Pós SABCS 2017

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Oncologia Clínica
INGOH

DOENÇA INICIAL

SAN ANTONIO BREAST CANCER SYMPOSIUM®

SABCS, December 5 -9, 2017

Increasing the dose intensity of adjuvant chemotherapy : an EBCTCG meta-analysis

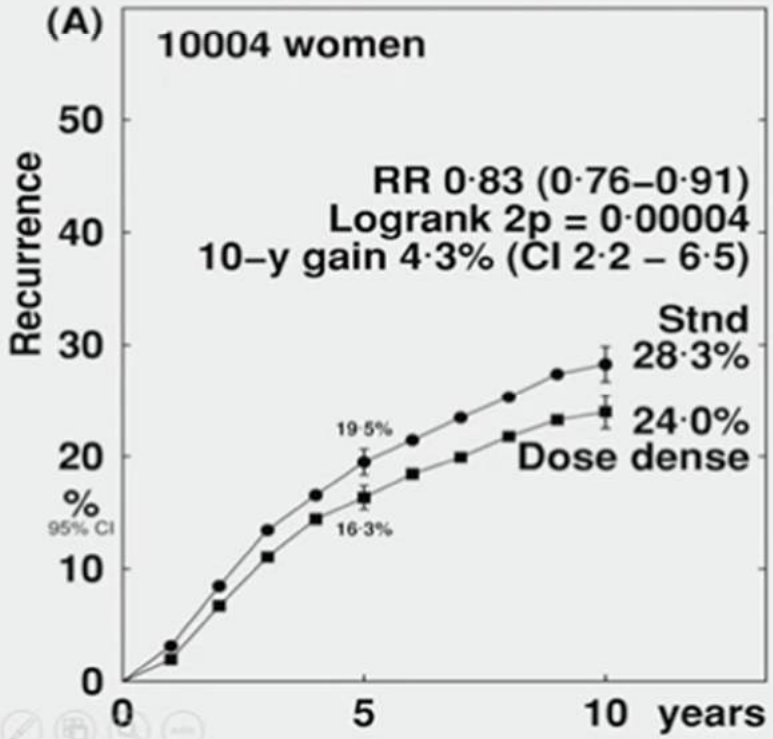
Richard Gray, Rosie Bradley, Jeremy Braybrooke, Christina Davies, Hongchao Pan, Richard Peto, Judith Bliss, David Cameron, John Mackey, Lucia Del Mastro, Sandra Swain, Michael Untch, Jonas Bergh, Kathleen Pritchard, Larry Norton, for the

Early Breast Cancer Trialists' Collaborative Group

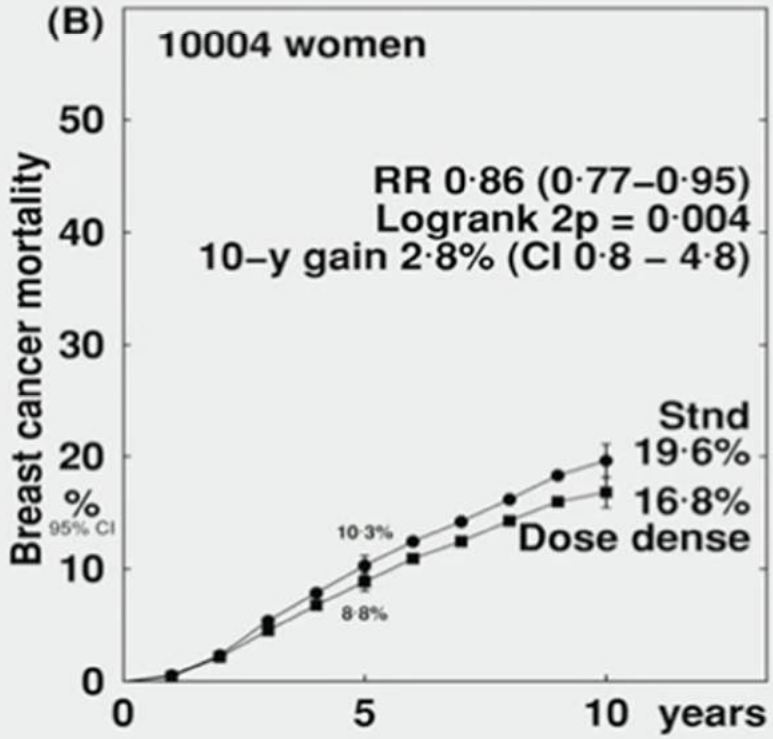
All authors declare no relevant conflict of interest

