RAGMA 23

16ª Revisión Anual GEICAM de Avances en Cáncer de Mama

Realidades y esperanzas

Avances en plataformas y biomarcadores

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Organizado por:

GEICAM investigación en cáncer de mama

Plataformas de expresión génica

Biomarkers for Adjuvant Endocrine and Chemotherapy in Early-Stage Breast Cancer: ASCO Guideline Update

Fabrice Andre, MD[1]; Nofisat Ismaila, MD, MSc[2]; Kimberly H. Allison, PhD[3]; William E. Barlow, PhD[4]; Deborah E. Collyar, BSc[5]; Senthil Damodaran, MD, PhD[6]; N. Lynn Henry, MD, PhD[7]; Komal Jhaveri, MD[8,9]; Kevin Kalinsky, MD, MS[10]; Nicole M. Kuderer, MD[11]; Anya Litvak, MD[12]; Erica L. Mayer, MD, MPH[13]; Lajos Pusztai, MD[14]; Rachel Raab, MD[15]; Antonio C. Wolff, MD[16]; and Vered Stearns, MD[16]

1. Se puede considerar el uso de **OncotypeDx**, **MammaPrint**, **Breast Cancer Index (BCI)** y **Endopredict** en **postmenopáusicas** (>50 años) **ER+/HER2- en ganglios negativos o 1-3 positivos**.

2. **Prosigna y Breast Cancer Index (BCI)** pueden usarse en **postmenopáusicas ganglios negativos**.

3. **OncotypeDx** puede considerarse en **premenopáusicas ganglios negativos**.

4. Datos sugieren **beneficio de la QT en premenopáusicas 1-3 ganglios** independientemente de resultados de test genómico.

5. No hay datos en pacientes con 4 ganglios o más.

André F *et al*. JCO 2022

Biomarcadores

Biomarkers for Systemic Therapy in Metastatic Breast Cancer: ASCO Guideline Update

N. Lynn Henry, MD, PhD[1]; Mark R. Somerfield, PhD[2]; Zoneddy Dayao, MD[3]; Anthony Elias, MD[4]; Kevin Kalinsky, MD, MS[5]; Lisa M. McShane, PhD[6]; Beverly Moy, MD, MPH[7]; Ben Ho Park, MD, PhD[8]; Kelly M. Shanahan, MD[9]; Priyanka Sharma, MD[10]; Rebecca Shatsky, MD[11]; Erica Stringer-Reasor, MD[12]; Melinda Telli, MD[13]; Nicholas C. Turner, MD, PhD[14]; and Angela DeMichele, MD[15]

1. **PIK3CA** en tejido o sangre en candidatas a **alpelisib** en combinación con fulvestrant
2. **gBRCA1/2** en candidatas a **iPARP**
3. **PD-L1/CPS-score** en candidatas a **ICI** en combinación con quimioterapia
4. **dMMR/MSI** en candidatas a **ICI**
5. **Fusiones en NTRK** en candidatas a **inhibidores TRK**

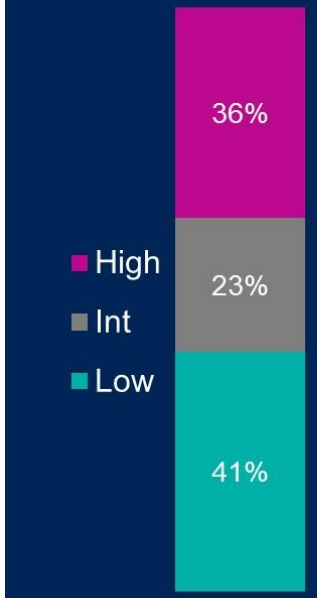
Henry NL *et al*. JCO 2022

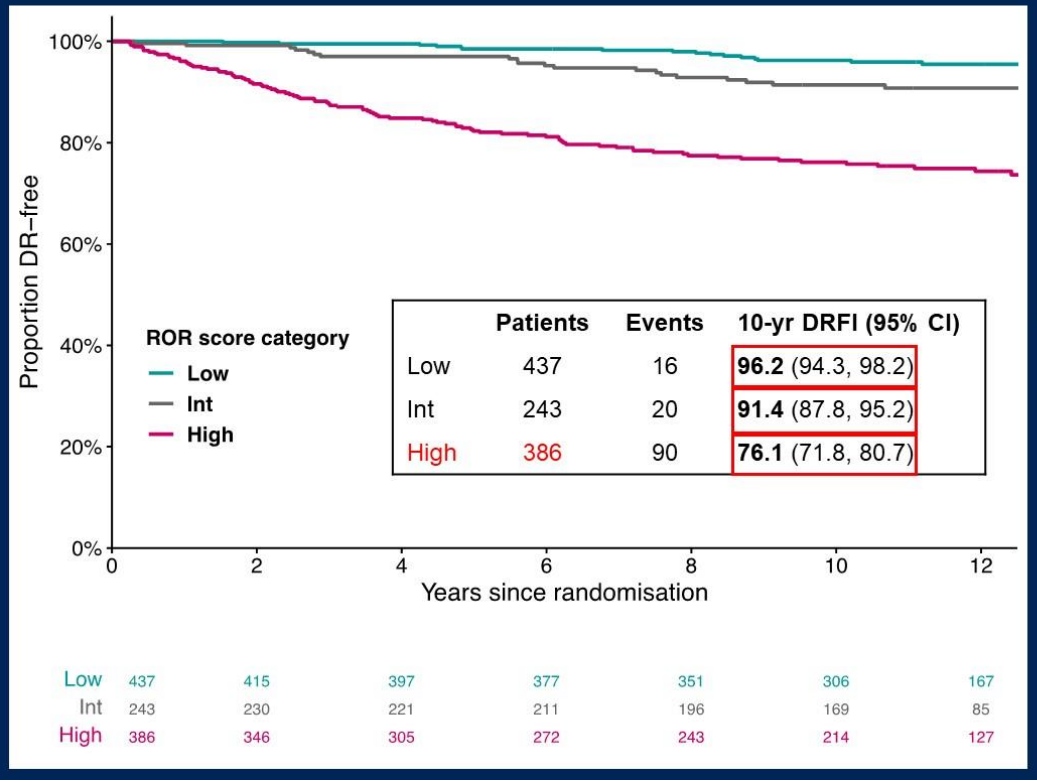
Plataformas de expresión génica

Plataformas de expresión génica-SOFT

PAM50 ROR scores are prognostic in premenopausal women with HR+/HER2- breast cancers

ROR score distribution





HR (95% CI)

Int vs low 1.4 (0.7, 2.7)

High vs low 2.7 (1.4, 5.1)

n=1066

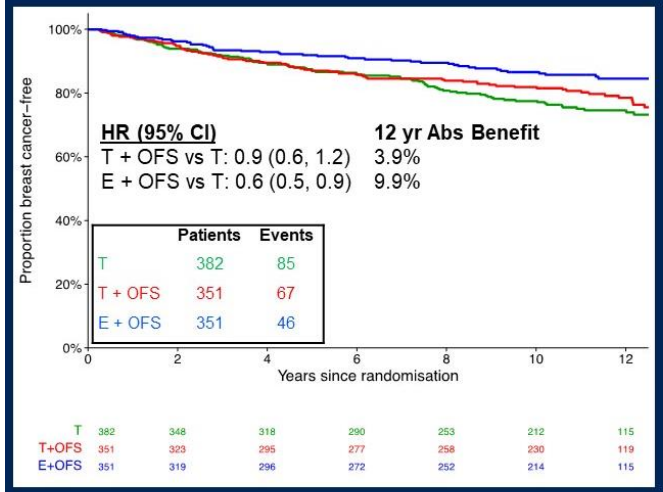
Brown LC. ASCO 2023

Plataformas de expresión génica-SOFT

PAM50 ROR Predictive results– overall cohort

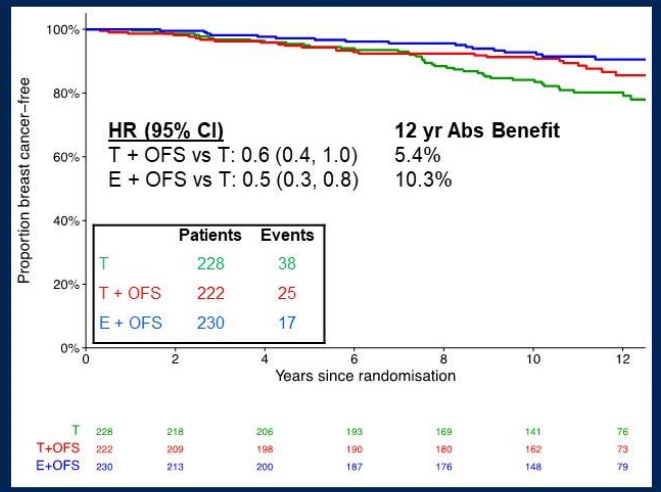
[Endpoint = BCFI]

Unselected (N=1084)



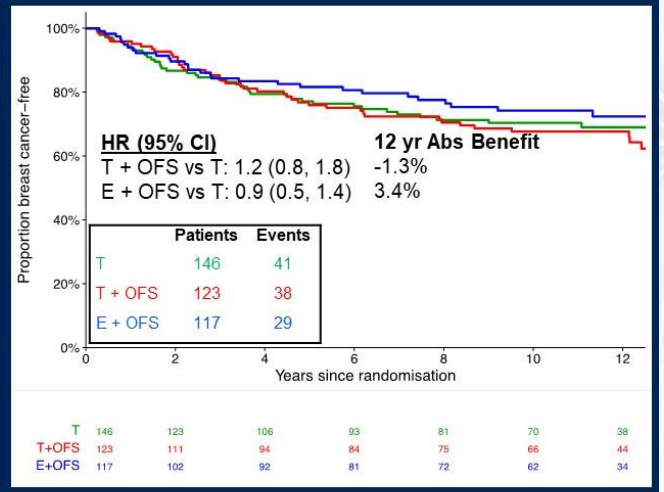
Chemo n=543 (50.1%)

ROR low/int (N=680, 64%)



Chemo n=212 (31.1%)

ROR high (N=386, 36%)



Chemo n=315 (81.6%)

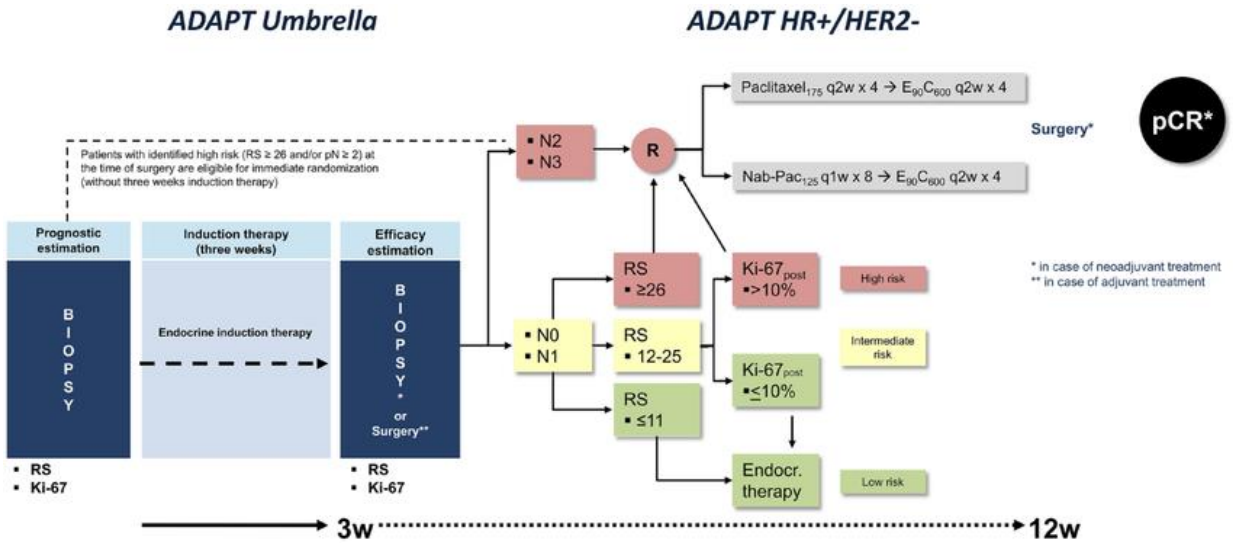
p_{int} (E + OFS) = 0.1; (T + OFS) = 0.2

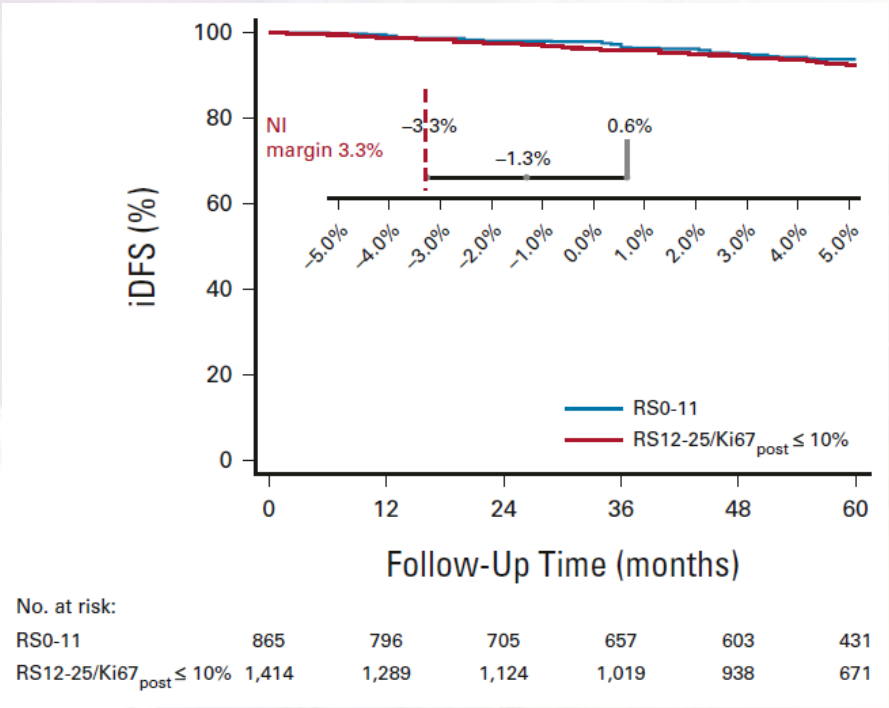
Brown LC. ASCO 2023

Plataformas de expresión génica-WGS-ADAPT

Endocrine Therapy Response and 21-Gene Expression Assay for Therapy Guidance in HR+/HER2– Early Breast Cancer

Ulrike A. Nitz, MD[1,2]; Oleg Gluz MD[1,2,3]; Sherko Kümmel, MD[1,4,5]; Matthias Christgen, MD, PhD[6]; Michael Braun, MD[7]; Bahriye Aktas, MD[8,9]; Kerstin Lüdtke-Heckenkamp, MD[10]; Helmut Forstbauer, MD[11]; Eva-Maria Grischke, MD[12]; Claudia Schumacher, MD[13]; Maren Darsow, MD[14]; Katja Krauss, MD[15]; Benno Nuding, MD[16]; Marc Thill, MD[17]; Jochem Potenberg, MD[18]; Christoph Uleer, MD[19]; Mathias Warm, MD[20]; Hans Holger Fischer, MD[21]; Wolfram Malter, MD[3]; Michael Hauptmann, PhD[22,23]; Ronald E. Kates, PhD[1]; Monika Gräser, MD[1,2,24]; Rachel Würstlein, MD[25]; Steven Shak, MD[26]; Frederick Baehner, MD[26]; Hans H. Kreipe, MD[6]; and Nadia Harbeck, MD, PhD[1,25]; for the West German Study Group



