SOLCA
NÚCLEO DE QUITO

7 DÉCADAS desde 1954
de atención especializada en cáncer

Cáncer de Mama Temprano

Consideraciones terapéuticas ante Enfermedad Residual post Neoadyuvancia

Sergio Rivero

- ONCOLOGIA CLÍNICA, Inst. FLEMING -

19/07/2024

Sergio Rivero MD.

- ✓ Especialista en Oncología Clínica Staff Departamento de Cáncer de Mama de IAF
- ✓ Miembro Centro Mamario IAF
- ✓ Coordinador Oncología Centro IAF/DIM Ramos Mejía
- ✓ Investigador estudios de investigación clínica en Cáncer Mama
- ✓ Docente de la Carrera de Especialista en Oncología de la UBA
- ✓ Miembro del Comité de Ética del IAF

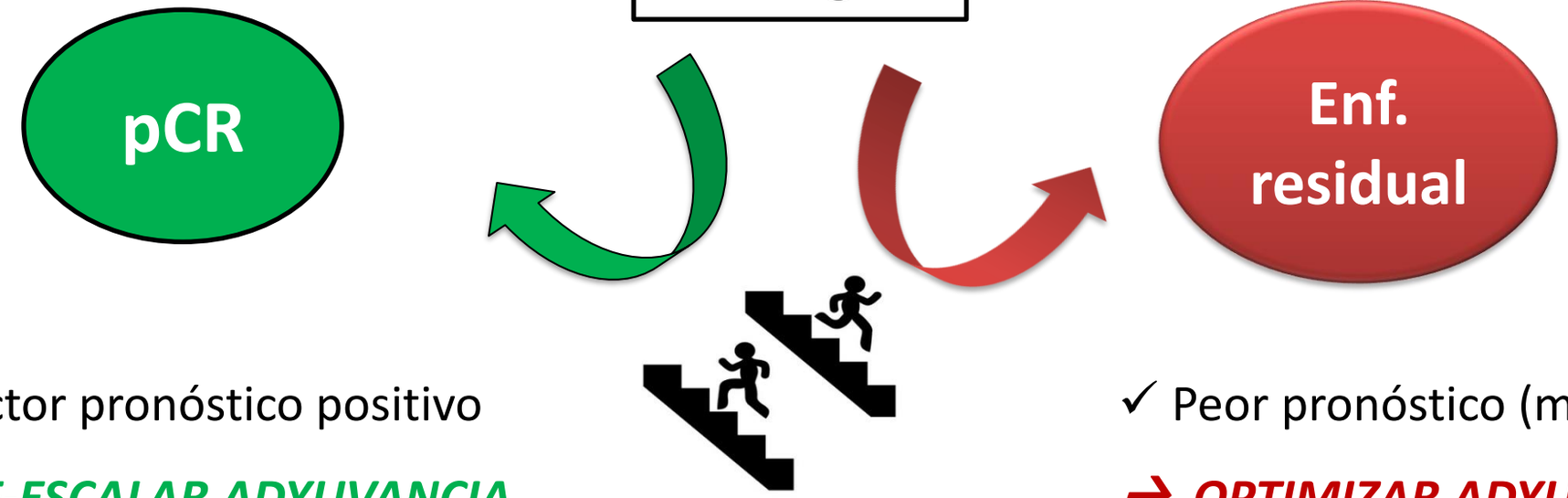
Conflictos de Interés:

- Honorarios por actividades académicas, investigación clínica y soporte económico para asistir a congresos y eventos académicos: Elea, Pfizer, Novartis, Raffo, Roche, Astrazeneca, Eli Lilly, Sanofi, Varifarma, Gador, Omics Oncotype Dx, Argenetics (Veracyte)

Neoadyuvancia

TN →	Her2 + →	Luminales →
QT + Inmunoterapia	QT + AntiHer2	QT

Cirugía

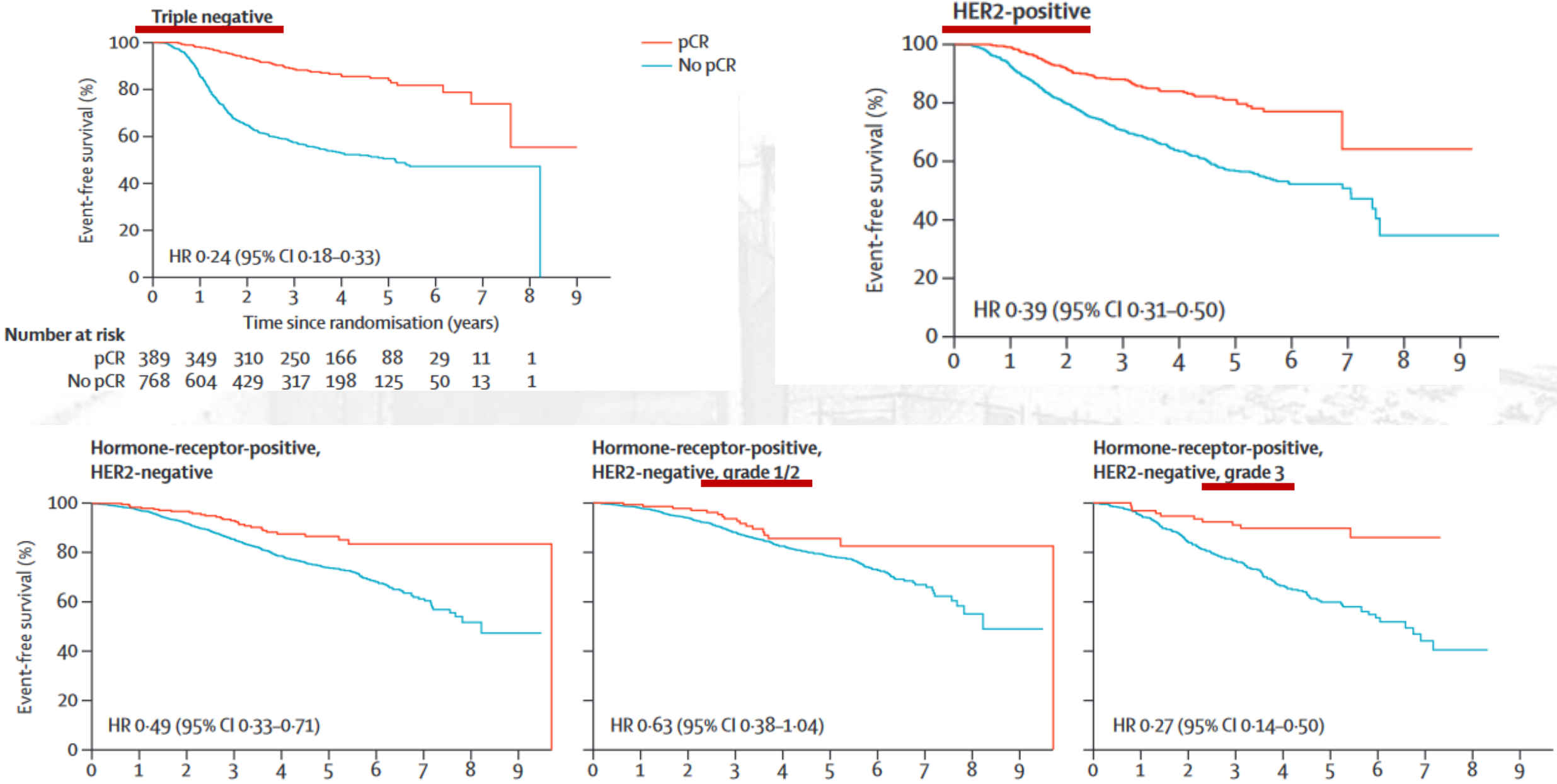


✓ Factor pronóstico positivo

→ *DE-ESCALAR ADYUVANCIA*

✓ Peor pronóstico (mayor RR)

→ *OPTIMIZAR ADYUVANCIA*



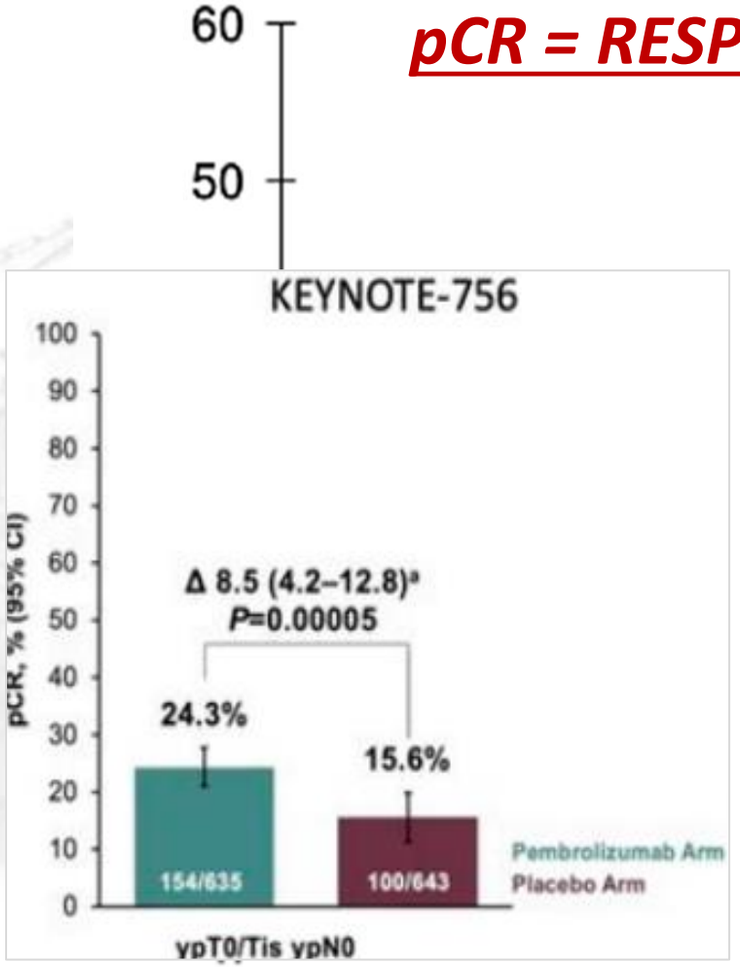
Cortazar et al. Lancet. 2019 Mar 9;393(10175):986

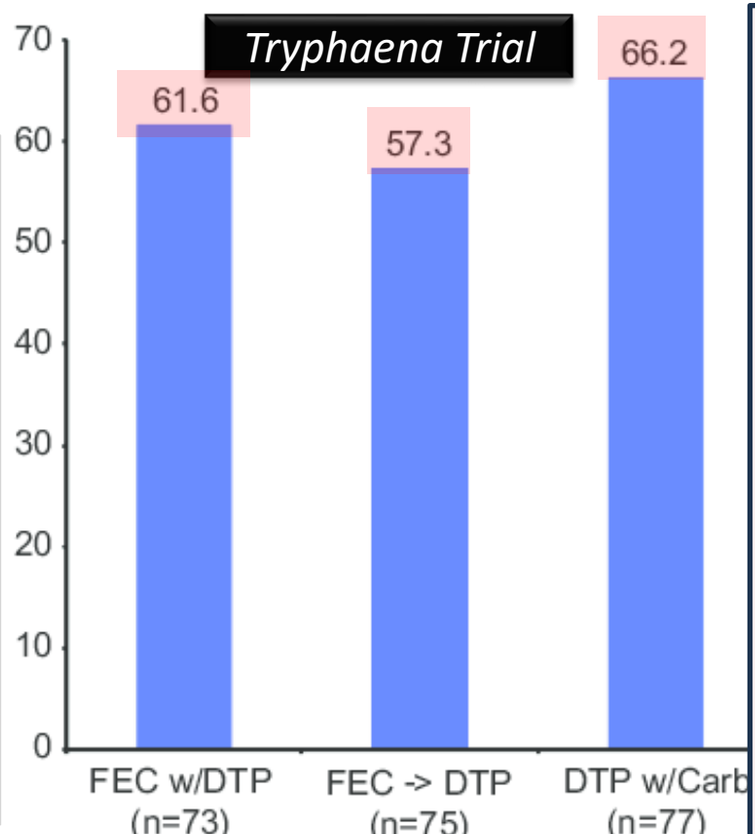
San Antonio Breast Cancer Symposium – December 4 - 8, 2012