2-weekly (dose dense) *vs* the same chemotherapy given 3-weekly

Any Recurrence

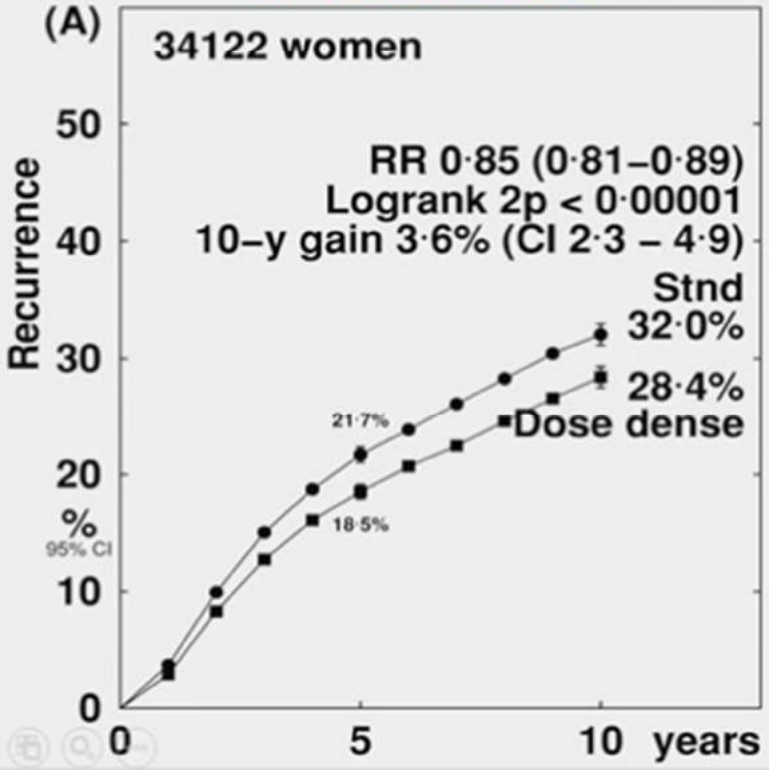


Breast Cancer Mortality

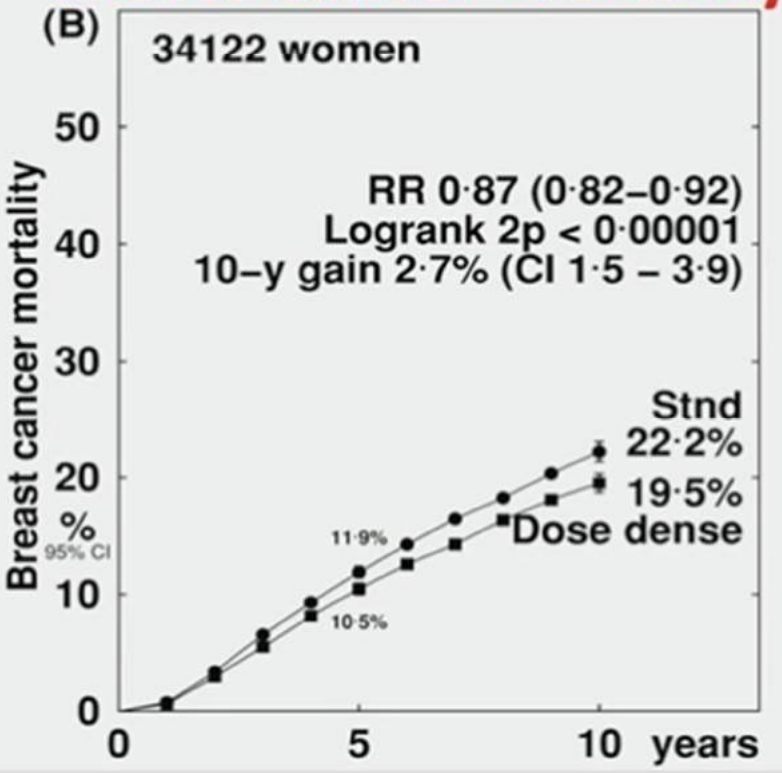


Pooled analysis of all 25 dose-dense and sequential trials

Recurrence

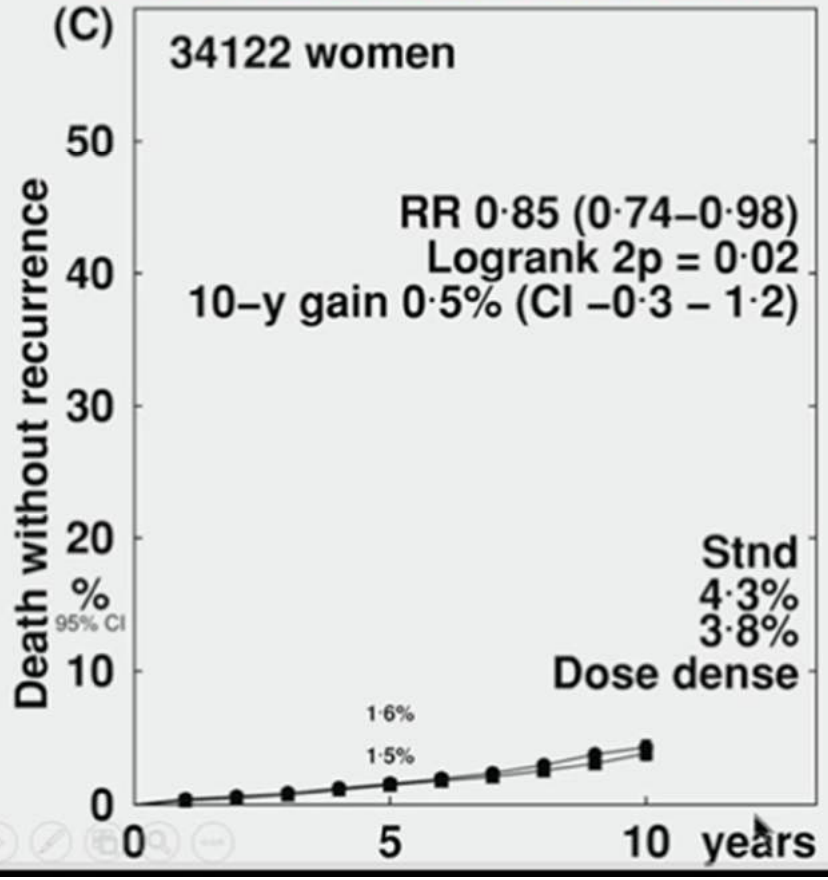


Breast Cancer Mortality

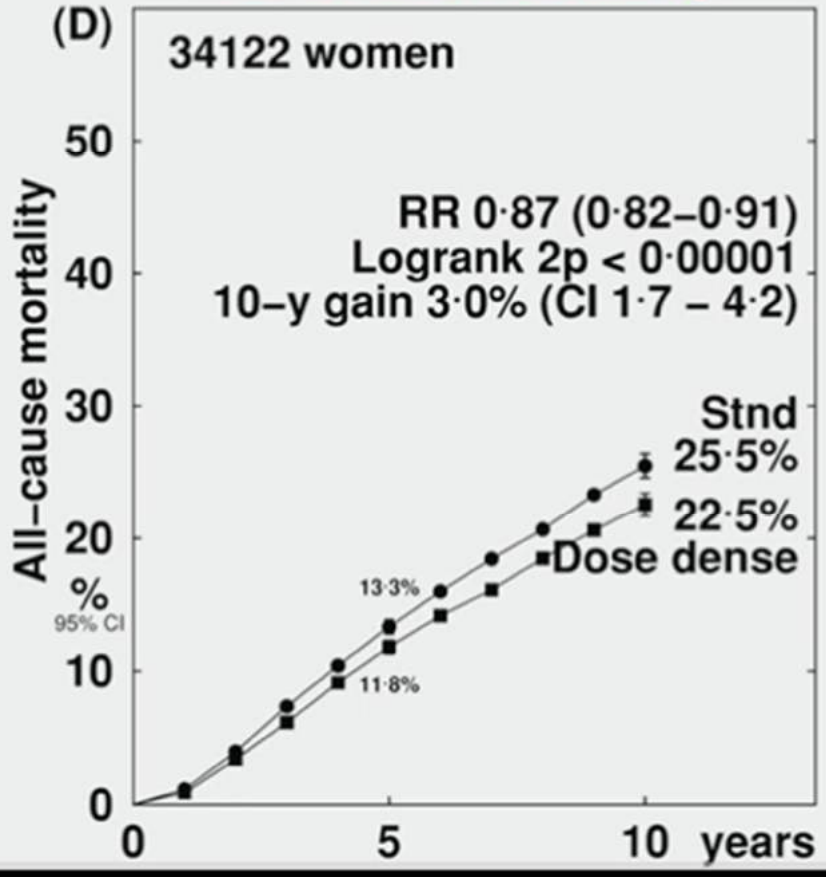


Pooled Analysis

Death without recurrence

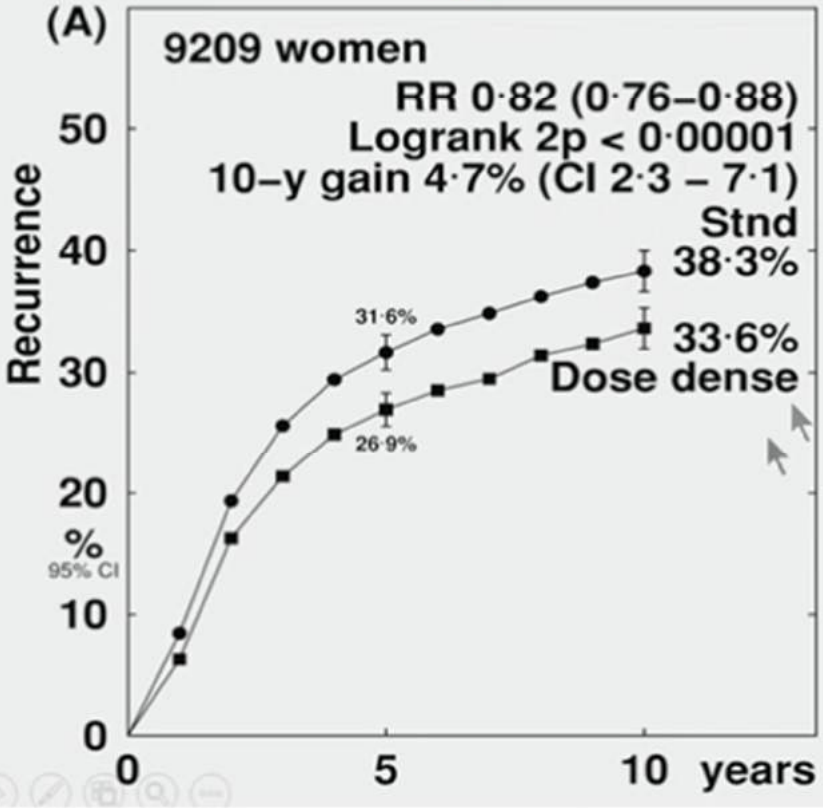


All cause mortality

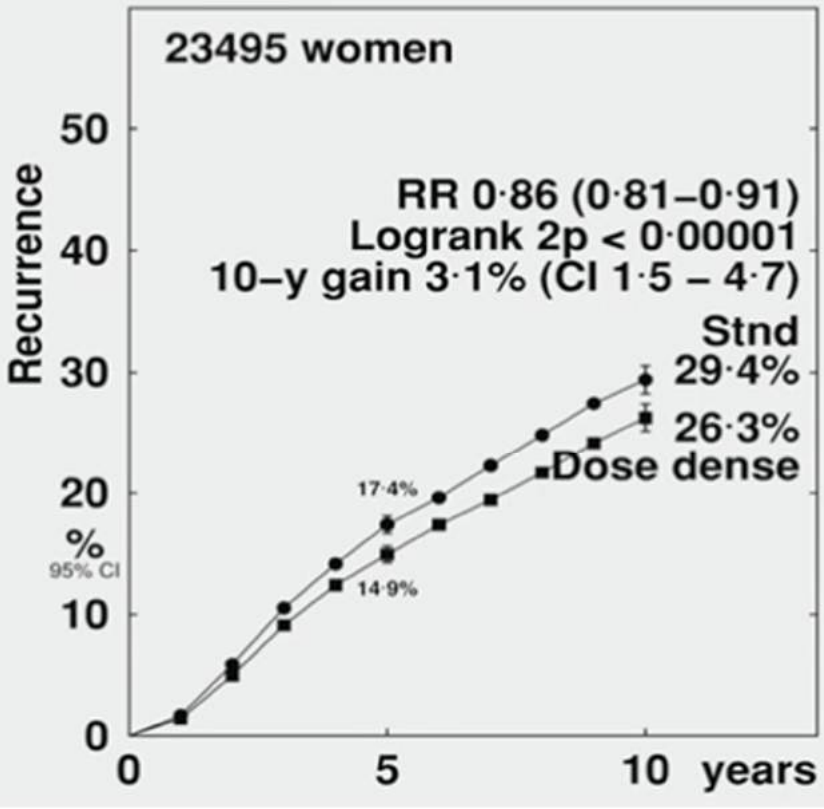


Pooled Analysis: recurrence by ER status

ER- Negative



ER - Positive



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NSABP B-47 (NRG Oncology)
Phase III RCT Comparing Adjuvant Chemotherapy with AC→Weekly Paclitaxel or TC x 6 with or without Trastuzumab for 1 Year in High-risk, Invasive Breast Cancer Negative for HER2 by ISH and with IHC 1+ or 2+ (HER2-Low IBC)

Louis Fehrenbacher, Reena S. Cecchini, Charles E. Geyer, Jr., Priya Rastogi, Joseph P. Costantino, James N. Atkins, John Crown, Jonathan Polikoff, Jean-Francois Boileau, Louise Provencher, Christopher Stokoe, Timothy D. Moore, André Robidoux, Virginia Borges, Kathy S. Albain, Sandra M. Swain, Soonmyung Paik, Eleftherios P. Mamounas, Norman Wolmark

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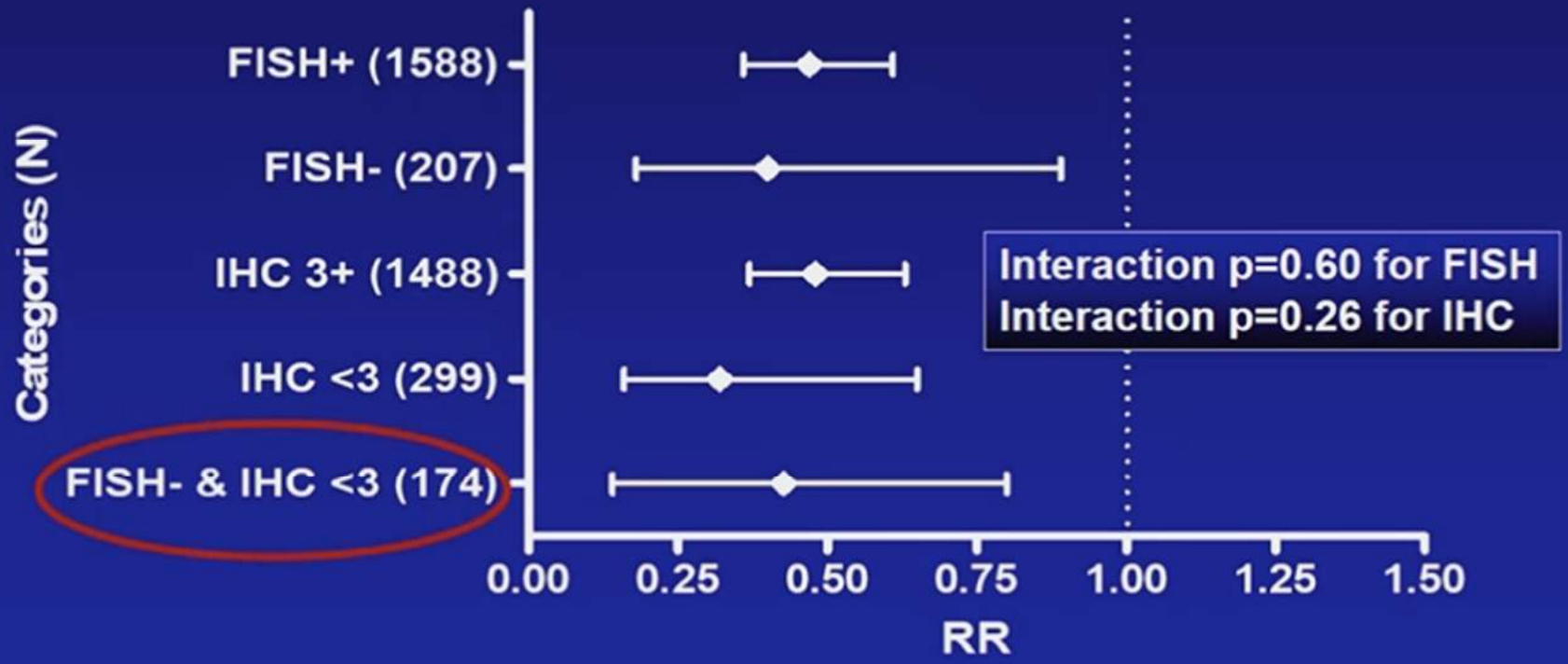
RR of ACTH/ACT for DFS (NSABP B-31)



