Endocrine Therapy for Early and Late Stage Breast Cancer: Therapeutic Updates

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NATALEE Study Design[1-3]

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

N=5101[b]

R 1:1[c]

Ribociclib 400 mg/d
3 wk on/1 wk off
for 3 y

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

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

Primary End Point
- iDFS using STEEP criteria

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

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

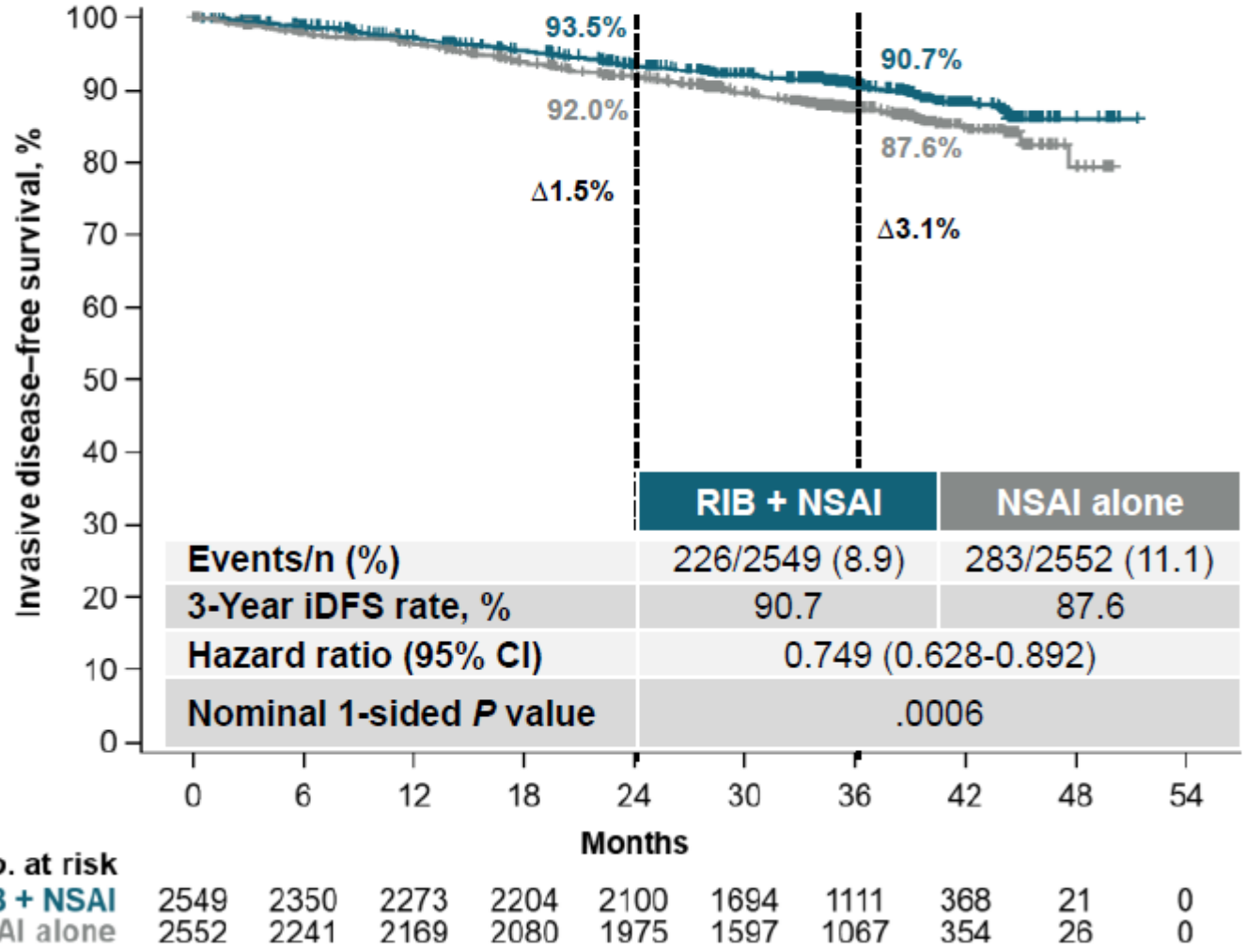
Randomization stratification
Anatomical stage: II vs III
Menopausal status: men and premenopausal women vs postmenopausal women
Receipt of prior (neo)adjuvant chemotherapy: yes vs no
Geographic location: North America/Western Europe/Oceania vs rest of world

ct, circulating tumor; EBC, early breast cancer; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; iDFS, invasive disease–free survival; N, node; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; PK, pharmacokinetics; PRO, patient-reported outcome; R, randomized; STEEP, Standardized Definitions for Efficacy End Points in Adjuvant Breast Cancer Trials.

[a] Enrollment of patients with stage II disease was capped at 40%. [b] 5101 patients were randomized from Jan 10, 2019 to April 20, 2021. [c] Open-label design. [d] Per investigator choice.

1. Slamon D, et al. ASCO 2023. Oral LBA500. 2. Slamon DJ, et al. *J Clin Oncol*. 2019;37(15 suppl). Abstract TPS597. 3. Slamon DJ, et al. *Ther Adv Med Oncol*. 2023;15:17588359231178125.

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.

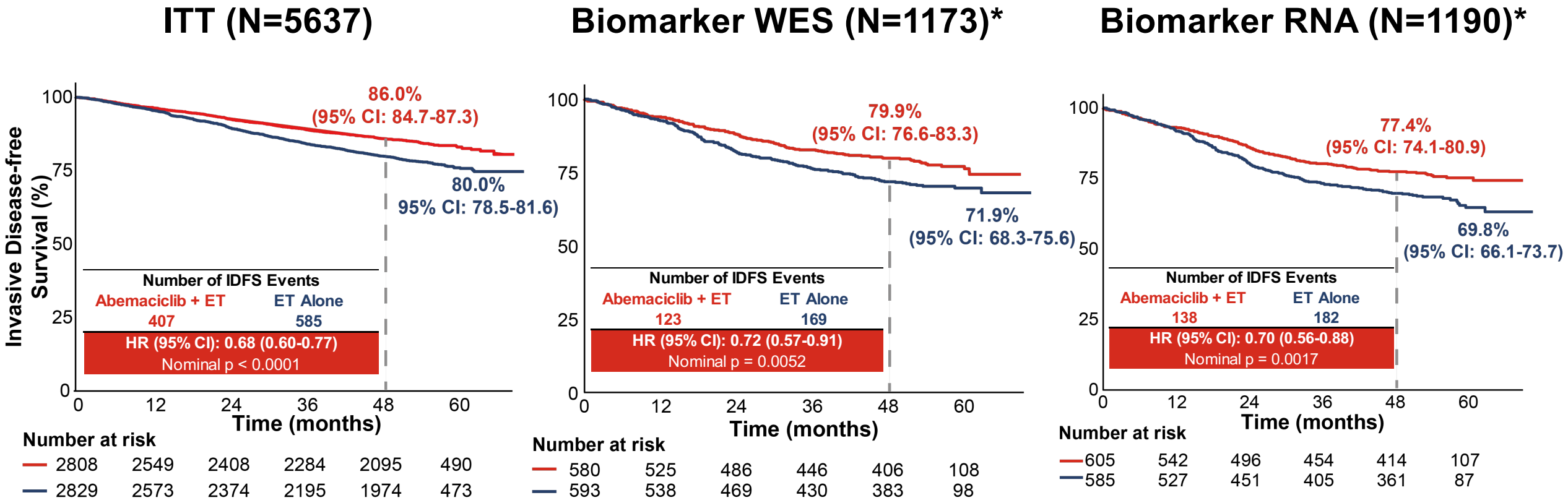
- The median follow-up for iDFS was 33.3 months (maximum, 51 months)—an additional 5.6 months from the second interim efficacy analysis[1]
- The absolute iDFS benefit with ribociclib plus NSAI was 3.1% at 3 years
- The risk of invasive disease was reduced by 25.1% with ribociclib plus NSAI vs NSAI alone

All subgroups had iDFS benefit with ribo+NSAI
- Stage II/ Stage III
- Node neg or bode positive
- Ki-67 ≤20%
- Ki-67 >20%

DRFS also remains significantly improved with no new safety concerns

Hortobagyi G et al. GS03-03

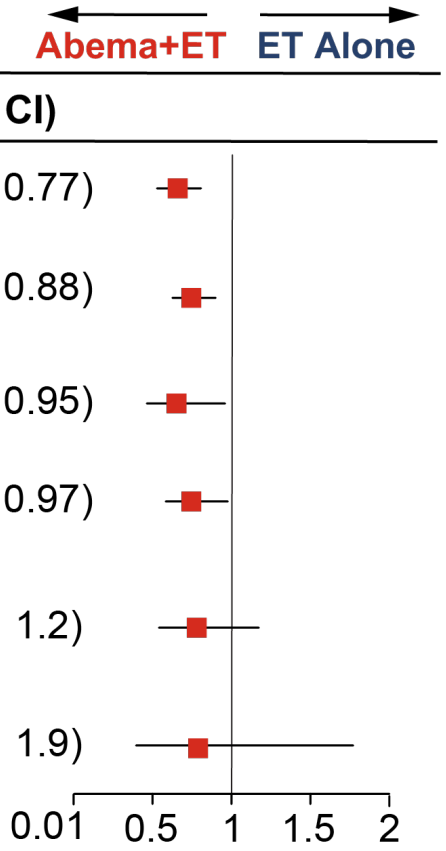
Abemaciclib benefit was consistently observed in biomarker subset of monarchE



