20as Jornadas HITOS ONCOLÓGICOS: LO MEJOR DE 2025
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20 ANIVERSARIO

Inhibidores de ciclinas en cáncer de mama inicial

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GENERALITAT VALENCIANA

19 de noviembre de 2025

Aglaye
EufRósine
TaLía

bemaciclib
ibociclib
Pa bociclib

CDK4-6 inhibitors represent the most important milestone in the luminal ABC treatment history since the introduction of Tamoxifen. Currently, ciclibs are accepted as the standard of care in first line: They improve PFS with relevant impact on OS and a favourable safety profile.
Next step was apparently obvious and expected...

PALLAS Trial

- II-III HR+ HER2-
- Prior Surgery+/- CHEMO
- Within 12 m of diag
- Within 6 m of starting HT

N = 5761 pts

R

Endocrine Therapy (at least 5 years): AI or TAMOX +/- LH-rH agonist

- ❑ IIA vs IIB-III
- ❑ Chemo vs No
- ❑ >50 vs < 50
- ❑ America vs Europe vs Other

Endocrine Therapy + PALBOCICLIB 125 mg/d x 21 /28 days, x 2 years

- iDFS
- BCFS

dRFS
LRFS
OS

PALLAS Trial: Patients

58,7%: High risk:

- ≥4 nodes involved (≥N2), or
- 1-3 nodes with either T3/T4 and/or G3 disease

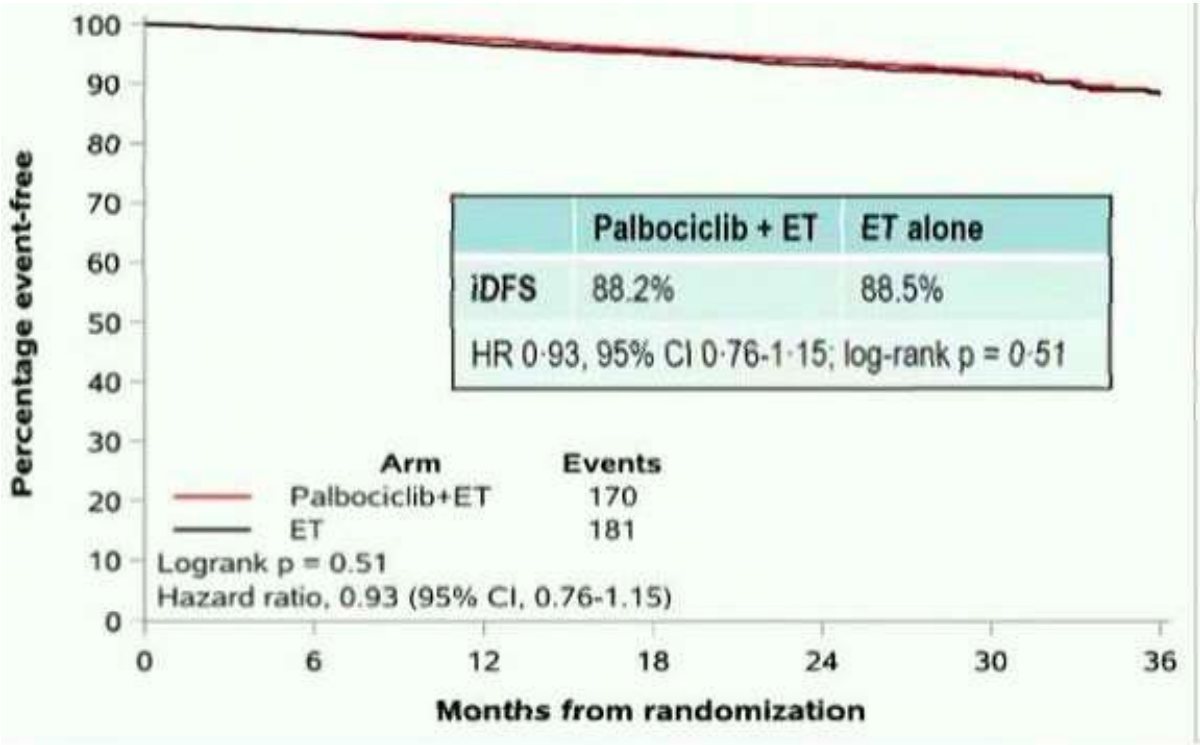
Variable	Palbociclib + ET (N=2,883)	ET (N=2,877)
Age (y) – median (range)	52 (25 – 90)	52 (22 – 85)
Stage		
IIA	504 (17·5%)	509 (17·7%)
IIB	968 (33·6%)	951 (33·1%)
III	1402 (48·6%)	1408 (48·9%)
T-Stage		
T0/T1/Tis/TX	557 (19·3%)	500 (17·4%)
T2	1603 (55·6%)	1636 (56·9%)
T3/T4	722 (25·0%)	741 (25·8%)
N-Stage		
N0	367 (12·7%)	383 (13·3%)
N1	1427 (49·5%)	1415 (49·2%)
N2	703 (24·4%)	709 (24·6%)
N3	385 (13·4%)	370 (12·9%)
Histologic Grade		
G1	300 (10·4%)	313 (10·9%)
G2	1622 (56·3%)	1658 (57·6%)
G3	836 (29·0%)	767 (26·7%)
Prior Chemotherapy	2384 (82·7%)	2370 (82·4%)
Initial Adjuvant Endocrine Therapy		
Aromatase inhibitor	1954 (67·8%)	1918 (66·7%)
Tamoxifen	923 (32·0%)	949 (33·0%)
Concurrent Adjuvant LHRH Agonist	532 (18·5%)	604 (21.1%)

ESMO 2020

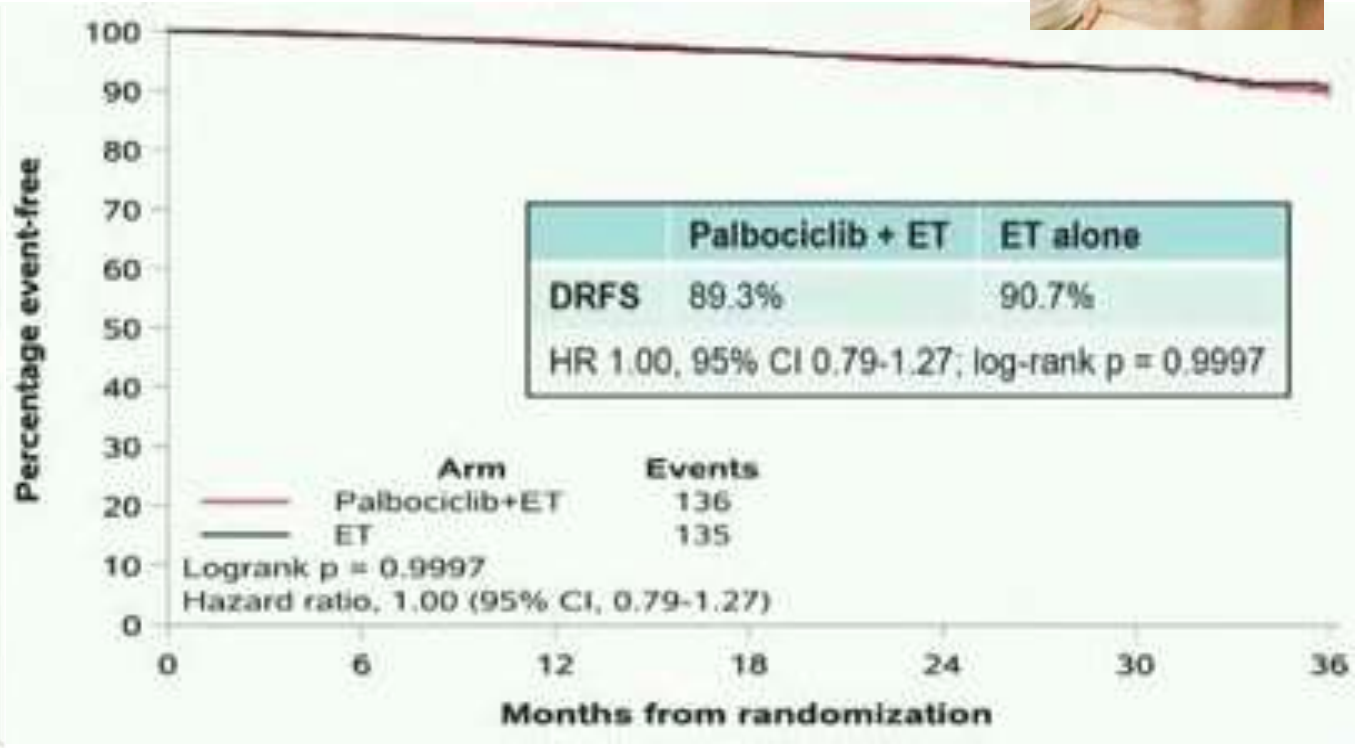
PALLAS Trial

- At IA2, with 351 iDFS events, the futility boundary for iDFS was crossed.
- The IDMC subsequently recommended discontinuation of palbociclib in remaining Arm A patients.

iDFS



dDFS



Reflexiones sobre el PALLAS

- Muchas interrupciones y retrasos en el brazo experimental: Quimioterapia previa en el 82%
- 41% de pacientes incluídas: “bajo riesgo” de recaída.
- Análisis en función de cumplimiento terapéutico: Sin diferencias *(Gnant M, et al. JCO 2022)*
- Análisis en función de dosis administrada de palbociclib: Sin diferencias. *(Gnant M, et al. JCO 2022)*
- **Escenario biológico de la adyuvancia ≠ metastásica**
- ¿Ineficacia de Palbociclib en este contexto?

Penelope B Trial

Looking for the luminal high risk-patient

- **II-III HR+ HER2-**
- 16 weeks **NACT** Tax based
- **No pCR**

Residual Disease

- **CPS-EG ≥ 3**
- **CPS-EG 2 ypN+**

N = 1250 pts

RTP

R

Endocrine Therapy (TAM, AI +/- LH-rH agonist + PLACEBO x 13 cycles

- ❑ CPS-EG sore ≥ 3 *v* 2/ypN+
- ❑ Ki-67 (≤ 15% *v* > 15%)
- ❑ ypN0-1 *v* ypN2-3
- ❑ >50 vs < 50
- ❑ Asian *v* non-Asian

