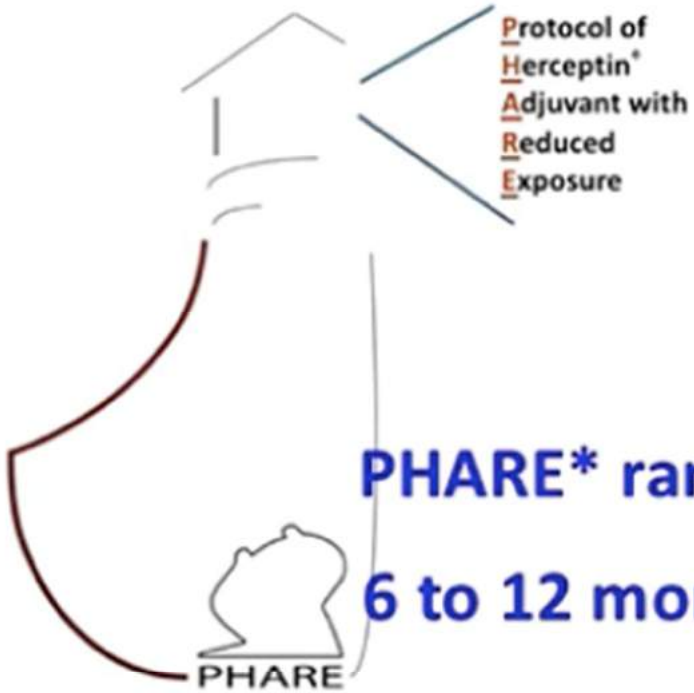
Destaques de SABCS 2018

Leandro Gonçalves Oliveira

Oncologista Clínico - INGOH



INSTITUT NATIONAL DU CANCER

PHARE* randomized trial final results comparing 6 to 12 months of trastuzumab in adjuvant early breast cancer

Xavier Pivot, Gilles Romieu, Marc Debled, Jean-Yves Pierga, Pierre Kerbrat, Thomas Bachelot, Alain Lortholary, Marc Espié, Pierre Fumoleau, Daniel Serin, Jean-Philippe Jacquin, Christelle Jouannaud, Maria Rios, Sophie Abadie-Lacourtoisie, Laurence Venat-Bouvet, Laurent Cany, Stéphanie Catala, David Khayat, Laetitia Gambotti, Iris Pauporté, Celine Faure-Mercier, Sophie Paget, Julie Henriquez, Jean-Marie Grouin.

*lighthouse in French

Objectives

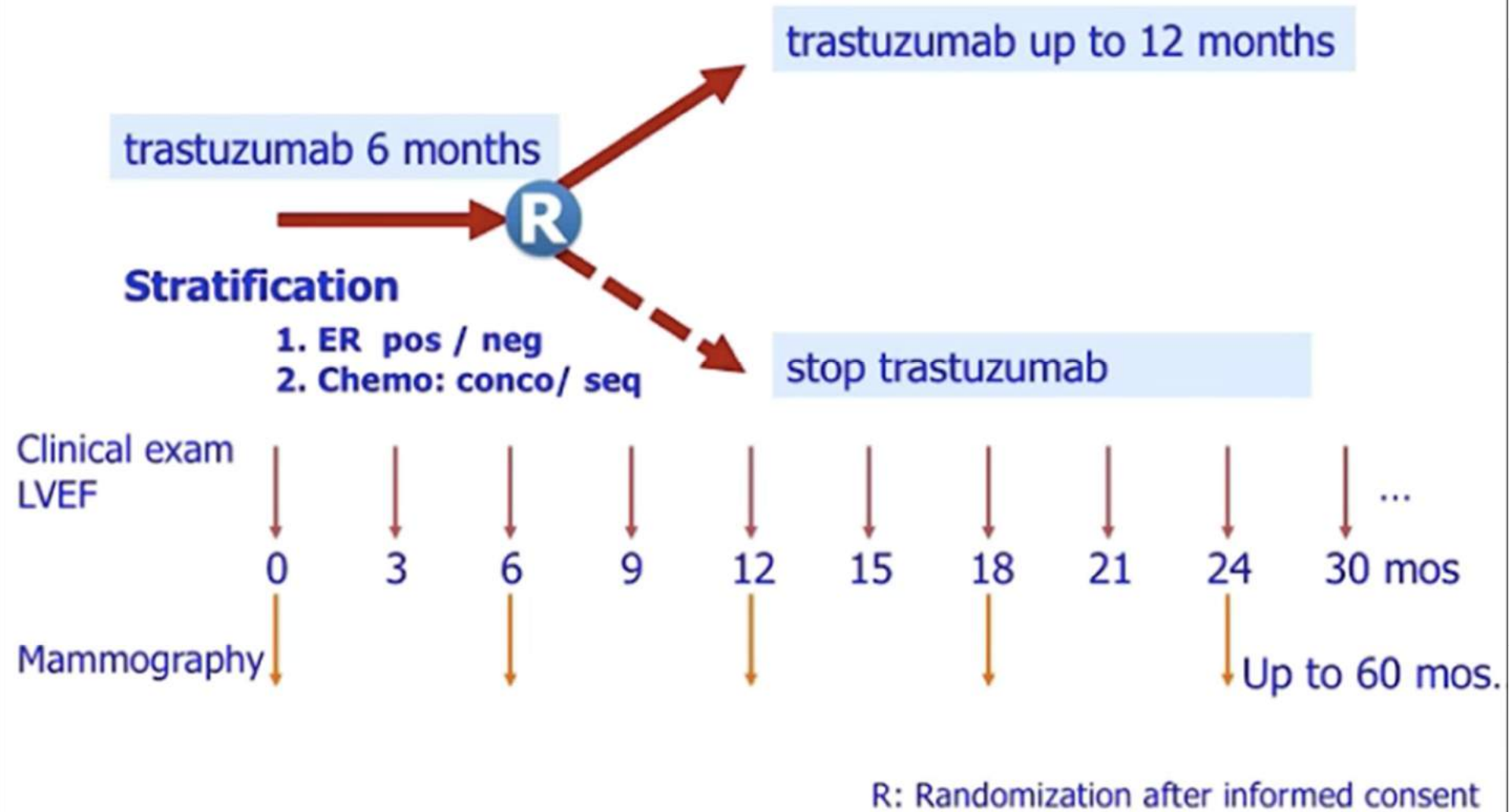
- **Primary objective**
  - Compare the effect of 6 months versus 12 months of treatment with trastuzumab in HER2+ over expression early breast cancer
  - Primary endpoint: Disease-Free Survival (DFS)
    - local, regional, or distant recurrence, contralateral breast, second non-breast malignancies, or death from any cause
- **Secondary objectives**
  - Cardiotoxicity
  - Overall survival
  - Distant metastasis Free Survival

X Pivot et al, ESMO 2012, LBA5_PR

Statistical Methods

- **Non inferiority randomized trial**
  - 2% variation in terms of absolute difference of recurrence
  - The 95% CI HR margins should not cross the 1.15 boundary
  - HR were estimated from the stratified Cox model

Study design



R: Randomization after informed consent

Treatment Characteristics

	12 months n=1690	6 months n=1690
Type of Chemotherapy		
No Anthracyclines	10.2%	11.8%
Anthracyclines no taxanes	15.9%	15.5%
Anthracyclines and Taxanes	73.9%	72.7%
Concomitant Chemotherapy	57.5%	56.9%
Sequential Chemotherapy	42.5%	43.1%
Radiotherapy	87.7%	88.2%
Hormonotherapy	50.6%	50.2%
Trastuzumab duration, mean (sd)	11.8 (2.03)	6.3 (1.46)

DFS Events

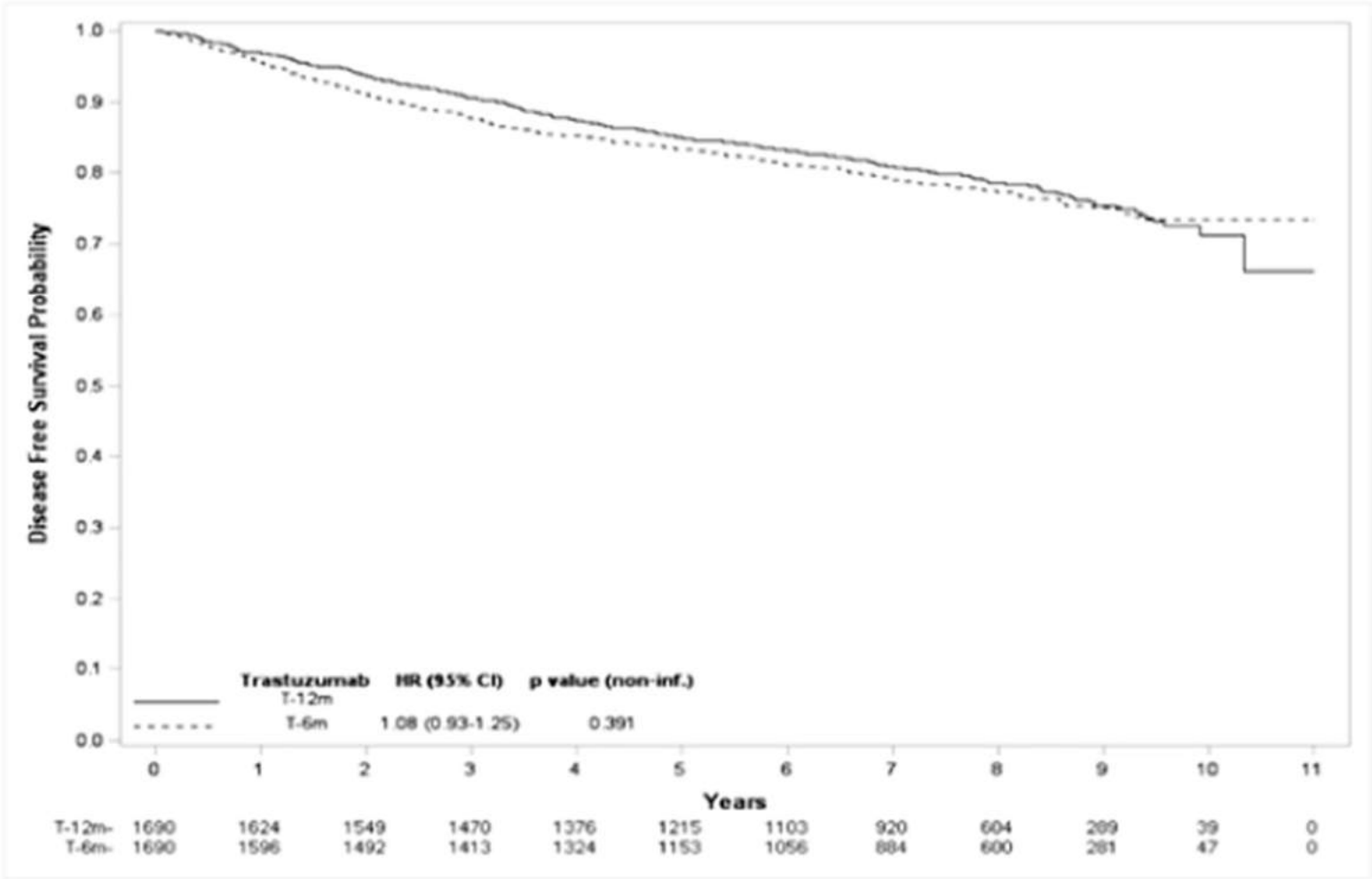
7.5 years median Follow-up

	12 mos (n=1690)	6 mos (n=1690)
DFS Events **(n=704)**	20.4%	21.2%
Local Recurrence	2.1%	2.5%
Regional Recurrence	1%	1.1%
Distant Recurrence	9.6%	11.1%
Controlateral Breast Cancer	1.6%	2%
2nd Primary Malignancy	4.6%	3.6%
Death	1.4%	1.1%

Disease Free Survival

HR: 1.08 (95%CI: 0.93-1.25) p=0.39

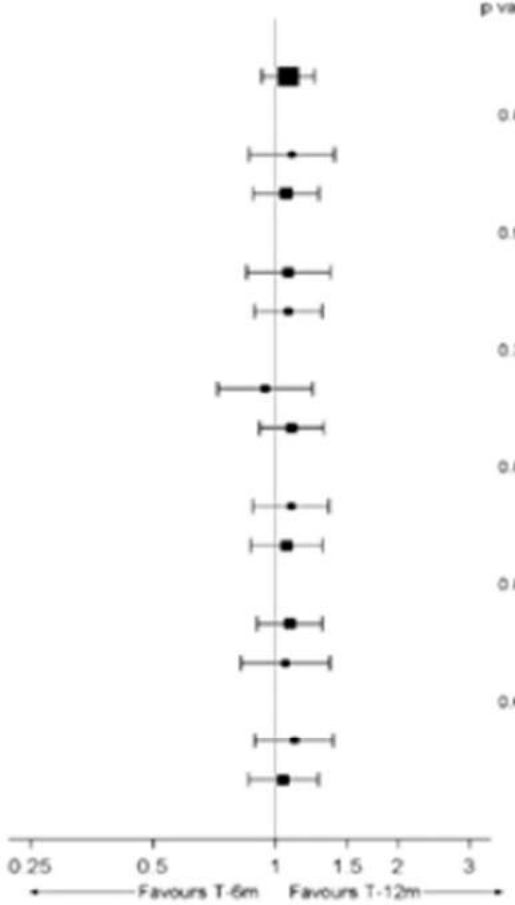
Non-inferiority margin = 1.15



1 : Adjusted for stratification factors : Oestrogen receptor status (+ vs -) and chemotherapy (concomitant vs sequential)

Subgroup effects

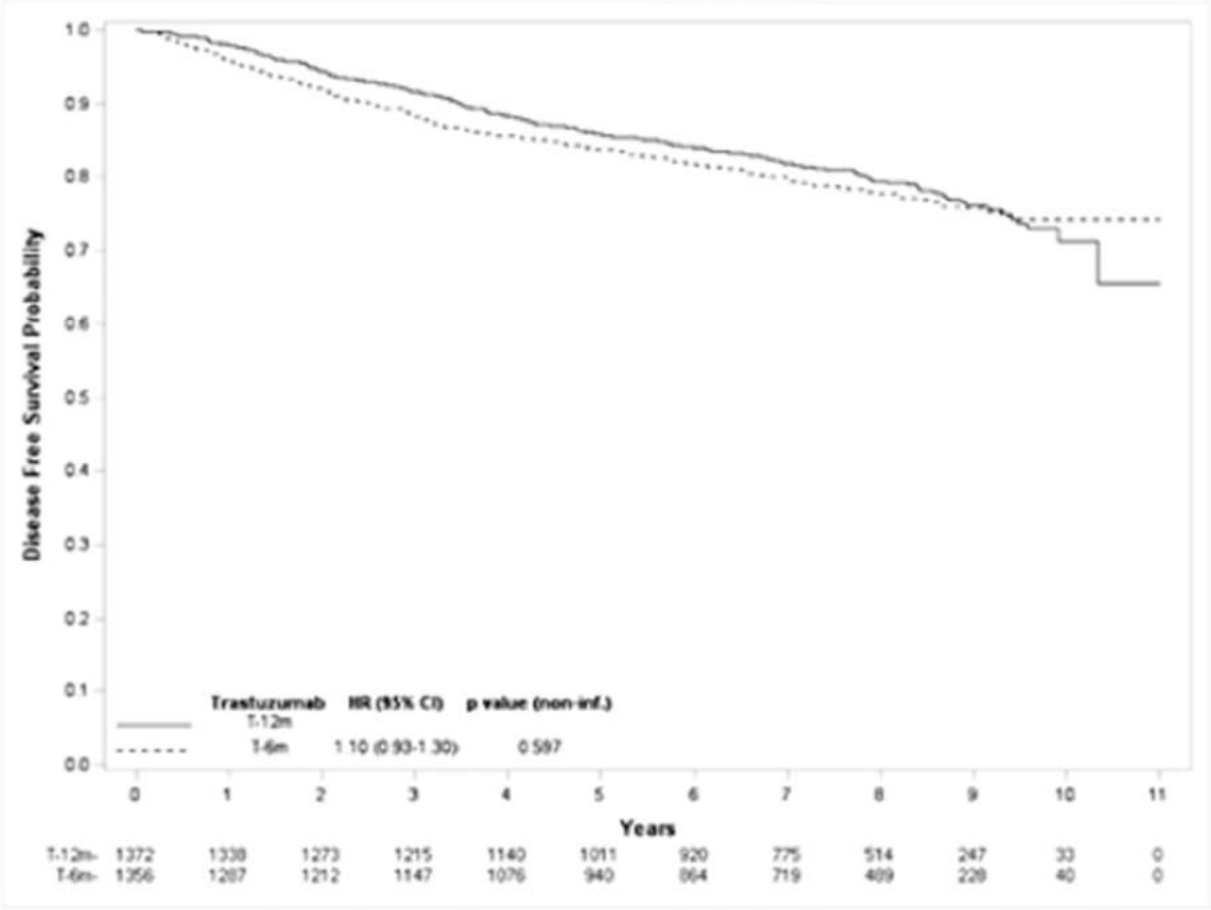
Subgroup	T-6m Events/N (%)	T-12m Events/N (%)	HR (95% CI)*	p value #
All	359/1690 (21.2)	345/1690 (20.4)	1.07 (0.93, 1.25)	
Age (Years)				0.83
< 50	132/594 (22.2)	129/600 (21.5)	1.10 (0.86, 1.40)	
≥ 50	227/1096 (20.7)	216/1090 (19.8)	1.06 (0.88, 1.28)	
Nodal status				0.99
Negative	138/915 (15.1)	135/927 (14.6)	1.08 (0.85, 1.37)	
Positive	217/759 (28.6)	203/746 (27.2)	1.08 (0.89, 1.30)	
Tumour size (cm)				0.36
< 2	100/703 (14.2)	113/742 (15.2)	0.94 (0.72, 1.24)	
≥ 2	244/950 (25.7)	222/912 (24.3)	1.10 (0.91, 1.32)	
Oestrogen Receptor				0.85
Negative	169/695 (24.3)	164/715 (22.9)	1.09 (0.88, 1.35)	
Positive	190/995 (19.1)	181/975 (18.6)	1.07 (0.87, 1.31)	
Progesterone Receptor				0.87
Negative	238/986 (24.1)	222/969 (22.9)	1.09 (0.90, 1.30)	
Positive	120/701 (17.1)	119/712 (16.7)	1.06 (0.82, 1.36)	
Chemotherapy				0.67
Sequential	163/729 (22.4)	150/718 (20.9)	1.11 (0.89, 1.39)	
Concomitant	196/961 (20.4)	195/972 (20.1)	1.05 (0.86, 1.28)	



* HR: unadjusted Hazard Ratio - # p value is the test of interaction between treatment and each subgroup unadjusted for multiplicity.