*biomarker subsets are enriched in IDFS events and thus IDFS event rates are higher than in the ITT population

Consistent abemaciclib treatment benefit across all intrinsic molecular subtypes

	Abemaciclib + ET		ET Alone		
	Events/n (%)	4-yr IDFS Rate (95% CI)	Events/n (%)	4-yr IDFS Rate (95% CI)	HR (95% CI)
ITT	407/2808 (14%)	86.0 (84.7−87.3)	585/2829 (21%)	80.0 (78.5−81.6)	0.68 (0.60, 0.77)
Biomarker Subset	138/605 (23%)	77.4 (74.1−80.9)	182/585 (31%)	69.8 (66.1−73.7)	0.70 (0.56, 0.88)
LumA	28/230 (12%)	87.5 (83.2−92)	45/228 (20%)	81.4 (76.3−86.8)	0.59 (0.37, 0.95)
LumB	65/265 (25%)	76.3 (71.2−81.7)	88/262 (34%)	66.6 (61.1−72.7)	0.70 (0.51, 0.97)
HER2E	32/69 (46%)	52.6 (41.8−66.2)	34/59 (58%)	42.5 (31.4−57.5)	0.74 (0.46, 1.2)
Basal	9/21 (43%)	57.1 (39.5−82.8)	8/15 (53%)	46.7 (27.2−80.2)	0.75 (0.29, 1.9)



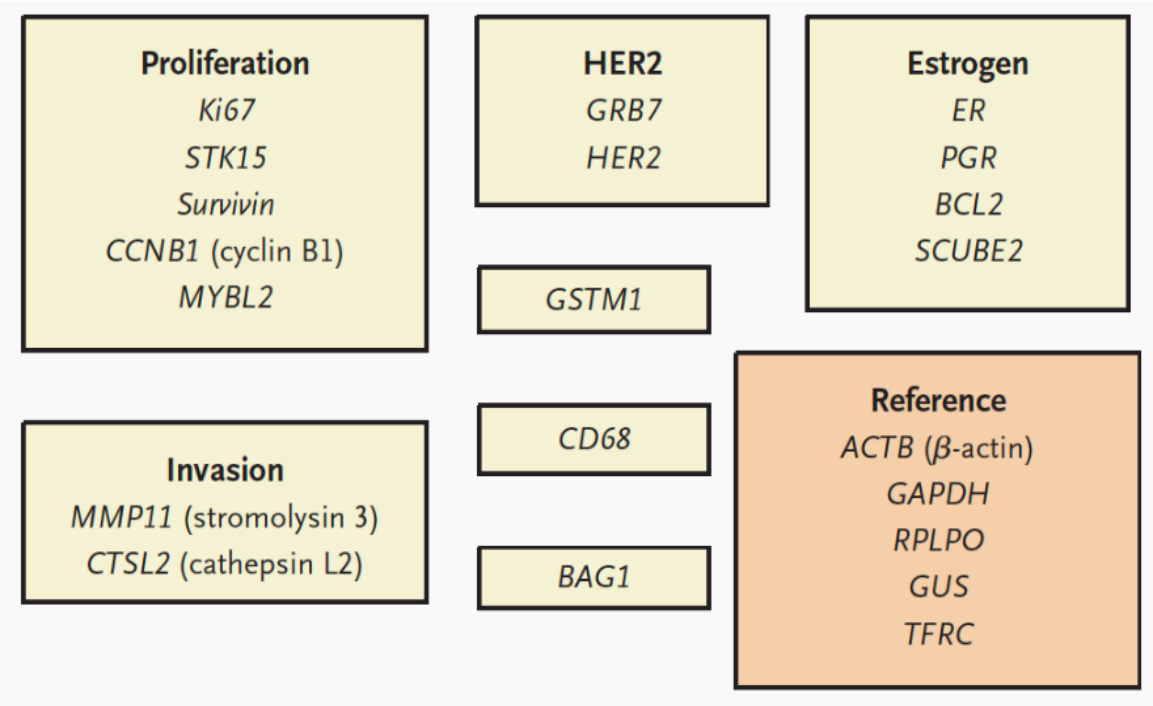
Interaction p-value (all subtypes) = 0.621

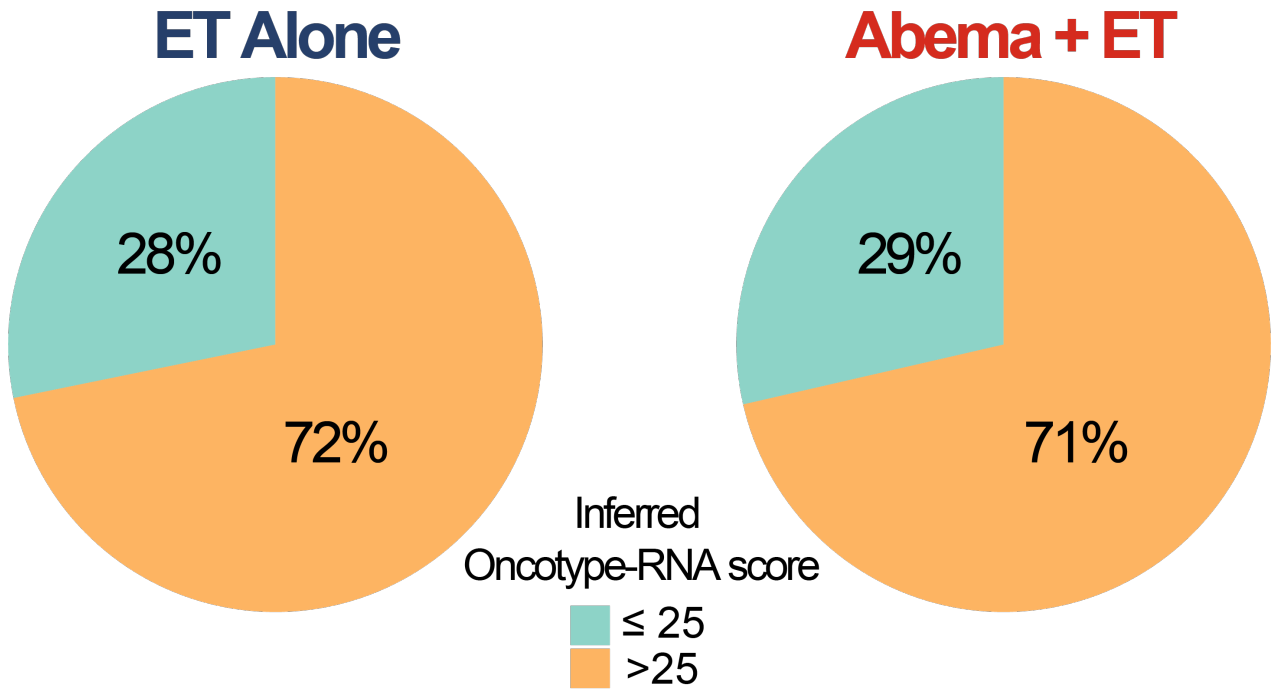
- The selected biomarker subset is enriched for IDFS events using case-cohort design
- IDFS rates are presented as indicative of relative prognosis across subtypes but do not inform the actúal risk of recurrence within each subtype because of IDFS event enrichment

LumA = luminal A, LumB = luminal B, HER2E = Human Epidermal Growth Factor Receptor 2 – Enriched

Inferred 21-gene Oncotype risk scores

21-gene Oncotype expression signature score inferred from RNAseq



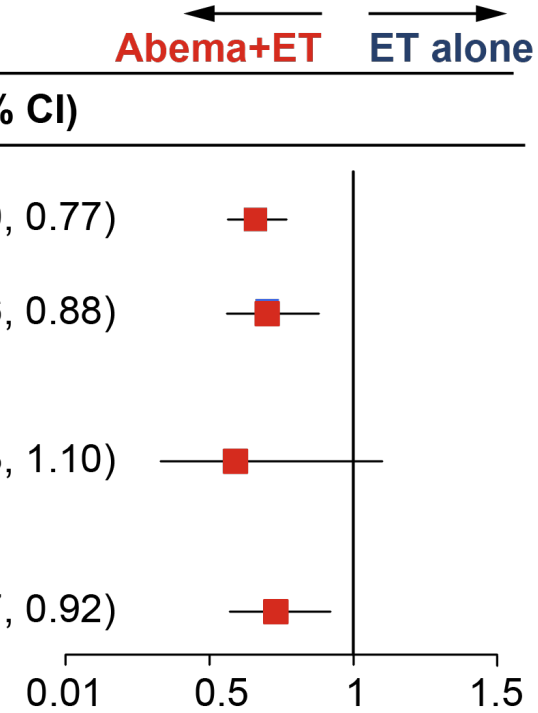


Observed high percentage of tumors with >25 risk score, reflective of the high-risk patient population

