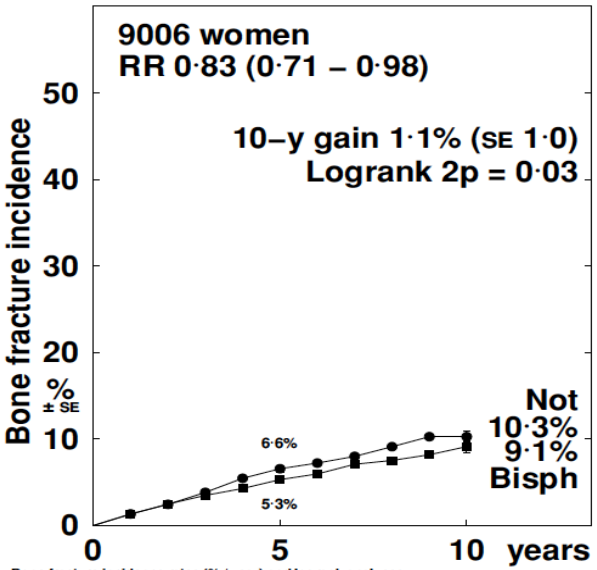
## All women




Bone fracture incidence rates (% / year) and logrank analyses

| Allocation | Years 0 – 4 | Years 5 – 9 | Year 10+ |
|---|---|---|---|
| Bisph | 1·06 (309 / 29021) | 0·88 (106 / 12112) | 0·40 (7 / 1767) |
| Not | 1·27 (371 / 29143) | 0·89 (108 / 12200) | 0·43 (8 / 1852) |
| Rate ratio, from (O–E) / V | 0·82 SE 0·07 −32·5 / 164·7 | 0·97 SE 0·14 −1·7 / 51·4 | 0·75 SE 0·47 −1·0 / 3·5 |

## Postmenopausal women



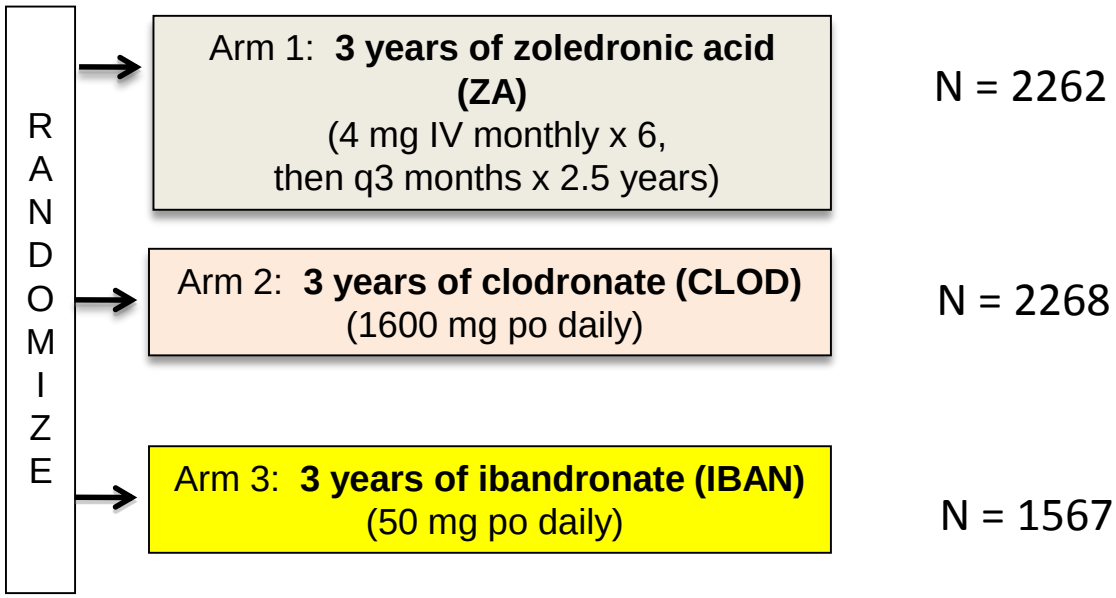

Bone fracture incidence rates (% / year) and logrank analyses

| Allocation | Years 0 – 4 | Years 5 – 9 | Year 10+ |
|---|---|---|---|
| Bisph | 1·11 (217 / 19572) | 0·81 (58 / 7128) | 0·82 (4 / 486) |
| Not | 1·35 (262 / 19456) | 0·86 (60 / 6946) | 1·06 (5 / 471) |
| Rate ratio, from (O–E) / V | 0·81 SE 0·08 −24·0 / 115·2 | 0·94 SE 0·18 −1·6 / 28·1 | 0·63 SE 0·56 −0·9 / 2·0 |