Note: RR adjusted for ER and nodal status

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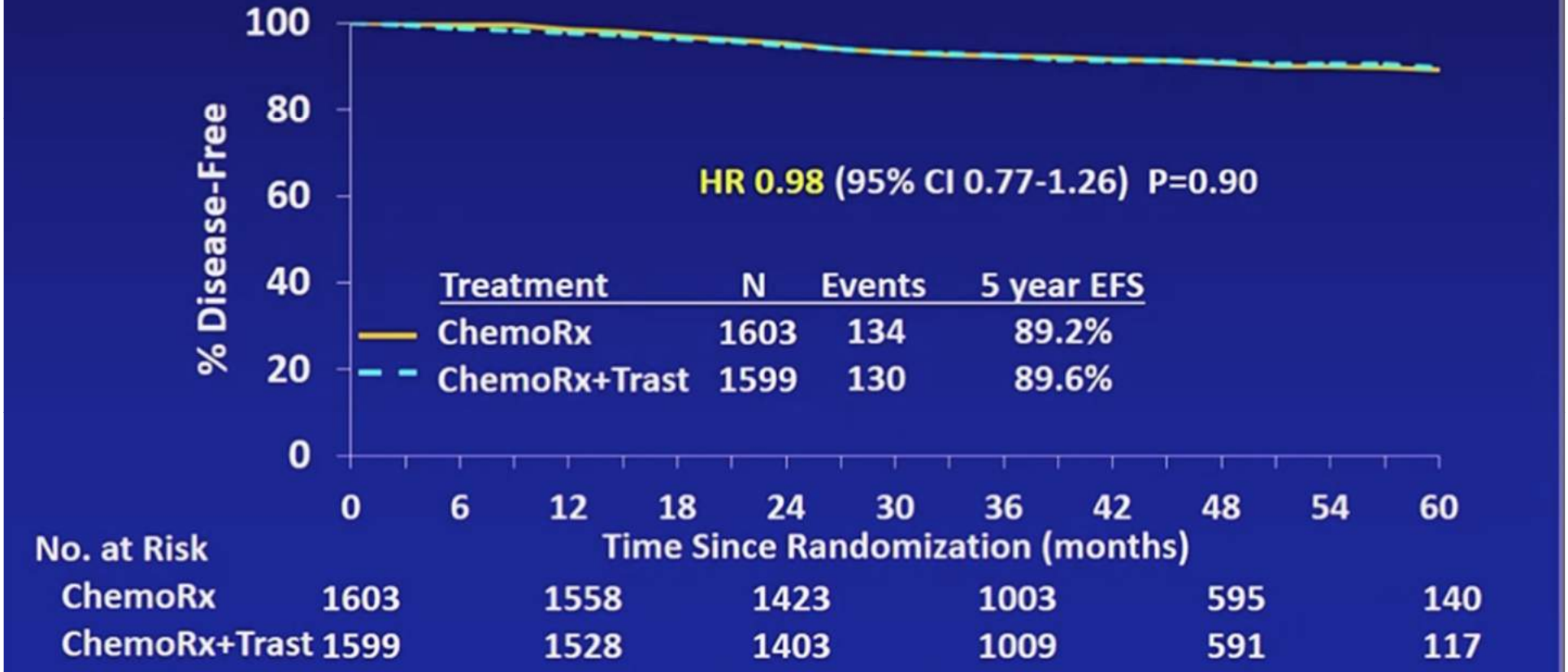
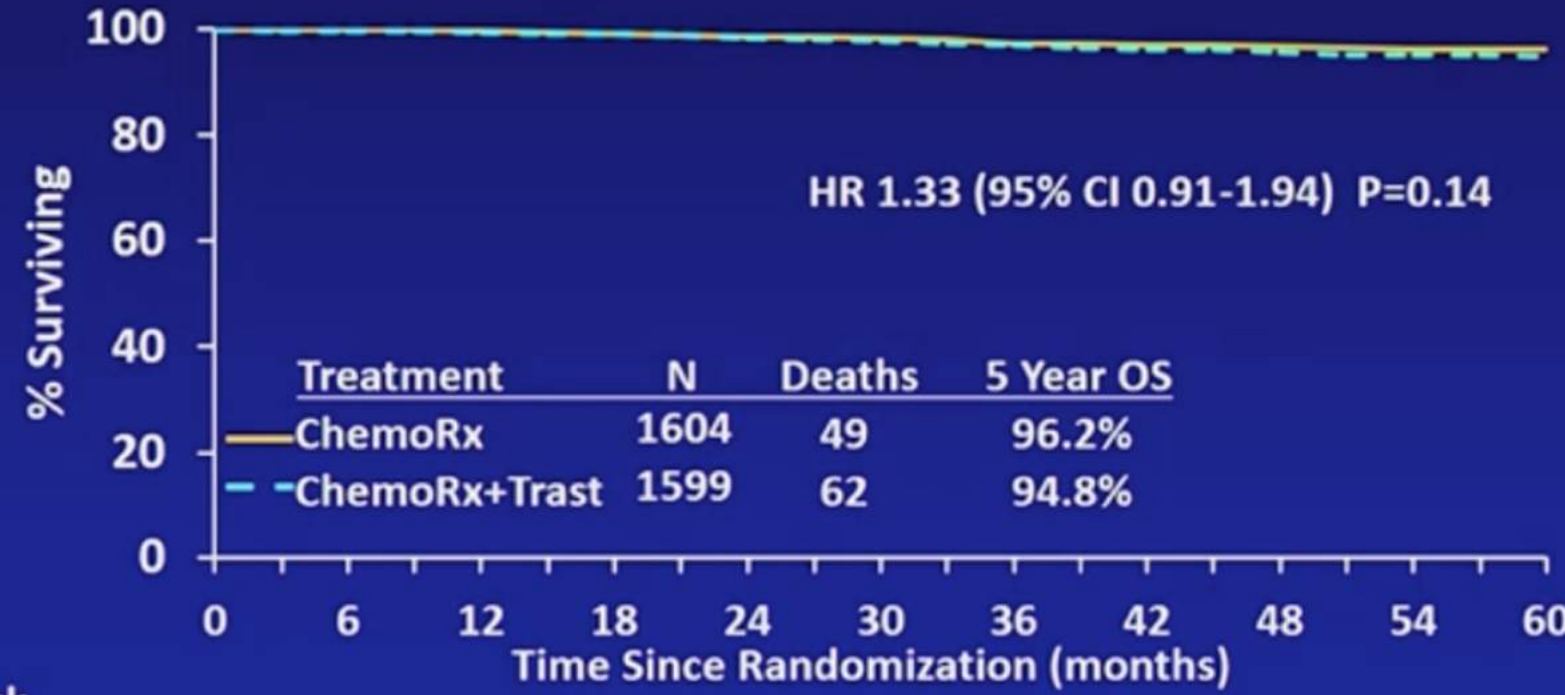
B-47: Invasive Disease-Free Survival



No. at Risk						
ChemoRx	1603	1558	1423	1003	595	140
ChemoRx+Trast	1599	1528	1403	1009	591	117

B-47: Overall Survival



No. at Risk

ChemoRx	1604	1577	1507	1099	703	169
ChemoRx+Trast	1599	1563	1497	1113	683	149

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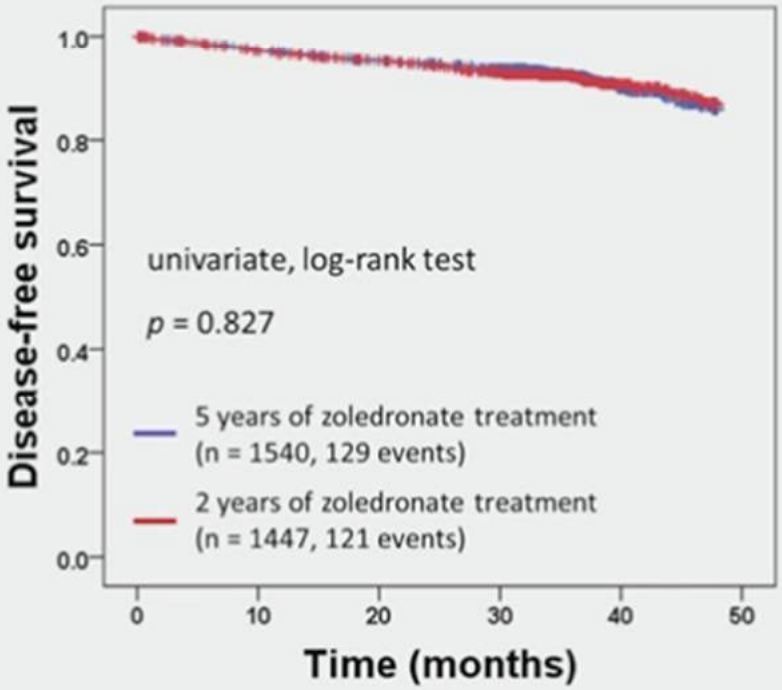
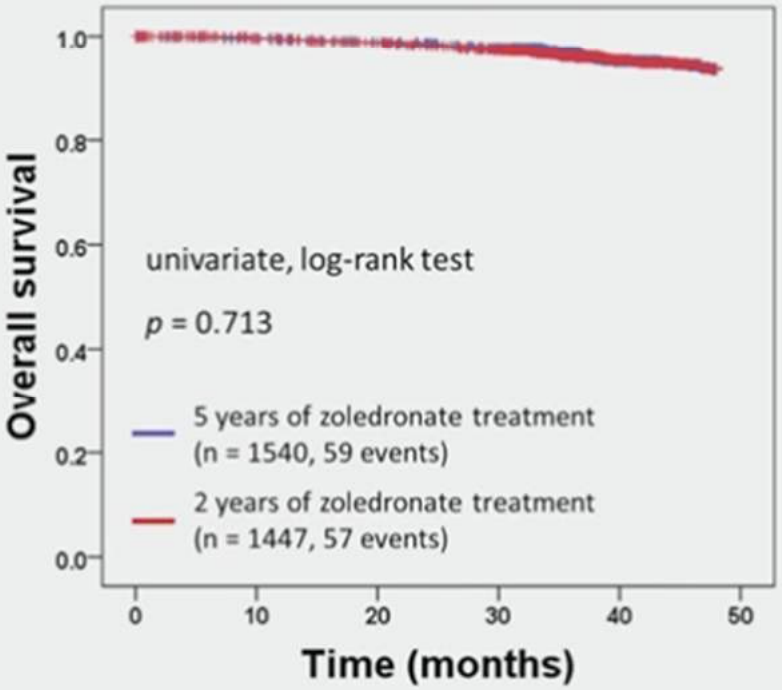
Extended adjuvant bisphosphonate treatment over five years in early breast cancer does not improve disease-free and overall survival compared to two years of treatment: Phase III data from the SUCCESS A study

Wolfgang Janni, Thomas WP Friedl, Tanja Fehm, Volkmar Mueller, Werner Lichtenegger, Jens Blohmer, Ralf Lorenz, Helmut Forstbauer, Emanuel Bauer, Visnja Fink, Inga Bekes, Jens Huober, Julia Jückstock, Andreas Schneeweiss, Hans Tesch, Sven Mahner, Sara Y Brucker, Georg Heinrich, Lothar Häberle, Peter A. Fasching, Matthias W Beckmann, Robert Coleman, Brigitte Rack

SUCCESS
BIG-Member

Adapted disease-free survival (DFS) and overall survival (OS) by zoledronate treatment arm





SUCCESS
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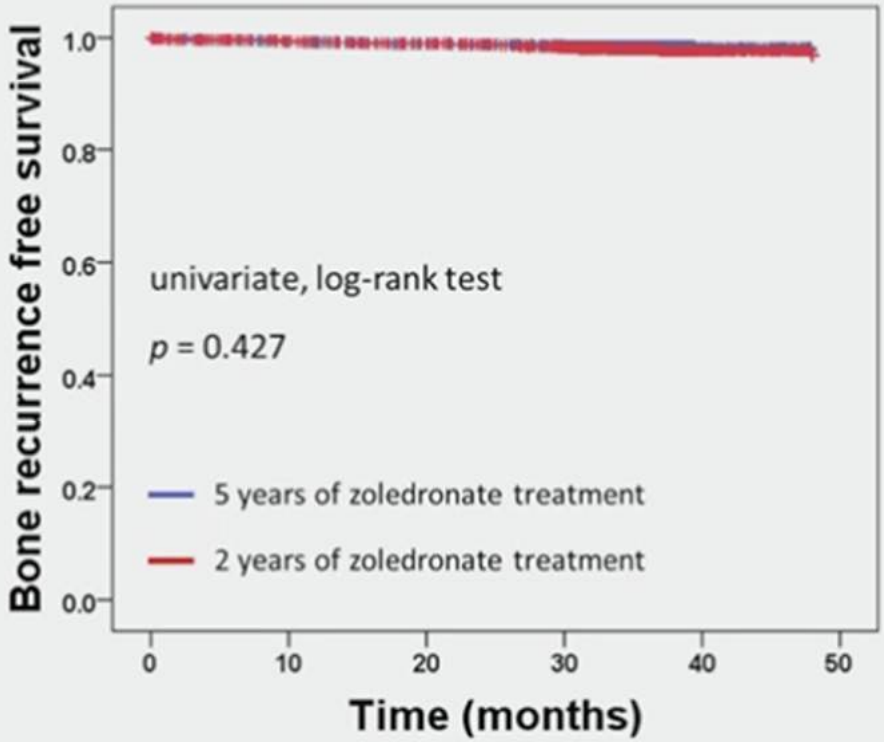
Bone recurrences by zoledronate treatment arm
(as of 2 years after the start of zoledronate treatment)