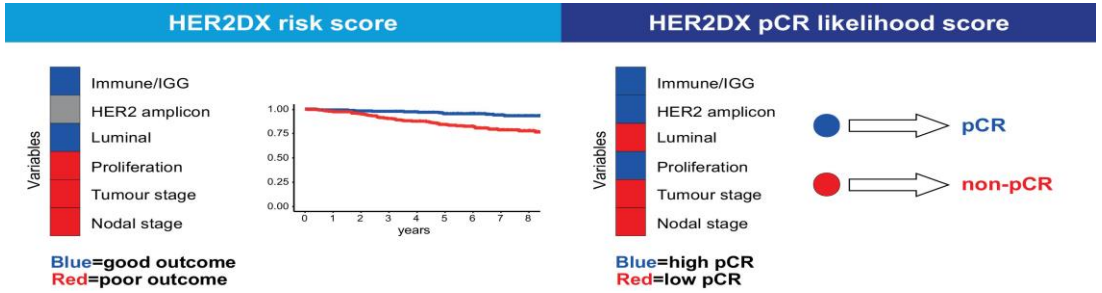


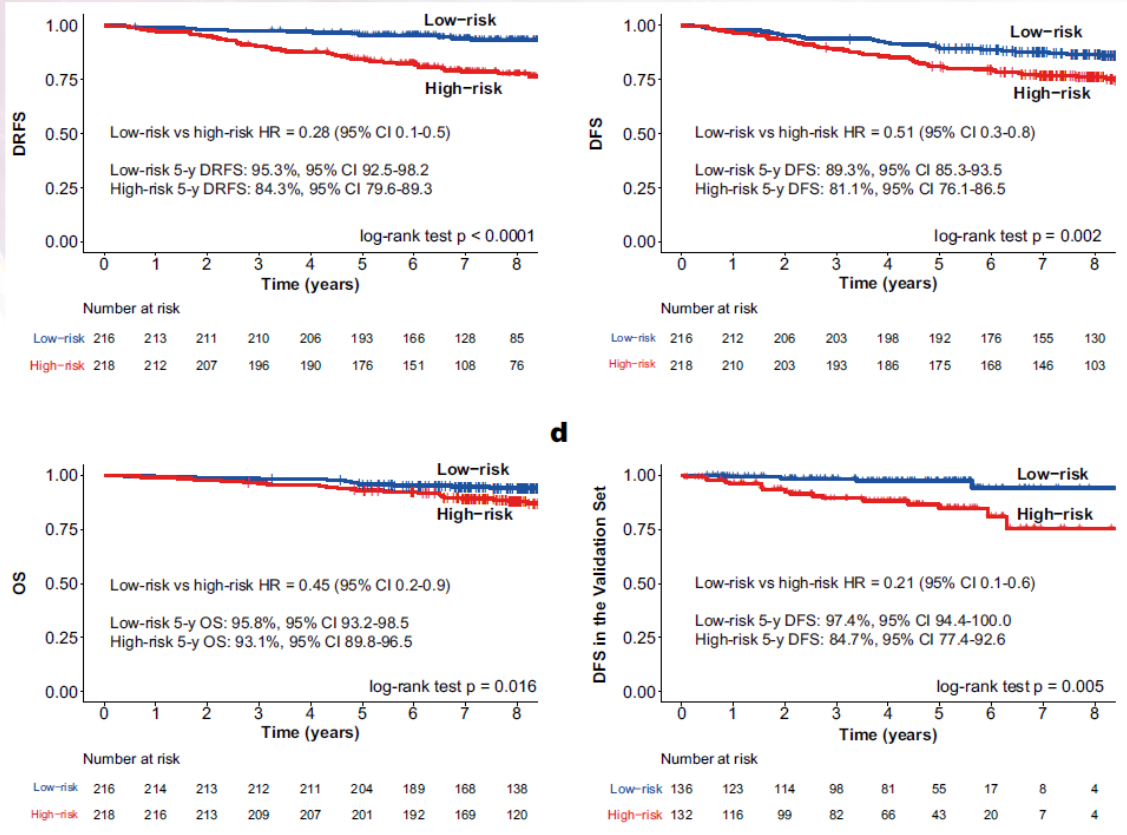
Nitz *et al*. JCO 2022

Plataformas de expresión génica-HER2+

Development and validation of the new HER2DX assay for predicting pathological response and survival outcome in early-stage HER2-positive breast cancer

Aleix Prat,[a,b,c,d,e,1,] Valentina Guarneri,[f,1] Tomás Pascual,[c] Fara Brasó-Maristany,[a] Esther Sanfeliu,[a,g] Laia Paré,[h] Francesco Schettini,[a,b,c] Débora Martínez,[a] Pedro Jares,[g,i] Gaia Griguolo,[f] Maria Vittoria Dieci,[f] Javier Cortés,[j,k] Antonio Llombart-Cussac,[l] Benedetta Conte,[a,b,c] Mercedes Marín-Aguilera,[h] Nuria Chic,[a,b,c] Joan Anton Puig-Butillé,[i,m] Antonio Martínez,[g] Patricia Galván,[a] Yi-Hsuan Tsai,[h] Blanca González-Farré,[a,g] Aurea Mira,[n] Ana Vivancos,[k] Patricia Villagrasa,[h] Joel S. Parker,[o] Pierfranco Conte,[f,2] and Charles M. Perou[p,2]*





Prat A *et al*. eBioMedicine 2022

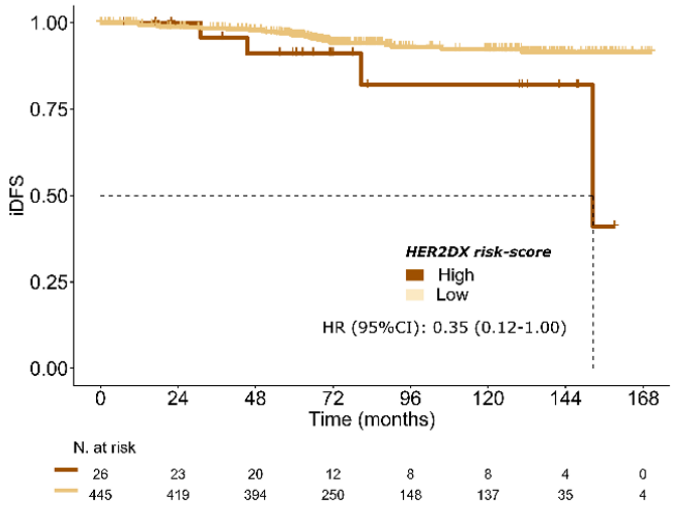
Plataformas de expresión génica-HER2+

original reports

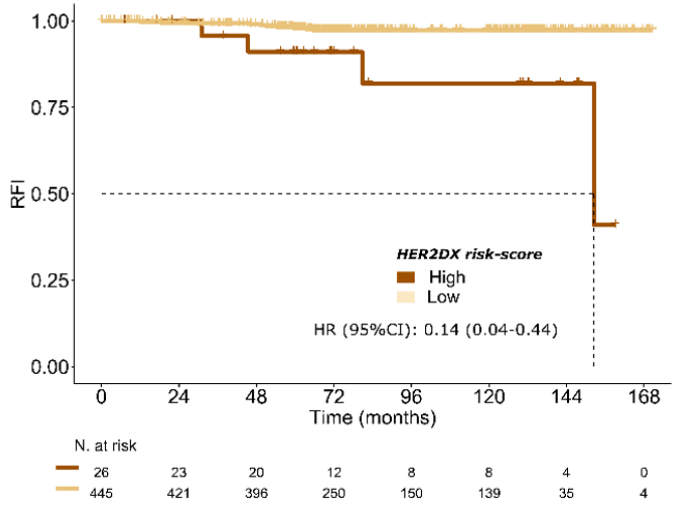
Adjuvant Trastuzumab Emtansine Versus Paclitaxel in Combination With Trastuzumab for Stage I HER2-Positive Breast Cancer (ATEMPT): A Randomized Clinical Trial

Sara M. Tolaney, MD, MPH[1,2]; Nabihah Tayob, PhD[1]; Chau Dang, MD[3]; Denise A. Yardley, MD[4]; Steven J. Isakoff, MD, PhD[5]; Vicente Valero, MD[6]; Meredith Faggen, MD[1]; Therese Mulvey, MD[5]; Ron Bose, MD, PhD[7]; Jiani Hu, MSc[1]; Douglas Weckstein, MD[1]; Antonio C. Wolff, MD[8]; Katherine Reeder-Hayes, MD, MBA, MSc[9]; Hope S. Rugo, MD[10]; Bhuvaneswari Ramaswamy, MD[11]; Dan Zuckerman, MD[12]; Lowell Hart, MD[13]; Vijayakrishna K. Gadi, MD, PhD[14]; Michael Constantine, MD[1]; Kit Cheng, MD[15]; Frederick Briccetti, MD[1]; Bryan Schneider, MD[16]; Audrey Merrill Garrett, MD[17]; Kelly Marcom, MD[18]; Kathy Albain, MD[19]; Patricia DeFusco, MD[20]; Nadine Tung, MD[2,21]; Blair Ardman, MD[22]; Rita Nanda, MD[23]; Rachel C. Jankowitz, MD[24]; Mothaffar Rimawi, MD[25]; Vandana Abramson, MD[26]; Paula R. Pohlmann, MD, PhD, MSc[27]; Catherine Van Poznak, MD[28]; Andres Forero-Torres, MD[29]; Minetta Liu, MD[30]; Kathryn Ruddy, MD[30]; Yue Zheng, MSc[1]; Shoshana M. Rosenberg, ScD, MPH[1,2]; Richard D. Gelber, PhD[1,2]; Lorenzo Trippa, PhD[1,2]; William Barry, PhD[1]; Michelle DeMeo, BS[1]; Harold Burstein, MD, PhD[1,2]; Ann Partridge, MD, MPH[1,2]; Eric P. Winer, MD[1,2]; and Ian Krop, MD, PhD[1,2]

A. iDFS in the combined population (outliers)



A. RFI in the combined population (outliers)

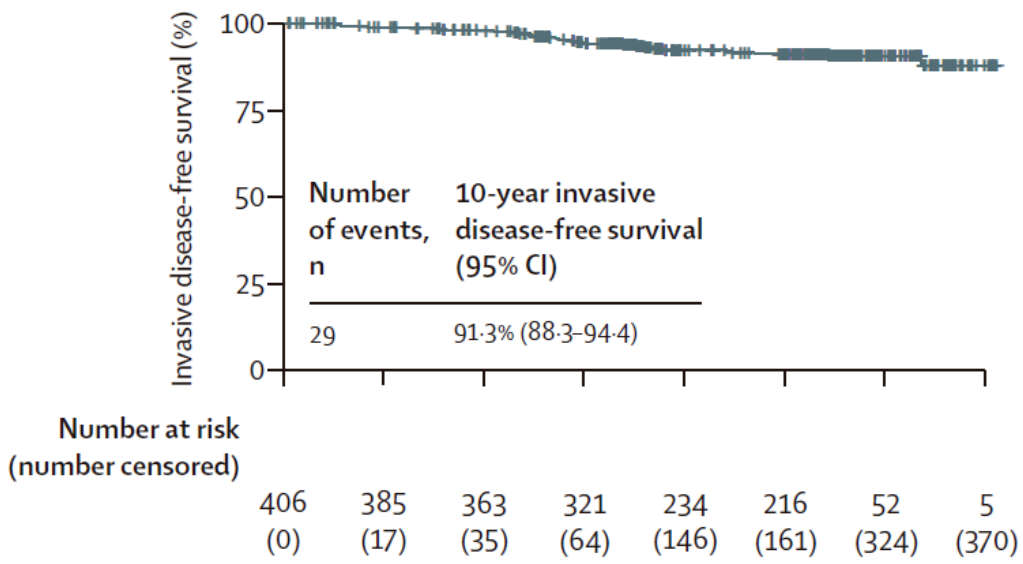


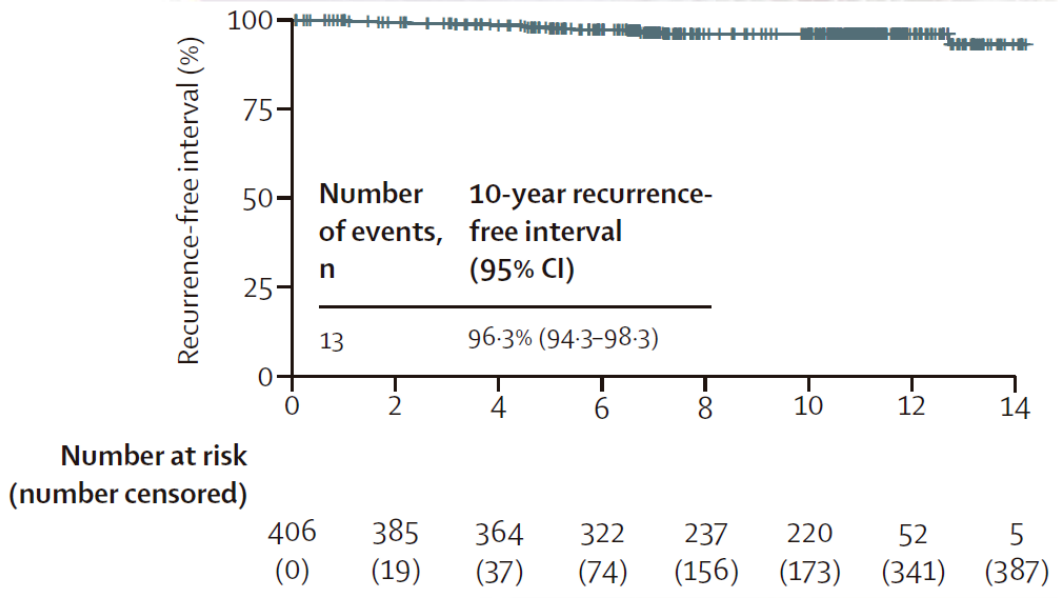
Tolaney S. SABCS 2022

Plataformas de expresión génica-HER2+

Adjuvant paclitaxel and trastuzumab for node-negative, HER2-positive breast cancer: final 10-year analysis of the open-label, single-arm, phase 2 APT trial

Sara M Tolaney, Paolo Tarantino, Noah Graham, Nabihah Tayob, Laia Parè, Guillermo Villacampa, Chau T Dang, Denise A Yardley, Beverly Moy, P Kelly Marcom, Kathy S Albain, Hope S Rugo, Matthew J Ellis, Iuliana Shapira, Antonio C Wolff, Lisa A Carey, Romualdo Barroso-Sousa, Patricia Villagrasa, Michelle DeMeo, Molly DiLullo, Jorge Gomez Tejeda Zanudo, Jakob Weiss, Nikhil Wagle, Ann H Partridge, Adrienne G Waks, Clifford A Hudis, Ian E Krop, Harold J Burstein, Aleix Prat, Eric P Winer

