XXIII JORNADA DE REVISIÓN DEL

CONGRESO AMERICANO DE ONCOLOGÍA

Cáncer de mama precoz

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ICO Institut Català d'Oncologia

IDI BELL Institut d'Investigació Biomèdica de Bellvitge

UNIVERSITAT DE BARCELONA

SOLTI INNOVATIVE BREAST CANCER RESEARCH

Disclosures

- **Advisor/Consultant:** AstraZeneca-Daiichi; Gebro; Pfizer; Pierre-Fabre; SeaGen
- **Speaker honoraria:** AstraZeneca-Daiichi; Eisai; Gilead; Lilly; Novartis; Roche;
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- **Grant/Research funding to the Institution:** Roche
- **Non-financial disclosure:** member of the SOLTI Executive Board and Scientific Committee

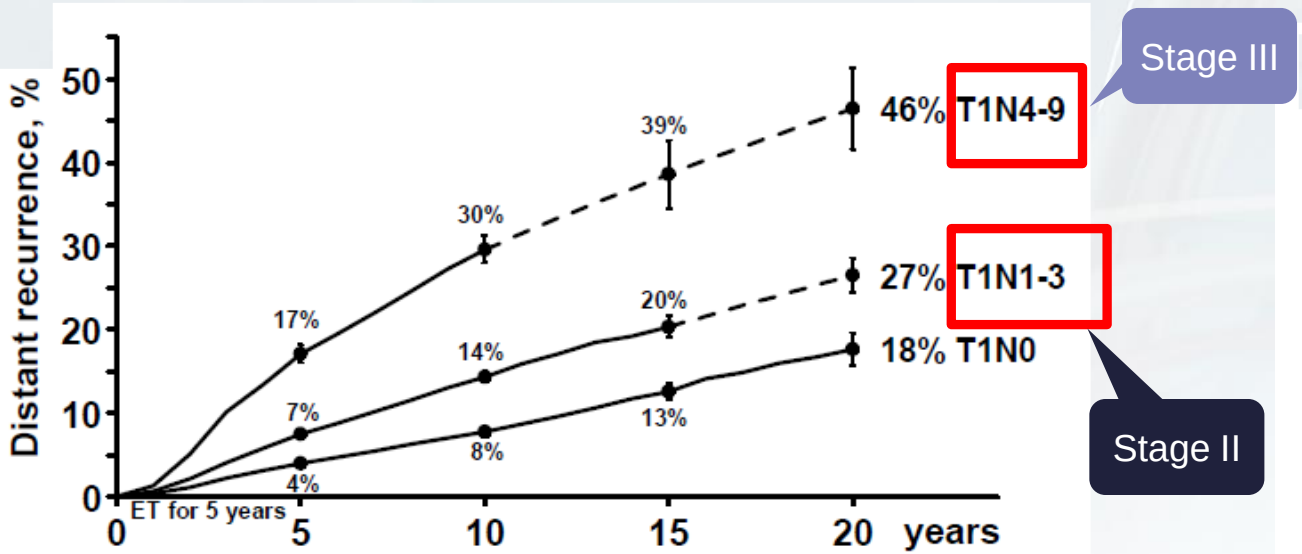
2023 ASCO ANNUAL MEETING
#ASCO23

Outline

- **#LBA500:** Ribociclib and endocrine therapy as adjuvant treatment in patients with HR+/HER2− early breast cancer: Primary results from the phase III **NATALEE trial**. D Slamon, et al.
- **#501** Efficacy and safety **results by age in monarchE**: Adjuvant abemaciclib combined with endocrine therapy (ET) in patients with HR+, HER2-, node-positive, high-risk early breast cancer (EBC). E Hamilton, et al.
- **#503 Effects of ovarian ablation or suppression** on breast cancer recurrence and survival: Patient-level meta-analysis of 14,993 pre-menopausal women in 25 randomized trials. Richard G. Gray et al.
- **#LBA506** 3-year invasive disease-free survival (iDFS) of the strategy-based, randomized phase II **PHERGain** trial evaluating chemotherapy (CT) de-escalation in human epidermal growth factor receptor 2-positive (HER2[+]) early breast cancer (EBC). Javier Cortes et al.
- **#LBA637** Nine-weeks versus one-year trastuzumab for early-stage HER2+ breast cancer: 10-year update of the **Short-HER** phase III randomized trial. PF Conte et al.
- **#510** Prognosis and trends in chemotherapy use for patients with **stage IA triple-negative breast cancer (TNBC):** A population-based study. P Tarantino et al

Risk of recurrence in patients with HR+ early-BC treated with adjuvant ET

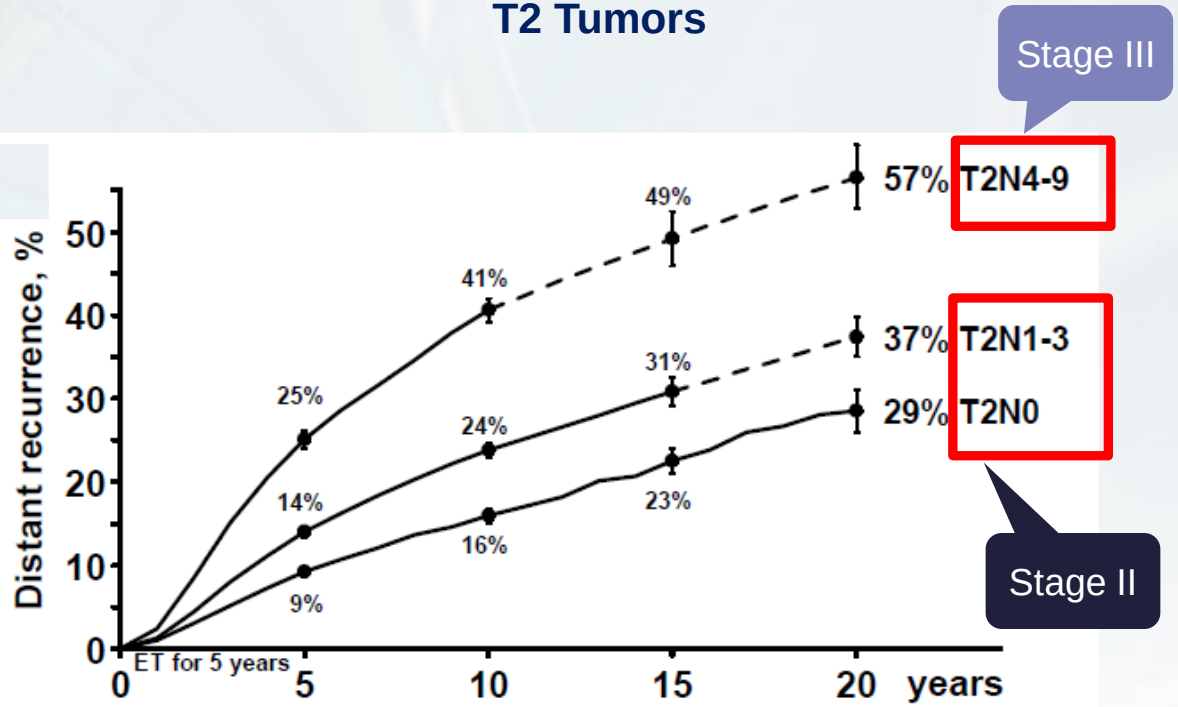
T1 Tumors



No. at risk (and, in each 5-year period, no. of events and annual rate)

T1N4-9	5033	(818, 3.7%)	3517	(340, 3.2%)	956	(47, 2.6%)	115	(7, 2.9%)	18
T1N1-3	17171	(1203, 1.5%)	13305	(652, 1.5%)	4282	(130, 1.6%)	552	(20, 1.5%)	102
T1N0	19682	(744, 0.8%)	16107	(425, 0.8%)	5701	(153, 1.1%)	1323	(39, 1.3%)	263

T2 Tumors



No. at risk (and, in each 5-year period, no. of events and annual rate)

T2N4-9	7300	(1750, 5.7%)	4599	(629, 4.6%)	1209	(74, 3.5%)	144	(6, 1.7%)	34
T2N1-3	14765	(1923, 3.0%)	10271	(769, 2.5%)	2968	(111, 1.9%)	397	(19, 2.1%)	81
T2N0	10243	(902, 1.9%)	7974	(410, 1.6%)	2870	(119, 1.6%)	659	(29, 1.7%)	151

Pan H, et al. N Engl J Med. 2017;377:1836-1846

Real world clinical outcomes in stage II and III HR+/HER2- EBC after initiation of ET

- Retrospective analysis of ConcertAI'sde-identified electronic medical records dataset among pts treated at US academic and community oncology clinics from January 1, 1995 to April 30, 2021
- Stage II BC was 4x' as common as stage III and had a 41% risk of invasive disease recurrence within 10 years of starting adjuvant ET

Population	2-Year Event Risk (95% CI), %	3-Year Event Risk (95% CI), %	5-Year Event Risk (95% CI), %	10-Year Event Risk (95% CI), %
Overall (N = 3133)	11.1 (10.1-12.3)	16.3 (15.0-17.7)	26.1 (24.5-27.9)	45.0 (42.7-47.3)
Stage II (n = 2535)	9.4 (8.3-10.7)	13.8 (12.4-15.2)	22.7 (21.0-24.6)	40.5 (38.0-43.1)
Stage III (n = 598)	18.4 (15.5-21.8)	27.1 (23.6-31.0)	40.4 (36.2-44.9)	62.9 (57.9-67.9)

O'Shaughnessy et al, SABCS 2022

2023 ASCO ANNUAL MEETING

Ribociclib and endocrine therapy as adjuvant treatment in patients with HR+/HER2− early breast cancer: primary results from the Phase III NATALEE trial

Dennis Slamon,[1] Daniil Stroyakovskiy,[2] Denise A. Yardley,[3] Chiun-Sheng Huang,[4] Peter A. Fasching,[5] John Crown,[6] Aditya Bardia,[7] Stephen Chia,[8] Seock-Ah Im,[9] Miguel Martin,[10] Sherene Loi,[11] Binghe Xu,[12] Sara Hurvitz,[13] Carlos Barrios,[14] Michael Untch,[15] Rebecca Moroose,[16] Frances Visco,[17] Rodrigo Fresco,[18] Tetiana Taran,[19] Gabriel N. Hortobagyi[20]

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PRESENTED BY: Dennis Slamon MD, PhD

NATALEE study design[1,2]

- Adult patients with HR+/HER2− EBC
- Prior ET allowed up to 12 mo
- **Anatomical stage IIA**[a]
  - **N0** with:
    - Grade 2 and evidence of high risk:
      - Ki-67 ≥ 20%
      - Oncotype DX Breast Recurrence Score ≥ 26 *or*
      - High risk via genomic risk profiling
    - Grade 3
  - **N1**
- **Anatomical stage IIB**[a]
  - N0 or N1
- **Anatomical stage III**
  - N0, N1, N2, or N3

N = 5101[b]

Who

How much

R 1:1[c]

Ribociclib
400 mg/day
3 weeks on/1 week off
for 3 y

NSAI
Letrozole or anastrozole[d] for ≥ 5 y
+ goserelin in men and premenopausal women

NSAI
Letrozole or anastrozole[d] for ≥ 5 y
+ goserelin in men and premenopausal women

Why

Primary End Point
- iDFS using STEEP criteria

Secondary End Points
- Recurrence-free survival
- Distant disease–free survival
- OS
- PROs
- Safety and tolerability
- PK

What downsides

Exploratory End Points
- Locoregional recurrence–free survival
- Gene expression and alterations in tumor ctDNA/ctRNA samples

Randomization stratification
Anatomical stage: II vs III
Menopausal status: men and premenopausal women vs postmenopausal women
Receipt of prior (neo)adjuvant chemotherapy: yes vs no
Geographic location: North America/Western Europe/Oceania vs rest of world

[a] Enrollment of patients with stage II disease was capped at 40%. [b] 5101 patients were randomized from 10 Jan 2019 to 20 April 2021. [c] Open-label design. [d] Per investigator choice.
CT, chemotherapy; ctDNA/RNA, circulating tumor DNA/RNA; EBC, early breast cancer; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; IDFS, invasive disease-free survival; N, node; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PAM50, prediction analysis of microarray 50; PK, pharmacokinetics; PRO, patient reported outcome; R, randomized; STEEP, Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials.
1. ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT03701334. Accessed April 6 2023. 2. Slamon DJ, et al. *J Clin Oncol*. 2019;37(15 suppl) [abstract TPS597].