Overall Survival

	HR (95% CI)	P value
adjusted HR [1]	1.13 (0.92-1.39)	0.26
unadjusted HR	1.12 (0.91-1.38)	0.29
adjusted HR [2]	1.07 (0.86-1.32)	0.55



1 : Adjusted for stratification factors : Oestrogen receptor status (+ vs -) and chemotherapy (concomitant vs sequential)

2 : adjusted for Oestrogen-receptor status (+ vs -), chemotherapy (concomitant vs sequential), Age (< 50 vs ≥ 50) , Tumour size (< 2 vs ≥ 2 cm), progesterone-receptor status (+ vs -), nodal status (+ vs -).

PERSEPHONE: 6 versus 12 months of adjuvant trastuzumab in patients with HER2 positive early breast cancer: Randomised phase 3 non-inferiority trial with definitive 4-year disease-free survival results

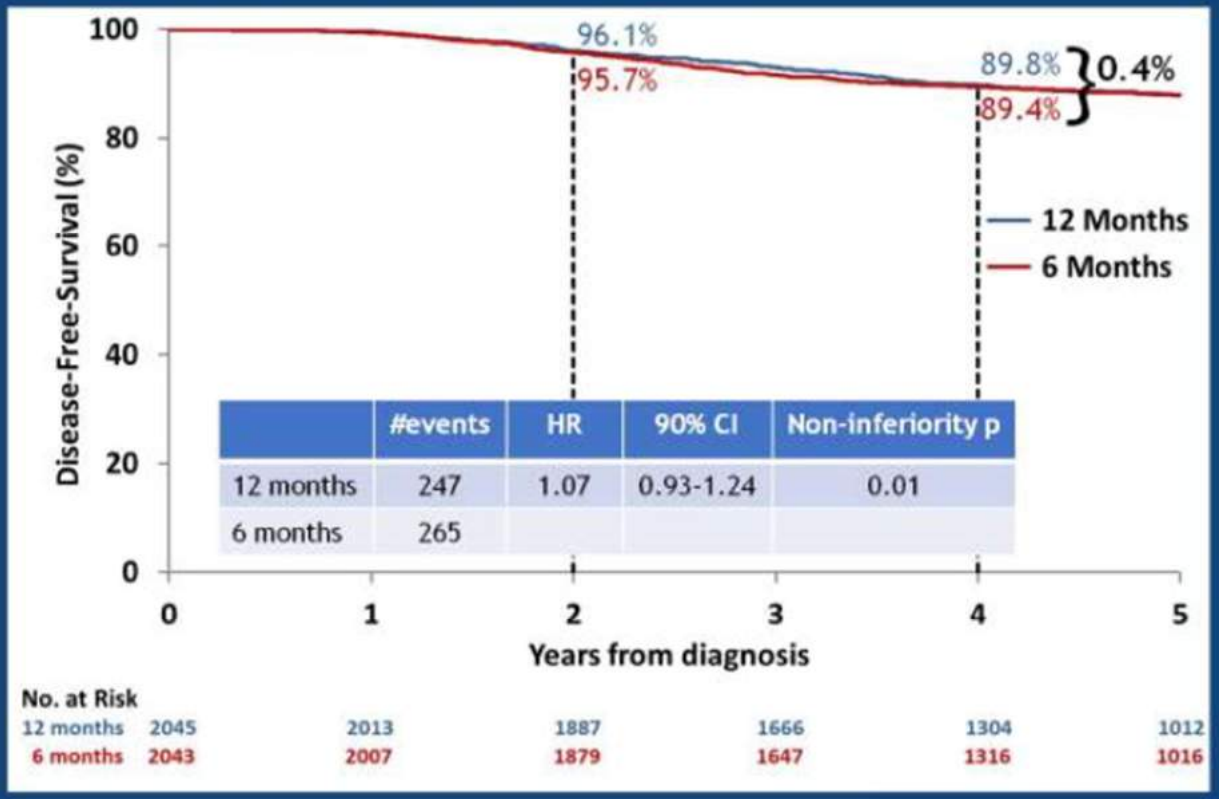
Helena Earl, Louise Hiller, Anne-Laure Vallier, Shrushma Loi, Donna Howe, Helen Higgins, Karen McAdam, Luke Hughes-Davies, Adrian Harnett, Mei-Lin Ah-See, Richard Simcock, Daniel Rea, Janine Mansi, Jean Abraham, Carlos Caldas, Claire Hulme, David Miles, Andrew Wardley, David Cameron, Janet Dunn, on behalf of the PERSEPHONE Trial Investigators

PRESENTED AT: 2018 ASCO ANNUAL MEETING #ASCO18

PRESENTED BY: Prof Helena Earl MD PhD

https://warwick.ac.uk/fac/med/research/ctu/trials/cancer/persephone

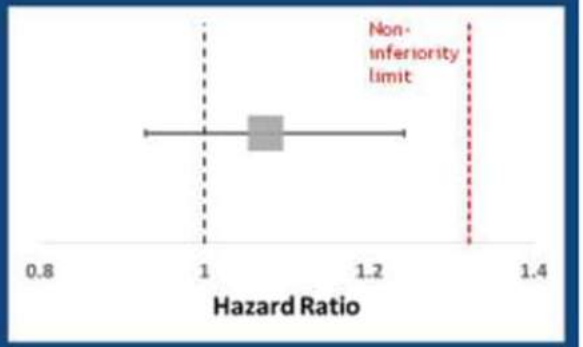
Disease-free survival



	#events	HR	90% CI	Non-inferiority p
12 months	247	1.07	0.93-1.24	0.01
6 months	265			

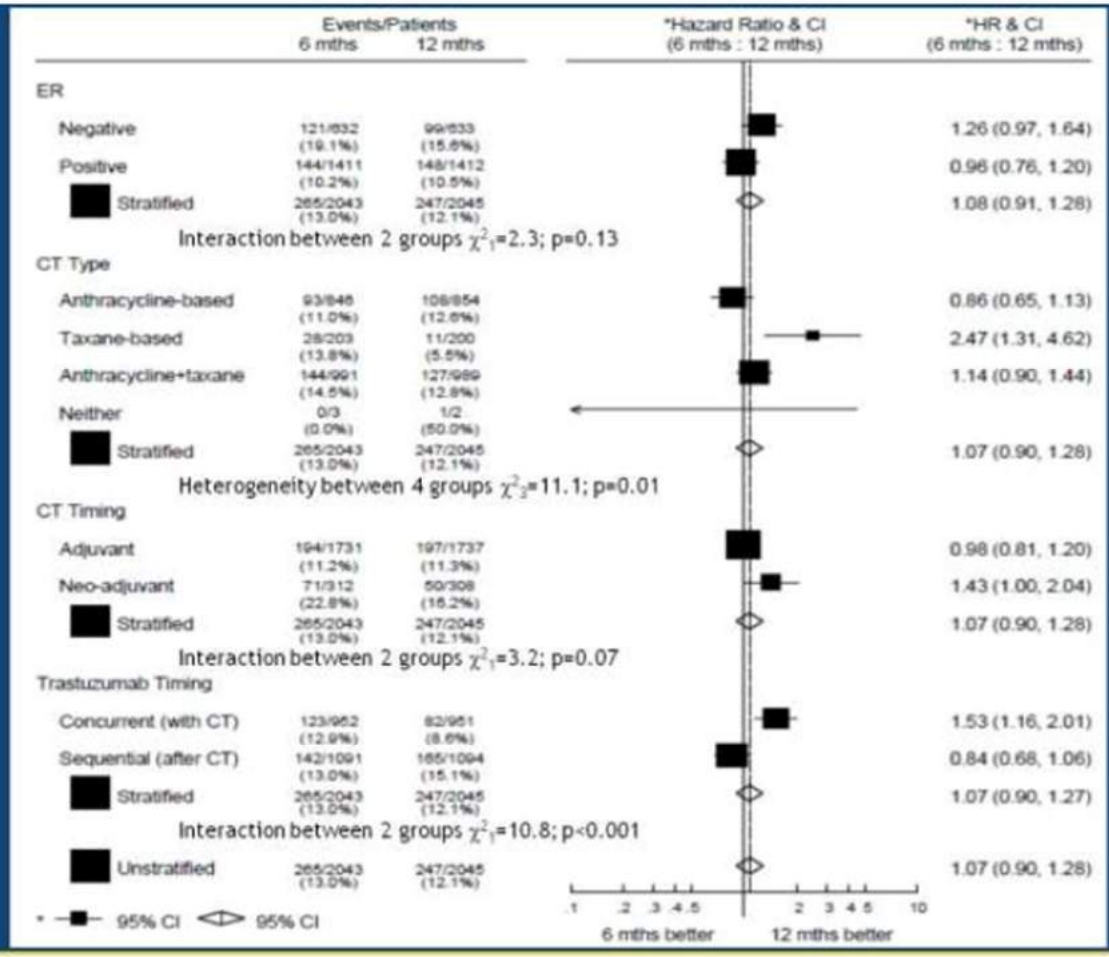
No. at Risk

12 months	2045	2013	1887	1666	1304	1012
6 months	2043	2007	1879	1647	1316	1016



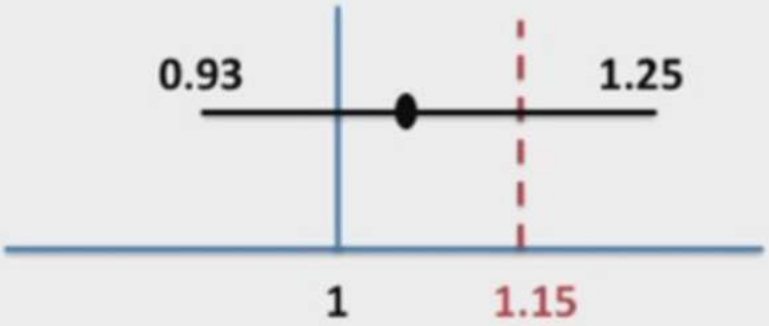
DFS:

Pre-defined subgroup analysis



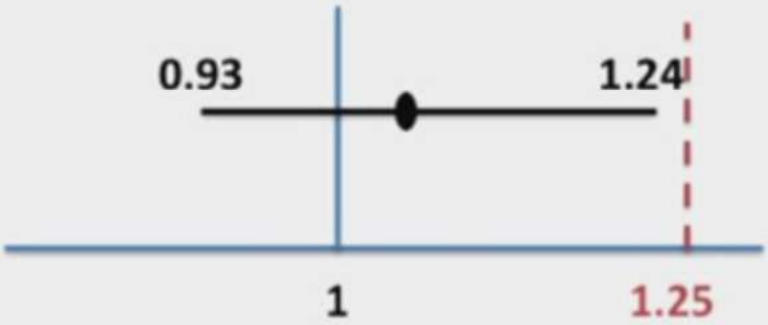
Conclusion

PHARE failed to show that 6 months of trastuzumab is non inferior to 12 months



HR: 1.08 (95%CI: 0.93-1.25) p=0.39

PERSEPHONE Showed that 6 months of trastuzumab is non inferior to 12 months



HR: 1.07 (90%CI: 0.93-1.24) p=0.01

San Antonio Breast Cancer Symposium®, December 4-8, 2018

Abs GS03-01. Randomized trial of low dose tamoxifen to prevent recurrence of breast intraepithelial neoplasia. Study TAM01

A.DeCensi*, M.Puntoni, A.Guerrieri Gonzaga, S.Caviglia, F.Avino, L.Cortesi, M.Donadio, M.Grazia Pacquola, F.Falcini, M.Gulisano, M.Digennaro, A.Carriello, K.Cagossi, G.Pinotti, M.Lazzeroni,D.Serrano, D.Branchi, S.Campora, M.Petrera, T.Buttiron Webber, L.Boni and B.Bonanni

Ente Ospedaliero Ospedali Galliera Genova
Ospedale di rilievo nazionale e di alta specializzazione

IEO Istituto Europeo di Oncologia

Queen Mary University of London

Barts and The London Queen Mary's School of Medicine and Dentistry

EudraCT Number
2007-007740-10
ClinicalTrials.gov
NCT01357772

Background

- **IEN** accounts for 15-25% of all breast neoplasms with heterogenous spectrum of disorders (ADH, DCIS, LCIS).
- **Dose de-escalation** now considered given lack of benefit of XRT+5 yr tamoxifen on mortality in DCIS.
- **Tamoxifen** side effects, including Endom Ca, DVT and menopausal symptoms, are a barrier for prevention.
- The **minimal active dose** of tamoxifen is unknown.
- **Our hypothesis:** a lower dose (5 mg/d) and a shorter duration (3y) was as effective and less toxic than 20 mg/d.

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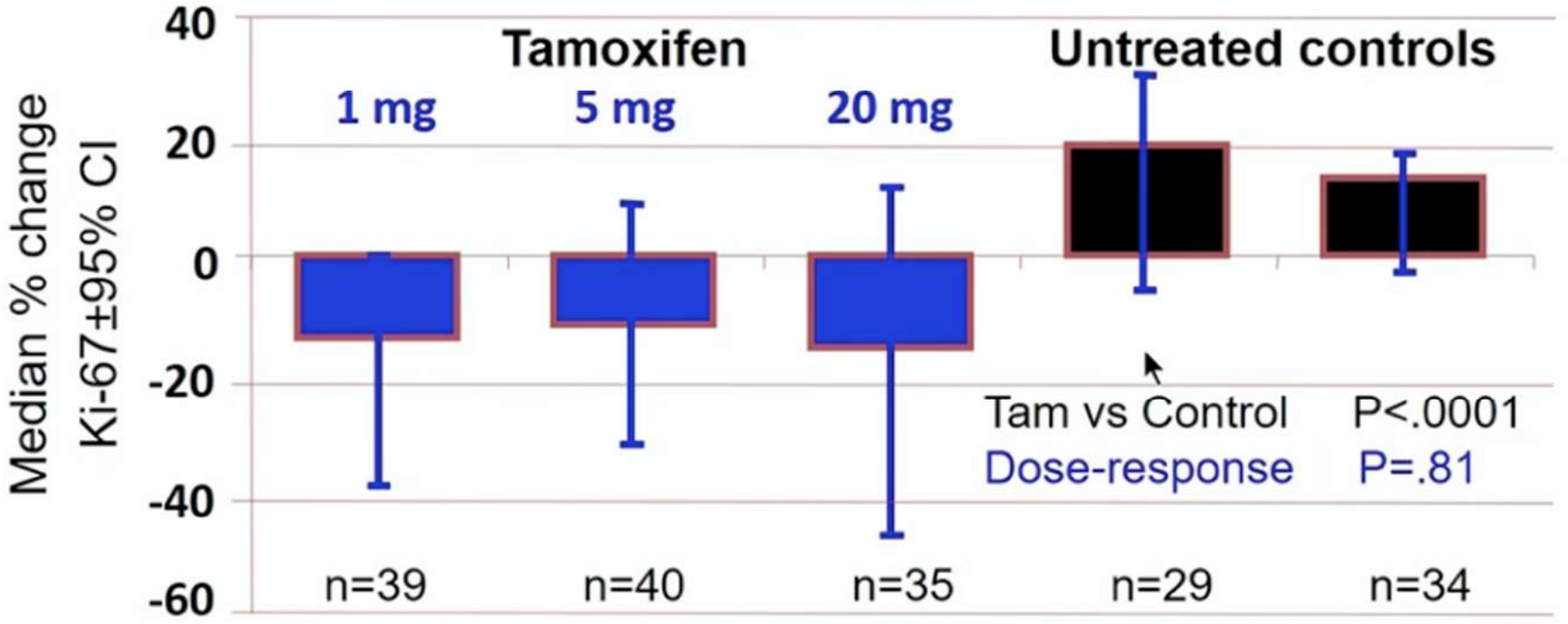
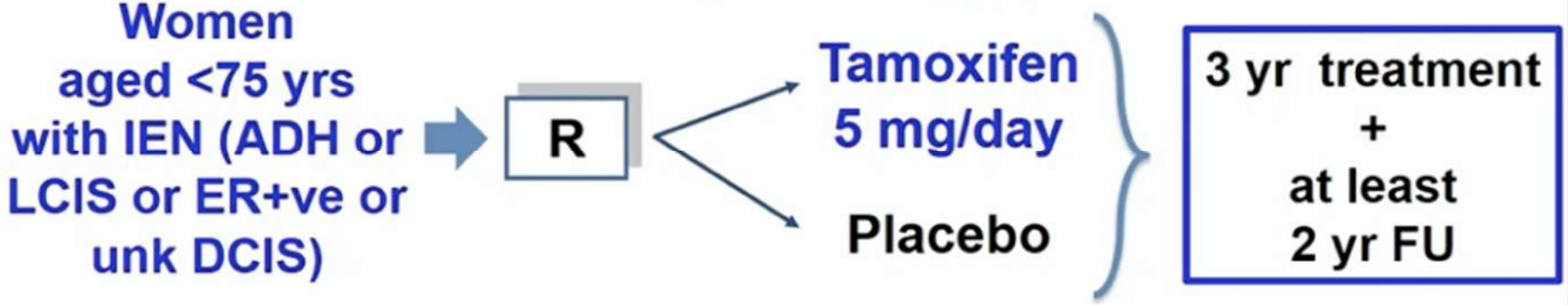
Lower doses non inferior to 20 mg/d in decreasing ki-67 in a randomized presurgical trial