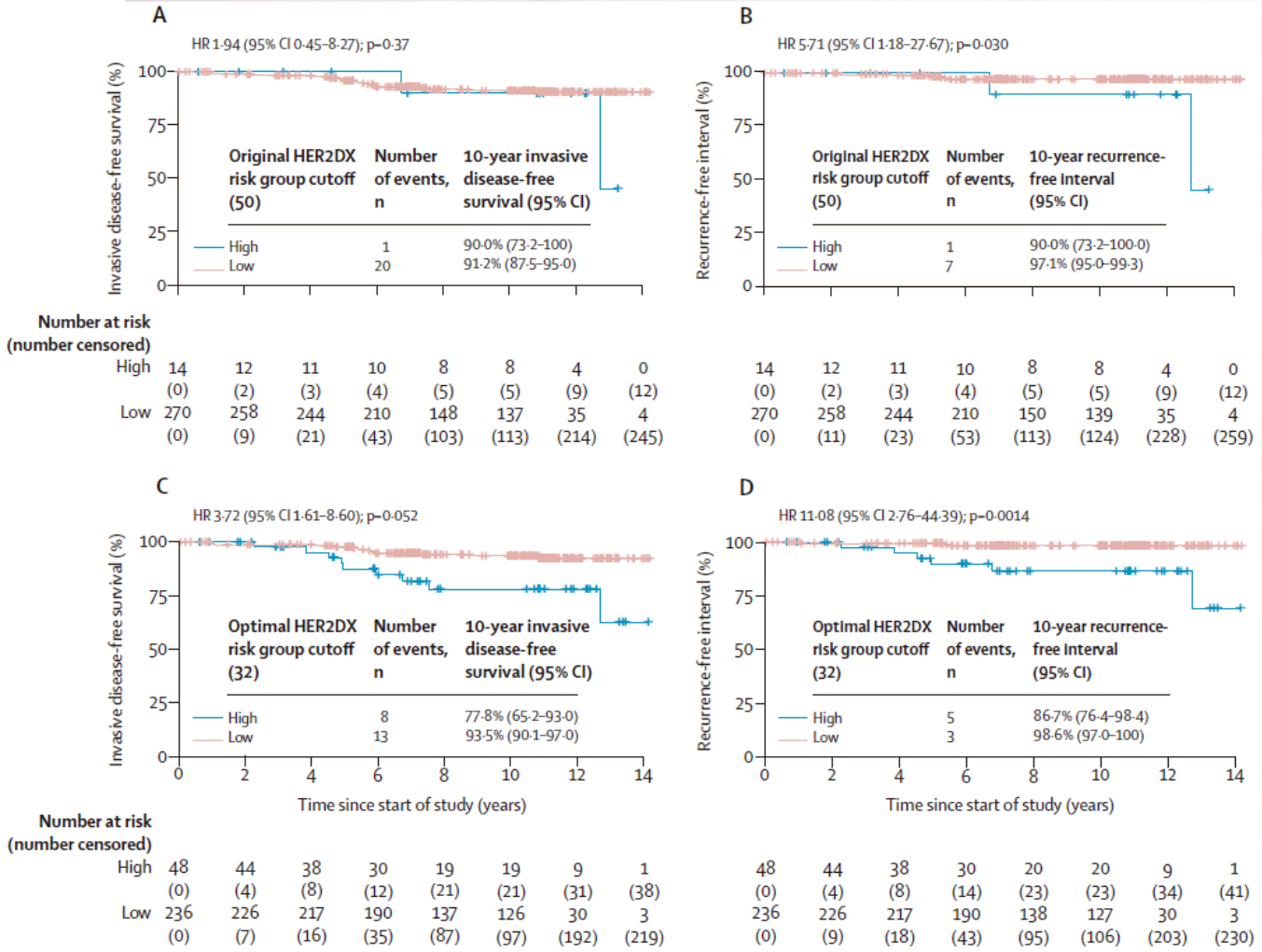




Tolaney S *et al*. Lancet Oncol 2023

Plataformas de expresión génica-HER2+

	Number of samples	Invasive disease-free survival		Recurrence-free interval	
		HR (95% CI)	p value	HR (95% CI)	p value
HER2DX risk score (10-unit increment)	284	1·24 (1·00–1·52)	0·047	1·45 (1·09–1·93)	0·011



Tolaney S *et al*. Lancet Oncol 2023

Plataformas de expresión génica-HER2+

JAMA Oncology | Brief Report

Assessment of the HER2DX Assay in Patients With *ERBB2*-Positive Breast Cancer Treated With Neoadjuvant Paclitaxel, Trastuzumab, and Pertuzumab

Adrienne G. Waks, MD; Esther R. Ogayo, BS; Laia Paré, PhD; Mercedes Marín-Aguilera, PhD; Fara Brasó-Maristany, PhD; Patricia Galván, PhD; Oleguer Castillo, MS; Olga Martínez-Sáez, MD; Ana Vivancos, PhD; Patricia Villagrasa, PhD; Guillermo Villacampa, MSc; Paolo Tarantino, MD; Neelam Desai, MD; Jennifer Guerriero, PhD; Otto Metzger, MD; Nadine M. Tung, MD; Ian E. Krop, MD, PhD; Joel S. Parker, PhD; Charles M. Perou, PhD; Aleix Prat, MD, PhD; Eric P. Winer, MD; Sara M. Tolaney, MD, MPH; Elizabeth A. Mittendorf, MD, PhD

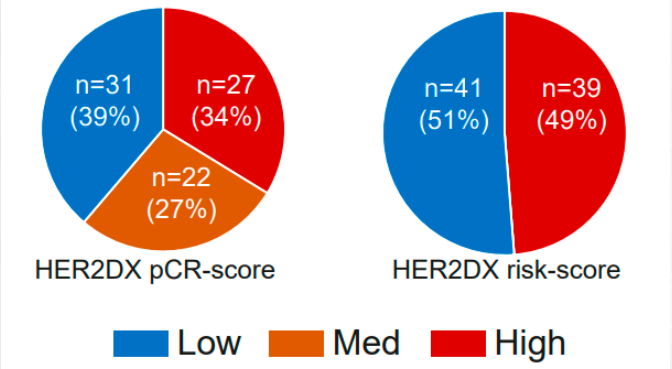


Table. Association of Pretreatment Baseline Variables With pCR in 80 Patients With *ERBB2*-Positive Early-Stage Breast Cancer Treated With Neoadjuvant THP in the DAPHNe Clinical Trial

Characteristic	No.	pCR rate, %	Univariable		Multivariable	
			OR (95% CI)	*P* value	OR (95% CI)	*P* value
Overall cohort	80	60.0				
HER2DX pCR score (continuous variable)	80	NA	1.05 (1.03-1.08)	<.001	1.03 (1.01-1.07)	.03
HER2DX pCR score groups						
Low	31	29.0	1 [Reference]	NA	NA	NA
Medium	22	63.6	4.30 (1.34-14.36)	.01	NA	NA
High	27	92.6	30.60 (1.30-156.90)	<.001	NA	NA
HER2DX *ERBB2* score (continuous variable)	80	NA	1.05 (1.02-1.08)	<.001	1.03 (1.00-1.07)	.04

Waks AG *et al*. JAMA Oncol 2023

Plataformas de expresión génica-HER2+

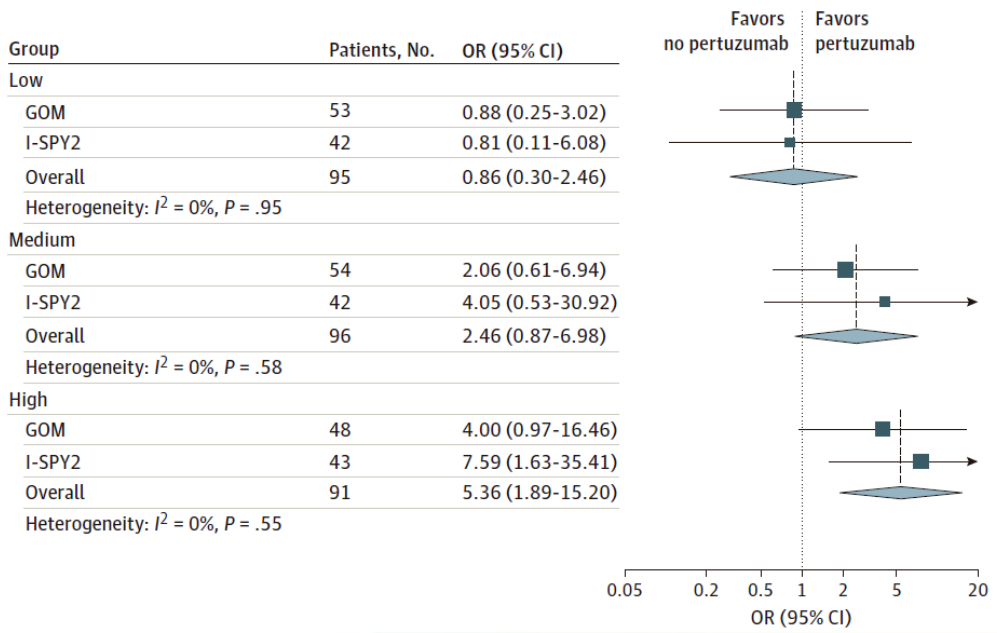
JAMA Oncology | Brief Report

Assessment of a Genomic Assay in Patients With *ERBB2*-Positive Breast Cancer Following Neoadjuvant Trastuzumab-Based Chemotherapy With or Without Pertuzumab

Coralia Bueno-Muiño, MD; Isabel Echavarría, MD; Sara López-Tarruella, MD; Marta Roche-Molina, MD; María del Monte-Millán, MD; Tatiana Massarrah, MD; Yolanda Jerez, MD; Francisco Ayala de la Peña, MD; José Ángel García-Sáenz, MD; Fernando Moreno, MD; Álvaro Rodríguez-Lescure, MD; Diego Malón-Giménez, MD; Ana Isabel Ballesteros García, MD; Mercedes Marín-Aguilera, PhD; Patricia Galván, PhD; Fara Brasó-Maristany, PhD; Adrienne G. Waks, MD; Sara M. Tolaney, MD, MPH; Elizabeth A. Mittendorf, MD, PhD; Ana Vivancos, PhD; Patricia Villagrasa, PhD; Joel. S. Parker, PhD; Charles M. Perou, PhD; Laia Paré, PhD; Guillermo Villacampa, PhD; Aleix Prat, MD, PhD; Miguel Martín, MD, PhD

Characteristic	Patients, No.	pCR rate
HER2DX pCR score (10-unit increase)	155	NA
HER2DX pCR score groups		
Low	53	28.3%
Medium	54	70.4%
High	48	75.0%
Clinical tumor stage		
cT1-cT2	113	60.2%
cT3-cT4	42	50.0%
Clinical nodal stage		
cN0	56	69.6%
cN1-cN3	99	50.5%
PAM50		
ERBB2 enriched	80	68.8%
Non-*ERBB2* enriched	75	45.3%
Treatment		
TCH	67	52.2%
TCHP	88	61.4%

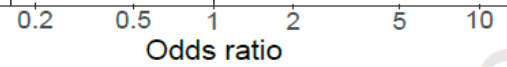
Figure. Association of HER2DX Pathologic Complete Response (pCR) Groups With Response to Pertuzumab in a Combined Patient-Level Analysis (N = 282)



Bueno-Muiño C *et al*. JAMA Oncol 2023

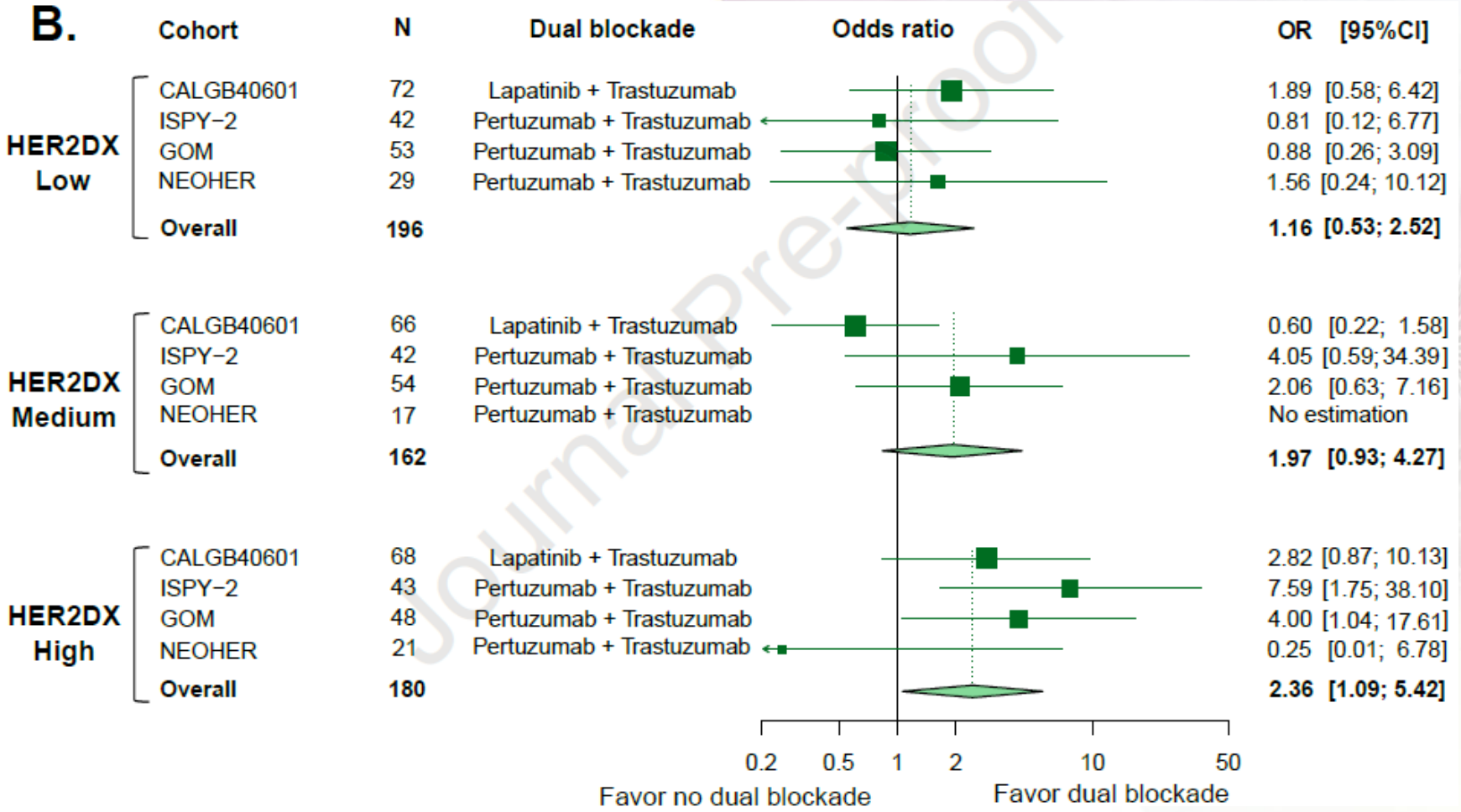
Plataformas de expresión génica-HER2+

Variable		N	pCR rate	OR (95%CI)	p-value	OR (95%CI)	p-value
HER2DX pCR score (10-units increment)		765	-	1.46 (1.37, 1.57)	<0.001	1.59 (1.43, 1.77)	**<0.001**
HER2DX pCR score groups	Low	257	20.2%	Reference		Reference*	
	Med	246	55.3%	4.87 (3.30, 7.28)	<0.001	4.89 (3.12, 7.75)*	**<0.001***
	High	262	74.0%	11.25 (7.51, 17.10)	<0.001	13.96 (7.64, 26.08)*	**<0.001***
Age (10-years increment)		631	-	0.85 (0.74, 0.98)	0.023	0.89 (0.76, 1.03)	0.13
Clinical tumor stage	T1	132	47.7%	Reference		Reference	
	T2-T3-T4	491	50.9%	1.14 (0.77, 1.67)	0.515	1.06 (0.68, 1.67)	0.79
Clinical nodal stage	N0	231	50.6%	Reference		Reference	
	N1-N2-N3	201	48.8%	0.93 (0.63, 1.35)	0.695	0.85 (0.59, 1.22)	0.39
Hormone receptor	Negative	277	66.1%	Reference		Reference	
	Positive	486	40.7%	0.35 (0.26, 0.48)	<0.001	0.93 (0.57, 1.52)	0.78
PAM50	Basal	82	52.4%	Reference		Reference	
	Her2	316	66.1%	1.77 (1.08, 2.90)	0.023	3.33 (1.85, 6.07)	**<0.001**
	LumA	153	28.1%	0.35 (0.20, 0.62)	<0.001	2.01 (0.95, 4.27)	0.07
	LumB	131	35.1%	0.49 (0.28, 0.86)	0.013	2.30 (1.10, 4.87)	**0.03**
	Normal	78	50.0%	0.91 (0.49, 1.69)	0.758	3.51 (1.68, 7.43)	**<0.001**
Systematic therapy	TH	115	48.7%	Reference		Reference	
	AC−TDM1−P	52	57.7%	1.44 (0.74, 2.80)	0.282	1.50 (0.72, 3.19)	0.28
	AC−TH	66	33.3%	0.53 (0.28, 0.98)	0.046	0.62 (0.30, 1.26)	0.19
	AC−THP	61	55.7%	1.33 (0.71, 2.49)	0.374	2.15 (1.02, 4.60)	**0.04**
	HL	84	29.8%	0.45 (0.24, 0.80)	0.008	0.26 (0.12, 0.55)	**<0.001**
	TCH	69	53.6%	1.22 (0.67, 2.22)	0.518	1.85 (0.88, 3.91)	0.10
	TCHP	89	60.7%	1.63 (0.93, 2.86)	0.090	3.85 (1.87, 8.10)	**<0.001**
	THL	103	54.4%	1.26 (0.74, 2.14)	0.403	1.27 (0.70, 2.29)	0.43
	THP	126	54.0%	1.24 (0.74, 2.05)	0.414	1.80 (0.95, 3.43)	0.07