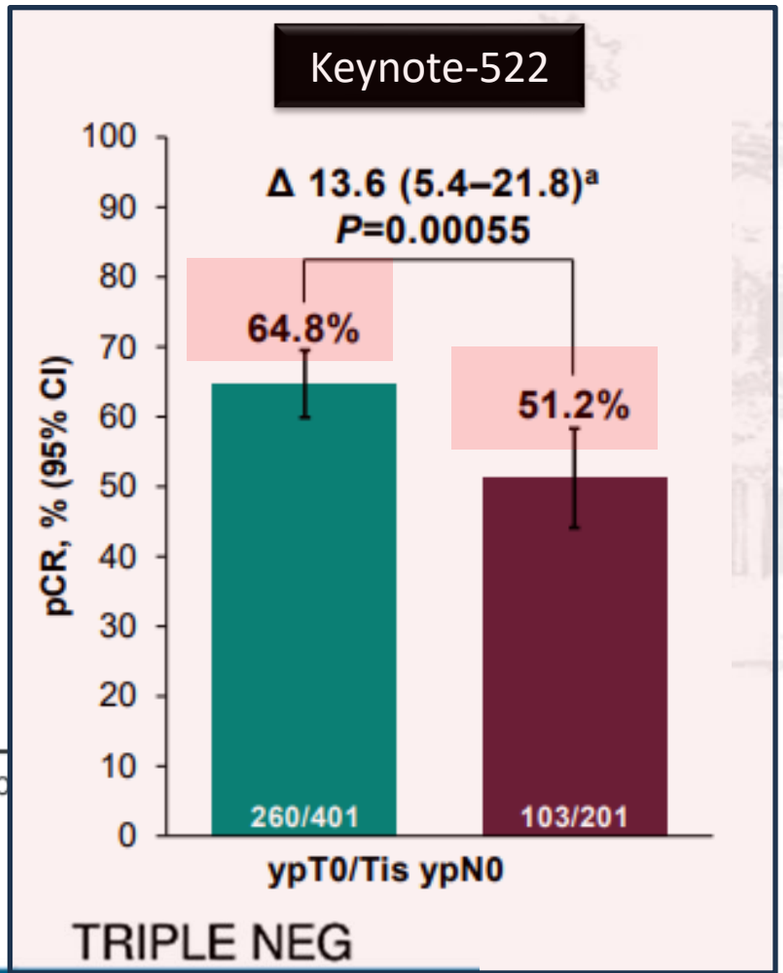
pCR Rates by Tumor Subtypes

CTNeoBC

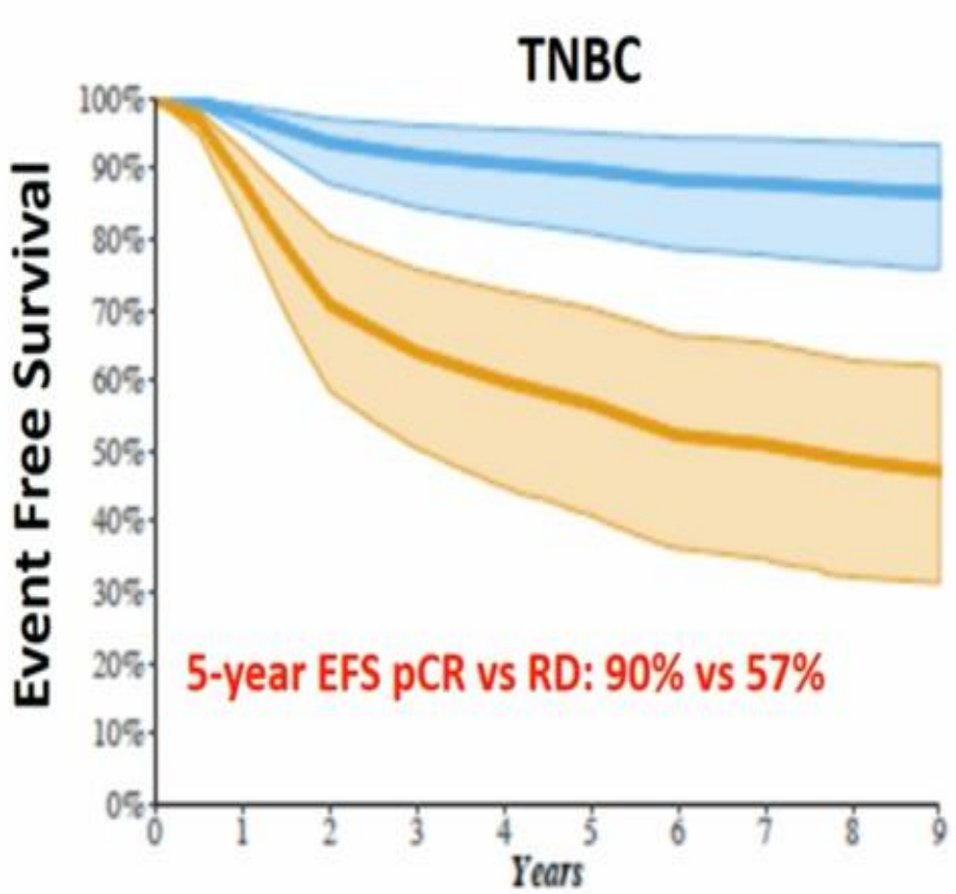
pCR = RESPUESTA COMPLETA PATOLÓGICA







Determina 2 escenarios:



Residual disease (RD) group

Spring L et al. SABCS 2018

QT: AC/T
+/- platinos
+/- Inmunoterapia
(Keynote 522)

- **pCR**:
  implica mejores resultados a largo plazo

- **Enfermedad residual post QTNA**:
  Implica mayor riesgo de recurrencia y menor supervivencia

1) Capecitabine
2) gBRCAm : iPARP
3) Pembrolizumab

Considerar ADYUVANCIA

SAN ANTONIO BREAST CANCER SYMPOSIUM

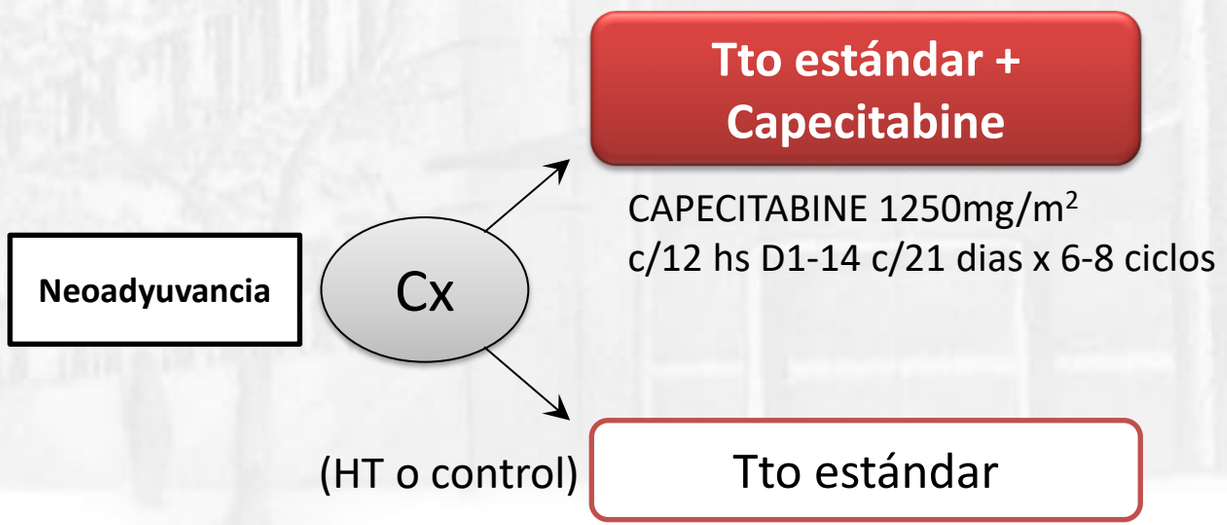
Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy

N. Masuda, S.-J. Lee, S. Ohtani, Y.-H. Im, E.-S. Lee, I. Yokota, K. Kuroi, S.-A. Im, B.-W. Park, S.-B. Kim, Y. Yanagita, S. Ohno, S. Takao, K. Aogi, H. Iwata, J. Jeong, A. Kim, K.-H. Park, H. Sasano, Y. Ohashi, and M. Toi

N Engl J Med 2017;376:2147-59.

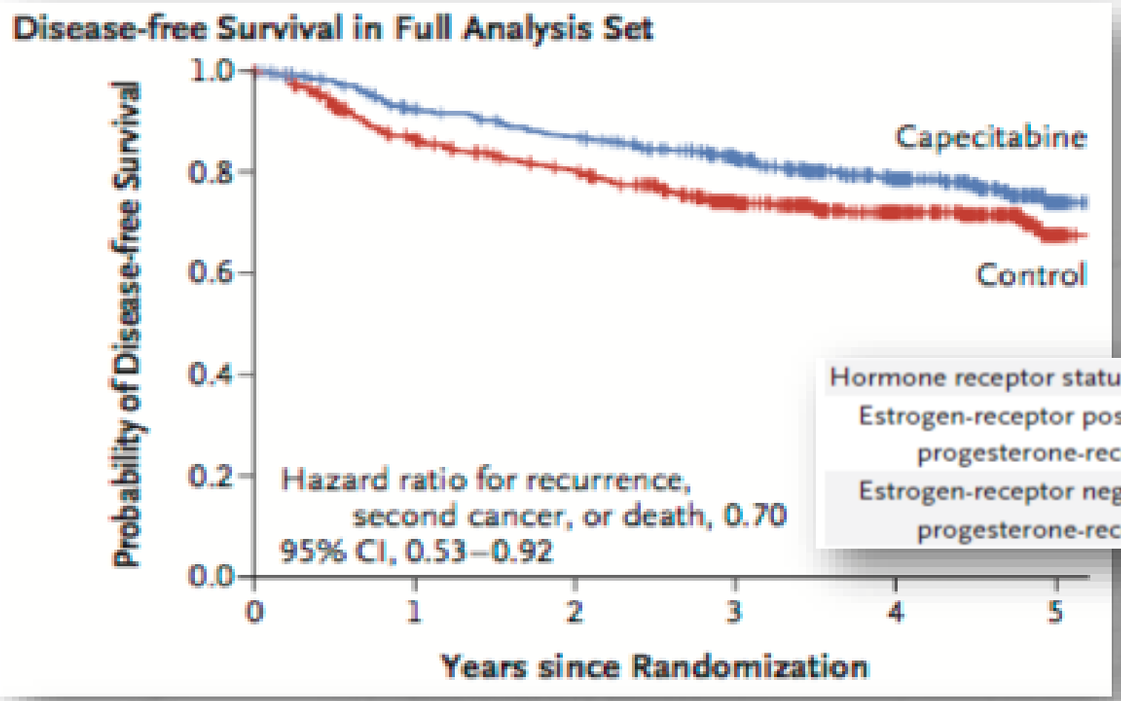
CREATEx

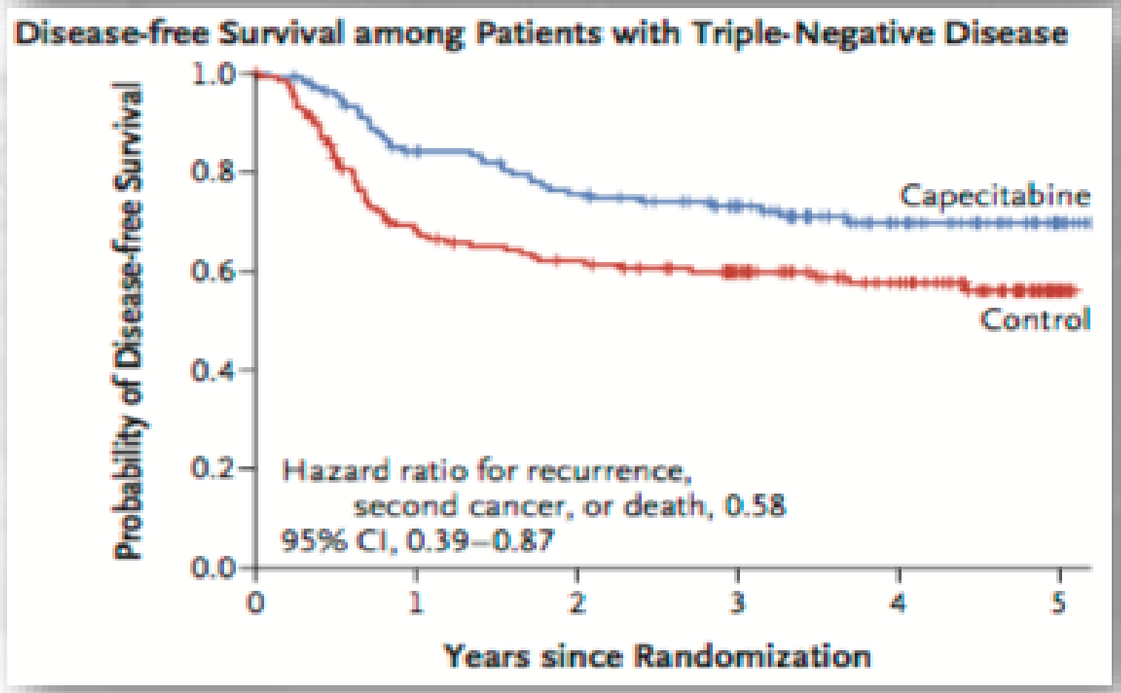
- Estudio aleatorizado, multicéntrico FIII
- Nº 910 (2007-2012)
- Población asiática
- Estadio I-IIIB Her2 neg y enfermedad residual post QTNA
- EP 1º SLR 2º SG

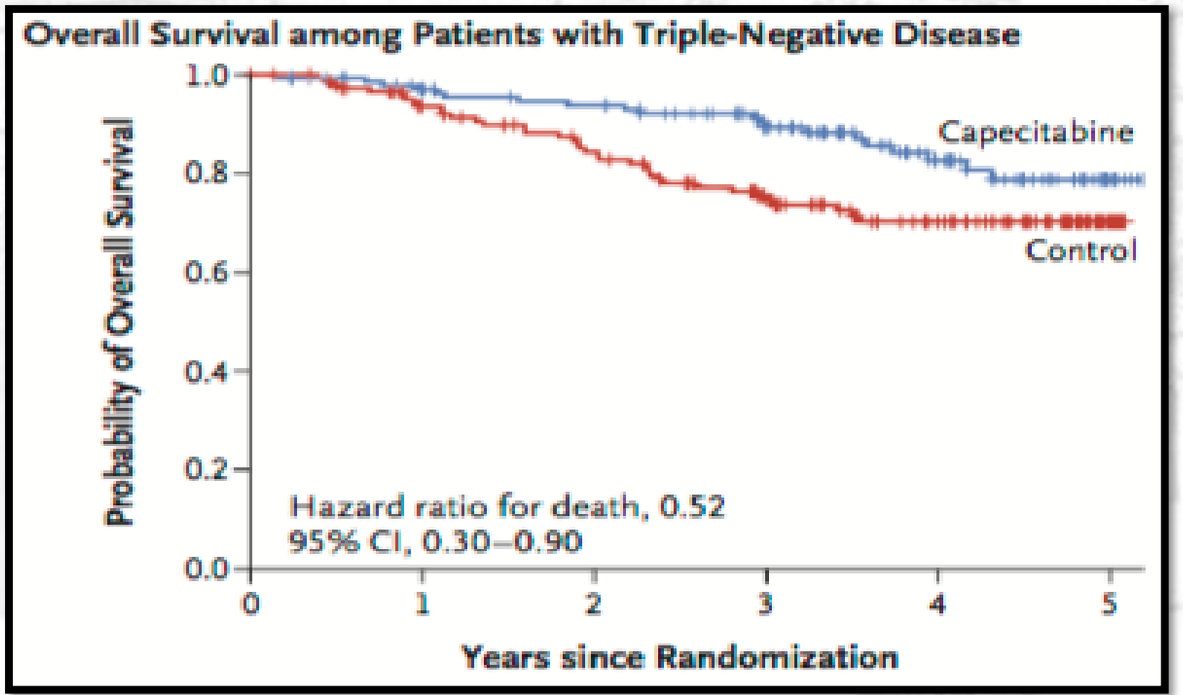


Characteristic	Capecitabine Group (N=443)	Control Group (N=444)
Age at enrollment — yr		
Median	48	48
Range	25–74	25–74
Menopausal status — no. (%)		
Premenopausal	262 (59.1)	248 (55.9)
Postmenopausal	181 (40.9)	196 (44.1)
Body-mass index†		
Median	22.6	23.0
Range	15.6–39.9	15.6–41.2
Tumor size at diagnosis — no./total no. (%)		
≤2 cm	68/442 (15.4)	61/444 (13.7)
>2 to ≤5 cm	244/442 (55.2)	275/444 (61.9)
>5 cm	65/442 (14.7)	69/444 (15.5)
Skin or chest-wall infiltration of any size — no./total no. (%)	65/442 (14.7)	39/444 (8.8)
Hormone-receptor status — no. (%)		
Estrogen-receptor positive or progesterone-receptor positive	304 (68.6)	297 (66.9)
Estrogen-receptor negative and progesterone-receptor negative	139 (31.4)	147 (33.1)
Neoadjuvant chemotherapy — no. (%)		
Sequential anthracycline and taxane	357 (80.6)	372 (83.8)
Concurrent anthracycline and taxane	63 (14.2)	53 (11.9)
Anthracycline-containing chemotherapy only or docetaxel and cyclophosphamide only	23 (5.2)	19 (4.3)
Fluorouracil plus anthracycline‡	262 (59.1)	271 (61.0)
Pathological-effect grade — no./total no. (%)§		
0	19/434 (4.4)	13/435 (3.0)
1a or 1b	232/434 (53.5)	220/435 (50.6)
2 or 3	183/434 (42.2)	202/435 (46.4)
No. of lymph nodes involved on histologic assessment — no. (%)		
0	176 (39.7)	171 (38.5)
1–3	165 (37.2)	174 (39.2)
≥4	102 (23.0)	99 (22.3)