Paik, et al. 2004 N Engl J Med 351:2817-2826; Buss, et al. 2021

Treatment benefit observed in inferred Oncotype risk scores

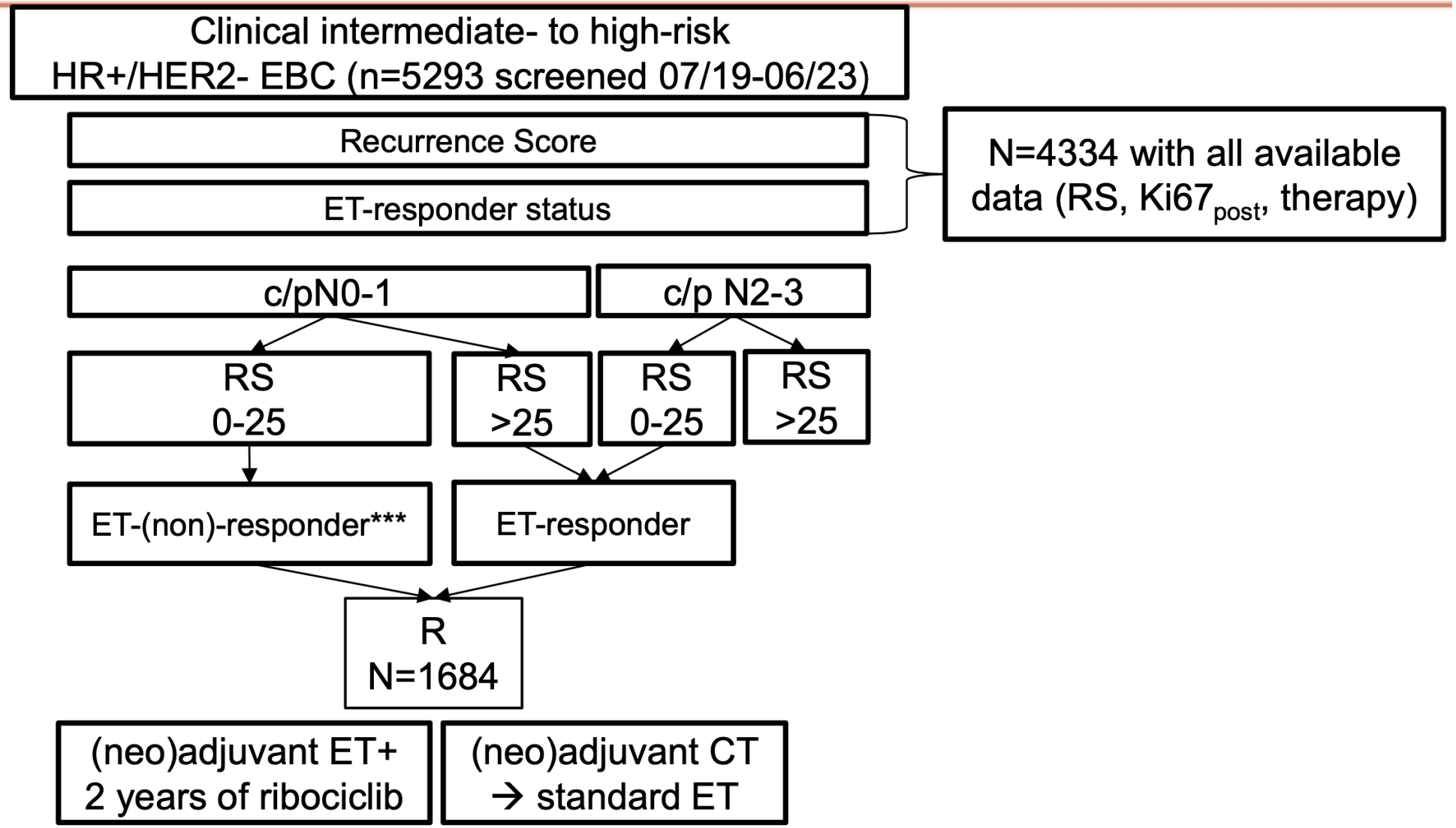
	Abemaciclib + ET		ET Alone		
	Events/n (%)	4yr IDFS Rate (95% CI)	Events/n (%)	4yr IDFS Rate (95% CI)	HR (95% CI)
ITT	407/2808 (14%)	86.0 (84.7−87.3)	585/2829 (21%)	80.0 (78.5−81.6)	0.68 (0.60, 0.77)
Biomarker Subset	138/605 (23%)	77.4 (74.1−80.9)	182/585 (31%)	69.8 (66.1−73.7)	0.70 (0.56, 0.88)
Inferred Oncotype-RNA score <=25	18/173 (10%)	90.2 (85.8−94.9)	28/165 (17%)	84.2 (78.7−90.1)	0.59 (0.33, 1.10)
Inferred Oncotype-RNA score>25	120/432 (28%)	72.3 (68.1−76.8)	154/420 (37%)	64.1 (59.6−69)	0.73 (0.57, 0.92)



Interaction p-value (inferred Oncotype scores high and low) = 0.532

- The selected biomarker subset is enriched for IDFS events using case-cohort design
- IDFS rates are presented as indicative of relative prognosis across subtypes but do not inform the actúal risk of recurrence within each subtype because of IDFS event enrichment