DeCensi et al. *JNCI* 95: 779, 2003

Study Design



Primary endpoint: Incidence of invasive breast cancer or DCIS

- 500 participants enrolled from 14 centers in Italy
- Visit and QoL every 6 months, Mx every year
- Median follow up = 5.1 years (IQR 3.9-6.3)

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Main subject and tumor characteristics (n = 500)

	Tamoxifen N=253	Placebo N=247
Age, mean (SD)	54 (9.6)	54 (9.1)
Pre-menopausal, %	46	44
BMI, mean (SD)	25.7 (4.8)	25.3 (4.2)
ADH, %	20	20
LCIS, %	11	10
DCIS, %	69	70
ER/PR+ve/unknown, %	66 / 34	67 / 33
HER 2-neu 3+, %	8	9
Quadrantectomy/Mastectomy %	84 / 16	82 / 18
Radiotherapy, %	43	43

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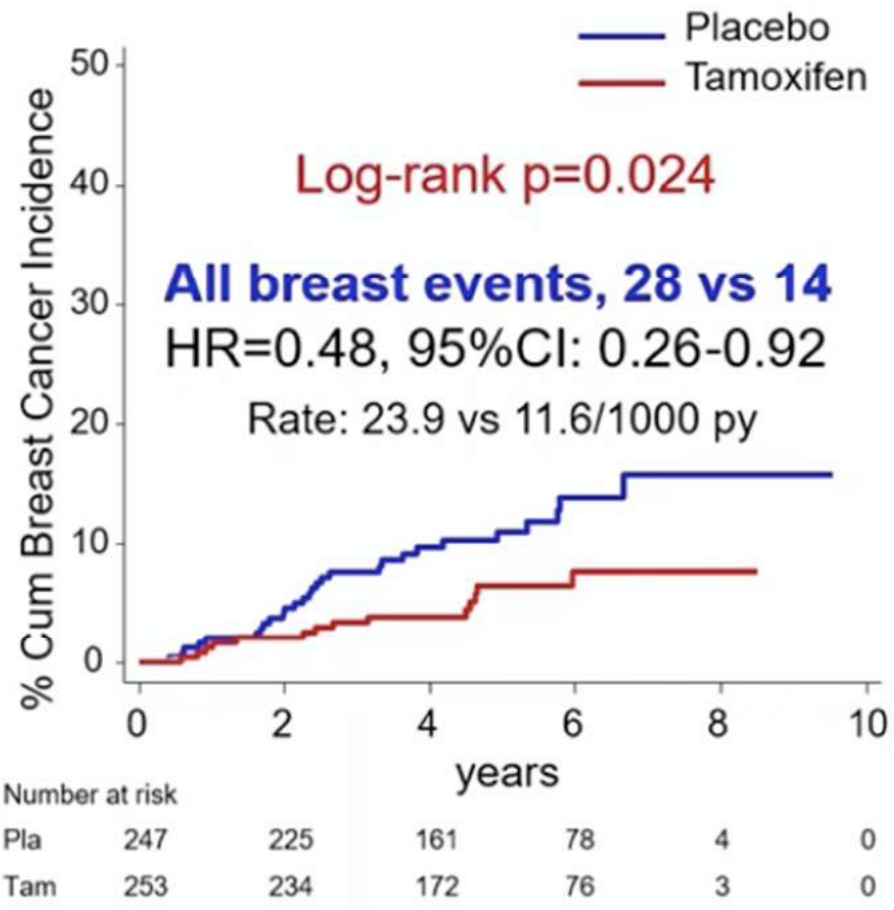

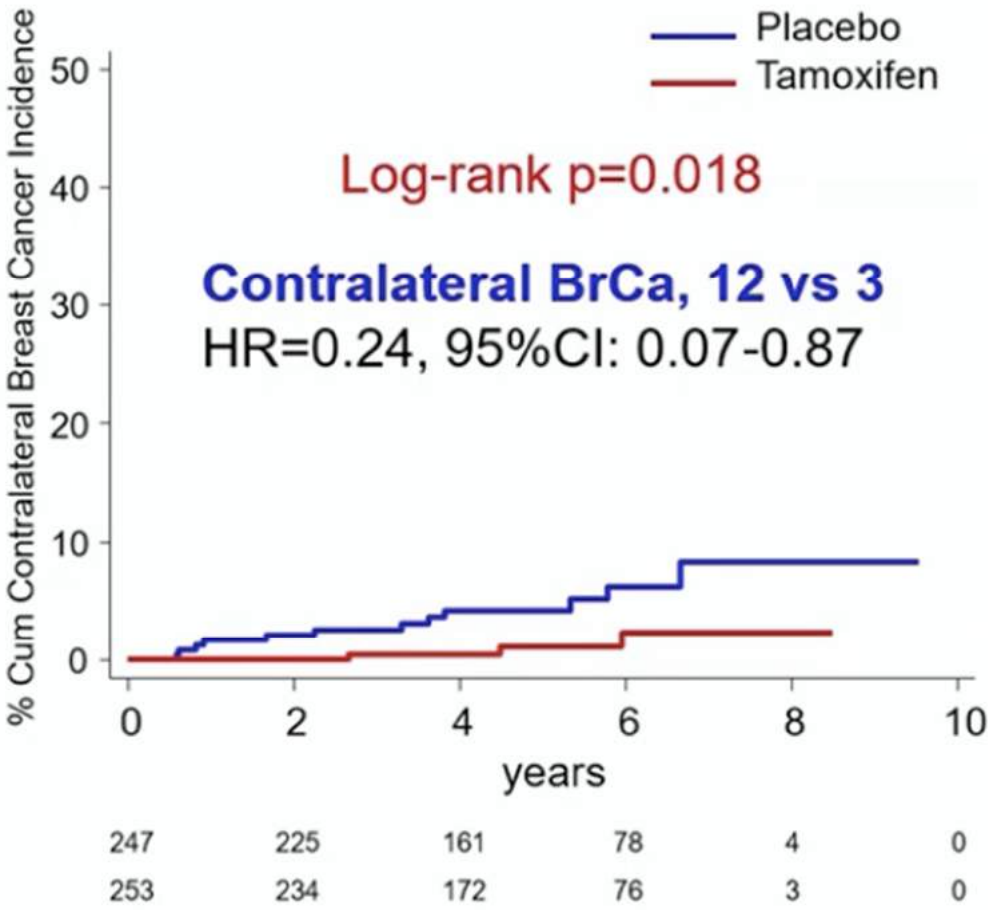

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Serious adverse events

	Tamoxifen	Placebo
Endometrial cancer	1	0
DVT or PE	1	1
Other neoplasms	4	6
Coronary heart disease	2	2
Other	3	5
Death	1	2
Total	12	16

20 mg/d, expected Endometrial Cancer: **2.7**; DVT+PE: **2.4**[1]

[1]NSABP-P1 trial (Fisher et al. *JNCI* 90:1371-88, 1998)

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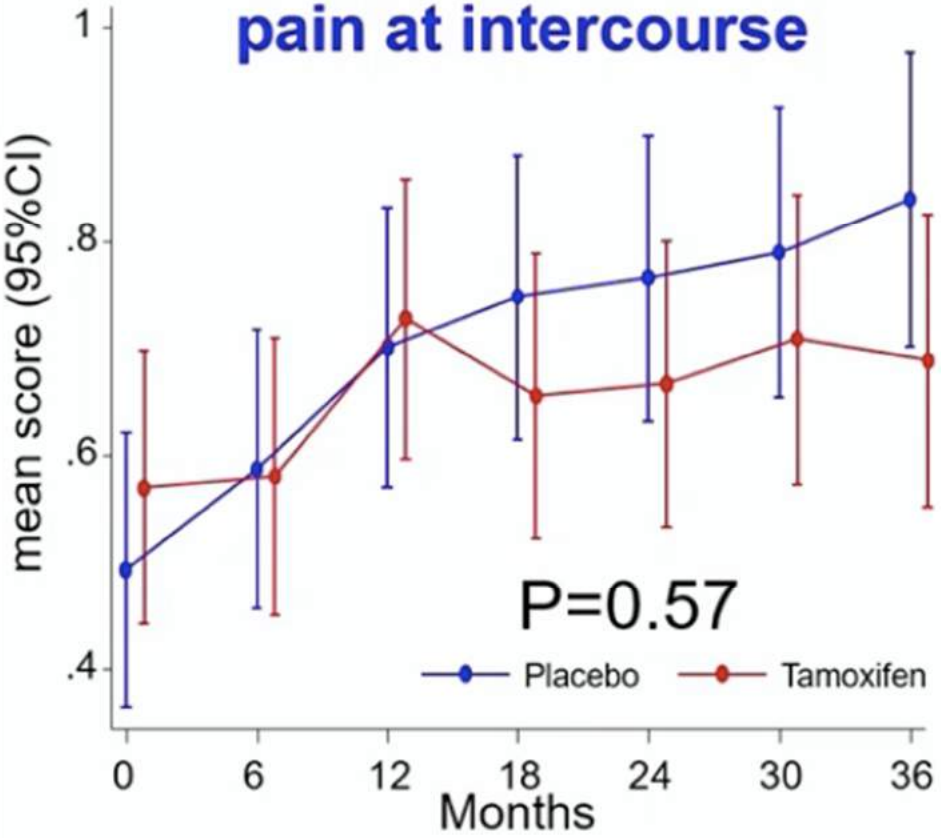
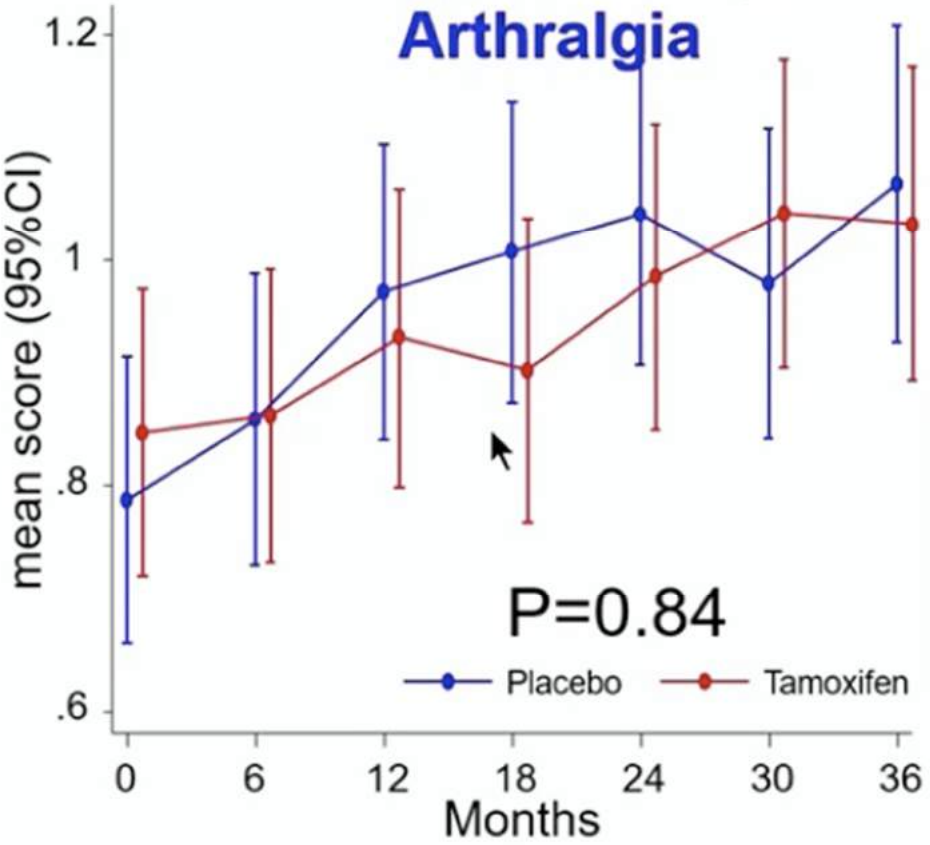
Vaginal dryness or pain at intercourse



Musculoskeletal pain/ Arthralgia



BCPSC, Stanton et al. *JNCI* 97:448-456, 2005

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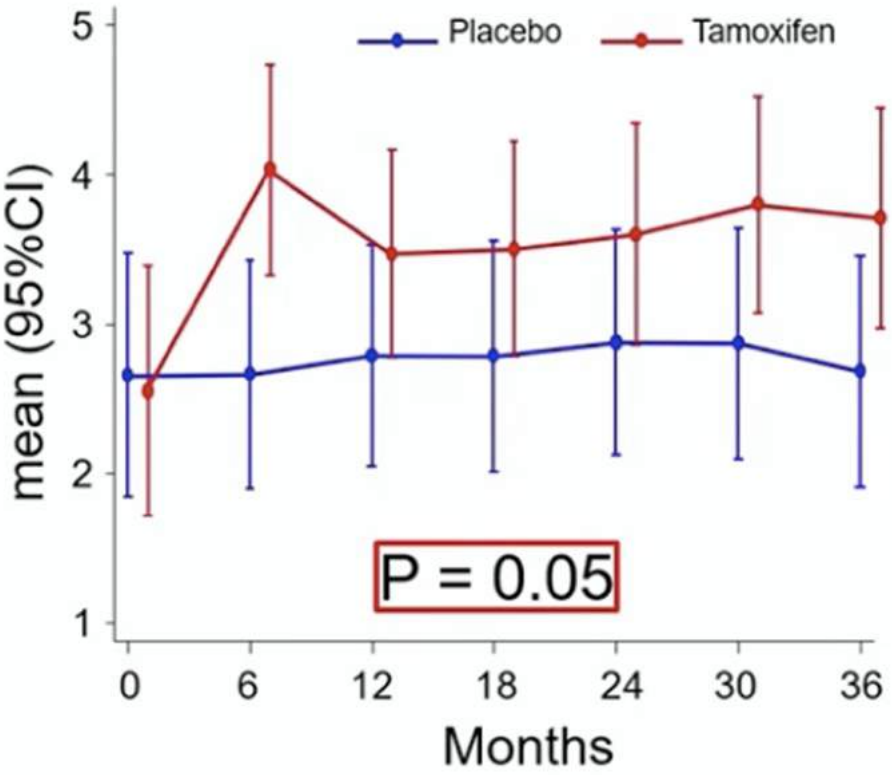
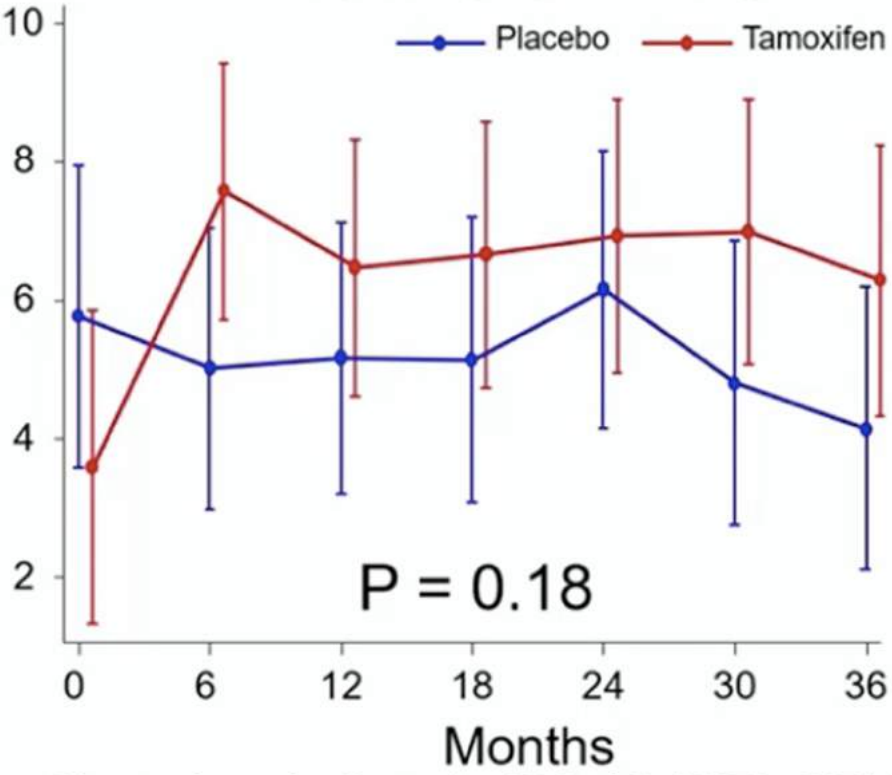
Daily hot flashes frequency



Daily hot flashes score

Frequency by Intensity



Sloan, Loprinzi et al. *JCO* 19:4280, 2001

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Estimate of treatment impact at 5 years

Number needed to treat*	22 (95% CI, 20-27)
Number needed to harm**	218 (95% CI, 193-265)
Likelihood of benefit	10 (218/22)

*5 year cumulative incidence of breast events: 6.4% on T and 11.0% on P
**5 year cumulative incidence of SAE: 0.87% on T and 0.41% on P

Conclusions

- Tamoxifen 5 mg/day for 3 years **halves the recurrence** of breast intraepithelial neoplasia in line with 20 mg/day (HR=0.58, 95% CI, 0.42-0.81)[1]
- Low dose Tamoxifen decreased contralateral breast cancer by 75%, suggesting a **strong preventive** potential
- Rate of endometrial cancer and DVT/PE on 5 mg (0.85/1000 py) **not different from placebo** and **2.5 times lower** than 20 mg[2]
- **Menopausal symptoms not worsened** except for a borderline effect on hot flashes
- Our results have external validity and are **generalizable**

[1]Allred et al. NSABP B-24 trial. *JCO* 30:1268-73, 2012
[2]Fisher et al. NSABP-P1 trial. *JNCI* 90:1371-88, 1998