Endocrine Therapy + PALBOCICLIB 125 mg/d x 21 /28 days, x 13 cycles

- **iDFS**
- iDFS exc 2nd non breast
- dDFS
- LRFS
- OS
- Safety
- Compliance

25% of patients with non pCR. DFS 70-77% 5 years

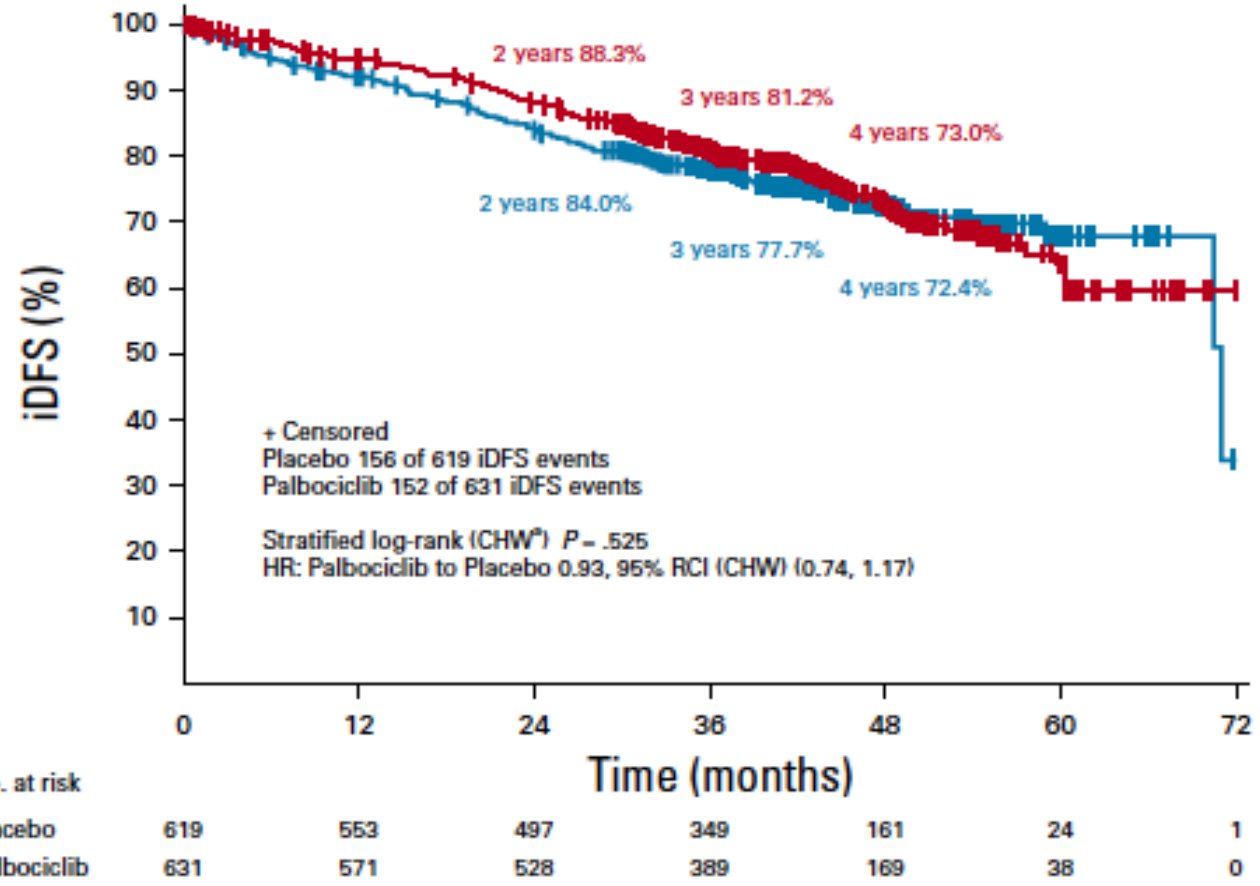
Hypothesis: HR for palbociclib/placebo: 0.685 (from 77% to 83.6% 3-year iDFS rate).
iDFS events: 255. Sample size.1,100 patients.

Loibl S, et al. JCO 2021

Penelope B Trial: Site of first iDFS event

Median FU of 42.8 months (92% complete). 308 events confirmed.
Palbociclib did not improve iDFS: HR: 0.93 (95%CI, 0.74 to 1.17) and two-sided weighted log-rank test p 0.525.

First iDFS Event	Palbociclib (n = 631), No. (Valid %)	Placebo (n = 619), No. (Valid %)	Overall (N = 1,250), No. (Valid %)
Patients with event	152 (24.1)	156 (25.2)	308 (24.6)
Site of first invasive disease event[a]			
Distant recurrence	116 (76.3)	111 (71.2)	227 (73.7)
Invasive locoregional recurrence	21 (13.8)	27 (17.3)	48 (15.6)
Contralateral breast cancer	2 (1.3)	5 (3.2)	7 (2.3)
Second primary invasive nonbreast cancer	9 (5.9)	9 (5.8)	18 (5.8)
Death without previous event	4 (2.6)	4 (2.6)	8 (2.6)



Loibl S, et al. JCO 2021

Reflexiones sobre PENELOPE-B

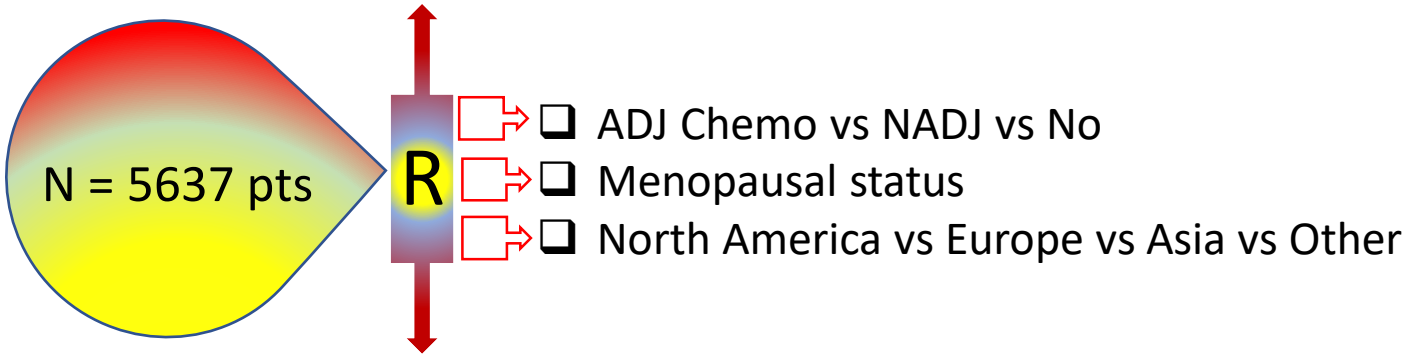
- 20% no completó los 13 ciclos (En PALLAS, 37% no completó dos años de palbociclib)
- Estudio robusto, contra placebo a doble ciego.
- Pacientes de alto riesgo. Casi el 100% recibió RTP.
- El brazo control se comportó exactamente como se hipotetizó en el diseño del estudio: iDFS a 3 años 77%
- ¿Es el palbociclib? ¿Un año?

MONARCH E Trial

- HR+ HER2- **High risk N+**
- Prior Surgery+/- CHEMO
- Within 16 m of surgery
- Within 12 w of starting ET

- N2-N3 (≥ 4 nodes)
- N1a + T > 5 cm
  or GIII
  or Ki-67 ≥ 20%
  517 pts

Endocrine Therapy (5 10 y): AI or TAMOX +/- LH-rH agonist



Endocrine Therapy (5-10 y) **+ ABEMACICLIB** 150 mg tid, x **2 years**

- **iDFS**
- dRFS

OS
Pk
Safety
PROs

Hypothesis: **β** 0.15. HR of 0.73 at a cumulative two-sided **α** level of .05, with a 5-year IDFS rate of 82.5% in the control arm. 390 iDFS events (ITT)

Monarch E: Patients

95%

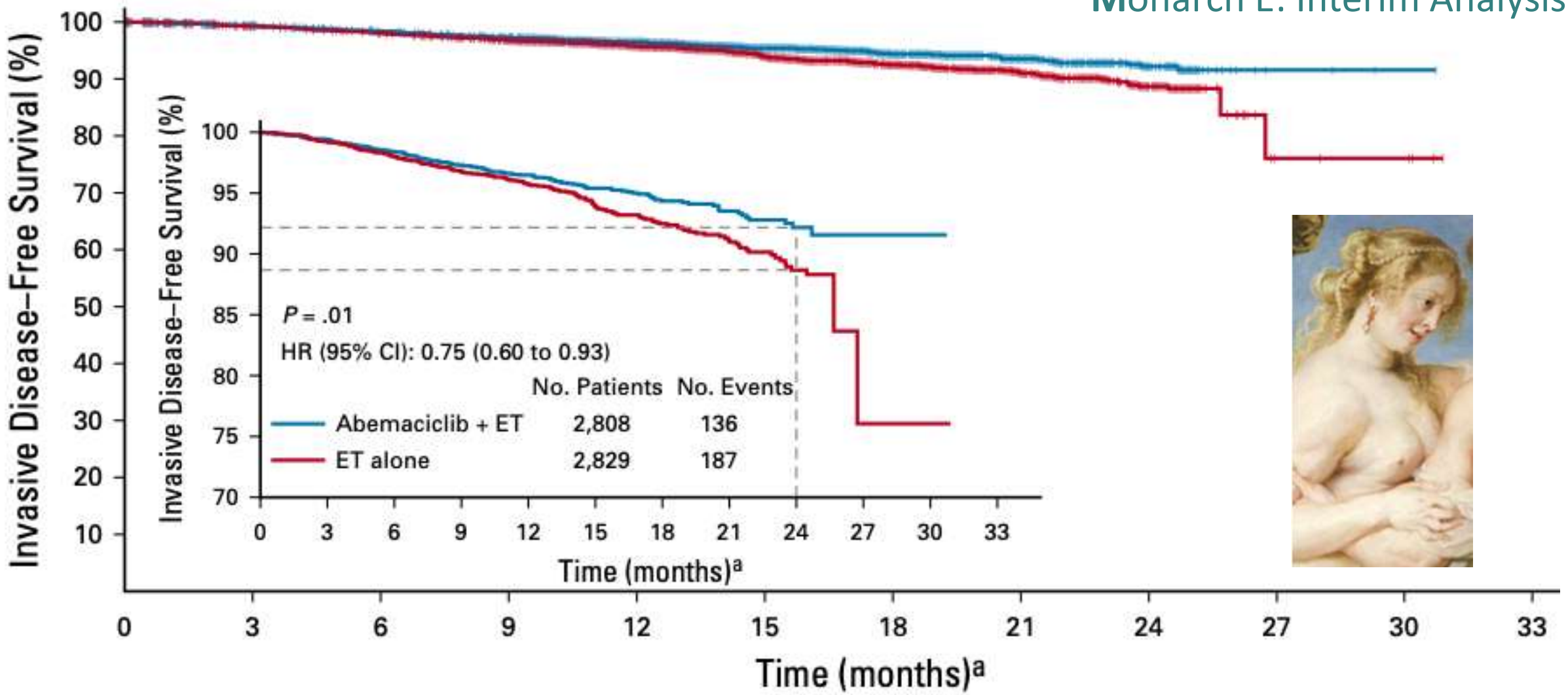
		Abemaciclib + ET N=2808, %	ET Alone N=2829, %
Age	Median (range)	51 (23-89)	51 (22-86)
Age categories	<65 years	84.4	85.4
Gender	Female	99.3	99.5
Menopausal Status[1]	Premenopausal	43.5	43.5
	Postmenopausal	56.5	56.5
Prior Chemotherapy[1]	Neoadjuvant	37.0	37.0
	Adjuvant	58.5	58.2
	None	4.5	4.7
Baseline ECOG PS	0	85.7	83.8
Pathologic Tumor Size	<2 cm	27.8	27.1
	2 - 5 cm	48.9	50.2
	≥5 cm	21.6	21.6
Number of Positive Lymph Nodes	1-3	39.8	40.4
	≥4	59.9	59.6
Histological Grade	Grade 1	7.4	7.6
	Grade 2	49.0	49.3
	Grade 3	38.7	37.6
Central Ki-67	<20%	33.9	34.4
	≥20%	44.9	43.6
	Unavailable	21.1	21.8

Monarch E: Analysis Timepoints

Analysis Timepoints	Interim Analysis[a,1-2]	Primary Outcome[3]	Additional Follow-up 1 (AFU1)
Date	16 March 2020	08 July 2020	01 April 2021
Median Follow-up (months)	15.5	19.1	27.1
IDFS Events	323	395	565
Off Study Treatment	26.4%	41.0%	89.6%
Completed 2-year Treatment Period	12.5%	25.5%	72.2%

[1] *J O'Shaughnessy, et al. ESMO Virtual Plenary, Oct 2021*
[2] *SBR Johnston, et al JCO 2020*
[3] *P Rastogi , et al. SABCS 2020*