EBCTCG, Lancet 2015, in press

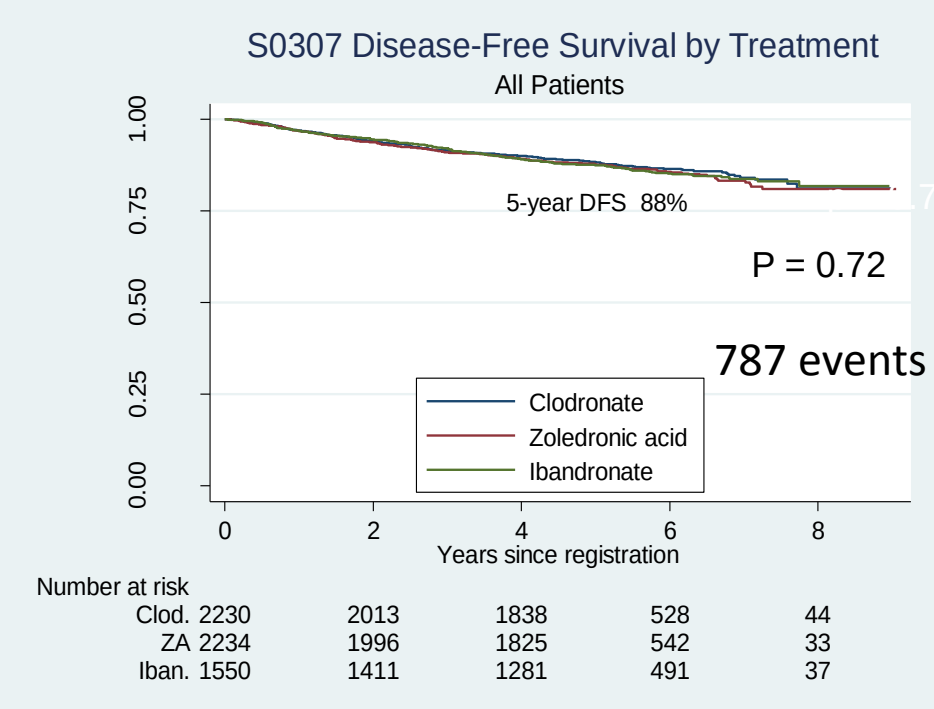
# SAFETY DATA FROM 3 DIFFERENT AGENTS

## S0307: Study Design




Gralow J et al. ASCO 2015, abs

# S0307 PRIMARY ENDPOINT:DISEASE-FREE SURVIVAL




Median Follow-up 5.4 years

No differences in DDFS or OS

No differences by ER, Her2

No differences in >60 years

# RISKS ASSOCIATED WITH ADJUVANT BISPHOSPHONATES

**Generally well tolerated**

- Low rate of troublesome GI adverse events with oral therapy
- Occasional bone pain and myalgia with IV aminobisphosphonates
- Low rate of ONJ
- Minimal rate of renal adverse events
- No reports of atypical femoral fractures in this disease setting

| S0307 | ONJ rate |
|---|---|
| Zoledronic Acid | 27/2094 (1.27%) |
| Clodronate | 7/2151 (0.31%) |
| Ibandronate | 11/1507 (0.71%) |
| p=0.003 | |

**[1]AZURE – 26 (1.7%)**

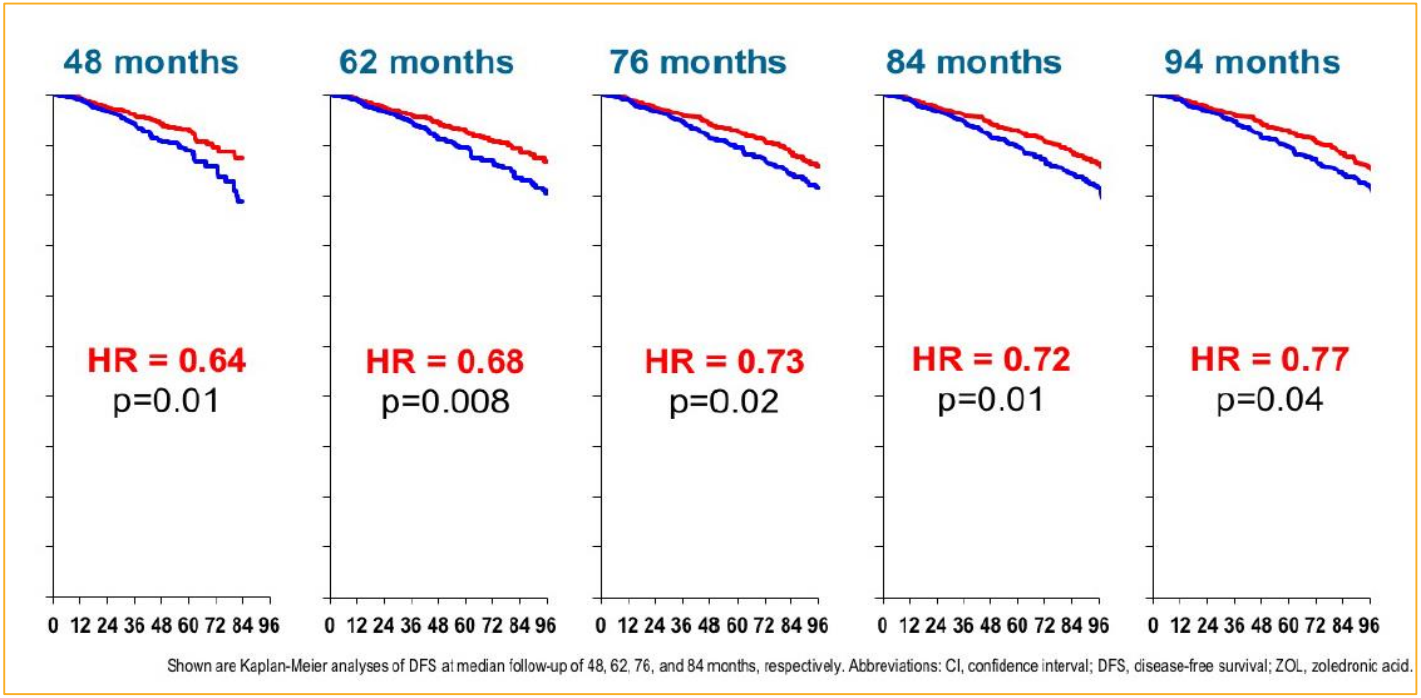
**[2]NSABP-B34 – 1 (0.06%)**

**[3]GAIN – 2 (0.1%)**

[1]Coleman et al Lancet Oncology 2014; [2]Paterson et al Lancet Oncology 2012; [3]von Minckwitz et al. J Clin Oncol 2013