Tamoxifen for Prevention of Breast Cancer: Report of the National Surgical Adjuvant Breast and Bowel Project P-1 Study

Bernard Fisher, Joseph P. Costantino, D. Lawrence Wickerham, Carol K. Redmond, Maureen Kavanah, Walter M. Cronin, Victor Vogel, André Robidoux, Nikolay Dimitrov, James Atkins, Mary Daly, Samuel Wieand, Elizabeth Tan-Chiu, Leslie Ford, Norman Wolmark, and other National Surgical Adjuvant Breast and Bowel Project Investigators

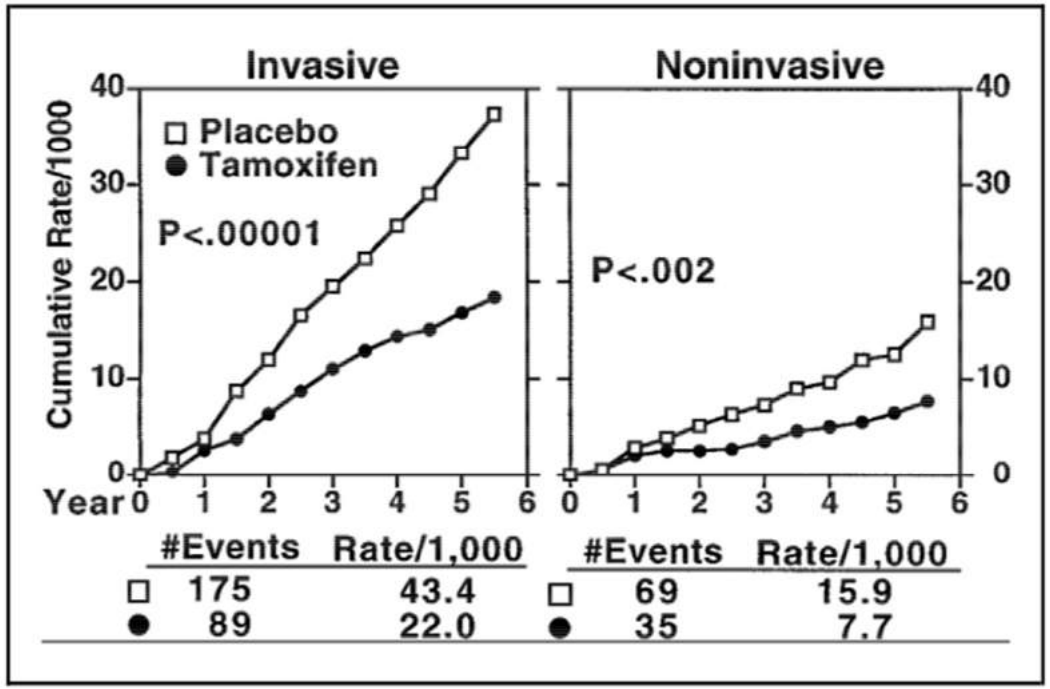


Fig. 2. Cumulative rates of invasive and noninvasive breast cancers occurring in participants receiving placebo or tamoxifen. The *P* values are two-sided.

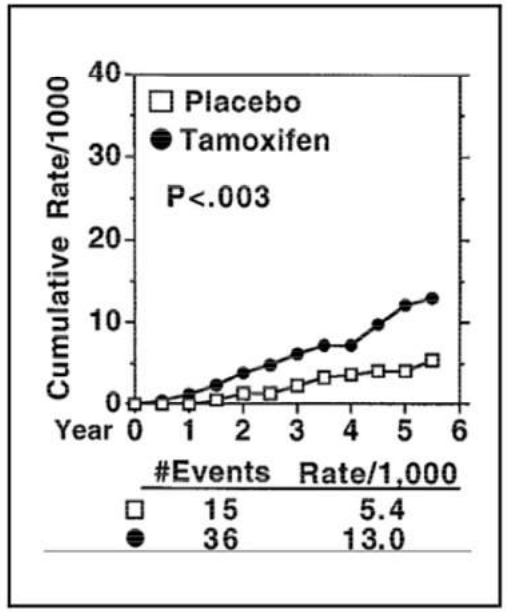


Fig. 5. Cumulative rates of invasive endometrial cancer occurring in participants receiving placebo or tamoxifen. The *P* value is two-sided.

Reduçao 49%

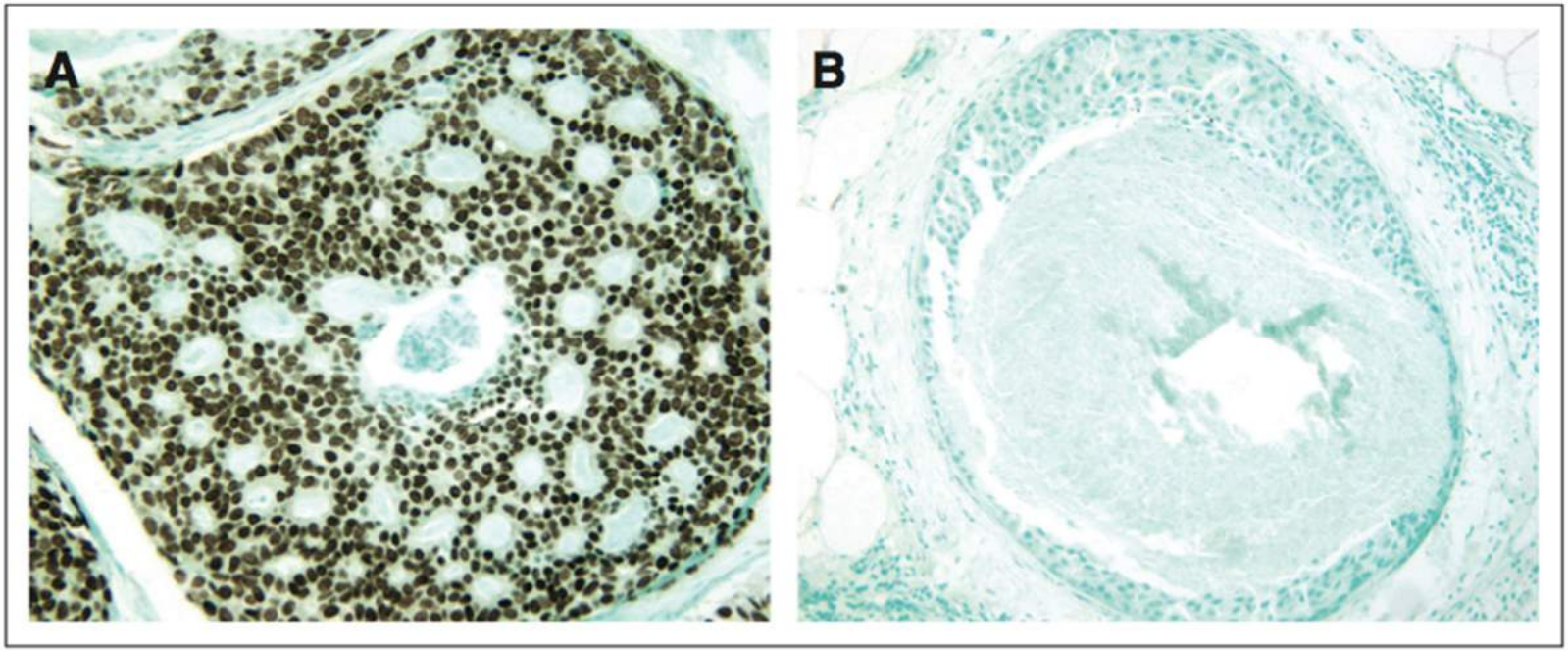
VOLUME 30 · NUMBER 12 · APRIL 20 2012

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Adjuvant Tamoxifen Reduces Subsequent Breast Cancer in Women With Estrogen Receptor–Positive Ductal Carcinoma in Situ: A Study Based on NSABP Protocol B-24

D. Craig Allred, Stewart J. Anderson, Soonmyung Paik, D. Lawrence Wickerham, Iris D. Nagtegaal, Sandra M. Swain, Elefetherios P. Mamounas, Thomas B. Julian, Charles E. Geyer Jr, Joseph P. Costantino, Stephanie R. Land, and Norman Wolmark



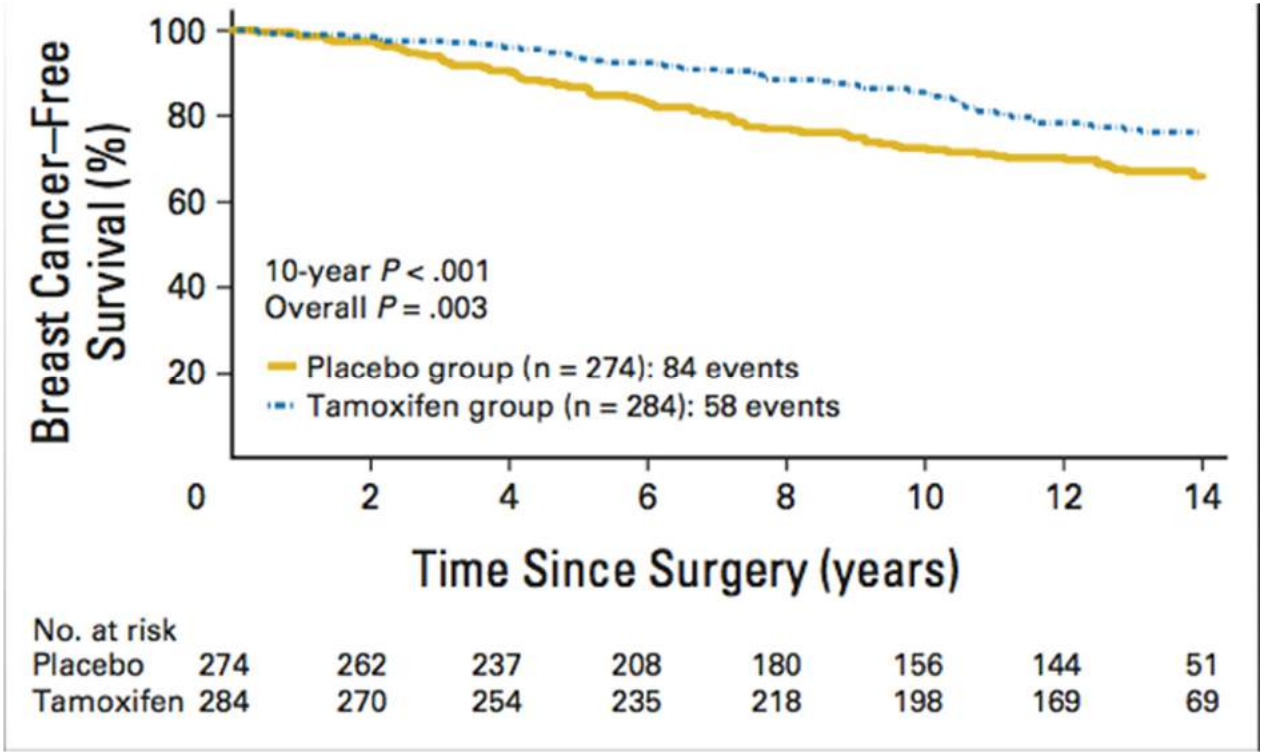


Table 3. Multivariate Analyses* of Patients With DCIS in NSABP B-24

Model Variable†	Time to Any Breast Cancer As First Event		
	HR	95% CI	*P*
Patients with known ER status (n = 732)			
Treatment (placebo‡ *v* tamoxifen)	0.643	0.481 to 0.861	.003
Age at entry, years (≤ 49‡ v ≥ 50)	0.609	0.457 to 0.812	< .001
All patients with follow-up (n = 1,799)			
Treatment (placebo‡ *v* tamoxifen)	0.687	0.563 to 0.837	< .001
Age at entry, years (≤ 49‡ v ≥ 50)	0.621	0.510 to 0.756	< .001

Table 4. Cumulative Incidence of Developing Subsequent Breast Cancer After Treatment at 10 Years in Patients With ER-Negative DCIS in NSABP B-24*

Event	Placebo (%)	Tamoxifen (%)	HR	95% CI	*P*†
Any breast cancer					
Total	25	21	0.84	0.45 to 1.58	.59
Central	23	27	1.09	0.47 to 2.51	.85
Institutional	28	15	0.58	0.22 to 1.56	.28
Ipsilateral breast cancer					
Total	18	21	1.06	0.51 to 2.20	.87
Central	19	24	1.23	0.48 to 3.20	.67
Institutional	16	18	0.84	0.27 to 2.66	.77

SAN ANTONIO BREAST CANCER SYMPOSIUM

SABCS, December 4 -8, 2018

Extended Aromatase Inhibitor treatment following 5 or more years of endocrine therapy: a meta-analysis of 22,192 women in 11 randomised trials

Early Breast Cancer Trialists' Collaborative Group

All authors declare no relevant conflict of interest

SAN ANTONIO BREAST CANCER SYMPOSIUM

Extended AI treatment after 5+ years of prior endocrine therapy: methods

Meta-analysis of individual patient data on postmenopausal women with ER-positive (99%) or ER-unknown (1%) tumours in trials of:

Any third-generation AI (exemestane, anastrozole, letrozole) vs no further adjuvant therapy **following**:

a) ≈ 5 years of tamoxifen alone (n=7,500)

b) ≈ 5-10 years of tamoxifen then AI (n=12,600)

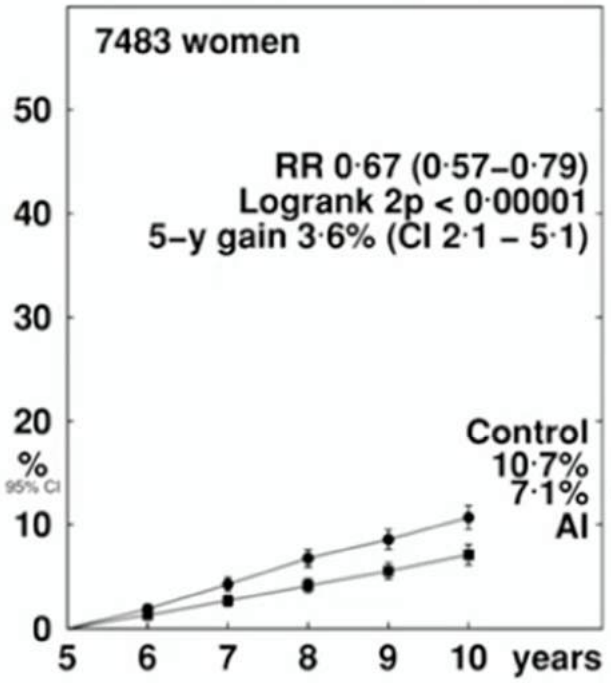
c) ≈ 5 years of AI alone (n=4,800)

Endocrine treatment prior to treatment divergence

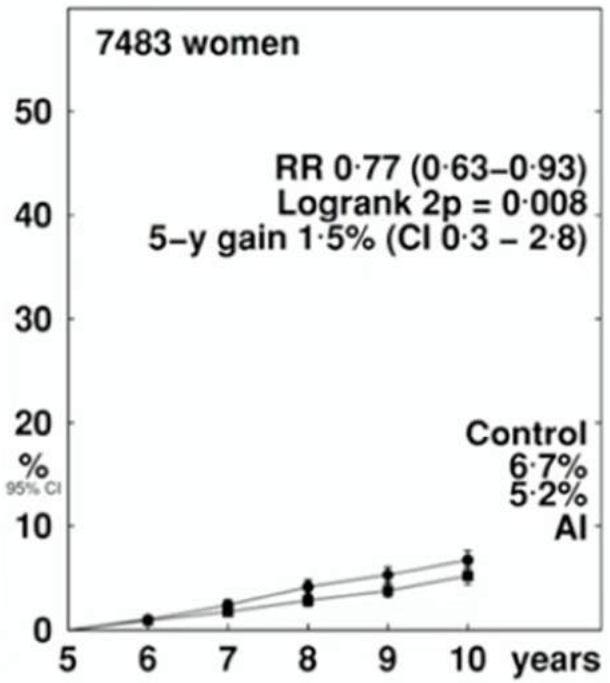
Trial (recruitment period)	(a) Tamoxifen alone	(b) Tamoxifen then AI	(c) AI alone
ABCSG VIa (1990–1995)	442	393	-
MA.17 (1998–2002)	4959	-	-
NSABP B-33 (2001–2003)	1550	-	-
ATENA (2001–2005)	358	-	-
SALSA (2004–2010)	-	3392	-
GIM 4 (2005–2015)	-	2031	-
NSABP B-42 (2006–2010)	-	1532	2387
DATA (2006–2009)	-	1827	-
LATER (2007–2012)	174	138	39
IDEAL (2007–2011)	-	1263	510
AERAS (2007–2012)	-	(≈255)	(≈1442)
MA.17R (2009–2015)	-	1473	386
All trials (% with data)	**7,483 (100%)**	**12,304 (98%)**	**4764 (70%)**
Median follow-up (yrs)	**4.9**	**6.1**	**6.5**

(a) Trials of AI after ≈5 years of Tamoxifen alone

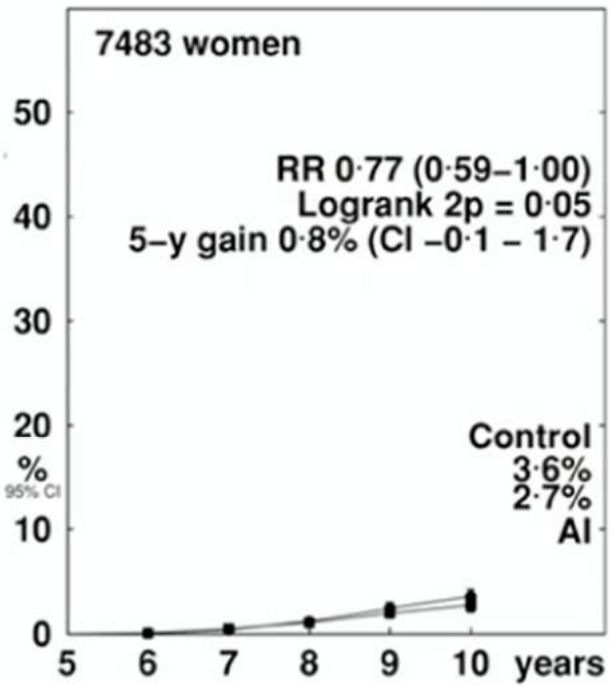
Any recurrence (distant, local or new primary)