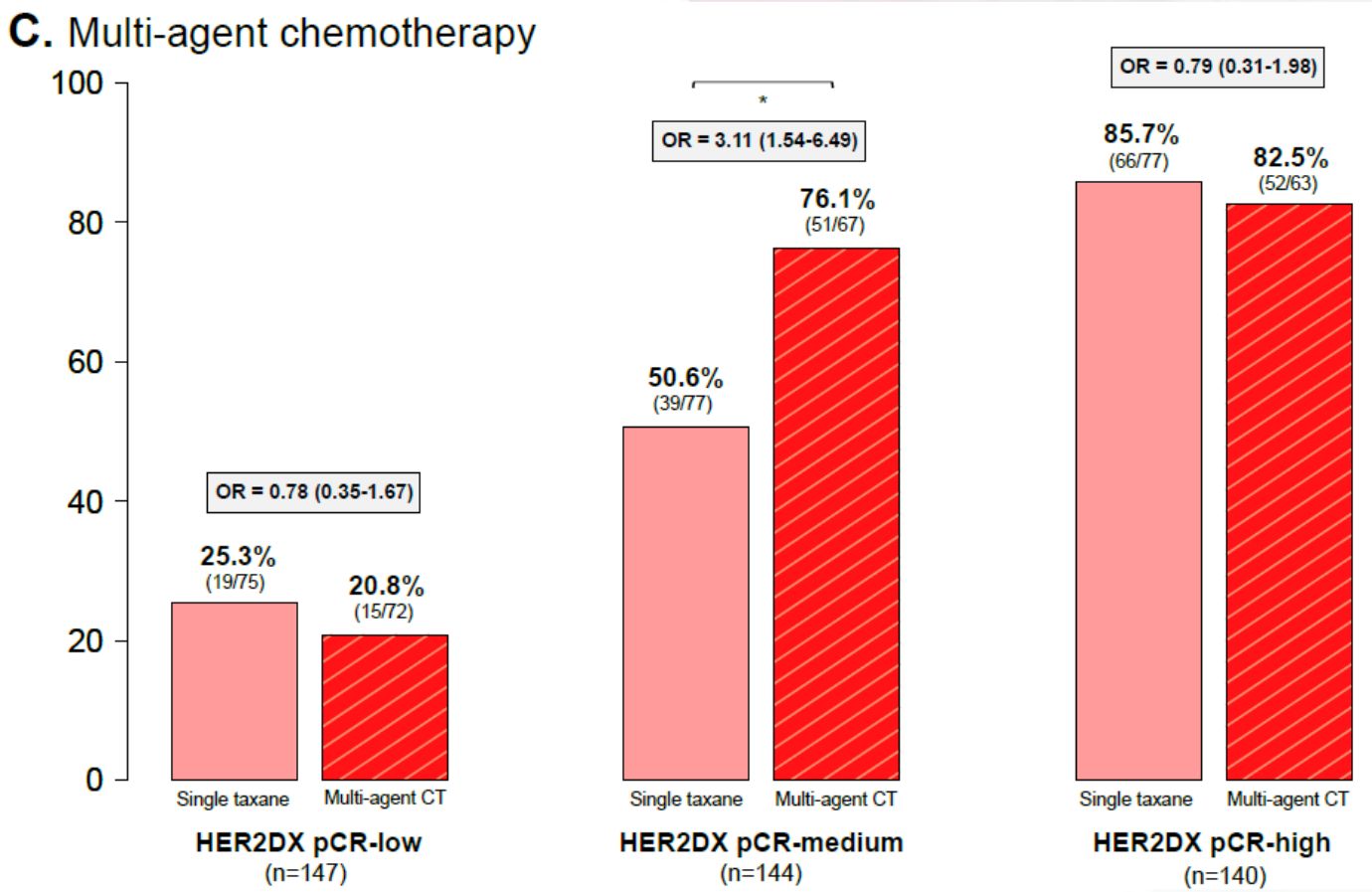
Villacampa G *et al*. Annals Oncol 2023

Plataformas de expresión génica-HER2+



Villacampa G *et al*. Annals Oncol 2023

Plataformas de expresión génica-HER2+

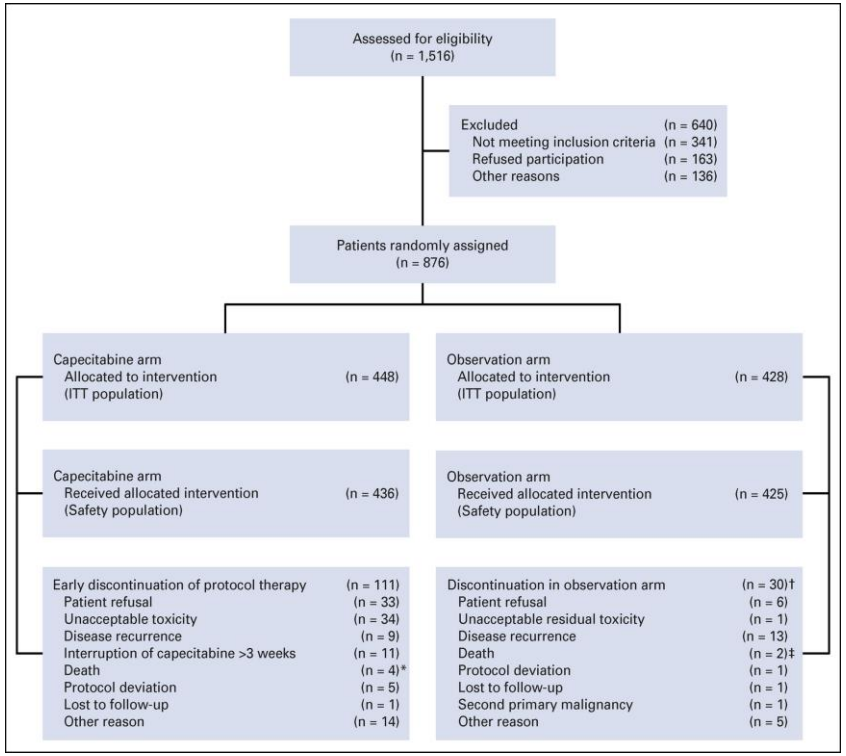


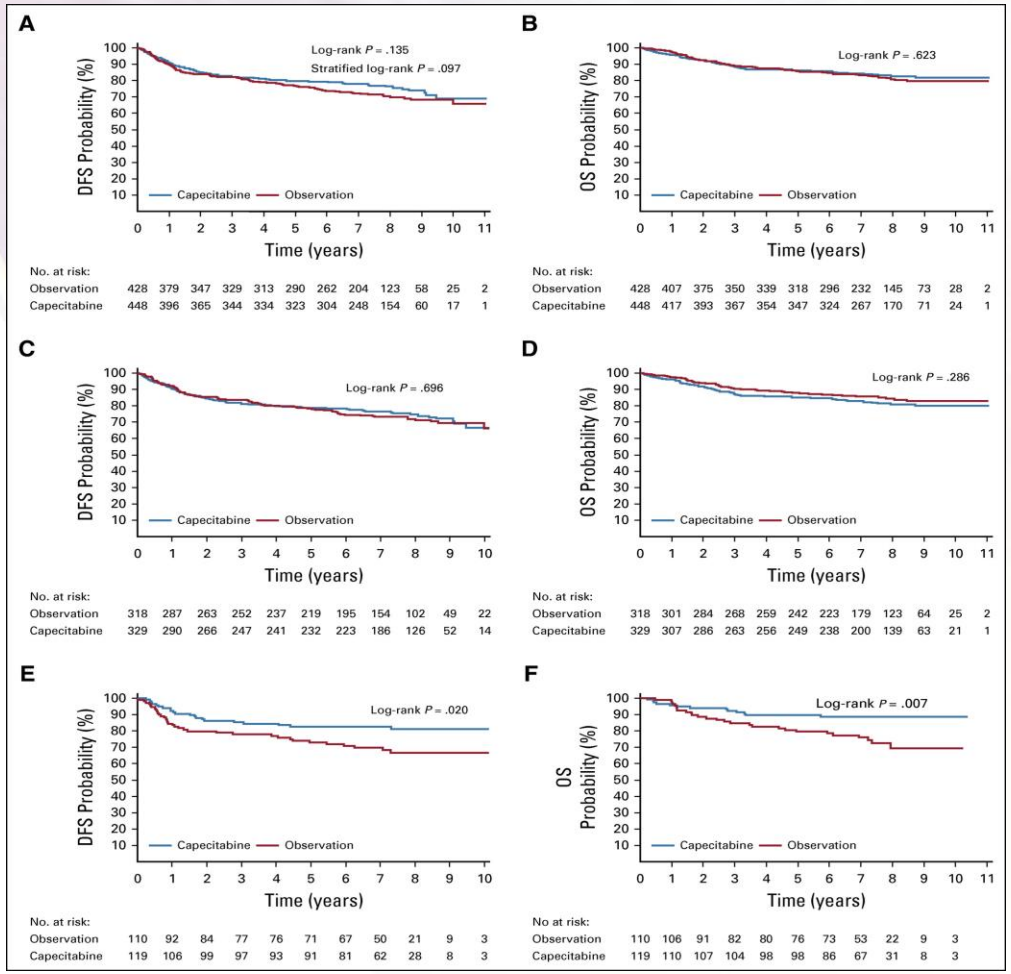
Villacampa G *et al*. Annals Oncol 2023

Plataformas de expresión génica-TNBC

Triple-Negative PAM50 Non-Basal Breast Cancer Subtype Predicts Benefit from Extended Adjuvant Capecitabine

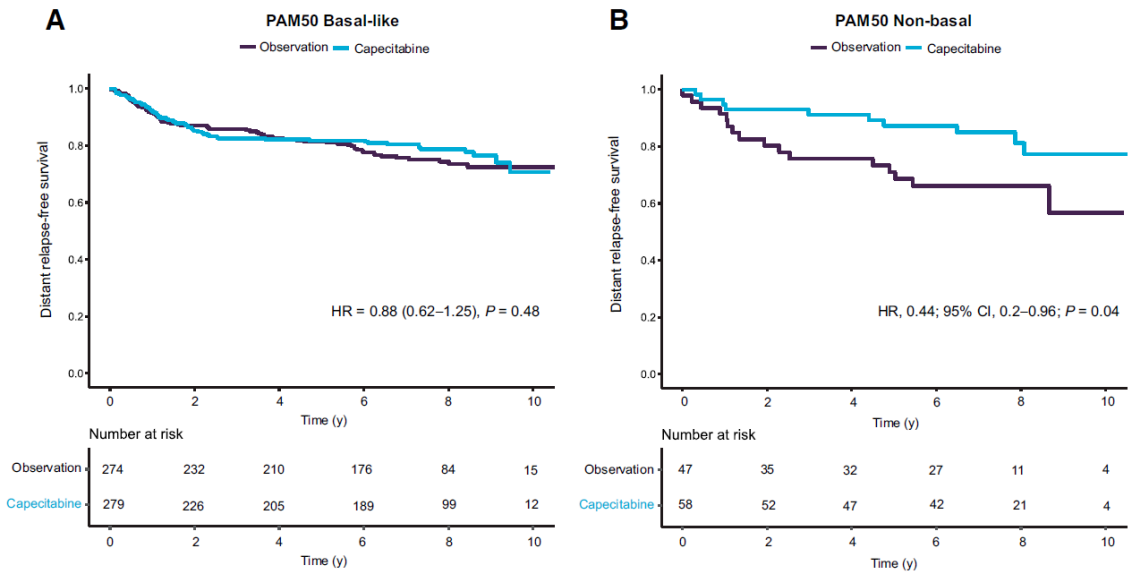
Karama Asleh[1,2], Ana Lluch[3,4,5], Angela Goytain[1], Carlos Barrios[6,7], Xue Q. Wang[1], Laura Torrecillas[7,8], Dongxia Gao[1], Manuel Ruiz-Borrego[3,9], Samuel Leung[1], José Bines[7,10], Ángel Guerrero-Zotano[3,11], Jose Ángel García-Sáenz[3,12], Juan Miguel Cejalvo[3,4,5], Jesus Herranz[3], Roberto Torres[7,13], Juan de la Haba-Rodriguez[3,14,15], Francisco Ayala[3,16], Henry Gómez[7,17,18], Federico Rojo[3,19,20], Torsten O. Nielsen[1], and Miguel Martin[3,20,21]

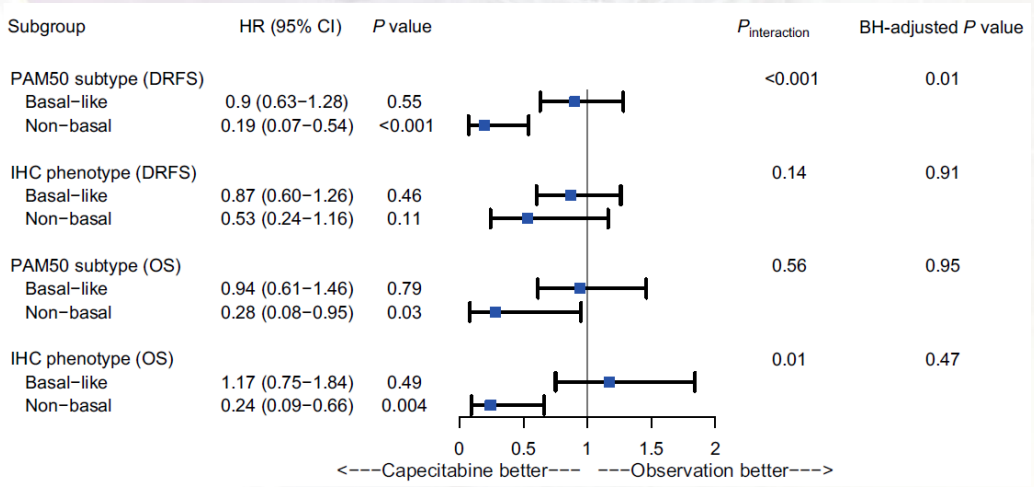




Asleh K *et al*. Clin Cancer Res 2023; Lluch A *et al*. JCO 2020

Plataformas de expresión génica-TNBC





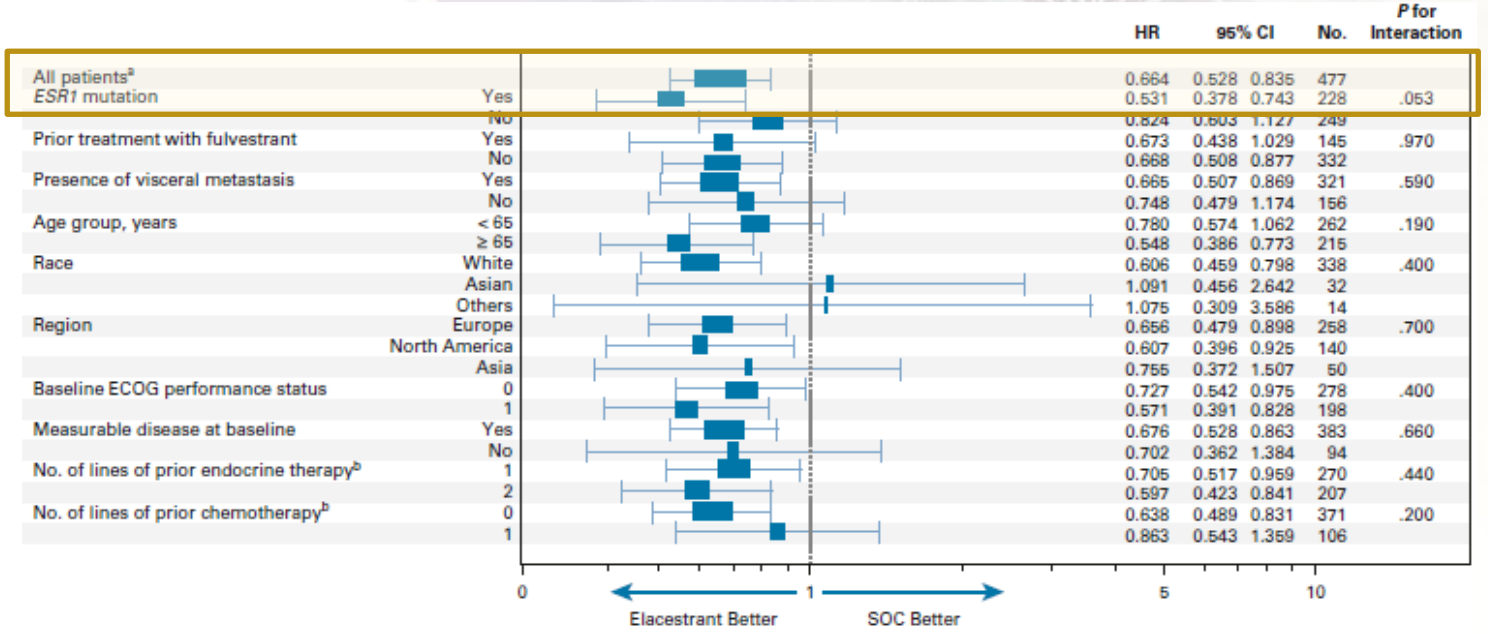
Asleh K *et al*. Clin Cancer Res 2023

ESR1

ESR1

Elacestrant (oral selective estrogen receptor degrader) Versus Standard Endocrine Therapy for Estrogen Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Advanced Breast Cancer: Results From the Randomized Phase III EMERALD Trial