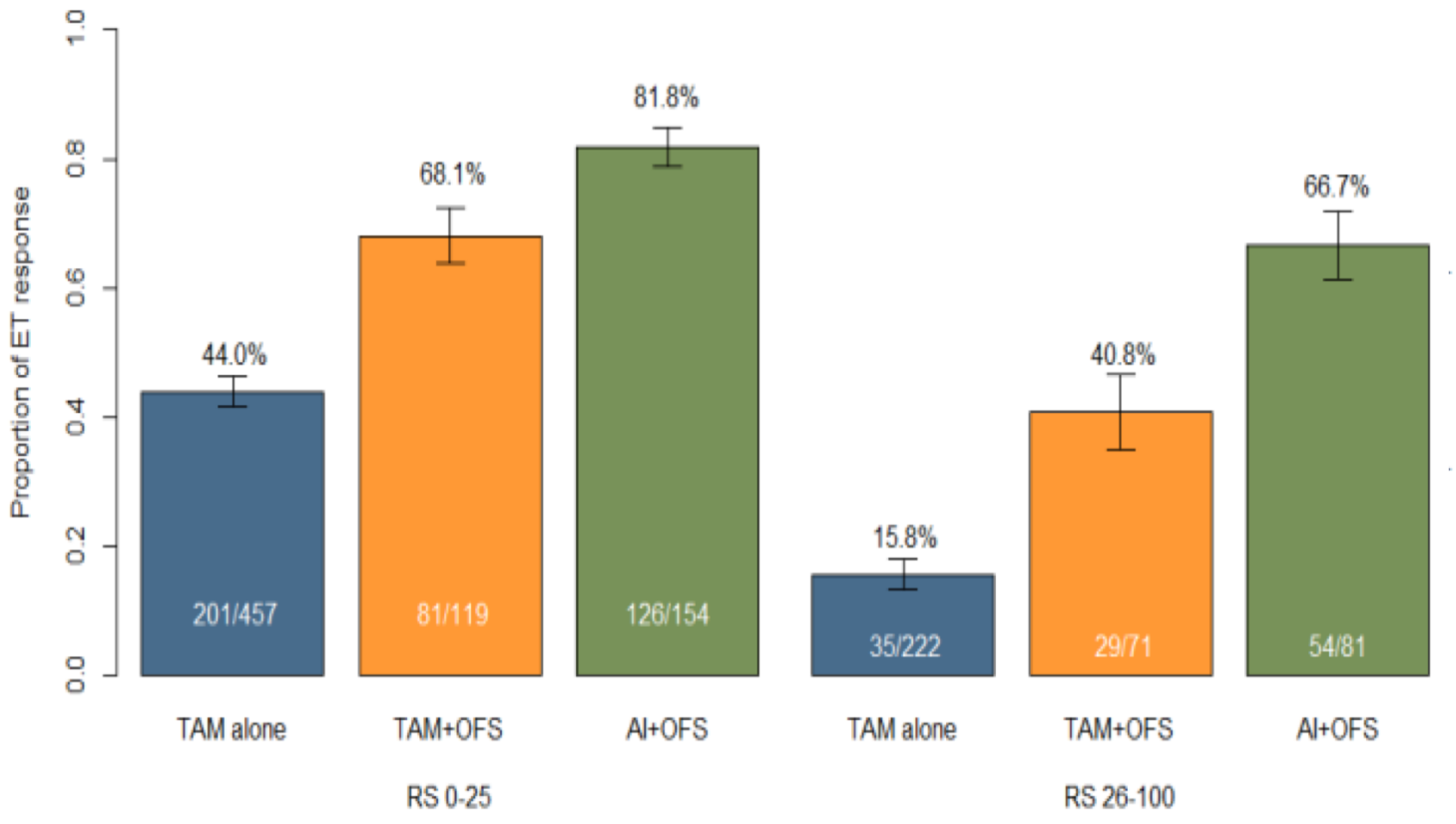
ADAPTcycle



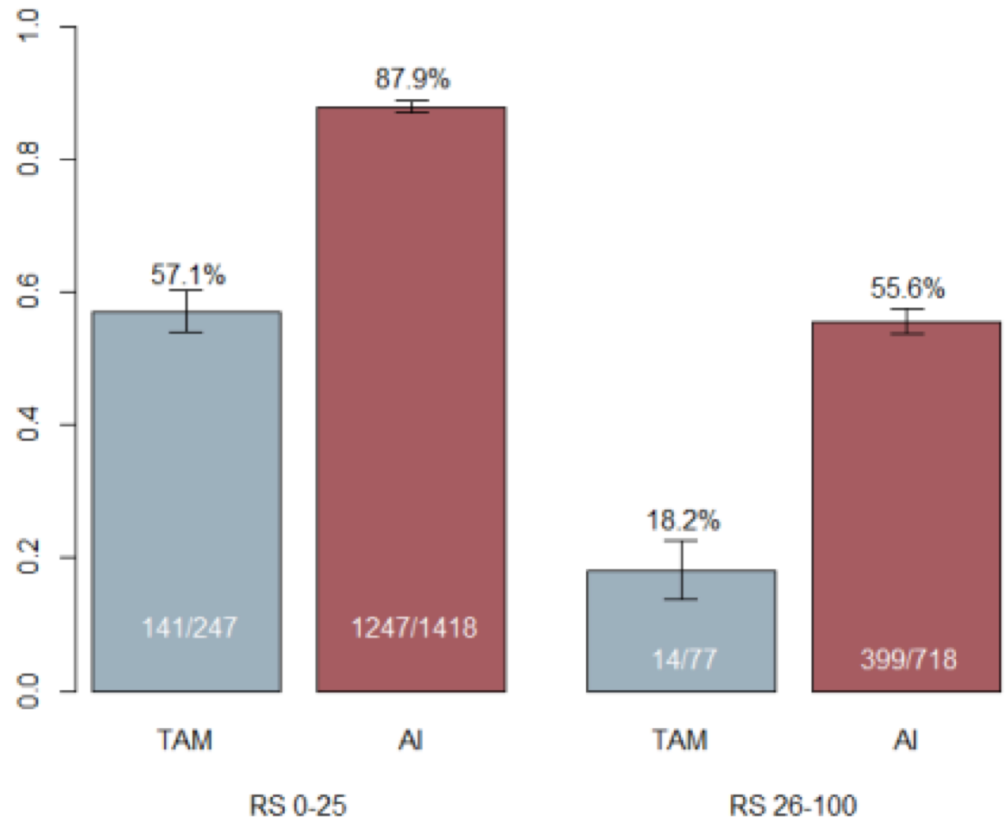
*** Participation of premenopausal N1 and N0 with RS 16-25 irrespective of ET-responder status allowed by investigator's decison, postmenopausal only if several risk factors

ET-response rates and Recurrence Score

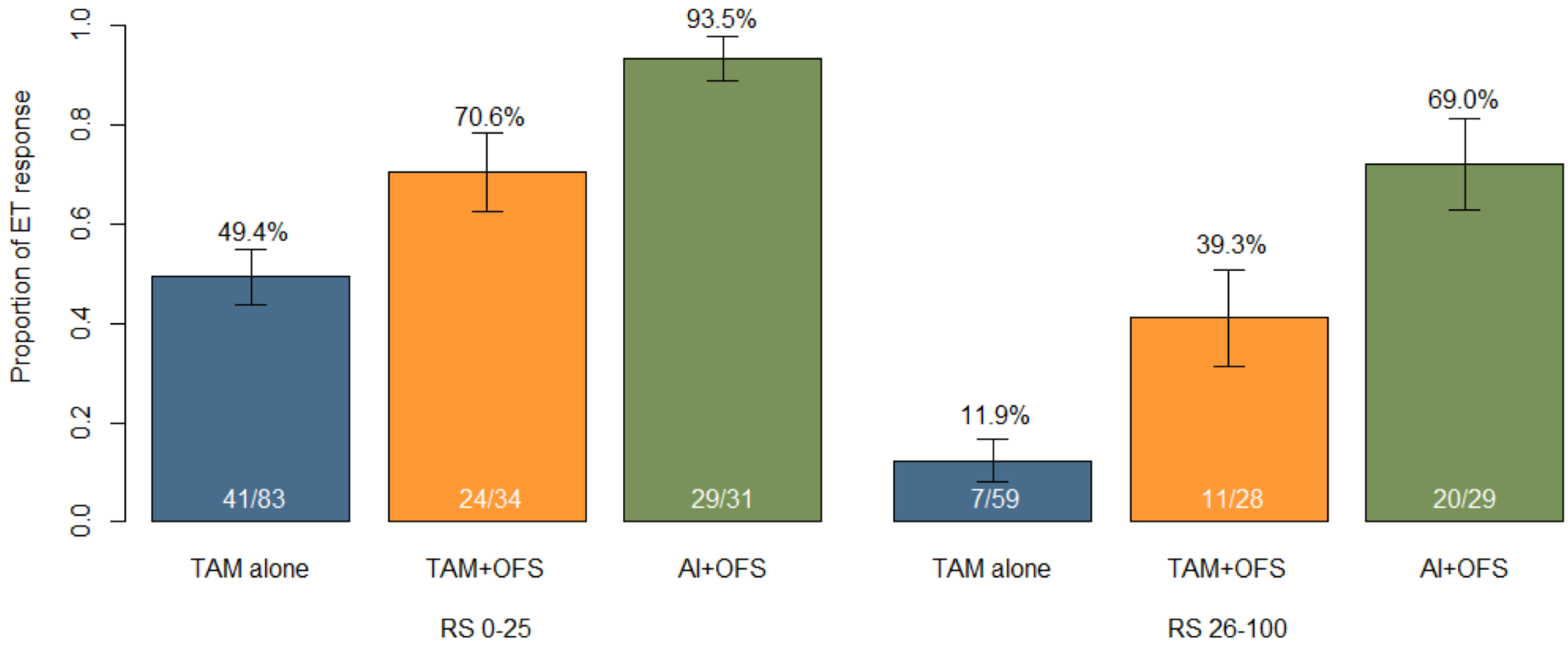
in ≤50y and premenopausal



in >50y or postmenopausal



ET-response rates and Recurrence Score in ≤40y (premenopausal)