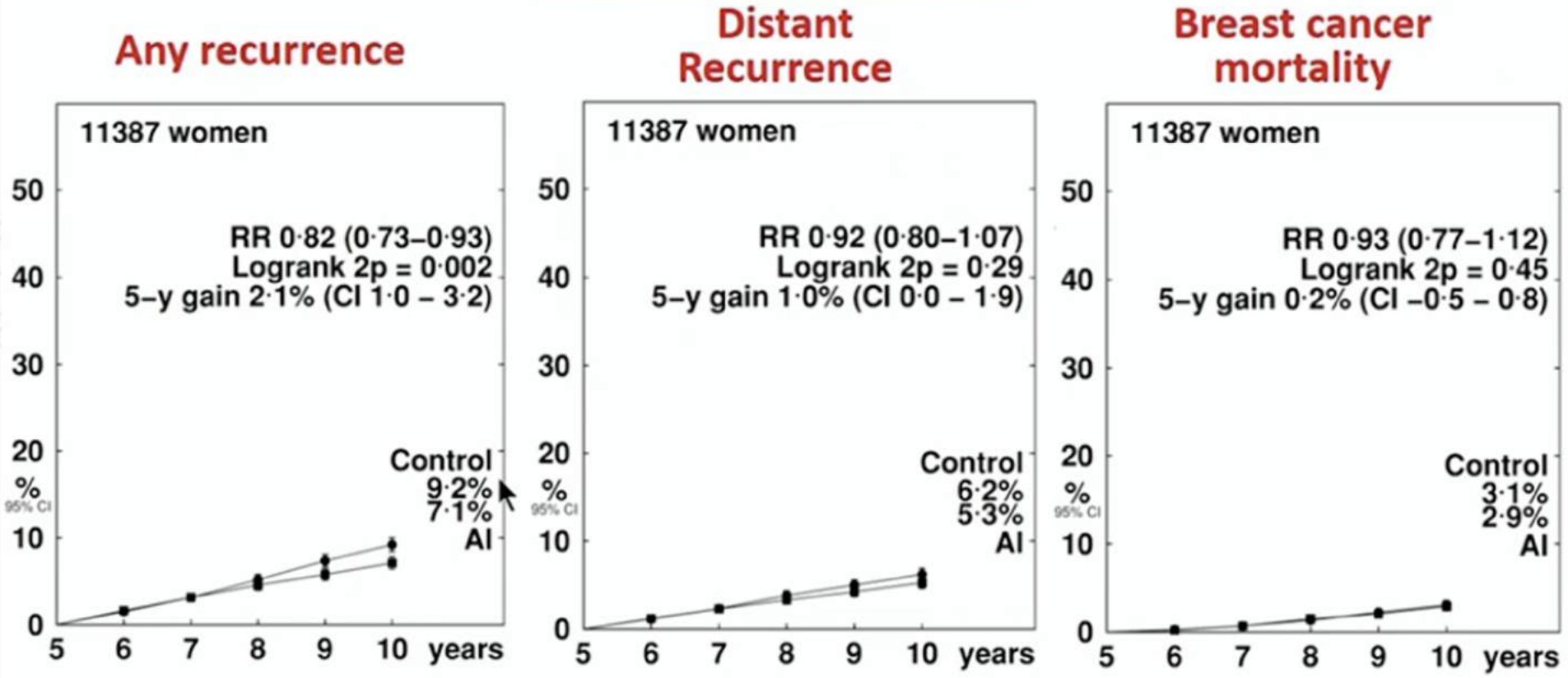
Distant Recurrence



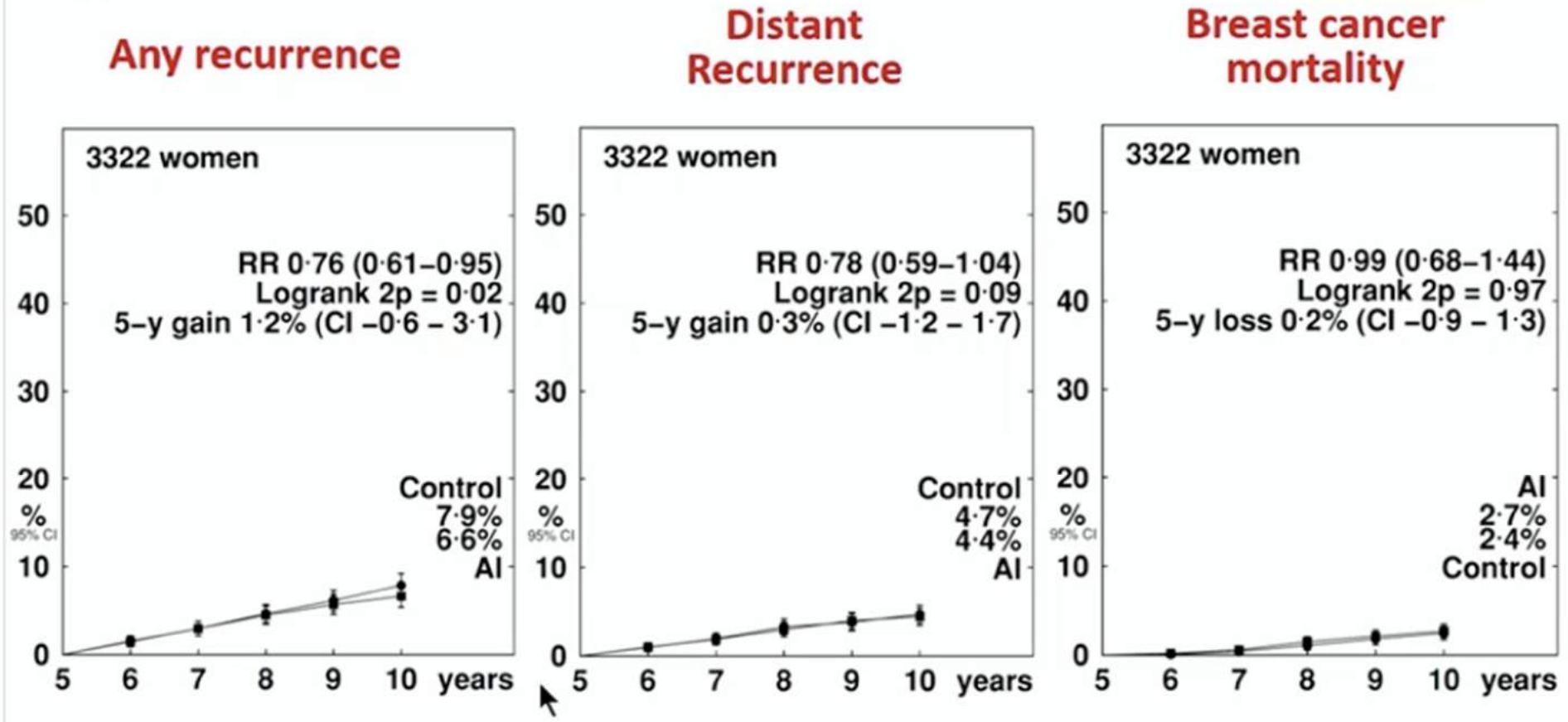
Breast cancer mortality



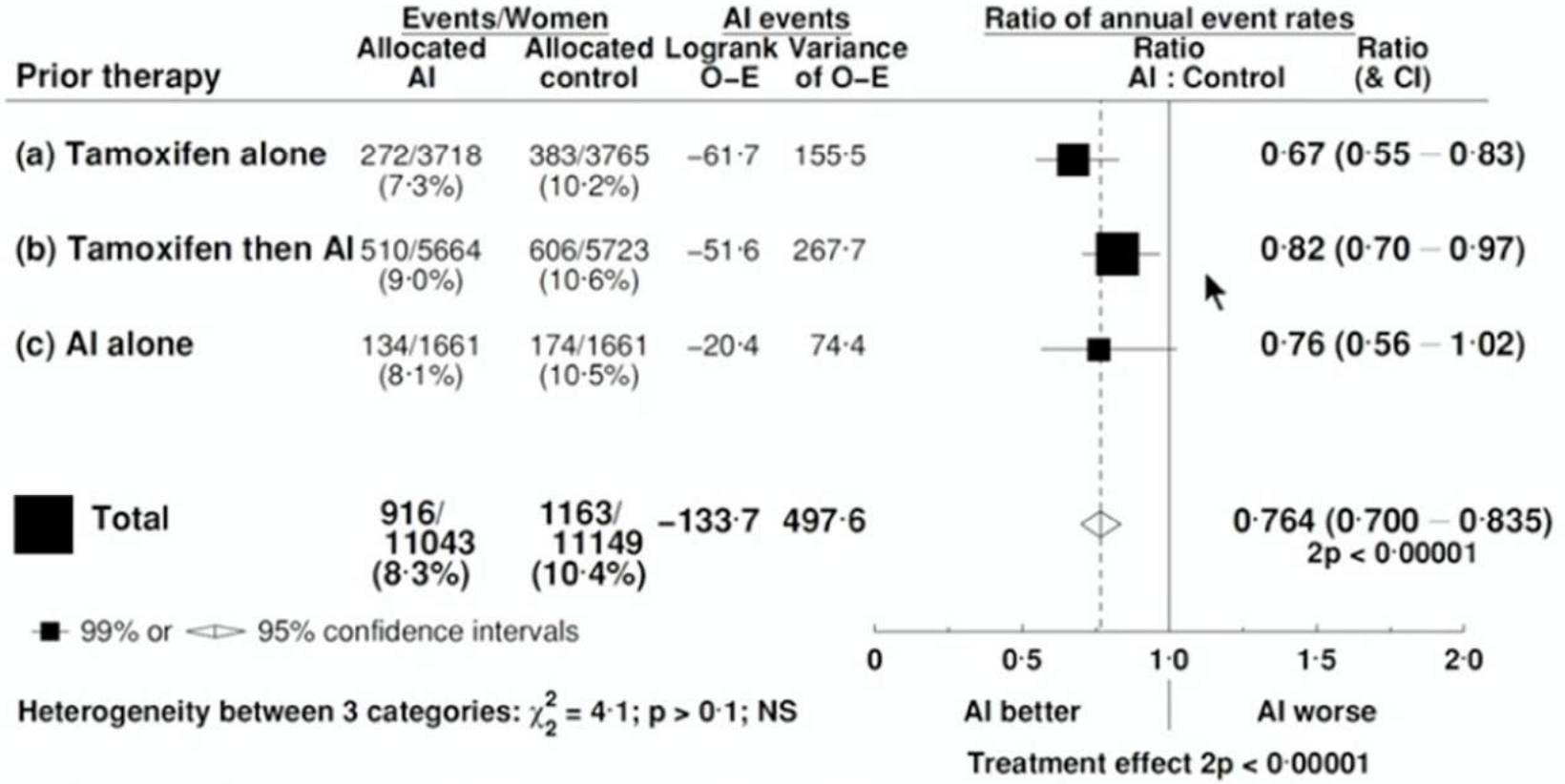
(b) Trials of Extended AI following 5-10 years of Tamoxifen then AI



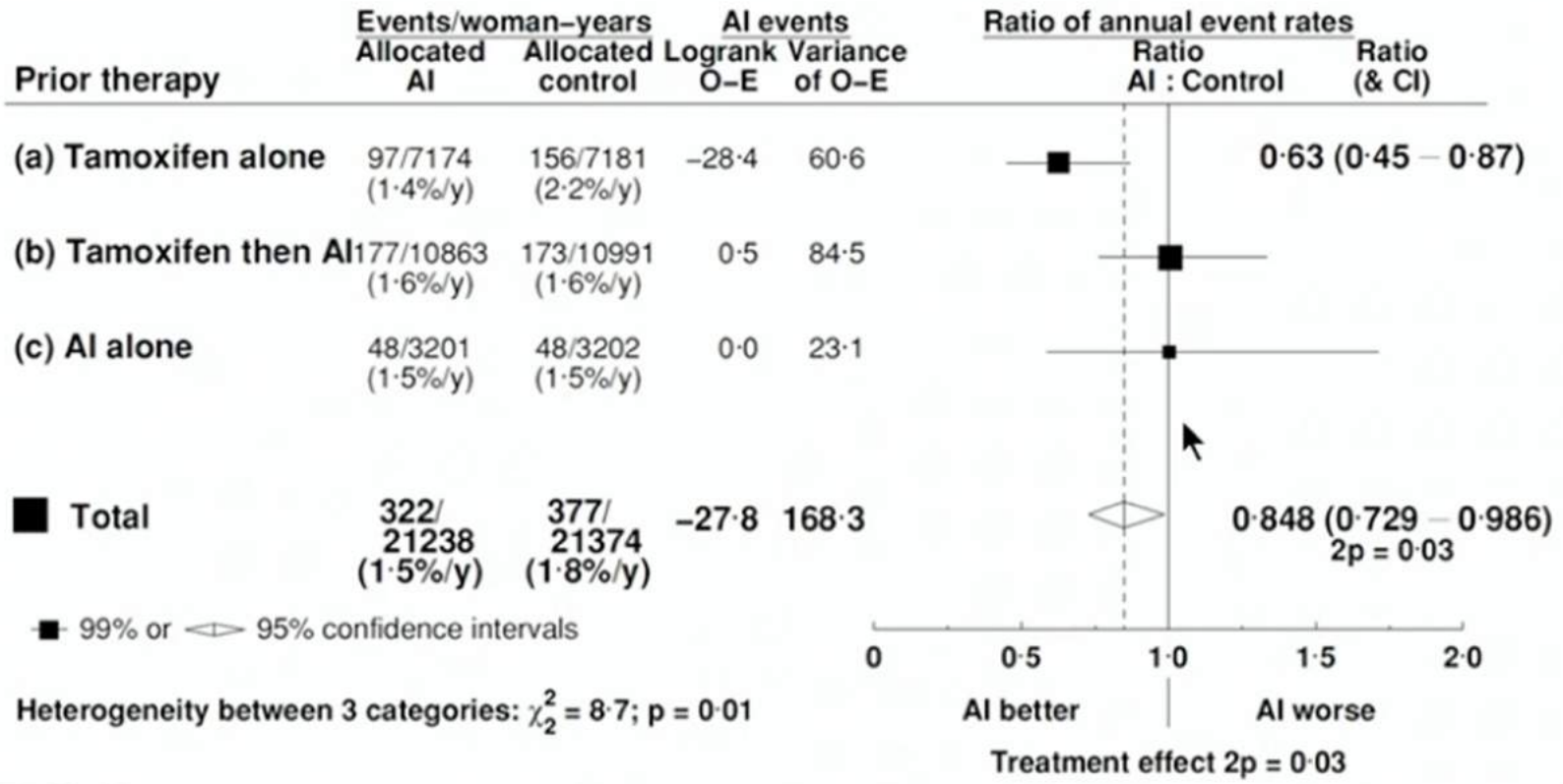
(c) Trials of Extended AI following 5 years of AI alone



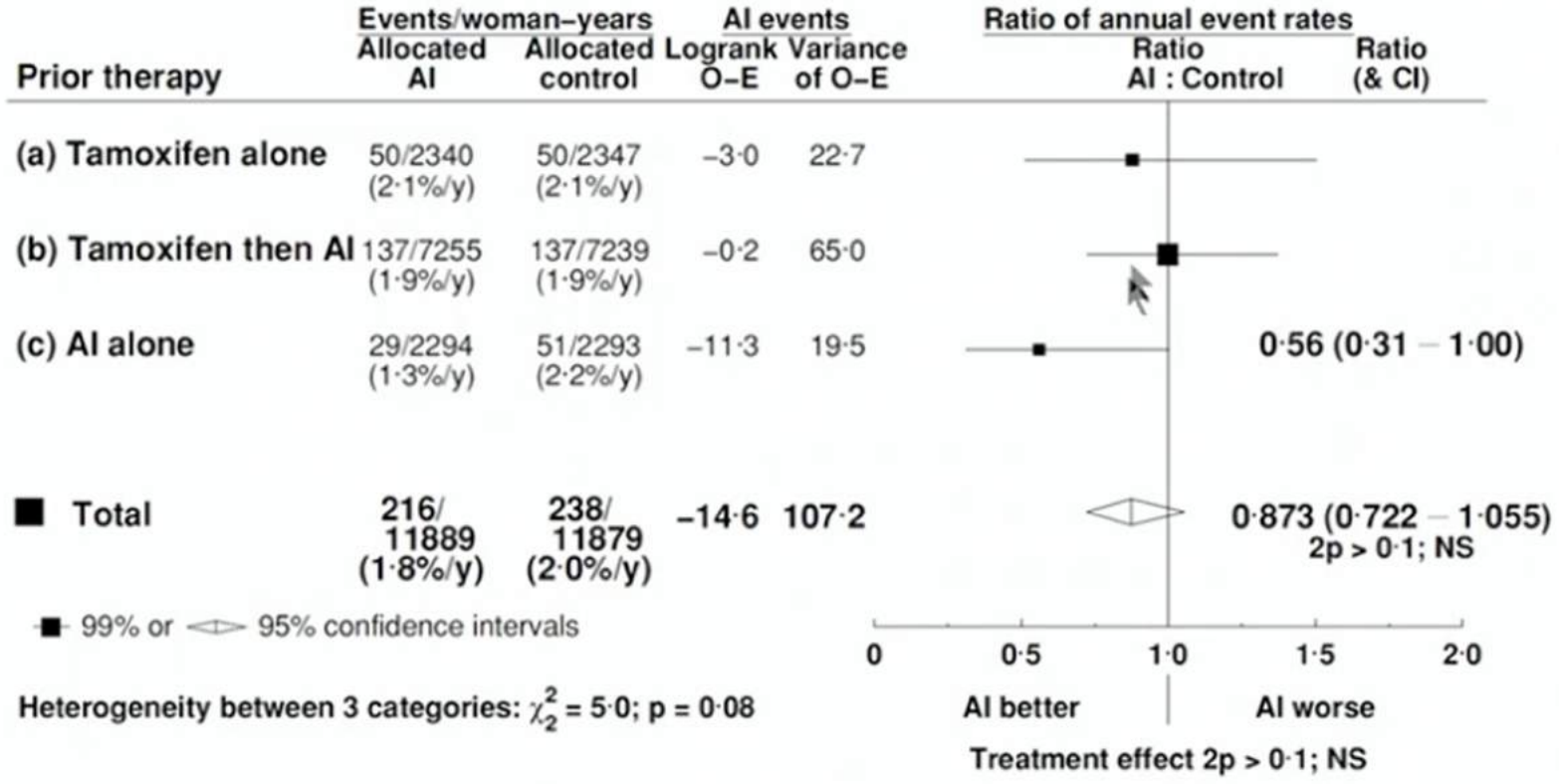
Effect on recurrence by prior endocrine therapy



