

VII SIMPOSIO NACIONAL
de **ONCOLOGÍA** de **PRECISIÓN**

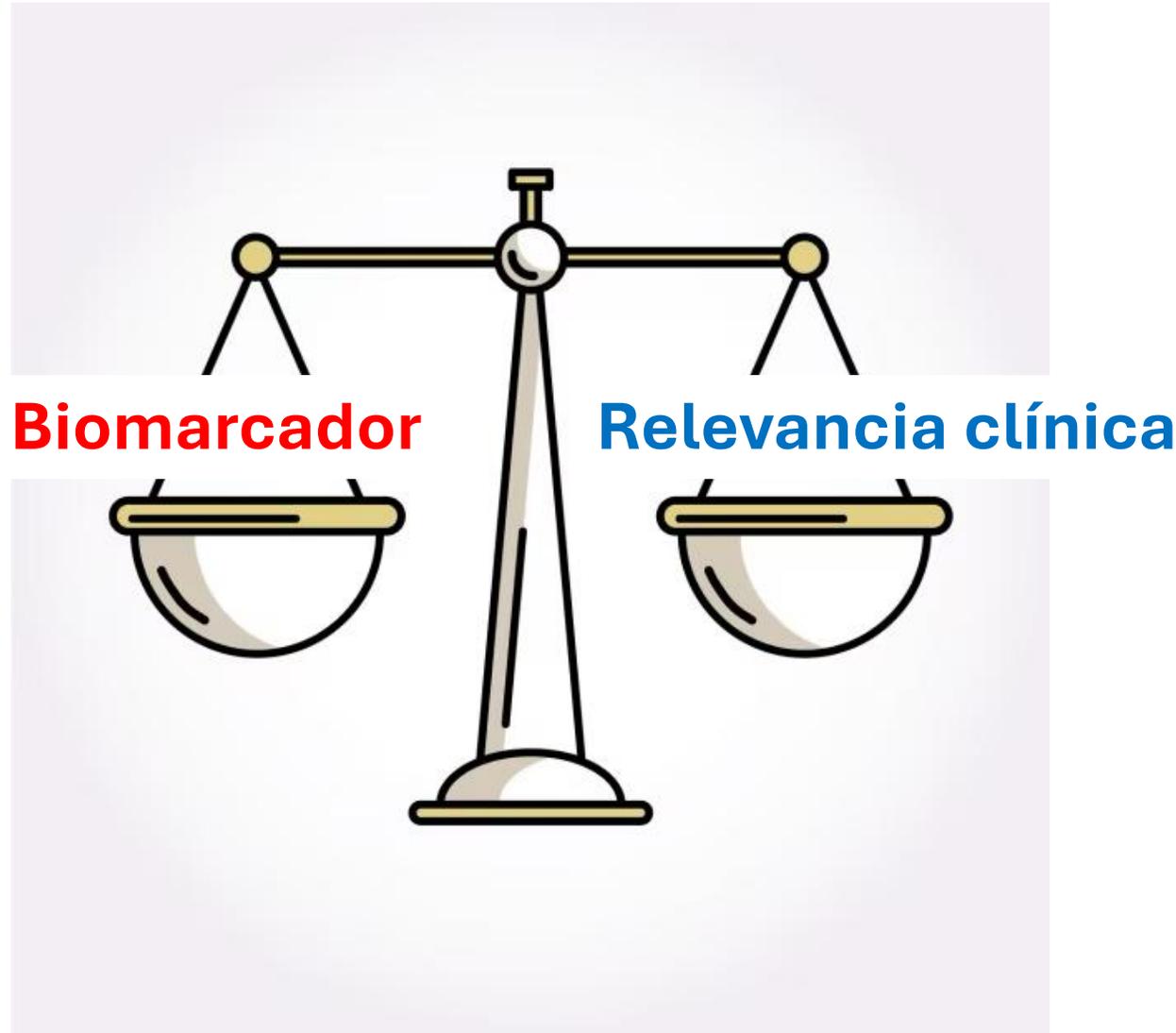
Vigo, 20 y 21 de febrero de 2025

Lo mejor del cáncer de mama en 2024

Fernando Moreno Antón



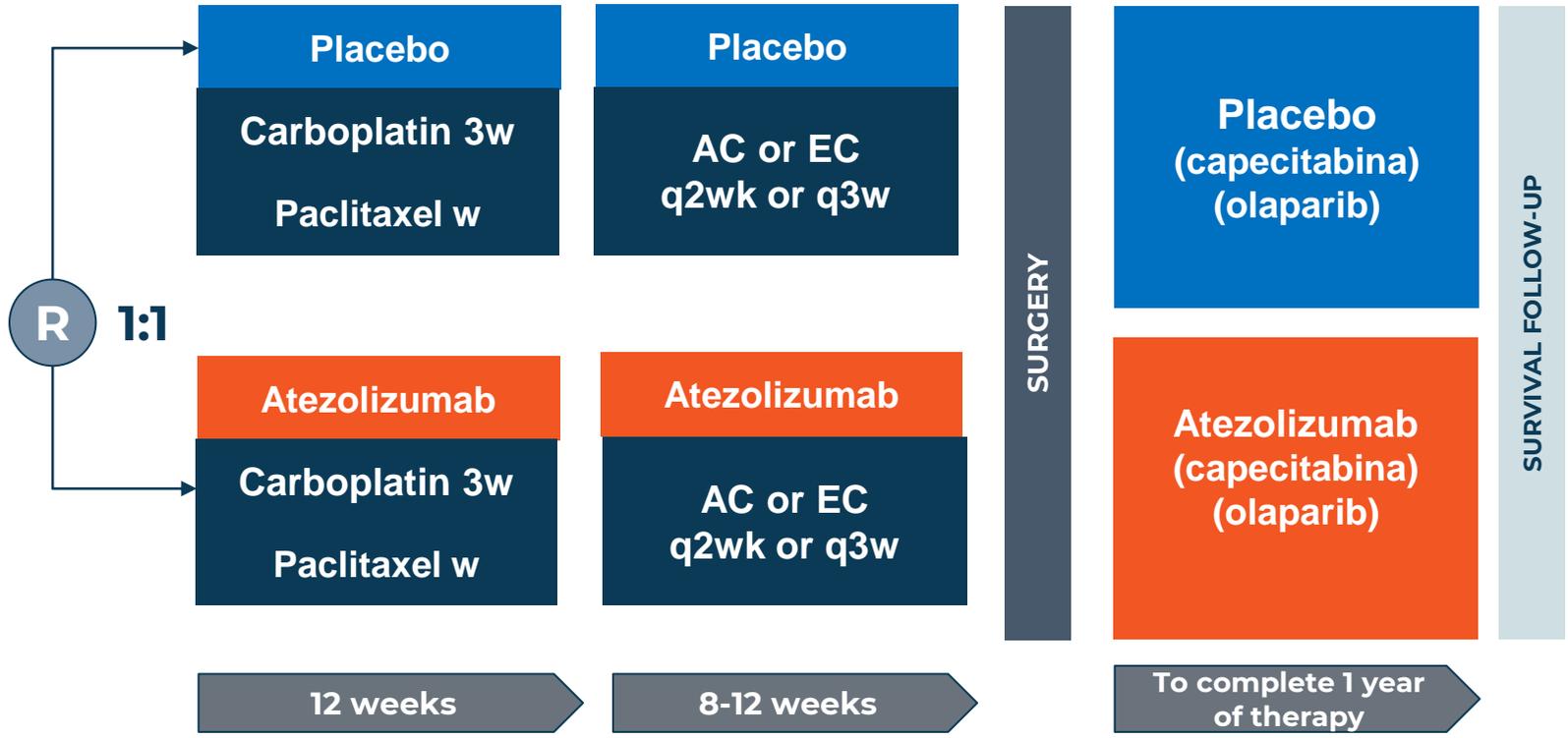
Lo mejor del cáncer de mama en 2024



Gepardouze: Study Design

N = 1550

- Invasive Breast Cancer Diagnosed by Core Needle Biopsy
- Negative for ER, PgR, HER2 on Central Testing by ASCO/CAP
- Clinical Stage T1c if node-positive (cN1,cN2 or cN3), T2 or T3 irrespective of nodal status



Primary efficacy endpoint

- Event-free survival (EFS)