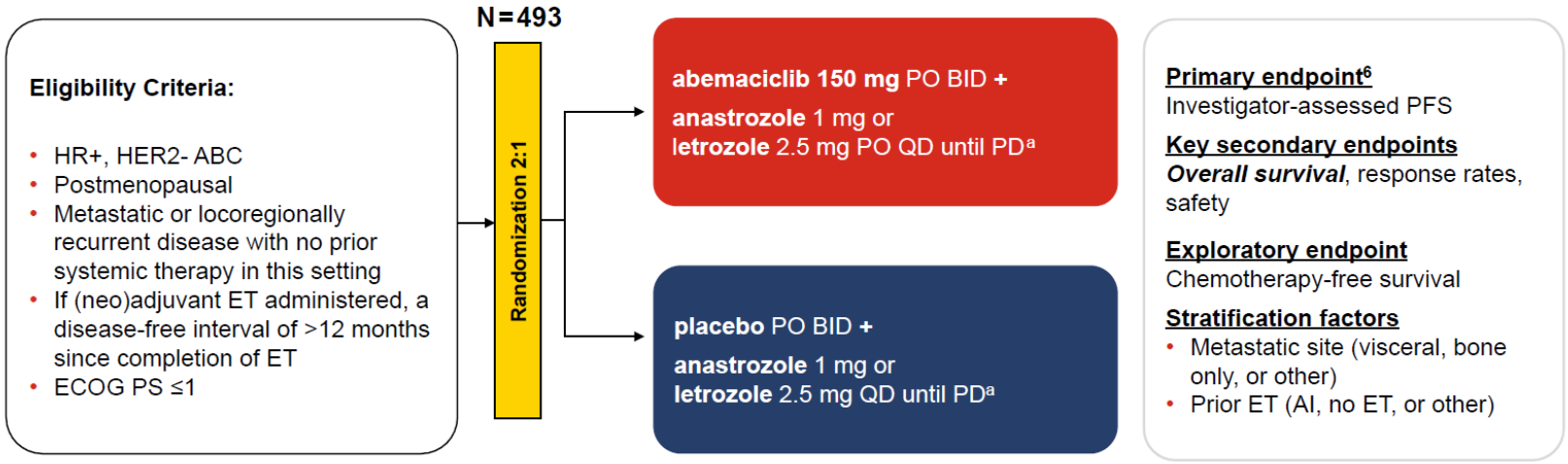


Conclusions

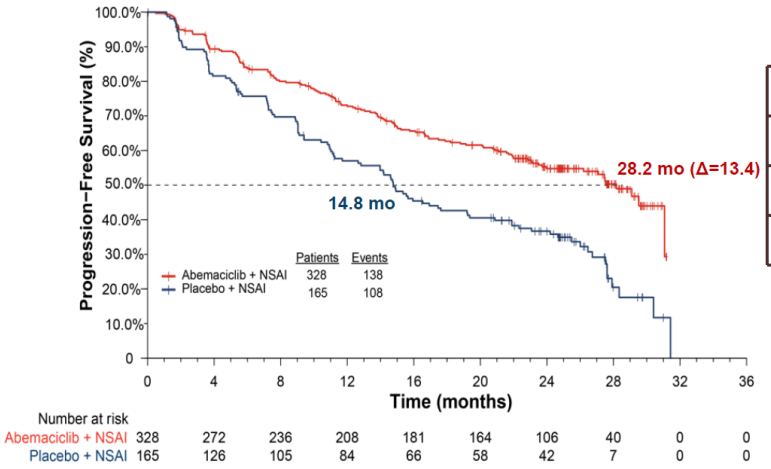
- In ADAPT, ET-response is associated with improved prognosis and identifies a subgroup of premenopausal N0-1 pts with excellent prognosis on ET alone
- ADAPTcycle screening cohort (n=4,334)
  - confirms ADAPT ET-response rates
  - shows first prospective data on $Ki67_{post}$ in premenopausal pts with <u>all</u> available ET options
  - demonstrates that adding OFS to TAM or AI substantially improves probability of ET-response in premenopausal pts - rates comparable to AI-treated postmenopausal pts
- → **with optimal ET, no difference in ET-sensitivity between pre- and postmenopausal pts observed**
- ADAPTcycle follow-up will demonstrate impact of ET-response (with and w/o OFS) on survival
- Based on ADAPT and ADAPTcycle, optimal ET (type / duration) for ET-response assessment:

  2-4w AI in postmenopausal pts; 4w GnRH and AI (started simultaneously) in premenopausal pts
- **ET-response should be considered in addition to gene expression testing for routine decision-making regarding chemotherapy use in HR+/HER2- N0-1 EBC to maximize the number of patients in whom chemotherapy can be spared**

MONARCH 3: Final OS results of 1L abemaciclib + NSAI inhibitor for HR+, HER2− advanced breast cancer



PFS benefit, leading to global regulatory approval



	abemaciclib + NSAI	placebo + NSAI
Median PFS (months)	28.2	14.8
HR (95% CI) 2-sided *P* value	0.540 (0.418-0.698) nominal p=0.000002*	
Pre-planned Final PFS Analysis[5] Data cut: 03 Nov 2017		

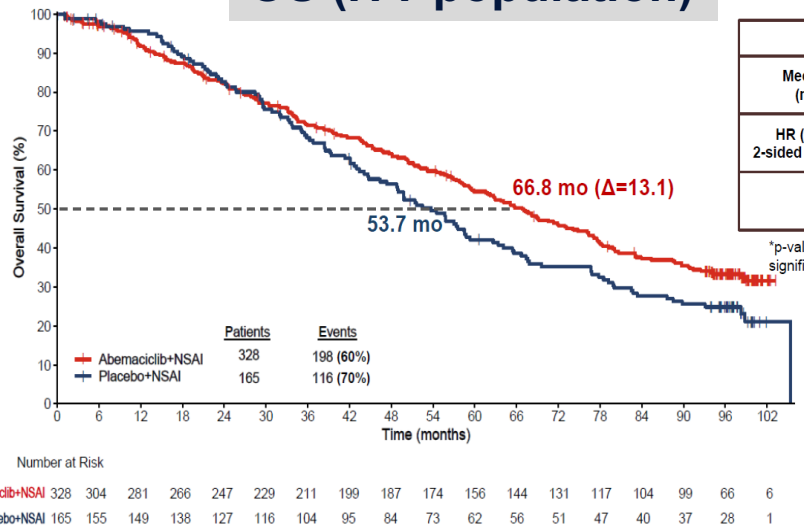
*Statistical significance was reached at the interim PFS analysis[6]

- At the final PFS data cut with a median follow-up of 26.7 months, PFS was prolonged by a median 13.4 months in patients receiving abemaciclib. At that time, OS was immature with 29.5% events observed across both arms
- Final OS:
  - ~315 events in the ITT
  - Data cutoff: Sep 29, 2023
  - Median follow up: 8.2 years
  - % of patients on treatment
    - Abemaciclib, 7%
    - Placebo, 3.0%

Goetz M, et al. SABCS 2023. Abstract GS01-12

MONARCH 3: Final OS results of 1L abemaciclib + NSAI inhibitor for HR+, HER2− advanced breast cancer

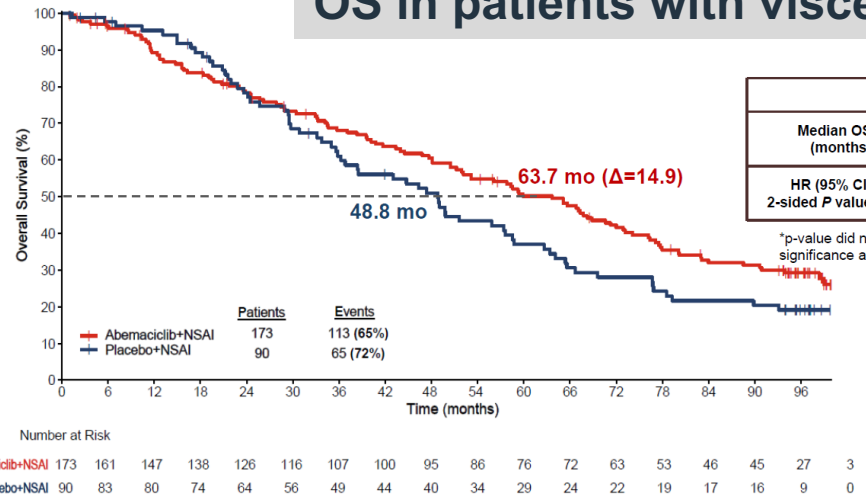
OS (ITT population)



	abemaciclib + NSAI	placebo + NSAI
Median OS (months)	66.8	53.7
HR (95% CI) 2-sided *P* value	0.804 (0.637-1.015) p=0.0664*	
Final OS Analysis Data cut: 29 Sep 2023		

*p-value did not reach threshold (0.034) for statistical significance at this final analysis

OS in patients with visceral disease

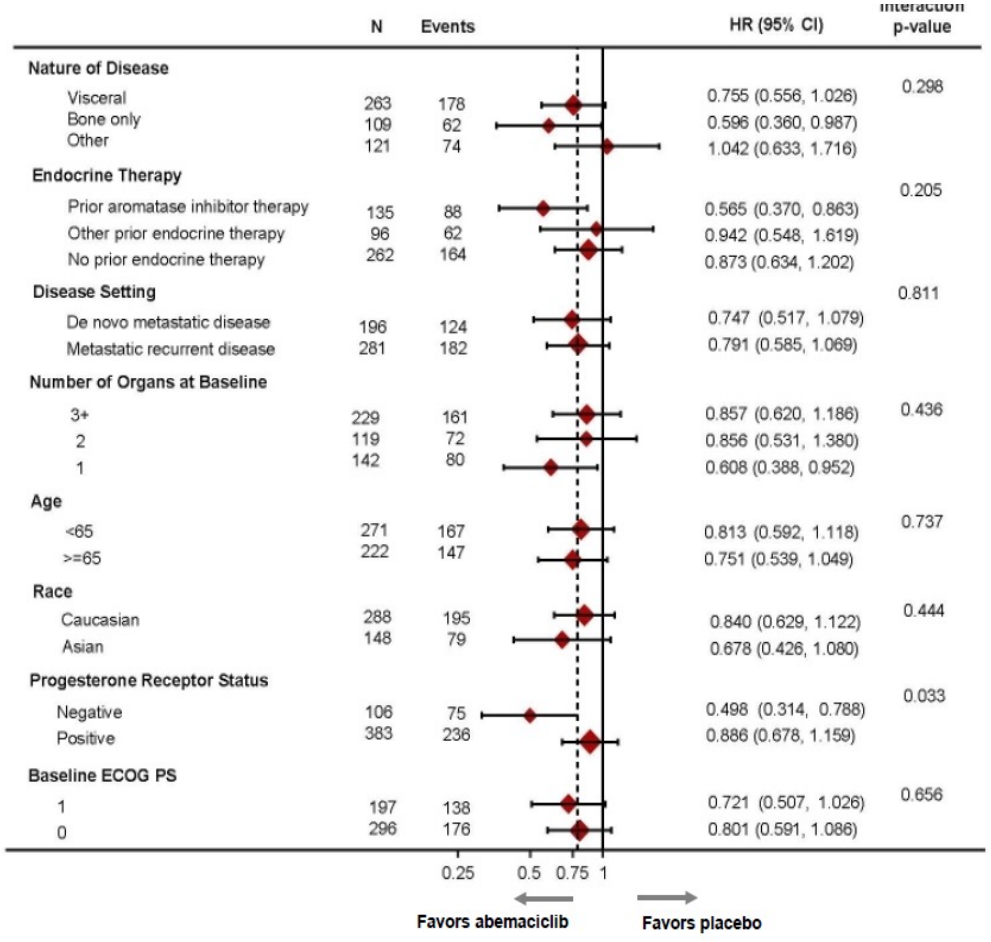


	abemaciclib + NSAI	placebo + NSAI
Median OS (months)	63.7	48.8
HR (95% CI) 2-sided *P* value	0.758 (0.558-1.030) p=0.0757*	