Effect on recurrence in years 0-1 after treatment divergence by prior endocrine therapy

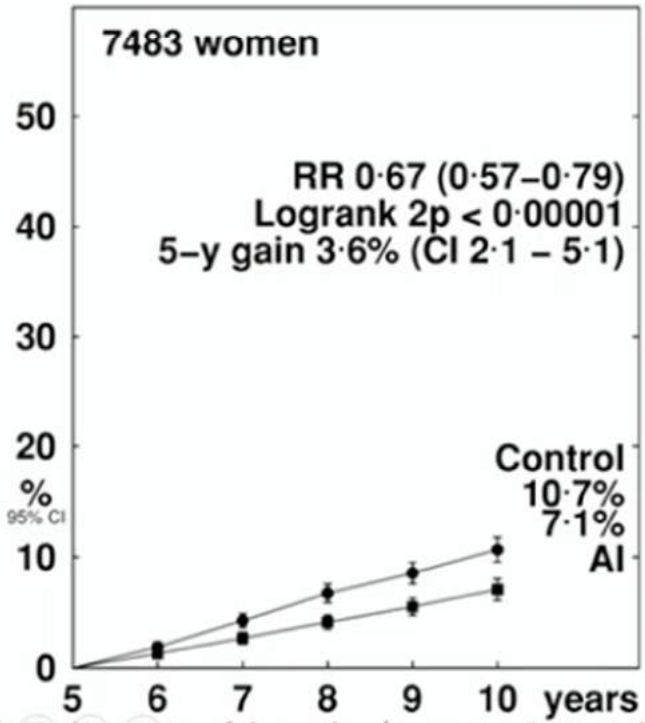


Effect on recurrence in years 5+ after treatment divergence by prior endocrine therapy

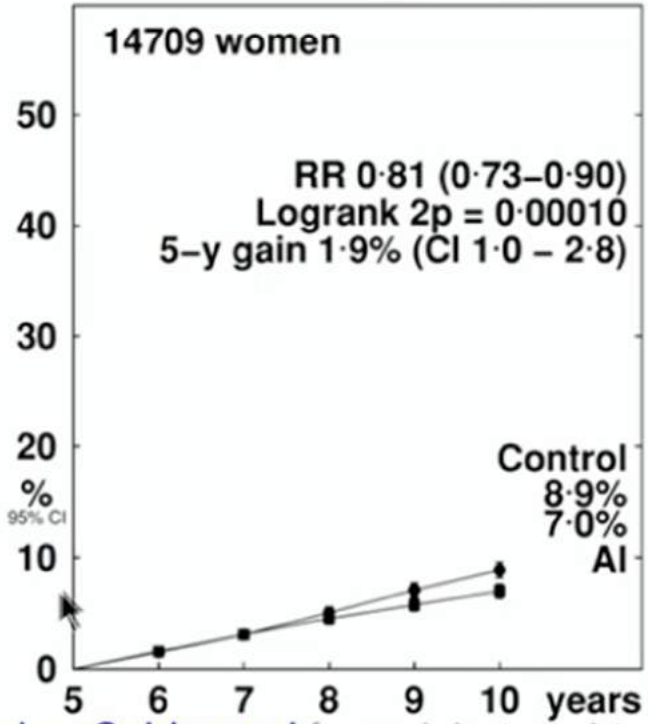


Summary: effect of extended AI therapy after 5-10 yrs on recurrence differs by type of prior endocrine therapy

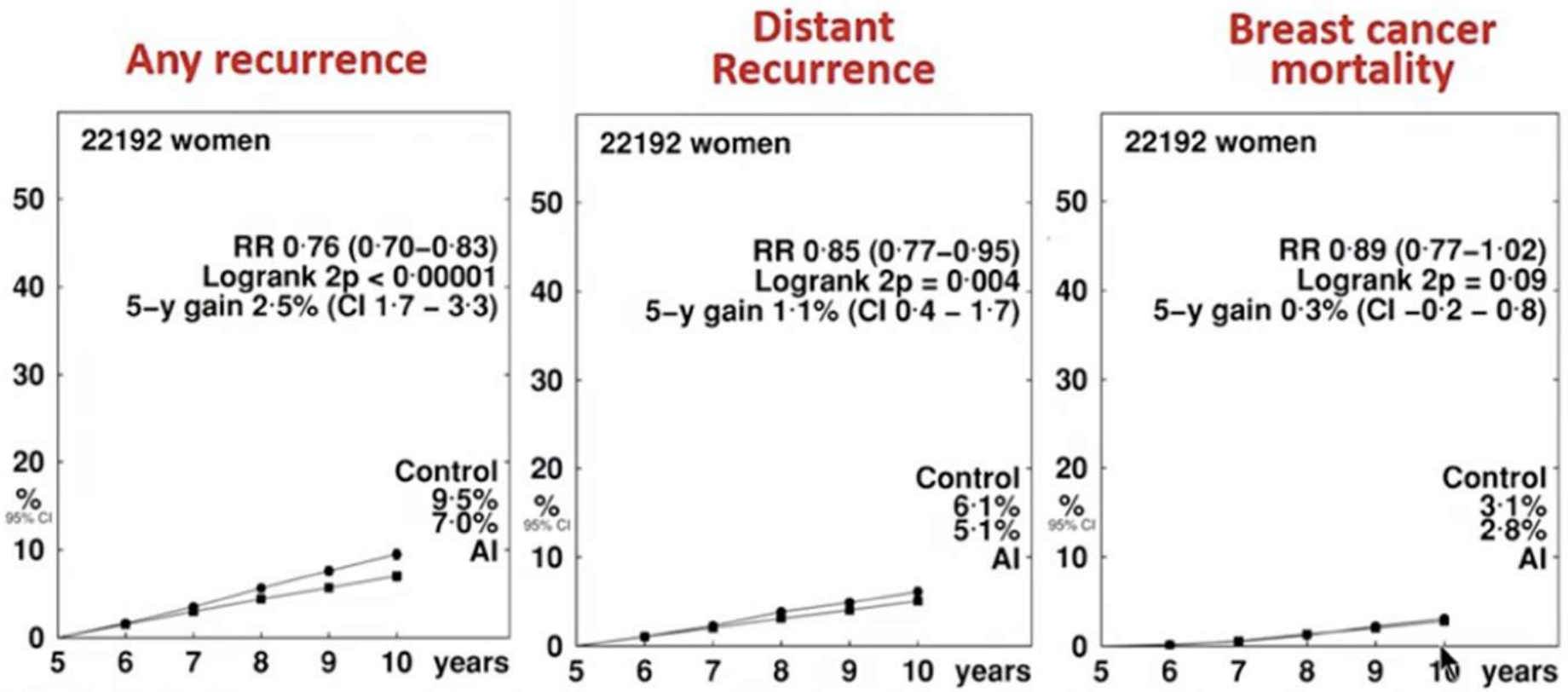
Prior tamoxifen (a)



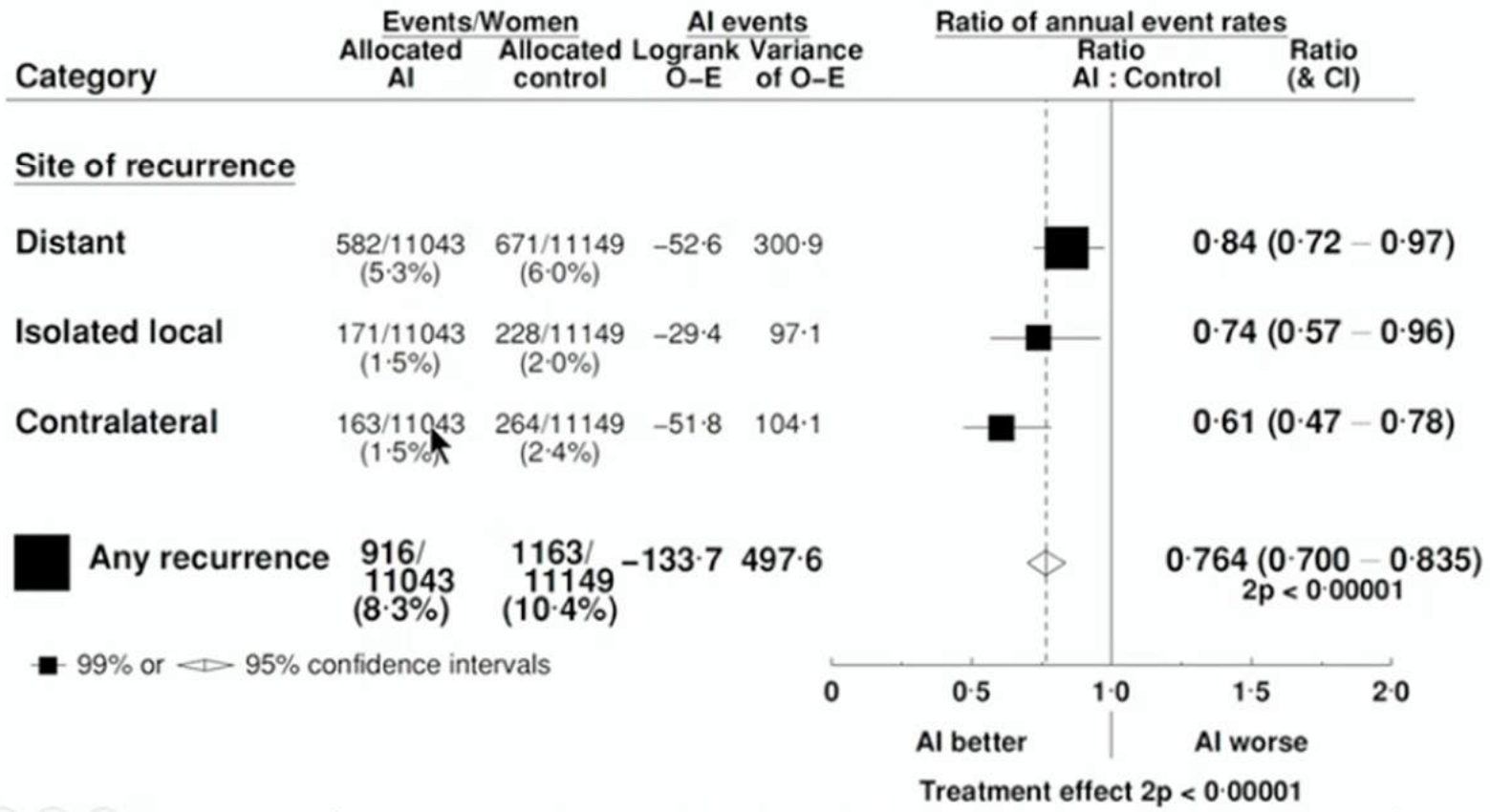
Prior AI (b + c)



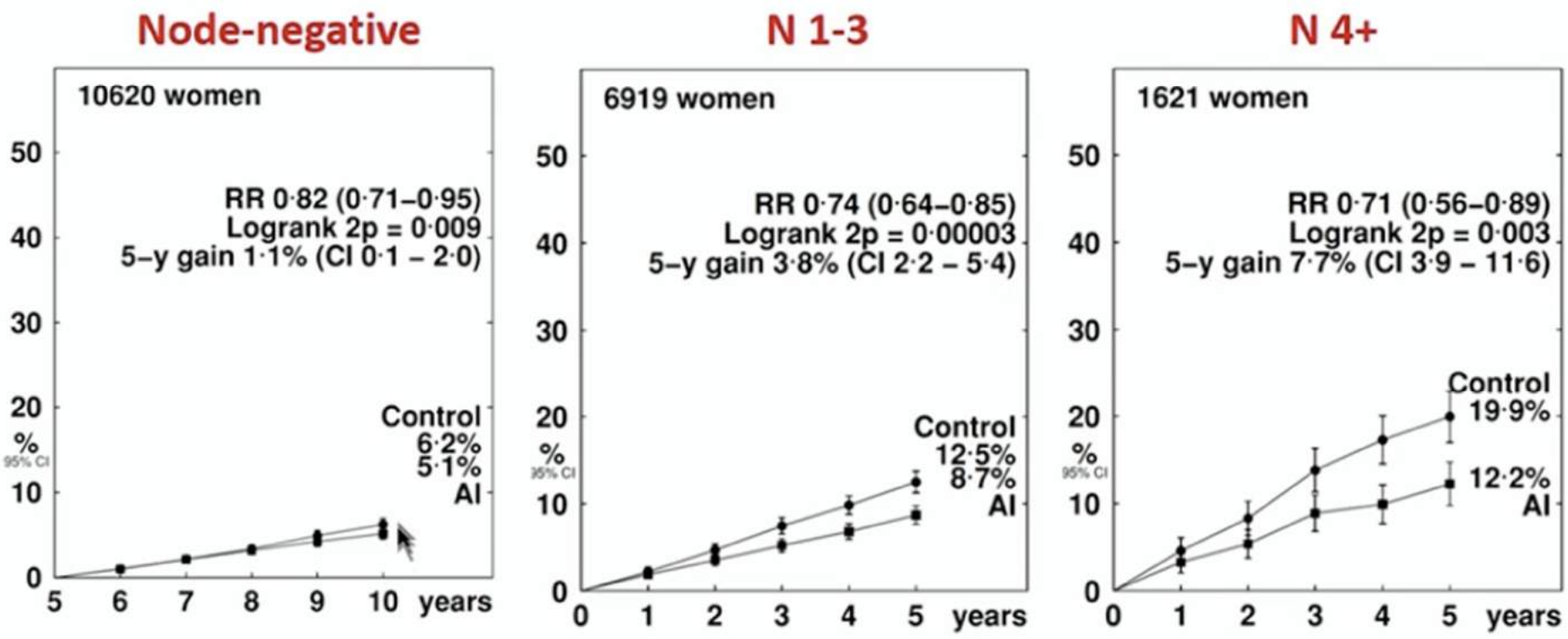
Combined results from all trials of Extended AI following 5-10 years of any prior endocrine therapy



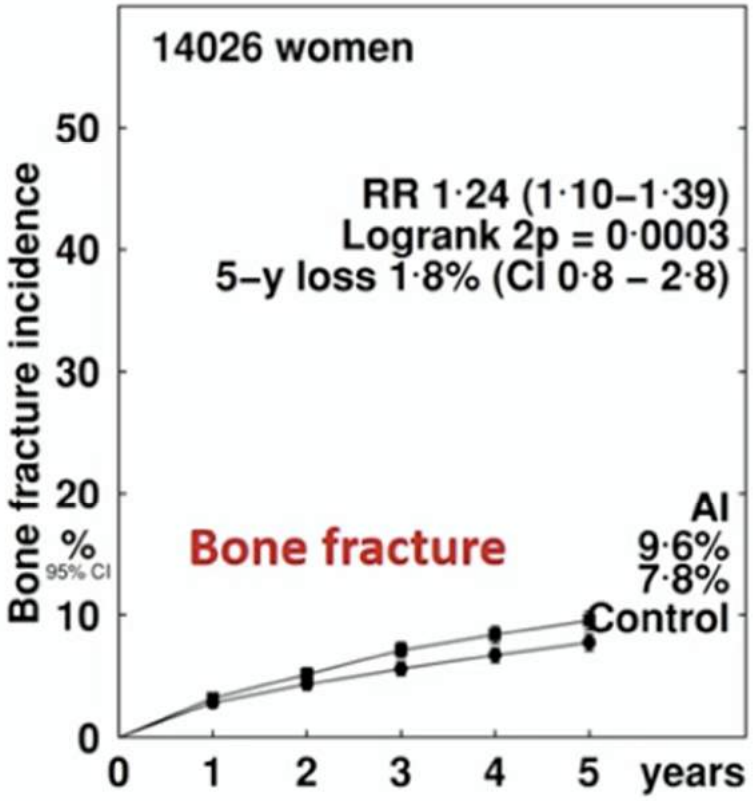
Recurrence by site – combined results from all trials