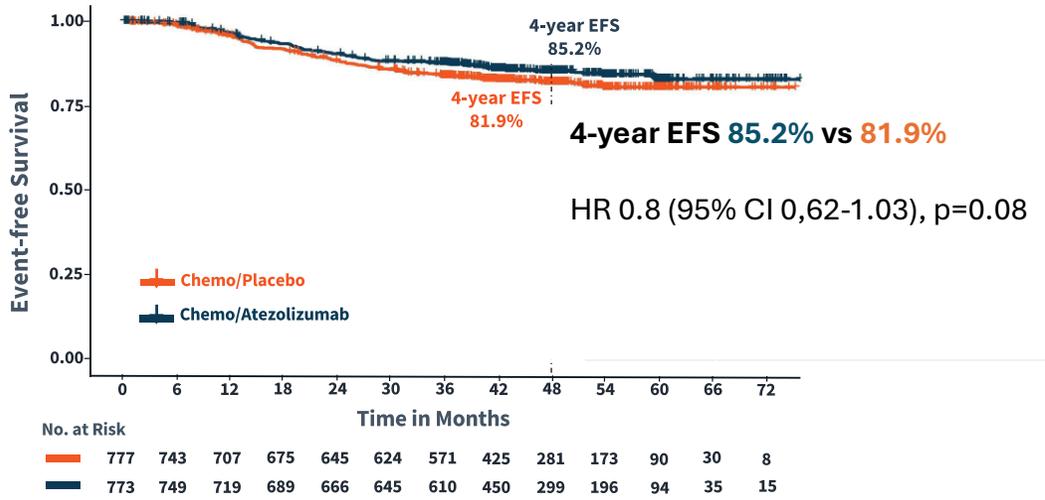
Secondary efficacy endpoints

- Overall survival (OS)
- Pathologic complete response (pCR) in the breast and lymph nodes (ypT0/Tis ypN0)