Monarch E: Interim Analysis



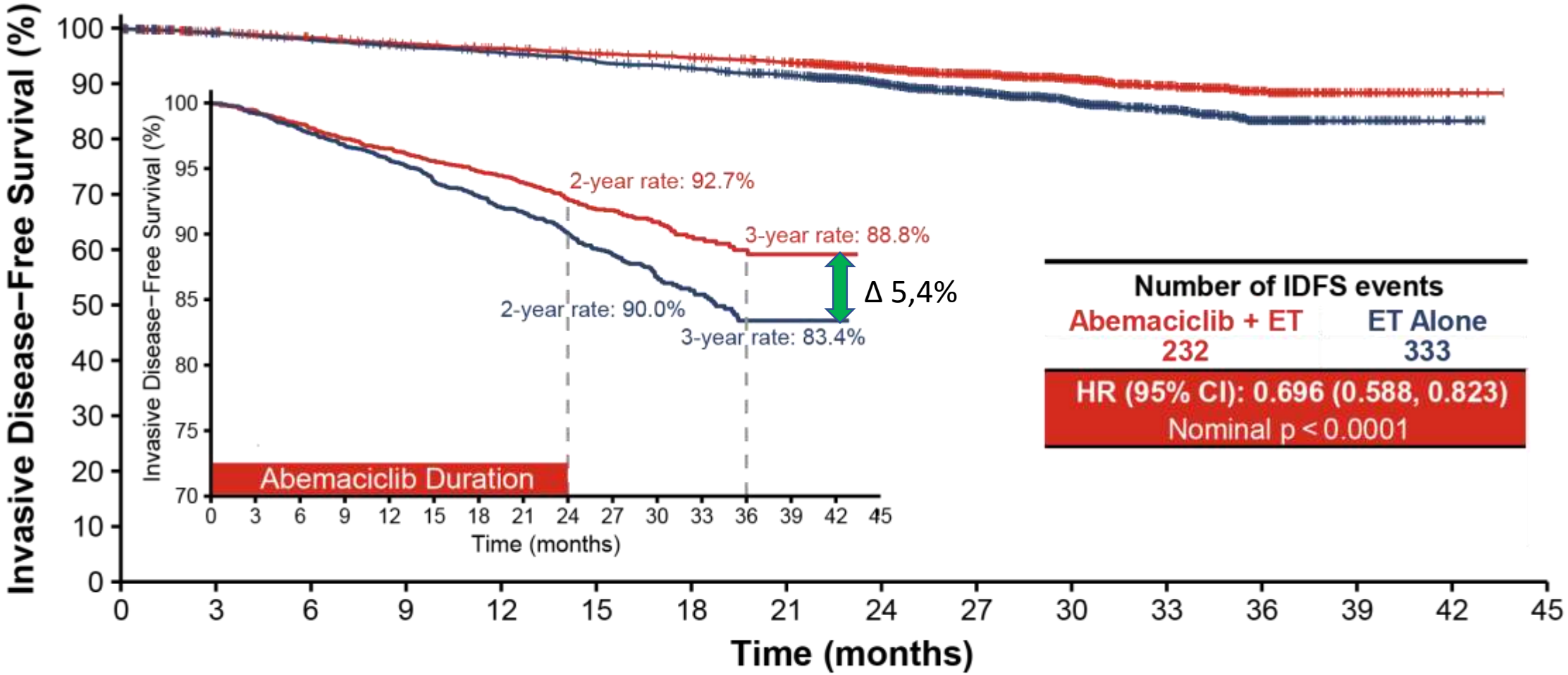
No. at risk:

2,808	2,676	2,613	2,543	1,996	1,371	918	566	245	3	1	0
2,829	2,699	2,649	2,562	2,013	1,405	932	586	262	7	6	0

SRD Johnston, et al. J Clin Oncol 2020; 38:3987-3998.

Median follow-up: 27,1 months

Monarch E: iDFS.Additional FU

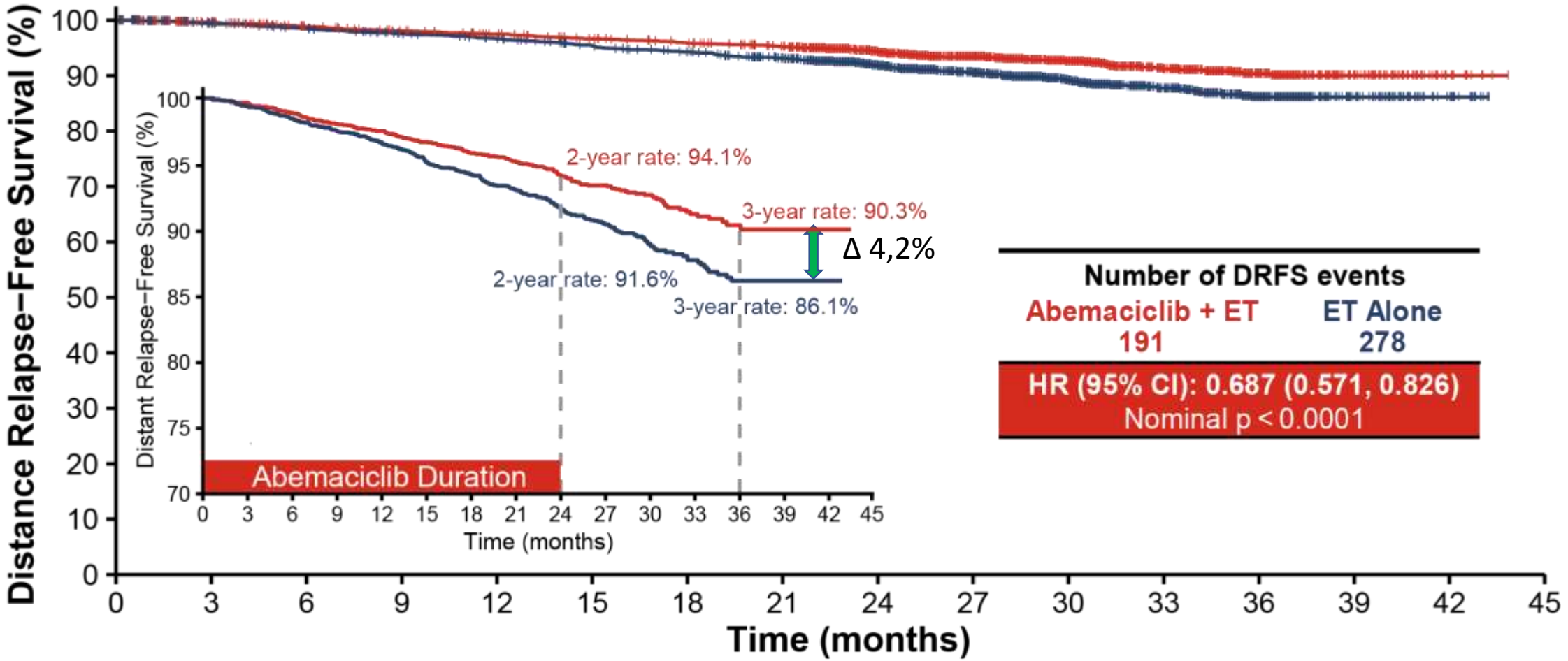


Number at risk																
Abemaciclib + ET	2808	2680	2621	2579	2547	2508	2477	2430	1970	1287	919	522	275	67	8	0
ET Alone	2829	2700	2652	2608	2572	2513	2472	2400	1930	1261	906	528	281	64	10	0

J O'Shaughnessy, et al. ESMO Virtual Plenary, Oct 2021

Median follow-up: 27,1 months

Monarch E: **dDFS**. Additional FU

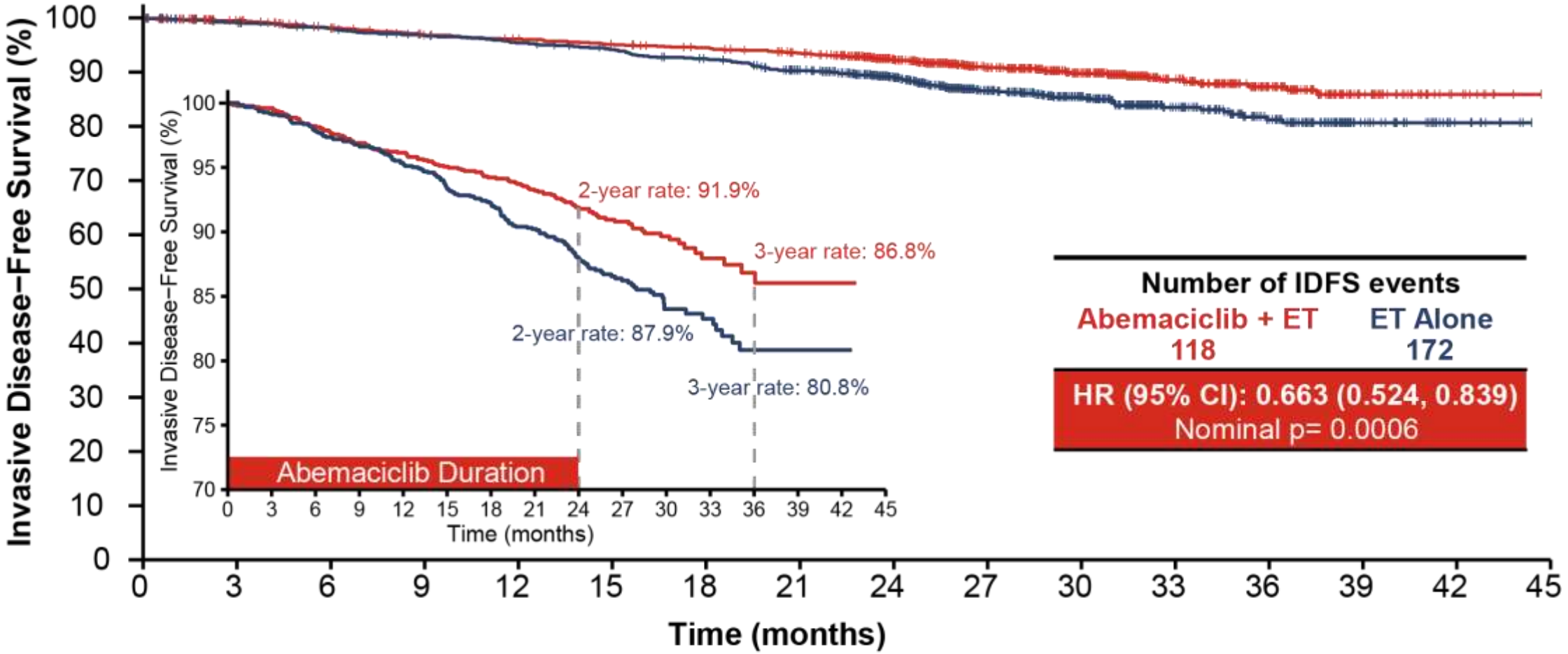


Number at risk																
Abemaciclib + ET	2808	2684	2629	2595	2566	2529	2497	2455	1990	1300	930	530	281	68	8	0
ET Alone	2829	2704	2660	2622	2591	2535	2499	2427	1955	1287	924	537	287	66	10	0

J O'Shaughnessy, et al. ESMO Virtual Plenary, Oct 2021

IDFS in ITT Ki-67 High (≥ 20%) Population

Median follow-up: 27,1 months

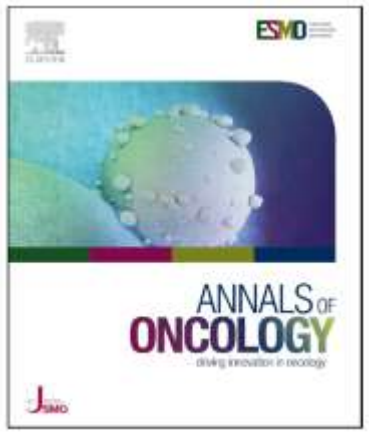


Number at risk																
Abemaciclib + ET	1262	1221	1189	1167	1155	1139	1123	1094	870	546	377	203	109	25	2	0
ET Alone	1236	1197	1177	1158	1142	1114	1096	1041	827	520	367	198	107	25	3	0

J O'Shaughnessy, et al. ESMO Virtual Plenary, Oct 2021

Monarch E: Ki-67 iDFS. Additional FU

	Patients	Events	
Cohort 1 Ki-67-high			
Abemaciclib + ET	1017	104	HR = 0.63 (95% CI 0.49-0.80)
ET alone	986	158	
Cohort 1 Ki-67-low			
Abemaciclib + ET	946	62	HR = 0.70 (95% CI 0.51-0.98)
ET alone	968	86	



N Harbeck, et al. Ann Oncol 2021

Reflexiones iniciales sobre Monarch E

- Impacto significativo sobre iDFS y dDFS
- La selección de pacientes de alto riesgo, ¿implica haber incluído más pacientes “metastásicas” que se han beneficiado del ciclib?
- ¿Es abemaciclib diferente en este contexto?
- ¿Es la pauta continua la clave?
- Ki-67 tiene claro valor pronóstico, pero NO es predictivo de beneficio para Abemaciclib
- ¿Qué % de pacientes recibieron iCDK4/6 a la recaída?