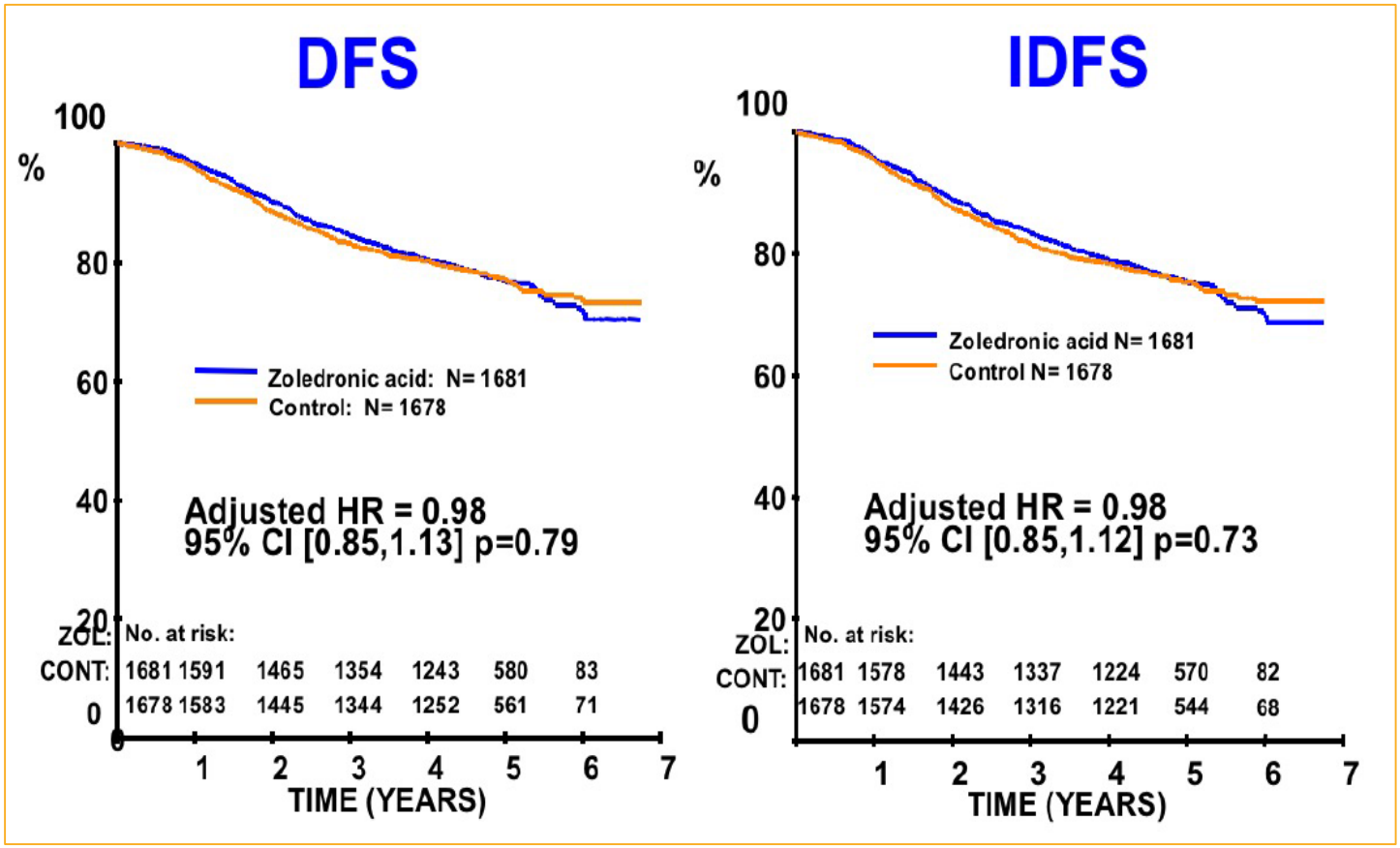
# What about disease recurrence?

# ABCSG-12: DFS ACCORDING TO FOLLOW-UP




Zoledronic Acid improved DFS when compared to control in all analyses

# AZURE: DFS AND IDFS RESULTS




Coleman et al SABCS 2010

# EFFICACY OF BONE-MODIFYING AGENTS ACROSS STUDIES

| Study | Overall DFS Result (95% CI) | P Value |
|---|---|---|
| AZURE (n = 3359)[1] | 0.98 (0.85-1.13) | .79 |
| ABCSG XII (n = 1803)[2] | 0.71 (0.55-0.92) | .011 |
| ZO-FAST (n = 1065)[3] | 0.66 (0.44-0.97) | .04 |
| NSABP-B34 (n = 3323)[4] | 0.91 (0.78-1.07) | .27 |
| CLODROPLAC (n = 1069)*[5] | 0.69 (0.48-0.99) | .043 |
| GAIN (n = 2994)[6] | 0.95 (0.77-1.16) | .59 |

*Analysis relates to bone metastasis-free survival.


*Coleman RE, et al. N Engl J Med. 2011;365:1396-1405*
*De Boer R, et al. SABCS 2011. Abstract S1-3.*
*Powles T, et al. Breast Cancer Res. 2006;8:R13.*
*Gnant M, et al. SABCS 2011. Abstract S1-2.*
*Paterson A, et al. SABCS 2011. Abstract S2-3.*
*Mobus V, et al. SABCS 2011. Abstract S2-4.*