- Distant disease-free survival (DDFS)
- Disease-free survival (DFS)
- Toxicity

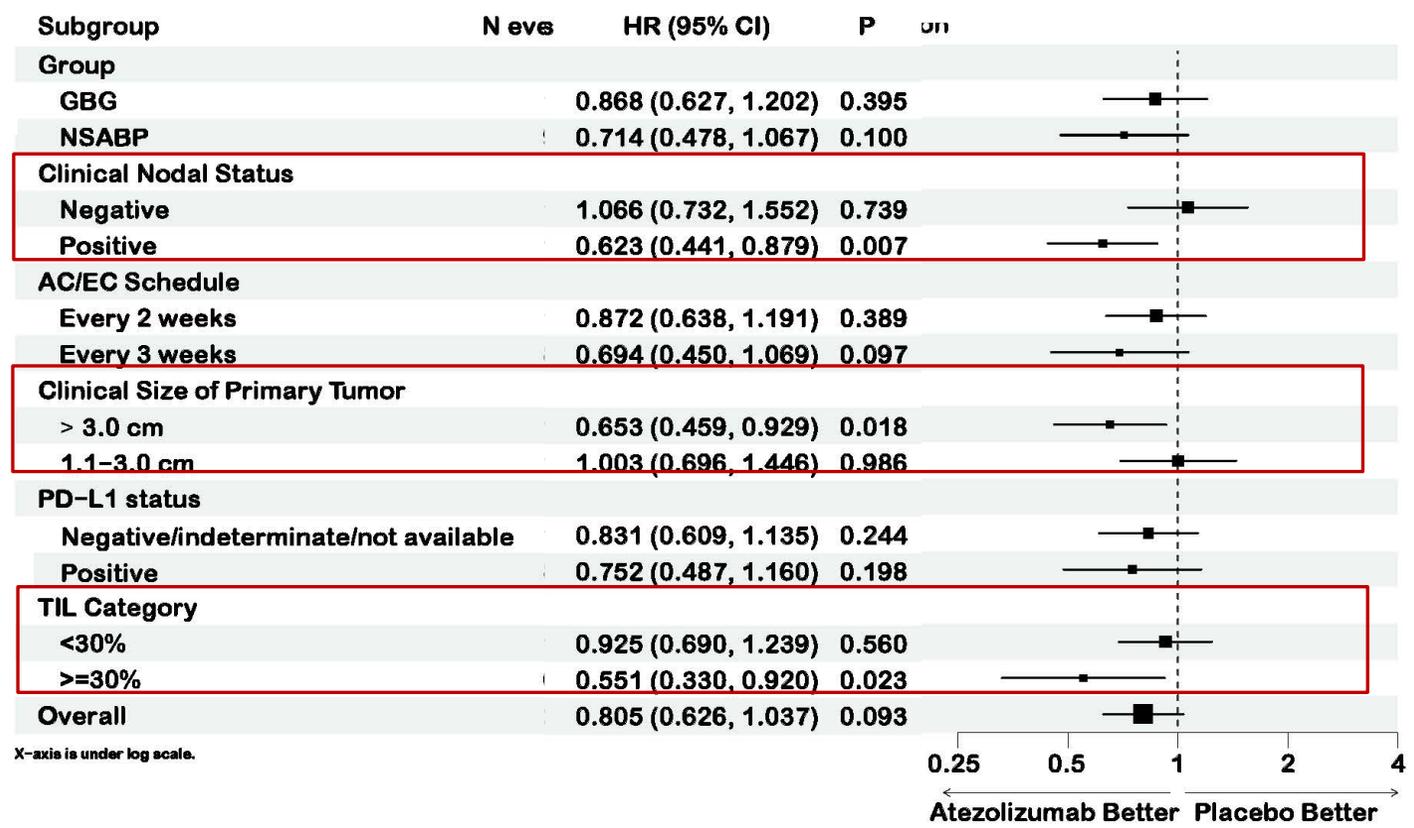
Gepardouze Results: Primary objective

Event-free Survival



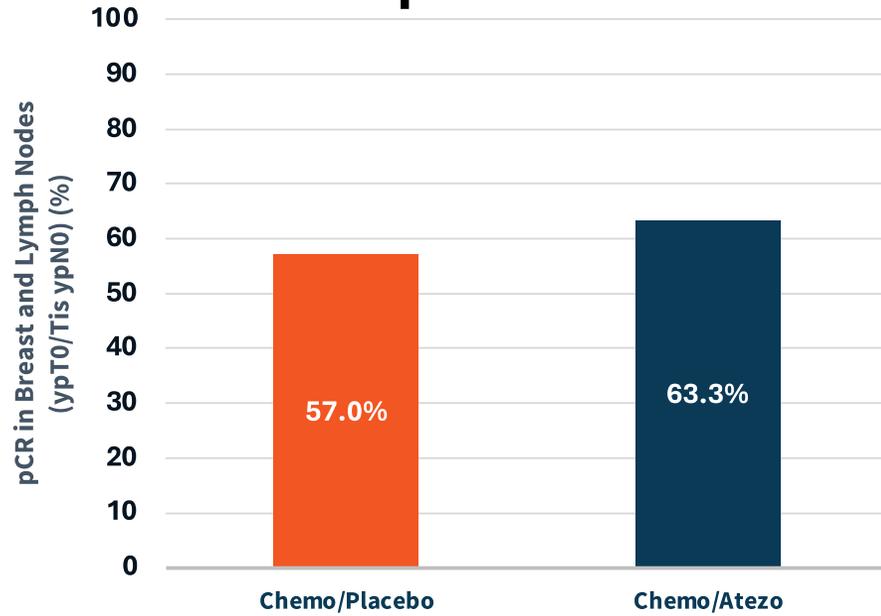
Median follow-up 46.9 months

EFS Subgroup Analysis



Gepardouze Results: Secondary objectives

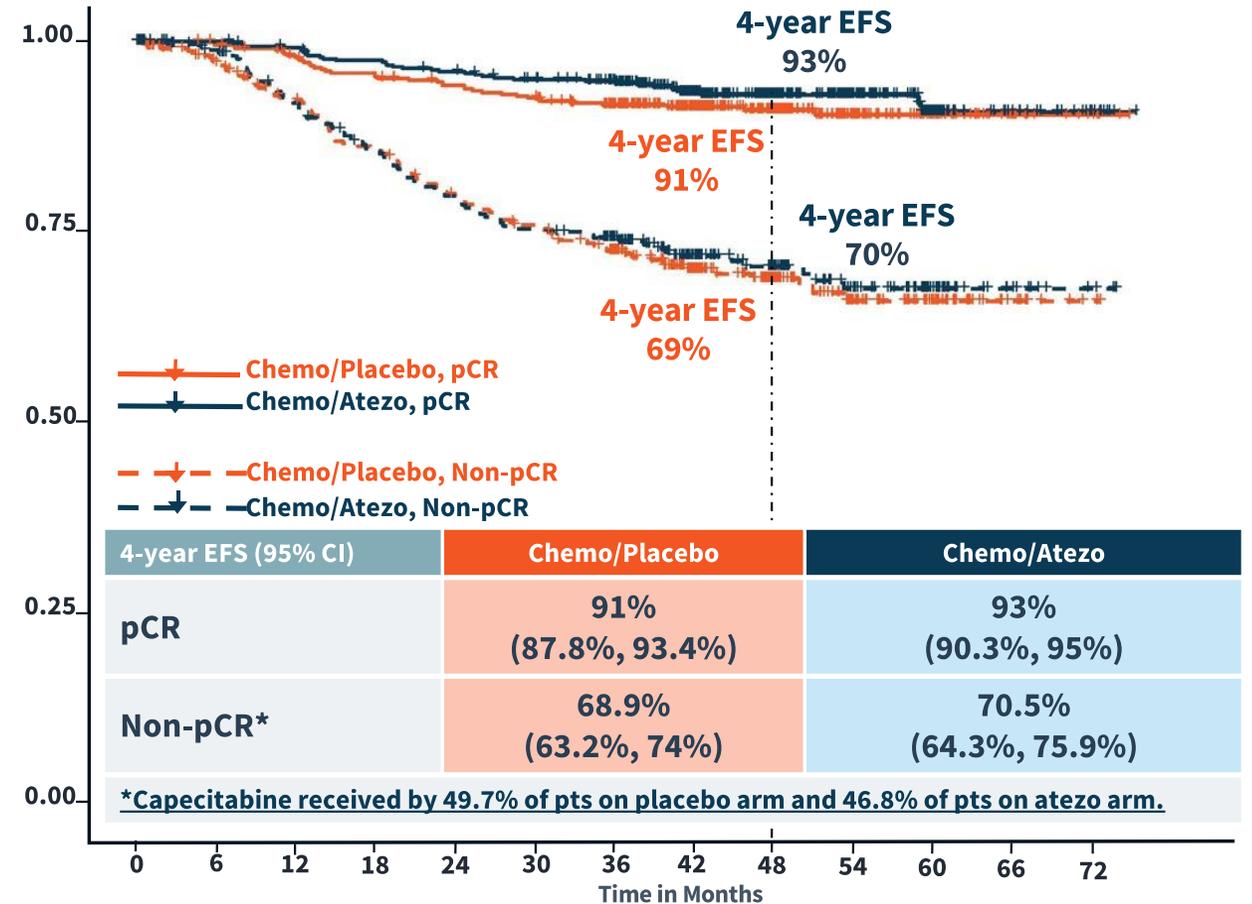
pCR rate



	Chemo/Placebo n = 777	Chemo/Atezo n = 773
% pCR ^a (95% CI)	57.0% (53.5%, 60.5%)	63.3% (59.9%, 66.7%)
Difference in % pCR (95% CI)	6.3% (1.4%, 11.1%) (p _{adj} = 0.0091) ^b	

^a Those with missing pCR status are considered as non-responders.
^b 2-sided CMH test adjusted by stratification factors collapse of PD-L1 status.

Event-free Survival by pCR



Estudio Gepardouze: Conclusiones



- Aumento de pCR (57 % vs 63 %)
- Beneficio en EFS en N+, T > 3 cm, TILS \geq 30%



Análisis de biomarcadores



- Ausencia de beneficio en objetivo principal (EFS)
- ↑ Efectos adversos inmunomediados

Advanced BC: ESR1 mutations

- **Mutations in ESR1** result in estrogen-independent ER activation and **resistance to AIs**
- **Oral SERDs** have demonstrated activity in **ESR1 mutated breast cancer**

Imlunestrant EMBER-3	Giredestrant aceLERA	Amcenenestrant AMEERA-3	Camizestrant SERENA-2	Elacestrant EMERALD
?				



EMBER-3 trial: Design

ER+, HER2- ABC

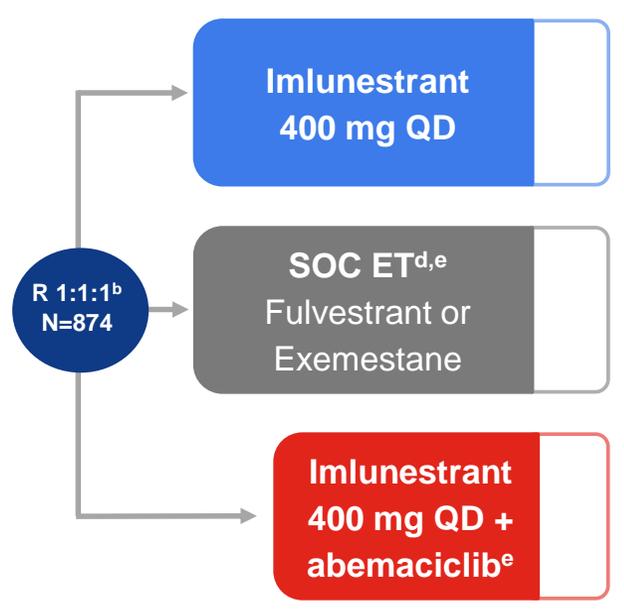
Men and Pre-^a/Post-menopausal women

Prior therapy:

- **Adjuvant:** Recurrence on or within 12 months of completion of AI ± CDK4/6i
- **ABC:** Progression on first-line AI ± CDK4/6i
- No other therapy for ABC

Stratification Factors:

- Prior CDK4/6i therapy (Y/N)
- Visceral metastases (Y/N)
- Region^c



Primary Endpoints

Investigator-assessed PFS for^f:

- A vs B in patients with *ESR1*^{m,g}
- A vs B in all patients
- C vs A in all^h patients

Key Secondary Endpoints

- OS, PFS by BICR, and ORR
- Safety

Exploratory Endpoints

- PFS and OS for C vs B in all^h patients

EMBER-3 trial. Results (1)

ER+, HER2- ABC

Men and Pre-^a/Post-menopausal women

Prior therapy:

- **Adjuvant:** Recurrence on or within 12 months of completion of AI ± CDK4/6i
- **ABC:** Progression on first-line AI ± CDK4/6i
- No other therapy for ABC

R 1:1:1^b
N=874

Imlunestrant
400 mg QD

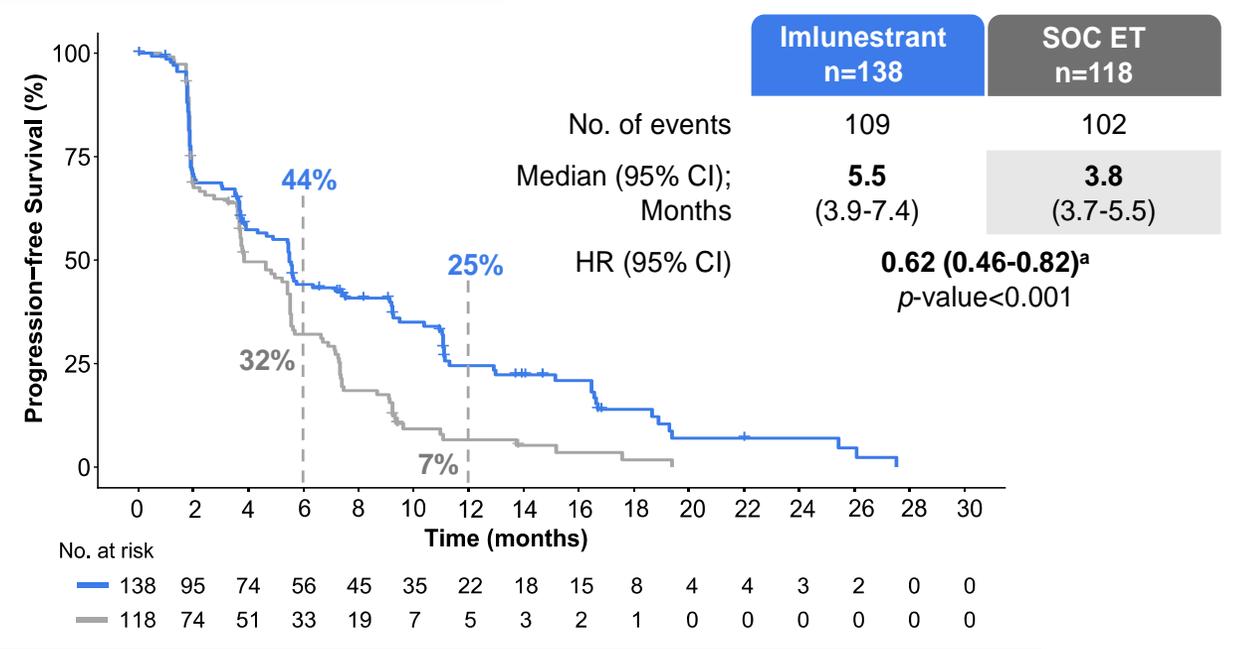
SOC ET^{d,e}
Fulvestrant or Exemestane

Stratification Factors:

- Prior CDK4/6i therapy (Y/N)
- Visceral metastases (Y/N)
- Region^c

Primary Endpoint: Imlunestrant vs SOC ET

Investigator-assessed PFS in **Patients with ESR1m**

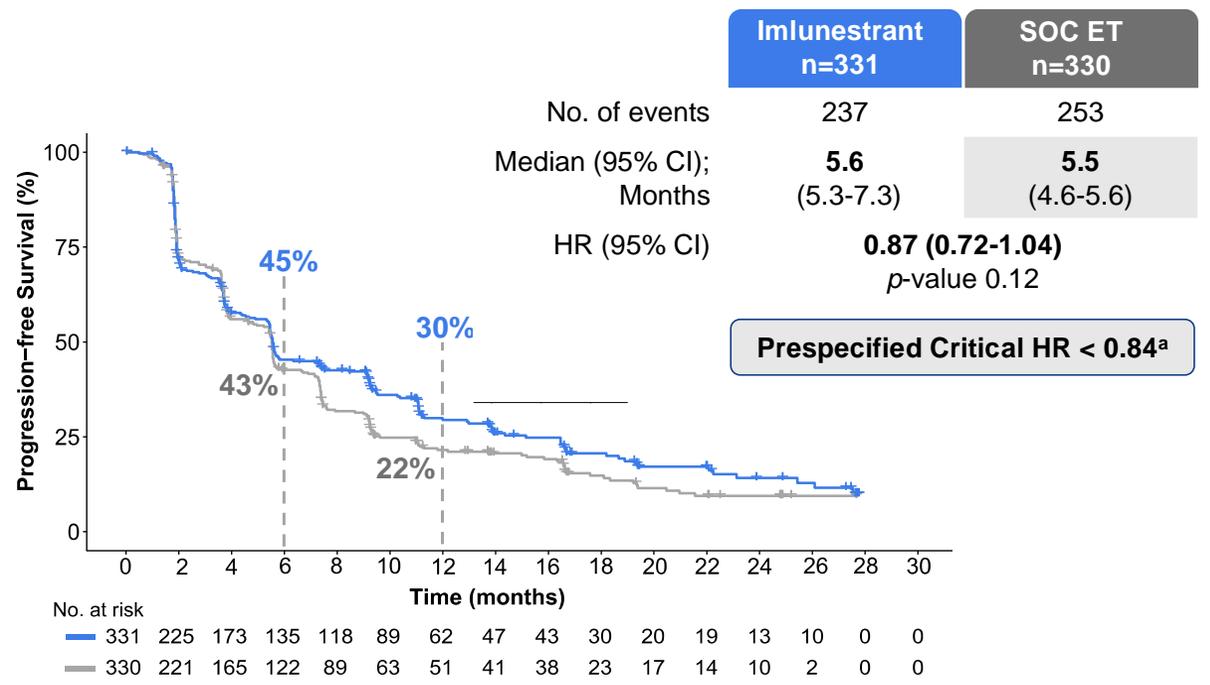
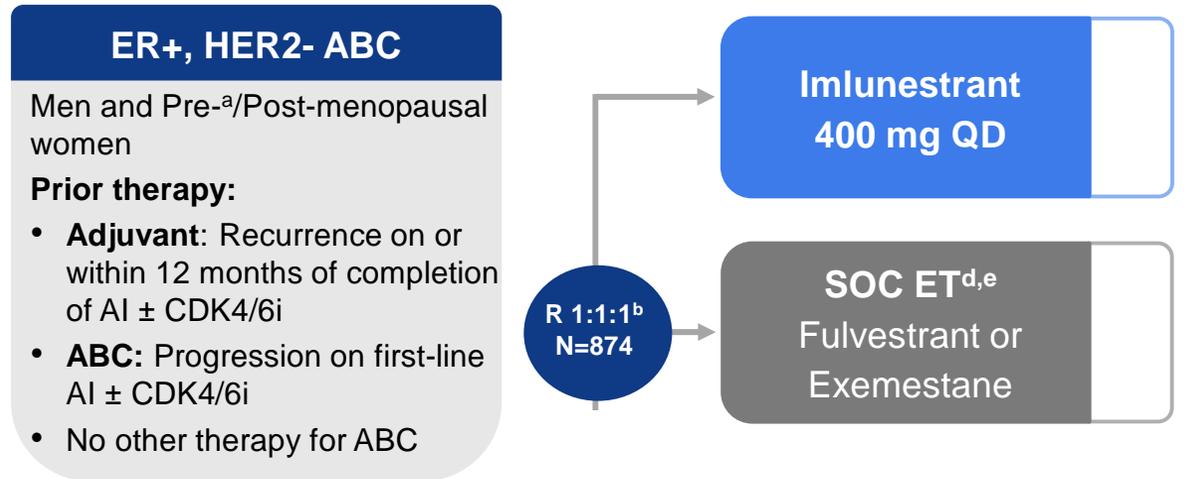


Imlunestrant led to a 38% reduction in the risk of progression or death in patients with ESR1m

EMBER-3 trial. Results (2)

Primary Endpoint: Imlunestrant vs SOC ET

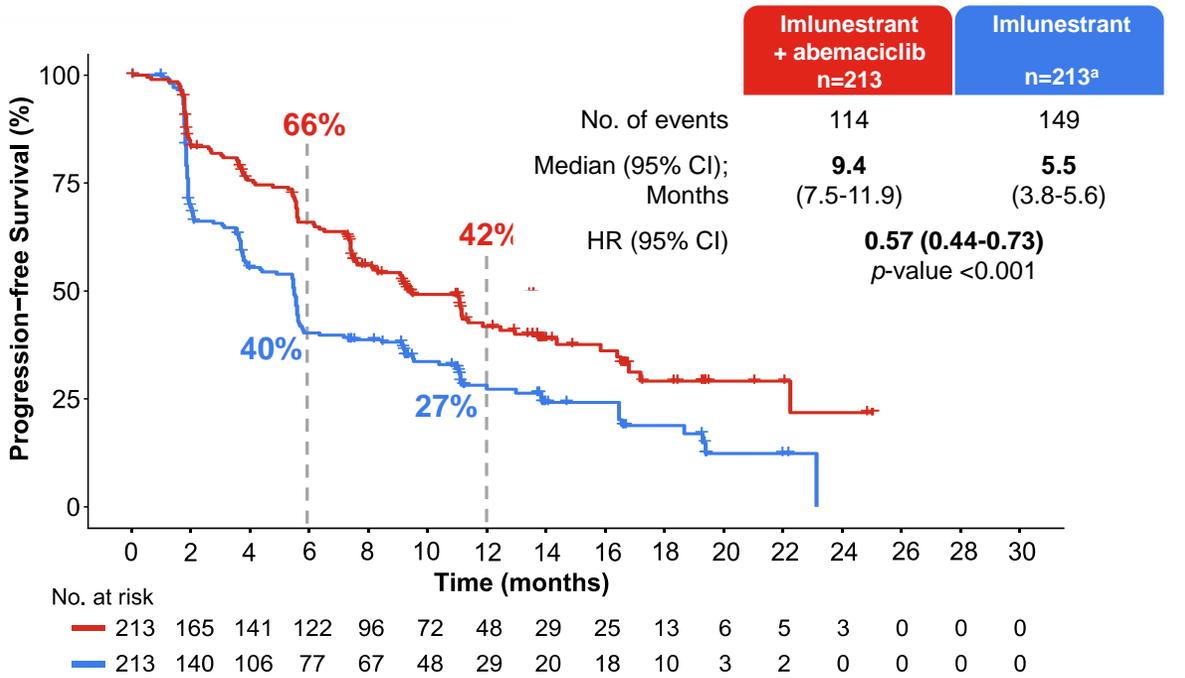
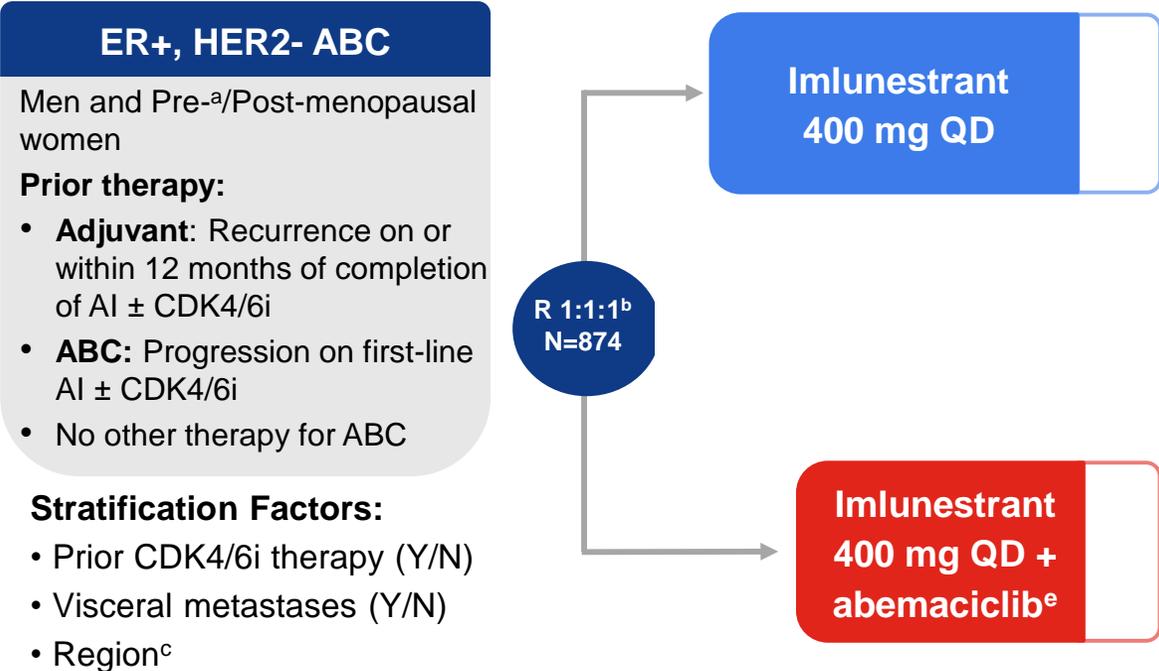
Investigator-assessed PFS in **All Patients**