Baseline characteristics

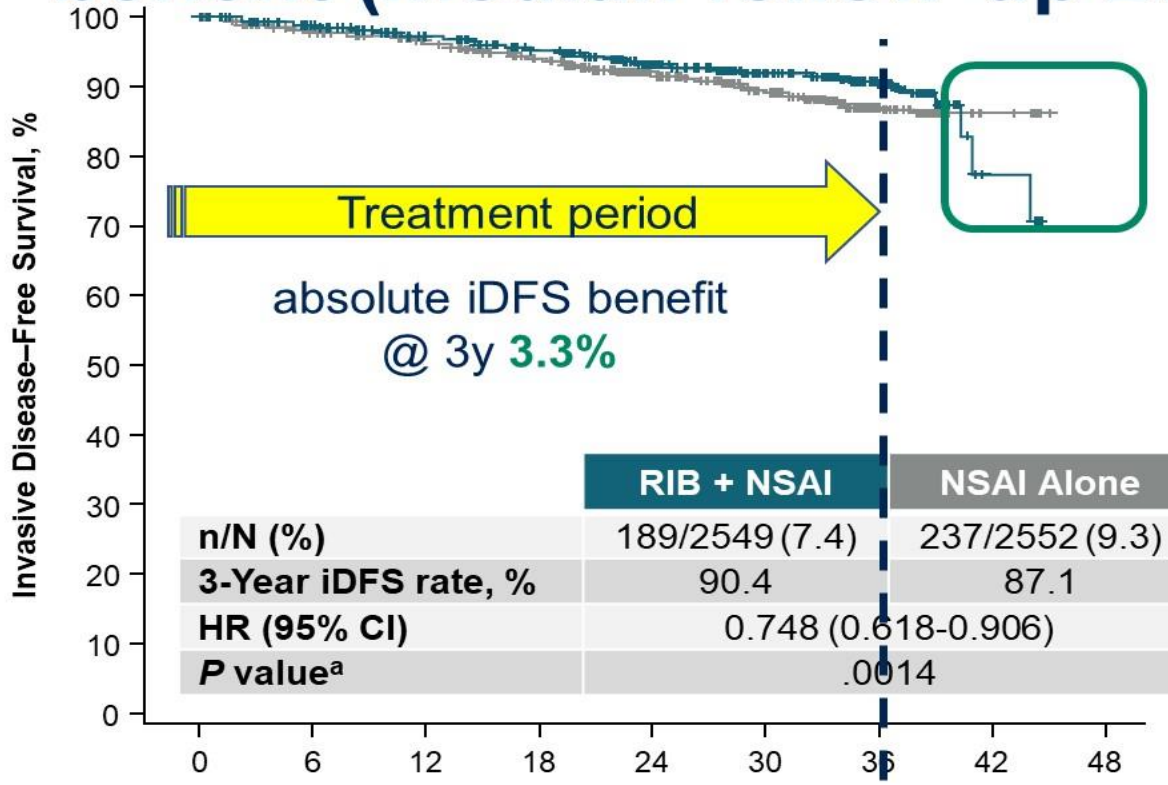
Parameter	RIB + NSAI n = 2549	NSAI Alone n = 2552	All Patients N = 5101
Age, median (min-max), years	52 (24-90)	52 (24-89)	52 (24-90)
Menopausal status, n (%)			
Men[a] and premenopausal women	1126 (44)	1132 (44)	2258 (44)
Postmenopausal women	1423 (56)	1420 (56)	2843 (56)
Anatomical stage,[b,c] n (%)			
Stage IIA	479 (19)	521 (20)	1000 (20)
Stage IIB	532 (21)	513 (20)	1045 (20)
Stage III	1528 (60)	1512 (59)	3040 (60)
Nodal status at diagnosis, n (%)			
NX	272 (11)	264 (10)	536 (11)
N0	694 (27)	737 (29)	1431 (28)
N1	1050 (41)	1049 (41)	2099 (41)
N2/N3	483 (19)	467 (18)	950 (19)
Prior ET, n (%)[d]			
Yes	1824 (72)	1801 (71)	3625 (71)
Prior (neo)adjuvant CT, n (%)			
Yes	2249 (88)	2245 (88)	4494 (88)
ECOG PS, n (%)			
0	2106 (83)	2132 (84)	4238 (83)
1	440 (17)	418 (16)	858 (17)

CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; N0, no nodal involvement; N1, 1-3 axillary lymph nodes; N2, 4-9 axillary lymph nodes; N3, ≥ 10 axillary lymph nodes or infra- or supraclavicular lymph nodes; NSAI, nonsteroidal aromatase inhibitor; NX, regional nodes were not assessed; OFS, ovarian function suppression; RIB, ribociclib.

[a] In the RIB + NSAI arm, there were 11 men (0.4%); in the NSAI alone arm, there were 9 men (0.4%). [b] A total of 14 patients with stage I disease were included: 9 (0.4%) in the RIB + NSAI arm and 5 (0.2%) in the NSAI alone arm. [c] Stage is derived using TNM from surgery for patients having not received (neo)adjuvant treatment or as worst stage derived using TNM at diagnosis and TNM from surgery for patients having received (neo)adjuvant treatment. [d] Prior OFS was received by 670 patients (26.3%) in the RIB + NSAI arm and 620 (24.3%) in the NSAI alone arm.

PRESENTED BY: Dennis Slamon MD, PhD

NATALEE: Ribociclib achieved highly significant iDFS benefit (median follow-up 27.7 months)



	RIB + NSAI	NSAI Alone
n/N (%)	189/2549 (7.4)	237/2552 (9.3)
3-Year iDFS rate, %	90.4	87.1
HR (95% CI)	0.748 (0.618-0.906)	
P value[a]	.0014	

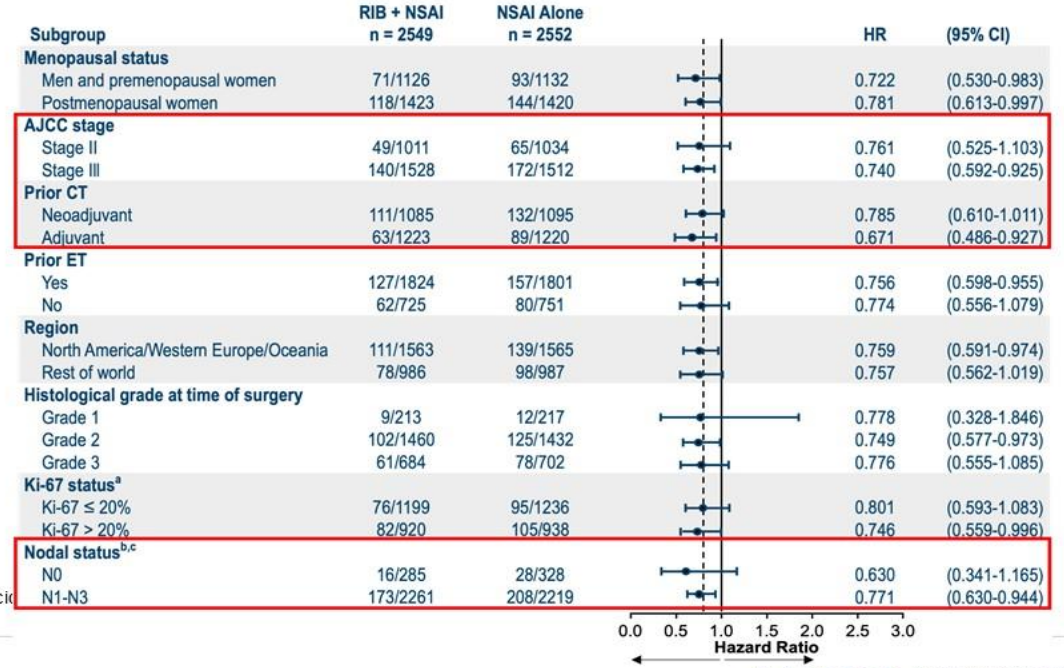
No. at risk									
RIB + NSAI	2549	2350	2274	2193	1718	1111	311	12	0
NSAI alone	2552	2240	2166	2071	1631	1067	286	13	0

iDFS, invasive disease–free survival; IDMC, Independent Data Monitoring Committee; HR, hazard ratio; NSAI, nonsteroidal aromatase inhibitor; RIB, ribocic
[a] One-sided *P* value.

Patients who completed ribociclib

2 years (including ongoing)	1449 (57)
3 years	515 (20)

iDFS benefit consistent across key subgroups



Subgroup	RIB + NSAI n = 2549	NSAI Alone n = 2552	HR	(95% CI)
Menopausal status				
Men and premenopausal women	71/1126	93/1132	0.722	(0.530-0.983)
Postmenopausal women	118/1423	144/1420	0.781	(0.613-0.997)
AJCC stage				
Stage II	49/1011	65/1034	0.761	(0.525-1.103)
Stage III	140/1528	172/1512	0.740	(0.592-0.925)
Prior CT				
Neoadjuvant	111/1085	132/1095	0.785	(0.610-1.011)
Adjuvant	63/1223	89/1220	0.671	(0.486-0.927)
Prior ET				
Yes	127/1824	157/1801	0.756	(0.598-0.955)
No	62/725	80/751	0.774	(0.556-1.079)
Region				
North America/Western Europe/Oceania	111/1563	139/1565	0.759	(0.591-0.974)
Rest of world	78/986	98/987	0.757	(0.562-1.019)
Histological grade at time of surgery				
Grade 1	9/213	12/217	0.778	(0.328-1.846)
Grade 2	102/1460	125/1432	0.749	(0.577-0.973)
Grade 3	61/684	78/702	0.776	(0.555-1.085)
Ki-67 status[a]				
Ki-67 ≤ 20%	76/1199	95/1236	0.801	(0.593-1.083)
Ki-67 > 20%	82/920	105/938	0.746	(0.559-0.996)
Nodal status[b,c]				
N0	16/285	28/328	0.630	(0.341-1.165)
N1-N3	173/2261	208/2219	0.771	(0.630-0.944)

NATALEE: Ribociclib at 400-mg dose was safe and well tolerated

	RIB + NSAI n = 2524		NSAI Alone n = 2444	
AESIs, %	**Any Grade**	**Grade ≥ 3**	**Any Grade**	**Grade ≥ 3**
Neutropenia[a]	62.1	43.8	4.5	0.8
Febrile neutropenia	0.3	0.3	0	0
Liver-related AEs[b]	25.4	8.3	10.6	1.5
QT interval prolongation	5.2	1.0	1.2	0.5
ECG QT prolonged	4.2	0.2	0.7	0
ILD pneumonitis[d]	1.5	0	0.8	0.1
Other clinically relevant AEs,%				
Arthralgia	36.5	1.0	42.5	1.3
Nausea	23.0	0.2	7.5	0.04
Headache	22.0	0.4	16.5	0.2
Fatigue	21.9	0.7	12.7	0.2
Diarrhea	14.2	0.6	5.4	0.1
VTE	1.4	0.6	0.6	0.2

- Most frequent all-grade AEs (RIB + NSAI vs NSAI alone) leading to discontinuation: Liver-related AEs: 8.9% vs 0.1% and Arthralgia: 1.3% vs 1.9%
- Most of RIB AE discontinuations occurred early in treatment: Median time of these discontinuations was 4 months
- **19% discontinued ribociclib** due to AE
- **4%** discontinued NSAI in control arm due to AE

- **monarchE**[1]: **6%** (180/2794) early discontinuations in abemaciclib arm due to AE
- **PenelopeB**[2]: **5%** (33/628) early discontinuations in palbociclib arm due to AE

AE, adverse event; AESI, adverse event of special interest; ILD, interstitial lung disease; MedDRA, Medical Dictionary for Regulatory Activities; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.
[a] This is a grouped term that combines neutropenia and neutrophil count decreased. [b] This is a grouped term that includes all preferred terms identified by standardized MedDRA queries for drug-related hepatic disorders. [c] This is a grouped term. [d] This is a grouped term that includes all preferred terms identified by standardized MedDRA queries for interstitial lung disease.

[1]Johnston et al, Lancet Oncol 2022; [2]Loibl et al, JCO 2021.

Harbeck N ASCO 2023, discussant

Efficacy and Safety Results by Age in monarchE: Adjuvant Abemaciclib Combined with Endocrine therapy (ET) in Patients with HR+, HER2-, Node-Positive, High-Risk Early Breast Cancer (EBC).