Francois-Clement Bidard, MD[1,2]; Virginia G. Kaklamani, MD[3]; Patrick Neven, MD[4]; Guillermo Streich, MD[5]; Alberto J. Montero, MD[6]; Frédéric Forget, MD[7]; Marie-Ange Mouret-Reynier, MD[8]; Joo Hyuk Sohn, MD[9]; Donatienne Taylor, MD[10]; Kathleen K. Harnden, MD[11]; Hung Khong, MD[12]; Judit Kocsis, MD[13]; Florence Dalenc, MD[14]; Patrick M. Dillon, MD[15]; Sunil Babu, MD[16]; Simon Waters, MD[17]; Ines Deleu, MD[18]; José A. García Sáenz, MD[19]; Emilio Bria, MD[20]; Marina Cazzaniga, MD[21]; Janice Lu, MD[22]; Philippe Aftimos, MD[23]; Javier Cortés, MD[24,25,26,27]; Shubin Liu, MS[28]; Giulia Tonini, PhD[29]; Dirk Laurent, MD[30]; Nassir Habboubi, MD[31]; Maureen G. Conlan, MD[32]; and Aditya Bardia, MD[33]



Bidard FC *et al*. JCO 2022

ESR1

Testing for *ESR1* Mutations to Guide Therapy for Hormone Receptor–Positive, Human Epidermal Growth Factor Receptor 2–Negative Metastatic Breast Cancer: ASCO Guideline Rapid Recommendation Update

Harold J. Burstein, MD, PhD[1]; Angela DeMichele, MD[2]; Mark R. Somerfield, PhD[3]; and N. Lynn Henry, MD, PhD[4]; for the Biomarker Testing and Endocrine and Targeted Therapy in Metastatic Breast Cancer Expert Panels

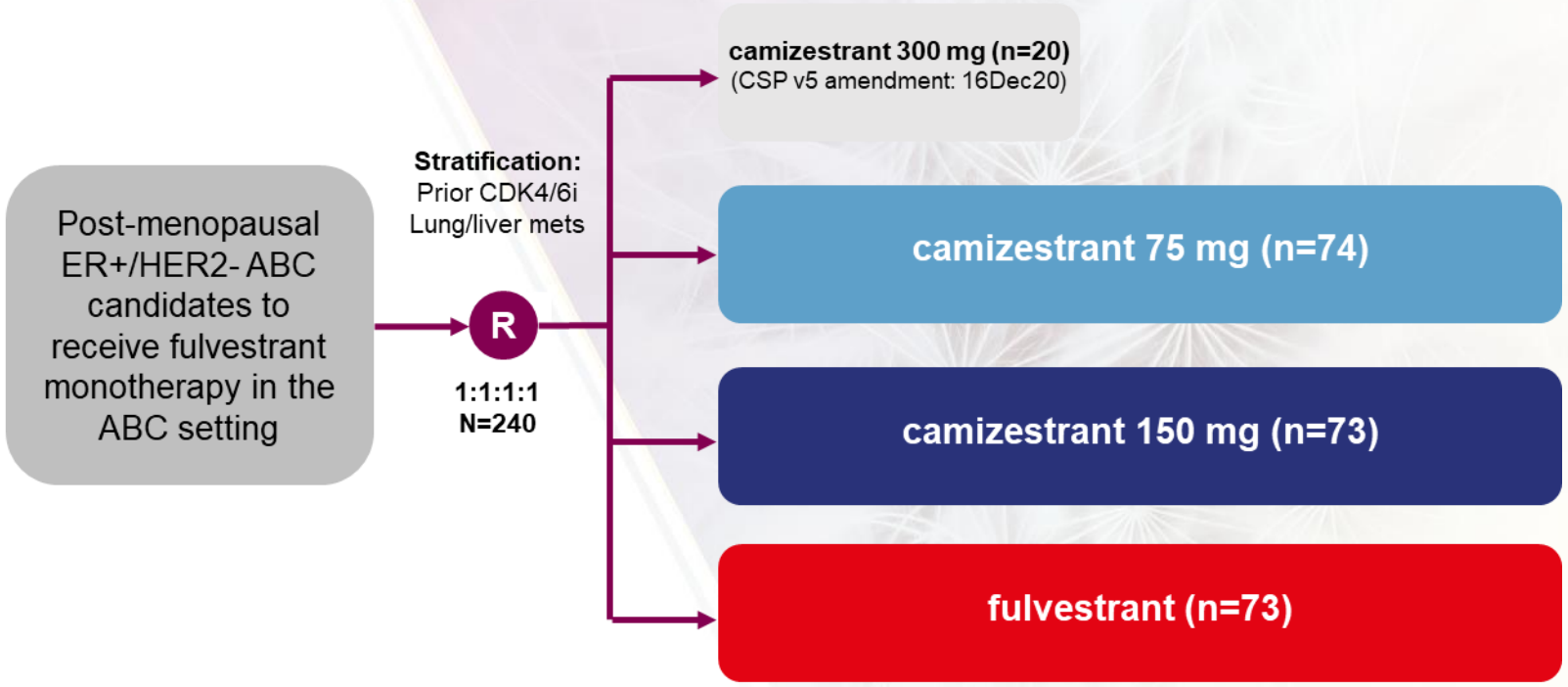
Se recomienda testeo rutinario de mutaciones en **ESR1** a la recurrencia o progression a ET, preferentemente en **ctDNA**

Burstein H *et al*. JCO 2023

SERENA-2 study overview

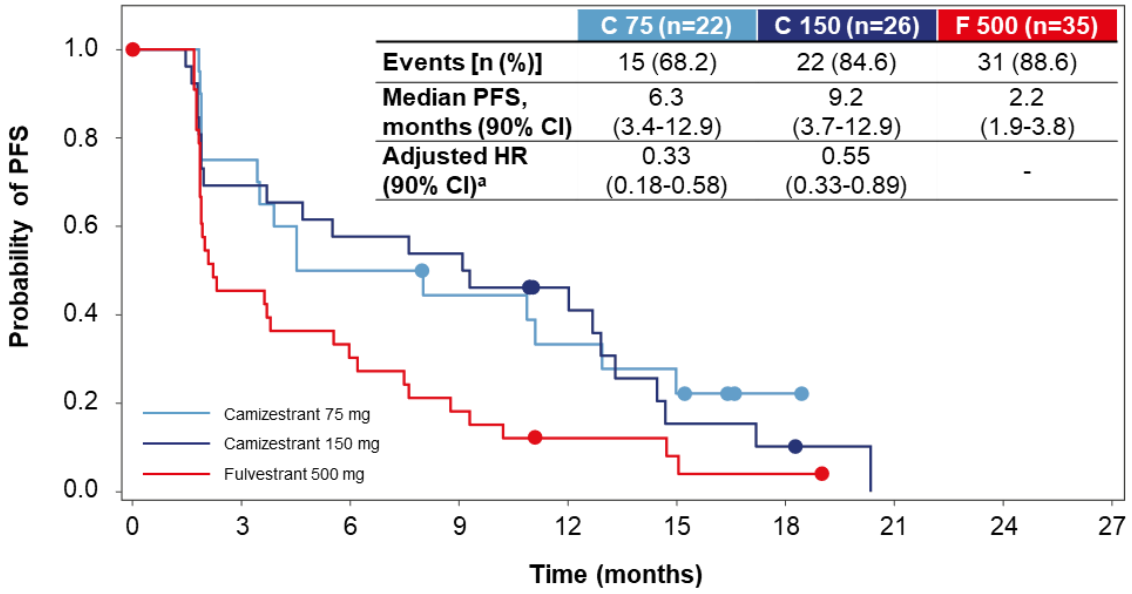
Key inclusion/exclusion criteria:

- Recurrence or progression on at least one line of ET
- No prior fulvestrant or oral SERD in ABC
- No more than one line of ET in ABC setting
- No more than one line CT in ABC setting
- Measurable and non-measurable disease



PFS in patients by detectable *ESR1*m

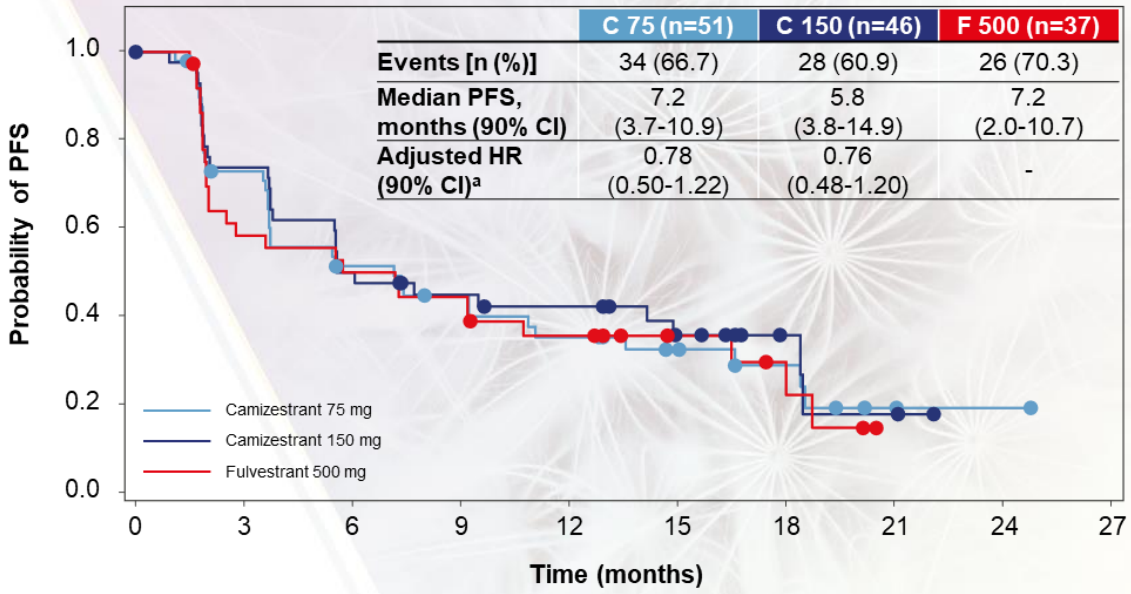
*ESR1*m detectable at baseline



	C 75 (n=22)	C 150 (n=26)	F 500 (n=35)
Events [n (%)]	15 (68.2)	22 (84.6)	31 (88.6)
Median PFS, months (90% CI)	6.3 (3.4-12.9)	9.2 (3.7-12.9)	2.2 (1.9-3.8)
Adjusted HR (90% CI)[a]	0.33 (0.18-0.58)	0.55 (0.33-0.89)	-

C 75	22	15	10	8	6	4	1	0
C 150	26	18	15	14	9	3	2	0
F	35	15	10	6	3	2	1	0

*ESR1*m not detectable at baseline



	C 75 (n=51)	C 150 (n=46)	F 500 (n=37)
Events [n (%)]	34 (66.7)	28 (60.9)	26 (70.3)
Median PFS, months (90% CI)	7.2 (3.7-10.9)	5.8 (3.8-14.9)	7.2 (2.0-10.7)
Adjusted HR (90% CI)[a]	0.78 (0.50-1.22)	0.76 (0.48-1.20)	-

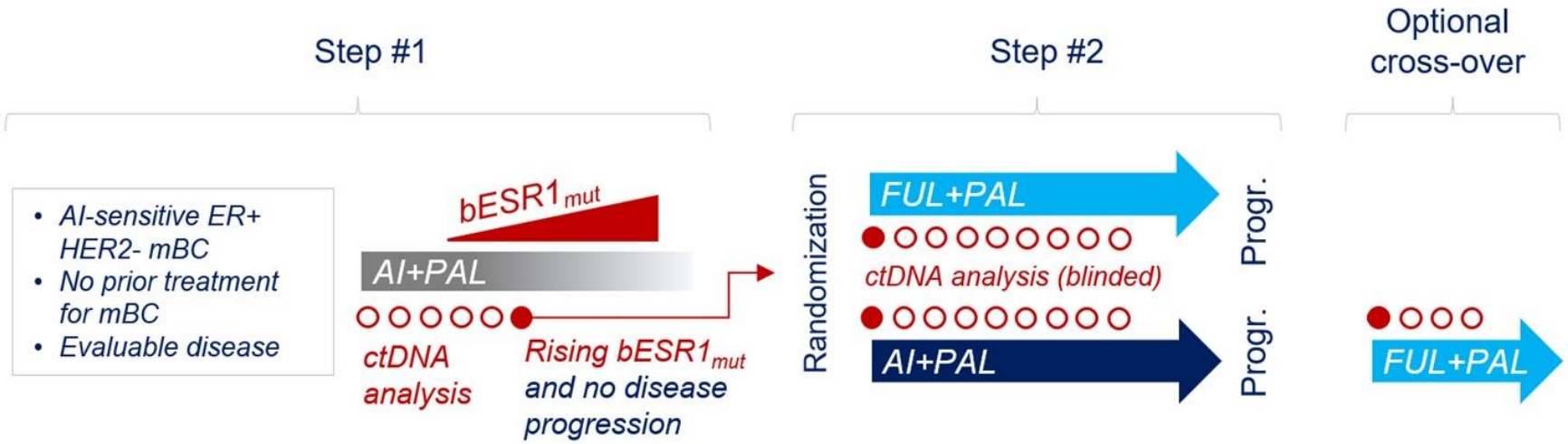
C 75	51	34	23	19	15	10	6	2	1	0
C 150	46	31	21	17	15	9	4	2	0	
F	37	21	18	16	11	6	4	1	0	

Oliveira M. SABCS 2022

ESR1

PADA-1

- Strategy: **targeting rising *bESR1$_{mut}$* when they become detectable** under AI+Palbociclib (PAL) [1]