PFS difference of imlunestrant vs SOC ET in all patients did not reach significance

EMBER-3 trial. Results (3)

Primary Endpoint: Imlunestrant + Abemaciclib vs Imlunestrant Investigator-assessed PFS in **All Patients**



Consistent benefit of imlunestrant + abemaciclib regardless of *ESR1m* status and previous iCDK exposure

Estudio EMBER 3: Conclusiones

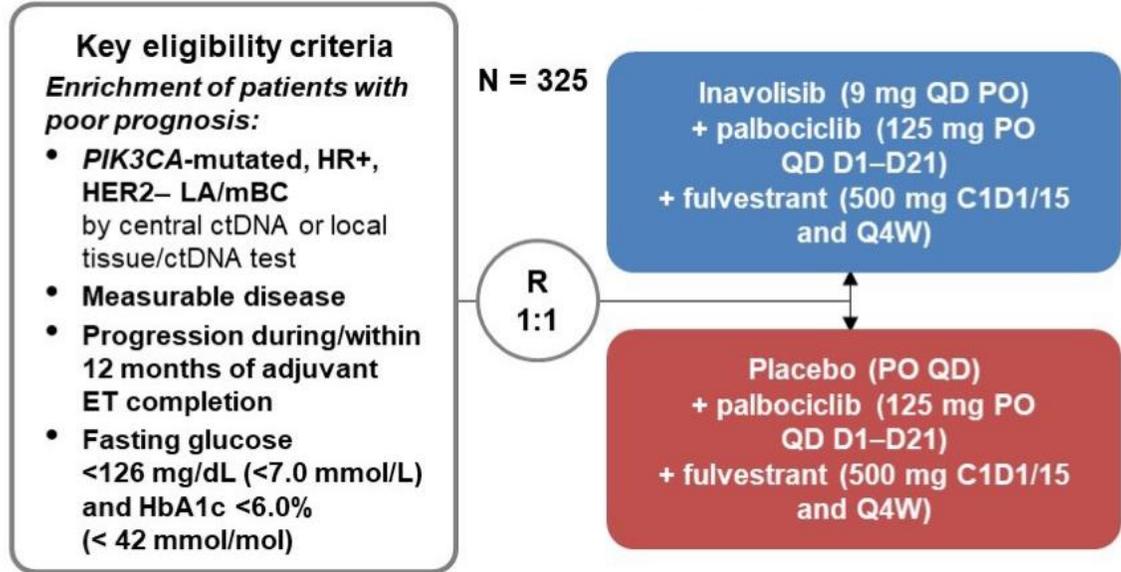


- Imlunestrant ↑ PFS vs fulvestrant en pacientes con mutación de ESR1
- Imlunestrant + abemaciclib ↑ PFS vs Imlunestrant independiente de ESR1



- Magnitud de beneficio limitado
- Datos inmaduros de SG
- Inclusión de pacientes sin iCDKs previo
- Imlunestrant no es un brazo standard de tratamiento
- Sugiere que el beneficio es a expensas de la utilización de iCDKs

INAVO 120: Trial Design



Statistical methods

- For efficacy endpoints and TTCD, hazard ratios were estimated using a Cox proportional hazard model with 95% CI and Kaplan–Meier methodology was used to estimate the medians with the Brookmeyer–Crowley method used for the 95% CI

Efficacy endpoints

- PFS by investigator
- OS
- ORR, BOR, CBR, DOR
- Time from randomization to end or discontinuation of next-line treatment, or death from any cause (proxy for PFS2)
- Time from randomization to first subsequent chemotherapy after treatment discontinuation

Safety endpoints

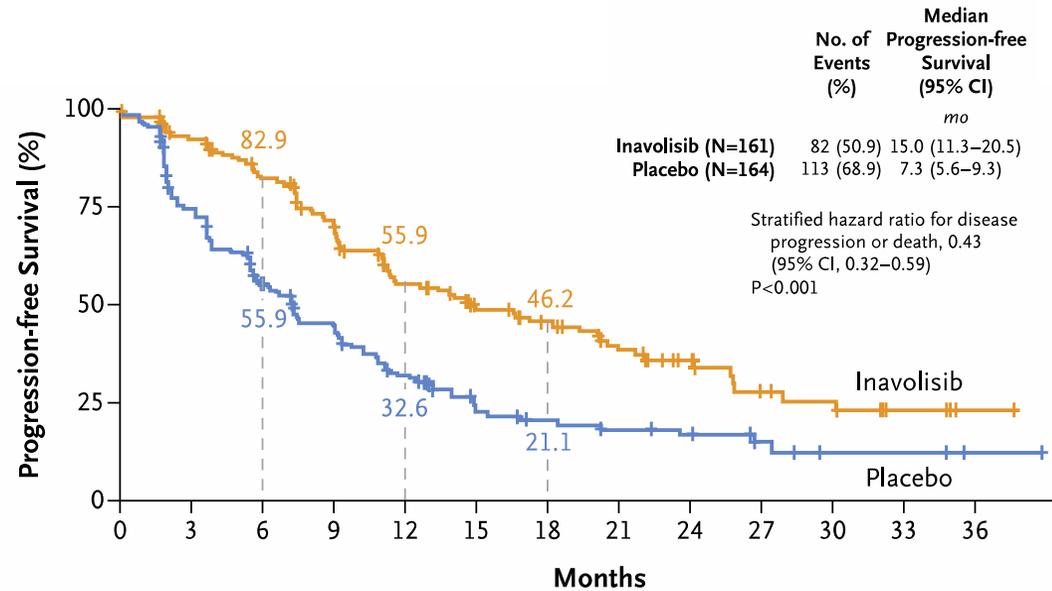
Key selected AEs (hyperglycemia, diarrhea, rash, and stomatitis/mucosal inflammation)*

Patient-reported outcomes endpoints†

- **BPI-SF: TTCD in worse pain^{‡§}**
- **EORTC QLQ-C30: mean change from baseline in HRQoL, physical functioning, and role functioning^{||}**
- **PRO-CTCAE: presence, frequency of occurrence, severity, and/or degree of interference with daily function of selected symptomatic treatment toxicities**
- **An overall bother item: overall bother experienced due to side effects of treatment**