Erika Hamilton[1], Jee Hyun Kim[2], Natalja Eigeliene[3], Dimitrios Mavroudis[4], Dragos Mircea Median[5], Heloisa Marconato[6], Sergii Shevnya[7], Ozgur Ozyilkan[8], Juan Manuel Puig[9], Catherine Shannon[10], Maria Munoz[11], Belen San Antonio[11], Ran Wei[11], Astra M. Liepa[11], Joyce O'Shaughnessy[12], Stephen R. D. Johnston[13], Valentina Guarneri[14]

[1]Sarah Cannon Research Institute/Tennessee Oncology, Nashville, Tennessee, USA, [2]Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea, [3]The Wellbeing Services County of Ostrobothnia, Vaasa, Finland, [4]University General Hospital of Heraklion, Heraklion, Greece, [5]Spitalul Clinic Filantropia, Bucharest, Romania, [6]Hospital de Cancer de Londrina, Paraná, Brazil , [7]Vinnytsia Regional Clinical Oncology Dispensary, Vinnytsia, Ukraine, [8]Baskent University Faculty of Medicine, Dept. of Medical Oncology, Adana, Turkey, [9]Centro Polivalente de Asistencia e Inv. Clinica CER-San Juan, San Juan, Argentina, [10]Mater Adult Hospital Brisbane, Brisbane, Australia, [11]Eli Lilly and Company, Indianapolis, Indiana, USA, [12]Baylor University Medical Center, Texas Oncology, US Oncology, Dallas, Texas, USA, [13]Royal Marsden Hospital, NHS Foundation Trust, London, United Kingdom, [14]University of Padua, Medical Oncology 2, Istituto Oncologico Veneto IOV-IRCCS, Padua, Italy

Sponsored by Eli Lilly and Company

Older Patients had More Comorbidities, Higher Baseline ECOG PS Scores, and Received Less Prior (Neo) Adjuvant Chemotherapy

Baseline factors, %		Overall n=5637	<65 n=4787	≥65 n=850
Pathological tumor size (mm)	<20	27	28	23
	20-<50	50	48	57
	≥50	22	22	19
No. positive lymph nodes[a]	1-3	40	41	36
	≥4	60	59	64
Histopathological grade	G1	8	8	7
	G2	49	49	52
	G3	38	38	37
Prior (neo) adjuvant chemotherapy	Yes	94	97	82
	No	6	3	18
ECOG PS[b]	0	85	86	77
	1	15	14	23
Treated patients, %		n=5591	n=4751	n=840
No. pre-existing comorbidities	0	17	19	6
	1-3	48	48	44
	≥4	35	33	51
Initial endocrine therapy	Aromatase inhibitors	68	64	95
	Tamoxifen	31	36	5

Values that do not add up to 100% are due to rounding or missing data; [a]n=14 patients with 0 positive lymph nodes were inadvertently enrolled; [b]n=3 patients with an ECOG PS score of >1 were inadvertently enrolled

Older Patients Derived Similar Abemaciclib Benefit to ITT Population

	IDFS			DRFS		
	ITT	<65	≥65	ITT	<65	≥65
Events/N						
Abemaciclib + ET	**336**/2808	**270**/2371	**66**/437	**281**/2808	**230**/2371	**51**/437
ET alone	**499**/2829	**414**/2416	**85**/413	**421**/2829	**353**/2416	**68**/413
HR (95% CI)	**0.664** (0.578, 0.762)	**0.646** (0.554, 0.753)	**0.767** (0.556, 1.059)	**0.659** (0.567, 0.767)	**0.647** (0.548, 0.764)	**0.748** (0.520, 1.077)
Interaction p-value	NA	0.35		NA	0.49	
4-year rate, %						
Abemaciclib + ET	**85.8**	**86.5**	**82.0**	**88.4**	**88.8**	**86.1**
ET alone	**79.4**	**79.8**	**76.8**	**82.5**	**82.6**	**81.5**
Absolute benefit	**6.4**	**6.7**	**5.2**	**5.9**	**6.2**	**4.6**

Consistent results were observed in Cohort 1

Hamilton et al. ASCO 2023

monarchE: Dose Adjustments were More Common in Older Patients

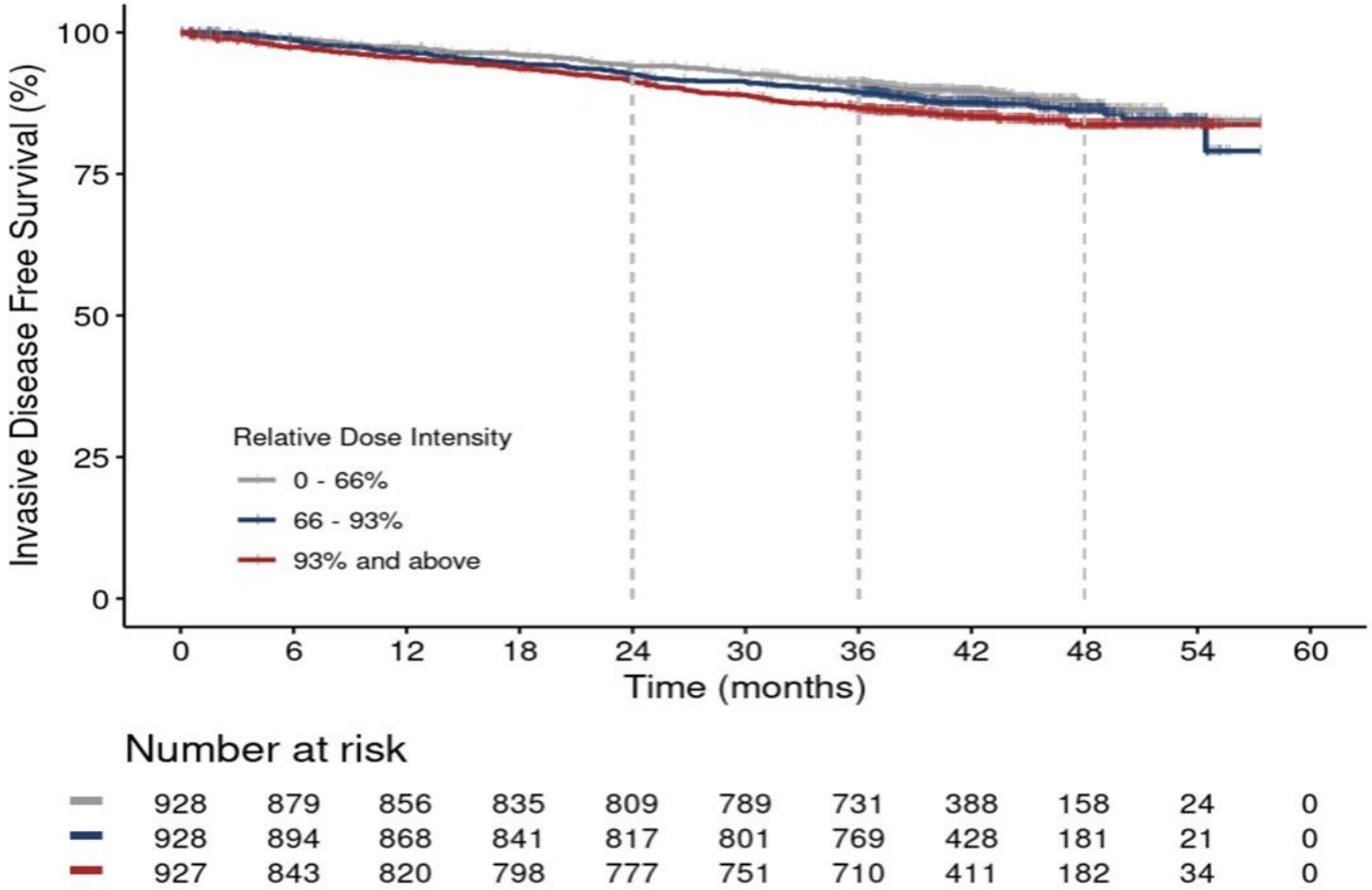
- Older Patients derive similar benefit (iDFS, DRFS) from abemaciclib as ITT population
- QoL was similar between arms and across age subgroups

	Abemaciclib + ET		
Abemaciclib dose adjustments due to AEs, %	**Overall** n=2791	**<65** n=2361	**≥65*** n=430
Interruptions	62	60	68
Reductions	44	42	55
Discontinuations	18	15	38
Discontinuations without prior dose reductions	**10**	**8**	**19**

*Patients ≥75 years have higher rates of abemaciclib dose adjustments and discontinuations due to AEs

monarchE: Abemaciclib Benefit is Maintained when Dose Modifications are Undertaken to Manage AEs

IDFS according to RDI in patients treated with abemaciclib (all ages included)



- Dose adjustments result in lower relative dose intensity (RDI*). To explore the impact of dose adjustments on abemaciclib efficacy:
  - Patients treated with abemaciclib were classified into 3 equal sized subgroups according to their RDI
  - IDFS rates were estimated within each subgroup

- **4-year IDFS rates were generally consistent** (87.1% vs 86.4% vs 83.7% from the lowest RDI group to the highest)
  - Similar findings were observed in Cohort 1 patients treated with abemaciclib

***RDI is defined as the average daily dose of abemaciclib received over the treatment duration, relative to the full dose (150mg BID)**

Comparison of NATALEE and monarchE Populations

AJCC Anatomical Staging[1]	TN (M0)	NATALEE[2]	monarchE[3]
Stage IIA	T0N1	✓	Only if grade 3 or Ki-67 ≥20%
	T1N1	✓	Only if grade 3 or Ki-67 ≥20%
	T2N0	Only if G3; or G2 with Ki-67 ≥20% or high genomic risk[a]	✗
Stage IIB	T2N1	✓	Only if grade 3 or Ki-67 ≥20%
	T3N0	✓	✗
Stage IIIA	T0N2	✓	✓
	T1N2	✓	✓
	T2N2	✓	✓
	T3N1	✓	✓
	T3N2	✓	✓
Stage IIIB	T4N0	✓	✗
	T4N1	✓	Only if tumor size ≥5 cm or grade 3 or Ki-67 ≥20%
	T4N2	✓	✓
Stage IIIC	Any TN3	✓	✓

NATALEE allowed:
- Any **N1, N2, N3**
- **N0**: **T2** [(*G2 + high genomic risk or Ki-67≥ 20%) or G3*)], **T3, T4**

monarchE allowed:
- Any **N2**, **N3**
- **N1** only if G3 or tumor size ≥ 5cm or Ki-67≥20%

N0 not allowed in monarchE

[a] High risk as determined by Oncotype DX/Prosigna/MammaPrint/EndoPredict

Slamon D, et al. ASCO 2023. LBA500; Harbeck N, et al. Ann Oncol. 2021;32:1571-1581.

2023 ASCO ANNUAL MEETING

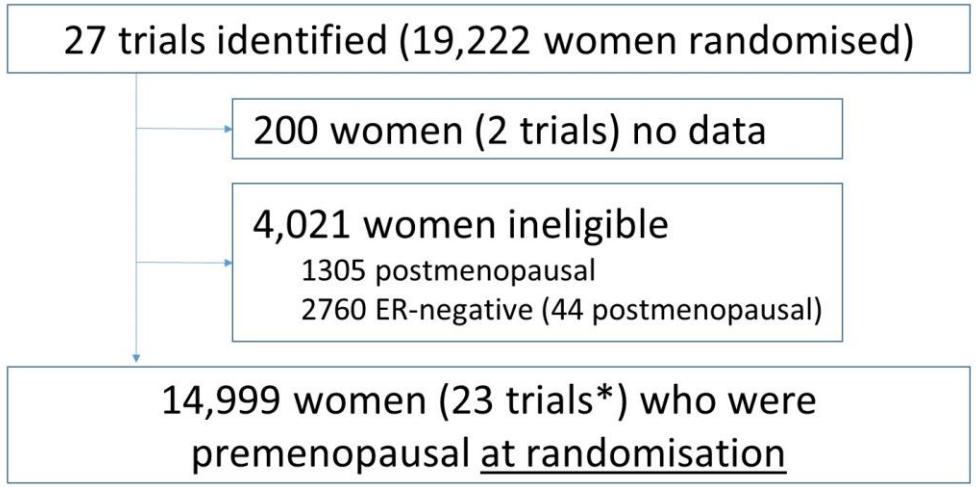
Effects of ovarian ablation or suppression on breast cancer recurrence and survival: patient-level meta-analysis of 14,999 pre-menopausal women in 25 randomized trials

Early Breast Cancer Trialists Collaborative Group (EBCTCG)

Writing Committee: Richard Gray, Rosie Bradley, Jeremy Braybrooke, Mike Clarke, Robert Hills, Richard Peto, Jonas Bergh, Sandra Swain, Rodrigo Arriagada, Judith Bliss, Allan Hackshaw, Hyun-Ah Kim, Woo Chul Noh, John Yarnold, Nancy Davidson, Prudence Francis, Meredith Regan

PRESENTED BY: Richard Gray, Emeritus Professor of Medical Statistics, University of Oxford

Randomised trials of ovarian ablation/suppression



*2 trials included only postmenopausal women

- No chemotherapy: 12 trials (3,934 women)
- Chemotherapy given prior to randomisation (3 trials)
- Post-randomisation chemotherapy (14 trials: 7,786)