New Adjuvant TriAl with LEE011

The third one

- **II-III HR+ HER2-**
- **NACT or ACT**
- **Surgery and RT**
- < 18 months from Dx

III N_{0-3}
IIb (N_0 and N_1)
IIa (N_1)
IIa (N_0)

N = 5101 pts

R

Endocrine Therapy (AI +/- LH-rH agonist) + PLACEBO x 13 cycles

- ❑ II *vs* III
- ❑ Premenopausal *vs* Postmenopausal
- ❑ Neoadjuvant *vs* not.
- ❑ North Am+ West Eur + Oceania *vs* rest of the World

Endocrine Therapy + RIBOCICLIB 400 mg/d x 21 /28 days, x 3 years

- **iDFS**
- RFS
  dDFS
  OS
  QoL
  Safety
  Compliance
  Pk

- 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

¿Son diferentes en eficacia Abema y Ribo?

New Adjuvant TriAl with LEE011

The third one

- **IIA,IIB, III HR+ HER2-**
- **NACT or ACT**
- **Surgery and RT**
- ET < 12 months

N = 5101

· Stage II recruitment capped alt 40%
· Enrollment: Jan 2019→ April 2021

R

Endocrine Therapy (LET or ANA +/- LH-rH agonist for ≥ 5 years

- ❑ II *vs* III
- ❑ Premenopausal *vs* Postmenopausal
- ❑ Neoadjuvant *vs* not.
- ❑ North Am+ West Eur + Oceania *vs* rest of the World

Endocrine Therapy **+ Ribociclib** 400 mg/d x 21 /28 days, for 3 years

- **iDFS**
  - RFS
    dDFS
    OS
    QoL-PROs
    Safety
    Pks
    - LRR-FS
    - ctDNA/ctRNA

Hypothesis: 500 events: 85% power to detect a hazard ratio for invasive disease, recurrence, or death of 0.76 at a one-sided alpha level of 0.025.

¿Afectación axilar?

- **Anatomical stage IIA**
- **N_0** with:
  - Grade 3 and evidence of high risk
    - Ki-67 ≥20%
    - Oncotype DX Breast Recurrence Score≥26 ***or***
    - High risk via genomic risk profiling
  - Grade 3
- **N_1**

- **Anatomical stage IIB**
- **N_0** or **N_1**

- **Anatomical stage III**
- **N_0**, **N_1**, **N_2**, or **N_3**

T1N1,
T1N2,
T1N3
T2N1
T2N2
T2N3
T3N1
T3N2
T3N3
T4N1
T4N2
T4N3
Any ypN1
Any ypN2
Any ypN3

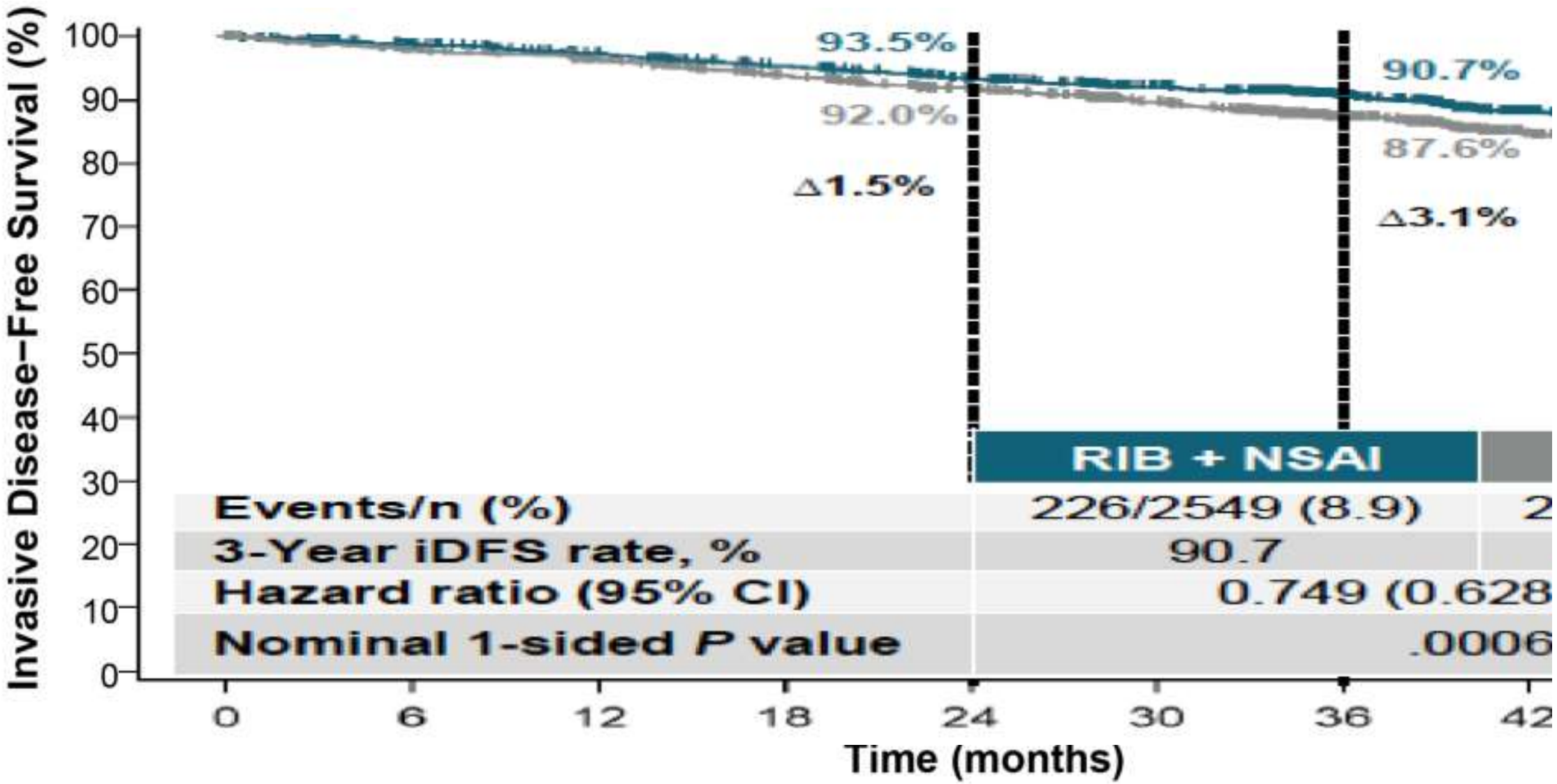
Table 1. Demographic and Baseline Clinical Characteristics.*

Characteristic	Ribociclib + NSAI (N=2549)	NSAI Alone (N=2552)	All Patients (N=5101)
Median age (range) — yr	52 (24–90)	52 (24–89)	52 (24–90)
Menopausal status — no. (%)			
Premenopausal women	1115 (43.7)	1123 (44.0)	2238 (43.9)
Postmenopausal women	1423 (55.8)	1420 (55.6)	2843 (55.7)
Nodal status at diagnosis — no. (%)‡			
NX	272 (10.7)	264 (10.3)	536 (10.5)
N0	694 (27.2)	737 (28.9)	1431 (28.1)
N1	1050 (41.2)	1049 (41.1)	2099 (41.1)
N2 or N3	483 (18.9)	467 (18.3)	950 (18.6)
Data missing	50 (2.0)	35 (1.4)	85 (1.7)
Nodal status at surgery — no. (%)‡			
NX	2 (0.1)	5 (0.2)	7 (0.1)
N0	378 (14.8)	418 (16.4)	796 (15.6)
N1	1062 (41.7)	1039 (40.7)	2101 (41.2)
N2 or N3	1105 (43.4)	1089 (42.7)	2194 (43.0)
Data missing	2 (0.1)	1 (<0.1)	3 (0.1)

4295/5101: 84%

Slamon D, et al. NEJM 2024

Median follow-up for iDFS: 36 months



Slamon D, et al. SABCS 2023

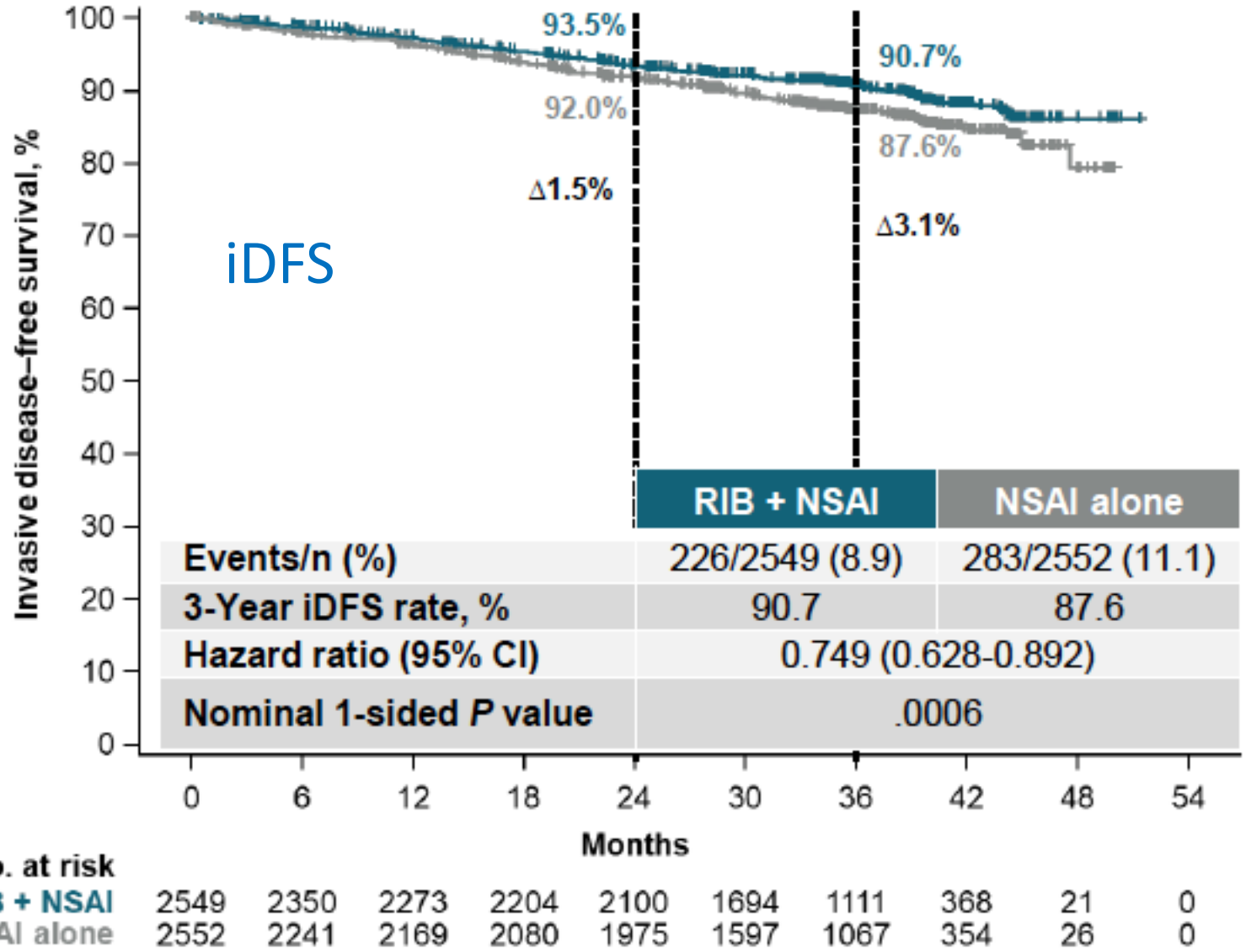
Median follow-up for iDFS: 33.3 months

Final iDFS Analysis

Data cutoff: July 21, 2023
iDFS events: n=509

- **Ribociclib + NSAI, n=2549**
- NSAI ongoing: 1914 (75.1%)
- **RIB ongoing: 528 (20.7%)**