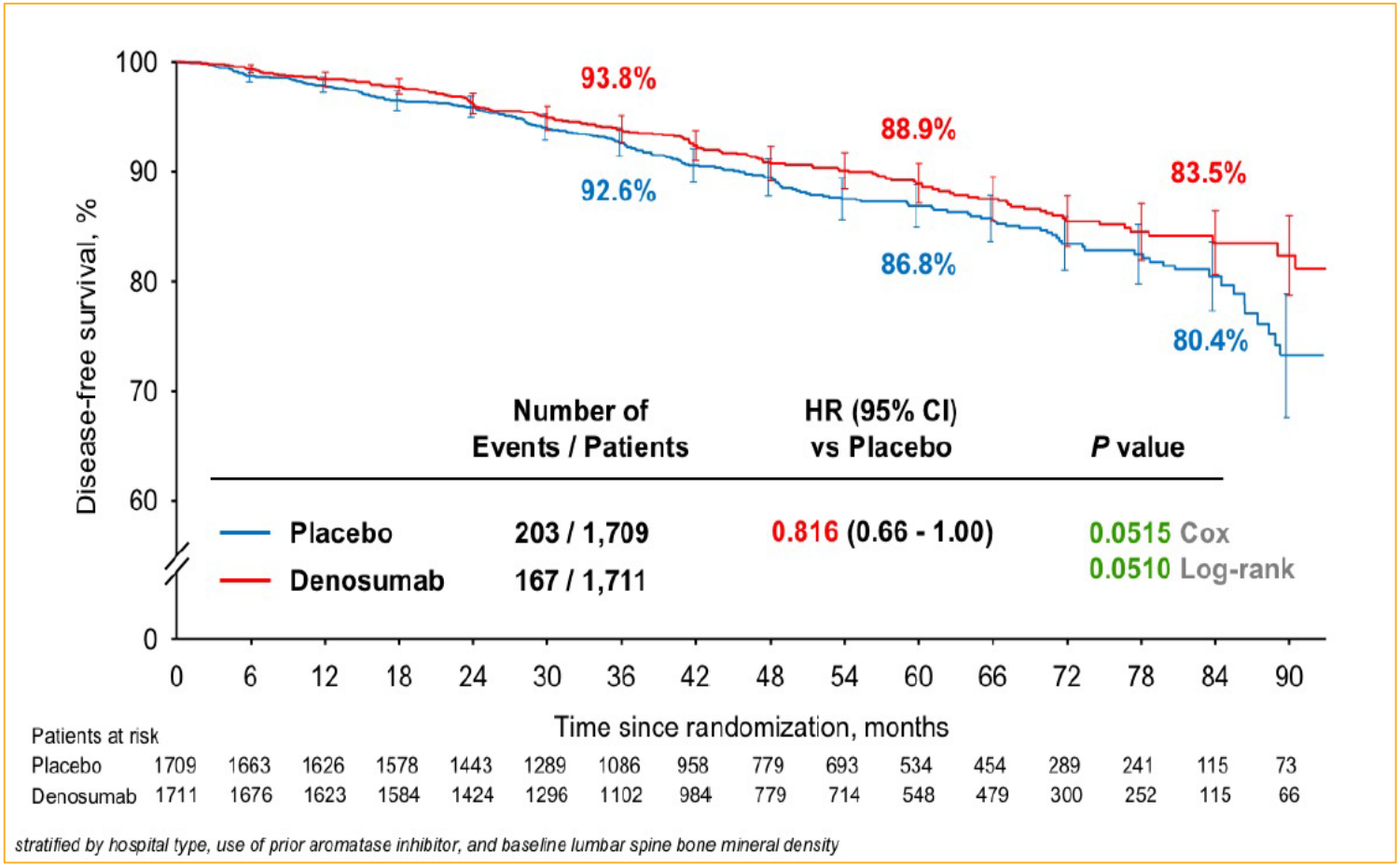
# CONSISTENT EFFECT AMONG POSTMENOPAUSAL WOMEN

| Study | "Postmenopausal" DFS (95% CI) | P Value |
|---|---|---|
| AZURE (n = 1041)[1] | 0.75 (0.59-0.96) | .02 |
| ABCSG XII (n = 1390)[2] | 0.66 (0.48-0.92)* | .013 |
| ZO-FAST (n = 1065)[3] | 0.66 (0.44-0.97) | .04 |
| NSABP-B34 (n = 2139)[4] | 0.68 (0.5-0.92) | .013 |
| CLODROPLAC† (n = 539)[5] | 0.66 (0.49-0.93) | .007 |
| GAIN (n = 1557)[6] | 0.75 (0.49-1.14)‡ | .17 |

*Includes patients > 40 yrs on goserelin; no significant effect for patients < 40 yrs.
†Analysis relates to OS.
‡≥ 60 yrs at study entry.

*Coleman RE, et al. N Engl J Med. 2011;365:1396-1405*
*De Boer R, et al. SABCS 2011. Abstract S1-3.*
*Powles T, et al. Breast Cancer Res. 2006;8:R13.*
*Gnant M, et al. SABCS 2011. Abstract S1-2.*
*Paterson A, et al. SABCS 2011. Abstract S2-3.*
*Mobus V, et al. SABCS 2011. Abstract S2-4.*

# ABCSG-18 RESULTS OF THE DFS ITT ANALYSIS




*stratified by hospital type, use of prior aromatase inhibitor, and baseline lumbar spine bone mineral density*