*p-value did not reach threshold (0.009) for statistical significance at this final analysis

Goetz M, et al. SABCS 2023. Abstract GS01-12

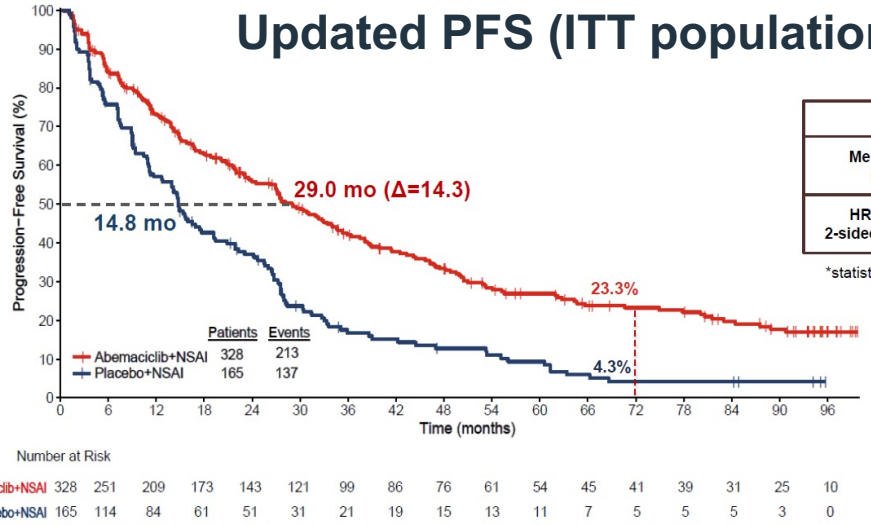
OS subgroup analysis



Consistent OS effect size observed across subgroups

MONARCH 3: Updated PFS and chemotherapy-free survival

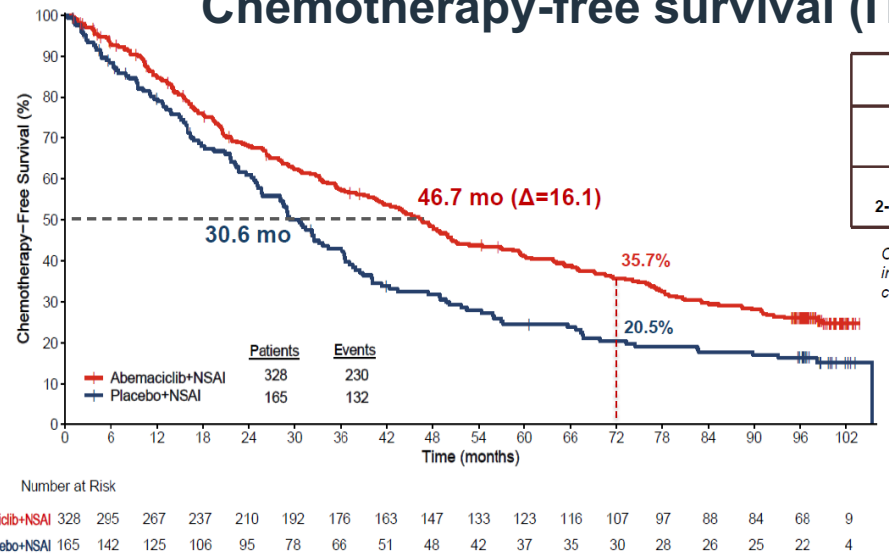
Updated PFS (ITT population)



	abemaciclib + NSAI	placebo + NSAI
Median PFS (months)	29.0	14.8
HR (95% CI) 2-sided *P* value	0.535 (0.429-0.668) nominal p=<0.0001*	

*statistical significance was reached at the interim PFS analysis[5]

Chemotherapy-free survival (ITT population)



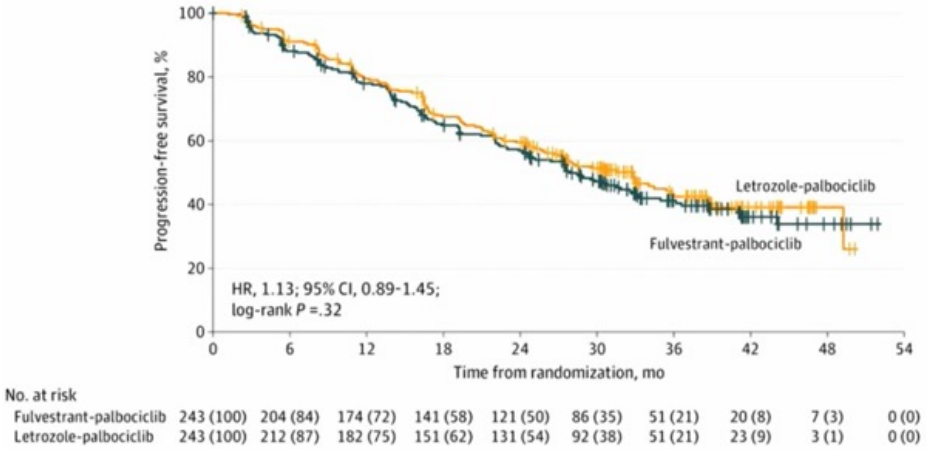
	abemaciclib + NSAI	placebo + NSAI
Median CFS (months)	46.7	30.6
HR (95% CI) 2-sided *P* value	0.693 (0.557-0.863) nominal p=0.0010	

Chemotherapy-free survival defined as the time to the initiation of subsequent chemotherapy or death from any cause, whichever was earlier

Goetz M, et al. SABCS 2023. Abstract GS01-12

PARSIFAL-LONG: Extended follow-up of fulvestrant/ palbociclib vs. letrozole/ palbociclib for HER2− advanced breast cancer

The PARSIFAL trial



Failed to show improvement in PFS of palbociclib + fulvestrant over fulvestrant/palbociclib vs. letrozole/ palbociclib with a median follow-up of 32 m

Extended follow up

The PARSIFAL-Long trial

N=389

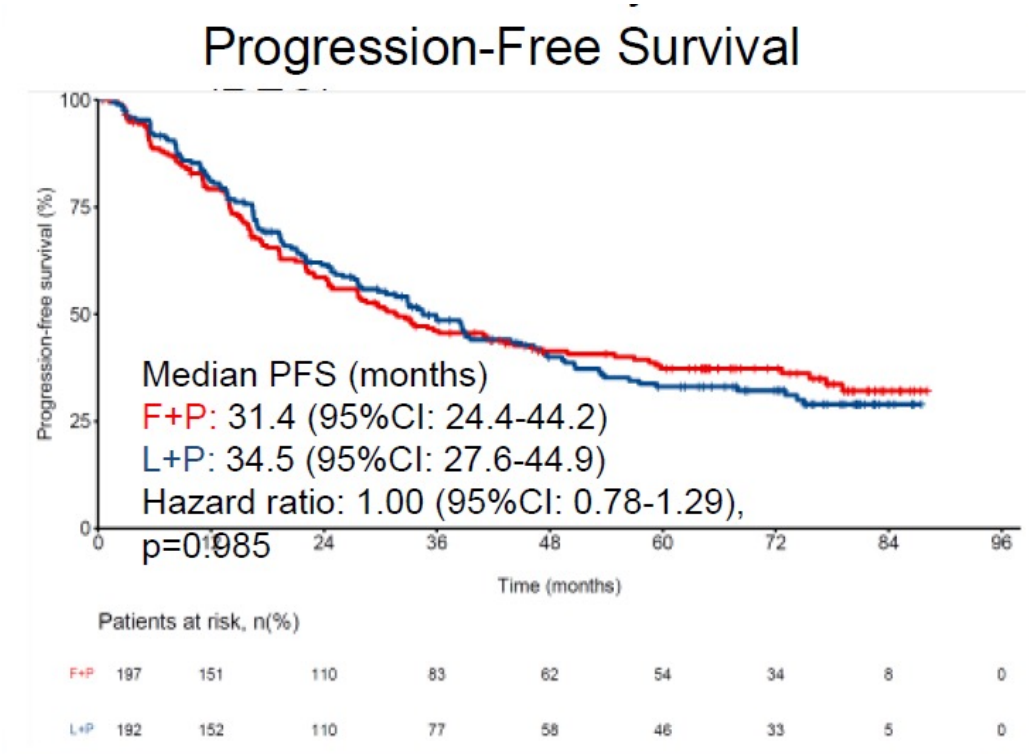
Primary objective: Efficacy (i.e OS)