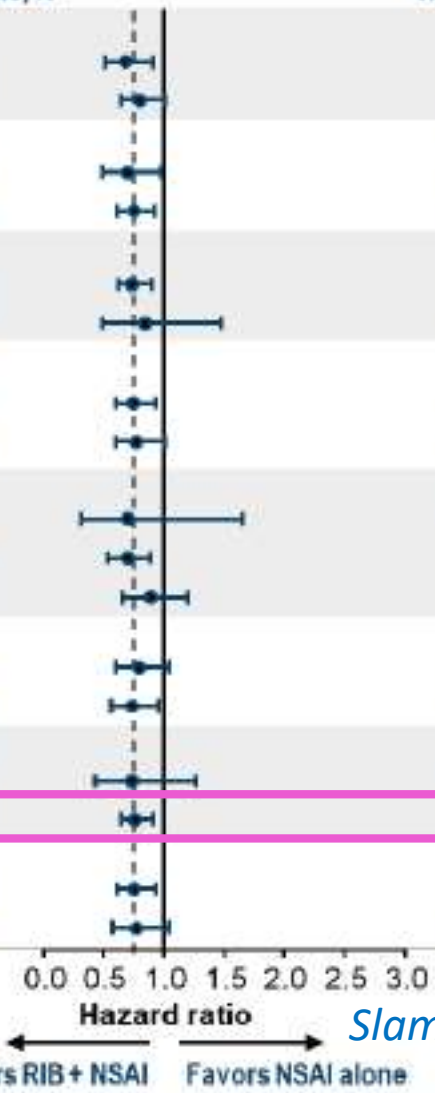
- Stopped RIB: 1996 (78.3%)
- Completed 3 years: 1091 (42.8%)
- **Early discontinuation: 905 (35.5%)**
- Discontinued due to AEs: 498 (19.5%)



Slamon D, et al. SABCS 2023

NATALEE TRIAL. IDFS: KEY PRESPECIFIED SUBGROUPS

Subgroup	RIB + NSAI Events/n	RIB + NSAI 3-y iDFS rate, %	NSAI alone Events/n	NSAI alone 3-y iDFS rate, %	Hazard ratio	95% CI
Menopausal status						
Men and premenopausal women	83/1125	91.8	114/1132	88.2	0.688	0.519-0.913
Postmenopausal women	143/1424	89.7	169/1420	87.1	0.806	0.645-1.007
AJCC stage						
Stage II	55/1101	94.2	80/1034	92.6	0.700	0.496-0.986
Stage III	170/1528	88.1	203/1512	83.8	0.755	0.616-0.926
Prior CT						
Yes	203/2249	90.5	255/2245	87.1	0.746	0.620-0.897
No	23/300	92.0	28/307	91.2	0.852	0.491-1.479
Region						
North America/Western Europe/Oceania	131/1563	91.1	166/1565	87.5	0.748	0.595-0.941
Rest of world	95/986	90.1	117/987	87.6	0.774	0.591-1.015
Histological grade at time of surgery						
Grade 1	9/213	95.1	13/217	93.1	0.708	0.303-1.657
Grade 2	118/1460	91.5	155/1432	88.0	0.696	0.548-0.885
Grade 3	80/684	87.5	89/702	85.9	0.890	0.658-1.204
Ki-67 status[a]						
Ki-67 ≤20%	93/1199	91.8	117/1236	89.8	0.794	0.605-1.042
Ki-67 >20%	98/920	89.0	125/937	84.9	0.743	0.570-0.968
Nodal status[b,c]						
N0	20/285	93.2	31/328	90.6	0.723	0.412-1.268
N1-N3	206/2261	90.3	251/2219	87.1	0.759	0.631-0.912
Prior ET						
Yes	150/1826	91.4	186/1805	88.4	0.755	0.609-0.936
No	76/723	88.9	97/747	85.8	0.771	0.571-1.040

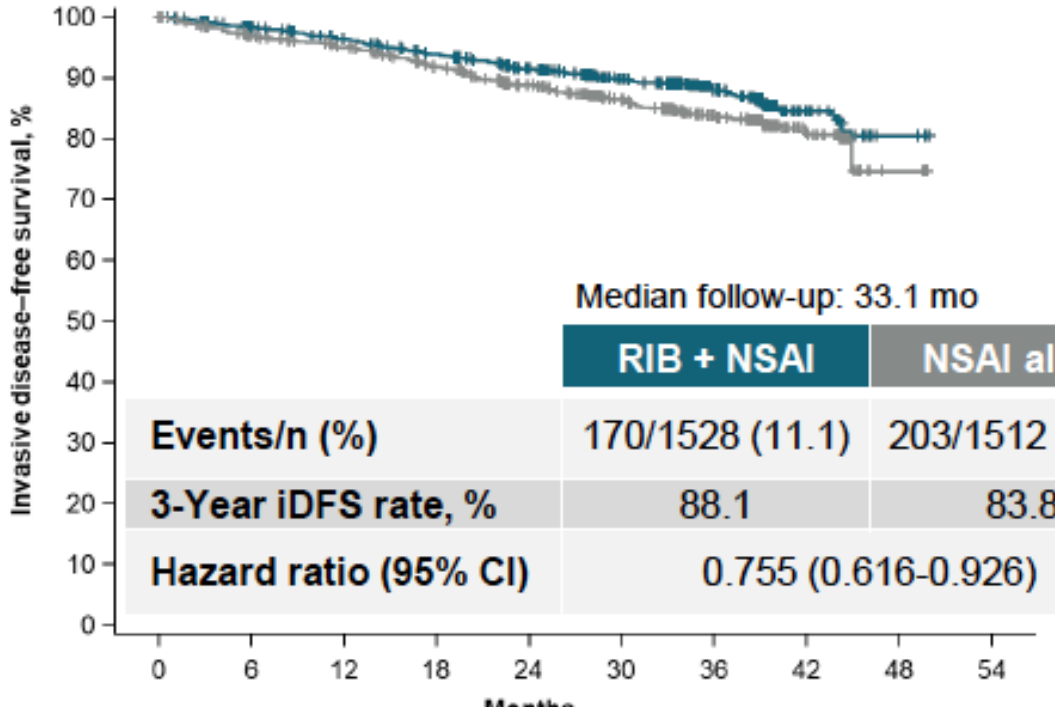


AJCC, American Joint Committee on Cancer; CT, chemotherapy.
[a] From archival tumor tissue. [b] Nodal status classification according to AJCC staging.
[c] Nodal status is from the worst stage derived per surgical specimen or at diagnosis.

Slamon D, et al. SABCS 2023

NATALEE TRIAL. IDFS: NODAL RISK

Stage III

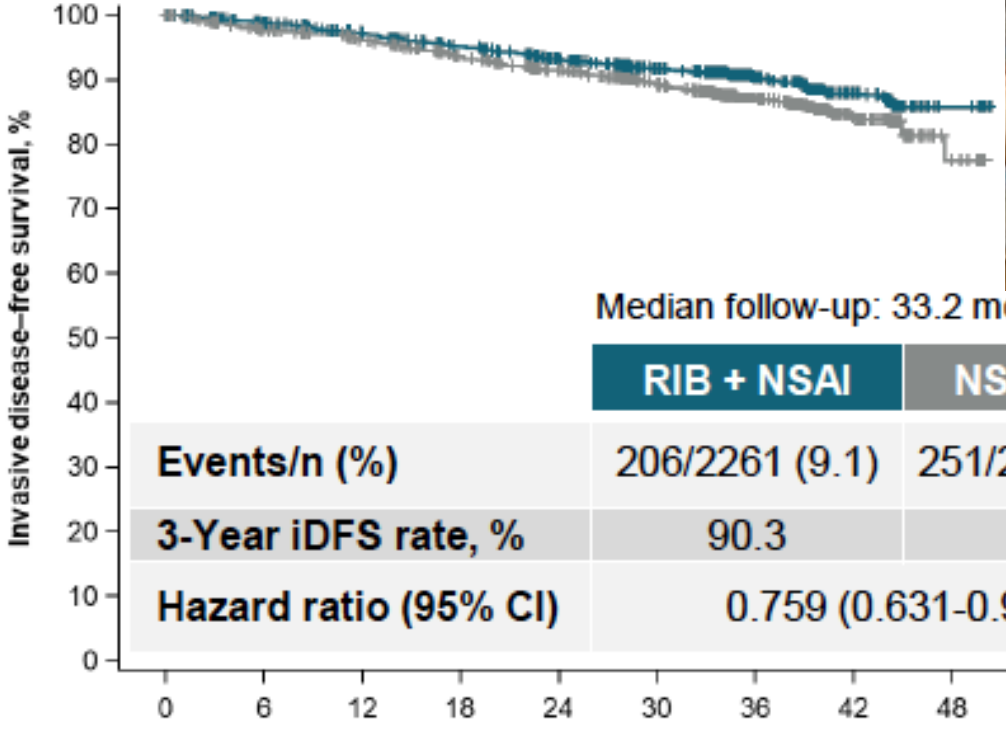


Median follow-up: 33.1 mo

	RIB + NSAI	NSAI alone
Events/n (%)	170/1528 (11.1)	203/1512 (13.4)
3-Year iDFS rate, %	88.1	83.8
Hazard ratio (95% CI)	0.755 (0.616-0.926)	

No. at risk										
RIB + NSAI	1528	1411	1362	1312	1232	844	496	174	6	0
NSAI alone	1512	1289	1241	1183	1099	753	456	151	8	0

N1-N3



Median follow-up: 33.2 mo

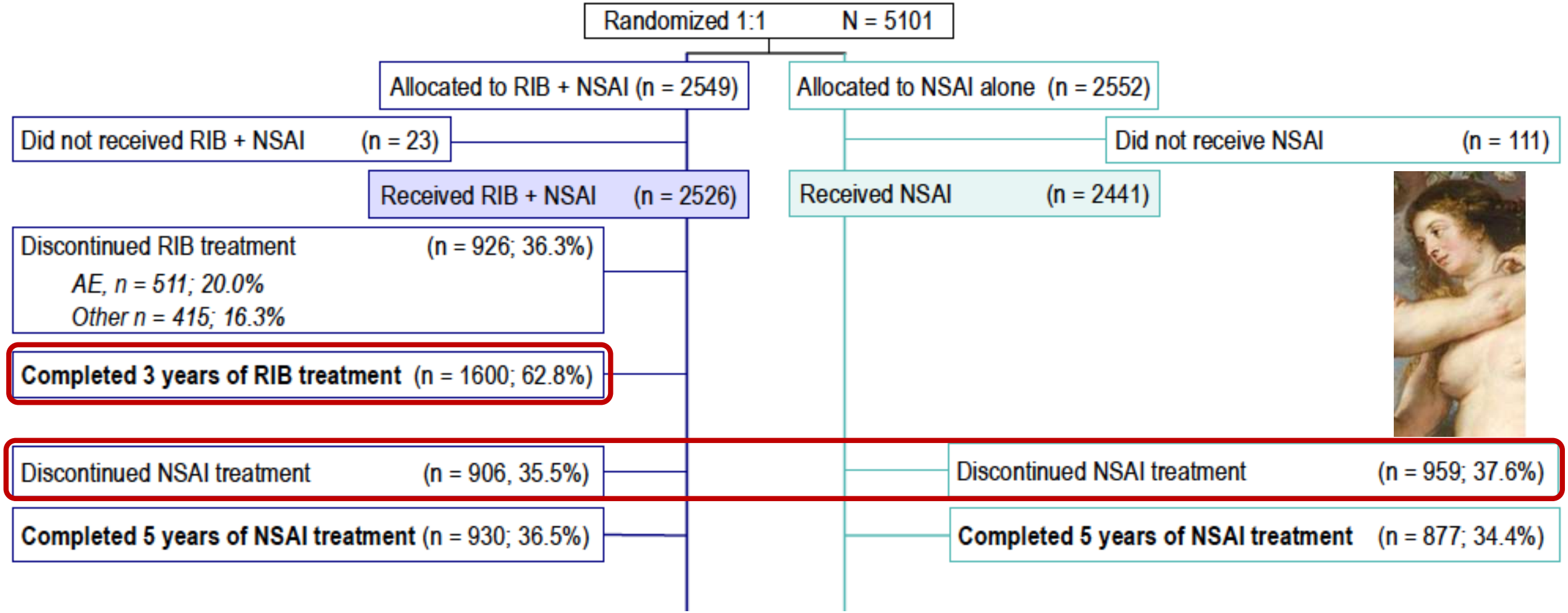
	RIB + NSAI	NSAI alone
Events/n (%)	206/2261 (9.1)	251/2219 (11.3)
3-Year iDFS rate, %	90.3	87.1
Hazard ratio (95% CI)	0.759 (0.631-0.912)	