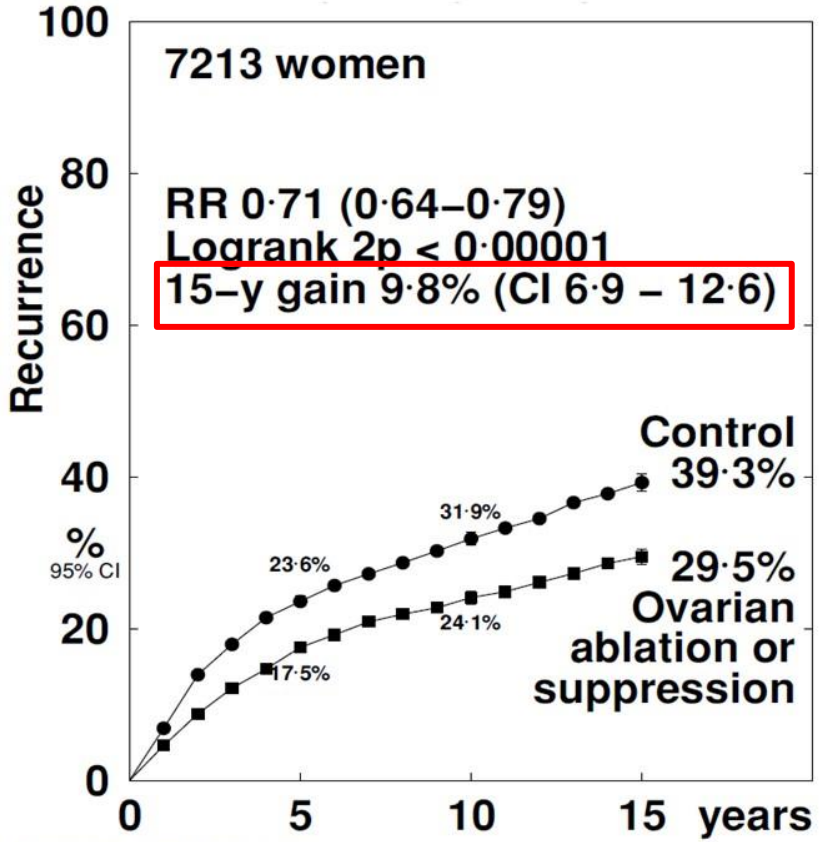
Methods

- Meta-analysis of individual patient data from trials of ovarian ablation (by surgery or irradiation) or ovarian suppression (usually GnRH-agonists) versus not (with all other treatments the same in each group)
- Pre-menopausal women with ER-positive, or unknown ER status, early stage breast cancer
- Primary outcomes: recurrence and cause specific mortality analysed by standard EBCTCG* methods

*EBCTCG OUP 1990, Lancet 2011, 2012

Ovarian ablation/suppression vs not: Recurrence

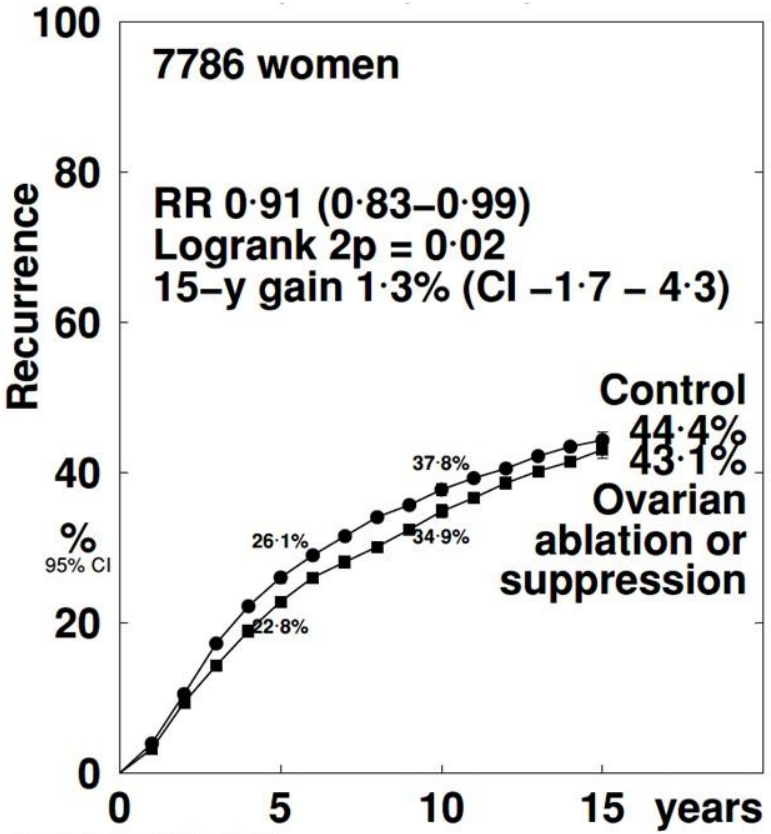
(A) No chemotherapy, or remained premenopausal after chemotherapy



Recurrence rates (% / year) and logrank analyses

Allocation	Years 0 – 4	Years 5 – 9	Years 10 – 14	Year 15+
Abl./suppr.	4·38 (667 / 15233)	1·79 (178 / 9933)	1·47 (78 / 5291)	1·30 (72 / 5520)
Control	5·12 (740 / 14445)	2·22 (198 / 8916)	2·34 (100 / 4273)	1·39 (54 / 3893)
Rate ratio, from	0·71 CI 0·62 – 0·81	0·73 CI 0·58 – 0·93	0·63 CI 0·45 – 0·89	0·90 CI 0·55 – 1·48
(O–E) / V	–77·8 / 226·2	–21·6 / 69·9	–14·8 / 32·6	–1·6 / 15·5

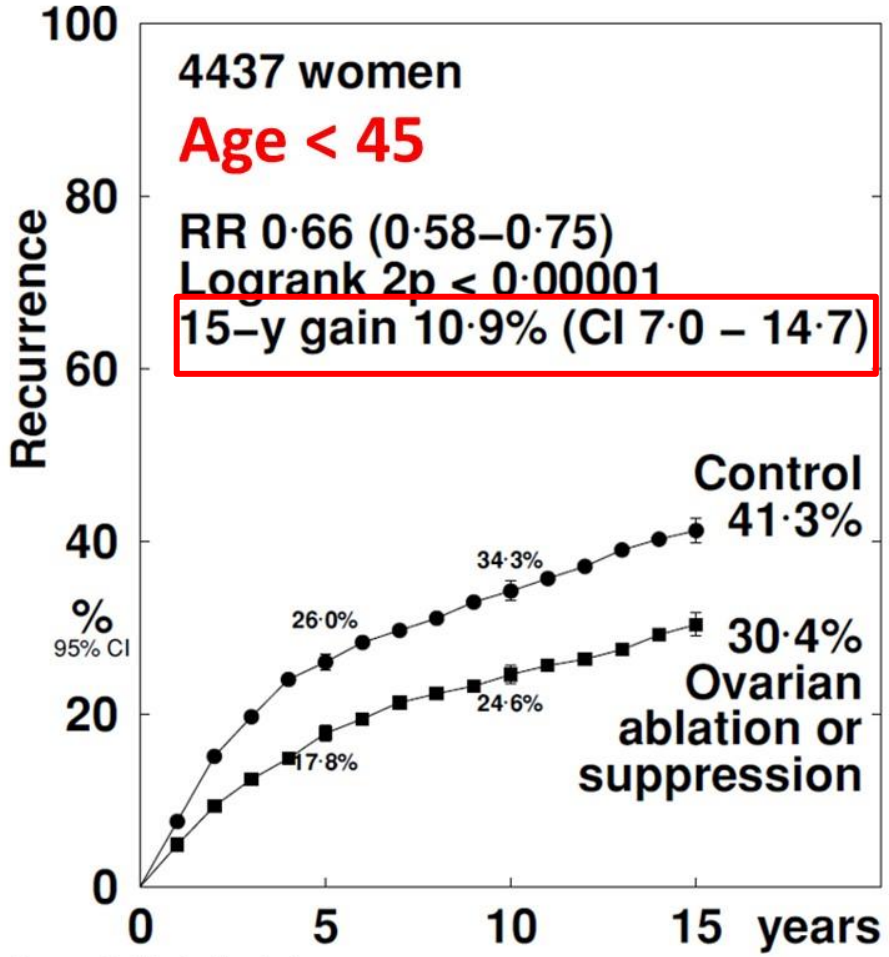
(B) Premenopausal before chemotherapy, uncertain after



Recurrence rates (% / year) and logrank analyses

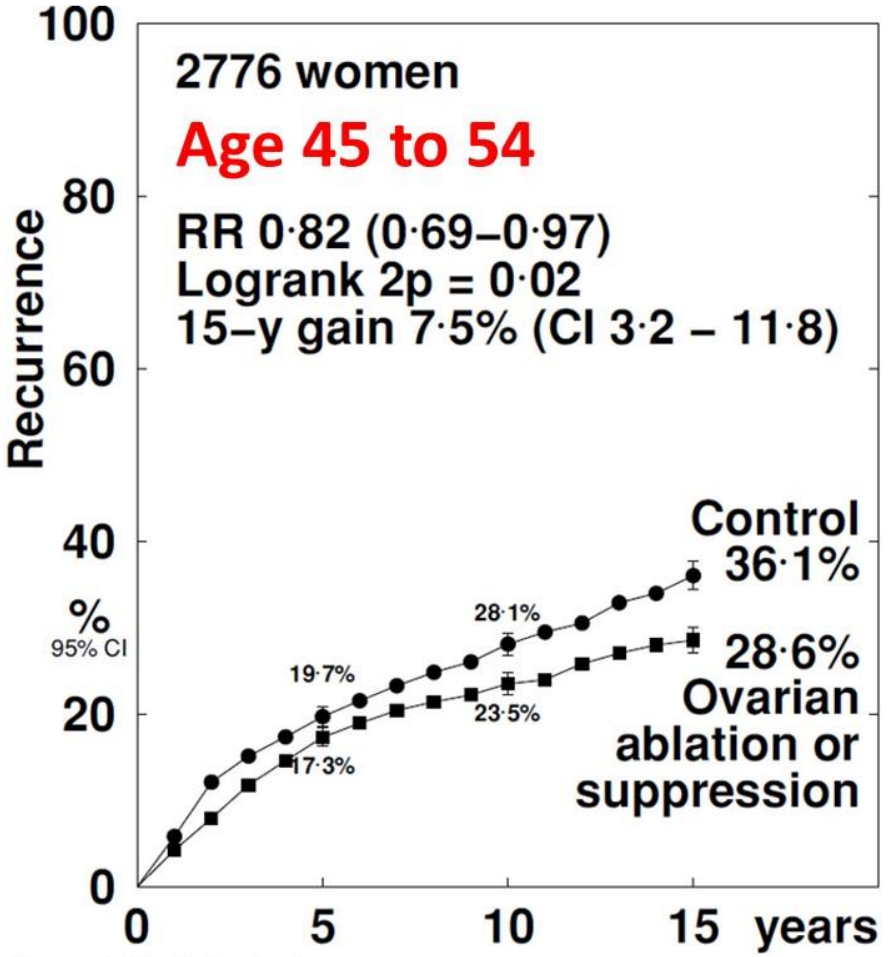
Allocation	Years 0 – 4	Years 5 – 9	Years 10 – 14	Year 15+
Abl./suppr.	5·29 (848 / 16038)	3·40 (345 / 10156)	2·73 (109 / 3993)	1·20 (21 / 1747)
Control	5·88 (950 / 16170)	3·51 (351 / 9996)	2·33 (91 / 3901)	0·95 (16 / 1676)
Rate ratio, from	0·85 CI 0·76 – 0·95	0·97 CI 0·82 – 1·15	1·18 CI 0·86 – 1·61	1·07 CI 0·53 – 2·18
(O–E) / V	–54·4 / 337·3	–4·1 / 135·6	6·5 / 39·6	0·5 / 7·6

Ovarian ablation/suppression vs not: Recurrence
(A) No chemotherapy or premenopausal after



Recurrence rates (% / year) and logrank analyses

Allocation	Years 0 – 4	Years 5 – 9	Years 10 – 14	Year 15+
Abl./suppr.	4·52 (412 / 9119)	1·86 (100 / 5384)	1·50 (41 / 2736)	1·11 (32 / 2885)
Control	5·77 (498 / 8637)	2·35 (110 / 4678)	2·41 (53 / 2201)	1·40 (30 / 2137)
Rate ratio, from	0·64 CI 0·55 – 0·75	0·75 CI 0·55 – 1·02	0·64 CI 0·40 – 1·01	0·65 CI 0·32 – 1·31
(O–E) / V	–66·8 / 149·9	–11·4 / 39·8	–8·0 / 17·6	–3·4 / 7·7