Bidard FC. ASCO 2023

Updated PFS results – primary endpoint

N= 1,017 pts enrolled in step #1

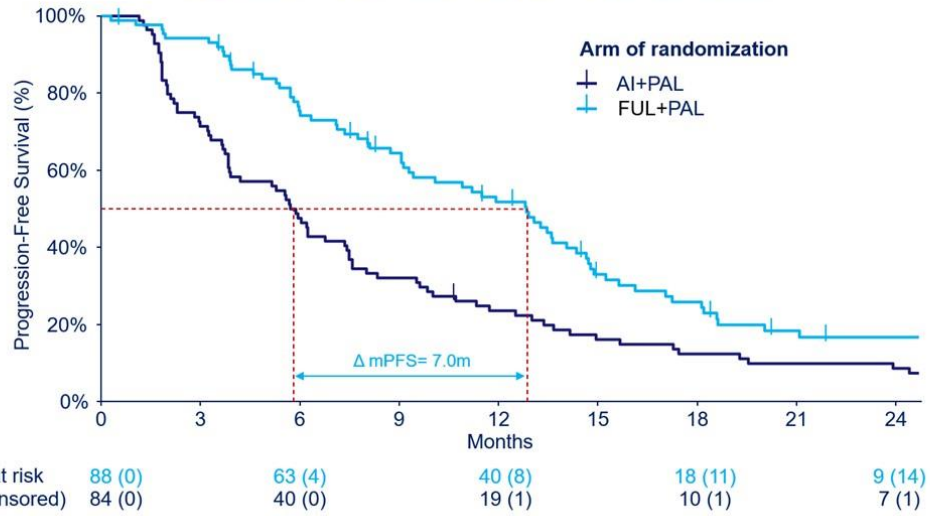
N= 283 pts with a rising *bESR1*$_{mut}$
while the study was ongoing

N= 172 pts randomized
- N= 88 pts allocated to FUL+PAL
- N= 84 pts allocated to AI+PAL

Data cut-off: June 21, 2022

Median FU from randomization: 28.2 months; N= 152 PFS events (89% maturity)

Progression-Free Survival, from randomization



FUL+PAL mPFS: 12.8 months, 95%CI [9.3;14.7]

AI+PAL mPFS: 5.8 months, 95%CI [3.9;7.5]

PFS HR= 0.54 [0.38;0.75]

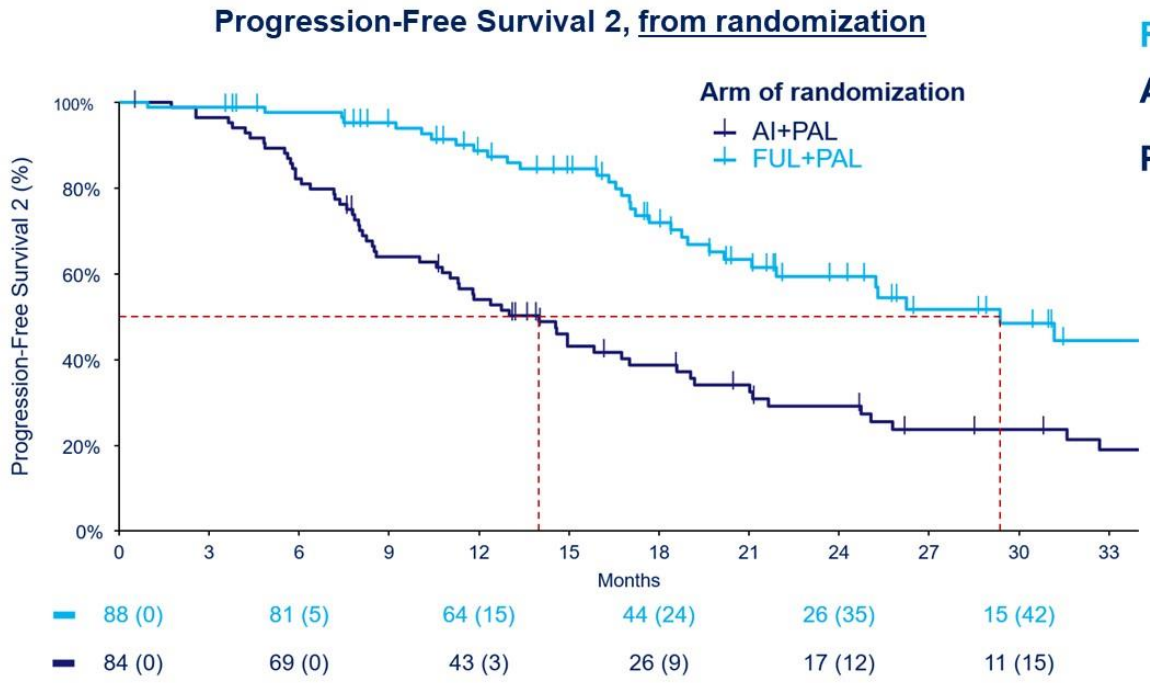
Optional cross-over (N=49 patients)

mPFS: 3.5 months, 95%CI [2.4;5.4]

[2] Bidar

PFS2 results – secondary endpoint

Data cut-off: June 21, 2022 N= 93 PFS2 events (54% maturity)



FUL+PAL mPFS2: 29.4 months, 95%CI [21.9;NR]

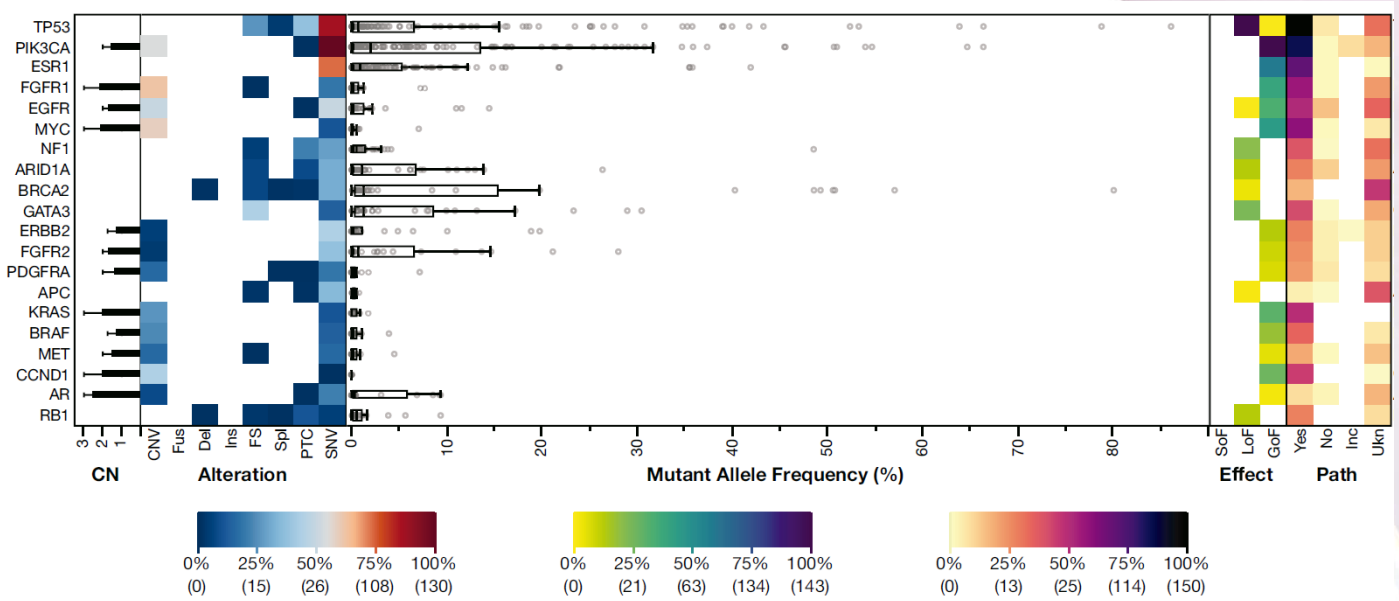
AI+PAL mPFS2: 14.0 months, 95%CI [11.0;18.6]

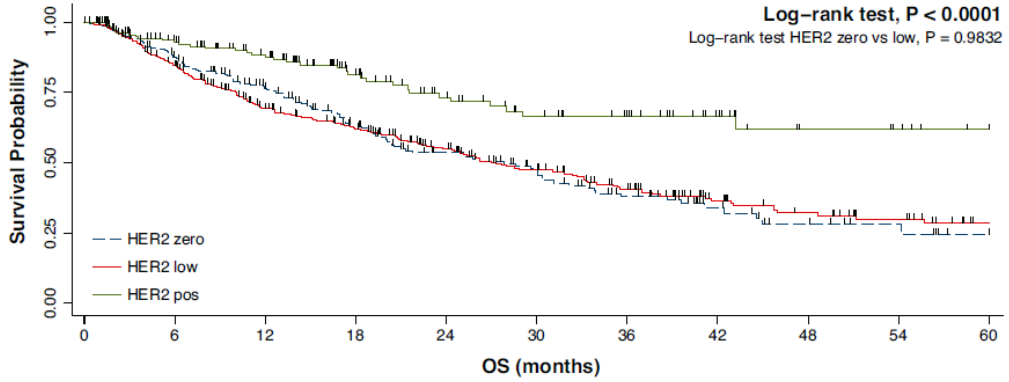
PFS2 HR= 0.37 [0.24;0.56]

Bidard FC. ASCO 2023

HER2-low

HER2-low





Number at risk											
HER2 zero	210	175	138	98	74	54	37	20	12	8	3
HER2 low	340	271	196	163	122	94	69	46	35	25	12
HER2 pos	166	133	110	66	47	37	28	17	10	7	4

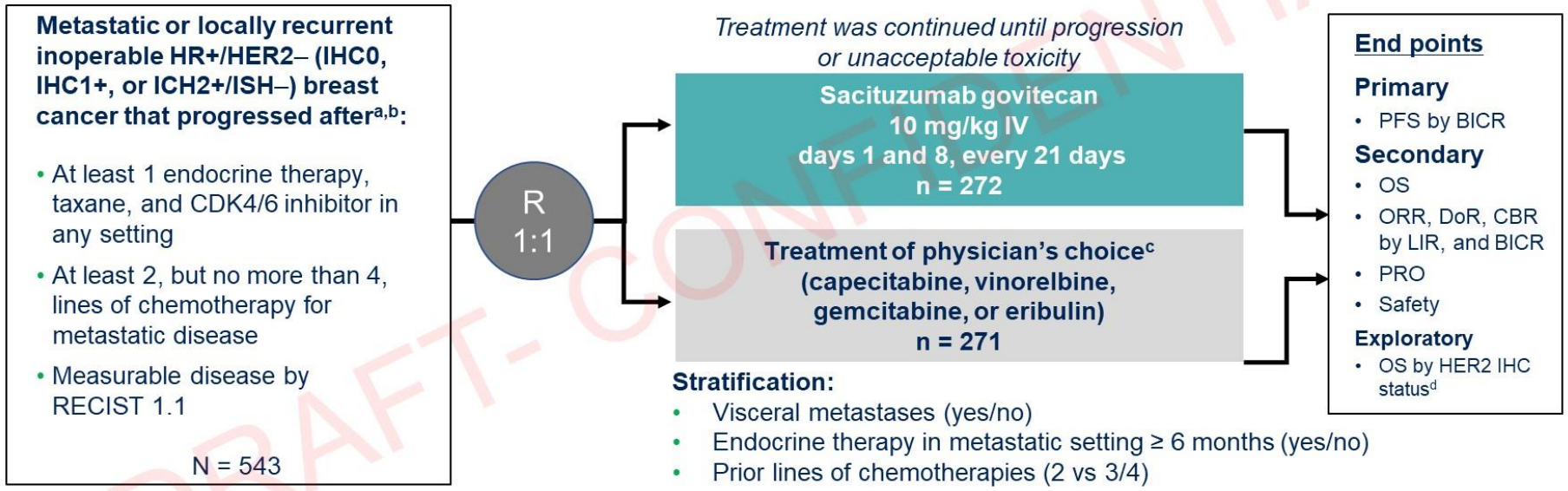
Mayor frecuencia de mutaciones en *PIK3CA* en HER2-low respecto a HER2-zero

No diferencias en *ERBB2*

No diferencias en supervivencia en HER2-low respecto a HER2-zero

Hensing WL *et al*. Clin Can Res 2023

TROPiCS-02: A Phase 3 Study of SG in Patients with HR+/HER2– mBC[1]



Overall Survival by HER2 IHC Status

HER2-low (IHC 1+, IHC2+/ISH-)[a]

	SG (n = 149)	TPC (n = 134)
Median OS,[b] mo (95% CI)	15.4 (13.5-19.1)	11.5 (10.1-12.9)
Unstratified HR (95% CI)	0.75 (0.57–0.97)	

No. of patients at risk (events)

SG	149 (0)	137 (11)	120 (27)	108 (39)	91 (56)	77 (70)	67 (80)	46 (94)	35 (100)	22 (106)	14 (109)	9 (111)	1 (112)	0 (113)
TPC	134 (0)	126 (5)	102 (27)	82 (47)	62 (67)	43 (85)	36 (92)	31 (96)	22 (101)	13 (102)	9 (103)	3 (106)	0 (106)	0 (106)

HER2 IHC0[a]

	SG (n = 101)	TPC (n = 116)
Median OS,[b] mo (95% CI)	13.6 (12.1-16.0)	10.8 (9.2-14.2)
Unstratified HR (95% CI)	0.85 (0.63–1.14)	

No. of patients at risk (events)

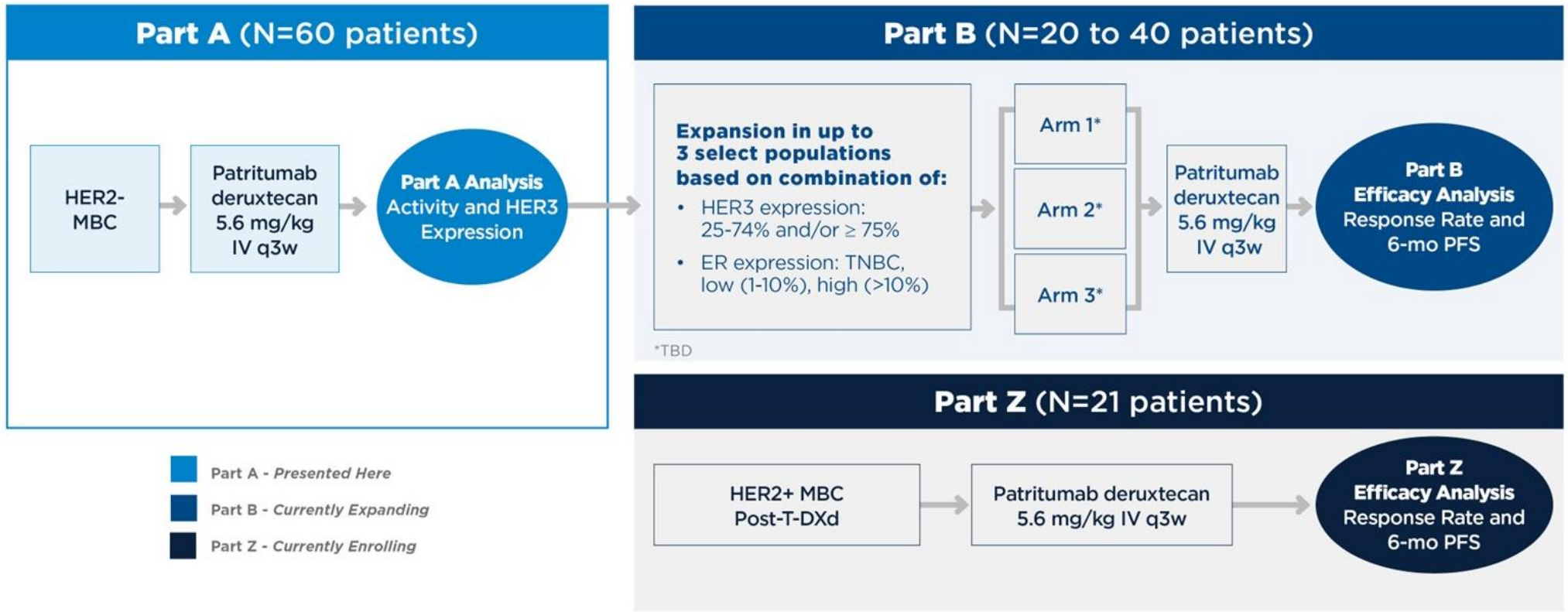
SG	101 (0)	94 (6)	83 (16)	76 (23)	60 (39)	45 (54)	34 (65)	22 (72)	15 (77)	10 (79)	4 (81)	4 (81)	0 (82)	0 (82)
TPC	116 (0)	107 (8)	82 (33)	71 (43)	52 (62)	44 (69)	38 (75)	29 (83)	20 (90)	12 (95)	5 (99)	4 (99)	1 (99)	0 (99)