No. at risk										
RIB + NSAI	2261	2085	2012	1951	1853	1458	934	301	16	0
NSAI alone	2219	1938	1873	1791	1697	1337	877	273	21	0

Slamon D, et al. SABCS 2023

Current data

Prespecified 5-y analysis of NATALEE: Median iDFS-FU: 55.4 months
All patients being **off ribociclib** treatment (median 2 years)



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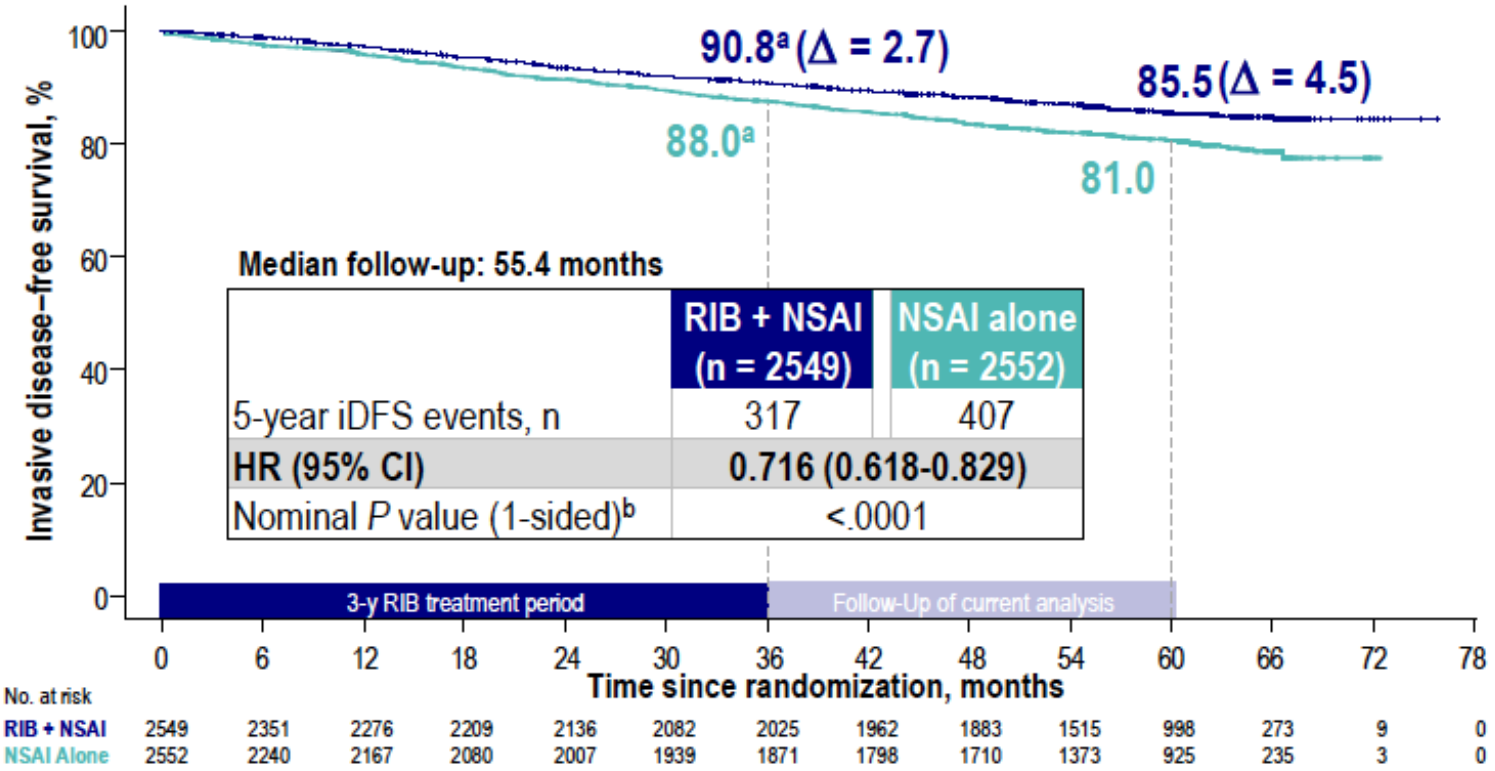
NATALEE:
Median iDFS-FU: 55.4 months



ITT Population	RIB + NSAI n = 2549	NSAI Alone n = 2552
iDFS event type, n (%)		
Distant recurrence	**207 (8.1)**	**290 (11.4)**
Local/regional invasive recurrence	29 (1.1)	56 (2.2)
Second primary nonbreast cancer	49 (1.9)	52 (2.0)
Death	23 (0.9)	14 (0.5)
Invasive contralateral breast tumor	14 (0.5)	14 (0.5)
Invasive ipsilateral breast tumor	8 (0.3)	11 (0.4)

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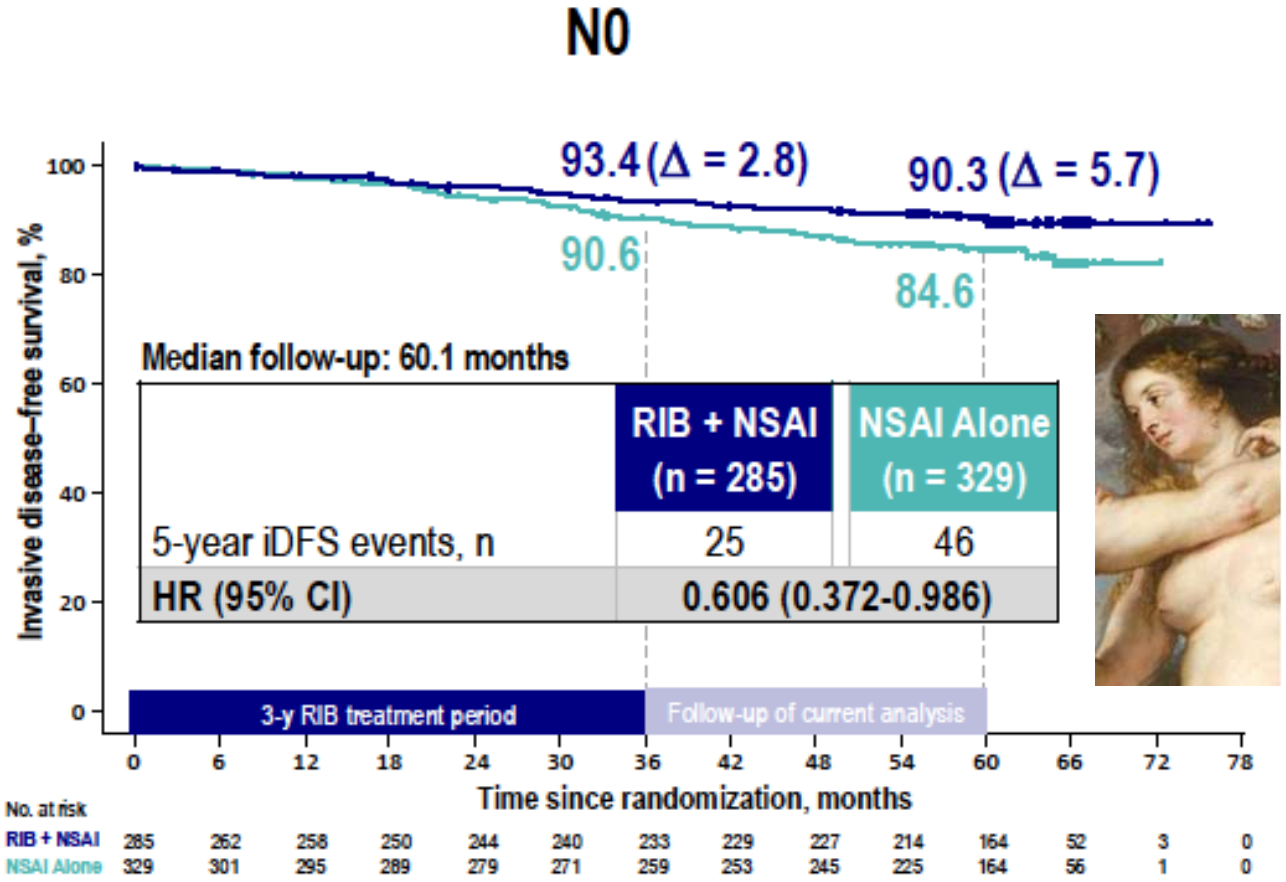
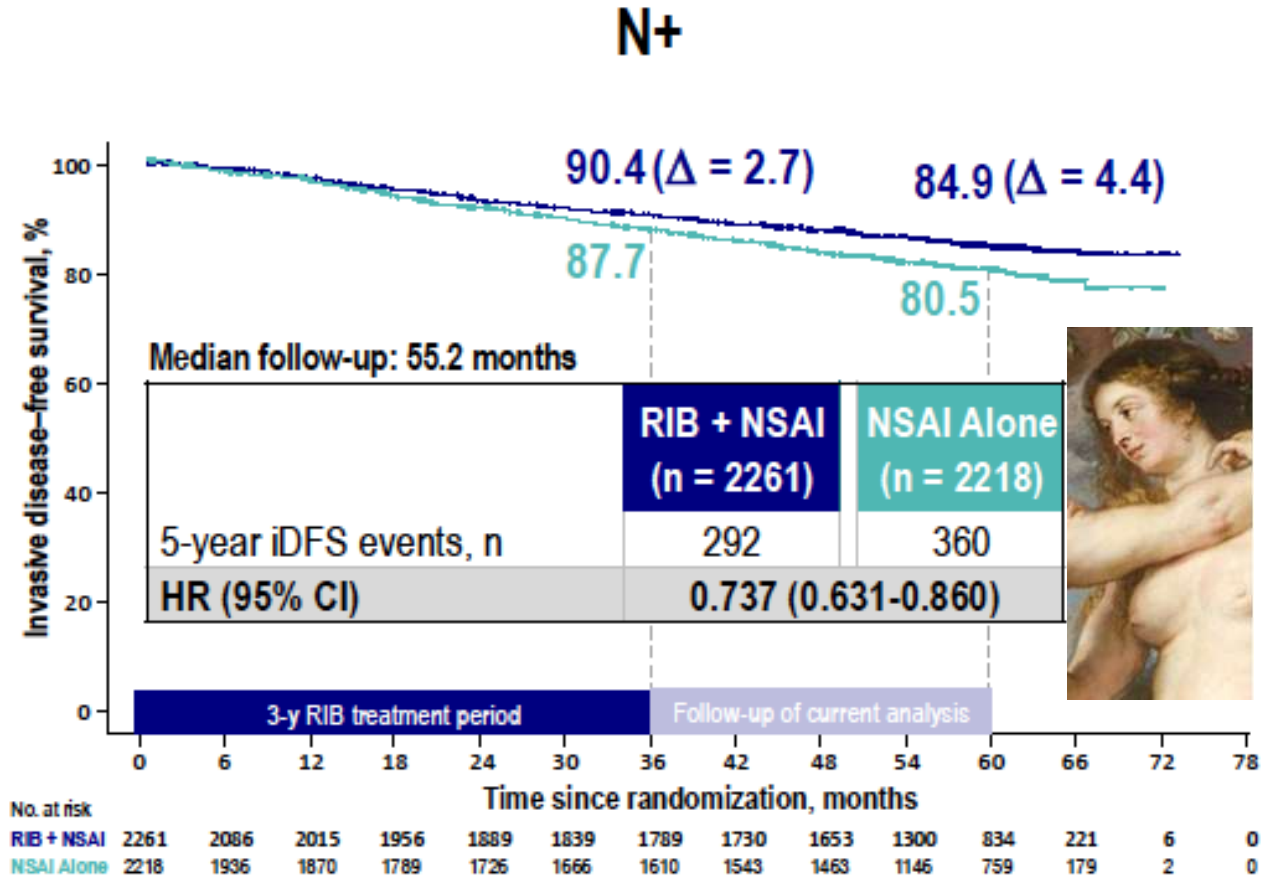
NATALEE:
Median iDFS by Nodal status