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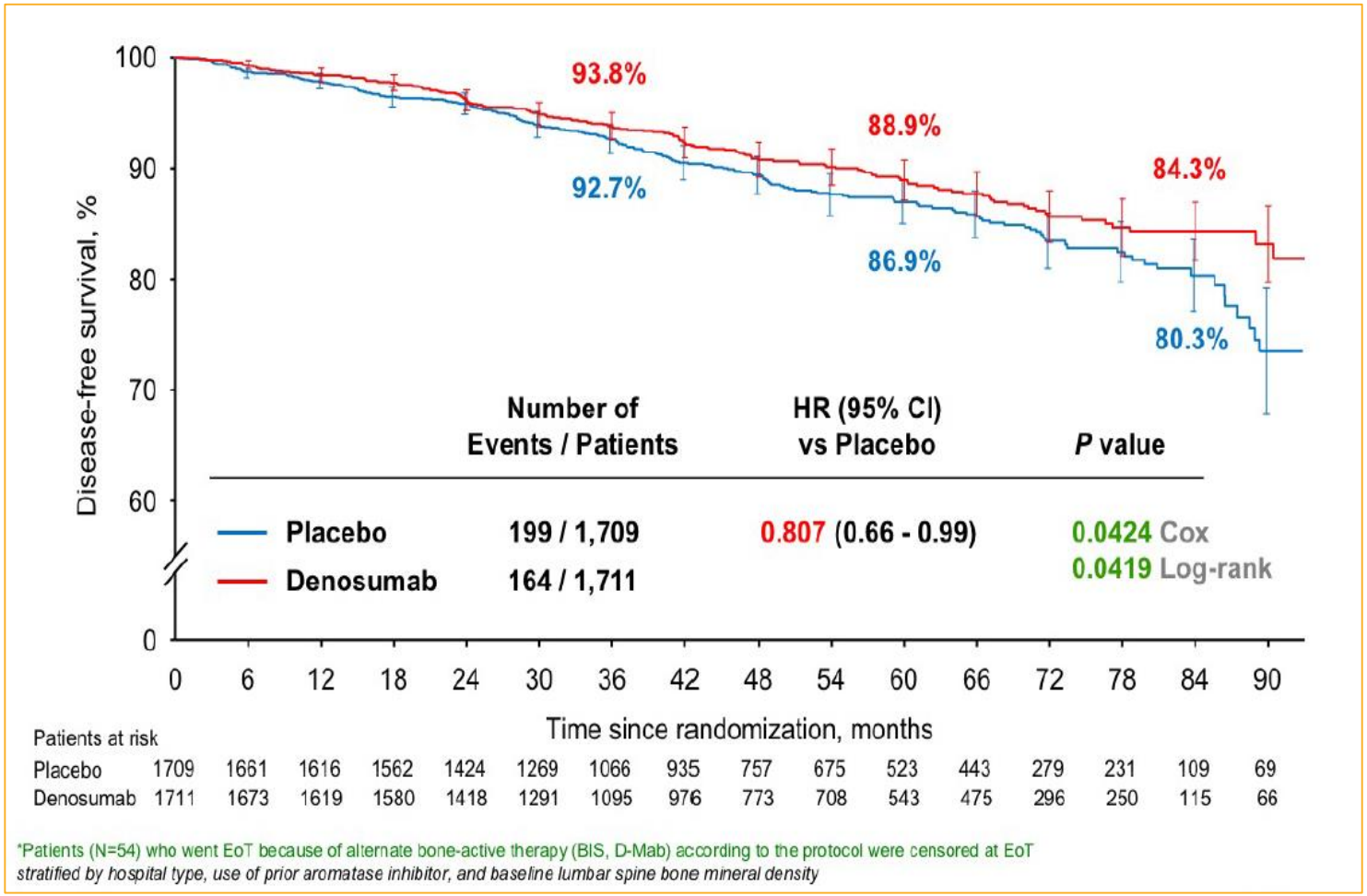
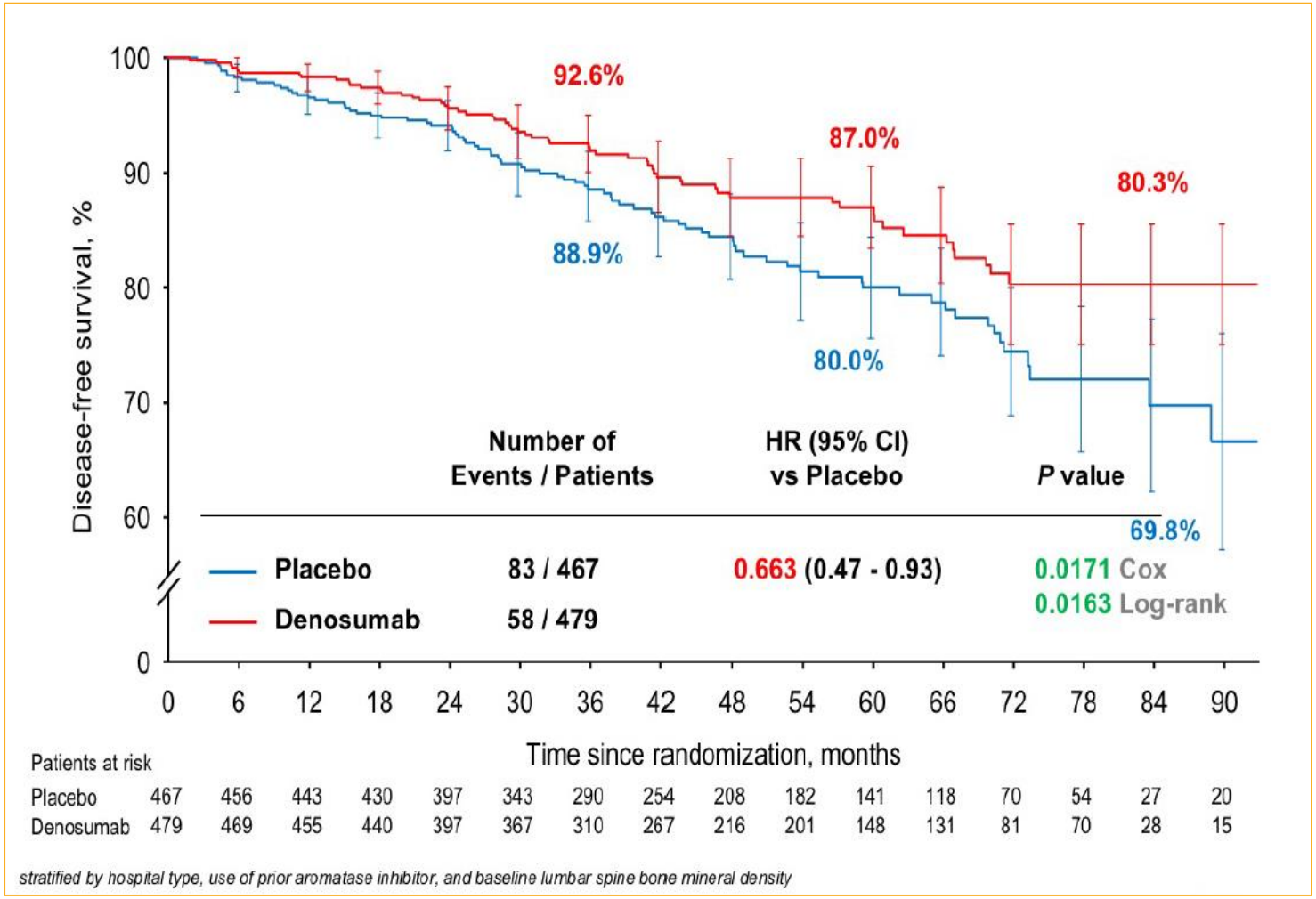
# ABCSG-18 SENSITIVITY ANALYSIS DFS (CROSS OVER CENSORED)