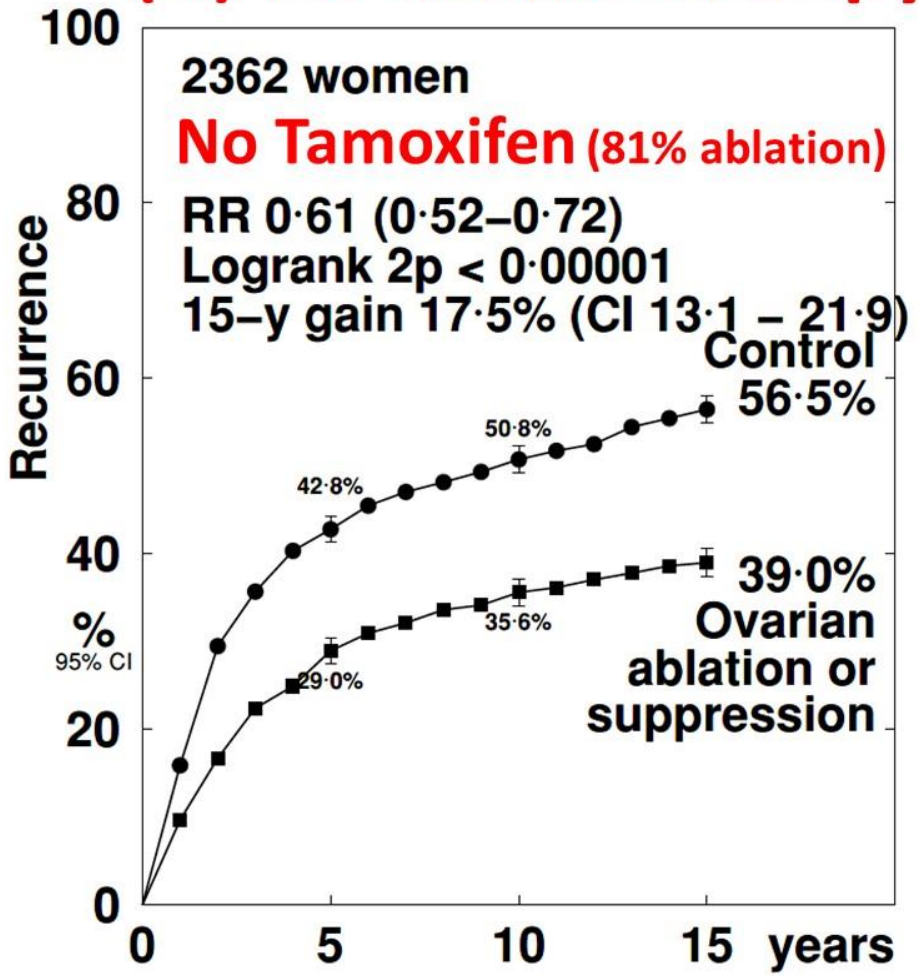


Recurrence rates (% / year) and logrank analyses

Allocation	Years 0 – 4	Years 5 – 9	Years 10 – 14	Year 15+
Abl./suppr.	4·17 (255 / 6113)	1·72 (78 / 4548)	1·45 (37 / 2555)	1·52 (40 / 2635)
Control	4·17 (242 / 5807)	2·08 (88 / 4238)	2·27 (47 / 2072)	1·37 (24 / 1756)
Rate ratio, from	0·87 CI 0·69 – 1·08	0·71 CI 0·50 – 1·02	0·63 CI 0·38 – 1·05	1·25 CI 0·62 – 2·52
(O–E) / V	–11·0 / 76·4	–10·1 / 30·1	–6·9 / 15·1	1·7 / 7·7

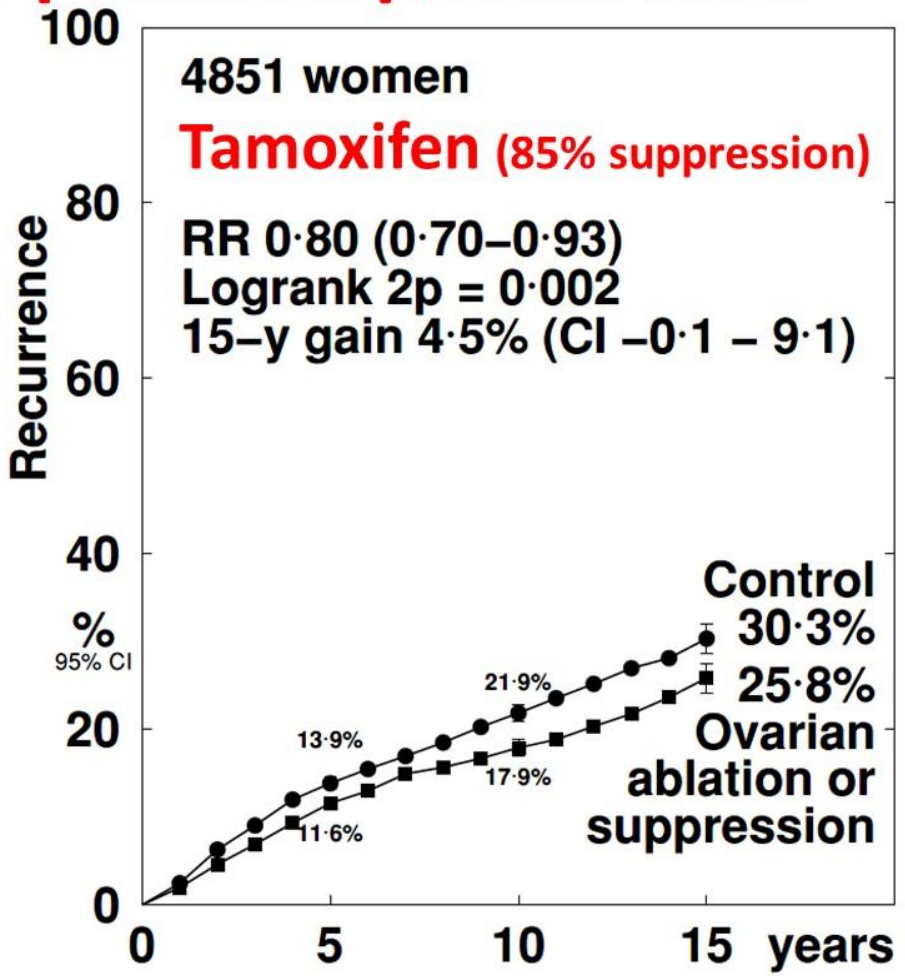
Ovarian ablation/suppress. vs not: Recurrence by tamoxifen use

(A) No chemotherapy or premenopausal after



Recurrence rates (% / year) and logrank analyses

Allocation	Years 0 – 4	Years 5 – 9	Years 10 – 14	Year 15+
Abl./suppr.	8·37 (412 / 4921)	2·22 (82 / 3691)	1·26 (37 / 2945)	1·28 (69 / 5395)
Control	10·82 (427 / 3945)	2·90 (80 / 2757)	2·47 (52 / 2103)	1·37 (52 / 3785)
Rate ratio, from	0·60 CI 0·49 – 0·72	0·66 CI 0·43 – 0·99	0·47 CI 0·27 – 0·81	0·85 CI 0·51 – 1·42
(O–E) / V	–51·8 / 100·0	–9·6 / 22·8	–9·8 / 12·9	–2·4 / 14·3

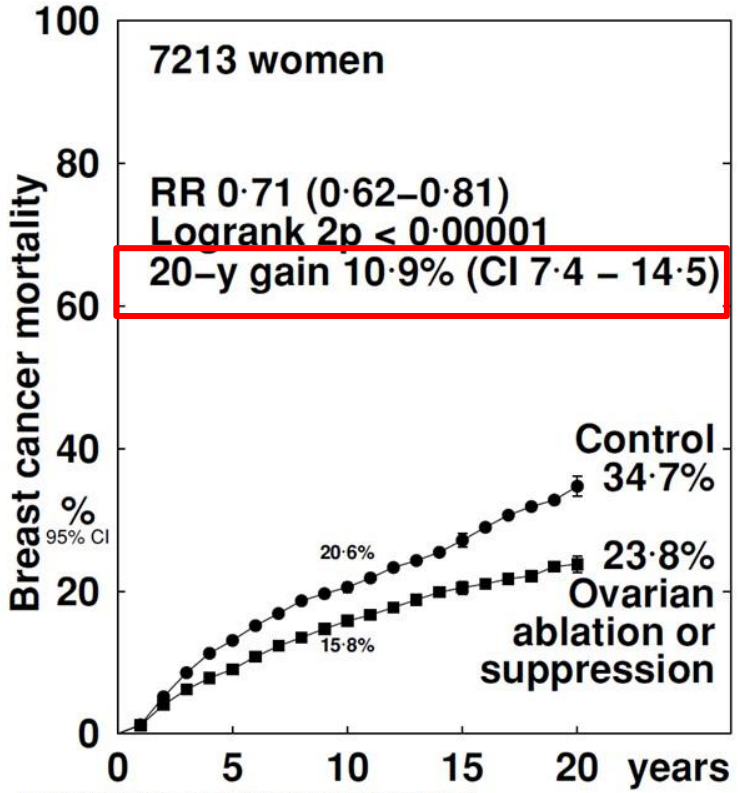


Recurrence rates (% / year) and logrank analyses

Allocation	Years 0 – 4	Years 5 – 9	Years 10 – 14	Year 15+
Abl./suppr.	2·47 (255 / 10311)	1·54 (96 / 6242)	1·75 (41 / 2346)	2·40 (3 / 125)
Control	2·98 (313 / 10499)	1·92 (118 / 6159)	2·21 (48 / 2169)	1·85 (2 / 108)
Rate ratio, from	0·81 CI 0·68 – 0·97	0·78 CI 0·58 – 1·03	0·77 CI 0·50 – 1·20	1·94 CI 0·30 – 12·52
(O–E) / V	–26·1 / 126·3	–12·0 / 47·1	–5·0 / 19·7	0·7 / 1·1

Ovarian ablation/suppression vs not: Mortality
(A) No chemotherapy or premenopausal after

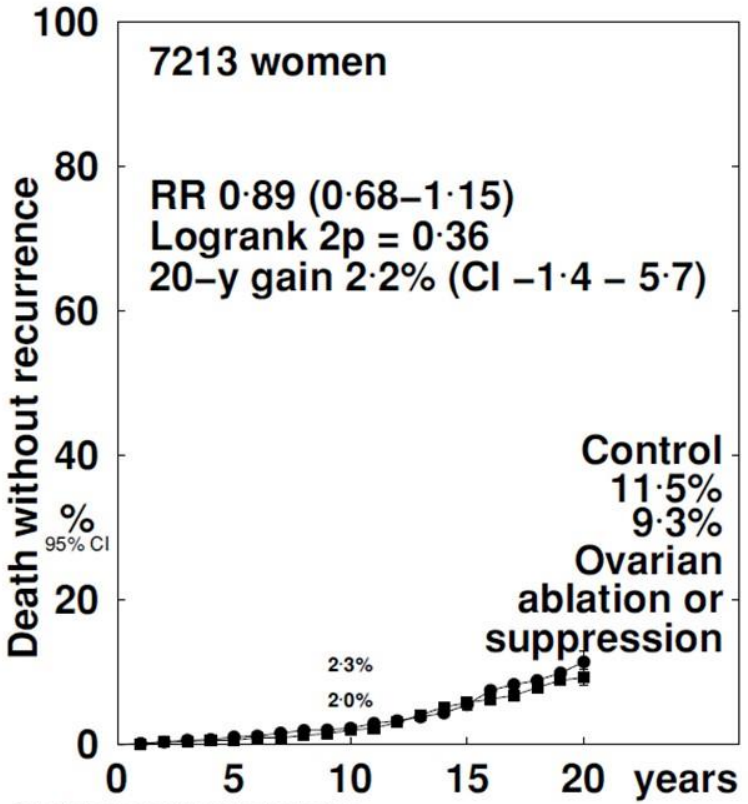
Breast cancer mortality



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

Allocation	Years 0 – 9	Years 10 – 19	Year 20+
Abl./suppr.	2·01 ci 1·84 – 2·18	1·18 ci 0·95 – 1·41	1·30 ci 0·93 – 1·68
Control	2·19 ci 2·01 – 2·37	1·78 ci 1·47 – 2·09	1·47 ci 1·01 – 1·93
Rate ratio, from	0·74 ci 0·63 – 0·86	0·58 ci 0·42 – 0·81	0·82 ci 0·43 – 1·56
(O–E) / V	–51·7 / 169·2	–19·5 / 35·9	–1·9 / 9·4

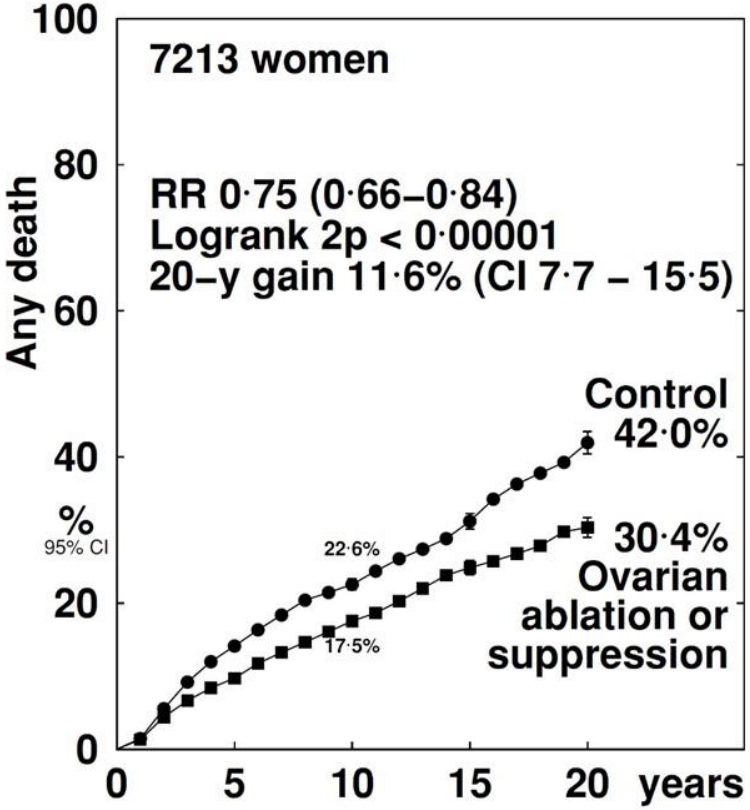
Death without recurrence



Death–without–recurrence rates (% / year) and logrank analyses

Allocation	Years 0 – 9	Years 10 – 19	Year 20+
Abl./suppr.	0·19 (49 / 25165)	0·73 (56 / 7648)	4·32 (146 / 3376)
Control	0·21 (50 / 23362)	0·86 (51 / 5905)	4·32 (106 / 2452)
Rate ratio, from	0·75 ci 0·46 – 1·22	0·89 ci 0·54 – 1·47	0·98 ci 0·67 – 1·44
(O–E) / V	–4·7 / 16·2	–1·8 / 15·4	–0·5 / 26·1