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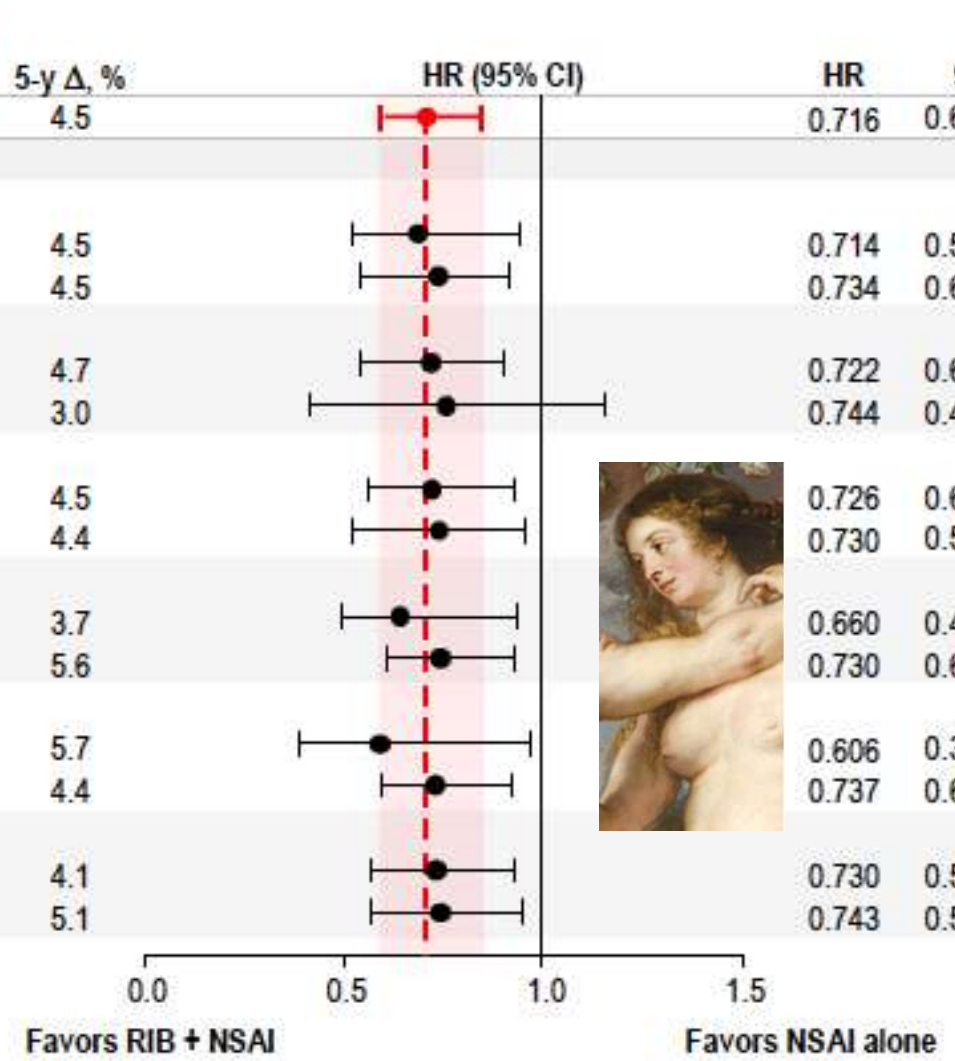
NATALEE:
Median iDFS-FU: 55.4 months

	RIB + NSAI		NSAI alone				
	Events/n	5-y iDFS rate, %	Events/n	5-y iDFS rate, %	5-y Δ, %	HR	95% CI
ITT	317/2549	85.5	407/2552	81.0	4.5	0.716	0.618-0.829
SUBGROUPS							
Menopausal status							
Premenopausal women and men	124/1126	87.1	162/1132	82.6	4.5	0.714	0.565-0.902
Postmenopausal women	193/1423	84.3	245/1420	79.7	4.5	0.734	0.608-0.887
Prior CT[a]							
Yes	290/2249	84.9	370/2245	80.2	4.7	0.722	0.619-0.842
No	27/300	89.6	37/307	86.6	3.0	0.744	0.453-1.222
Prior ET							
Yes	220/1832	85.8	278/1807	81.3	4.5	0.726	0.608-0.867
No	97/717	84.6	129/745	80.3	4.4	0.730	0.561-0.950
AJCC stage							
Stage II	75/1012	91.7	113/1034	87.9	3.7	0.660	0.493-0.884
Stage III	241/1527	81.2	294/1512	75.6	5.6	0.730	0.615-0.865
Nodal status[b]							
N0	25/285	90.3	46/329	84.6	5.7	0.606	0.372-0.986
N1-N3	292/2261	84.9	360/2218	80.5	4.4	0.737	0.631-0.860
Ki-67 status[c]							
Ki-67 ≤20%	132/1200	87.0	177/1241	83.0	4.1	0.730	0.583-0.915
Ki-67 >20%	138/919	83.2	172/932	78.1	5.1	0.743	0.594-0.930



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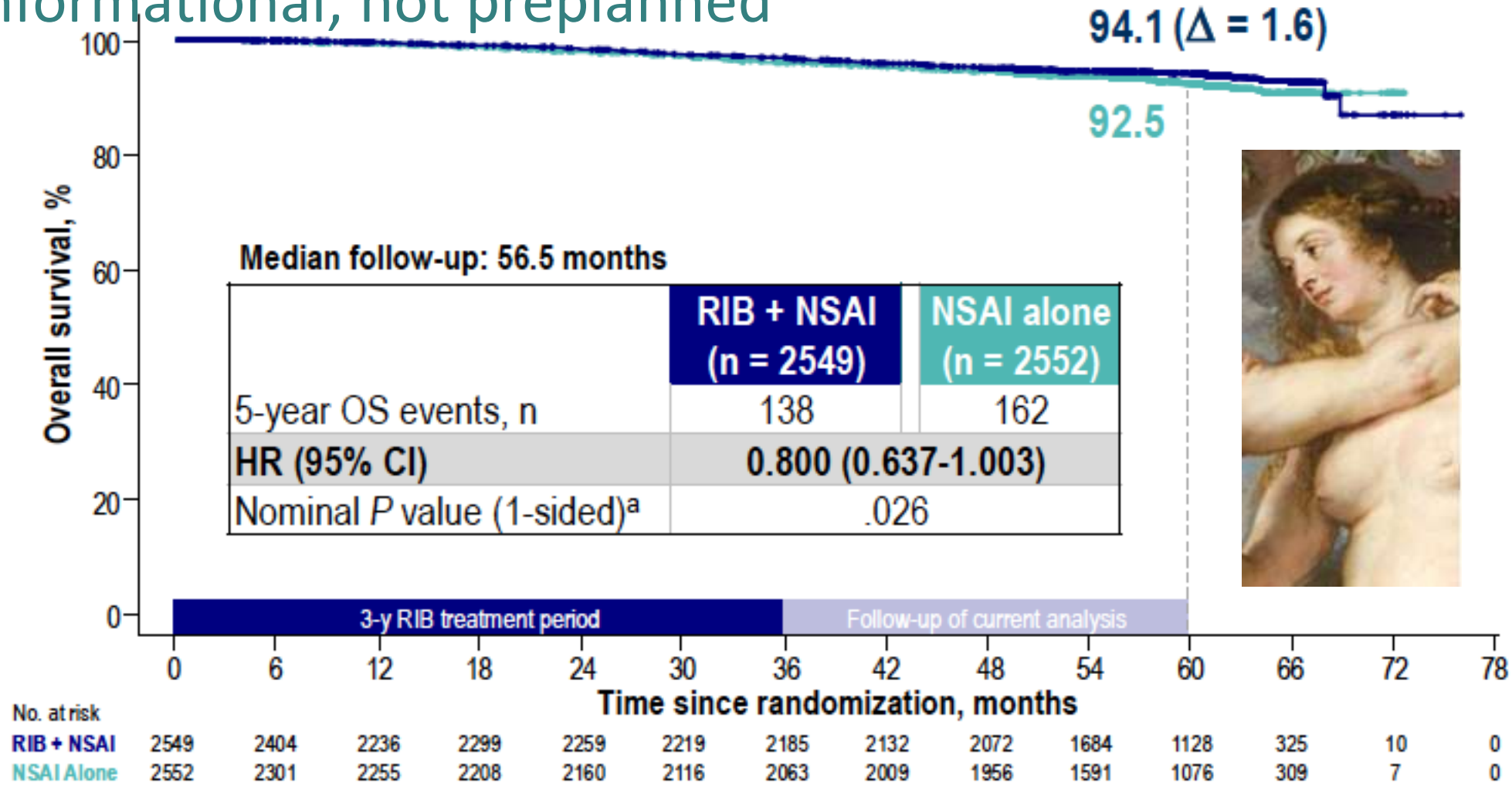
NATALEE:
OS-FU: Informational, not preplanned



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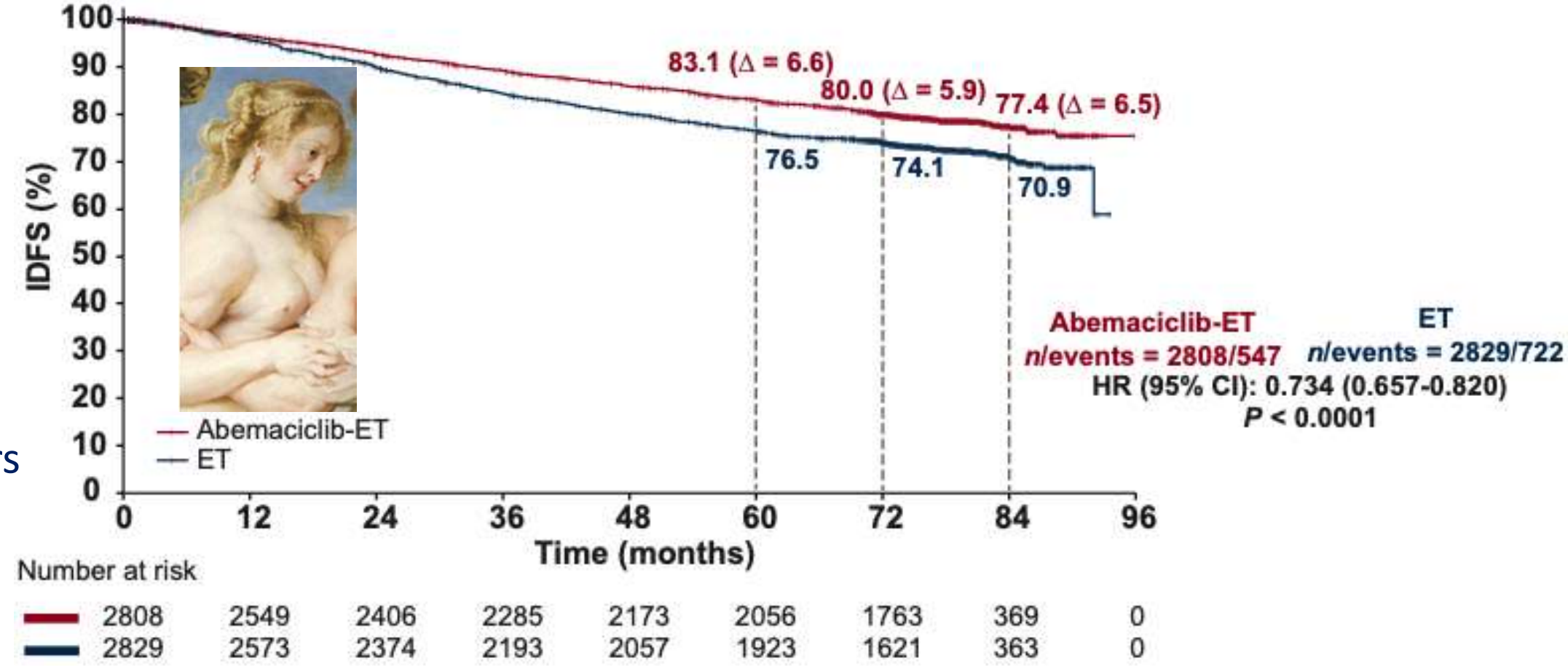
Monarch-E:
Median iDFS : 76 months.