Dosis 1250 mg/m2 c/12 hs 14 on 7 off x 8 ciclos
(4+4 o 4+5, 14 on 7 off)
- 30% completaron 8 cursos (78% reducción de dosis)







N ENGL J MED 384;25 NEJM.ORG JUNE 24, 2021

Adjuvant Olaparib for Patients with *BRCA1*- or *BRCA2*-Mutated Breast Cancer

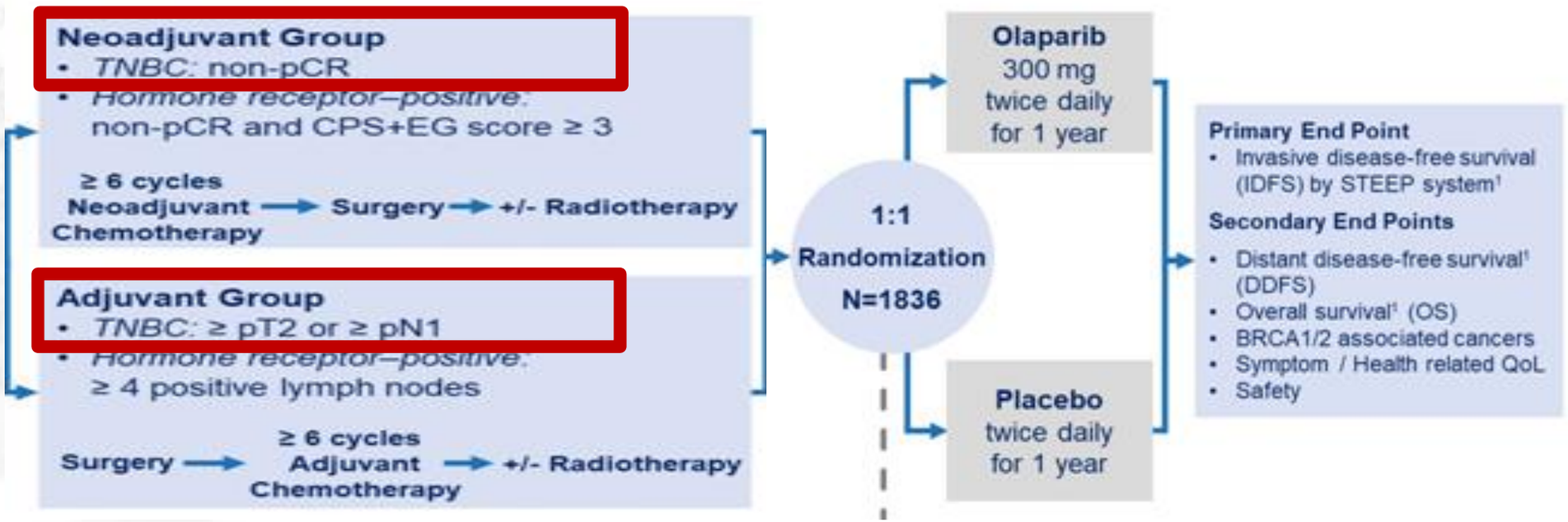
A.N.J. Tutt, J.E. Garber, B. Kaufman, G. Viale, D. Fumagalli, P. Rastogi, R.D. Gelber, E. de Azambuja, A. Fielding, J. Balmaña, S.M. Domchek, K.A. Gelmon, S.J. Hollingsworth, L.A. Korde, B. Linderholm, H. Bandos, E. Senkus, J.M. Suga, Z. Shao, A.W. Pippas, Z. Nowecki, T. Huzarski, P.A. Ganz, P.C. Lucas, N. Baker, S. Loibl, R. McConnell, M. Piccart, R. Schmutzler, G.G. Steger, J.P. Costantino, A. Arahmani, N. Wolmark, E. McFadden, V. Karantza, S.R. Lakhani, G. Yothers, C. Campbell, and C.E. Geyer, Jr., for the OlympiA Clinical Trial Steering Committee and Investigators*

OlympiA
OLaparib in Adjuvant BRCAm breast cancer

Table 1. Demographic and Disease Characteristics of the Patients at Baseline.*

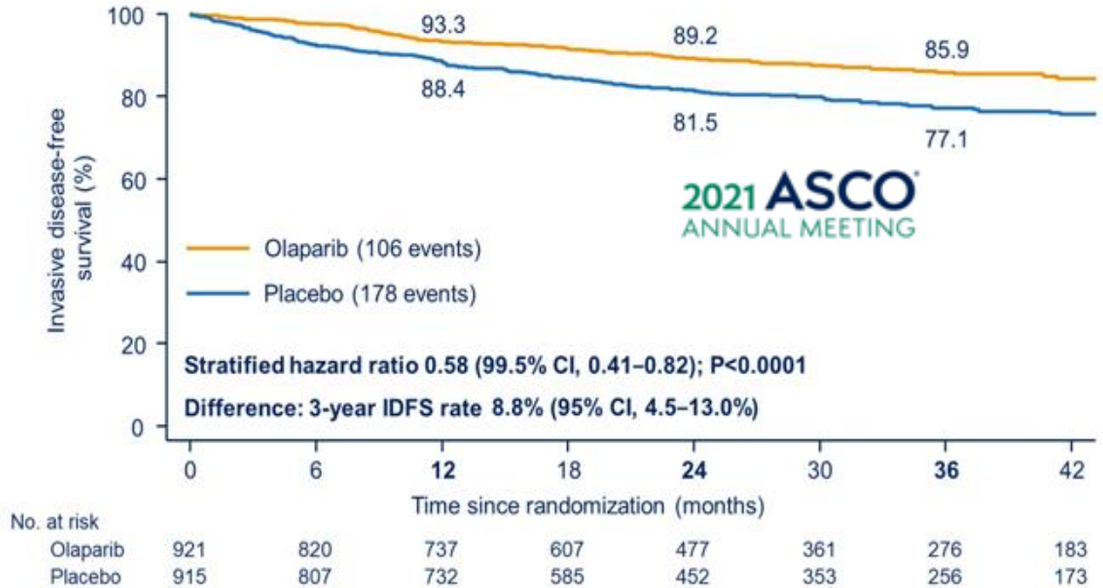
Hormone-receptor status — no. (%)‡		
Hormone-receptor positive and HER2 negative§	168 (18.2)	157 (17.2)
Triple-negative breast cancer¶	751 (81.5)	758 (82.8)
Germline *BRCA* mutation — no. (%)†		
BRCA1	657 (71.3)	670 (73.2)
BRCA2	261 (28.3)	239 (26.1)
BRCA1 and *BRCA2*	2 (0.2)	5 (0.5)

Fase 3 doble ciego randomizado
Her2 negativo, mutación germinal BRCA 1 o 2



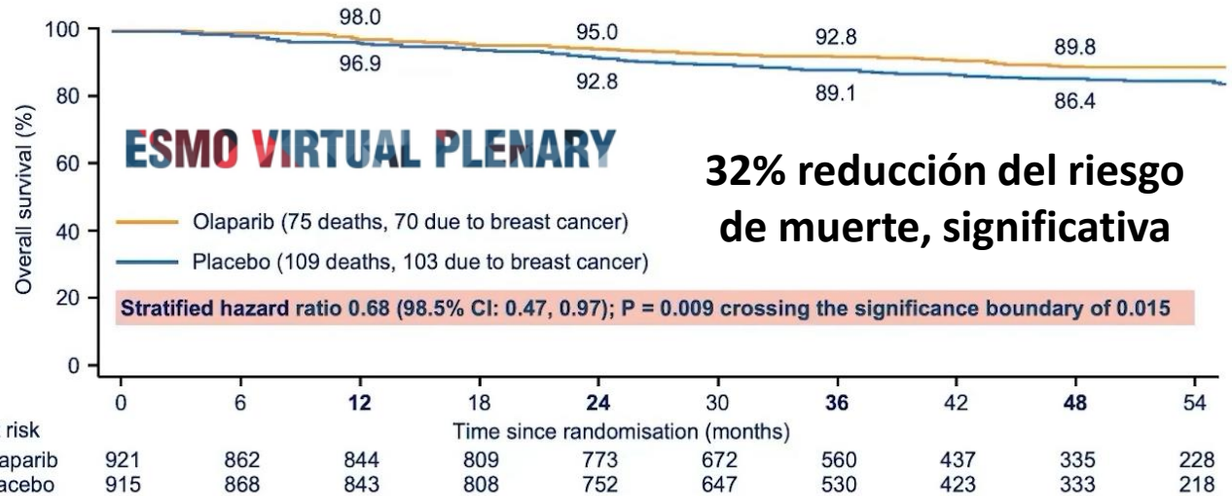
Tutt. NEJM. 2021;[Epub]. NCT02032823.

OlympiA: Invasive disease-free survival (ITT)



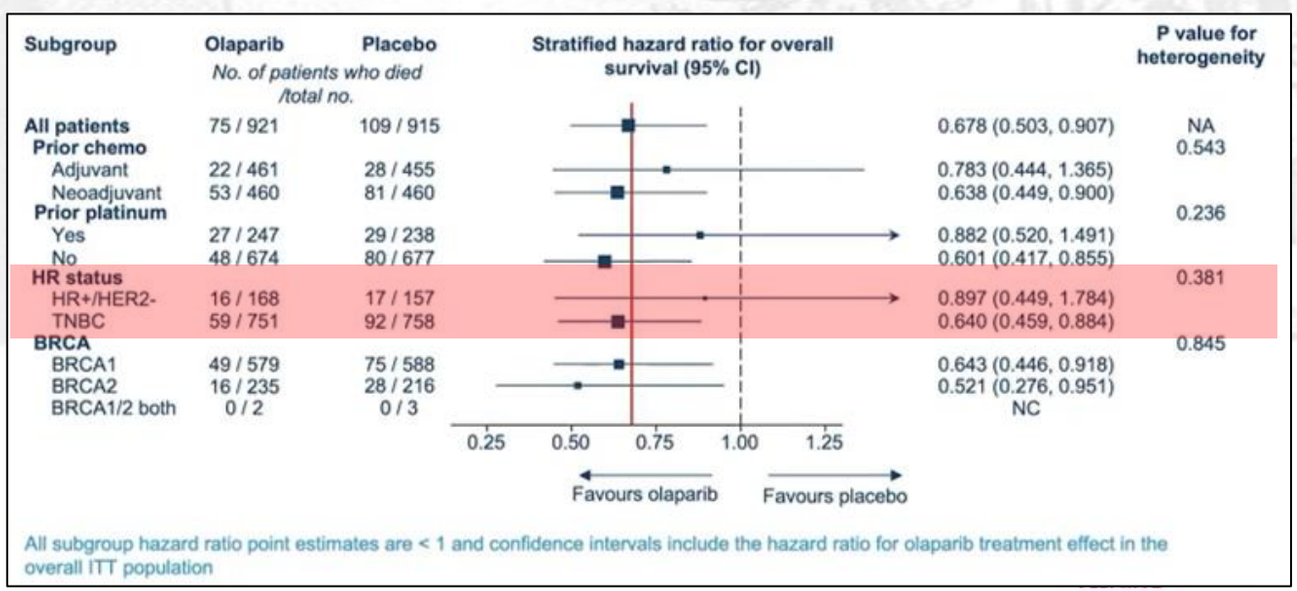
	Olaparib (N = 921)	Placebo (N = 915)
Number of patients with a first IDFS event	**106 (11.5%)**	**178 (19.5%)**
Distant recurrence	**72 (7.8%)**	**120 (13.1%)**
Distant CNS Recurrence	22 (2.4%)	36 (3.9%)
Distant excluding CNS Recurrence	50 (5.4%)	84 (9.2%)
Regional (Ipsilateral) Recurrence	6 (0.7%)	14 (1.5%)
Local (Ipsilateral) Recurrence	7 (0.8%)	11 (1.2%)
Contralateral invasive breast cancer	8 (0.9%)	12 (1.3%)
Second primary non-breast malignancies	11 (1.2%)	21 (2.3%)
Ovarian	1 (0.1%)	4 (0.4%)
Peritoneal	0 (0.0%)	0 (0.0%)
Fallopian tube	1 (0.1%)	4 (0.4%)
Other	9 (1.0%)	13 (1.4%)
Deaths without a prior IDFS event*	2 (0.2%)	0 (0.0%)

SECOND OVERALL SURVIVAL INTERIM ANALYSIS - OS IA 2 (ITT)



32% reducción del riesgo de muerte, significativa

98.5% confidence intervals are shown for the hazard ratio because P < 0.015 is required for statistical significance



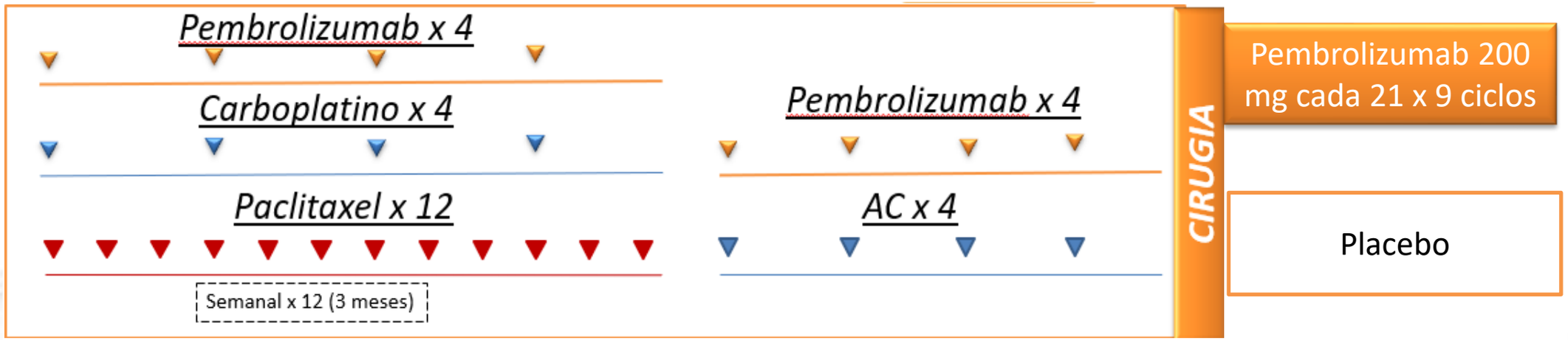
Tutt. NEJM. 2021;[Epub]. NCT02032823.