Bone recurrences as first distant recurrence*

- 5 years of zoledronate: 25 events
- 2 years of zoledronate: 28 events



* with or without concurrent other recurrence

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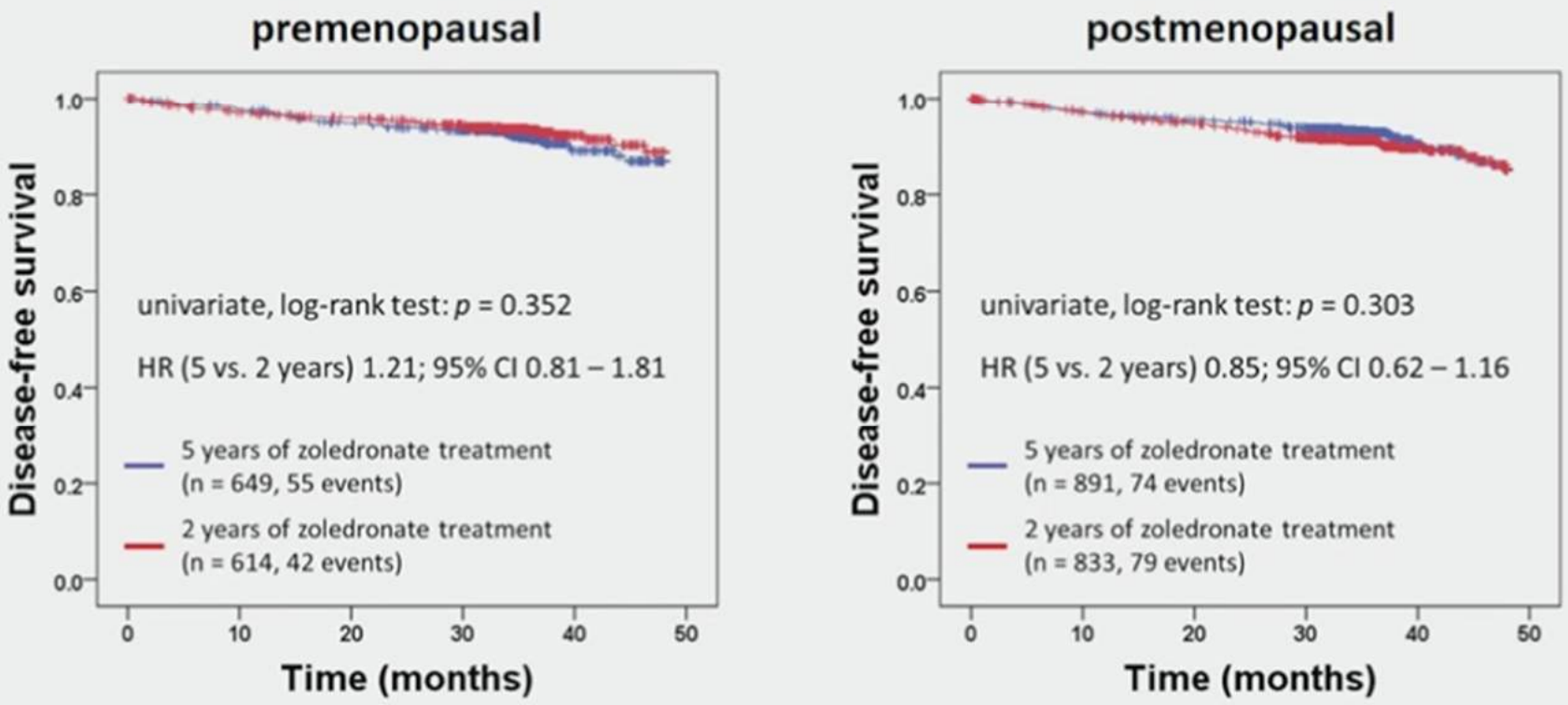
Subgroups – adapted DFS by menopausal status



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Adverse events by zoledronate treatment arm
(as of 2 years after the start of zoledronate treatment)

Patient cohort	Number of adverse events observed (% of patients affected)	
	all grades	grade 3/4
Total	2845 (37.0%)	257 (6.4%)
5 years of zoledronate	1954 (46.2%)	159 (7.6%)
2 years of zoledronate	891 (27.2%)	98 (5.1%)
	p<0.001	P=0.006

Conclusion

- At this early time point, our study showed no difference in DFS or OS between 5-years and 2-years of adjuvant zoledronate treatment following adjuvant chemotherapy in high-risk early breast cancer patients, irrespectively of menopausal status

- 5 years of adjuvant zoledronate treatment should not be considered currently in these patients in the absence of decreased bone density

GS3-01

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SAN ANTONIO BREAST CANCER SYMPOSIUM

A prospective randomized multi-center phase-III trial of additional 2 versus additional 5 years of Anastrozole after initial 5 years of adjuvant endocrine therapy – results from 3,484 postmenopausal women in the ABCSG-16 trial

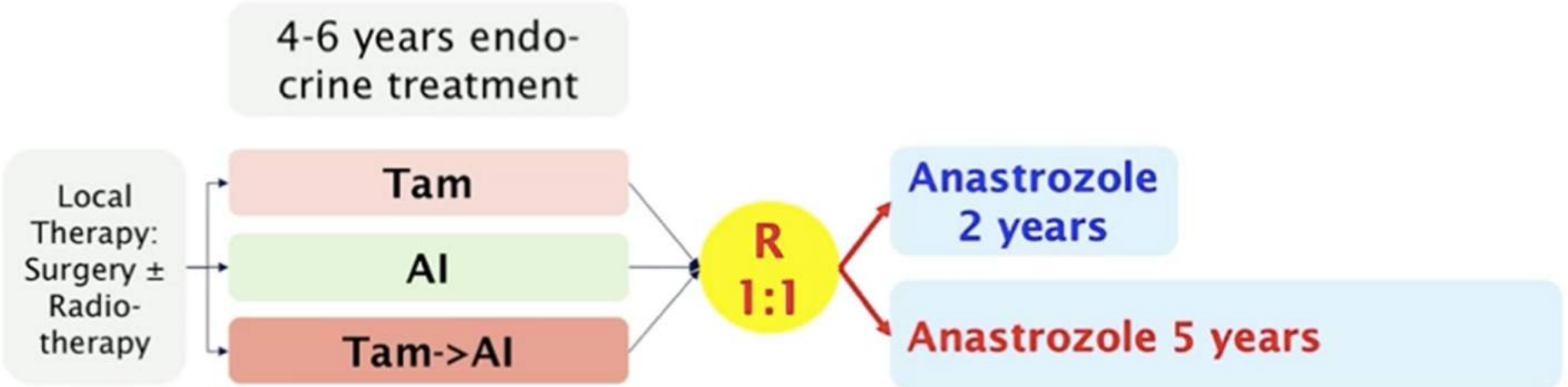
Professor Michael Gnant, MD, FACS
Medical University of Vienna, Vienna, Austria

Michael Gnant, Guenther Steger, Richard Greil, Florian Fitzal, Brigitte Mlineritsch, Diether Manfreda, Christoph Tausch, Marija Balic, Peter Dubsky, Martin Moik, Josef Thaler, Daniel Egle, Vesna Bjelic-Radisic, Ursula Selim, Ruth Exner, Christian Singer, Elisabeth Melbinger-Zeinitzer, Ferdinand Haslbauer, Herbert Stoeger, Ruth Helfgott, Paul Sevelda, Harald Trapl, Viktor Wette, Lidija Soelkner, Raimund Jakesz, on behalf of the Austrian Breast and Colorectal Cancer Study Group

ABCSG
AUSTRIAN BREAST & COLORECTAL CANCER STUDY GROUP

SAN ANTONIO BREAST CANCER SYMPOSIUM

ABCSG-16 Trial Design



N=3,484

Postmenopausal, HR+, T1-3, N0/N+, M0

Recruitment in 75 centers in Austria, 2004-2010

Median Follow-Up: 106.2 months (102.7-107.7)

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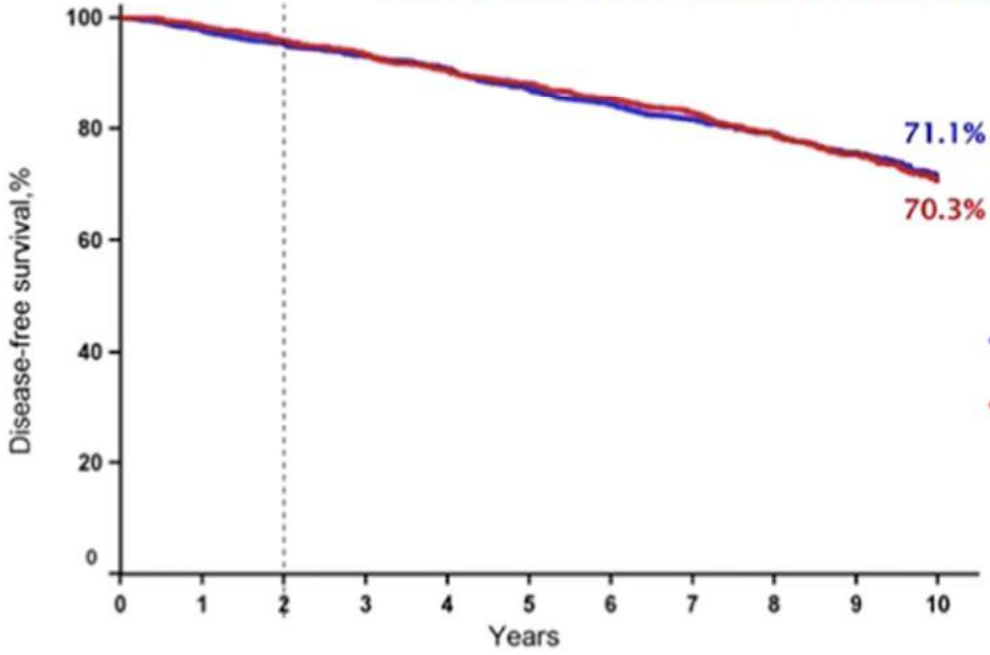
SAN ANTONIO BREAST CANCER SYMPOSIUM

ABCSG-16 Disease-Free Survival

Time from randomization to first DFS event



	Number of Events/Patients	Hazard ratio vs 2 years	P-value
2 years	378/1,731	1.007 (0.87, 1.16)	0.925
5 years	384/1,738		

Patients at risk:

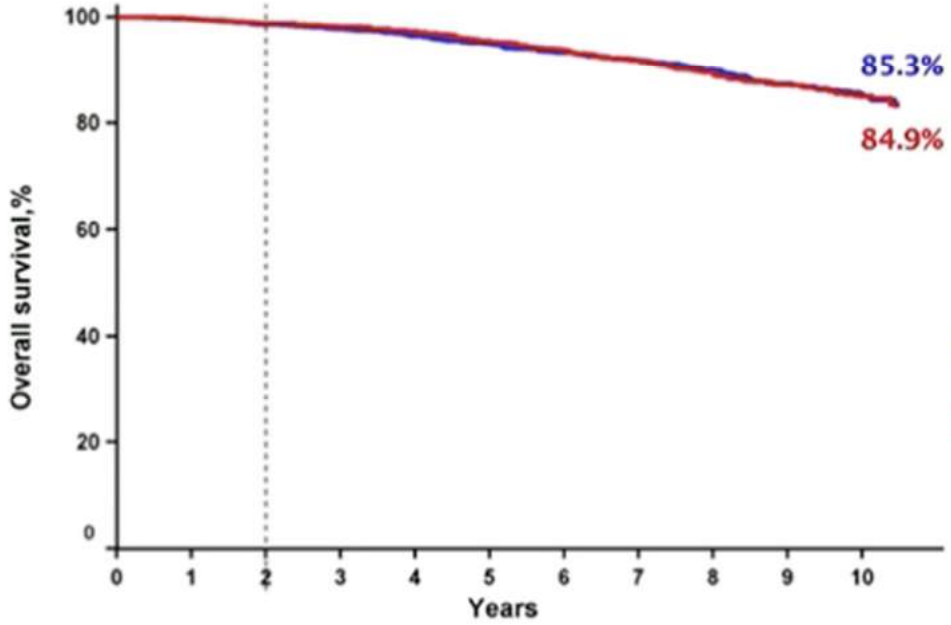
2 years	1731	1651	1601	1538	1477	1368	1206	990	741	540	214
5 years	1738	1667	1605	1551	1485	1399	1233	1026	779	554	209

ABCSG

ABCSG-16 Secondary End Point: Overall Survival

SAN ANTONIO BREAST CANCER SYMPOSIUM

Time from randomization to death from any cause



Patients at risk:

2 years	1731	1689	1661	1626	1594	1518	1352	1125	901	701	381
5 years	1738	1694	1659	1637	1606	1533	1362	1156	920	710	361

	Number of Events/Patients	Hazard ratio vs 2 years	P-value
2 years	192/1,731	1.007 (0.82,1.23)	0.947
5 years	194/1,738		