*Patients (N=54) who went EoT because of alternate bone-active therapy (BIS, D-Mab) according to the protocol were censored at EoT
*stratified by hospital type, use of prior aromatase inhibitor, and baseline lumbar spine bone mineral density*

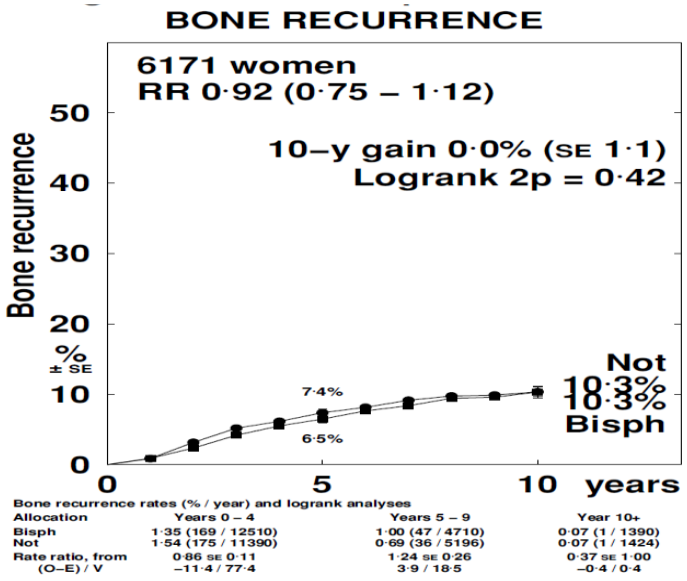
# ABCSG-18 SUBGROUP TUMOR SIZE > 2CM



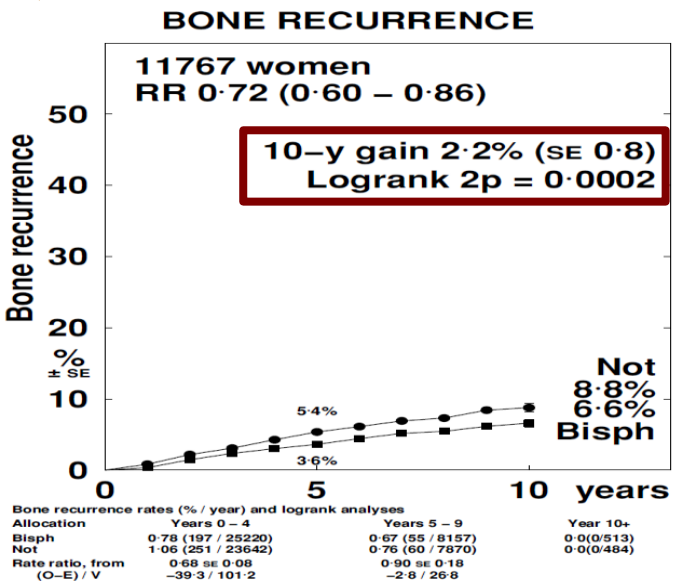

*stratified by hospital type, use of prior aromatase inhibitor, and baseline lumbar spine bone mineral density*