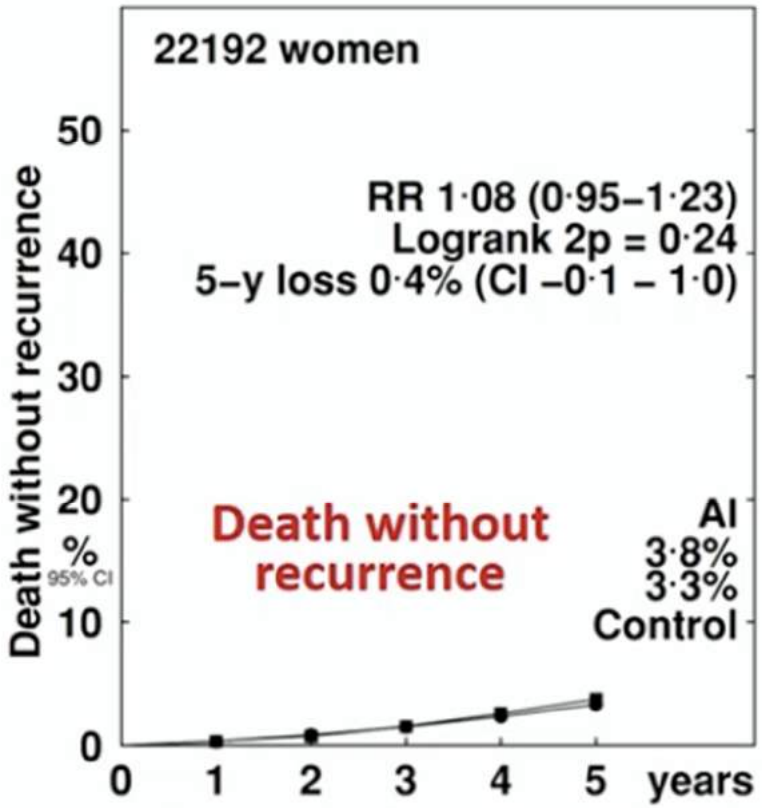


Recurrence by nodal status – all trials



Bone fracture and death without recurrence





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Conclusions: Benefits and risks of AI after 5+ years of prior endocrine therapy

- ≈35% proportional reduction in recurrence for women who have received ≈5 years of tamoxifen
- ≈ 20% proportional reduction in risk of recurrence for women receiving AI (with or without prior tamoxifen)
- Recurrence reductions apparent in first two years following prior tamoxifen, but not until the third year following prior AI
- Absolute benefits increase the more nodes were involved
- Risk of bone fracture increased by ≈25%

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Limitations

- Short follow-up: 10 or more years of follow-up is needed to assess the effects of extending AI on breast cancer mortality
- Need to obtain more information on side-effects, for example bone fractures
- Impact of AIs on Quality of Life was not assessed
- One trial (AERAS) still to be included

2018
DECEMBER 4-8
HENRY B. GONZALEZ CONVENTION CENTER, SAN ANTONIO, TEXAS, USA

SAN ANTONIO BREAST CANCER SYMPOSIUM®

A PROSPECTIVE RANDOMIZED MULTI-CENTER OPEN-LABEL PHASE Ⅲ TRIAL OF EXTENDING AROMATASE-INHIBITOR ADJUVANT THERAPY TO 10 YEARS - RESULTS FROM 1697 POSTMENOPAUSAL WOMEN IN THE N-SAS BC 05 TRIAL: ARIMIDEX EXTENDED ADJUVANT RANDOMIZED STUDY (AERAS)

Shoichiro Ohtani[1], Kotaro Iijima[2], Kenji Higaki[1], Yasuyuki Sato[3], Yasuo Hozumi[4], Yoshie Hasegawa[5], Hiroyuki Takei[6], Maki Tanaka[7], Hiroshi Yagata[8], Hideji Masuoka[9], Masahiko Tanabe[2], Chiyomi Egawa[10], Yoshifumi Komoike[11], Shigehira Saji[12], Toshitaka Nakamura[13], Yasuhiro Yanagita[14], Hiroshi Ohtsu[15], Hirofumi Mukai[16], Takuji Iwase[2]

[1]Hiroshima City Hiroshima Citizens Hospital, Hiroshima, [2]The Cancer Institute Hospital Of JFCR, Tokyo, [3]National Hospital Organization Nagoya Medical Center, Nagoya [4]University of Tsukuba Hospital /Ibaraki Prefectural Central Hospital, Tsukuba/Kasama, [5]Hirosaki municipal hospital, Hirosaki, [6]Saitama Cancer Center, Ina, [7]JCHO Kurume General Hospital, Kurume, [8]Saitama medical center, Saitama Medical University, Kawagoe, [9]Sapporo Kotoni Breast Clinic, Sapporo, [10]Kansai Rosai Hospital, Amagasaki, [11]Osaka International Cancer Institute, Osaka, [12]Fukushima Medical University, Fukushima, [13]University of Occupational and Environmental Health, Kitakyusyu, [14]Gunma Cancer Center, Ohta, [15]National Center for Global Health and Medicine, Tokyo, [16]National Cancer Center Hospital East, Kashiwa, Japan

Background

- Treatment with an aromatase inhibitor (AI) for 5 years as up-front monotherapy or after tamoxifen therapy for 2-3 years is the treatment of choice for hormone-receptor-positive breast cancer in postmenopausal women.
- Extending endocrine therapy is an important treatment of choice for reducing the risk of late breast cancer recurrence.
- Recently, DATA, IDEAL, MA17R, and NSABP B42 trials showed that extended AI therapy reduced the occurrence of secondary breast tumors. However, they had no or only a small impact on DDFS.
- Several studies investigated the safety and efficacy of additional treatment with AIs after a sequential regimen of tamoxifen and AI for 5 years. Only the AERAS study investigated the safety and efficacy of the same AI between for 10- and 5-years treatments.

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N-SAS BC 05 (AERAS) study design

Postmenopausal women with primary breast cancer who had received 4 years 9 months to 5 years 2 months of adjuvant therapy with anastrozole

Amendment; postmenopausal women who had received tamoxifen and then received anastrozole for more than 2 years, a total of 5 years of adjuvant therapy, were also allowed.

Stratification Factor
- Nodal status
- Prior adjuvant chemotherapy
- Choice of tamoxifen or anastrozole
- Institution

Registration Randomization 1:1

STOP GROUP
NO EXTENDED USE OF anastrozole

CONTINUAL GROUP
EXTENDED USE OF anastrozole for an additional 5 years

FOLLOW UP (median follow up period:4.9Y)

1697 Patients Randomized in ITT, Nov 2007-Nov 2012

Primary endpoint : DFS

Secondary endpoints:
- OS
- DDFS
- Safety
- HRQOL
- Cost-effectiveness

UMIN : 000000818

Patient Demographics and Disease Characteristics (1)

		STOP GROUP (N=843) n(%)	CONTINUAL GROUP (N=840) n(%)
Median age	Years	64.5	64.3
BMI		23.3	23.3
T-stage	T1	437 (51.8)	449 (53.4)
	T2	378 (44.8)	358 (42.6)
	T3/T4	28 (3.3)	33 (3.9)
N-stage	N0	667 (79.1)	650 (77.3)
	N1	163 (19.3)	171 (20.3)
	N2	13 (1.5)	19 (2.2)
Hormone receptor	ER +	836 (99.1)	830 (98.8)
	PgR +	627 (74.3)	618 (73.5)

Patient Demographics and Disease Characteristics (2)

		STOP GROUP (N=843) n(%)	CONTINUAL GROUP (N=840) n(%)
Radiotherapy	Yes	457 (54.2)	456 (54.2)
	No	383 (45.4)	385 (45.8)
Adjuvant chemotherapy	Yes	332 (39.3)	328 (39)
	N0	509 (60.3)	512 (60.9)
Endocrine therapy In first 5 years	TAM→ANA	76(9)	75(8.9)
	ANA	772 (91)	774 (91.1)

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Duration of Study Treatment

- Median duration of treatment was 4.9 years in both groups
- Overall, 75.2% of patients in STOP group and 70.1% of patients in CONTINUAL group completed 5 years of study treatment

Reason of early termination	STOP GROUP (%)	CONTINUAL GROUP (%)
Adverse events	0	9.6
Patient refusal	3	7.4
Changing hospital	2.2	2.2
Breast cancer recurrence	11.3	5.4
Second cancer (not breast-related)	5.4	1.9
Other	4.1	2.9

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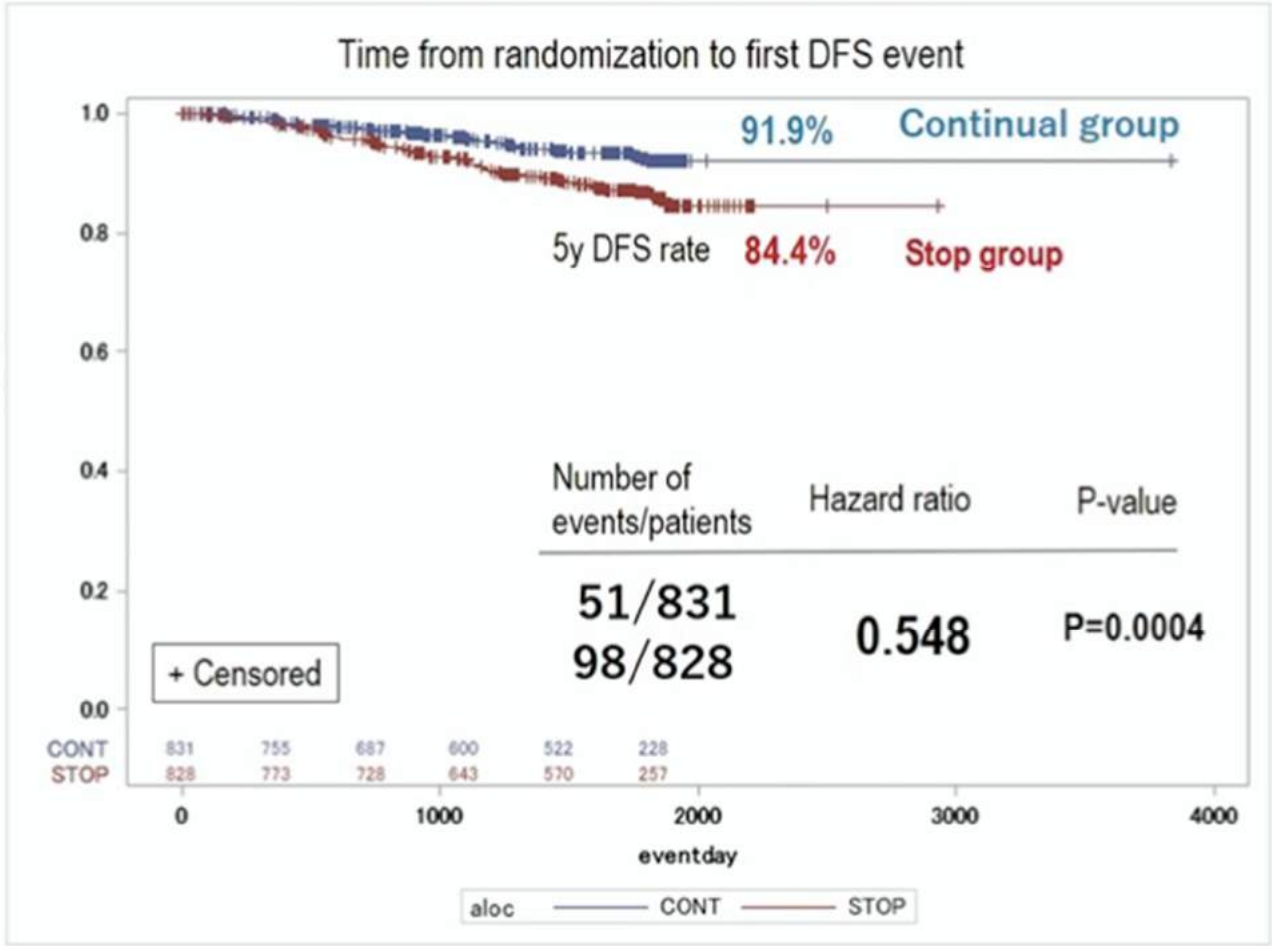
Disease-Free Survival



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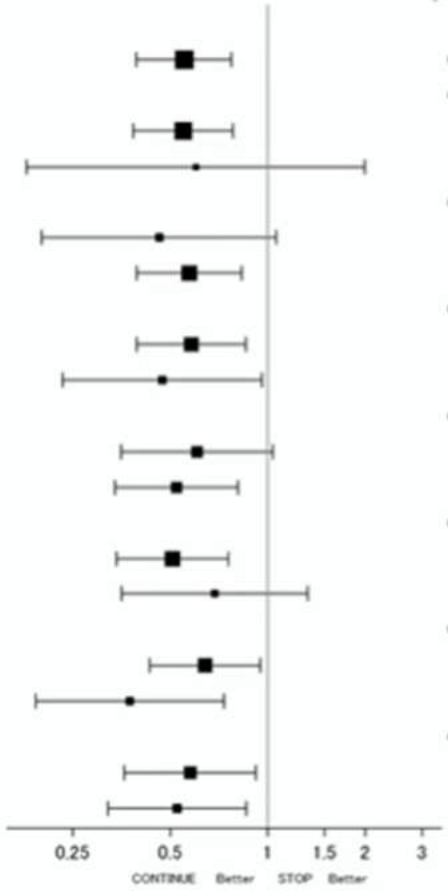
DFS Subgroups

Subgroup	CONTINUE Events/N (%)		STOP Events/N (%)		HR (95% CI)	P Value*
Overall	51/831	(6.1)	97/829	(11.7)	0.55 (0.39, 0.77)	0.0006
Prior TAM						0.5677
ANA	47/757	(6.2)	89/753	(11.8)	0.55 (0.39, 0.78)	
TAM->ANA	4/74	(5.4)	8/76	(10.5)	0.60 (0.18, 1.99)	
AGE						0.0487
<60 yr	8/200	(4.0)	18/204	(8.8)	0.46 (0.20, 1.06)	
≥60 yr	43/631	(6.8)	79/625	(12.6)	0.57 (0.40, 0.83)	
BMI						0.3088
<25	40/598	(6.7)	72/599	(12.0)	0.58 (0.40, 0.86)	
≥ 25	11/233	(4.7)	25/230	(10.9)	0.47 (0.23, 0.96)	
T-stage						0.0005
T1	21/427	(4.9)	36/415	(8.7)	0.60 (0.35, 1.04)	
≥T2	30/375	(8.0)	61/384	(15.9)	0.52 (0.34, 0.81)	
pN-stage						0.2881
pN0	36/621	(5.8)	76/634	(12.0)	0.51 (0.34, 0.76)	
≥pN1	15/181	(8.3)	21/165	(12.7)	0.69 (0.35, 1.33)	
Hormone status						0.6668
ER+PR+	39/580	(6.7)	67/587	(11.4)	0.64 (0.43, 0.95)	
any negative	12/222	(5.4)	30/212	(14.2)	0.38 (0.19, 0.73)	
Prior chemo.						0.0205
No	27/488	(5.5)	50/487	(10.3)	0.58 (0.36, 0.92)	
Yes	24/313	(7.7)	47/311	(15.1)	0.53 (0.32, 0.86)	



* P-Value is the test of interaction between treatment and each subgroup unadjusted for multiplicity.

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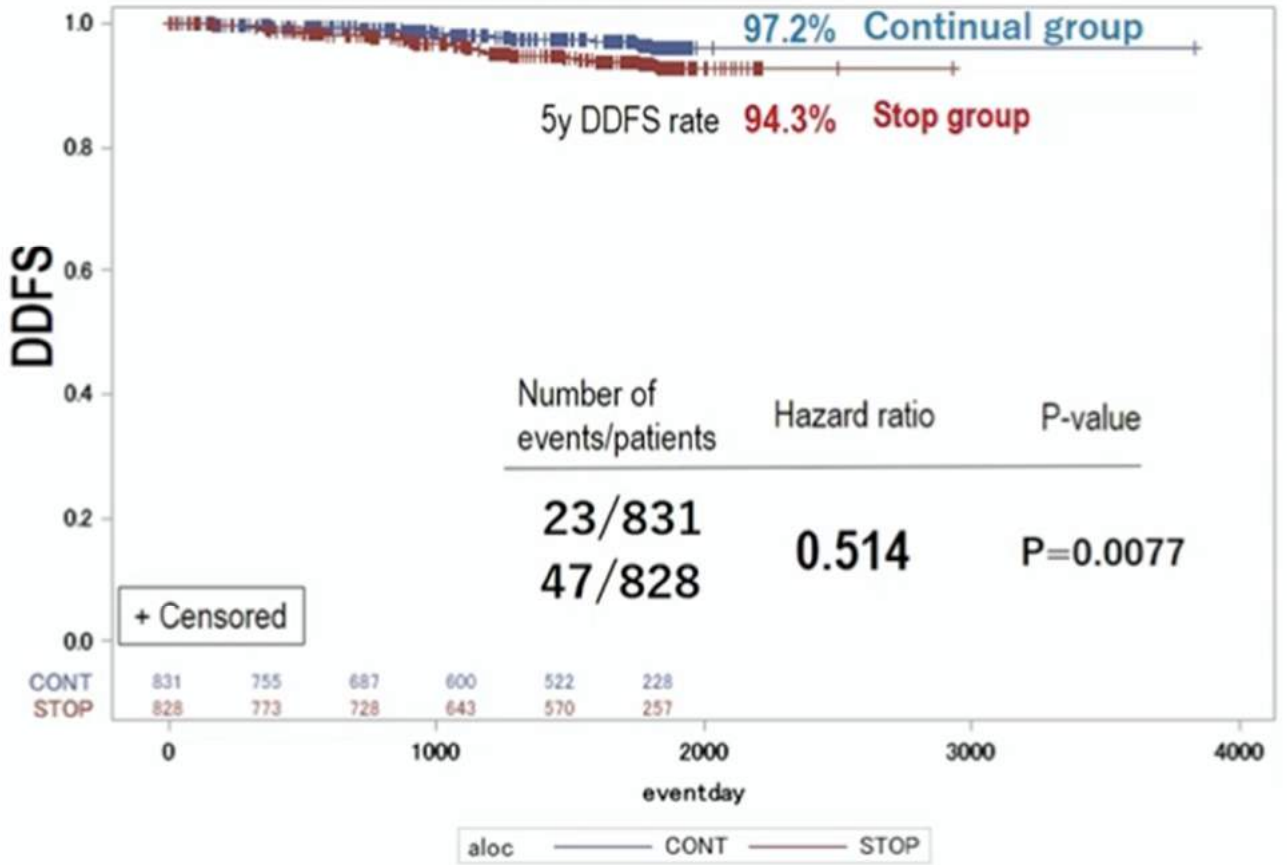
Distant Disease-Free Survival