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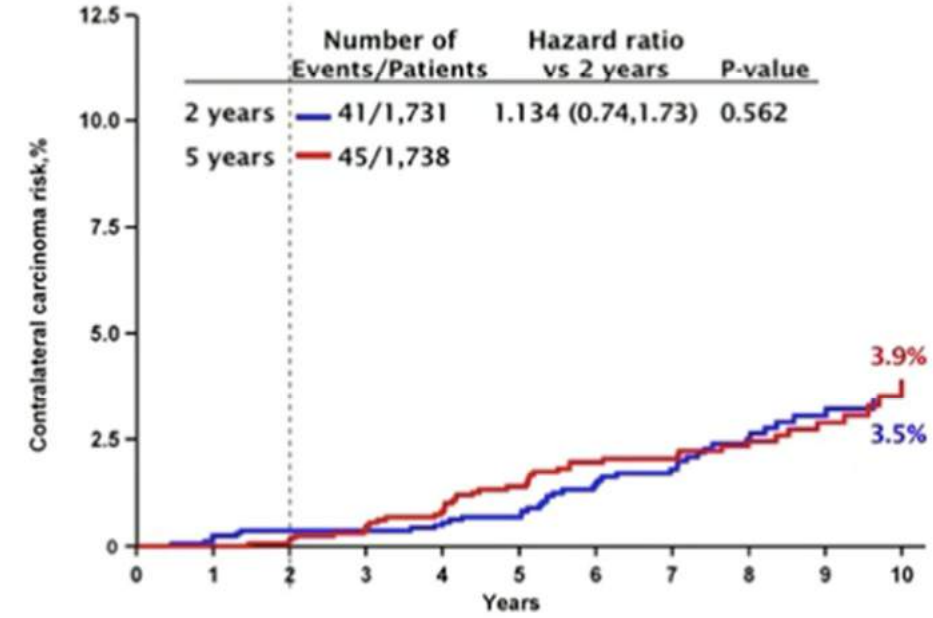
ABCSG-16 Secondary End Points

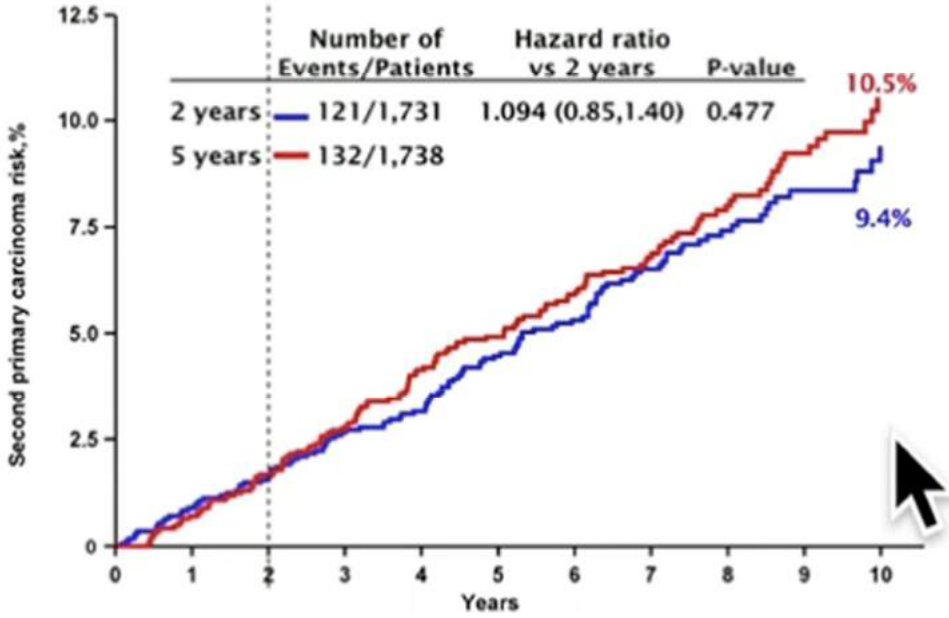
Contralateral Breast Cancer



Patients at risk:

2 years	1731	1662	1629	1585	1528	1448	1282	1058	794	588	252
5 years	1738	1676	1639	1602	1539	1454	1279	1065	821	599	235

Secondary Primary Cancer

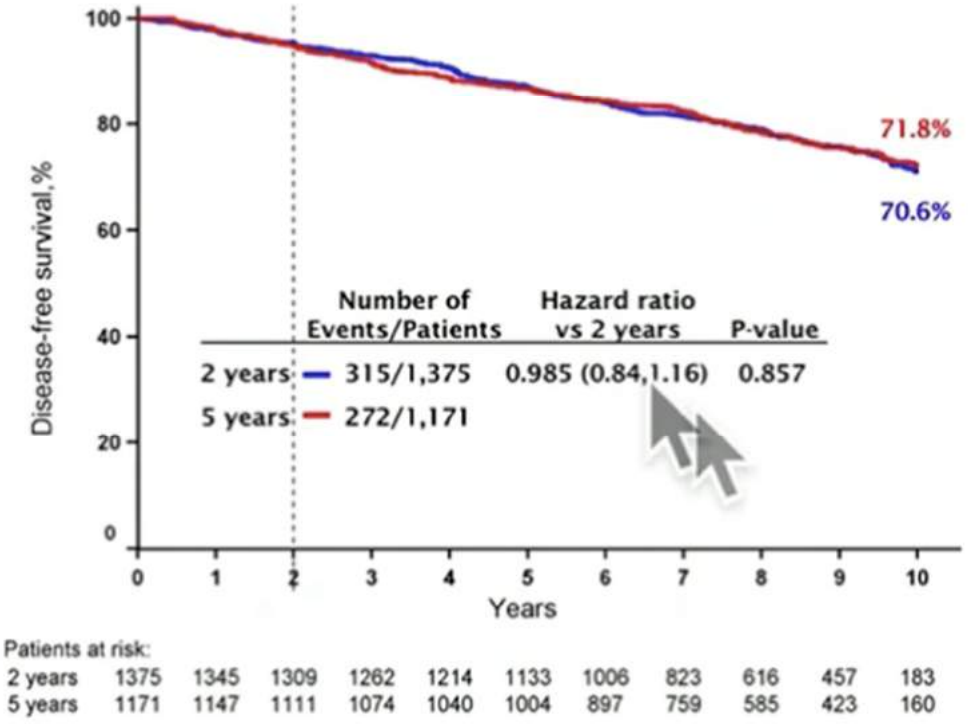


Patients at risk:

2 years	1731	1656	1616	1559	1502	1417	1261	1040	785	583	245
5 years	1738	1668	1618	1571	1502	1424	1253	1043	800	583	229

Exploratory: DFS in „Adherent“ Patients only

SAN ANTONIO BREAST CANCER SYMPOSIUM



Time to contralateral breast cancer

	Number of Events/Patients	Hazard ratio vs 2 years	P-value
2 years	35/1,375	1.071 (0.66,1.73)	0.781
5 years	32/1,171		

Time to second primary cancer

	Number of Events/Patients	Hazard ratio vs 2 years	P-value
2 years	101/1,375	1.250 (0.95,1.64)	0.106
5 years	109/1,171		

DFS in Adherence Subgroup including patients with AEs

	Number of Events/Patients	Hazard ratio vs 2 years	P-value
2 years	336/1,474	0.976 (0.84,1.14)	0.755
5 years	311/1,354		

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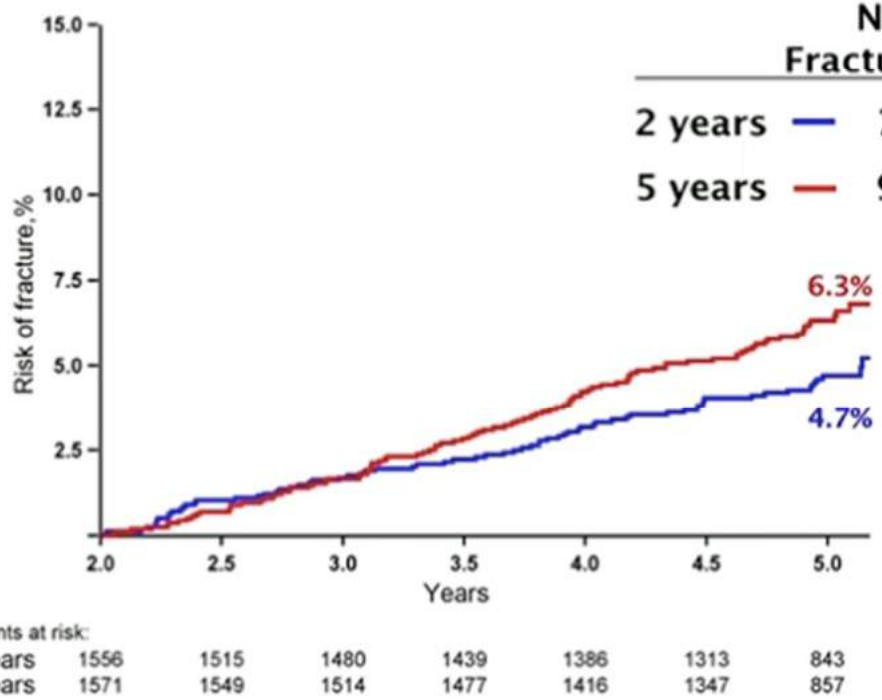
ABCSG-16 Fractures



	Number of Fractures/Patients	Hazard ratio vs 2 years	P-value
2 years	71/1,556	1.353 (1.00,1.84)	0.053
5 years	98/1,571		

San Antonio Breast Cancer Symposium, December 5-9, 2017

Pooled analysis of five randomized trials investigating temporary ovarian suppression with gonadotropin-releasing hormone analogs during chemotherapy as a strategy to preserve ovarian function and fertility in premenopausal early breast cancer patients

Matteo Lambertini[1], Halle C.F. Moore[2], Robert C.F. Leonard[3], Sibylle Loibl[4], Pamela Munster[5], Marco Bruzzone[6], Luca Boni[7], Joseph M. Unger[8], Richard A. Anderson[9], Keyur Mehta[4], Susan Minton[10], Francesca Poggio[6], Kathy S. Albain[11], Douglas J.A. Adamson[12], Bernd Gerber[13], Amy Cripps[14], Gianfilippo Bertelli[15], Sabine Seiler[4], Marcello Ceppi[6], Ann H. Partridge[16], and Lucia Del Mastro[6]

[1]Institut Jules Bordet and Université Libre de Bruxelles (U.L.B.), Brussels, Belgium. [2]Cleveland Clinic Foundation, Taussig Cancer Institute, Cleveland, OH. [3]Imperial College, London, UK. [4]GBG - German Breast Group, Neu-Isenburg, Germany. [5]UCSF - University of California, San Francisco, CA. [6]Ospedale Policlinico San Martino-IST, Genova, Italy. [7]AOU Careggi and Istituto Toscano Tumori, Firenze, Italy. [8]SWOG Statistical Center, Fred Hutchinson Cancer Research Center, Seattle, WA. [9]MRC Centre for Reproductive Health, University of Edinburgh, Edinburgh, UK. [10]Moffitt Cancer Center, Tampa, FL. [11]Loyola University Medical Center, Cardinal Bernardin Cancer Center, Maywood, IL. [12]Tayside Cancer Centre, Ninewells Hospital, Dundee, UK. [13]University Hospital Rostock, Rostock, Germany. [14]Nexgen Oncology, Dallas, TX. [15]Singleton Hospital, Swansea, UK. [16]Dana-Farber Cancer Institute, Boston, MA.