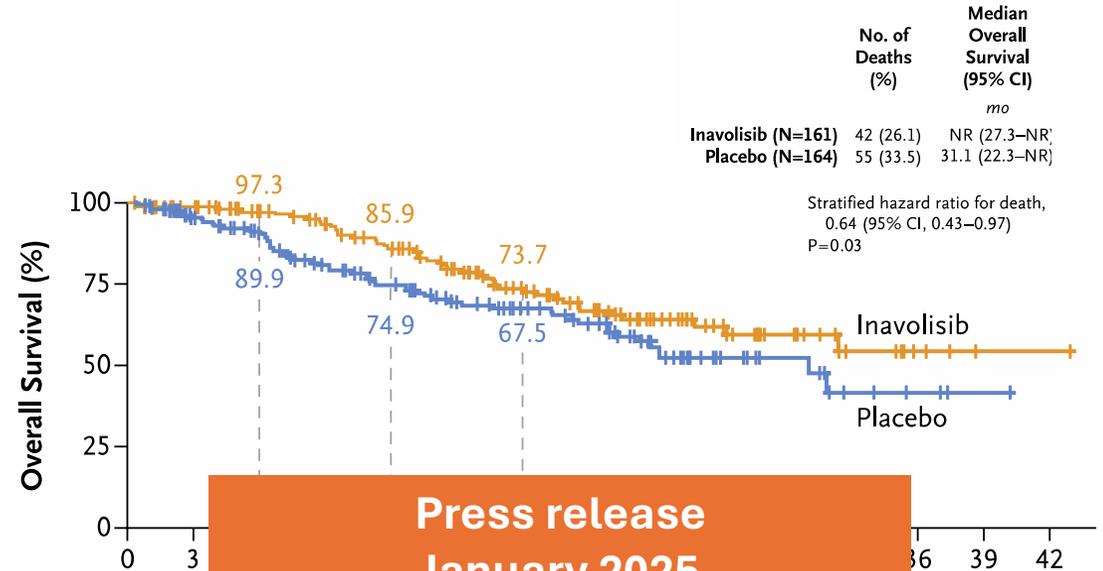
INAVO 120: Results

Progression-free Survival



No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36
Inavolisib	161	134	111	92	66	48	41	31	22	13	11	5	1
Placebo	164	113	77	59	40	23	19	16	12	6	3	3	1

Overall Survival

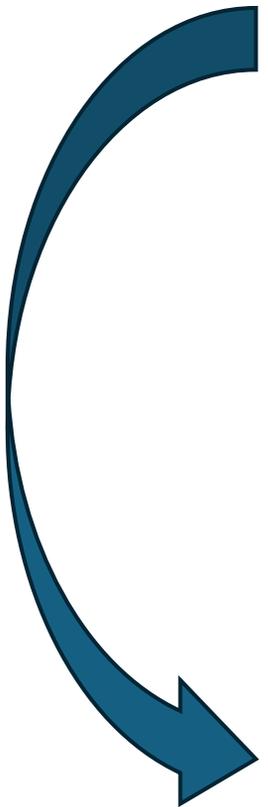


**Press release
January 2025
Statistically significant OS benefit**

No. at Risk	0	3	6	9	12	15	18	21	24	27	30	33	36	39	42
Inavolisib	161	143	127	114	101	85	69	56	38	26	17	8	4	1	1
Placebo	164	139	120	98	87	72	61	52	33	19	11	5	3	1	0

INAVO 120: Toxicity

Adverse Event	Inavolisib (N=162)		Placebo (N=162)	
	Any Grade	Grade 3 or 4	Any Grade	Grade 3 or 4
Neutropenia	144 (88.9)	130 (80.2)	147 (90.7)	127 (78.4)
Thrombocytopenia	78 (48.1)	23 (14.2)	73 (45.1)	7 (4.3)
Stomatitis and mucosal inflammation	83 (51.2)	9 (5.6)	43 (26.5)	0
Anemia	60 (37.0)	10 (6.2)	59 (36.4)	3 (1.9)
Hyperglycemia	95 (58.6)	9 (5.6)	14 (8.6)	0
Diarrhea	78 (48.1)	6 (3.7)	26 (16.0)	0
Nausea	45 (27.8)	1 (0.6)	27 (16.7)	0
Rash	41 (25.3)	0	28 (17.3)	0
Decreased appetite	38 (23.5)	0	14 (8.6)	0
Fatigue	38 (23.5)	0	21 (13.0)	2 (1.2)
Covid-19	37 (22.8)	3 (1.9)	17 (10.5)	1 (0.6)
Headache	34 (21.0)	0	22 (13.6)	0
Leukopenia	28 (17.3)	11 (6.8)	40 (24.7)	17 (10.5)
Ocular toxic effects	36 (22.2)	0	21 (13.0)	0



Discontinuation rate (inavolisib arm): 6.8%

Estudio INAVO 120: Conclusiones

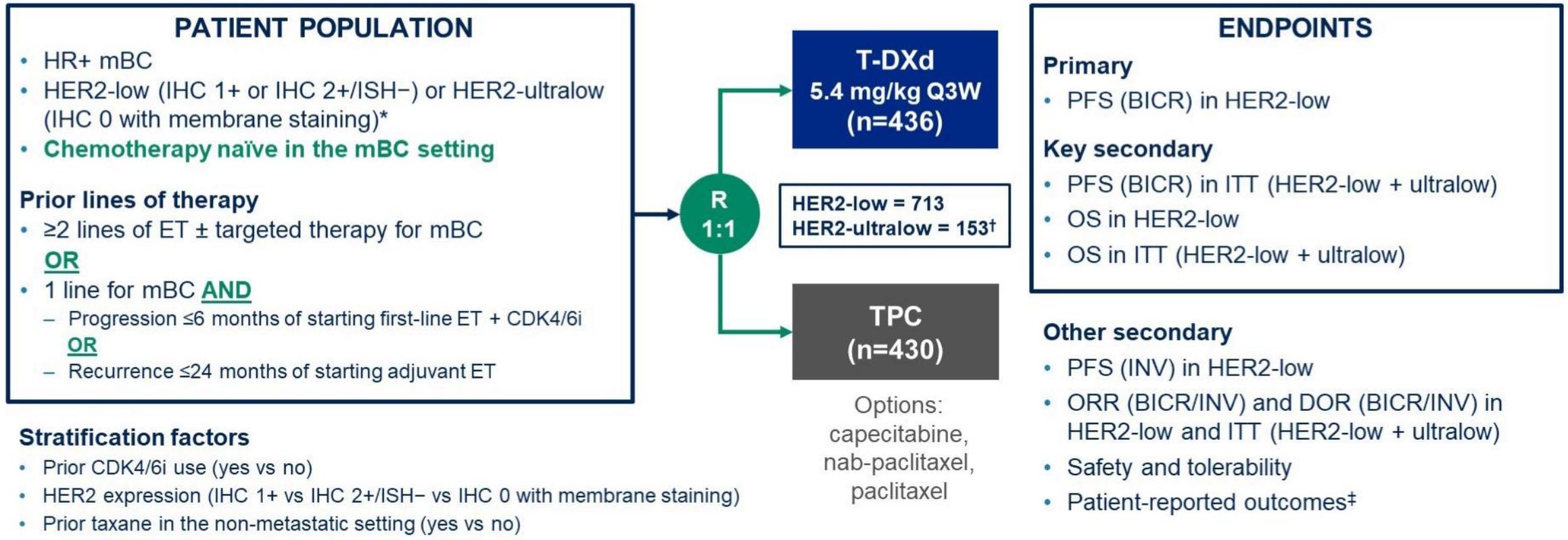


- **Beneficio en PFS & OS**
- **Biomarcador predictivo**
- **Perfil de seguridad más favorable comparado con otros inhibidores de PI3K**



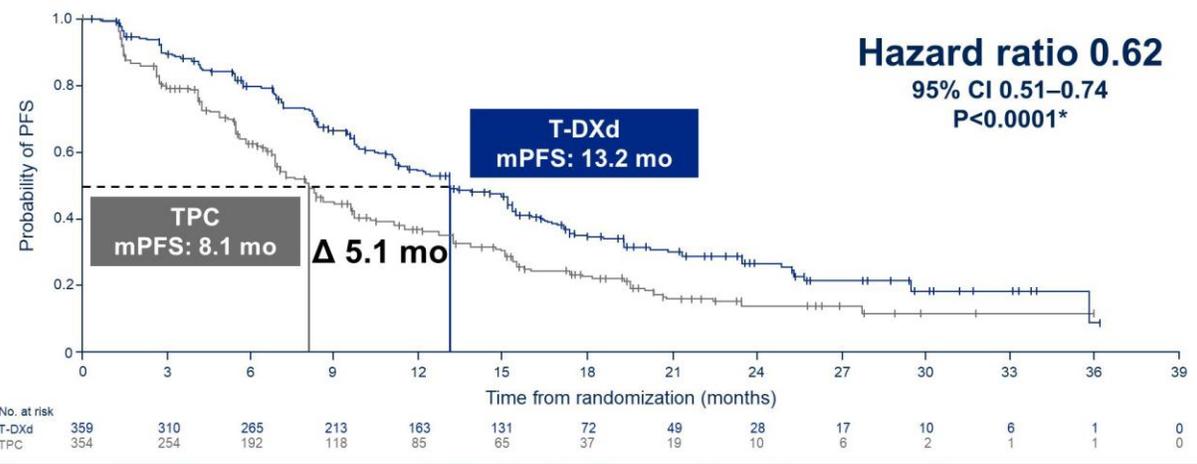
- **¿Aplicabilidad con otros iCDKs?**
- **¿Eficacia en pacientes previamente expuestos a iCDKs en adyuvancia?**