SG consistently improved OS vs TPC in the HER2 low (IHC 1+, IHC2+/ISH-) and the HER2 IHC0 groups

Tolaney S. ASCO 2023

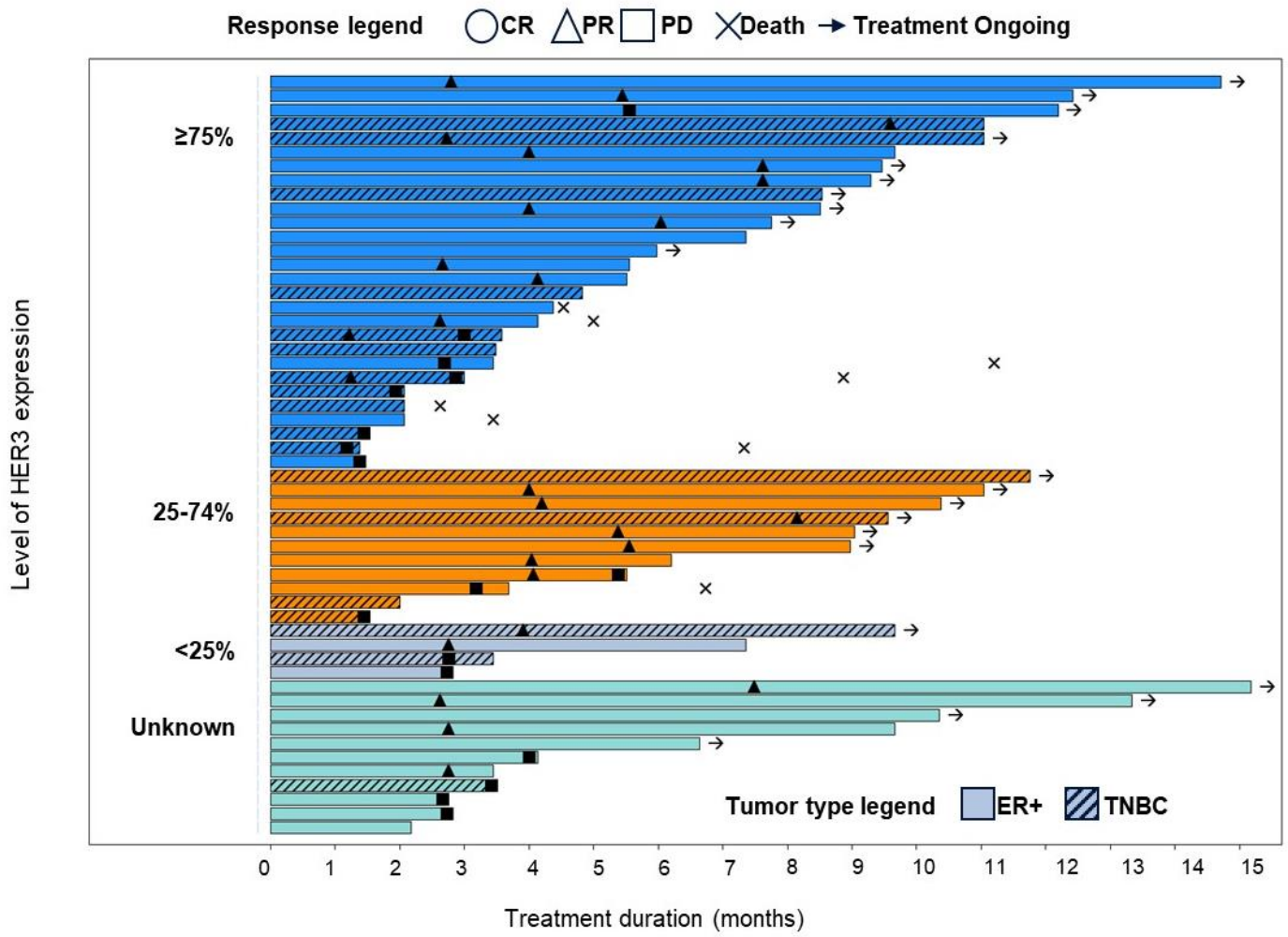
HER3

HER3



Hamilton E. ASCO 2023

HER3



Hamilton E. ASCO 2023

HER3

	Membrane HER3 ≥75% (N=30)	Membrane HER3 25%- 74% (N=13)	Membrane HER3 <25% (N=4)	Unknown Membrane HER3 Expression* (N=13)	Total (N=60) N (%)
Best Overall Response, n (%)					
Complete response (CR)	0	0	0	0	0
Partial response (PR)	**10 (33.3)**	**6 (46.2)**	**2 (50.0)**	**3 (23.1)**	**21 (35.0)**
Stable disease (SD)	13 (43.3)	4 (30.8)	1 (25.0)	8 (61.5)	26 (43.3)
Progressive disease (PD)	5 (16.7)	1 (7.7)	1 (25.0)	0	7 (11.7)
Missing/no post baseline	2 (6.7)	2 (15.4)	0	2 (15.4)	6 (10.0)
ORR, n (%)	**10 (33.3)**	**6 (46.2)**	**2 (50.0)**	**3 (23.1)**	**21 (35.0)**
95% CI	(17.3, 52.8)	(19.2, 74.9)	(6.8, 93.2)	(5.0, 53.8)	(23.1, 48.4)
CBR, n (%)**	**12 (40.0)**	**7 (53.8)**	**2 (50.0)**	**5 (38.5)**	**26 (43.3)**
95% CI	(22.7, 59.4)	(25.1, 80.8)	(6.8, 93.2)	(13.9, 68.4)	(30.6, 56.8)
DoR ≥6 months, n (%)†	4 (40.0)	2 (33.3)	2 (100)	2 (66.7)	10 (47.6)

Hamilton E. ASCO 2023

TROP-2

TROP-2

Figure 1. TROPiCS-02: A phase 3 study of SG in HR+/HER2– locally recurrent inoperable or metastatic breast cancer[a]

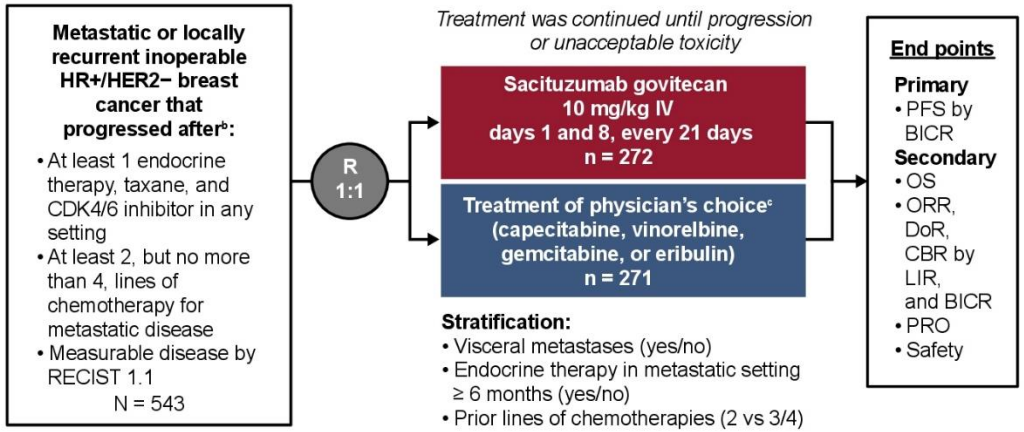
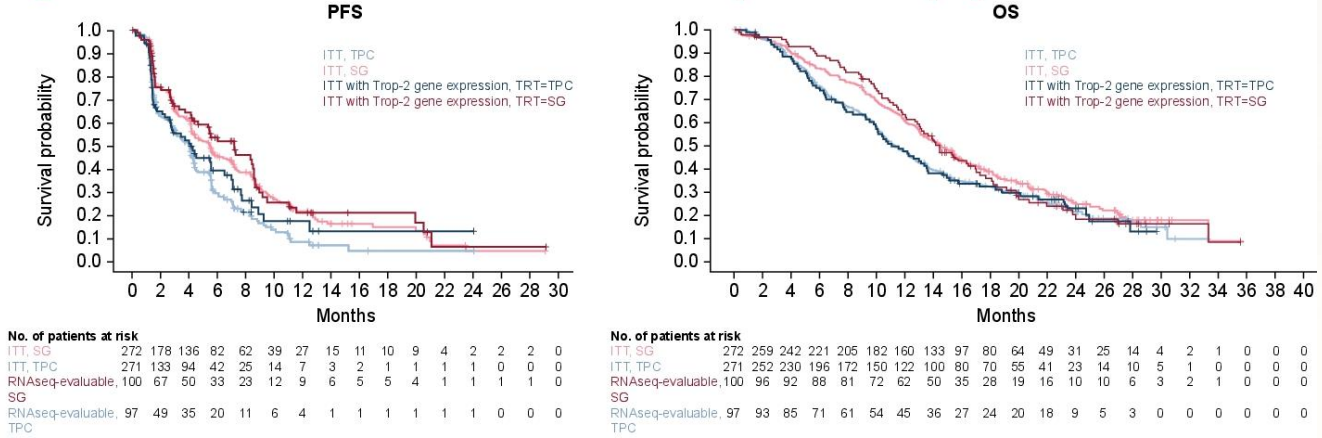


Figure 2. PFS and OS in the ITT and RNAseq-evaluable populations



ITT, intent-to-treat; OS, overall survival; PFS, progression-free survival; SG, sacituzumab govitecan; TPC, treatment of physician's choice.

Bardia A *et al*. ASCO 2023

ctDNA

ctDNA: MRD

N=1250
- HR+/HER2- breast cancer
- no pCR after NACT
- CPS-EG score ≥3 or ≥2 with ypN+

Primary Endpoint: iDFS

Stratification factors
- Nodal status: ypN 0-1 vs ypN2-3
- Age: ≤50 vs >50 yrs
- Ki-67: >15% vs ≤ 15%
- Region: Asian vs non Asian
- CPS-EG Score: ≥3 vs 2 and ypN+

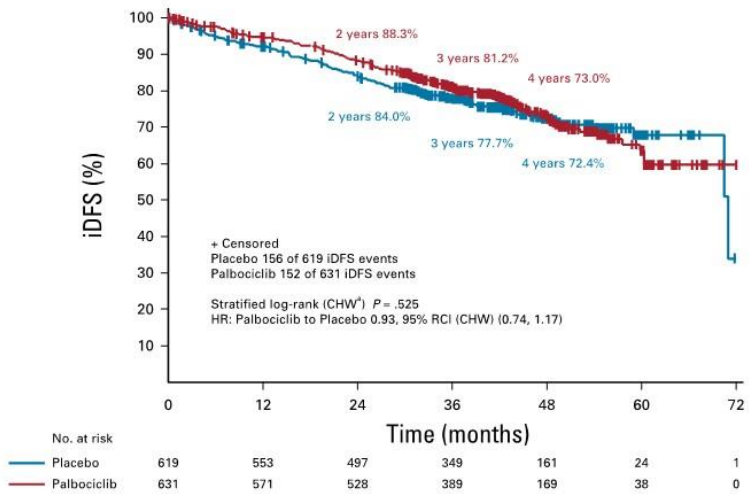
PENELOPE^B

Neoadjuvant Chemotherapy → **Surgery +/- Radiotherapy** → **R 1:1**

- **Palbociclib** 1 year
- **Placebo**

All patients received concomitantly endocrine therapy according to local standards.