KEYNOTE-522 Study Design (NCT03036488)

Schmid et al. GS3-03

Obj. 1rio
pCR y SLE

N : 1174



Characteristic	Pembrolizumab–Chemotherapy (N=784)	Placebo–Chemotherapy (N=390)
Age		
Median (range) — yr	49 (22–80)	48 (24–79)
<65 yr — no. (%)	701 (89.4)	342 (87.7)
Menopausal status — no. (%)		
Premenopausal	438 (55.9)	221 (56.7)
Postmenopausal	345 (44.0)	169 (43.3)
PD-L1 status — no. (%)†		
Positive	656 (83.7)	317 (81.3)
Negative	127 (16.2)	69 (17.7)
Primary tumor classification — no. (%)		
T1 to T2	580 (74.0)	290 (74.4)
T3 to T4	204 (26.0)	100 (25.6)
Nodal involvement — no. (%)		
Positive	405 (51.7)	200 (51.3)
Negative	379 (48.3)	190 (48.7)
Overall disease stage — no. (%)		
Stage II	590 (75.3)	291 (74.6)
Stage III	194 (24.7)	98 (25.1)

PDL1+ (CPS ≥ 1 IHC22C3 pharmDx)

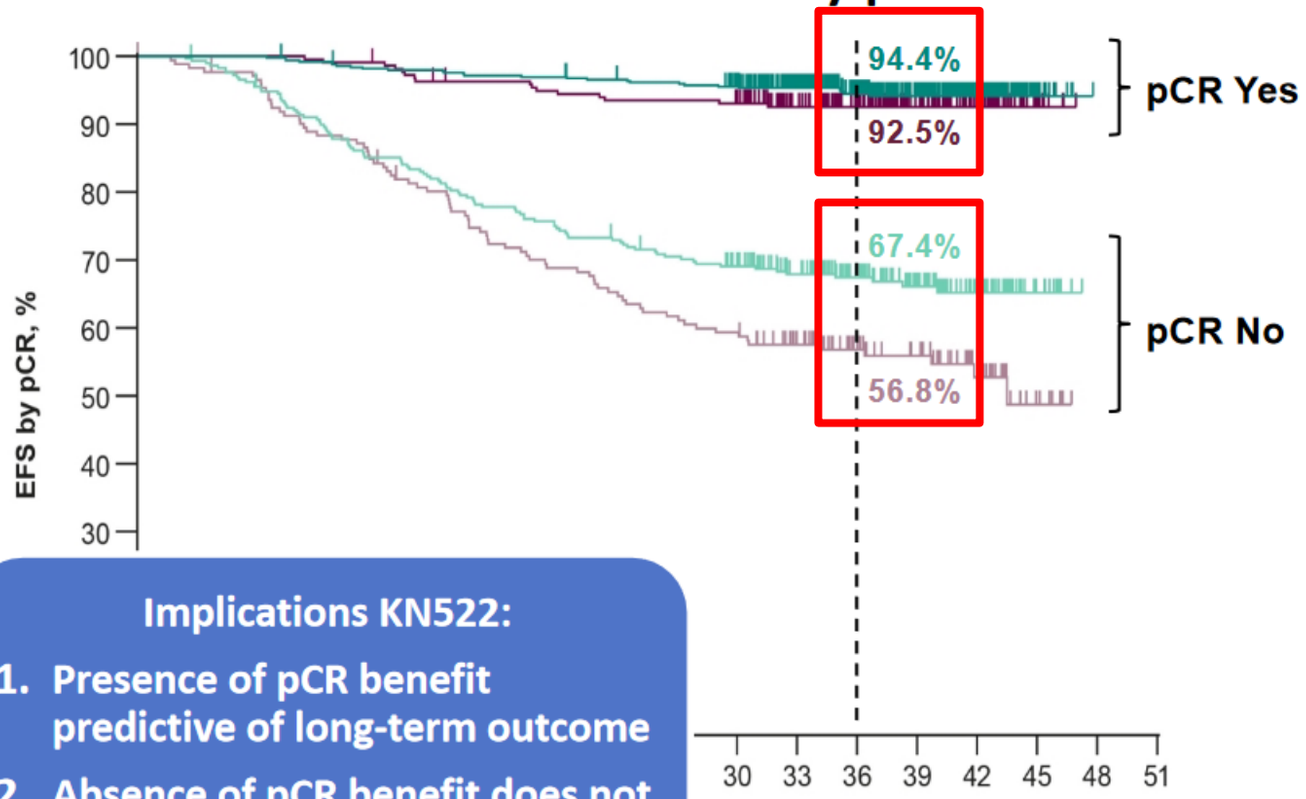
Schmid et a. Presented at: ESMO 2019

¿El beneficio en pCR se traduce en mejoría de la sobrevida?

KN522

Mayor impacto SLE en pacientes que no acceden a pCR

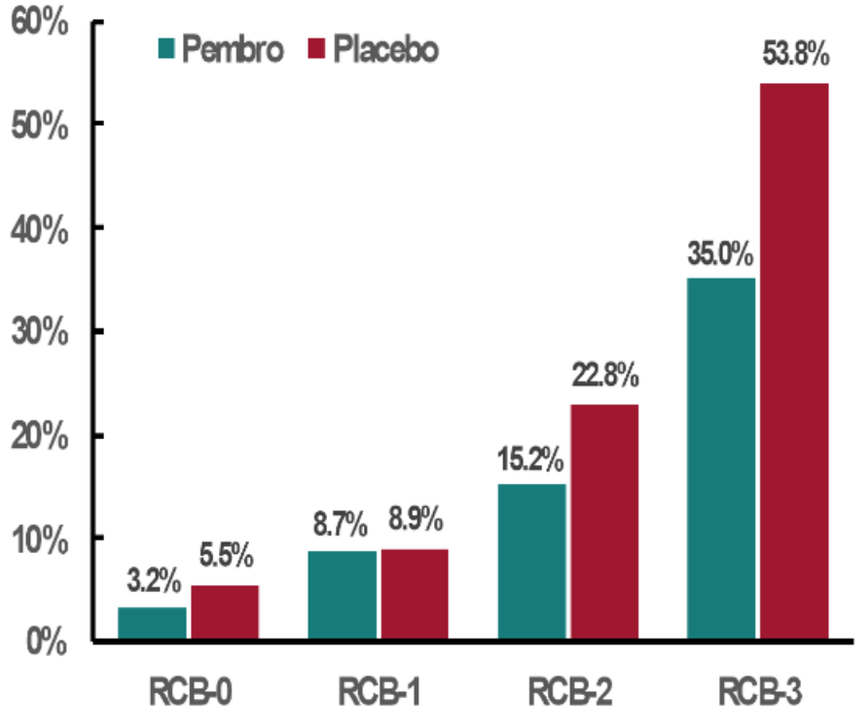
Event-free Survival by pCR



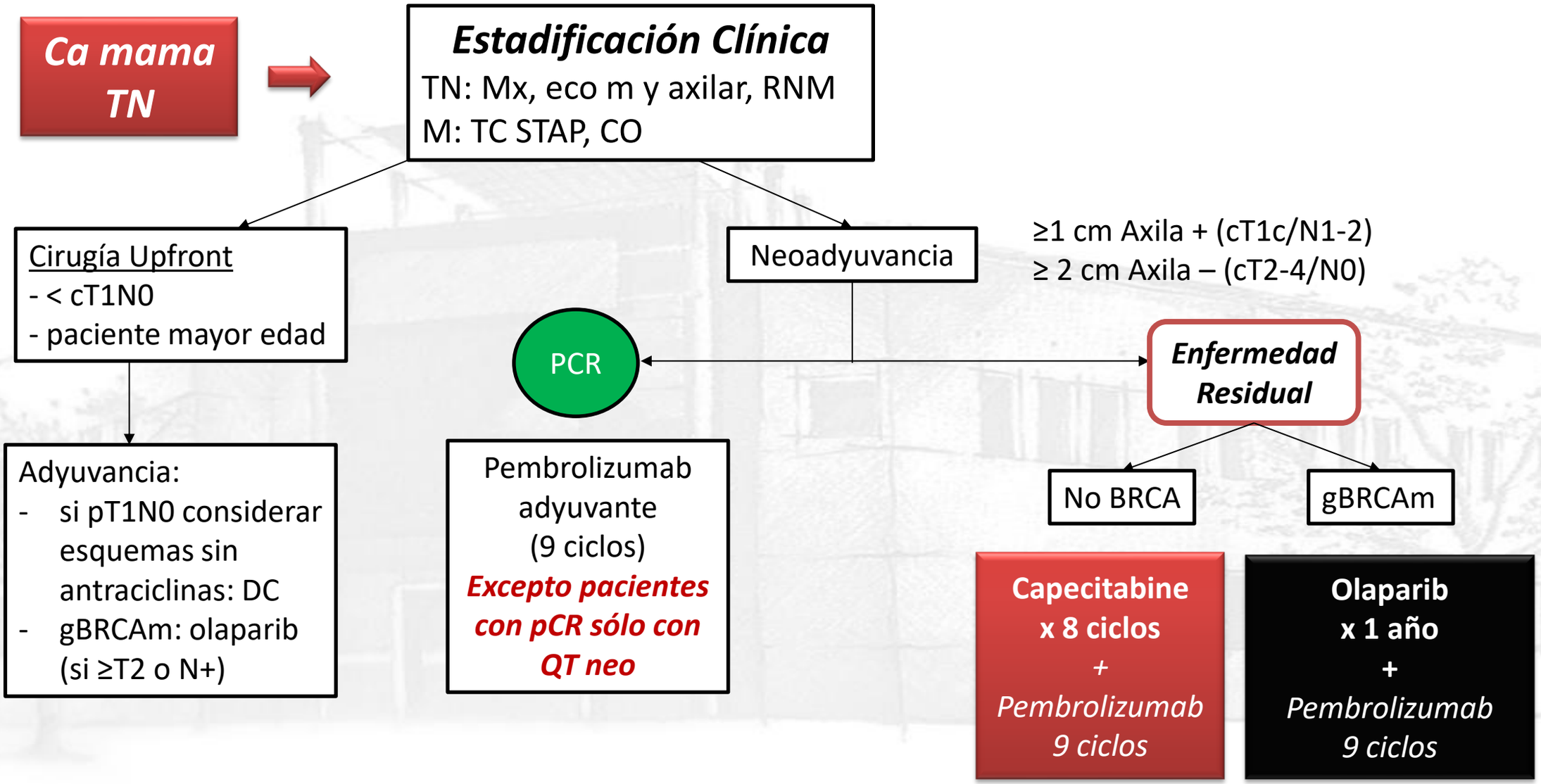
Implications KN522:

1. **Presence of pCR benefit predictive of long-term outcome**
2. **Absence of pCR benefit does not rule out substantial benefit**

Distant recurrences by RCB



Schmid et al, NEJM 2022; Pusztai, ASCO 2022


Ca mama TN
Estadificación Clínica
TN: Mx, eco m y axilar, RNM
M: TC STAP, CO
Cirugía Upfront
- < cT1N0
- paciente mayor edad
Adyuvancia:
- si pT1N0 considerar esquemas sin antraciclinas: DC
- gBRCAm: olaparib (si ≥T2 o N+)
Neoadyuvancia
≥1 cm Axila + (cT1c/N1-2)
≥ 2 cm Axila – (cT2-4/N0)
PCR
Pembrolizumab adyuvante (9 ciclos)
Excepto pacientes con pCR sólo con QT neo
Enfermedad Residual
No BRCA
gBRCAm
Capecitabine x 8 ciclos + Pembrolizumab 9 ciclos
Olaparib x 1 año + Pembrolizumab 9 ciclos