DESTINY-Breast 06. Design

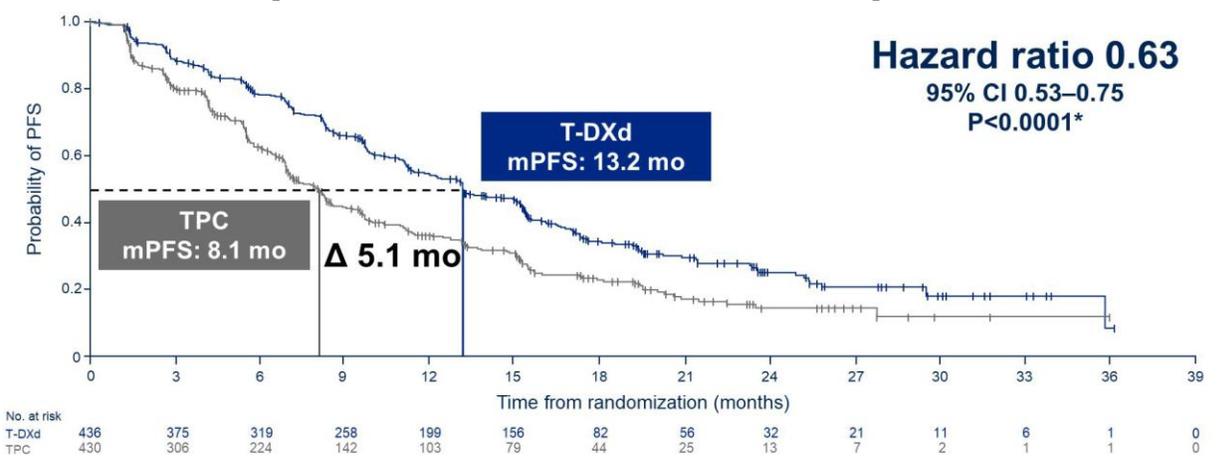


DESTINY-Breast 06. Results

Primary endpoint: PFS in HER2-low



Secondary endpoint: PFS in ITT (HER2-low & ultralow)

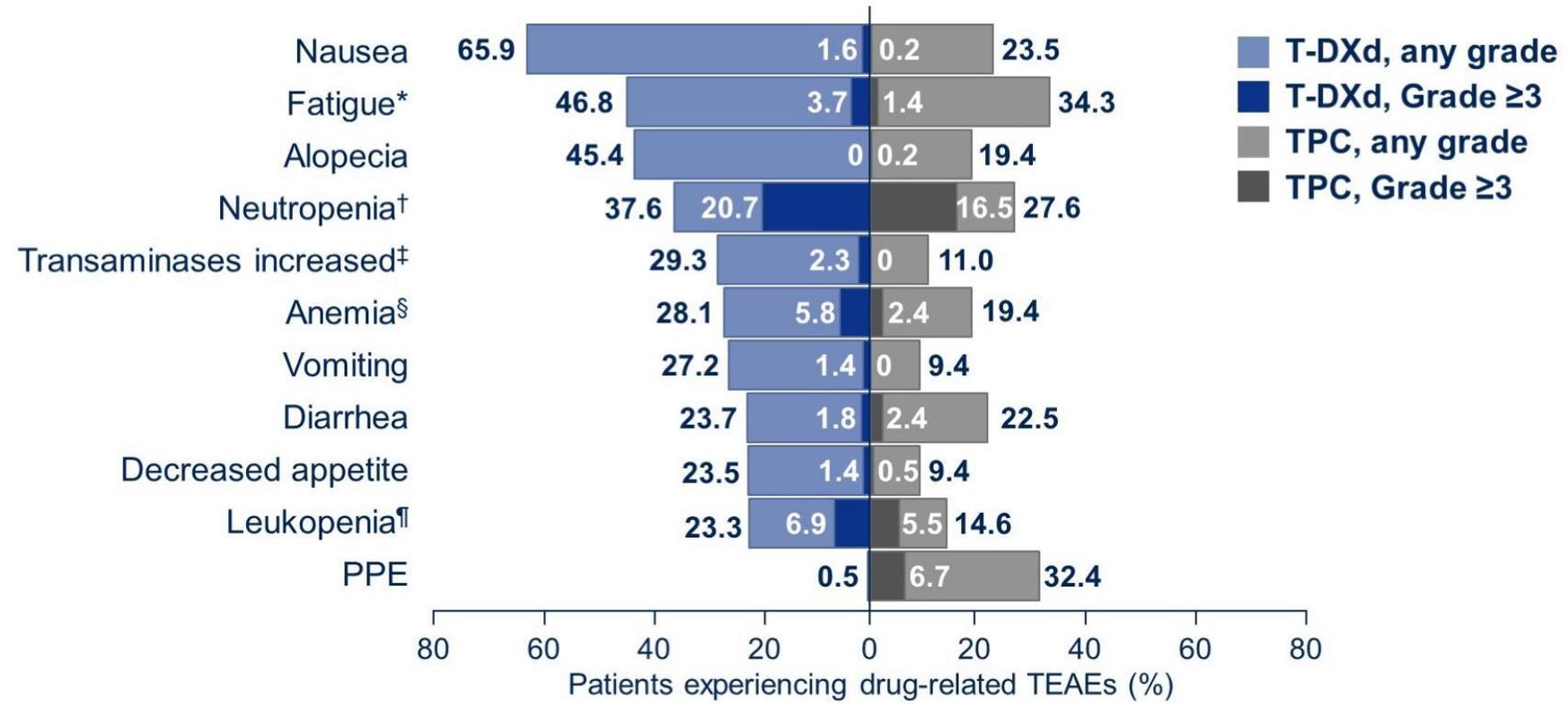


Secondary endpoint: ORR

	HER2-low*		ITT		HER2-ultralow*	
	T-DXd (n=359)	TPC (n=354)	T-DXd (n=436)	TPC (n=430)	T-DXd (n=76)	TPC (n=76)
Confirmed ORR, n (%)	203 (56.5)	114 (32.2)	250 (57.3)	134 (31.2)	47 (61.8)	20 (26.3)
Best overall response, n (%)						
Complete response	9 (2.5)	0	13 (3.0)	0	4 (5.3)	0
Partial response	194 (54.0)	114 (32.2)	237 (54.4)	134 (31.2)	43 (56.6)	20 (26.3)
Stable disease	125 (34.8)	170 (48.0)	148 (33.9)	212 (49.3)	22 (28.9)	42 (55.3)
Clinical benefit rate, n (%)†	275 (76.6)	190 (53.7)	334 (76.6)	223 (51.9)	58 (76.3)	33 (43.4)
Median duration of response, mo	14.1	8.6	14.3	8.6	14.3	14.1

DESTINY-Breast 06. Toxicity

Drug-related TEAEs in ≥20% of patients (either treatment group)



Adjudicated as drug-related interstitial lung disease / pneumonitis*

n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Grade 5	Any grade
T-DXd (n=434)	7 (1.6)	36 (8.3)	3 (0.7)	0	3 (0.7)	49 (11.3)
TPC (n=417)	0	1 (0.2)	0	0	0	1 (0.2)