Primary endpoint



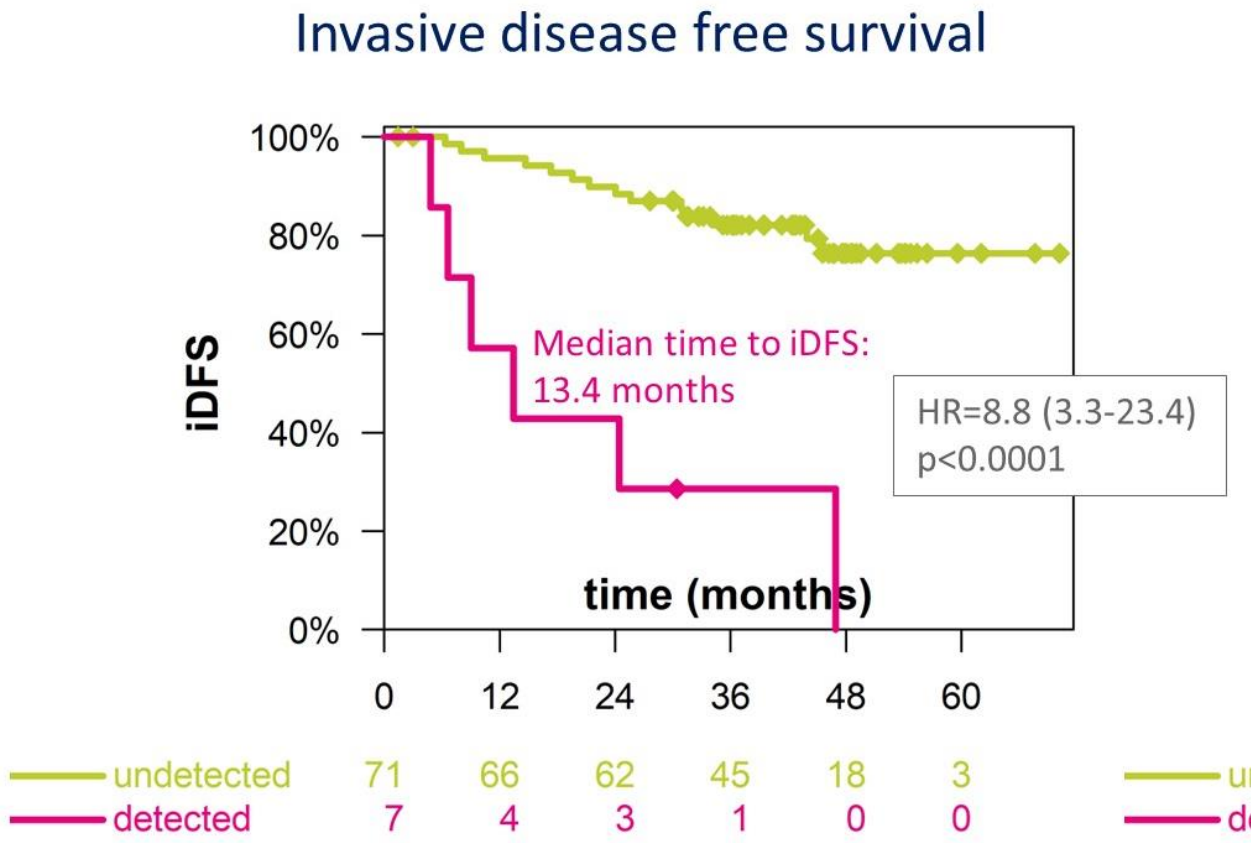
Samples for ctDNA analysis

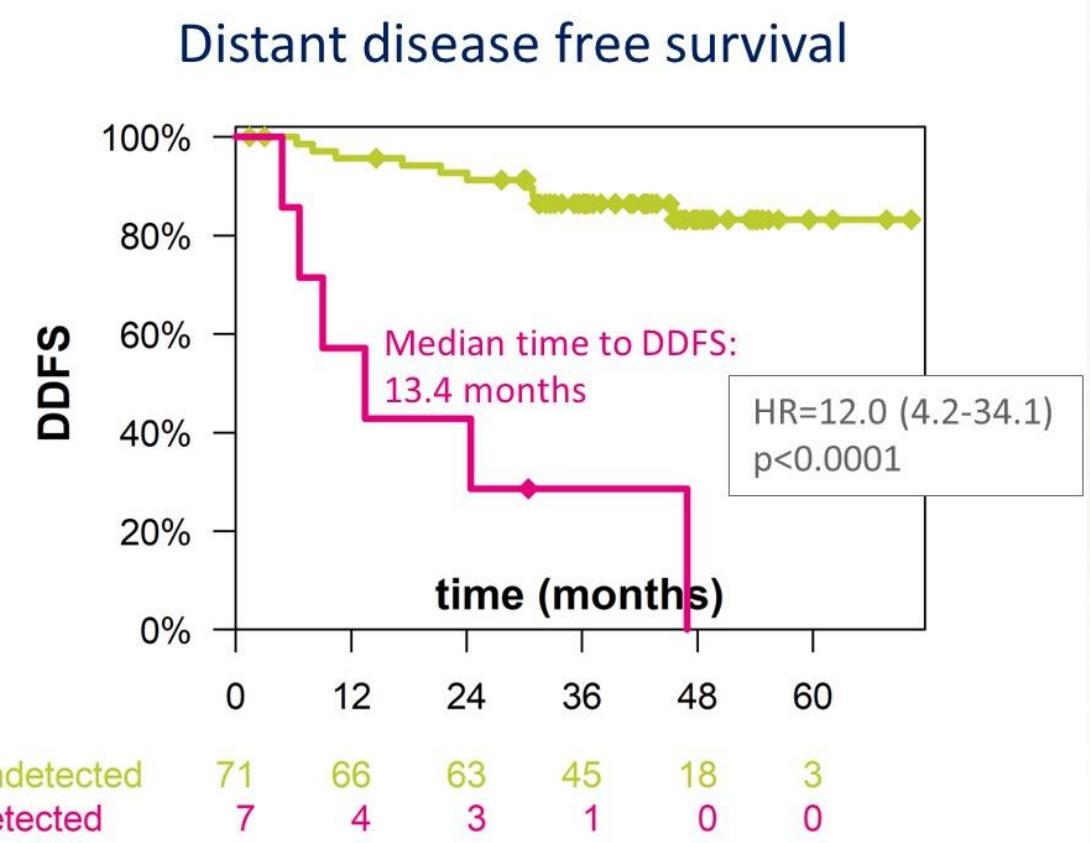
Baseline ↓ Cycle 7 ↓ EoT ↓

PenelopeB ET + Palbociclib/Placebo

Turner N. ASCO 2023

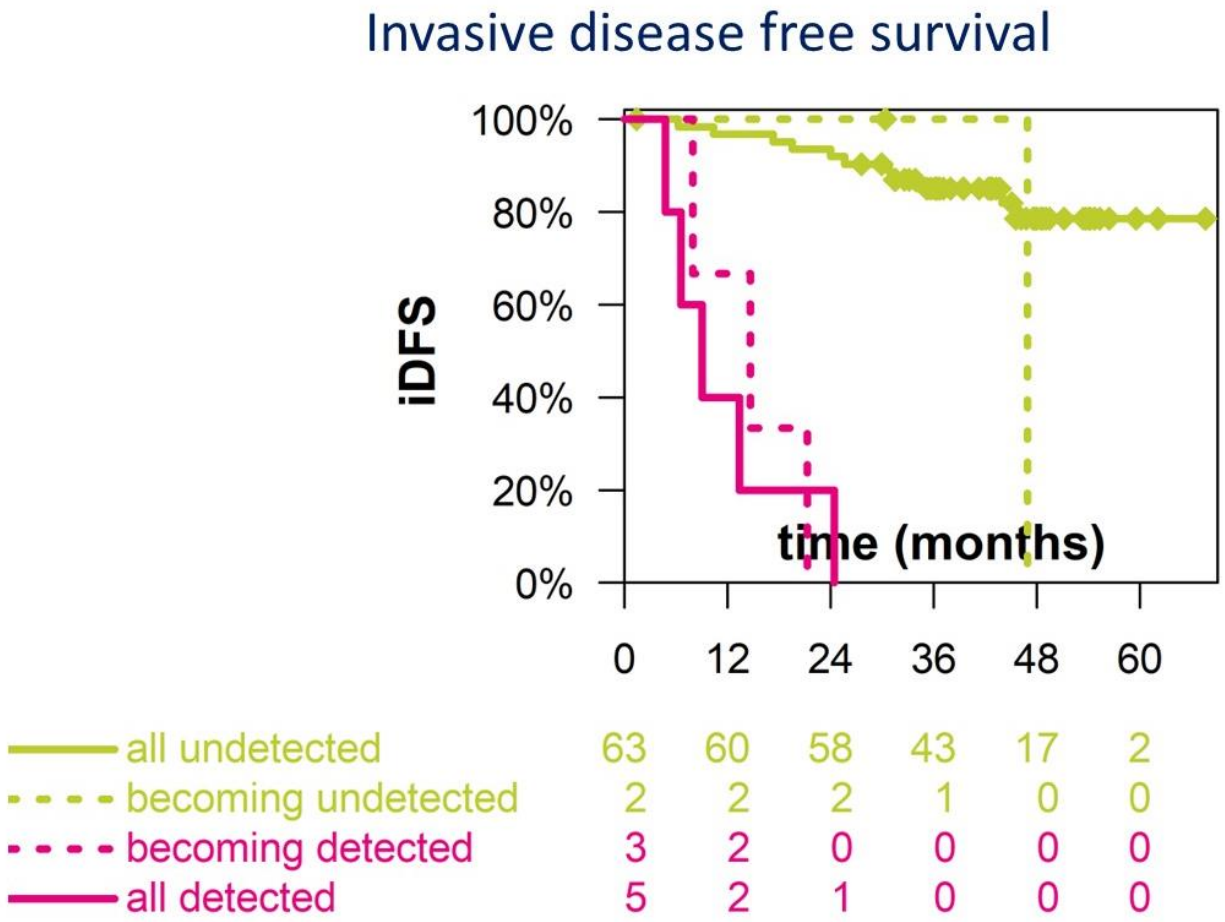
ctDNA: MRD





Turner N. ASCO 2023

ctDNA: MRD



iDFS by ctDNA dynamic groups

Patients with undetected baseline ctDNA, who become positive during treatment have poor outcome

Both patients who became undetected were on palbociclib

Analysis limited by small groups

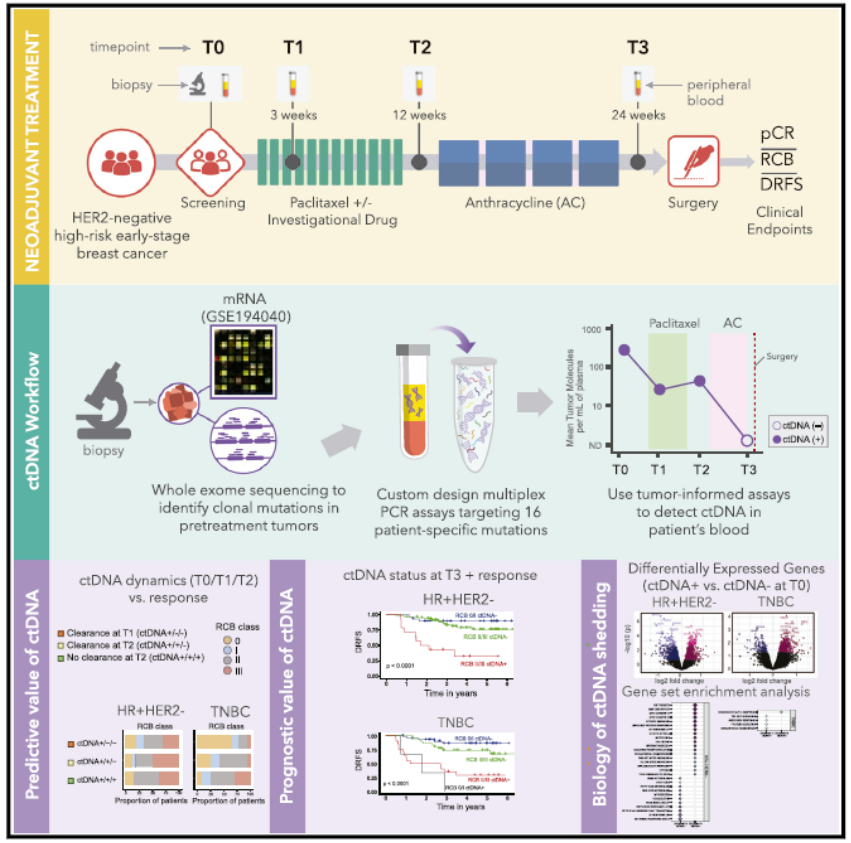
Turner N. ASCO 2023

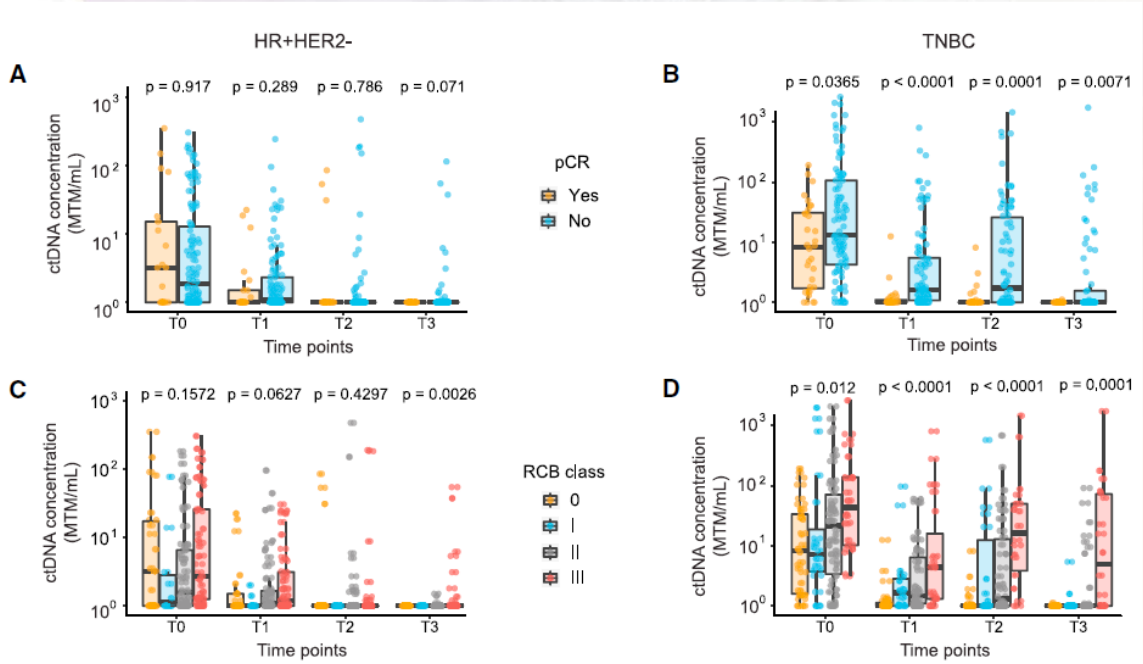
ctDNA: MRD

Article

Cancer Cell

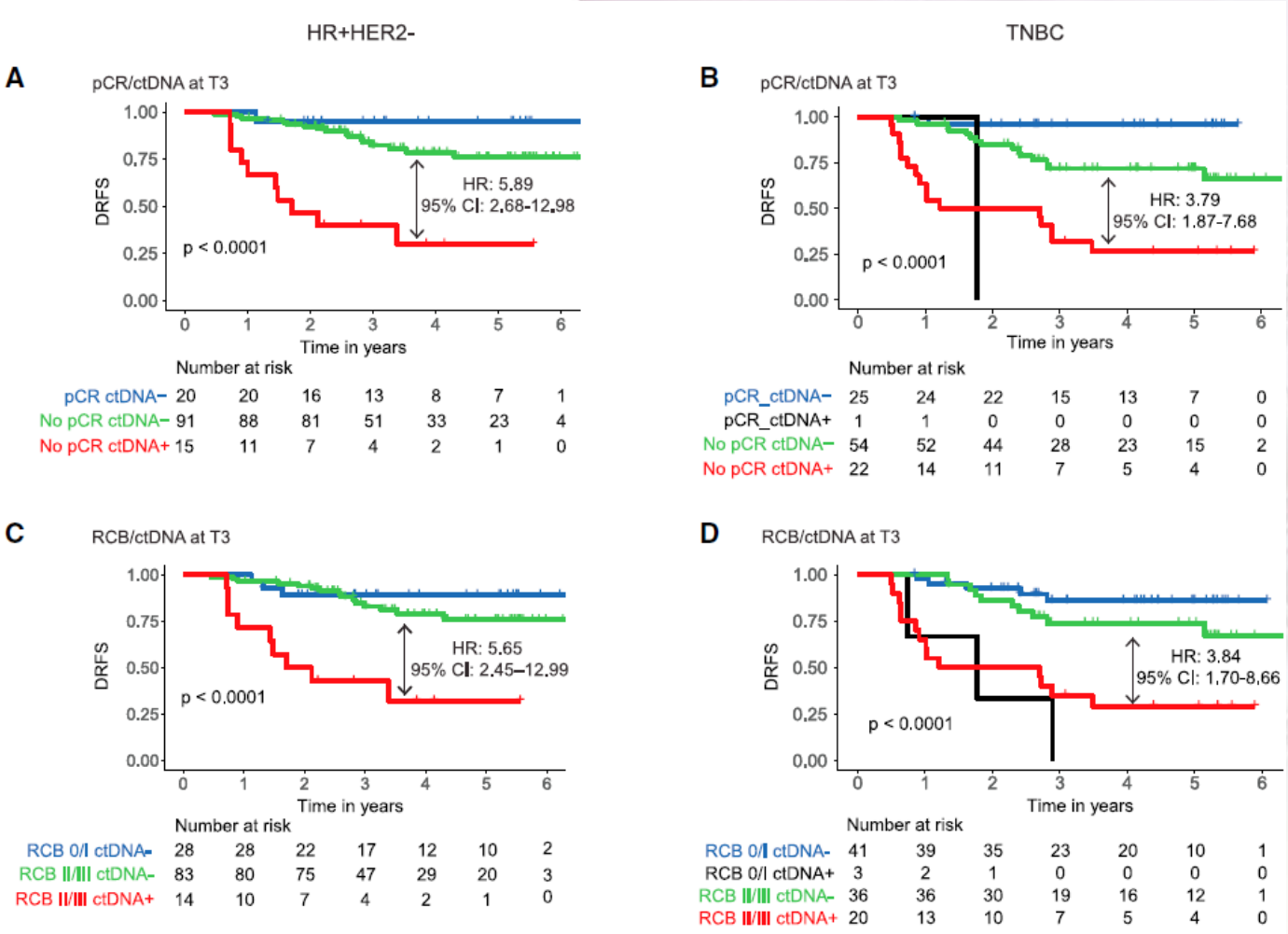
Clinical significance and biology of circulating tumor DNA in high-risk early-stage HER2-negative breast cancer receiving neoadjuvant chemotherapy





Magbanua M *et al*. Cancer Cell 2023

ctDNA: MRD



Magbanua M *et al*. Cancer Cell 2023

Conclusiones

El uso de las plataformas **OncotypeDx**, **Prosigna**, **MammaPrint**, **Breast Cancer Index (BCI)** y **Endopredict** está recomendado (con sus respectivas poblaciones validadas) para ayudar en la decision de administrar QT adyuvante o no en cáncer de mama luminal

- PAM50 no parece útil para seleccionar pacientes premenopáusicas óptimas para supresión ovárica
- RS podría complementar la monitorización dinámica de Ki67 para desescalar tratamiento neo/adyuvante
- **HER2DX** se propone como plataforma para ayudar en decisiones de escalada/desescalada de tratamiento en enfermedad HER2+ precoz

PIK3CA, gBRCA1/2, PD-L1/CPS-score, dMMR/MSI y fusiones en NTRK ya tenían una recomendación de testeo para guiar tratamientos en enfermedad metastásica (y adyuvante para gBRCA1/2), a lo que ahora se suma **ESR1**

- **HER2-low** no parece una entidad biológica única aunque es útil para seleccionar pacientes candidatas a T-DXd
- **HER-3** emerge como una nueva diana para nuevos ADCs, aunque su valor pronóstico/pedictivo no está claro
- **TROP-2** se mantiene como diana para algunos ADCs, sin aparente valor predictivo según niveles de expresión

El **ctDNA** sigue avanzando como alternativa al tejido para el estudio de alguno de estos biomarcadores, siendo óptimo para el estudio de mutaciones en ESR1 y demostrando validez clínica para la detección de enfermedad molecular residual, aún pendiente de demostrar utilidad clínica