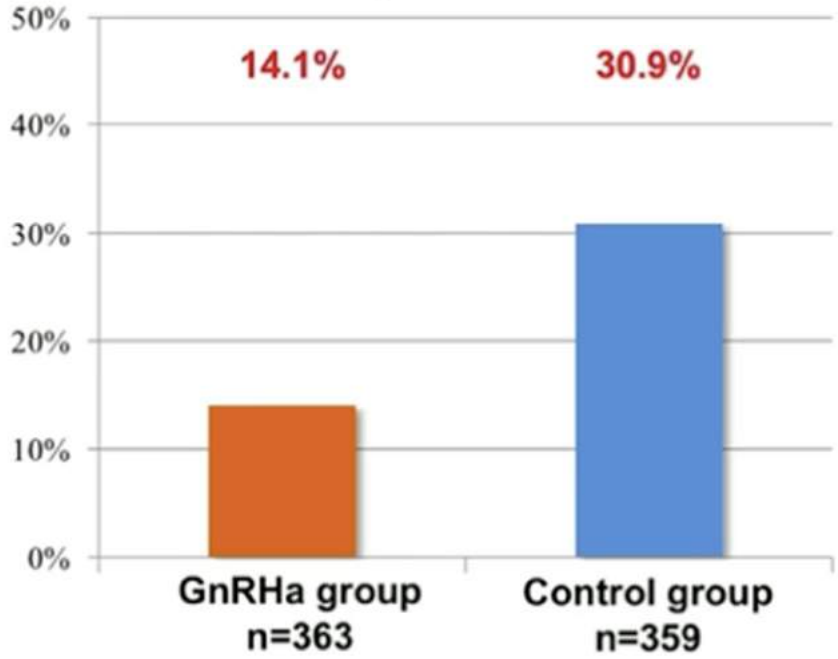
Study Characteristics

	PROMISE-GIM6[1,2]	POEMS/SWOG S0230[3]	Moffitt-led trial[4]	GBG-37 ZORO[5]	Anglo Celtic Group OPTION[6]
Definition of POI	No resumption of menstrual activity and postmenopausal levels of FSH and E2	Amenorrhea for the prior 6 months and postmenopausal levels of FSH	No maintenance of menses and no resumption of menses	No re-appearance of two consecutive menstrual periods within 21 to 35 days	Amenorrhea with elevated FSH
Timing of POI after chemotherapy	12 months	24 months	24 months	6 months	Between 12 and 24 months
Sample size	281	257	48	60	227
ER status for eligibility	ER-positive and ER-negative	ER-negative only	ER-positive and ER-negative	ER-negative only	ER-positive and ER-negative
Upper age limit for eligibility	≤ 45 years	≤ 49 years	≤ 44 years	≤ 45 years	None
Type of GnRHa	Triptorelin	Goserelin	Triptorelin	Goserelin	Goserelin

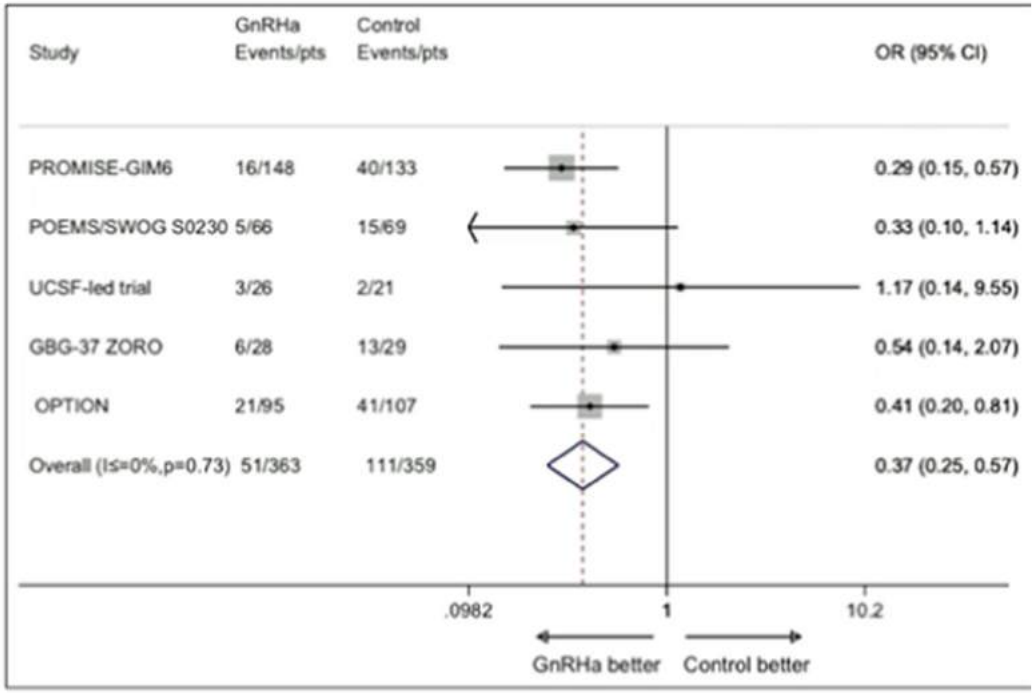
1. Del Mastro L et al, *JAMA* 2011;306:269-76. 2. Lambertini M et al, *JAMA* 2015;314:2632-40. 3. Moore HCF et al, *N Engl J Med* 2015;372:923-32.
4. Munster P et al, *J Clin Oncol* 2012;30:533-38. 5. Gerber B et al, *J Clin Oncol* 2011;29:2334-41. 6. Leonard RCF et al, *Ann Oncol* 2017;28:1811-16.

Premature-Ovarian Insufficiency Rate

OR* 0.38 (95% CI 0.26-0.57)
p<0.001



Meta-analysis approach

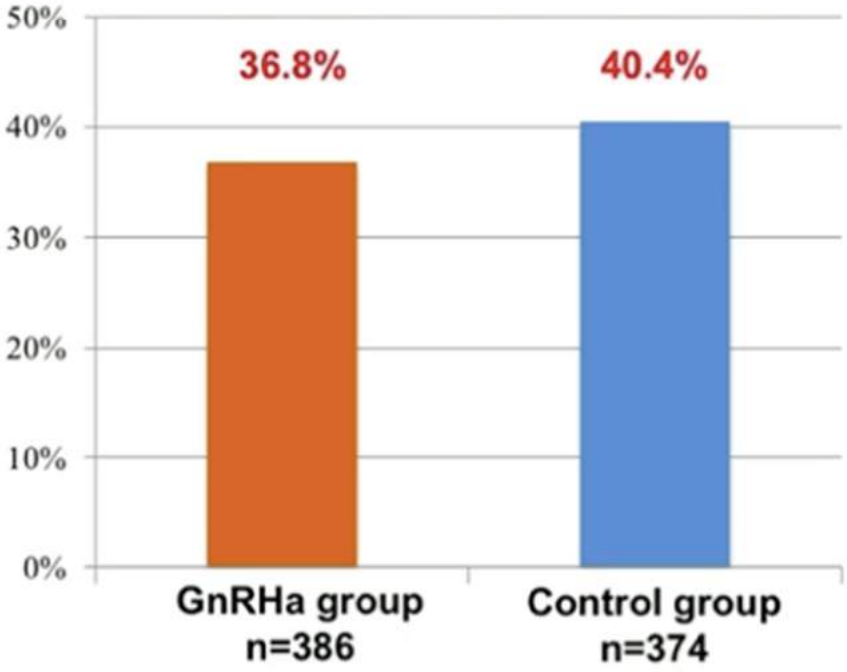


*Odds ratio (OR) adjusted for age, estrogen receptor status, type and duration of chemotherapy administered

Amenorrhea Rates

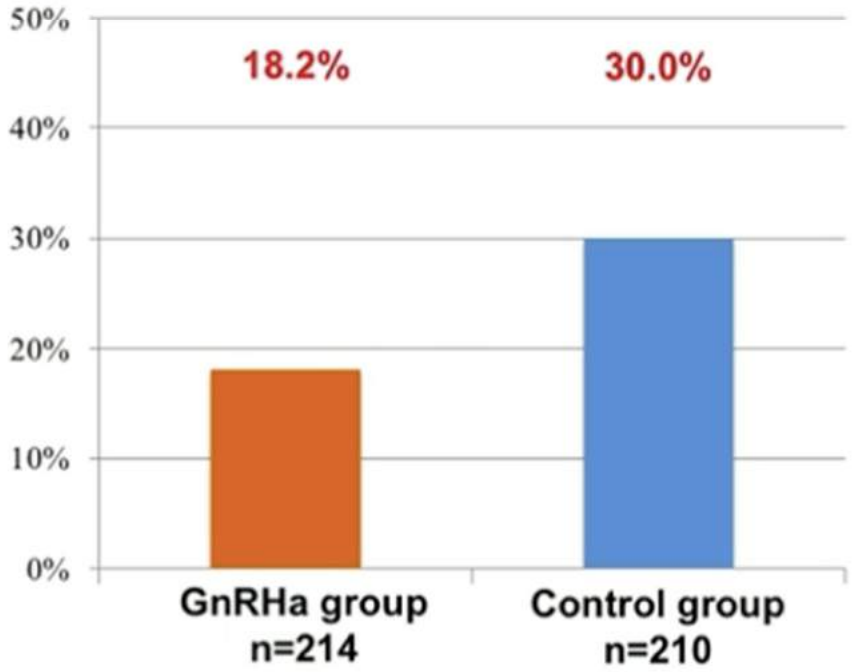
One-Year Amenorrhea

OR* 0.92 (95% CI 0.66-1.28); p=0.623



Two-Year Amenorrhea

OR* 0.51 (95% CI 0.31-0.85); p=0.009



*Odds ratio (OR) adjusted for age, estrogen receptor status, type and duration of chemotherapy administered

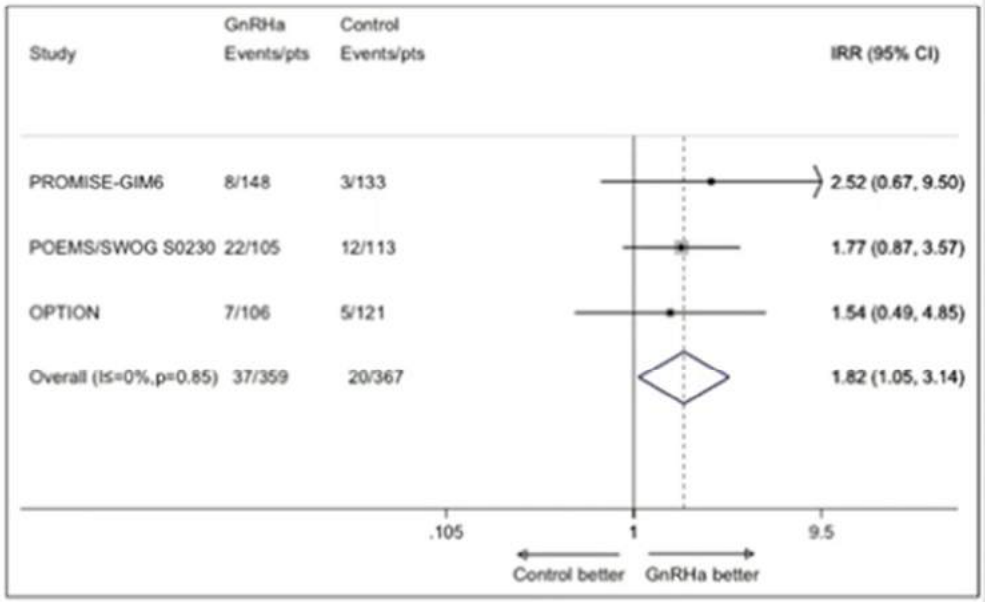
Post-Treatment Pregnancy Rate

GnRHa Group: 37/359 (10.3%)
vs.
Control Group: 20/367 (5.5%)

IRR* 1.83 (95% CI 1.06-3.15)
p=0.030

	GnRHa group (n = 37) No. (%)	Control group (n = 20) No. (%)
Age distribution, years		
≤ 40	37 (100)	20 (100)
≥ 41	0 (0.0)	0 (0.0)
Estrogen receptor status		
Positive	6 (16.2)	2 (10.0)
Negative	31 (83.8)	18 (90.0)

Meta-analysis approach



*Incidence rate ratio (IRR)

Randomized Comparison of Adjuvant Aromatase Inhibitor Exemestane plus Ovarian Function Suppression vs Tamoxifen plus Ovarian Function Suppression in Premenopausal Women with HR+ Early Breast Cancer: Update Of The Combined TEXT and SOFT Trials