SOLCA
NÚCLEO DE QUITO

Ca mama Her2 +

- ✓ **≥cT1 (1,5 cm)**
- ✓ **≥cN+**

Neoadyuvancia

QT + doble bloqueo antiHer2

PCR

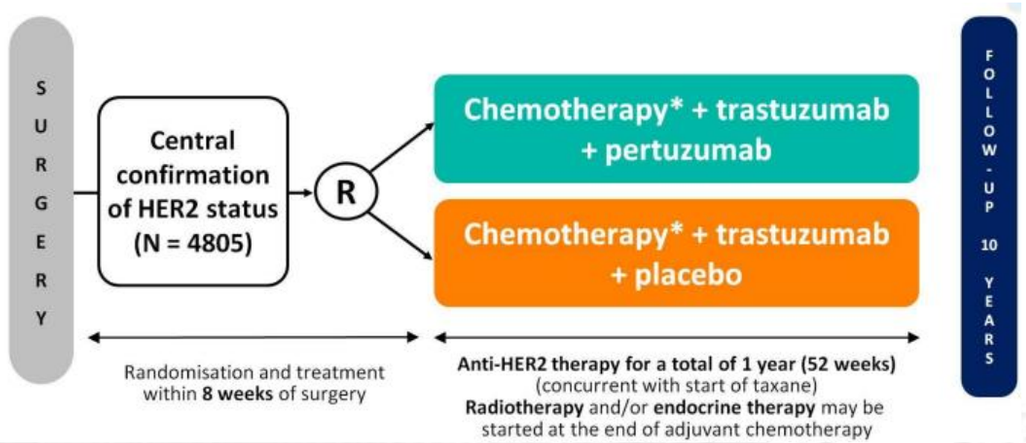
Enf residual

THCP (Neosphere- Tryphaena - Train2)
AC/T + T + P

ORIGINAL ARTICLE

Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer

Gunter von Minckwitz, M.D., Marion Procter, Ph.D., Evandro de Azambuja, M.D., Dimitrios Zardavas, M.D., Mark Benyunes, M.D., Giuseppe Viale, M.D., Thomas Suter, M.D., Amal Arahmani, Ph.D., Nathalie Rouchet, M.Sc., Emma Clark, M.Sc., Adam Knott, Ph.D., Istvan Lang, M.D., Christelle Levy, M.D., Denise A. Yardley, M.D., Jose Bines, M.D., Richard D. Gelber, Ph.D., Martine Piccart, M.D., and Jose Baselga, M.D., for the APHINITY Steering Committee and Investigators*



Characteristic	Pertuzumab Group (N=2400)	Placebo Group (N=2404)
Nodal status — no. of patients (%)		
0 positive nodes and tumor ≤1 cm*	90 (3.8)	84 (3.5)
0 positive nodes and tumor >1 cm*	807 (33.6)	818 (34.0)
1–3 positive nodes	907 (37.8)	900 (37.4)
≥4 positive nodes	596 (24.8)	602 (25.0)

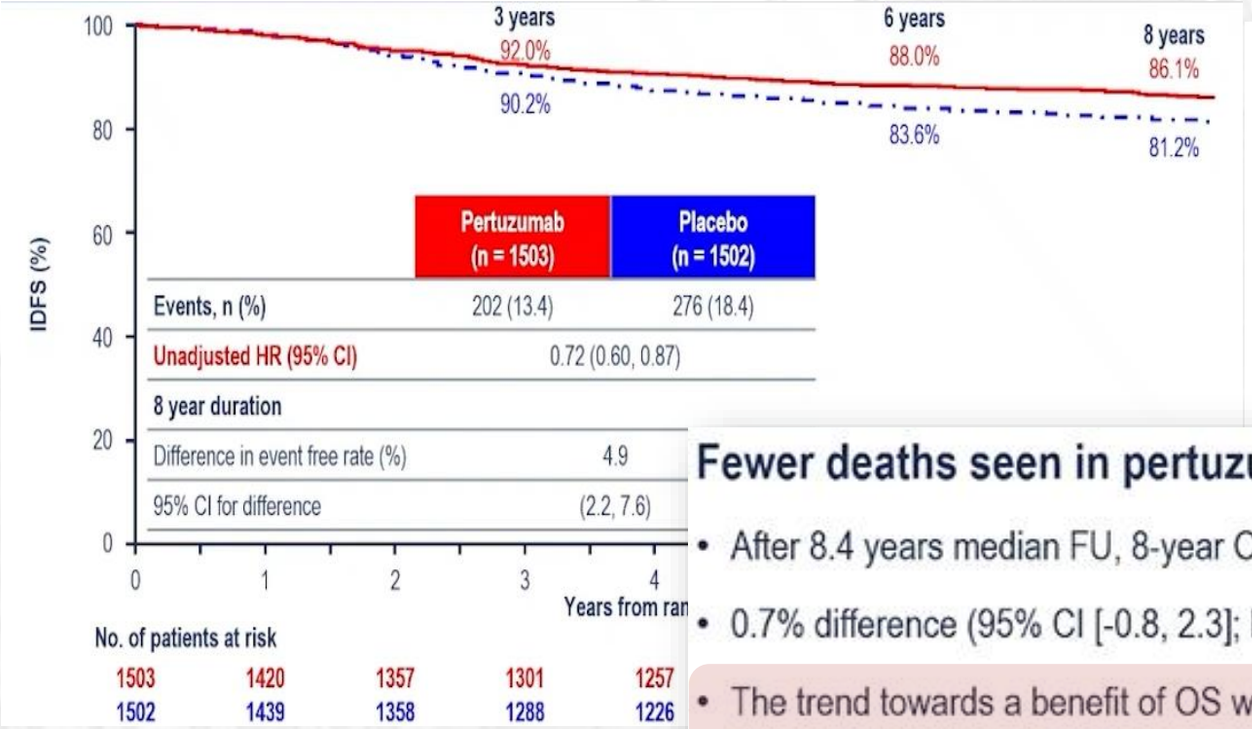
Updated results of APHINITY at 8.4 years compared with at 4 and 6 years median follow up

	4 yr IDFS (TP vs T)	4 yr IDFS Δ	6 yr IDFS (TP vs T)	6 yr IDFS Δ	8 yr IDFS (TP vs T)	8 yr IDFS Δ
ITT	92.3 vs 90.6%	1.7%	90.6 vs 87.8%	2.8%	88.4 vs 84.8%	2.6%
N0	96.7 vs 96.2%	0.5%	95.0 vs 94.9%	0.1%	92.3 vs 93.3	-1%
N+	**89.9 vs 86.7%**	**3.2%**	**87.9 vs 83.4%**	**4.5%**	**86.1 vs 81.2%**	**4.9%**
ER/PR+	93.0 vs 91.6%	1.4%	91.2 vs 88.2%	3%	88.9 vs 86.1%	2.8%
ER/PR-	91.0 vs 88.7%	2.3%	89.5 vs 87.0%	2.5%	87.5 vs 85.2%	2.3%

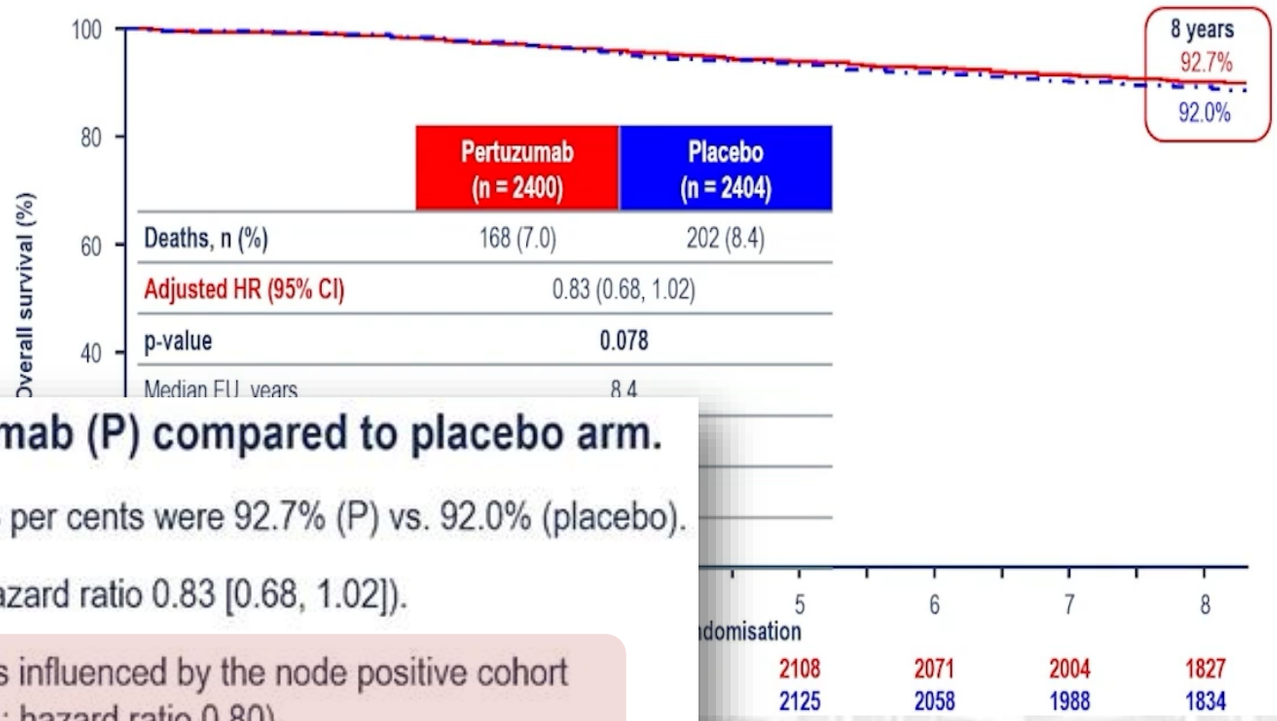
ALEXANDER FLEMING

von Minckwitz, Gunter; (2017). Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. New England Journal of Medicine, (), NEJMoa1703643–.

APHINITY Updated Descriptive IDFS Analysis at 8.4 Years Median FU by treatment regimen
Node-positive Cohort



APHINITY Interim Overall Survival Analysis at 8.4 years Median FU by Treatment Regimen (ITT Population)



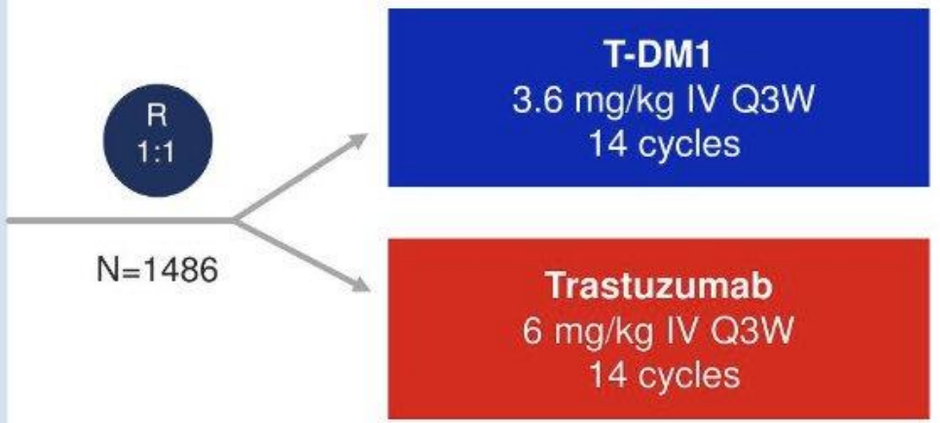
Fewer deaths seen in pertuzumab (P) compared to placebo arm.

- After 8.4 years median FU, 8-year OS per cents were 92.7% (P) vs. 92.0% (placebo).
- 0.7% difference (95% CI [-0.8, 2.3]; hazard ratio 0.83 [0.68, 1.02]).
- The trend towards a benefit of OS was influenced by the node positive cohort (8-year OS per cents 91.1% vs 89.2%; hazard ratio 0.80).
- Follow-up is very important to determine OS benefit of P.

Geyer et al SABCS 2018

KATHERINE Study Design

- cT1-4/N0-3/M0 at presentation (cT1a-b/N0 excluded)
- Centrally confirmed HER2-positive breast cancer
- Neoadjuvant therapy must have consisted of
  - Minimum of 6 cycles of chemotherapy
    - Minimum of 9 weeks of taxane
    - Anthracyclines and alkylating agents allowed
    - All chemotherapy prior to surgery
  - Minimum of 9 weeks of trastuzumab
    - Second HER2-targeted agent allowed
- Residual invasive tumor in breast or axillary nodes
- Randomization within 12 weeks of surgery



Radiation and endocrine therapy per protocol and local guidelines

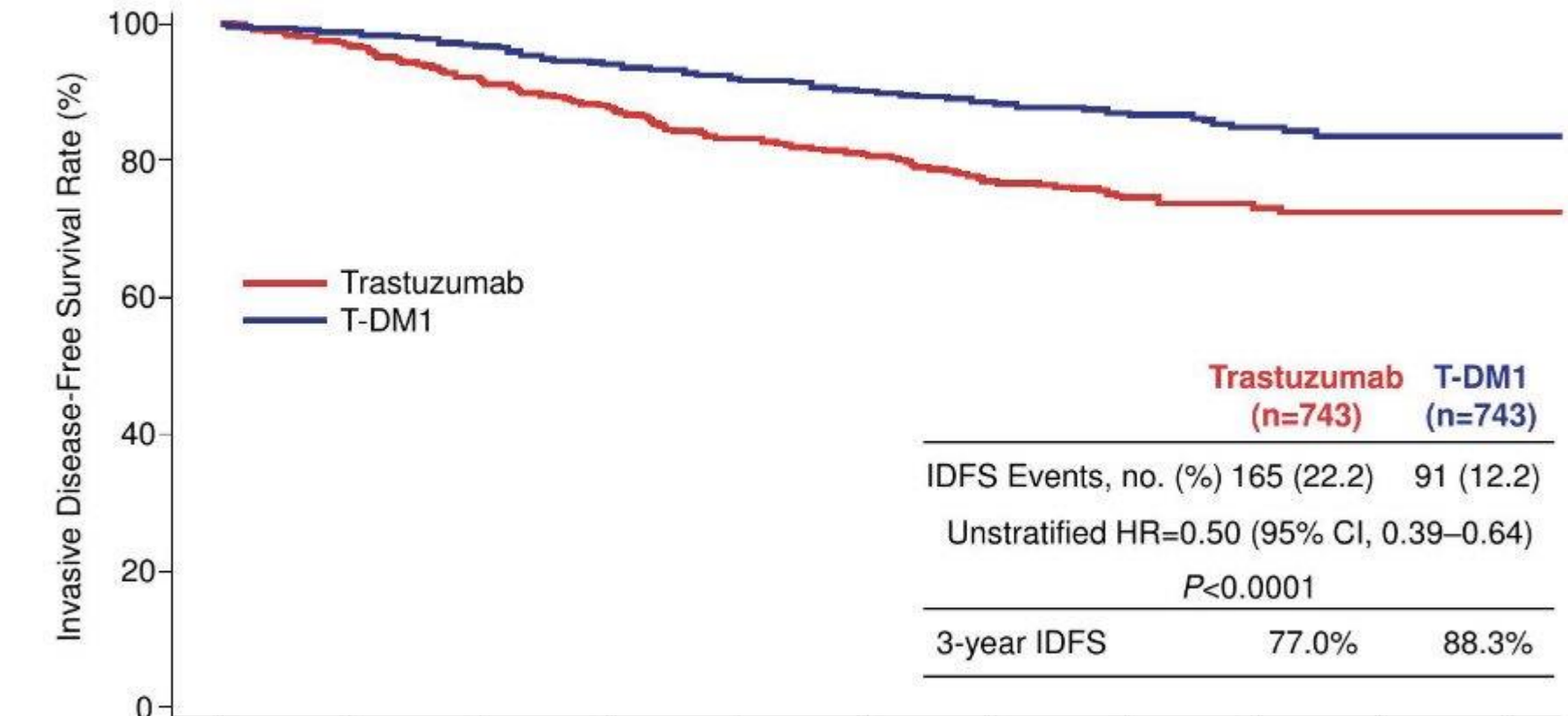
Stratification factors:

- Clinical presentat
- Hormone recepto
- Preoperative ther
- Pathological nod

Hormone-receptor status — no. of patients (%)		
Estrogen-receptor–negative and progesterone-receptor–negative or status unknown	203 (27.3)	209 (28.1)
Estrogen-receptor–positive, progesterone-receptor–positive, or both	540 (72.7)	534 (71.9)
Previous use of anthracycline — no. of patients (%)	564 (75.9)	579 (77.9)
Neoadjuvant HER2-targeted therapy — no. of patients (%)		
Trastuzumab alone	596 (80.2)	600 (80.8)
Trastuzumab plus pertuzumab	139 (18.7)	133 (17.9)
Trastuzumab plus other HER2-targeted therapy	8 (1.1)	10 (1.3)

IAF
INSTITUTO ALEXANDER FLEMING

Invasive Disease-Free Survival



	Trastuzumab (n=743)	T-DM1 (n=743)
IDFS Events, no. (%)	165 (22.2)	91 (12.2)
Unstratified HR=0.50 (95% CI, 0.39–0.64)		
P<0.0001		
3-year IDFS	77.0%	88.3%

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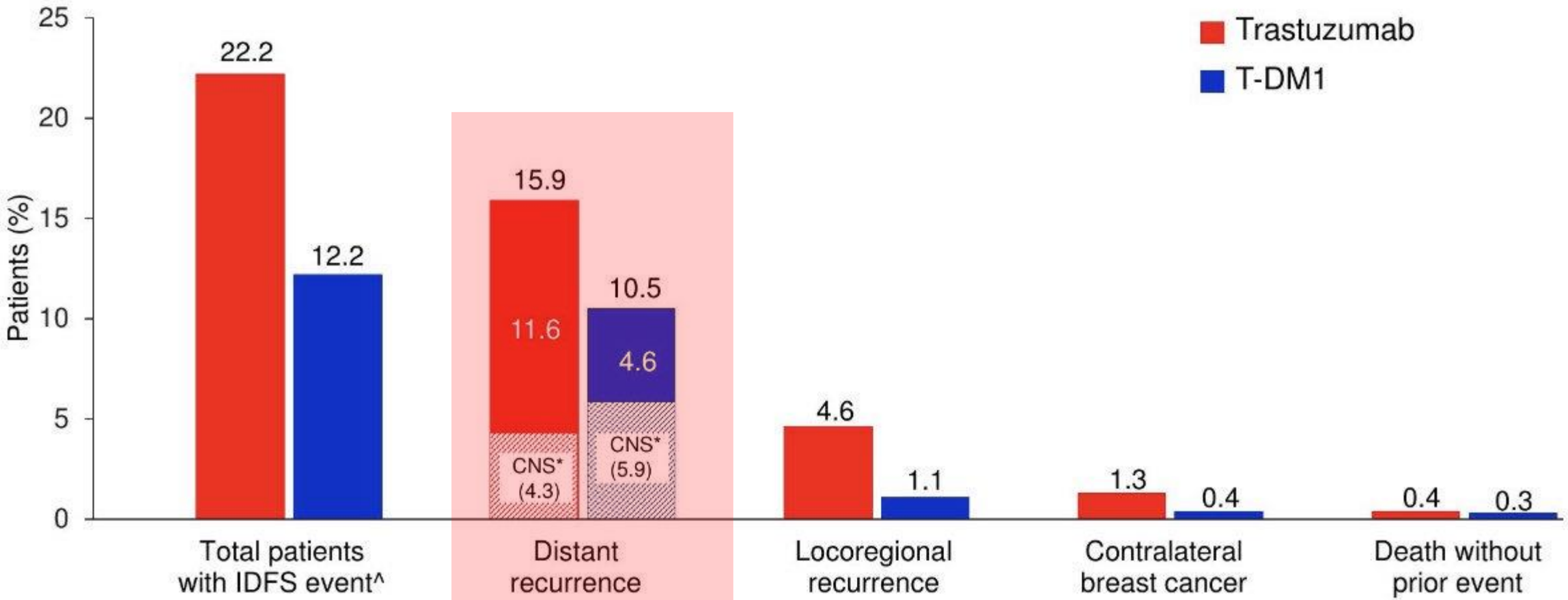
von Minckwitz G, *et al*. *N Engl J Med* 2018

First IDFS Events



^Patients who experience additional IDFS event(s) within 61 days of their first IDFS event are reported in the category according to the following hierarchy: [1] Distant recurrence; [2] Locoregional recurrence; [3] Contralateral breast cancer; [4] Death without prior event.

***CNS metastases as component of distant recurrence (isolated or with other sites).** **Trastuzumab** **T-DM1**

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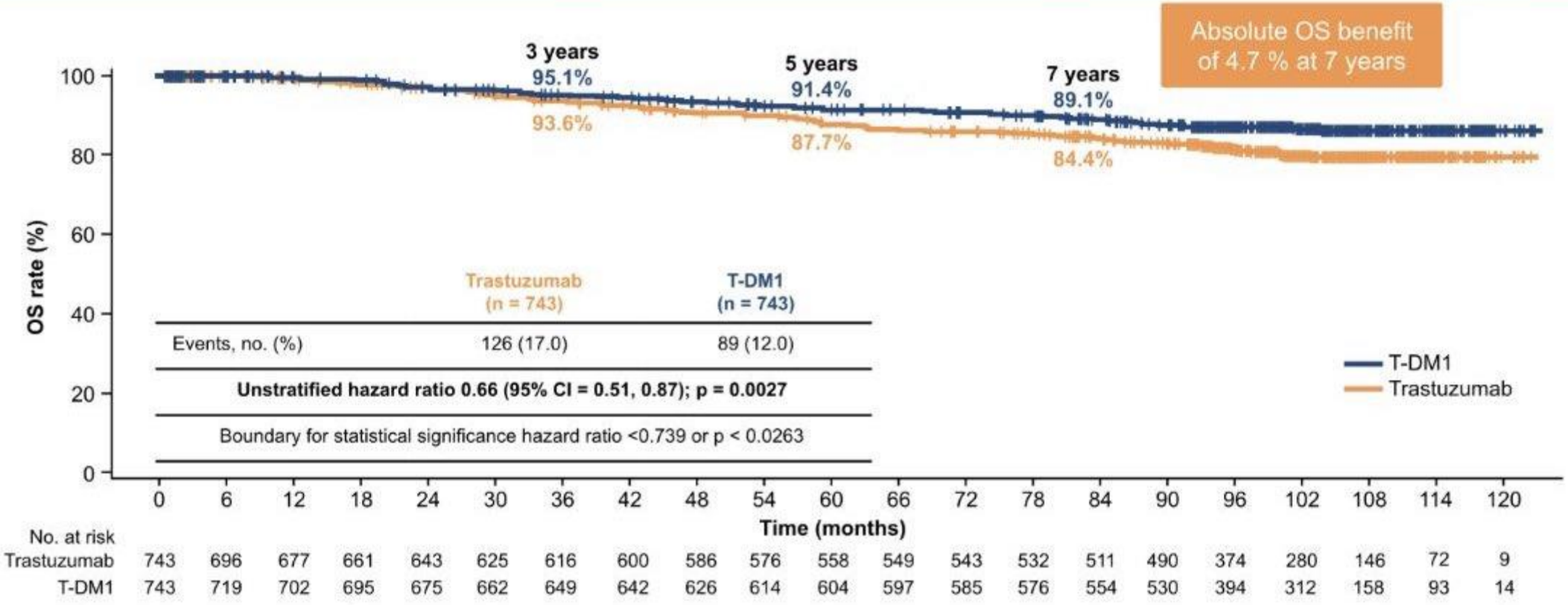
KATHERINE 2nd OS interim analysis; median follow-up 8.4 years (101 months)



Significant reduction in risk of death by 34% with T-DM1

CI, confidence interval; OS, overall survival; T-DM1, ado-trastuzumab emtansine.

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Pacientes con HER2 negativo en enfermedad residual postNeo

1486 pts Her2 positivo enroladas

1195 (80.4%) muestras neoadyuvancia

289 (19.4%) muestra quirúrgicas

Análisis exploratorio cambios estatus HER2

Muestras preneoadyuvancia:
845 pts Her2+

Additional testing

Muestras cirugía:
775 pacientes (91,7%) Her2 positivo
70 pacientes (8,3%) Her2 negativo

Eficacia: NO recurrencia en 70 pts con Her2 negativo que recibieron TDM1 (n28) y 11 eventos en la rama trastuzumab (n42)

CONCLUSIONES (bajo n)

- TDM1 debería continuarse en pacientes que negativizan HER2 postneoadyuvancia
- La evaluación de HER2 en la pieza quirúrgica no es necesaria

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Geyer et al SABCS 2018

Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial

Dr Martin et al

THE LANCET Oncology

- Fase III randomizado multicéntrico

Estratificado por RH, compromiso ganglionar (0 vs 1-3 vs ≥ 4), régimen trastuzumab ady (secuencial vs concurrente con QT)

Pts con ca mama HER2+ temprano operadas (E I-IIIc), N+ or N- y adyuvancia con trastuzumab completa ≤ 2 años previos a randomización* (N = 2840)

HT adyuvante concurrent en RH+

Neratinib 240 mg/d VO (1 año) (n = 1420)

Placebo (n = 1420)

Time from last trastuzumab dose to randomization		
≤1 y	1152 (81)	1145 (81)
>1 y	268 (19)	275 (19)
Prior neoadjuvant therapy	342 (24)	379 (27)
pCR	61 (4)	65 (5)
No pCR	258 (18)	298 (21)

Previous neoadjuvant or adjuvant therapy†				
Yes	1420 (100%)	1420 (100%)	1028 (100%)	1089 (100%)
Trastuzumab	1420 (100%)	1420 (100%)	1028 (100%)	1089 (100%)
Anthracycline only	136 (10%)	135 (10%)	102 (10%)	109 (10%)
Anthracycline plus taxane	962 (68%)	965 (68%)	725 (71%)	762 (70%)
Taxane only	318 (22%)	316 (22%)	198 (19%)	216 (20%)
Non-anthracycline or taxane	4 (<1%)	4 (<1%)	3 (<1%)	2 (<1%)

*Enmienda Feb 2010: inclusión sólo pacientes de alto riesgo (N+) y quienes completaban trastuzumab ≤ 1 año después de la randomización

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Holmes. SABCS 2020. Abstr PD3-03. Martin. Lancet Oncol. 2017;18:1688. Chan. Lancet Oncol. 2016;17:367. NCT00878709.

Final Efficacy Results of Neratinib in HER2-positive Hormone Receptor-positive Early-stage Breast Cancer From the Phase III ExteNET Trial

A 8 años OS en **no Pcr HR +**
Beneficio absoluto: 9.1%

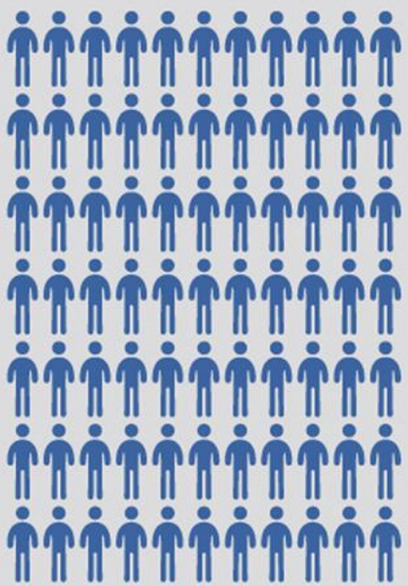
Chan et al. Clin Breast Cancer. 2021 Feb;21(1):80-91.e7