All cause mortality



Death rates (% / year) and logrank analyses

Allocation	Years 0 – 9	Years 10 – 19	Year 20+
Abl./suppr.	2·22 (602 / 27161)	1·89 (160 / 8488)	5·40 (193 / 3573)
Control	2·43 (628 / 25843)	2·55 (178 / 6991)	5·52 (145 / 2625)
Rate ratio, from	0·74 ci 0·64 – 0·85	0·66 ci 0·50 – 0·87	0·93 ci 0·67 – 1·30
(O–E) / V	–56·4 / 185·5	–21·3 / 51·3	–2·4 / 35·5

2023 ASCO ANNUAL MEETING

3-year invasive disease-free survival (iDFS) of the strategy-based, randomized phase II PHERGain trial evaluating chemotherapy (CT) de-escalation in human epidermal growth factor receptor 2-positive (HER2[+]) early breast cancer (EBC)

Javier Cortés[1,2,3], José Manuel Pérez-García[1,2], Manuel Ruiz-Borrego[4], Agostina Stradella[5], Begoña Bermejo[6], Santiago Escrivá-de-Romaní[7], Lourdes Calvo Martínez[8], Nuria Ribelles[9], Alfonso Cortés[10], Cinta Albacar[11], Marco Colleoni[12], Geraldine Gebhart[13], Aleix Prat[14], Kerrou Khaldoun[15], Peter Schmid[16], Serena Di Cosimo[17], Crina Popa[2], Daniel Alcalá-López[2], Miguel Sampayo-Cordero[2], Antonio Llombart-Cussac[2,18]

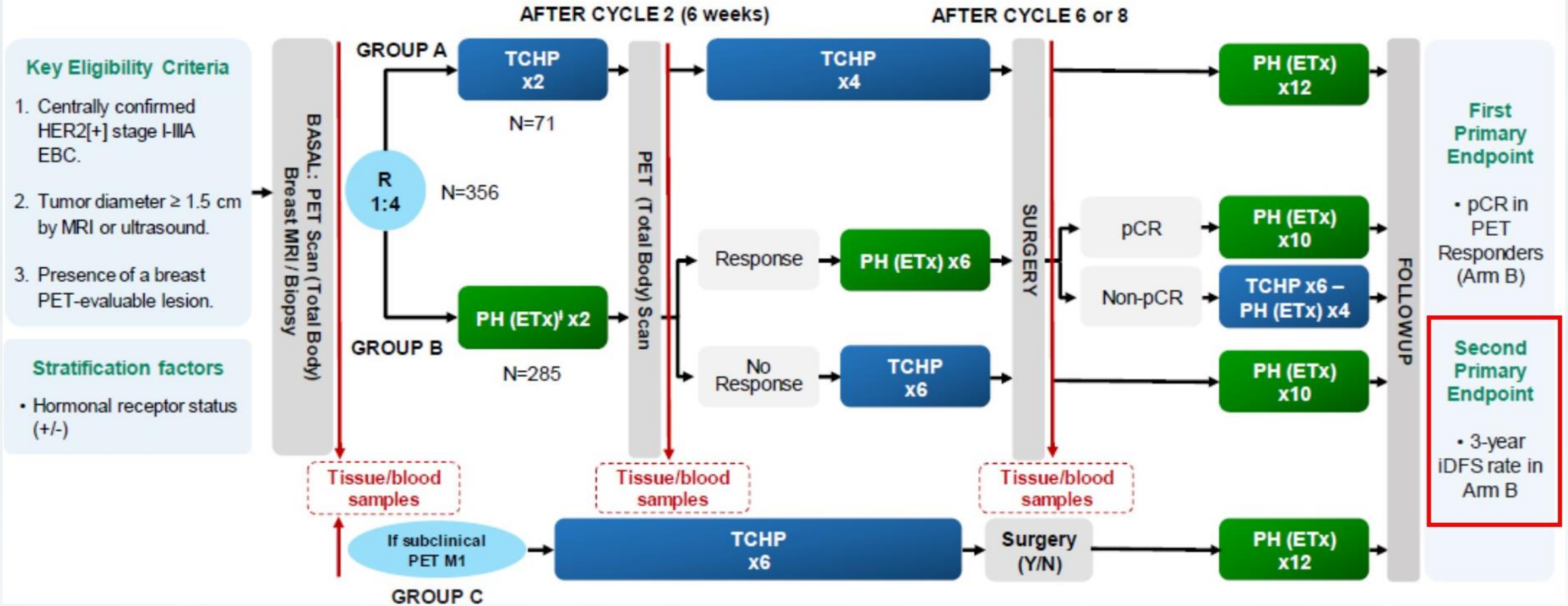
1.) International Breast Cancer Center (IBCC), Pangaea Oncology, Quiron Group, Barcelona, Spain; 2.) Medica Scientia Innovation Research (MEDSIR), Barcelona, Spain and Ridgewood, New Jersey, US; 3.) Universidad Europea de Madrid, Faculty of Biomedical and Health Sciences, Department of Medicine, Madrid, Spain; 4.) University Hospital Virgen del Rocío, Sevilla, Spain; 5.) Medical Oncology Department, Institut Català D'Oncologia, L'Hospitalet de Llobregat, Barcelona, Spain; 6.) Medical Oncology, Hospital Clínico Universitario de Valencia, Biomedical Research Institute INCLIVA, Medicine Department, Universidad de Valencia, Valencia and Oncology Biomedical Research National Network (CIBERONC-ISCIII), Madrid; 7.) Medical Oncology Department, Breast Cancer Group, Vall d'Hebron University Hospital, Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain; 8.) Hospital Universitario A Coruña, A Coruña, Spain; 9.) UGC Oncología Intercentros, Hospital Universitario Virgen de la Victoria, Instituto de Investigaciones Biomédicas de Málaga (IBIMA), Málaga, Spain; 10.) University Hospital Ramón y Cajal, Madrid, Spain; 11.) Hospital Universitari Sant Joan de Reus, Reus, Spain; 12.) European Institute of Oncology (IRCCS), Milan, Italy; 13.) Institut Jules Bordet–Université Libre de Bruxelles, Brussels, Belgium; 14.) Department of Medical Oncology, Hospital Clinic of Barcelona, Translational Genomics, Targeted Therapies Group, IDIBAPS, Department of Medicine, University of Barcelona, Barcelona, Spain; 15.) APHP, Tenon Hospital IUC-UPMC, Nuclear Medicine and PET Center Department, Sorbonne University, Paris, France; 16.) Barts Experimental Cancer Medicine Centre, Barts Cancer Institute, Queen Mary University of London, Barts Hospital NHS Trust, London, UK; 17.) Department of Advanced Diagnostics, Fondazione IRCCS Istituto Nazionale dei Tumori, Milano; 18.) Arnau de Vilanova Hospital, Universidad Católica de Valencia, Valencia, Spain.

PRESENTED BY: Dr. JAVIER CORTÉS MD PhD

phergain

ASCO AMERICAN SOCIETY OF CLINICAL ONCOLOGY
KNOWLEDGE CONQUERS CANCER

PHERGain Study Design

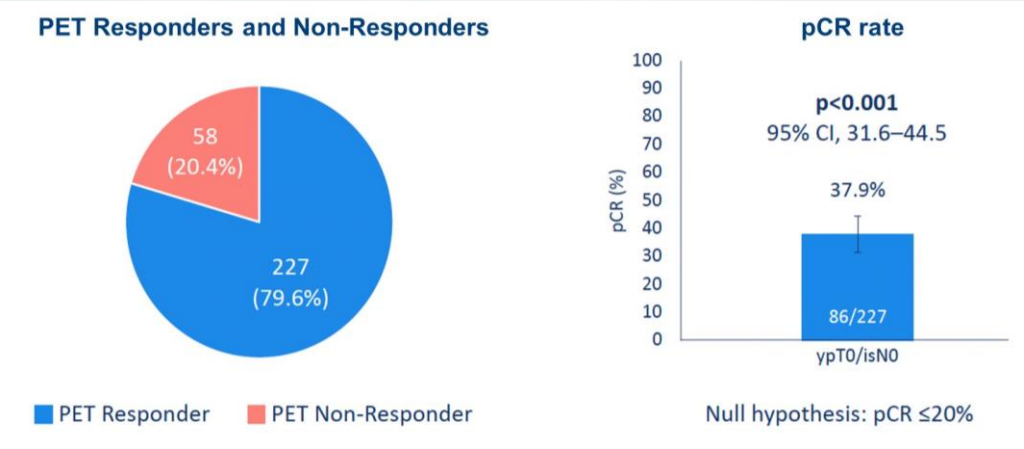


- De-escalation phase II study with a response-adapted strategy
- Patient charact.: 76.8% stage II; 51% cN0; ER+ 67.4%

Javier Cortés, ASCO 2023 #LBA506

PHERGain

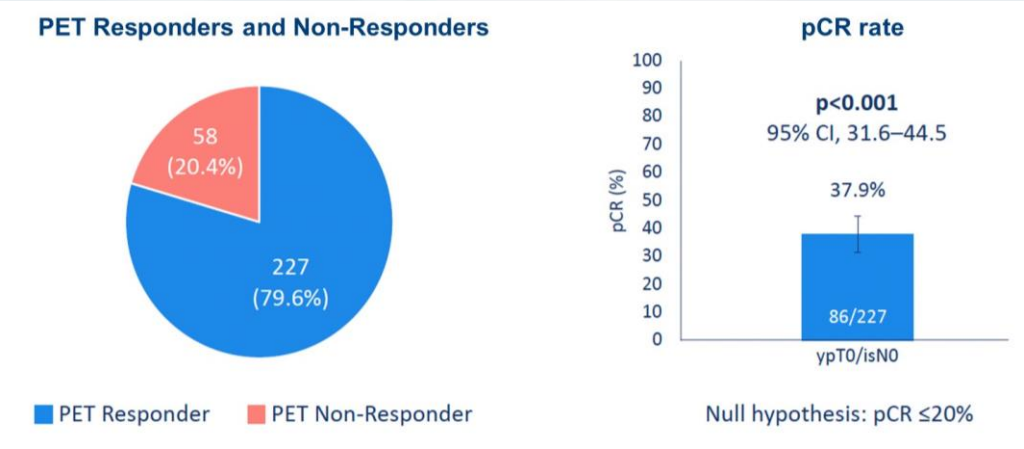
pCR in PET responders (primary endpoint)



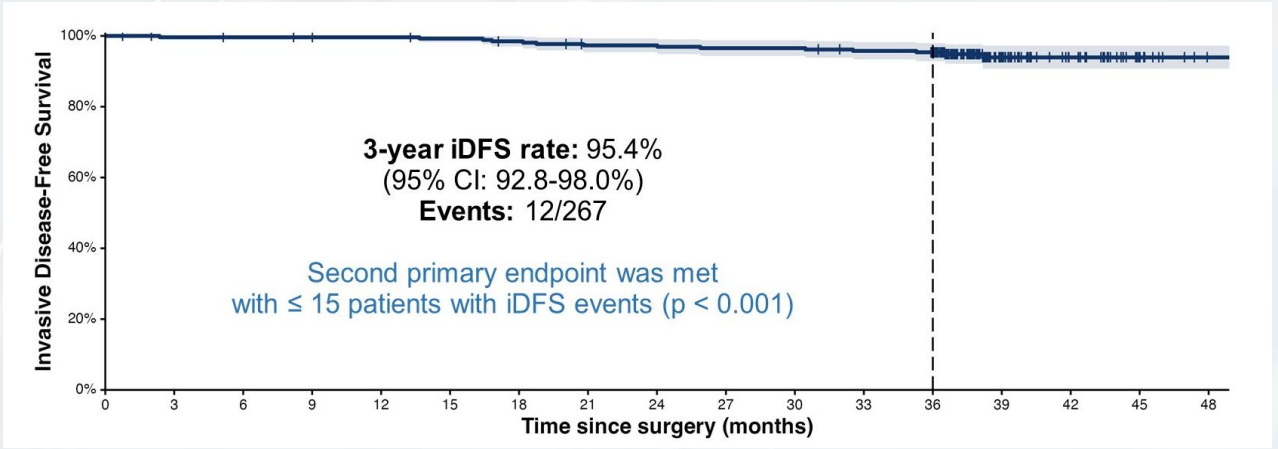
Pérez-García, Lancet Oncol 2021; Javier Cortés, ASCO 2023 #LBA506