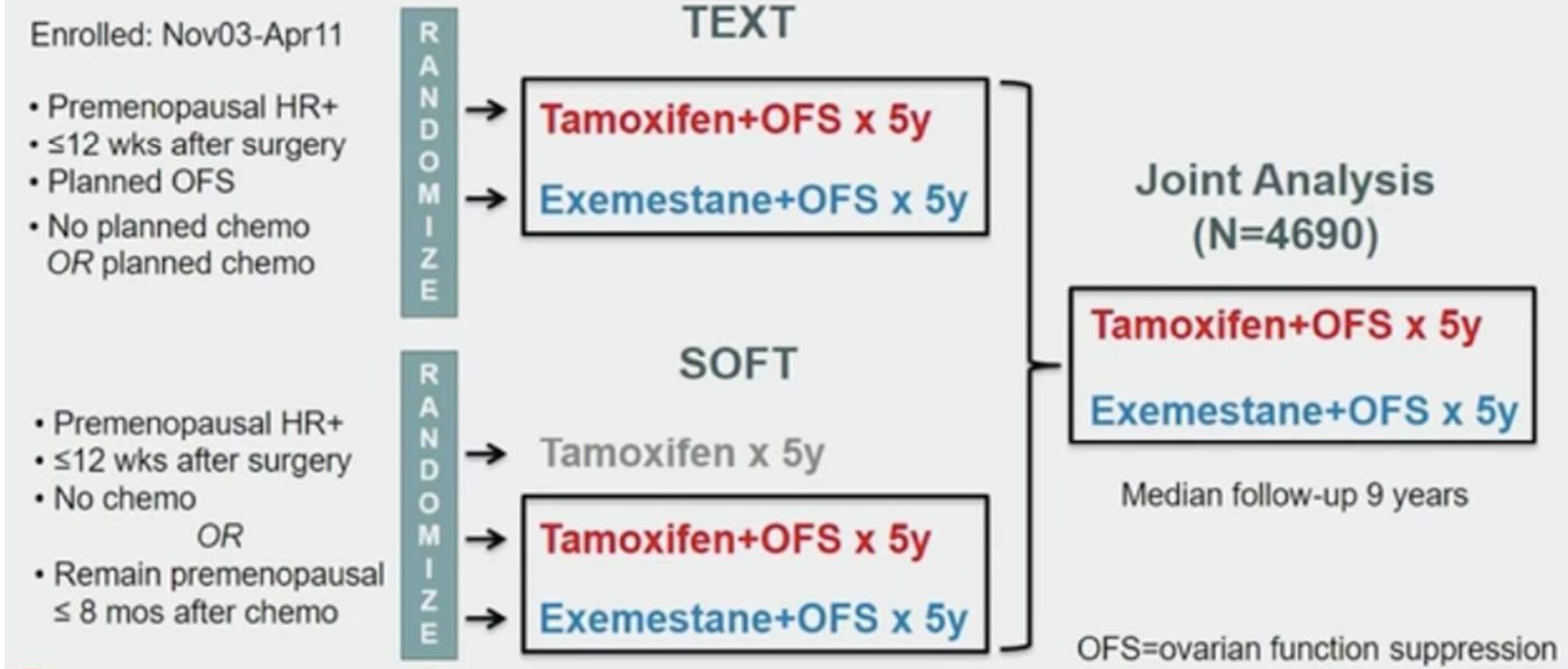
Prudence Francis

on behalf of Olivia Pagani, MD

TEXT and SOFT Investigators and

International Breast Cancer Study Group (IBCSG)

TEXT and SOFT Designs

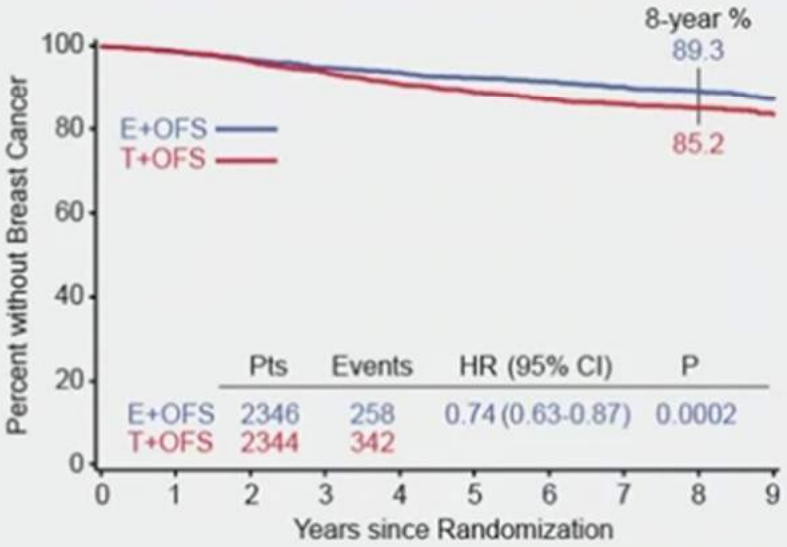


Patient Characteristics

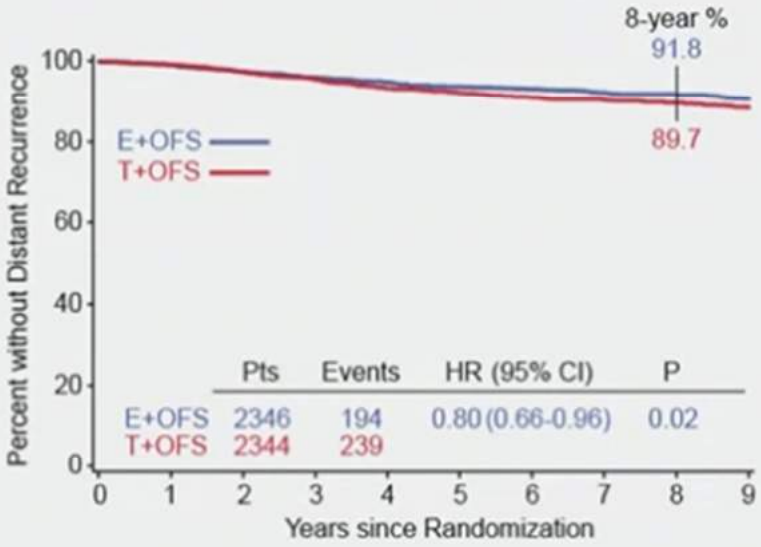
	No chemo TEXT (N=1053)	No chemo SOFT (N=943)	Chemo TEXT (N=1607)	Prior chemo SOFT (N=1087)	Overall (N=4690)
Age <40 yr	16%	9%	30%	49%	27%
LN +	21%	8%	66%	57%	42%
T-size >2cm	19%	15%	53%	47%	36%
HER2 +	5%	3%	17%	20%	12%
Surgery to random. (median)	1.5 mo	1.8 mo	1.2 mo	8.0 mo	1.6 mo

Significant Reductions in Recurrence

Breast Cancer-Free Interval



Distant Recurrence-Free Interval



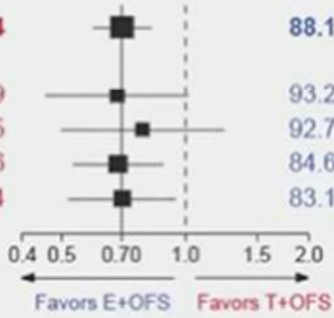
4.1% absolute improvement in 8-yr freedom from breast cancer for E+OFS

2.1% absolute improvement in 8-yr freedom from distant recurrence for E+OFS

HER2-negative Patients (N=4035)

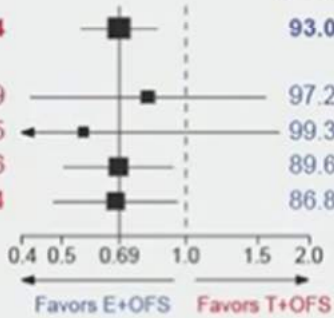
DFS

	E+OFS Events	E+OFS Pts	T+OFS Events	T+OFS Pts	8-Year DFS E+OFS	8-Year DFS T+OFS	Difference
All Patients	**250**	**2011**	**350**	**2024**	**88.1%**	**82.7%**	**+ 5.4%**
Cohort							
No Chemotherapy TEXT	40	492	59	499	93.2%	89.1%	+ 4.1%
No Chemotherapy SOFT	33	447	42	445	92.7%	91.3%	+ 1.4%
Chemotherapy TEXT	105	661	144	656	84.6%	77.7%	+ 6.9%
Prior Chemotherapy SOFT	72	411	105	424	83.1%	73.9%	+ 9.2%



DRFI

	E+OFS Events	E+OFS Pts	T+OFS Events	T+OFS Pts	8-Year DRFI E+OFS	8-Year DRFI T+OFS	Difference
All Patients	**144**	**2011**	**209**	**2024**	**93.0%**	**89.6%**	**+ 3.4%**
Cohort							
No Chemotherapy TEXT	16	492	20	499	97.2%	96.5%	+ 0.7%
No Chemotherapy SOFT	5	447	9	445	99.3%	98.3%	+ 1.0%
Chemotherapy TEXT	70	661	98	656	89.6%	84.6%	+ 5.0%
Prior Chemotherapy SOFT	53	411	82	424	86.8%	79.8%	+ 7.0%

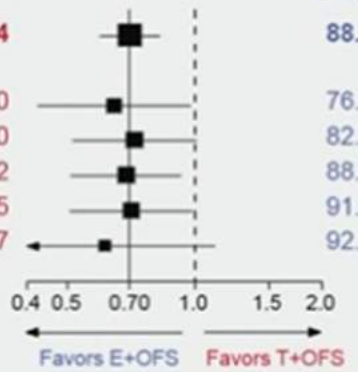


- Consistent relative treatment effects in all cohorts
- Larger absolute benefits of E+OFS in chemo cohorts
- Overall Survival HR=0.86 (0.68-1.10)

Treatment Effect by Age (HER2-neg)

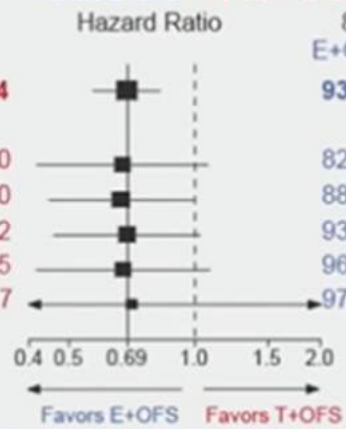
DFS

	E+OFS Events	E+OFS Pts	T+OFS Events	T+OFS Pts	8-Year DFS E+OFS	8-Year DFS T+OFS	Difference
All Patients	**250**	**2011**	**350**	**2024**	**88.1%**	**82.7%**	**+ 5.4%**
Age at Randomization							
< 35	38	180	54	170	76.9%	68.7%	+ 8.2%
35 - 39	63	333	77	320	82.7%	75.6%	+ 7.1%
40 - 44	72	641	106	662	88.6%	83.8%	+ 4.8%
45 - 49	58	657	87	695	91.9%	87.4%	+ 4.5%
50+	19	200	26	177	92.6%	86.2%	+ 6.4%



DRFI

	E+OFS Events	E+OFS Pts	T+OFS Events	T+OFS Pts	8-Year DRFI E+OFS	8-Year DRFI T+OFS	Difference
All Patients	**144**	**2011**	**209**	**2024**	**93.0%**	**89.6%**	**+ 3.4%**
Age at Randomization							
< 35	30	180	40	170	82.5%	74.9%	+ 7.6%
35 - 39	42	333	58	320	88.1%	82.5%	+ 5.6%
40 - 44	39	641	59	662	93.5%	90.7%	+ 2.8%
45 - 49	27	657	44	695	96.3%	93.7%	+ 2.6%
50+	6	200	8	177	97.9%	95.3%	+ 2.6%



Randomized Comparison of Adjuvant Tamoxifen plus Ovarian Function Suppression vs Tamoxifen in Premenopausal Women with HR+ Early Breast Cancer: Update of the SOFT Trial

Gini Fleming, MD

on behalf of SOFT Investigators and

International Breast Cancer Study Group (IBCSG)

SOFT: Suppression of Ovarian Function Trial

Enrolled: Dec 2003-Jan 2011

Stratification

Receipt of (neo)adjuvant chemotherapy

-No chemo, enrolled within 12 weeks of surgery (47%)
-Prior chemo, premenopausal E2 level within 8 months (53%)

Nodal status

-Positive (34.5%)

OFS method intended

-Triptorelin (91%)

RANDOMIZE

Median follow-up 8 years

Tamoxifen x 5y (n=1018)