Neratinib for Early-Stage HER2-Positive Breast Cancer

International, Randomized, Phase 3 ExteNET Trial

Intention-to-treat population

2840 patients
HER2+ early-stage breast cancer after prior trastuzumab



*According to labelling in the European Union and other

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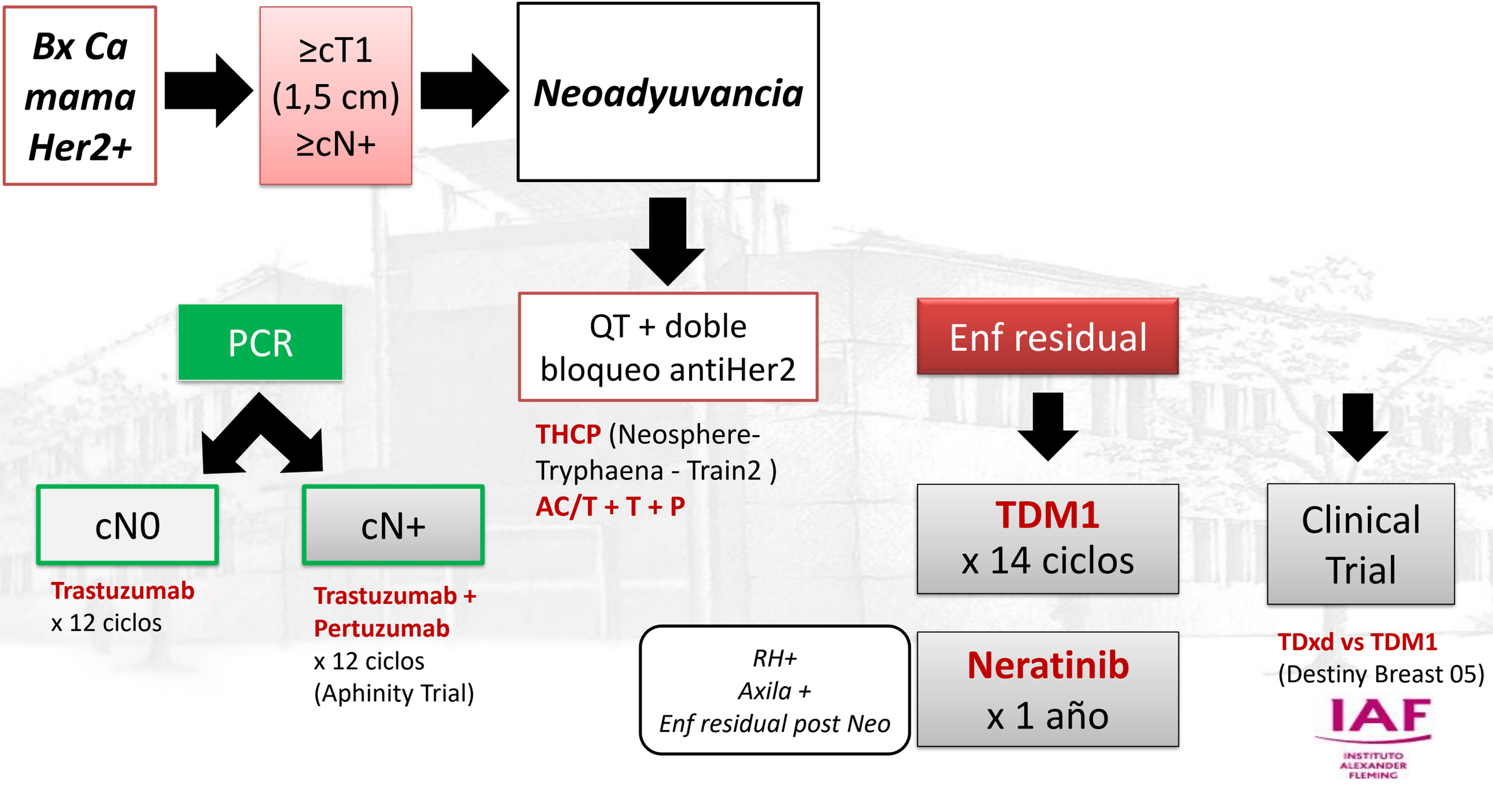
Bx Ca mama Her2+
≥cT1 (1,5 cm) ≥cN+
Neoadyuvancia
QT + doble bloqueo antiHer2
THCP (Neosphere-Tryphaena - Train2)
AC/T + T + P
PCR
cN0
Trastuzumab
x 12 ciclos
cN+
Trastuzumab + Pertuzumab
x 12 ciclos
(Aphinity Trial)
Enf residual
TDM1
x 14 ciclos
RH+
Axila +
Enf residual post Neo
Neratinib
x 1 año
Clinical Trial
TDxd vs TDM1
(Destiny Breast 05)
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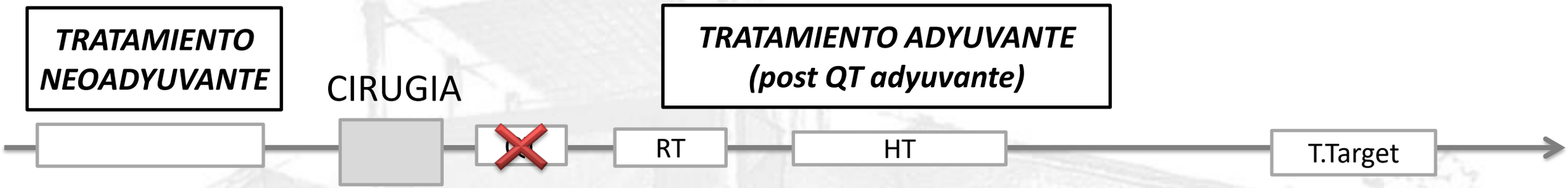
Manejo Ca mama temprano Luminal



Conservadora vs Radical

Alto Riesgo: N+, >T3, Lum B, Gh3, alto riesgo genómico, menor 35 años

QT:
ACx4 (dd)
→ **Taxanos**

(HT)

(QT + IT)
CA7FL / KN 756

- *Tumores inoperables de inicio (inflamatorios)*
- *> volumen enf. axilar*
- *Premenopausicas N+*

- ***Premen***: análogos LHRH 2-5 años + TMX o IA seguido de TMX/IA hasta 10 años
- ***Postmen*** 7-10 años IA o TMX (switch)

iCDK4:
Abemaciclib (2 años)
Ribociclib (3 años)

iPARP:
Olaparib (1 año)

Otros iCDK4-6 evaluados en adyuvancia de alto riesgo (pre/postmen)

	MonarchE	Pallas	Penelope	Natalee
Droga	Abemaciblib continuo	Palbociclib	Palbociclib	Ribociclib
Duración	2 años	2 años	1 año	3 años
Forma administración	150 mg c/12 hs Continuo	125 mg 1-21d cada 28	125 mg 1-21d cada 28 d	400 mg 1-21d cada 28 d
N	5637	5760	1250	Reclutando
Elegibilidad	4 ganglios o 1-3 con GH3 o ≥5 cm EII: 26% EIII: 74%	EII: 52% III: 48%	Ausencia de pCR post QT neoady (CPS EG score ≥3 o ≥2 con ypN+)	EII (N0 GH2-3 y/o Ki67 ≥ 20% o N1) EIII
Tasa discontinuación	27%	42%	19%	-
SLE	A 5a 83,6% vs % 76% (+)	A 3a 89% vs 90% (-)	A 4a 73,5% vs 72% (-)	A 3a 90,7% vs 87,6%

https://dailynews.ascopubs.org/do/10.1200/ADN.21.200483/full/

MonarchE and NATALEE Study Population

MonarchE: Abemaciclib x 2 yr

Randomization

- AI or tamoxifen +/- OFS
- Abemaciclib 150 mg po BID

AI or tamoxifen +/- OFS

Cohorte 1

- ≥4 ganglios
- 1-3 ganglios: - GH3 y/o
  - T ≥5 cm y/o

Cohorte 2

- Ki67 ≥20%

30% estadios temprano elegibles para NATALEE y no para MonarchE

NATALEE: Ribociclib x 3 yr

Randomization

- NSAI +/- OFS
- Ribociclib 400 mg po QD 21 days on/ 7 days off

NSAI +/- OFS

- N1 (1 a 3 ganglios) o N2 (≥4 ganglios)
- N0: - GH3
  - GH2 con Ki>20% o alto grado genómico

NSAI = Non-Steroidal Aromatase Inhibitor; OFS = Ovarian Function Suppression

Johnston S et al ESMO 2023; Slamon D et al ASCO 2023

- ***QT previa***

MonarchE

Prior chemotherapy[a]		
Neoadjuvant chemotherapy	1,039 (37.0)	1,048 (37.0)
Adjuvant chemotherapy	1,642 (58.5)	1,647 (58.2)
No chemotherapy	127 (4.5)	134 (4.7)

Natalee

Previous neoadjuvant or adjuvant chemotherapy — no. (%)			
Any	2249 (88.2)	2245 (88.0)	4494 (88.1)
Neoadjuvant	1085 (42.6)	1095 (42.9)	2180 (42.7)
Adjuvant	1223 (48.0)	1220 (47.8)	2443 (47.9)

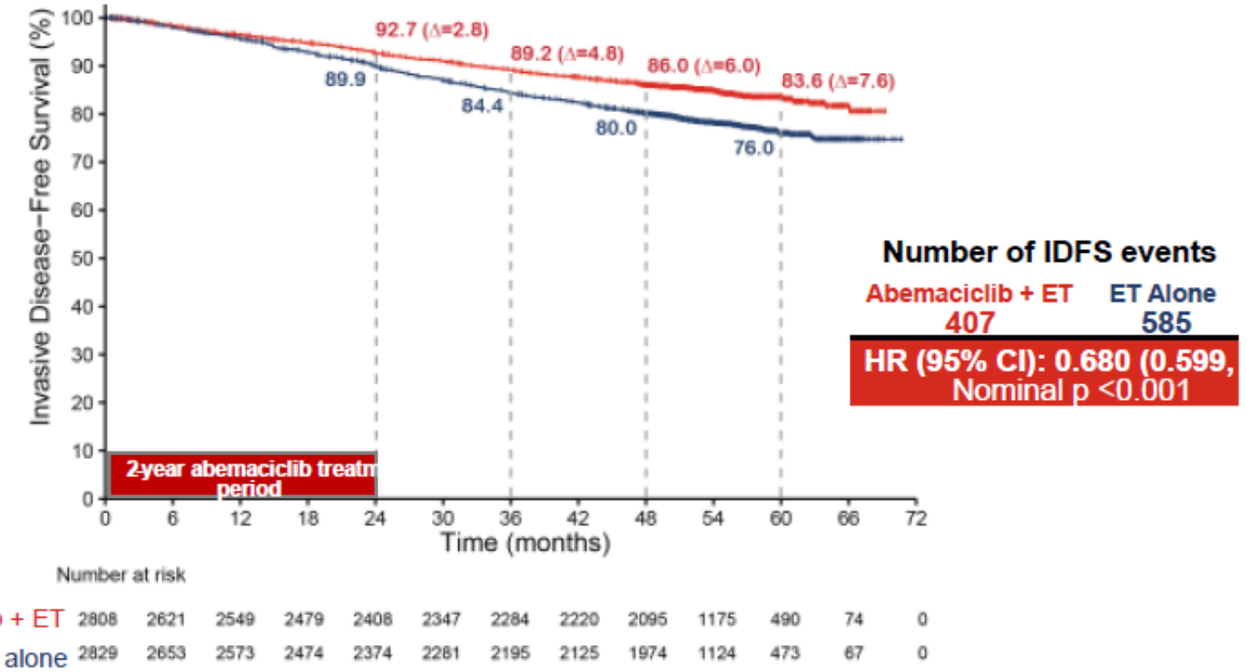
Estadificación MonarchE: anatómica o clínica (previo a tratamiento neoady.)

Estadificación Natalee: anatómica o clínica. El estado ganglionar se evaluó en el momento del diagnóstico (evaluación radiológica) y, después de la cirugía (evaluación patológica)

Johnston S et al ESMO 2023; Slamon D et al ASCO 2023

monarchE 5-yr Results

- Median follow-up time is 4.5 years (54 months)



Number of IDFS events

Abemaciclib + ET	ET Alone
407	585

HR (95% CI): 0.680 (0.599,
Nominal p <0.001

32% reduction in the risk of developing an IDFS event.

Harbeck et al. ESMO 2023

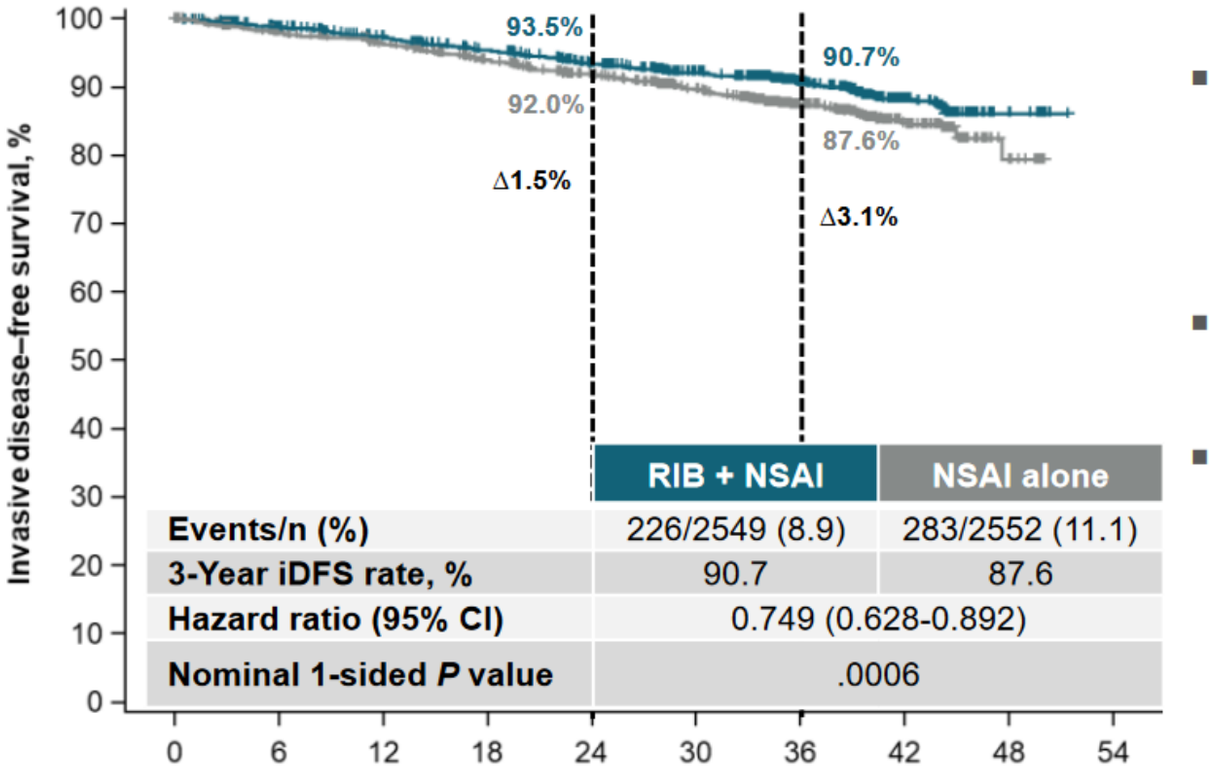
Prior chemotherapy					
Neoadjuvant	1,039	76	1,048	111	0.69 (0.52 to 0.93)
Adjuvant	1,642	52	1,647	69	0.77 (0.54 to 1.10)

Johnston S et al ESMO 2023: Slamon D et al ASCO 2023

Natalee

IDFS 3yr

Invasive Disease–Free Survival



	RIB + NSAI	NSAI alone
Events/n (%)	226/2549 (8.9)	283/2552 (11.1)
3-Year iDFS rate, %	90.7	87.6
Hazard ratio (95% CI)	0.749 (0.628-0.892)	
Nominal 1-sided *P* value	.0006	

No. at risk										
RIB + NSAI	2549	2350	2273	2204	2100	1694	1111	368	21	0
NSAI alone	2552	2241	2169	2080	1975	1597	1067	354	26	0