PHERGain

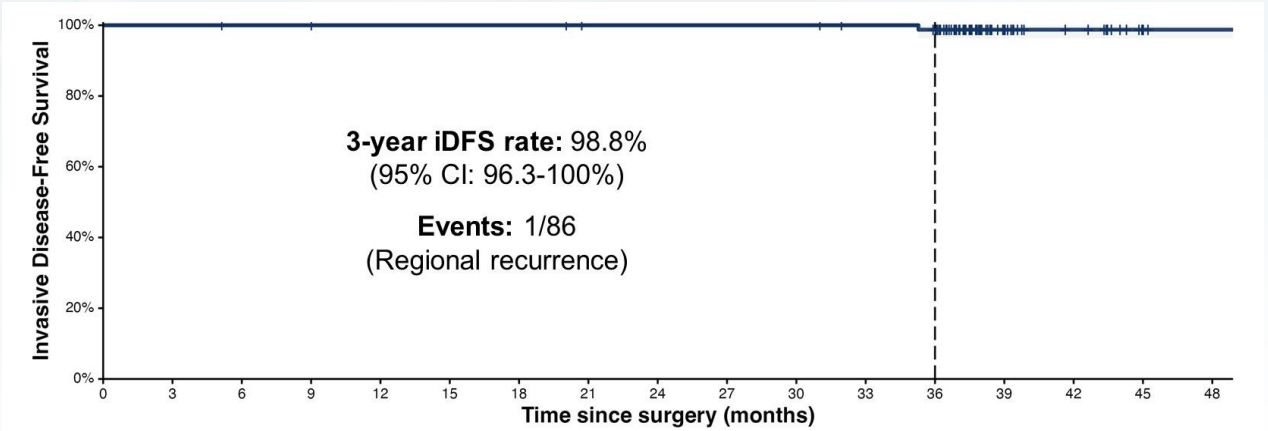
pCR in PET responders (primary endpoint)



3-years iDFS in group B N=267 (co-primary endpoint)



3-years iDFS without chemo in PET responders with pCR n=86 (subgroup analysis)



Pérez-García, Lancet Oncol 2021; Javier Cortés, ASCO 2023 #LBA506

2023 ASCO ANNUAL MEETING

Nine weeks versus one-year trastuzumab for early HER2+ breast cancer: 10-year update of the Short-HER phase III randomised trial

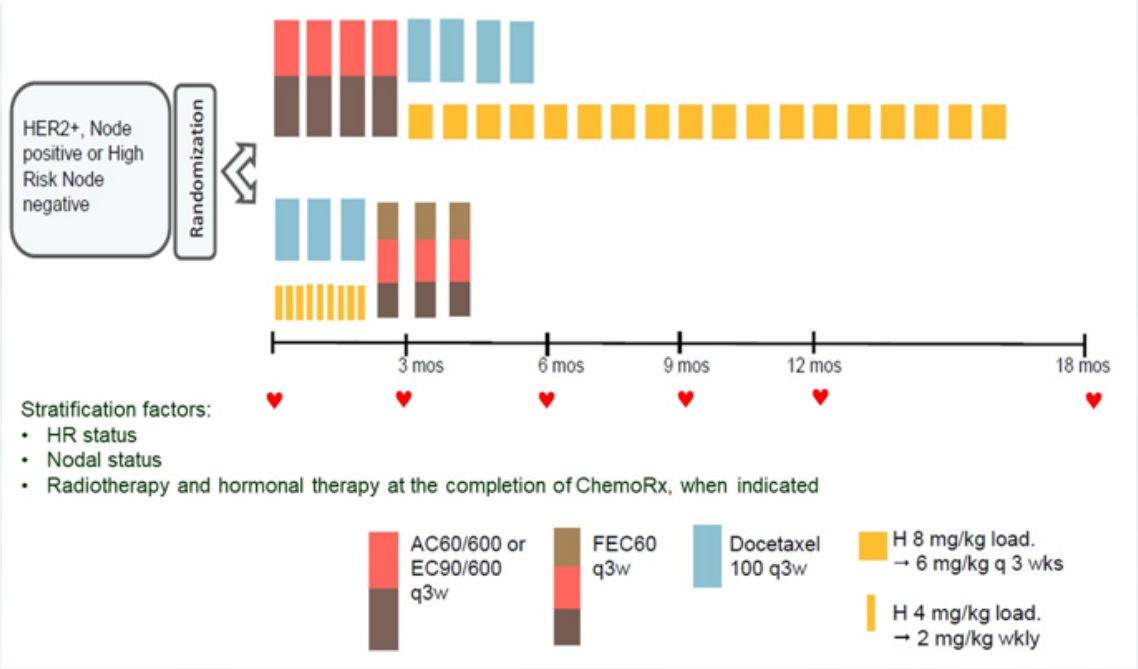
PF Conte, G Bisagni, F Piacentini, S Sarti, S Minichillo, E Anselmi, M Aieta, V Gebbia, A Schirone, A Musolino, O Garrone, A Beano, A Rimanti, F Giotta, A Turletti, MV Dieci, R Vicini, S Balduzzi, R D'Amico, V Guarneri.

S Camillo Hospital IRCCS, Istituto Oncologico Veneto IRCCS, University of Padova
on behalf of the ShortHER study team

PRESENTED BY: Pierfranco Conte MD

ShortHER

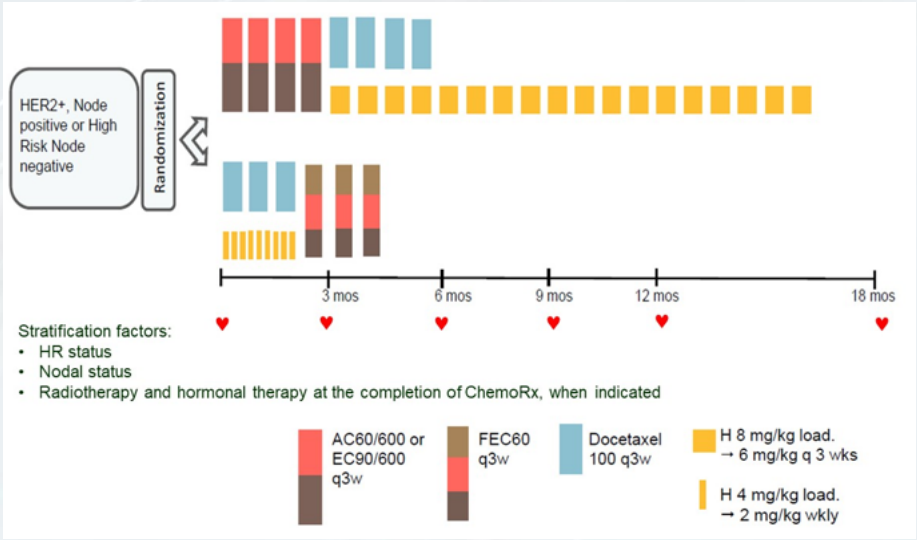
- 5y DFS: Long Arm 87.5%; Short Arm 85.4%; HR 1.15 (90% CI 0.91-1.46) → Non-inferiority cannot be claimed
- Significant lower cardiac toxicity for the short treatment HR 0.32 (95% CI 0.21-0.50; p<0.0001)

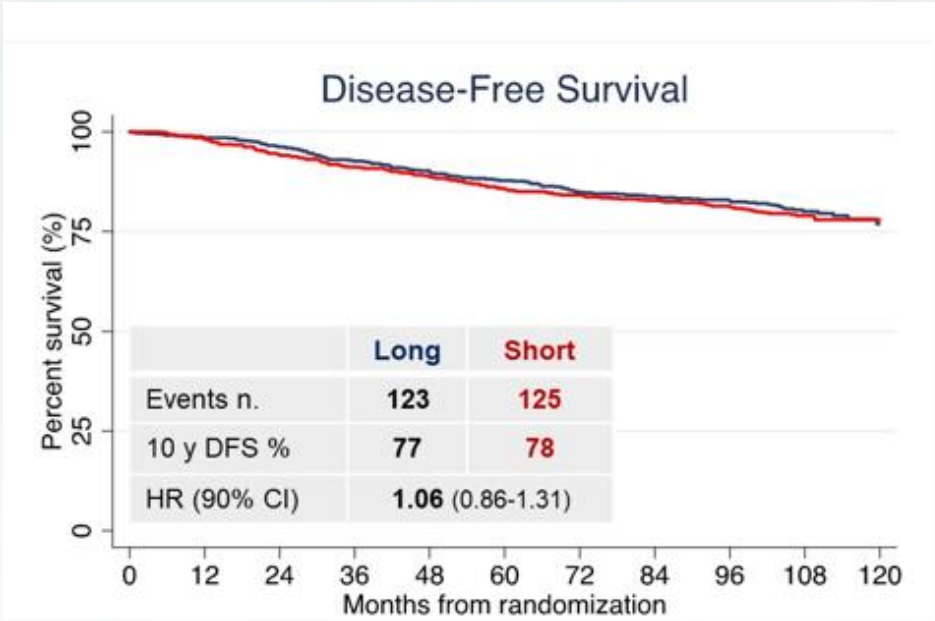


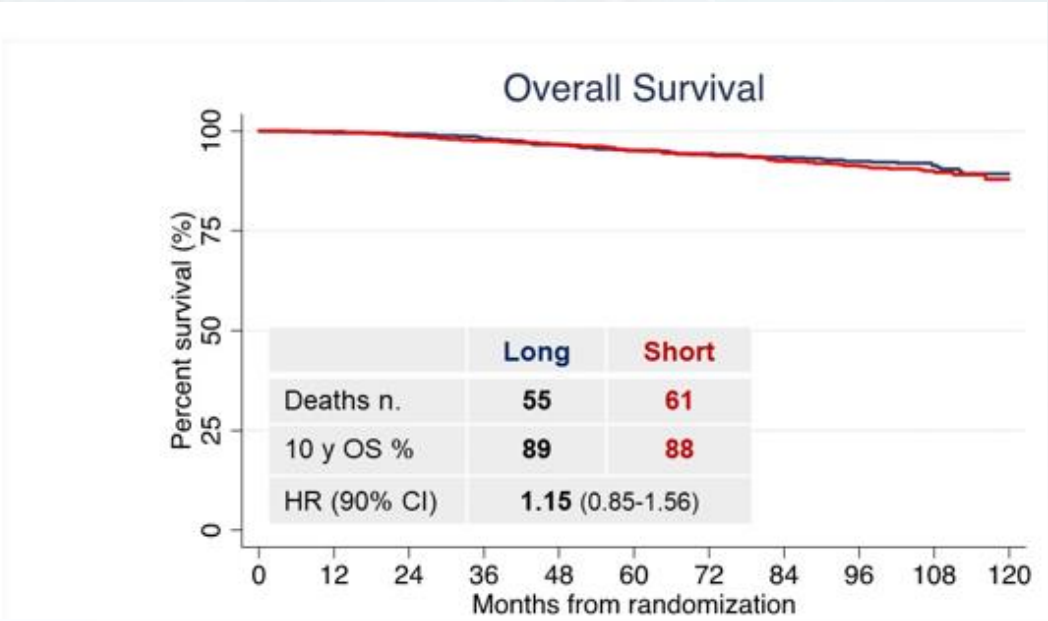
Conte P et al, Ann Oncol 2018 ;Pierfranco Conte, ASCO 2023 #637