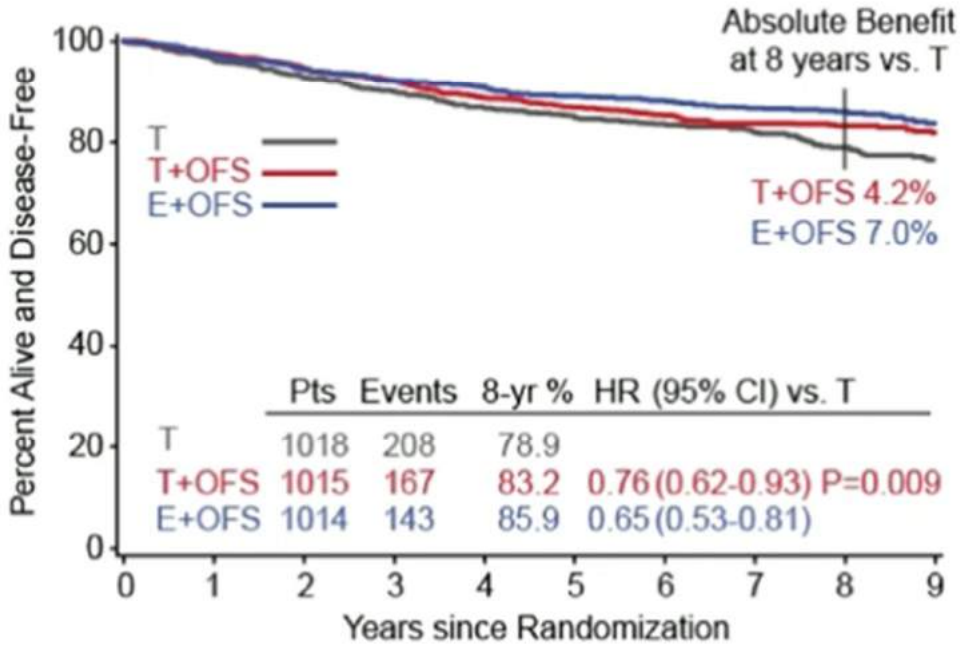
Tamoxifen+OFS x 5y (n=1015)

Exemestane+OFS x 5y (n=1014)

OFS=Ovarian Function Suppression

SOFT DFS

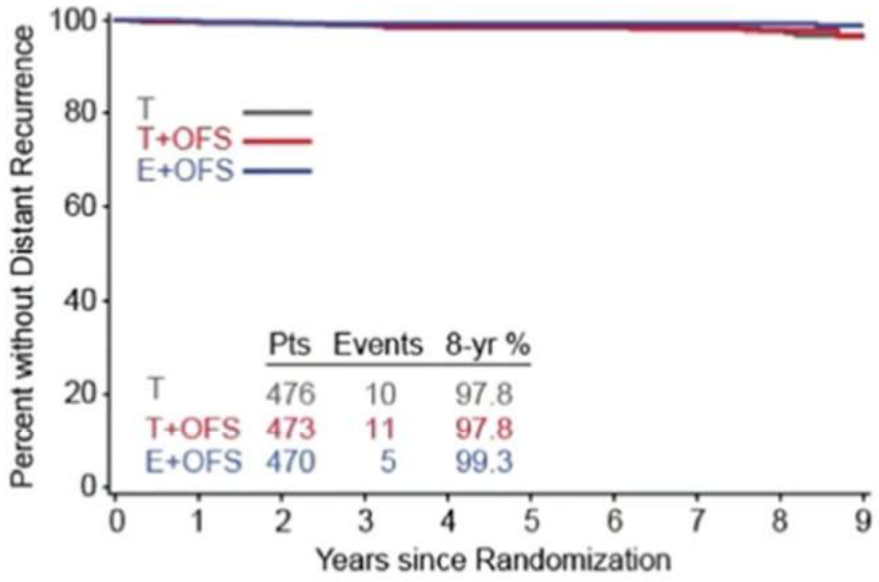
8 years median follow-up



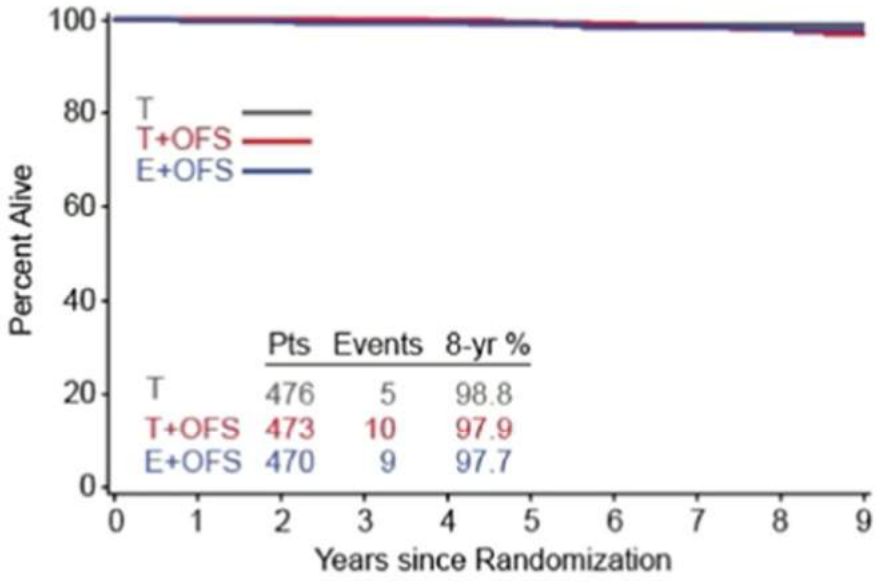
T+OFS significantly improves DFS vs T-alone in the overall population

SOFT Secondary Endpoints: No Chemo

Distant Recurrence-Free Interval



Overall Survival



No Chemo cohort remains at low risk of distant recurrence with T alone;
12 of 24 deaths were in setting of no distant recurrence

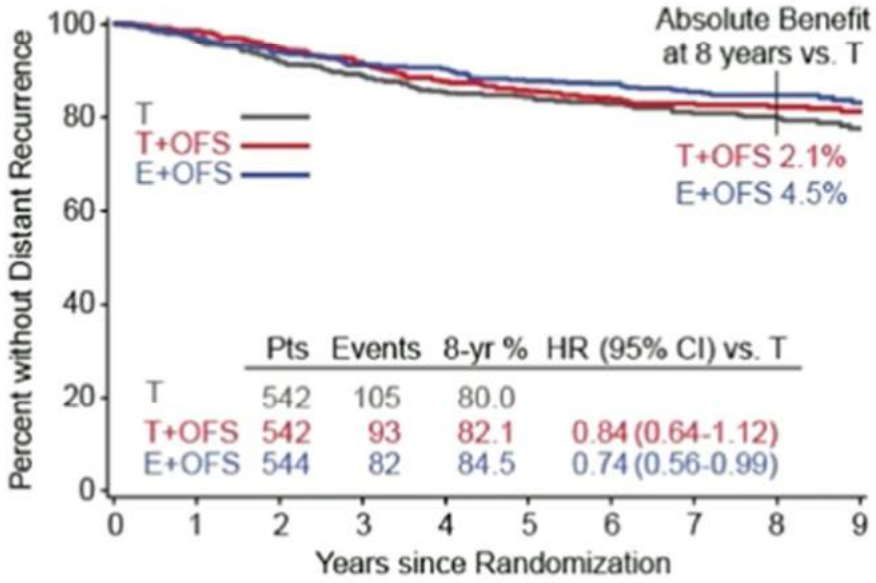
SOFT DFS

8 years median follow-up

	8-yr DFS T	8-yr DFS T + OFS	HR: T + OFS vs T	8-yr DFS E + OFS	HR: E + OFS vs T
All	**78.9%**	**83.2%**	0.76 (0.62-0.93)	**85.9%**	0.65 (0.53-0.81)
No chemo	**87.4%**	**90.6%**	0.76 (0.52-1.12)	**92.5%**	0.58 (0.38-0.88)
Prior chemo	**71.4%**	**76.7%**	0.76 (0.60-0.97)	**80.4%**	0.68 (0.53-0.88)
<35 years (n=350)	**64.3%**	**73.0%**	0.66 (0.41-1.07)	**77.4%**	0.52 (0.31-0.87)

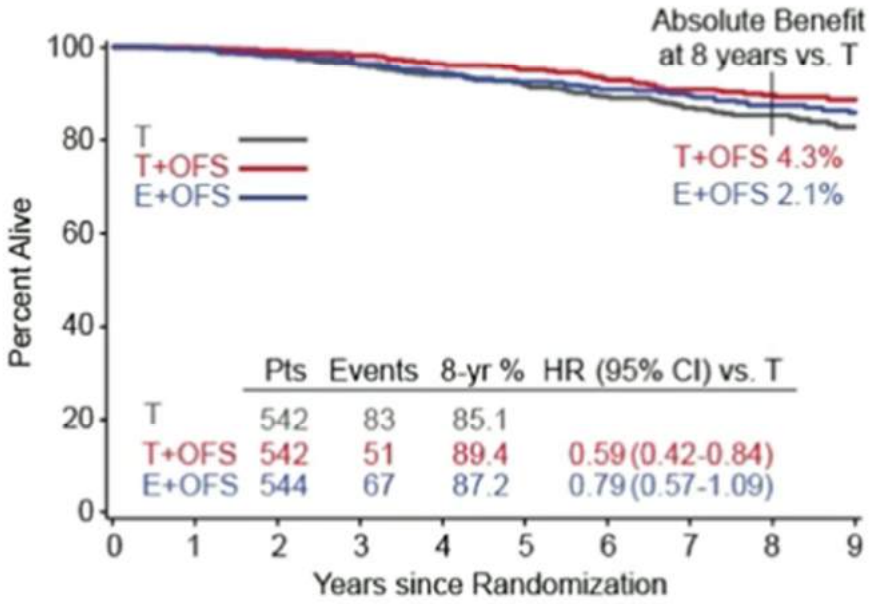
SOFT Secondary Endpoints: Prior Chemo

Distant Recurrence-Free Interval



	Pts	Events	8-yr %	HR (95% CI) vs. T
T	542	105	80.0	
T+OFS	542	93	82.1	0.84 (0.64-1.12)
E+OFS	544	82	84.5	0.74 (0.56-0.99)

Overall Survival



	Pts	Events	8-yr %	HR (95% CI) vs. T
T	542	83	85.1	
T+OFS	542	51	89.4	0.59 (0.42-0.84)
E+OFS	544	67	87.2	0.79 (0.57-1.09)

Prior Chemo cohort has small absolute OS improvements in OFS arms at 8 yrs

Selected Adverse Events

	T (N=1005)	T + OFS (N=1006)	E + OFS (N=1000)
Endometrial cancer (n)	**N=7**	**N=4**	N=3
Thrombosis/embolism (G2-4)	**2.2%**	**2.2%**	0.9%
Hot flashes (G3)	7.8%	**13.2%**	**10.7%**
Libido decrease (G2)	11.5%	**15.9%**	**17.5%**
Musculoskeletal symptoms (G3-4)	6.7%	5.9%	**12.0%**
Osteoporosis (G2-4; T score<-2.5)	3.9%	6.1%	**11.9%**
Depression (G3-4)	4.1%	4.5%	3.9%

Take home message

- Paciente 34 anos, nulípara, solteira, portadora de câncer de mama direita, submetida a cirurgia conservadora e PLS. CDI g3, 4,5cm, 1 linf +/3. RE 70% RP 10% HER 2 1+. Ki67 30%. Estadio (2018) IIA. M0. ECO normal. Sem comorbidades
- CONDUTAS DA ONCOLOGIA baseadas em

  SABCS 2017:

Take home message

- QT ADJUVANTE COM ESQUEMA DOSE-DENSA ADRIAMICINA E CICLOFOSFAMIDA X 4 14/14D +GCSF SEGUIDO POR PACLITAXEL x12

Take home message

- ZOLADEX (OU SIMILAR) MENSAL, CONCOMITANTE A QT PARA TENTATIVA DE PRESERVAÇAO DE FUNÇAO OVARIANA/ FERTILIDADE

Take home message

- HT ADJUVANTE COM ZOLADEX (OU SIMILAR) + EXEMESTANO (ou outro IA) POR 5 ANOS.
- DISCUTIR O BENEFÍCIO COM HT MAIS 2 ANOS DE HT (ATÉ LÁ OS RESULTADOS DEVEM ESTAR MAIS CLAROS...)

Take home message

- ÁCIDO ZOLEDRÔNICO 4MG 6/6M POR ATÉ 2 ANOS CASO NÃO HAJA OSTEOPENIA E/OU OSTEOPOROSE (NESTES CASOS POR 2-5 ANOS). REPOSIÇÃO DE CÁLCIO+ VITD

Take home message

- HER 2 1+: SEM INDICAÇÃO DE HERCEPTIN ADJUVANTE
- ATIVIDADES FÍSICAS, DIETA SAUDÁVEL, CONTROLE DO PESO

INGOH
Instituto Goiano de
Oncologia e Hematologia

Obrigado pela atenção!