All patients were off abemaciclib for four or more years



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Monarch-E:
First recurrence: 76 months.

	Abemaciclib + ET N=2555*	ET N=2565*
Patients with any disease recurrence, n (%)	**473 (18.5)**	**649 (25.3)**
Type of recurrence event, n (%)		
Distant recurrence	359 (14.1)	495 (19.3)
Locoregional recurrence	65 (2.5)	95 (3.7)
Second primary neoplasm	44 (1.7)	50 (1.9)
Contralateral breast cancer	13 (0.5)	21 (0.8)
Site of initial distant recurrence		
Bone	160 (6.3)	252 (9.8)
Liver	93 (3.6)	129 (5.0)
Lung	65 (2.5)	68 (2.7)
Lymph Node	29 (1.1)	43 (1.7)
Brain/Central Nervous System	25 (1.0)	31 (1.2)
Pleura	7 (0.3)	26 (1.0)

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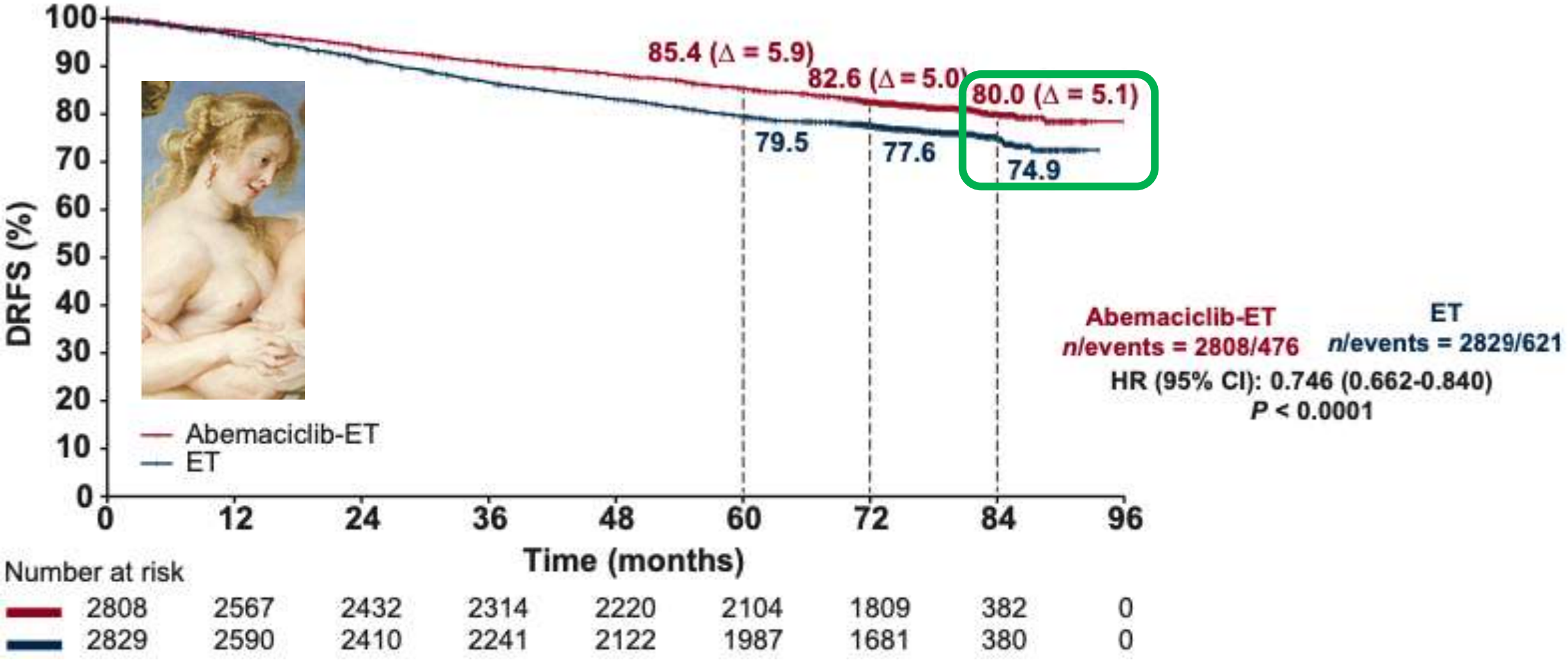
Monarch-E:
Median DRFS : 76 months.



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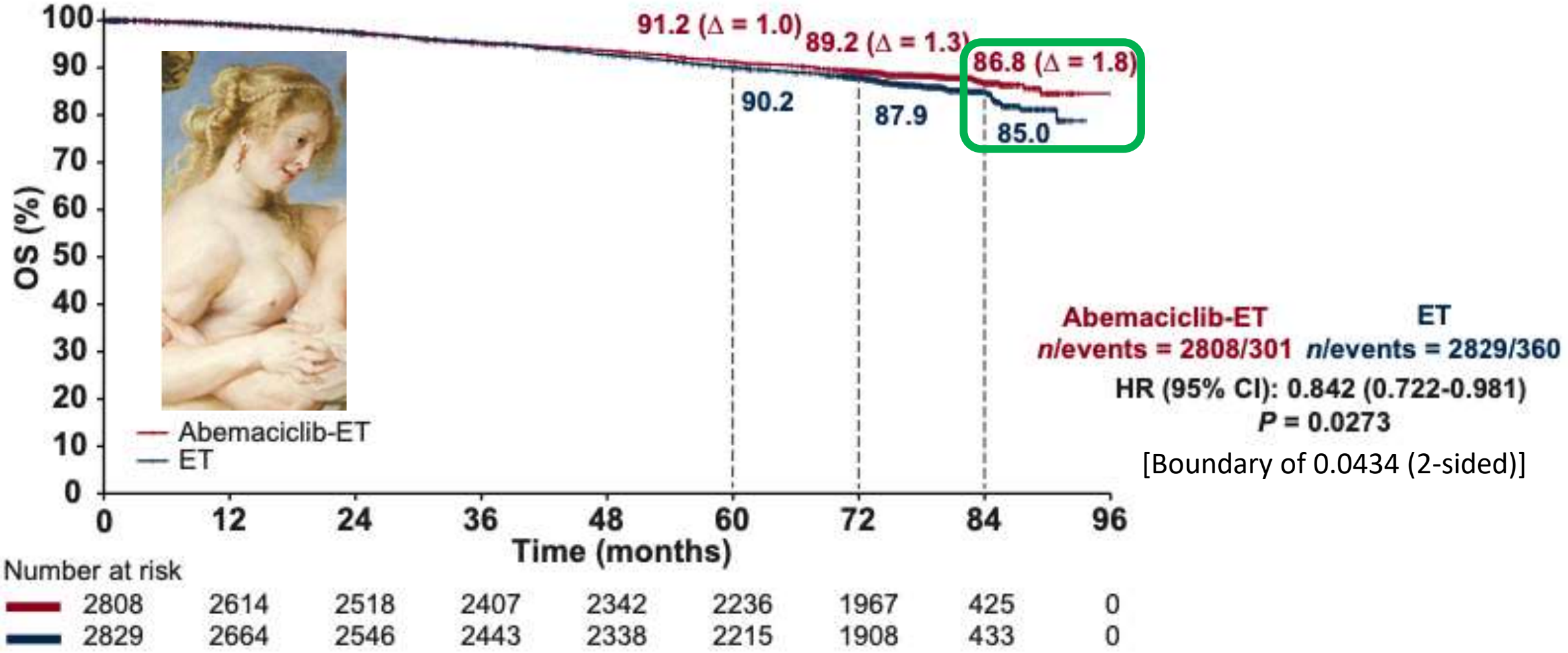
Monarch-E:
OS ITT Population : med FU 76 months.



Abemaciclib-ET *n*/events = 2808/301

ET *n*/events = 2829/360

HR (95% CI): 0.842 (0.722-0.981)

***P* = 0.0273**

[Boundary of 0.0434 (2-sided)]

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Monarch-E:

Systemic anticancer therapies received as first-line treatment in the metastatic setting.

Patients with distant recurrence who entered post-discontinuation follow-up	Abemaciclib—ET $N = 407$	ET $N = 565$
Any systemic therapy, *n* (%)	321 (78.9)	471 (83.4)
Endocrine therapy,[a] *n* (%)	190 (46.7)	330 (58.4)
Fulvestrant	117 (28.7)	188 (33.3)
Letrozole	40 (9.8)	95 (16.8)
Exemestane	20 (4.9)	18 (3.2)
Anastrozole	12 (2.9)	23 (4.1)
Tamoxifen	7 (1.7)	20 (3.5)
Targeted therapy, *n* (%)	135 (33.2)	276 (48.8)
CDK4/6i	122 (30.0)	267 (47.3)
Palbociclib	44 (10.8)	100 (17.7)
Ribociclib	54 (13.3)	90 (15.9)
Abemaciclib	23 (5.7)	83 (14.7)
PI3K/AKT/mTOR pathway inhibitors	13 (3.2)	4 (0.7)
Chemotherapy, *n* (%)	133 (32.7)	134 (23.7)
Other[b], *n* (%)	21 (5.2)	27 (4.8)
Bevacizumab	8 (2.0)	11 (1.9)

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My most critical views, in sum up

- **Most patients do not benefit** from adjuvant treatment with CDK4/6i.
- We don’t have effective tools to identify and select high risk patients who really benefit from CDK4/6 inh in the adjuvant setting.
- Most patients did not receive CDK4/6i at relapse*. Potential bias for OS analysis in the following years.
- Informative censoring to be explained*
- More FU is needed to understand the real long-term benefit of CDK4/6 inh in the adjuvant setting.
- New scenarios at relapse

My most positive views, in sum up

- Abemaciclib and Ribociclib add benefit in terms of iDFS in the adjuvant setting, mostly and **certainly meaningful** in terms of **DRFS** for patients who meet MONARCH E and NATALEE inclusion criteria.
- After a FU of 76 months, Abemaciclib demonstrates a **modest increase** in **OS** (1.8% in absolute terms). It takes a long time to demonstrate OS benefits in HR-pos HER2-neg breast cancer. Anyway there's a trend.
- Different **toxicity profiles** with no new findings after relevant follow up. Significant percentage of patients who do not complete the tratment.
- Financial toxicity...
- Daily practice "toxicity" for Med Oncs and HS for 2 or 3 years: More complexity in the day-to-day practice of oncologists and patients.

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GRACIAS