# EBCTCG OVERVIEW: BONE RECURRENCE BY MENOPAUSAL STATUS

## Premenopausal‡




## Postmenopausal

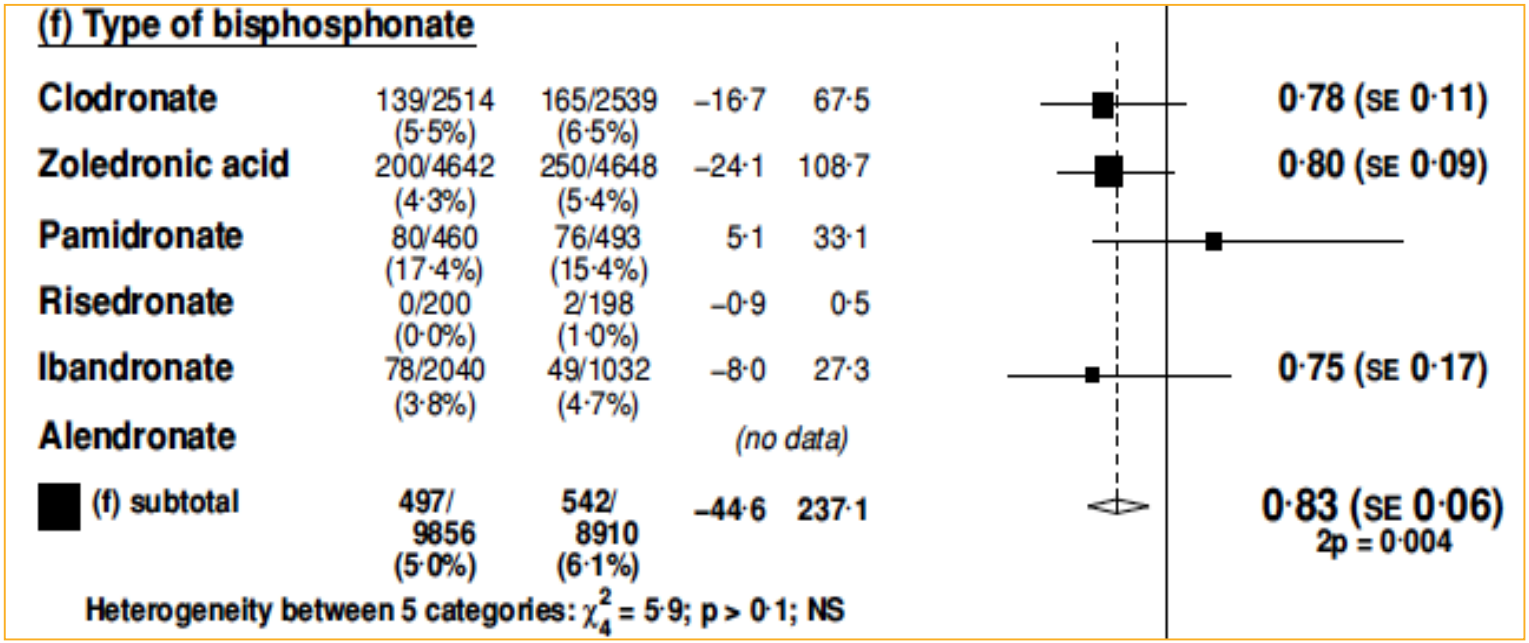



**Heterogeneity between menopausal groups $\chi^2_1 = 5.6$ ; P=0.02**

‡ includes women aged < 45 if unknown

EBCTCG, Lancet 2015

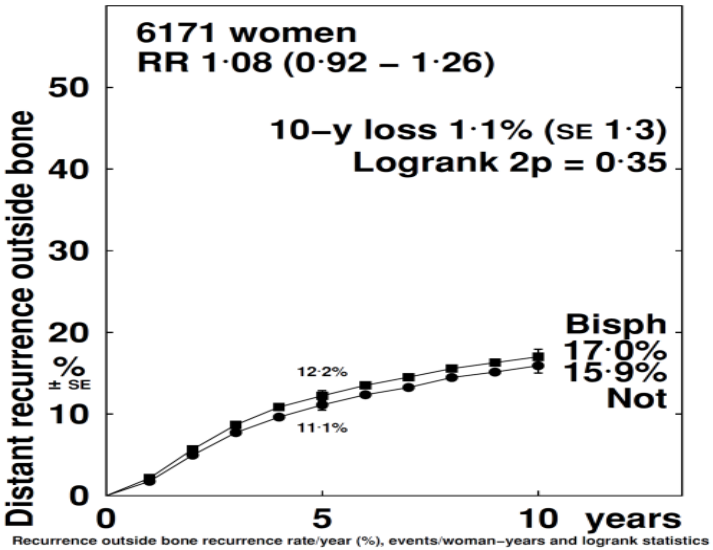
# SIMILAR EFFECTS ON BONE RECURRENCE IRRESPECTIVE OF TYPE OF BISPHOSPHONATE




EBCTCG, Lancet 2015

# NON-BONE DISTANT RECURRENCE BY MENOPAUSAL STATUS

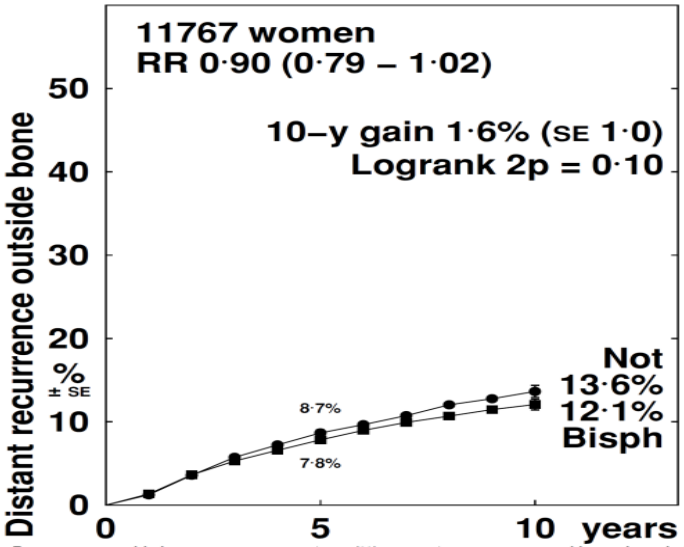
## Premenopausal‡




Recurrence outside bone recurrence rate/year (%), events/woman–years and logrank statistics

| Allocation | Years 0 – 4 | Years 5 – 9 | Year 10+ |
|---|---|---|---|
| Bisph | 2·64 (330 / 12510) | 1·25 (59 / 4710) | 0·43 (6 / 1390) |
| Not | 2·41 (275 / 11390) | 1·14 (59 / 5196) | 0·77 (11 / 1424) |
| Rate ratio, from (O–E) / V | 1·12 SE 0·09<br>14·2 / 128·4 | 1·03 SE 0·20<br>0·7 / 26·1 | 0·37 SE 0·36<br>–3·0 / 3·1 |

## Postmenopausal




Recurrence outside bone recurrence rate/year (%), events/woman–years and logrank statistics