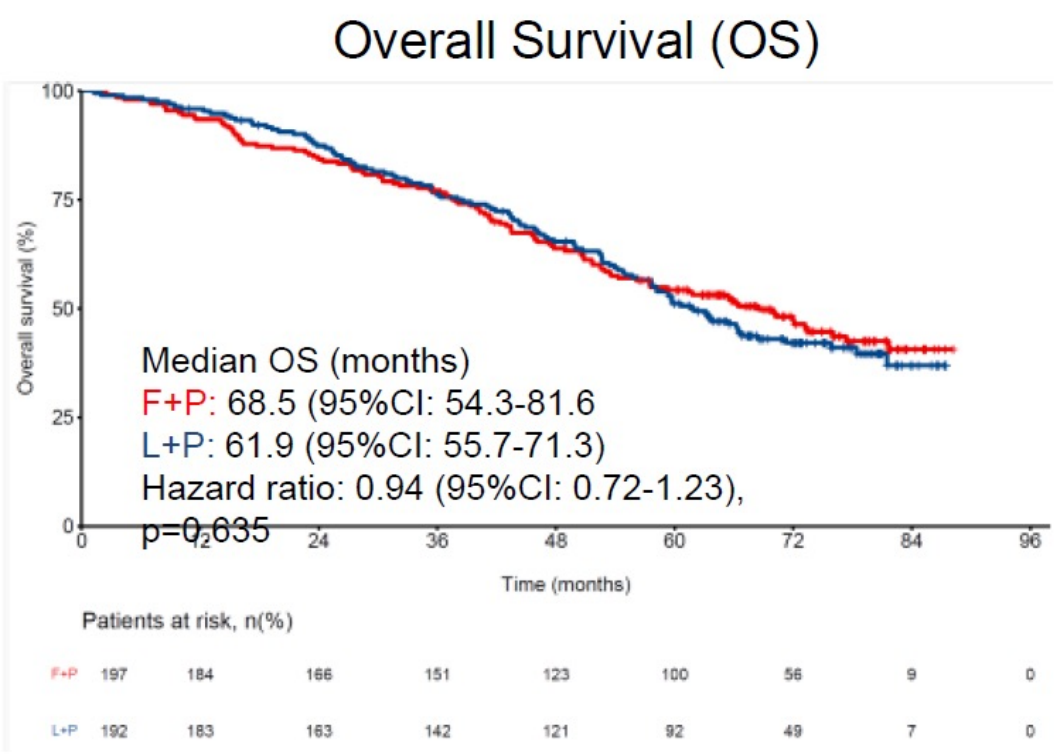
Secondary objective: PFS, PFS and OS by treatment arms

- Analysis included 32 of the original 47 sites
- 80.5% of patients from the PARSIFAL trial were included
- Baseline demographics and disease characteristics were similar between the PARIFAL-LONG and the overall PARSIFAL ITT population
- Median follow-up of 59.7 months (IQR: 36.3–72.9)

Llombart-Cussac, et al. SABCS 2023. Abstract RF01-03

PARSIFAL-LONG: Efficacy, PFS and OS





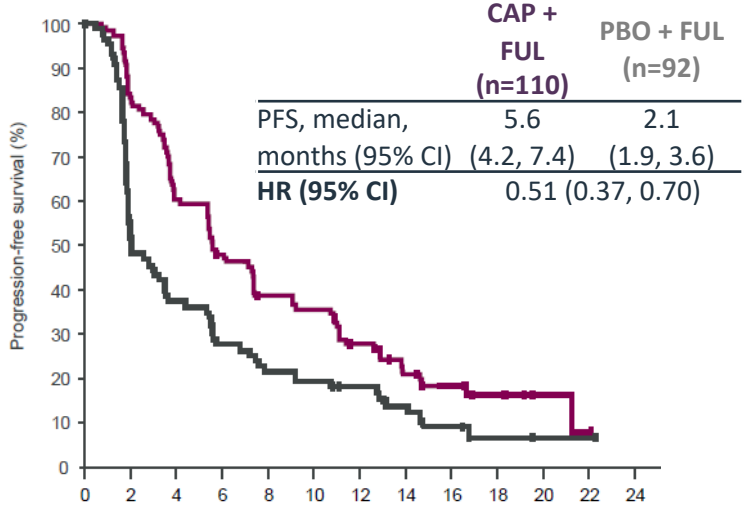
Medial follow-up: 59.7 months. Data cutoff: May 2023

Llombart-Cussac, et al. SABCS 2023. Abstract RF01-03

CAPltello-291 (Phase 3, exploratory analysis): Capivasertib and fulvestrant for AI-resistant HR+/HER2– advanced breast cancer

- **Objective:** Explore PFS by tumor PIK3CA/AKT1/PTEN-mutated status among patients from the CAPltell-291 study (including pooled analysis with inclusion of data from the Chinese extension cohort)
- **CAPltell-291 population:** Patients with HR+/HER2– advanced breast cancer after progression during during AI treatment with/without prior CDK4/6i therapy

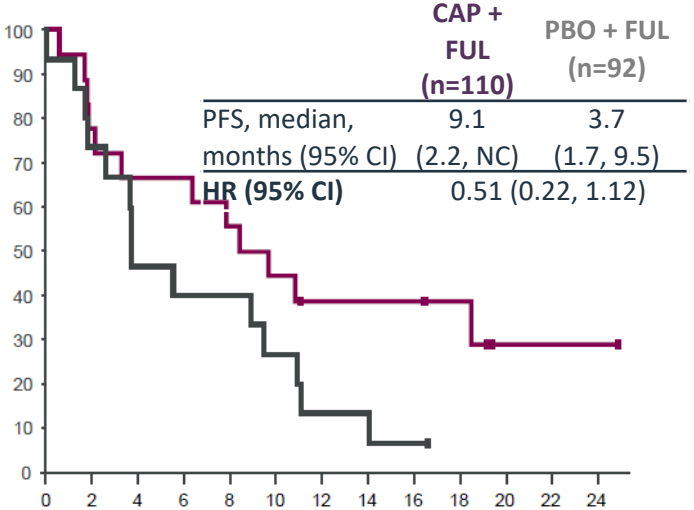
PIKCA alteration only



	CAP + FUL (n=110)	PBO + FUL (n=92)
PFS, median, months (95% CI)	5.6 (4.2, 7.4)	2.1 (1.9, 3.6)
HR (95% CI)	0.51 (0.37, 0.70)	

Patients at risk													
Capivasertib plus fulvestrant	110	90	65	51	40	37	27	17	13	7	2	1	0
Placebo plus fulvestrant	92	48	31	23	18	16	13	9	5	2	1	1	0

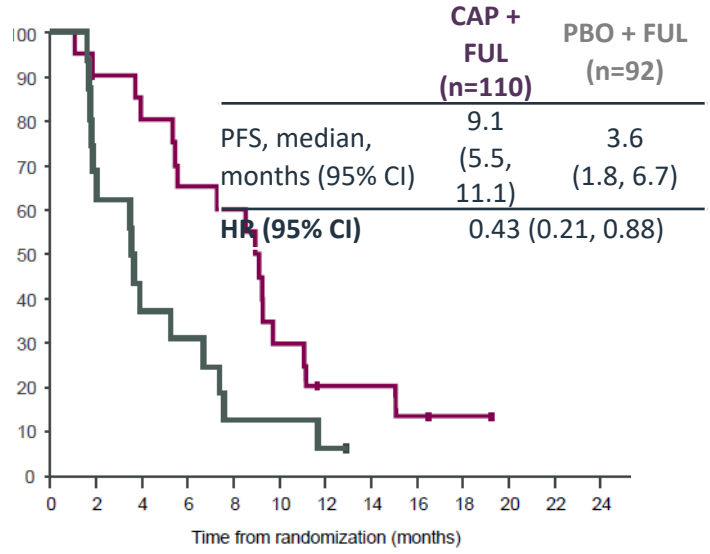
AKT1 alteration only



	CAP + FUL (n=110)	PBO + FUL (n=92)
PFS, median, months (95% CI)	9.1 (2.2, NC)	3.7 (1.7, 9.5)
HR (95% CI)	0.51 (0.22, 1.12)	

	18	14	12	12	10	8	6	6	6	4	1	1	1
	15	11	7	6	6	4	2	2	1	0	0	0	0

PTEN alteration only



	CAP + FUL (n=110)	PBO + FUL (n=92)
PFS, median, months (95% CI)	9.1 (5.5, 11.1)	3.6 (1.8, 6.7)
HR (95% CI)	0.43 (0.21, 0.88)	

	21	18	17	13	12	6	3	3	2	1	0	0	0
	16	11	6	5	2	2	1	0	0	0	0	0	0

Howell SJ, et al. SABCS 2023. Abstract PS17-03

EMERALD: Consistent Improvement in PFS vs SoC Across all Relevant *ESR1*-mut Subgroups

PFS Summary in *ESR1*-mut Patients With ≥12 Months of Prior CDK4/6 Inhibitor

		Median PFS, months (95% CI)		
Patients	% (n)	Elacestrant	SOC	HR (95% CI)
All *ESR1*-mut patients[9]	100 (159)	8.61 (4.14–10.84)	1.91 (1.87–3.68)	0.410 (0.262–0.634)
ESR1-mut and bone metastases[a]	86 (136)	9.13 (5.49–16.89)	1.91 (1.87–3.71)	0.381 (0.230–0.623)
ESR1-mut and liver and/or lung metastases[b]	71 (113)	7.26 (2.20–10.84)	1.87 (1.84–1.94)	0.354 (0.209–0.589)
ESR1-mut and *PIK3CA*-mut[c]	39 (62)	5.45 (2.14–10.84)	1.94 (1.84–3.94)	0.423 (0.176–0.941)
ESR1-mut and HER2-low expression[d]	48 (77)	9.03 (5.49–16.89)	1.87 (1.84–3.75)	0.301 (0.142–0.604)
ESR1-mut and *TP53*-mut	38 (61)	8.61 (3.65–24.25)	1.87 (1.84–3.52)	0.300 (0.132–0.643)

[a]85% of patients had bone and other sites of metastases (30% of these patients had no liver or lung involvement); [b]55% of patients had liver and other sites of metastases (10% of these patients had no lung or bone involvement); 25% of patients had lung and other sites of metastases (2% of these patients had no liver or bone involvement); [c]Includes E545K, H1047R, E542K amongst others; [d]HER2 IHC 1+, and 2+ with no ISH amplification. Data not available for all patients

Bardia A, O'Shaughnessy J, Bidard F-C, et al. San Antonio Breast Cancer Symposium 2023; PS16-01.