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ALL Events

	STOP GROUP (n=828)		CONTINUAL GROUP (n=831)	
	No. of Pts	%	No. of Pts	%
Local recurrence	32	3.8	15	1.8
Distant recurrence	47	5.6	23	2.7
Contralateral breast cancer	7	0.8	6	0.7
Second primary Cancer	35	4.3	13	1.5
Death	3	0.3	4	0.4

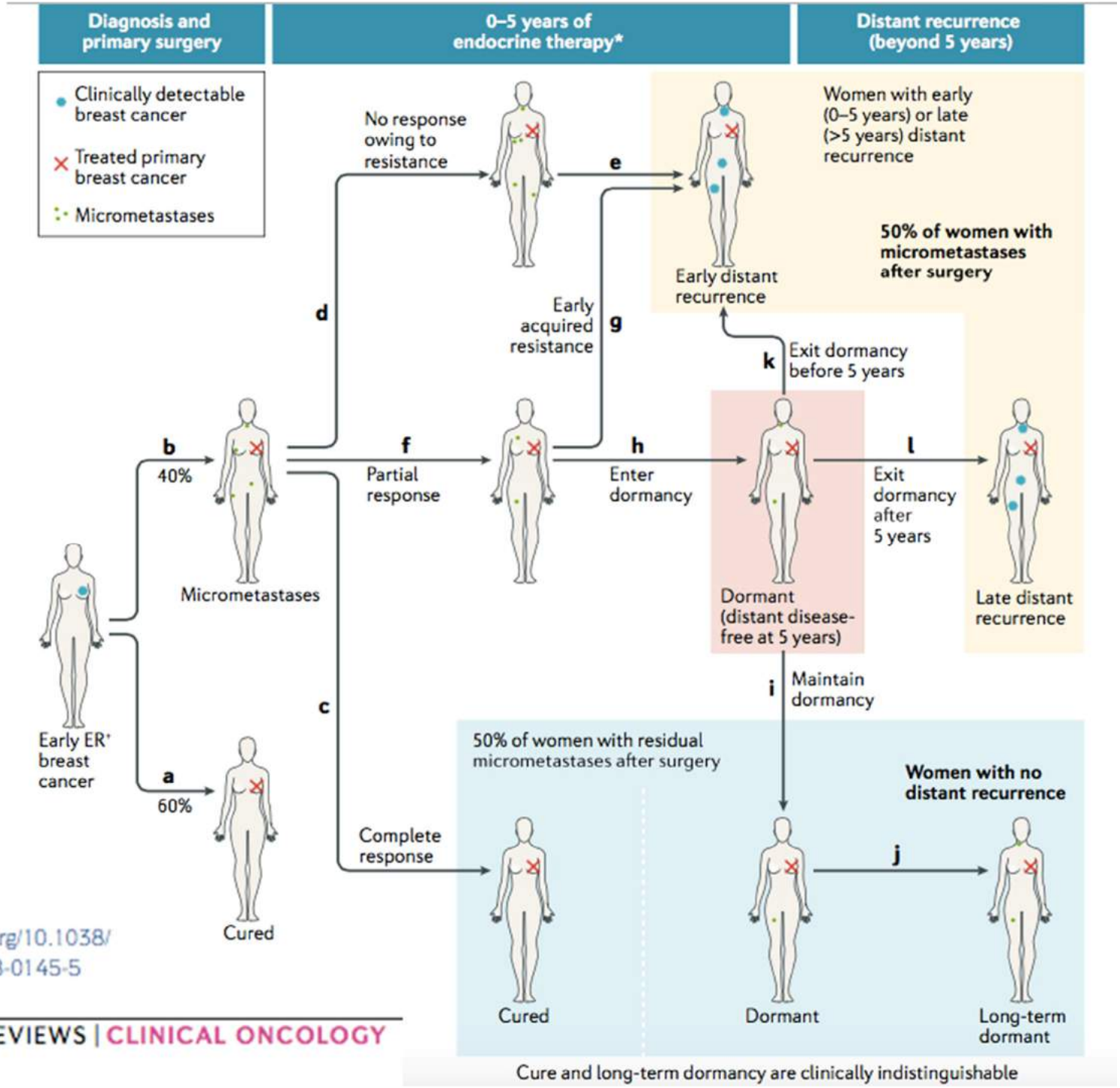
Predefined Adverse Events

	STOP GROUP (N=783)		CONTINUAL GROUP (N=783)	
	Any	Grade≥3	Any	Grade≥3
Bone fractures	1.1%	0.1%	2.8%	0.5%
Osteoporosis	28%	0.1%	33%	0.3%
Arthralgia	11.7%	0.1%	19.2%	0.8%
Stiff joints	4.9%	0%	11.7%	0.3%
Hot flashes	3.2%	0%	6.7%	0.5%
Headache	1.8%	0%	2.1%	0.1%

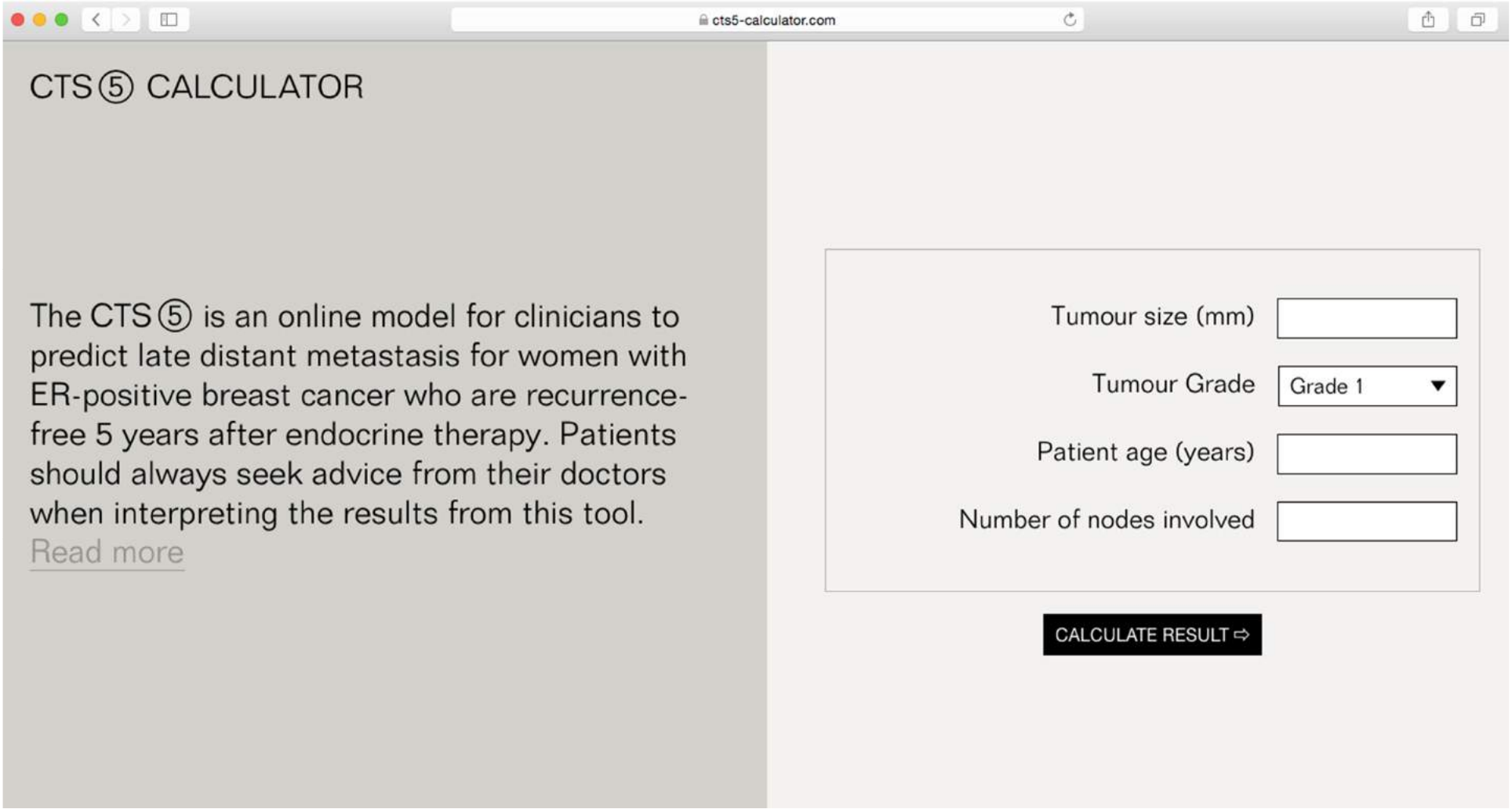
Conclusions

- The extension of treatment with an adjuvant aromatase inhibitor (anastrozole) to 10 years resulted in significantly higher rates of disease-free survival and distant disease-free survival than those with no additional anastrozole.

- However, the rate of overall survival with anastrozole was not higher than the rate of survival with no additional anastrozole.



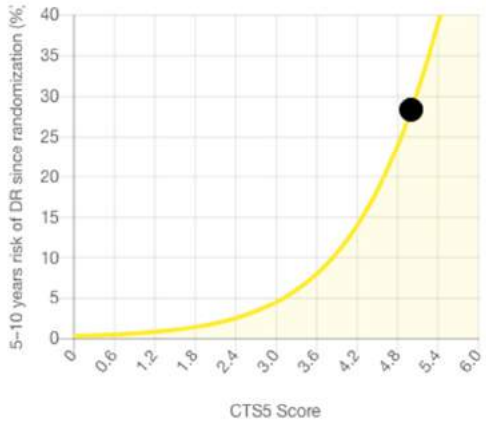
https://doi.org/10.1038/s41571-018-0145-5


cts5-calculator.com
CTS⑤ CALCULATOR
The CTS⑤ is an online model for clinicians to predict late distant metastasis for women with ER-positive breast cancer who are recurrence-free 5 years after endocrine therapy. Patients should always seek advice from their doctors when interpreting the results from this tool.
Read more
Tumour size (mm)
Tumour Grade
Grade 1
Patient age (years)
Number of nodes involved
CALCULATE RESULT ⇨

CTS⑤ CALCULATOR

Tumour size (mm)	40
Tumour Grade	Grade 2
Patient age (years)	65
Number of nodes involved	4

UPDATE RESULT ⇨

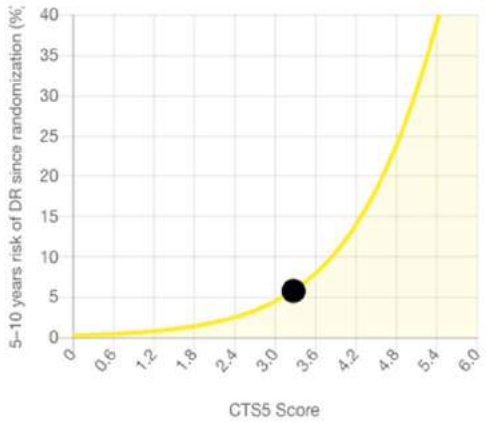


CTS5 SCORE	5–10 YEAR RISK	CTS5 RISK GROUP
5.01	28.3%	High

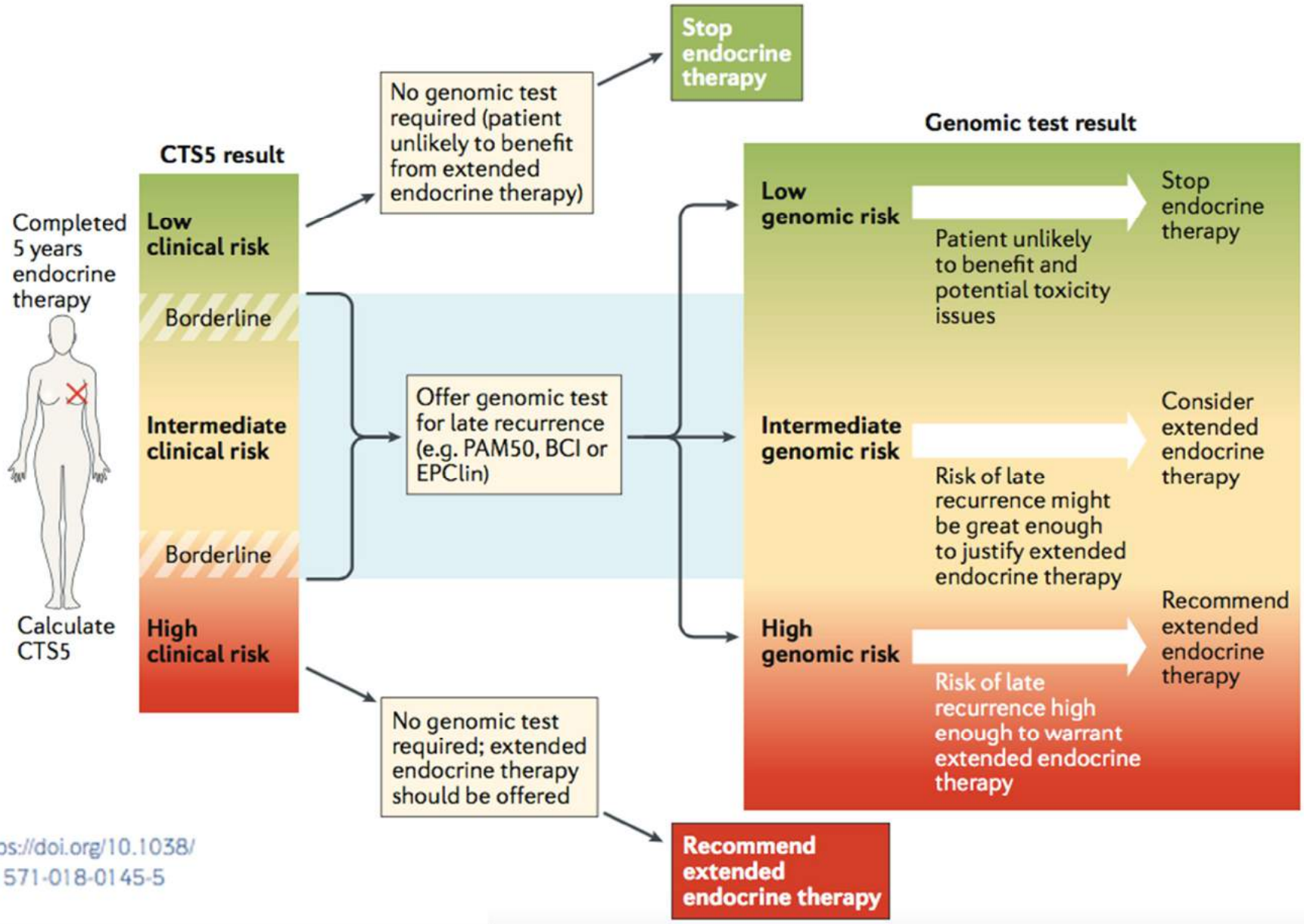
CTS⑤ CALCULATOR

Tumour size (mm)	20
Tumour Grade	Grade 2
Patient age (years)	65
Number of nodes involved	0

UPDATE RESULT ⇨



CTS5 SCORE	5–10 YEAR RISK	CTS5 RISK GROUP
3.28	5.7%	Intermediate



https://doi.org/10.1038/s41571-018-0145-5

Adjuvant Endocrine Therapy for Women With Hormone Receptor–Positive Breast Cancer: ASCO Clinical Practice Guideline Focused Update

Harold J. Burstein, MD, PhD[1]; Christina Lacchetti, MHSc[2]; Holly Anderson, RN[3]; Thomas A. Buchholz, MD[4]; Nancy E. Davidson, MD[5]; Karen A. Gelmon, MD[6]; Sharon H. Giordano, MD[4]; Clifford A. Hudis, MD[7]; Alexander J. Solky, MD[8]; Vered Stearns, MD[9]; Eric P. Winer, MD[1]; and Jennifer J. Griggs, MD[10]

TABLE 4. Prognostic Factors for Recurrence After 5 Years of Adjuvant Endocrine Therapy

Factor	Relationship
Anatomic stage	
Nodal status	N+ > N−[11]
Tumor size	Risk increase with increased T
Tumor pathology	
Higher grade	Higher grade > lower grade[11,12]
Lower levels of ER expression	Higher ER < lower ER
Genomic assay	
Intrinsic subtype	Luminal A < B[13]
21-gene recurrence score	Lower < higher[14]
PAM 50 ROR score	Lower < higher[15-17]
Breast cancer index score	Lower < higher[18-20]
EndoPredict clinical score	Lower < higher[21]

J Clin Oncol 37:423-438.

Take-home messages 1

- Estudos ainda não publicados
- 6 meses de trastuzumabe razoável para pacientes com alto risco cardíaco e em contextos com acesso limitado à medicação.
- Sem dados ainda para pacientes que receberam duplo bloqueio (neo)adjuvante ou para aquelas em tratamento com paclitaxel e trastuzumabe (APT trial).

Take-home messages 2

- Estudo ainda não publicado
- Tamoxifeno baixa dose seria uma excelente opção para pacientes apresentando sintomas importantes com a dose convencional ou possuem risco aumentado de toxicidade G3 devido às comorbidades.
- Opção atrativa de quimioprofilaxia para pacientes com hiperplasia atípica e neoplasia lobular *in situ*
- Aplicável para CDIS RE negativo?

Take-home messages 3

A forma correta de escrita da palavra é **estendido**. A palavra extendido está errada. **Estendido** é o particípio do verbo estender. ... Assumindo função de adjetivo, a palavra **estendido** é sinônima de estirado, aberto, desenrolado, esticado, deitado, dilatado e morto, entre outras.

Estendido ou extendido - Dúvidas de Português no Dicio

https://duvidas.dicio.com.br/estendido-ou-extendido/

Take-home messages 3

- Tarefa difícil: em quais pacientes não fazer terapia estendida? Pacientes e médicos tendem a super-estimar os riscos de recidiva
- Acesso limitado aos testes moleculares
- Pacientes com osteoporose/osteopenia em terapia estendida: qual a segurança em manter bifosfonados além de 3-5 anos?

Obrigado!