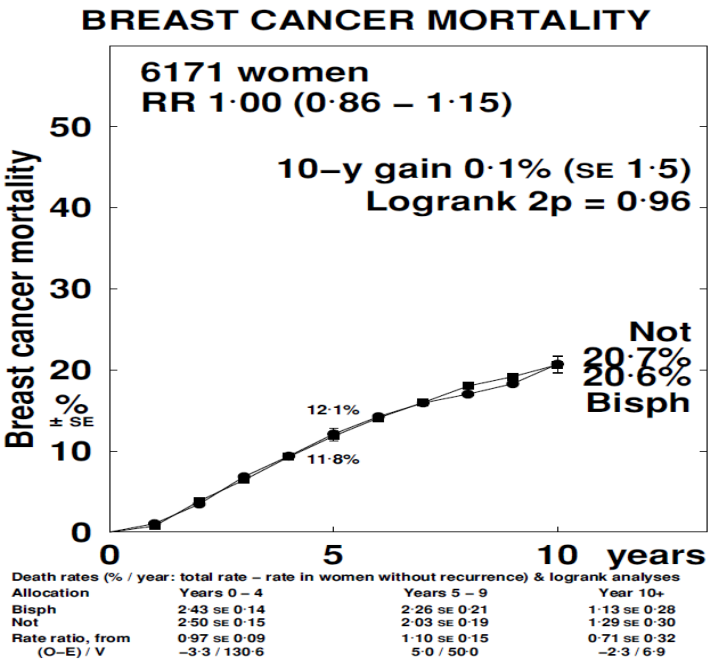
| Allocation | Years 0 – 4 | Years 5 – 9 | Year 10+ |
|---|---|---|---|
| Bisph | 1·67 (420 / 25220) | 1·04 (85 / 8157) | 0·78 (4 / 513) |
| Not | 1·81 (427 / 23642) | 1·17 (92 / 7870) | 1·65 (8 / 484) |
| Rate ratio, from (O–E) / V | 0·90 SE 0·07<br>–18·4 / 182·4 | 0·89 SE 0·15<br>–4·5 / 39·7 | 0·38 SE 0·49<br>–1·7 / 1·8 |

‡ includes women aged < 45 if unknown

EBCTCG, Lancet 2015

# BREAST CANCER MORTALITY BY MENOPAUSAL STATUS

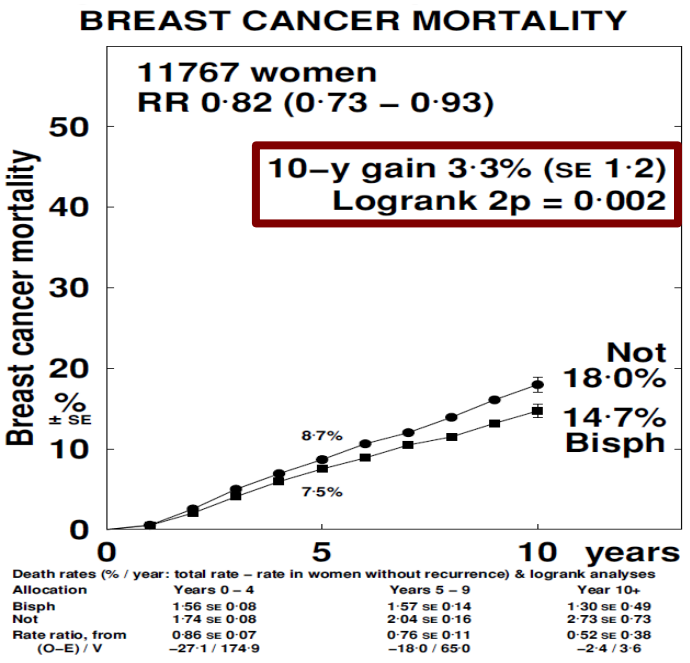
## Premenopausal‡




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

| Allocation | Years 0 – 4 | Years 5 – 9 | Year 10+ |
|---|---|---|---|
| Bisph | 2·43 SE 0·14 | 2·26 SE 0·21 | 1·13 SE 0·28 |
| Not | 2·50 SE 0·15 | 2·03 SE 0·19 | 1·29 SE 0·30 |
| Rate ratio, from (O–E) / V | 0·97 SE 0·09 –3·3 / 130·6 | 1·10 SE 0·15 5·0 / 50·0 | 0·71 SE 0·32 –2·3 / 6·9 |

## Postmenopausal




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

| Allocation | Years 0 – 4 | Years 5 – 9 | Year 10+ |
|---|---|---|---|
| Bisph | 1·56 SE 0·08 | 1·57 SE 0·14 | 1·30 SE 0·49 |
| Not | 1·74 SE 0·08 | 2·04 SE 0·16 | 2·73 SE 0·73 |
| Rate ratio, from (O–E) / V | 0·86 SE 0·07 –27·1 / 174·9 | 0·76 SE 0·11 –18·0 / 65·0 | 0·52 SE 0·38 –2·4 / 3·6 |

**‡ includes women aged < 45 if unknown**

EBCTCG, Lancet 2015

# SUMMARY OF RECOMMENDATIONS

***Recommendation 1***

- It is recommended that administration of bisphosphonates as adjuvant therapy be considered for postmenopausal patients with breast cancer (including patients premenopausal before treatment who have menopause induced by ovarian suppression) deemed candidates for adjuvant systemic therapy.

- The final decision of whether or not to administer bisphosphonates should be made during consultation between the patient and oncologist, taking into account patient and disease characteristics, including risk of recurrence, and weighing the potential benefits and risks (adverse effects).

***Qualifying Statements for Recommendation 1***

- While the EBCTCG meta-analysis[1] found benefit for bisphosphonates in all subgroups of postmenopausal patients, the absolute benefit was small. For patients with cancers assessed as having low risk of recurrence, the use of bisphosphonates may not result in clinically meaningful effect.

Ontario
Cancer Care Ontario
ASCO GUIDELINES

www.asco.org/breast-cancer-adjuvant-bisphosphonates-guideline

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