ShortHER

- **10-year DFS and OS**
- Final OS (co-primary endpoint) with a median FU of 9y

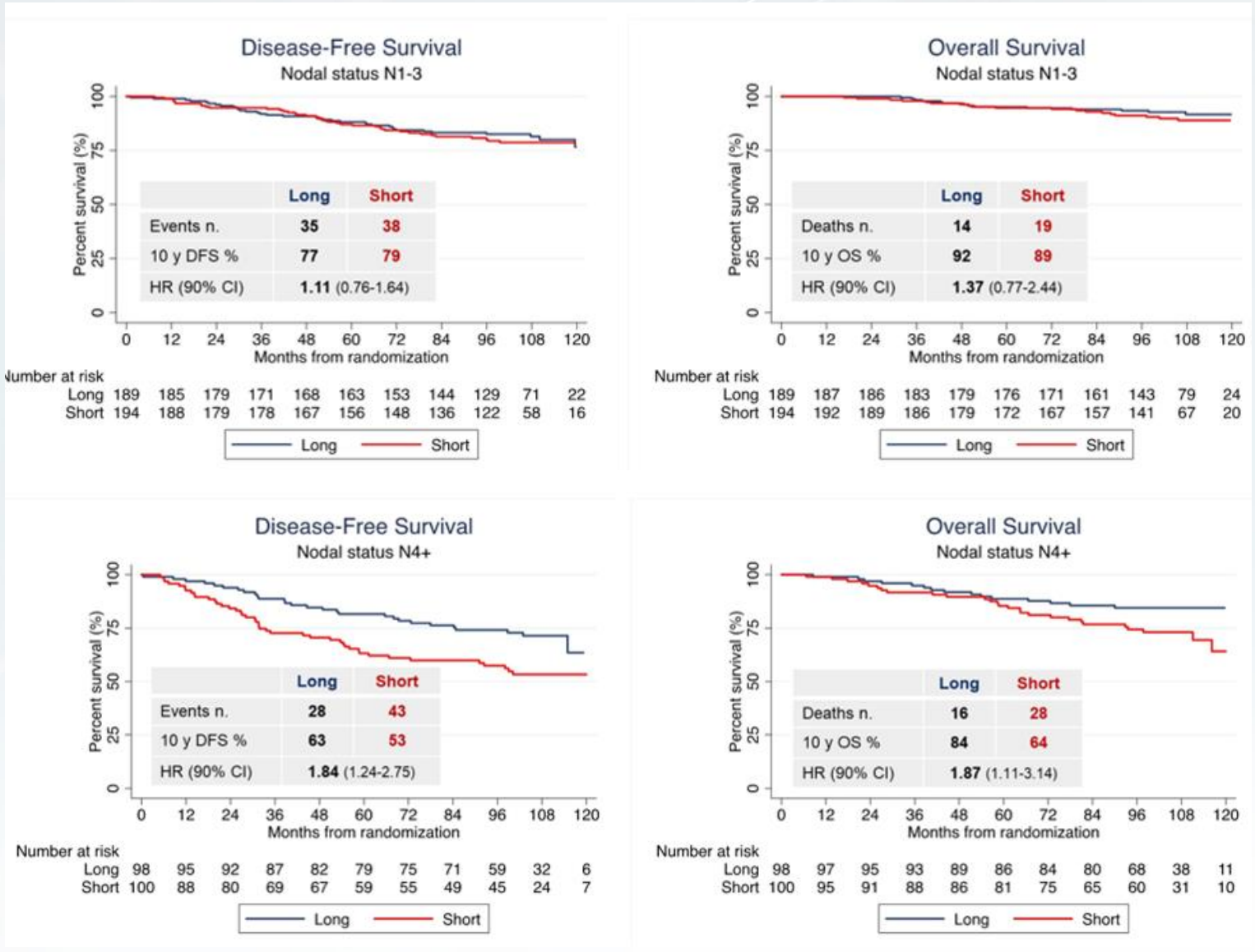






Conte P et al, Ann Oncol 2018 ;Pierfranco Conte, ASCO 2023 #637

ShortHER



Pierfranco Conte, ASCO 2023 #637

2023 ASCO ANNUAL MEETING

Prognosis and Treatment Outcomes for Patients with Stage IA Triple-negative Breast Cancer: A Population-based Study

Paolo Tarantino, Julieta Leone, Carlos T. Vallejo, Rachel A. Freedman, Adrienne G. Waks, Olga Martínez-Sáez, Ana Garrido-Castro, Filipa Lynce, Nabihah Tayob, Nancy U. Lin, Sara M. Tolaney and Jose P. Leone.

Dana-Farber Cancer Institute

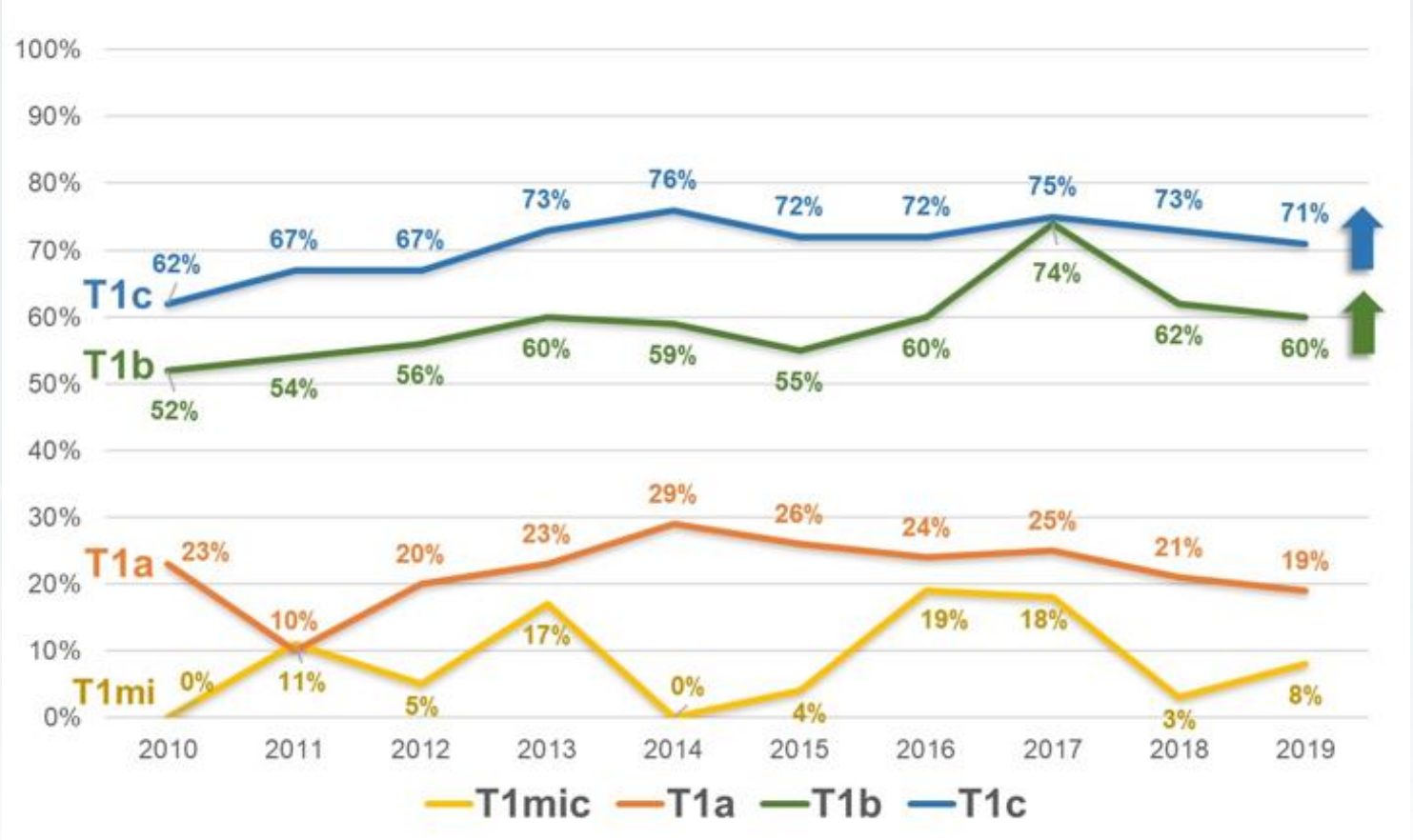
HARVARD MEDICAL SCHOOL

Boston, MA, USA

Population based study stage I TNBC

- N 8,601
- Women with Stage I TNBC from SEER
- Diagnosed 2010-2019

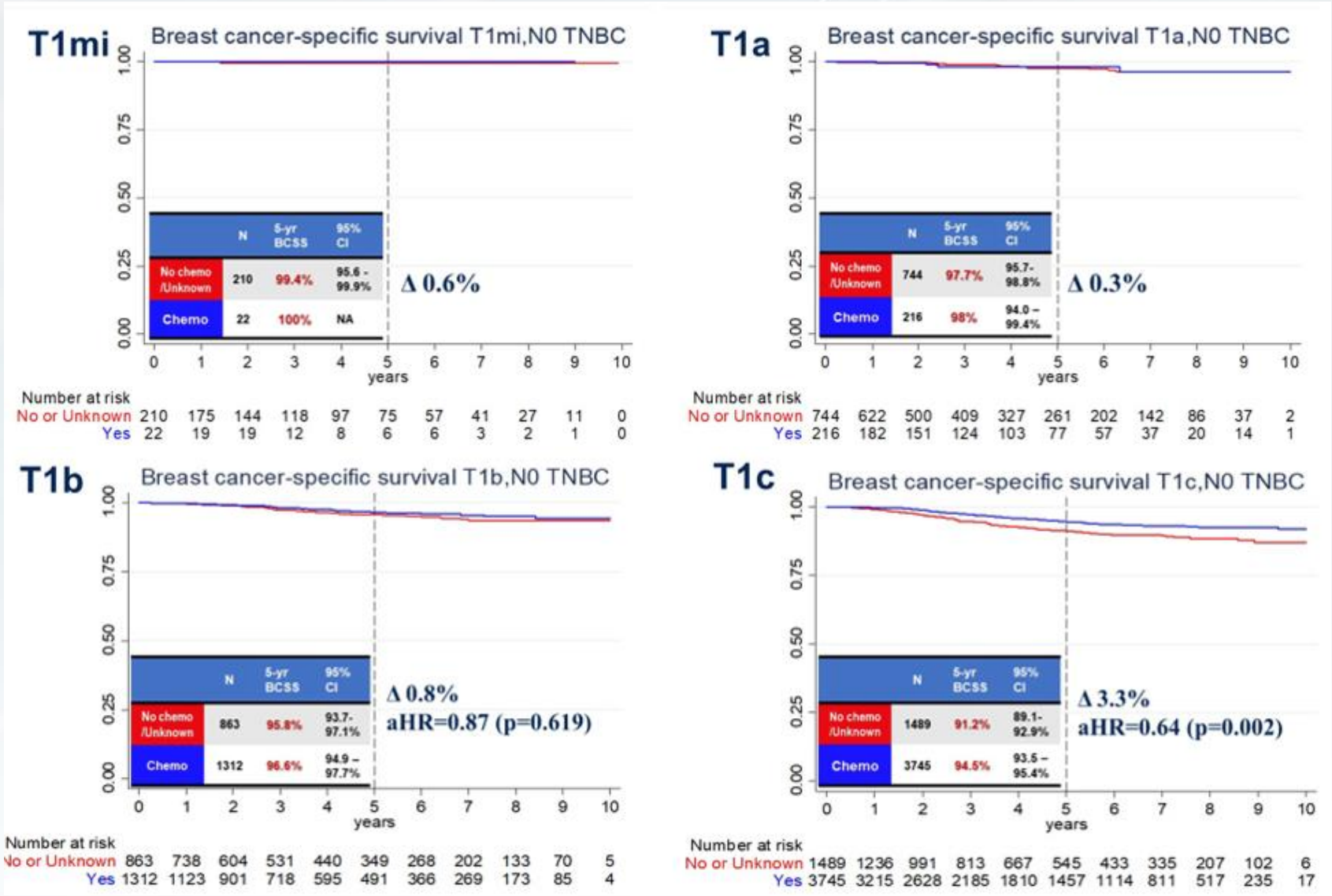
- 1ry Obj: BC specific survival
- 2ry Obj: trends & use of chemo over the time



The use of chemo significantly increased over time for pts with T1b and T1c TNBC

Paolo Tarantino, ASCO 2023

Population based study stage I TNBC



Paolo Tarantino, ASCO 2023

Conclusions in ER +/HER2- EBC

- **NATALEE** has reached its primary end point, and supports RIB + NSAI as a new treatment of choice in stage II-III ER+/HER2- EBC, including pts with node-negative disease (8% grade ≥3 liver-related AEs, and only 20% of pts have already completed 3y RIB)

- **In MonarchE**, pts ≥65y derive similar benefit (iDFS, DRFS) from adjuvant abema + ET, and showed similar AEs rate, although dose reductions and treatment discontinuations were higher in this group of pts

- **Ovarian ablation/suppression Oxford meta-analysis**: recurrence and survival benefit in women who received no prior chemotherapy, or who received chemo and remained premenopausal after it. Larger benefit in patients ≤ 45y, and in women who received no tamoxifen

Conclusions in HER2-positive/TN EBC

- **The PHERGain** study also mets the second primary endpoint with a 3yiDFS of 95.4% in pts in group B. Among CT-free pts, 3y iDFS was 98.8%. This approach identifies ∽1/3 of pts who could safely omit CT

- In **ShortHER**: 10y DFS and OS of long vs short duration of adjuvant trastuzumab are similar. However, pts with 4+ nodes and stage III have better DFS and OS with 1-year

- **Population-based study in stage I TNBC**: chemo significantly improved BCSS in pts with TNBC, but not for pts with T1b TNBC

Salut/ ICO Institut Català d'Oncologia

Muchas gracias por vuestra atención!

Institut Català d'Oncologia (ICO)

Hospital Universitari de Bellvitge (HUB)

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