Estudio Destiny Breast 06: Conclusiones

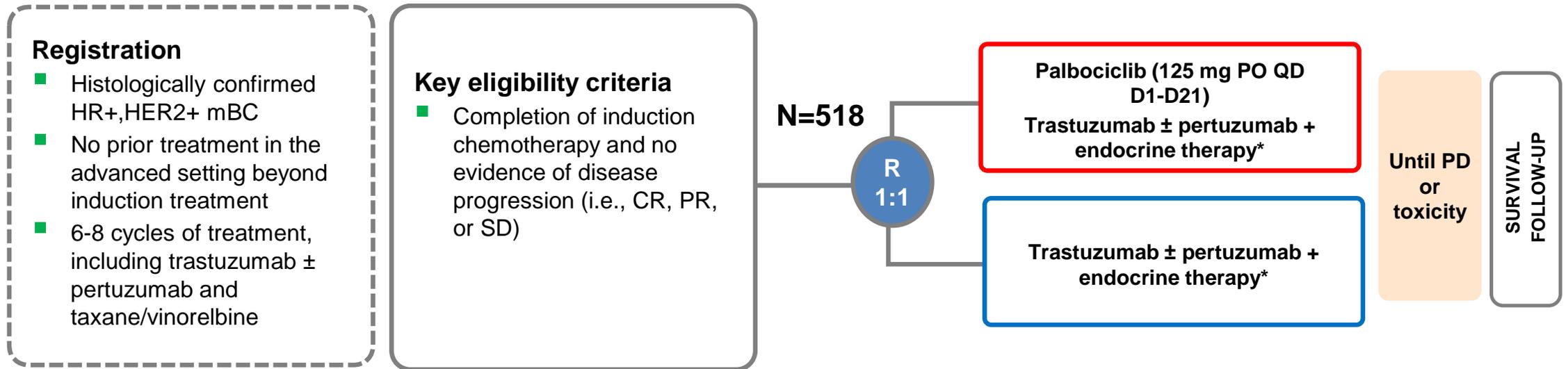


- **Población de estudio acorde a práctica clínica**
 - 90% iCDKs previo
 - 85% ≥ 2 líneas previas de terapia hormonal
- **Clasificación HER2 ultralow por laboratorio central**
- **Magnitud de beneficio en PFS & ORR**



- **Incremento toxicidad**
 - Grado ≥ 3
 - Mortalidad por tratamiento
- **Beneficio en OS en 1L?**
 - T-DXd \uparrow PFS & OS en 2-3L
- **Falta información sobre QoL**
- **Biomarcador (expresión HER2 IHC)**
 - Umbral mínimo expresión no definido
 - Variabilidad interobservador

PATINA Trial: Study Design

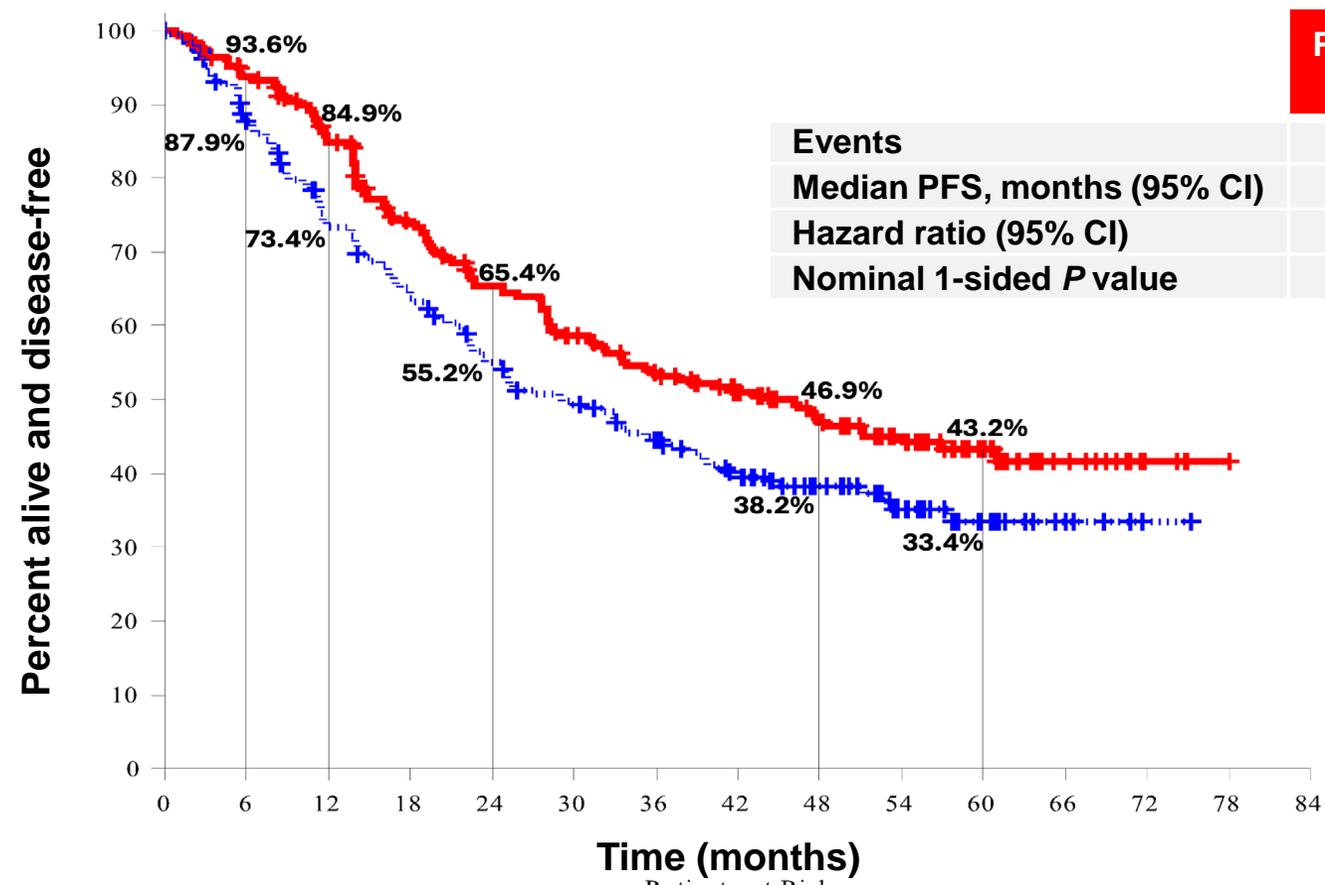


Stratification factors

- Pertuzumab use (yes vs no)
 - The non-pertuzumab option is limited to up to 20% of the population
- Prior anti-HER2 therapy in the (neo)adjuvant setting (yes vs no, including de novo)[†]
- Response to induction therapy (CR or PR vs SD) by investigator assessment[†]
- Type of endocrine therapy (fulvestrant vs aromatase inhibitor)

PATINA Trial: Results

Progression-free Survival



	Palbo + anti-HER2 and ET	Anti-HER2 and ET
Events	126/261	136/257
Median PFS, months (95% CI)	44.3 (32.4-60.9)	29.1 (23.3-38.6)
Hazard ratio (95% CI)	0.74 (0.58-0.94)	
Nominal 1-sided P value	0.0074	

Median follow-up on patients who are alive and disease-free, 52.6 months

	0	6	12	18	24	30	36	42	48	54	60	66	72	78	84
Palbo + HER2 + ET	261	231	203	168	146	128	113	94	78	55	33	14	4	1	0
HER2 + ET	257	198	159	137	116	102	87	68	51	29	14	6	1	0	0

CI=confidence interval; ET=endocrine therapy; HER2=human epidermal growth factor receptor 2; palbo=palbociclib.

PATINA Trial: Results

Toxicity

Adverse Events, n (%) [*]	Palbociclib + anti-HER2 and ET (N=261)			Anti-HER2 and ET (N=248)		
	Grade 2	Grade 3	Grade 4	Grade 2	Grade 3	Grade 4
Neutropenia	52 (19.9)	165 (63.2)	12 (4.6)	10 (4.0)	11 (4.4)	0 (0.0)
White blood cell count decreased	30 (11.5)	30 (11.5)	1 (0.4)	2 (0.8)	0 (0.0)	0 (0.0)
Fatigue	60 (22.9)	14 (5.4)	0 (0.0)	32 (12.9)	0 (0.0)	0 (0.0)
Stomatitis	45 (17.2)	11 (4.2)	0 (0.0)	3 (1.2)	0 (0.0)	0 (0.0)
Diarrhea	69 (26.4)	29 (11.1)	0 (0.0)	26 (10.5)	4 (1.6)	0 (0.0)
Upper respiratory tract infection	30 (11.5)	1 (0.4)	0 (0.0)	16 (6.5)	0 (0.0)	0 (0.0)
Urinary tract infection	26 (10.0)	2 (0.8)	0 (0.0)	19 (7.7)	1 (0.4)	0 (0.0)
Arthralgia	23 (8.8)	4 (1.5)	0 (0.0)	44 (17.7)	3 (1.2)	0 (0.0)
Ejection fraction decreased	22 (8.4)	1 (0.4)	0 (0.0)	21 (8.5)	8 (3.2)	0 (0.0)
Cardiac heart failure	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)	1 (0.4)	0 (0.0)



Discontinuation rate (palbociclib arm): 7.5%

Estudio PATINA: Conclusiones



- **Magnitud de beneficio en PFS**
 - **mPFS 44.3 meses**
 - **△ 15.2 meses**



- **Incremento toxicidad y necesidad monitorización**
- **Aplicabilidad en caso de cambio de tratamiento standard en 1ª línea (T-DXd)**