1. Slamon D. et al. ASCO 2023. Oral LBA500.

Prior CT				
Neoadjuvant	111/1085	132/1095	0.785	(0.610-1.011)
Adjuvant	63/1223	89/1220	0.671	(0.486-0.927)

Johnston S et al ESMO 2023: Slamon D et al ASCO 2023

N ENGL J MED 384;25 NEJM.ORG JUNE 24, 2021

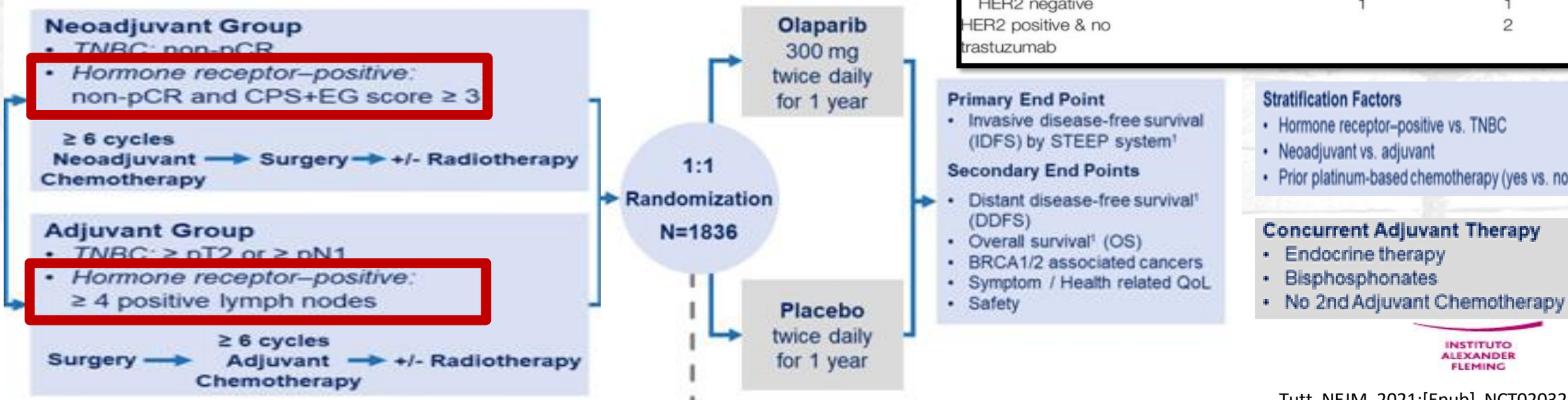
Adjuvant Olaparib for Patients with *BRCA1*- or *BRCA2*-Mutated Breast Cancer

A.N.J. Tutt, J.E. Garber, B. Kaufman, G. Viale, D. Fumagalli, P. Rastogi, R.D. Gelber, E. de Azambuja, A. Fielding, J. Balmaña, S.M. Domchek, K.A. Gelmon, S.J. Hollingsworth, L.A. Korde, B. Linderholm, H. Bandos, E. Senkus, J.M. Suga, Z. Shao, A.W. Pippas, Z. Nowecki, T. Huzarski, P.A. Ganz, P.C. Lucas, N. Baker, S. Loibl, R. McConnell, M. Piccart, R. Schmutzler, G.G. Steger, J.P. Costantino, A. Arahmani, N. Wolmark, E. McFadden, V. Karantza, S.R. Lakhani, G. Yothers, C. Campbell, and C.E. Geyer, Jr., for the OlympiA Clinical Trial Steering Committee and Investigators*

OlympiA
OLaparib in Adjuvant BRCAm breast cancer

Cancer Stage	CPS + EG Score	Neo-Bioscore (7 points)	Modified Neo-Bioscore (8 points)
Pretreatment Clinical Stage (CS)			
I	0	0	0
IIA	0	0	0
IIB	1	1	1
IIIA	1	1	1
IIIB	2	2	2
IIIC	2	2	2
Post-treatment Pathologic Stage (PS)			
0	0	0	0
I	0	0	0
IIA	1	1	1
IIB	1	1	1
IIIA	1	1	1
IIIB	1	1	1
IIIC	2	2	2
Tumor Marker			
ER negative	1	1	1
Grade 3	1	1	1
HER2 negative		1	1
HER2 positive & no trastuzumab			2

Fase 3 doble ciego randomizado
Her2 negativo, mutación germinal BRCA 1 o 2



INSTITUTO ALEXANDER FLEMING

Tutt. NEJM. 2021;[Epub]. NCT02032823.

In high-risk HR+HER2- gBRCAm pts: olaparib or abemaciclib?

Indication olaparib HR+HER2-

- Neoadjuvant: no pCR and CPS-EG ≥ 3*
- Adjuvant: ≥ 4 positive lymph nodes

Indication abemaciclib HR+HER2-

- FDA: N+ with high recurrence risk and Ki-67 ≥ 20%
- EMA: N+ with high recurrence risk
  - ≥ 4 positive lymph nodes
  - 1-3 pos lymph nodes and:
    T ≥ 5 cm or grade 3 or Ki-67 ≥ 20%

- Can olaparib be combined with abemaciclib (NCT03685331)?
- What is the efficacy of the combination compared to either one drug?

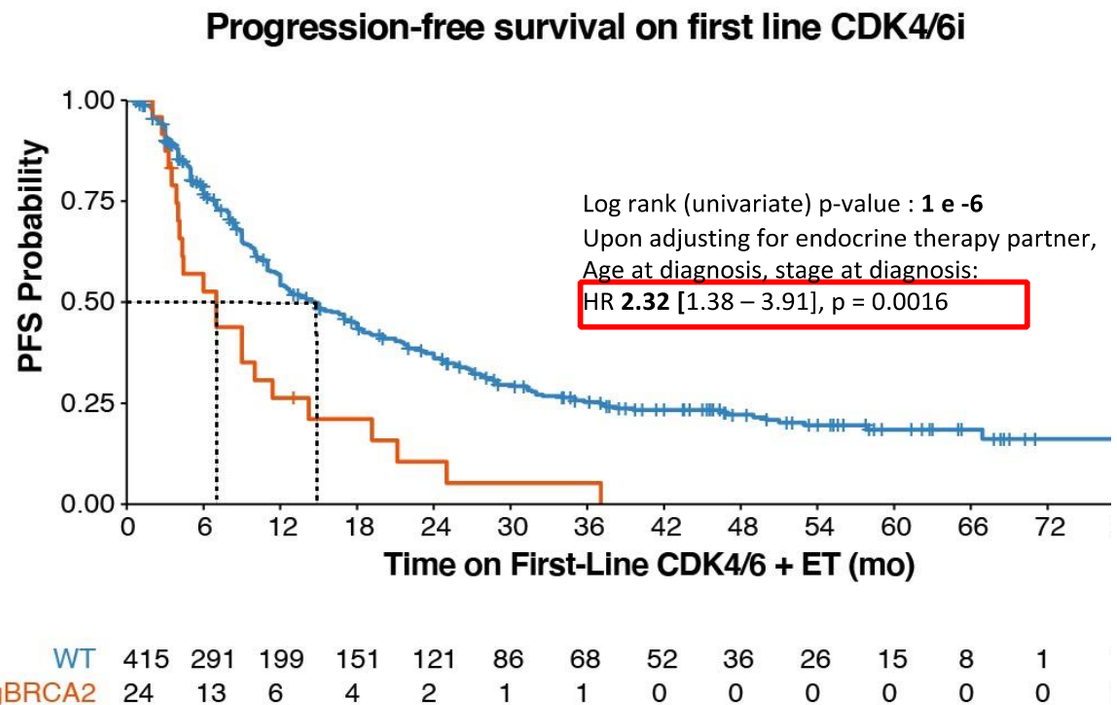
agent	Investigational arm	Placebo/control arm	HR (95% CI)[3]
	3-years invasive disease-free survival		
Olaparib[1]	83.5%	77.2%	0.70 (0.38-1.27)
abemaciclib[2]	88.8%	83.4%	0.70 (0.59-0.82)

*CPS+EG score: MD Anderson Cancer Center neoadjuvant therapy outcomes calculator; Mittendorf, JCO 2011

ALEXANDER FLEMING

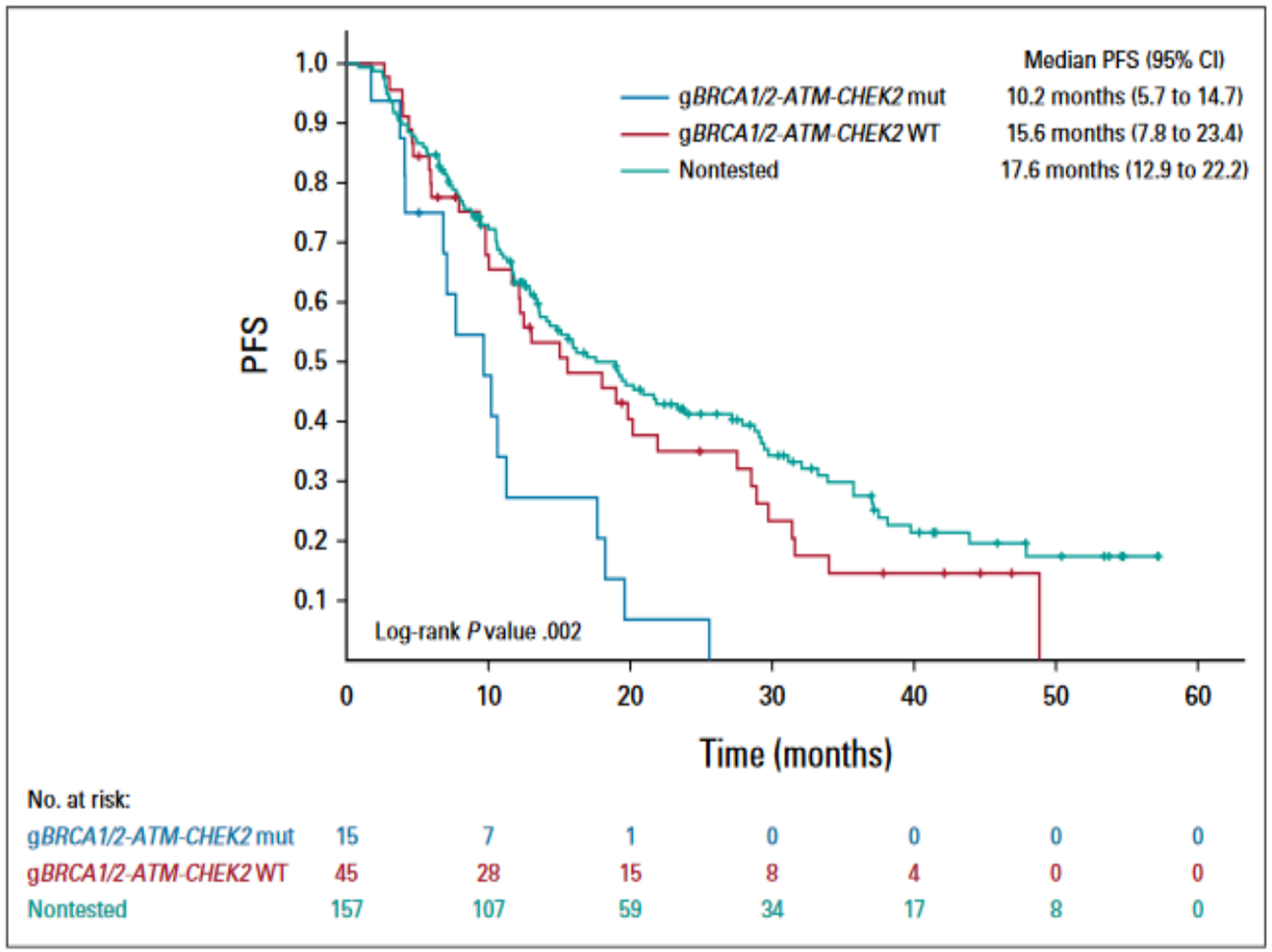
Tutt. NEJM. 2021;[Epub]. NCT02032823.

Inferior outcomes for gBRCAm pts with CDK4/6i in Metastatic HR+ Breast Cancer



BRCA2 status	Median PFS (mo) [95% CI]
gBRCA2 WT	14.7 [12 – 17.5]
gBRCA2 pathogenic variant	7.0 [4.0 – 10.0]

Safonov et al, SABCS 2021



Bruno et al. JCO Precis Oncol 6:e2100140. © 2022 by American Society of Clinical Oncology

Manejo Ca mama temprano Luminal

TRATAMIENTO NEOADYUVANTE

CIRUGIA

TRATAMIENTO ADYUVANTE (post QT adyuvante)

RT | HT | T.Target

~~Plataformas genómicas~~

Conservadora vs Radical

QT:
ACx4 (dd)
→ **Taxanos**

(HT)

(QT + INMUNOTERAPIA)
CA7FL / KN 756

Alto Riesgo: N+, >T3, Lum B, Gh3, alto riesgo genómico, menor 35 años

- ***Premen***: análogos LHRH 2-5 años + TMX o IA seguido de TMX/IA hasta 10 años
- ***Postmen*** 7-10 años IA o TMX (switch)

iCDK4:
 # Abemaciclib (2 años)
- 4 ganglios o
- 1-3 gg GH3 o T>5 cm

(# Ribociclib) (3 años)
- 4 ganglios o 1-3 gg

Axila neg: GH3 o GH2 con Ki>20% o plataforma genómica alto riesgo

iPARP en gBRCAm
 # Olaparib
(1 año)
Si neoady CPS EG score ≥3 (o ≥ 4 gg)

SOLCA
NÚCLEO DE QUITO

CONCLUSIONES

1) Si neoadyuvancia y enfermedad residual:
   - repetir IHQ en cirugía para definir adyuvancia (excepto Her2+++)
2) Si PCR, evaluar de-escalar tratamiento
3) Si Enf. Residual enfermedad de alto riesgo, evaluar sumar estrategias adyuvantes:

TN: - Pembrolizumab (si realizó neoadyuvancia con IT)
- gBRCAm olaparib
- sin gBRCAm Capecitabine

Her2: - TDM1
- (neratinib: axila +, RH+)

Luminales: - considerar estadificación clínica para iCDK4-6

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NÚCLEO DE QUITO

desde 1954
7 DÉCADAS
de atención especializada en cáncer

Muchas Gracias

UICC Member

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¡Juntos somos esperanza de vida!