INAVO120 study design

Key eligibility criteria

Enrichment of patients with poor prognosis:

- ***PIK3CA*-mutated, HR+, HER2- ABC** by central ctDNA* or local tissue/ctDNA test
- **Measurable disease**
- **Progression during/within 12 months of adjuvant ET completion**

- **No prior therapy for ABC**
- **Fasting glucose <126 mg/dL and HbA_{1C} <6.0%**

Enrolment period: December 2019 to September 2023

N=325

R 1:1

Inavolisib (9 mg QD PO) + palbociclib (125 mg PO QD D1–D21) + fulvestrant (500 mg C1D1/15 and Q4W)**

Placebo (PO QD) + palbociclib (125 mg PO QD D1–D21) + fulvestrant (500 mg C1D1/15 and Q4W)**

Until PD or toxicity

SURVIVAL FOLLOW-UP

Stratification factors:

- Visceral Disease (Yes vs. No)
- Endocrine Resistance (Primary vs. Secondary)†
- Region (North America/Western Europe; Asia; Other)

Endpoints

- Primary: PFS by Investigator
- Secondary: OS‡, ORR, BOR, CBR, DOR, PROs

* Central testing for *PIK3CA* mutations was done on ctDNA using FoundationOne®Liquid (Foundation Medicine). In China, the central ctDNA test was the PredicineCARE NGS assay (Huidu). † Defined per 4th European School of Oncology (ESO)–European Society for Medical Oncology (ESMO) International Consensus Guidelines for Advanced Breast Cancer.[1] Primary: relapse while on the first 2 years of adjuvant ET; Secondary: relapse while on adjuvant ET after at least 2 years or relapse within 12 months of completing adjuvant ET. ‡ OS testing only if PFS is positive; interim OS analysis at primary PFS analysis;
** Pre-menopausal women received ovarian suppression. ctDNA, circulating tumor DNA; R, randomized. 1. Cardoso F, *et al. Ann Oncol* 2018;**29:**1634–1657.

Demographics and baseline disease characteristics

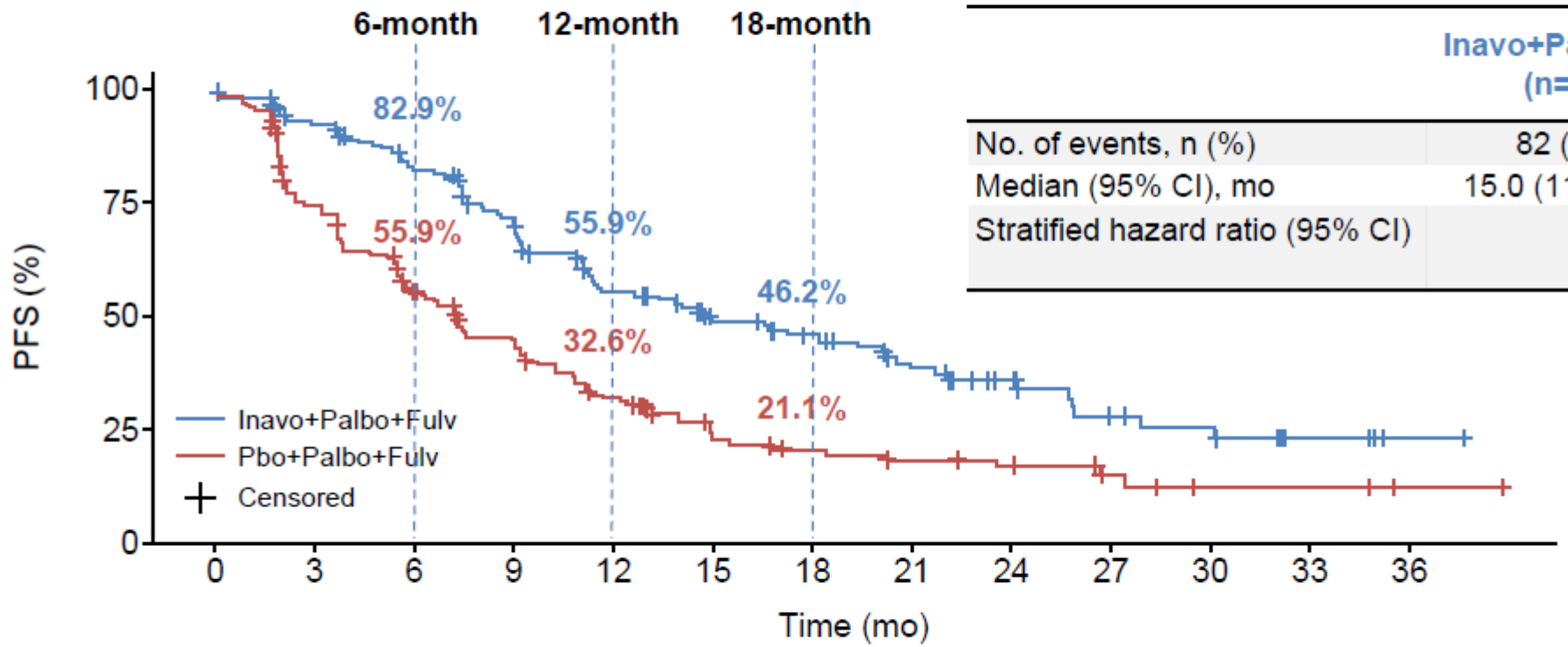
	Inavo+Palbo+Fulv (n=161)	Pbo+Palbo+Fulv (n=164)
Age (year)		
Median	53.0	54.5
Min–Max	27–77	29–79
Sex, n (%)		
Female	156 (96.9)	163 (99.4)
Race, n (%)		
Asian	61 (37.9)	63 (38.4)
Black or African American	1 (0.6)	1 (0.6)
White	94 (58.4)	97 (59.1)
ECOG PS, n (%)		
0	100 (62.1)	106 (64.6)
1	60 (37.3)	58 (35.4)
Menopausal status at randomization, n (%)		
Premenopausal	65 (40.4)	59 (36.0)
Postmenopausal	91 (56.5)	104 (63.4)

	Inavo+Palbo+Fulv (n=161)	Pbo+Palbo+Fulv (n=164)
Number of organ sites, n (%)		
1	21 (13.0)	32 (19.5)
2	59 (36.6)	46 (28.0)
≥3	81 (50.3)	86 (52.4)
Visceral disease, n (%)*	132 (82.0)	128 (78.0)
Liver	77 (47.8)	91 (55.5)
Lung	66 (41.0)	66 (40.2)
Bone only†	5 (3.1)	6 (3.7)
ER‡ and PgR status, n (%)		
ER+/PgR+	113 (70.2)	113 (68.9)
ER+/PgR-	45 (28.0)	45 (27.4)
Endocrine resistance , n (%)**		
Primary	53 (32.9)	58 (35.4)
Secondary	108 (67.1)	105 (64.0)

301 (92.6%) pts were enrolled per ctDNA testing (284 [94.4%] central, 17 [5.6%] local) and 24 (7.4%) were enrolled per local tissue testing

* "Visceral" (yes/no) refers to lung, liver, brain, pleural, and peritoneal involvement; † Patients with evaluable bone-only disease were not eligible; patients with disease limited to the bone but with lytic or mixed lytic/blastic lesions, and at least one measurable soft-tissue component per RECIST 1.1, may be eligible. ‡ Defined as 10% per ASCO-CAP guidelines. ** Endocrine resistance was defined per 4th ESO–[ESMO] International Consensus Guidelines for Advanced Breast Cancer. Primary resistance: Relapse while on the first 2 years of adjuvant endocrine therapy. Secondary resistance: Relapse while on adjuvant endocrine therapy after at least 2 years or relapse within 12 months of completing adjuvant endocrine therapy. ECOG PS, Eastern Cooperative Oncology Group Performance Status; ER, estrogen receptor, Fulv, fulvestrant; Inavo, inavolisib; Palbo, palbociclib; Pbo, placebo; PgR, progesterone receptor; RECIST, Response Evaluation Criteria in Solid Tumors.

Primary endpoint: PFS (investigator-assessed)



	Inavo+Palbo+Fulv (n=161)	Pbo+Palbo+Fulv (n=164)
No. of events, n (%)	82 (50.9)	113 (68.9)
Median (95% CI), mo	15.0 (11.3, 20.5)	7.3 (5.6, 9.3)
Stratified hazard ratio (95% CI)	**0.43 (0.32, 0.59) p<0.0001**	

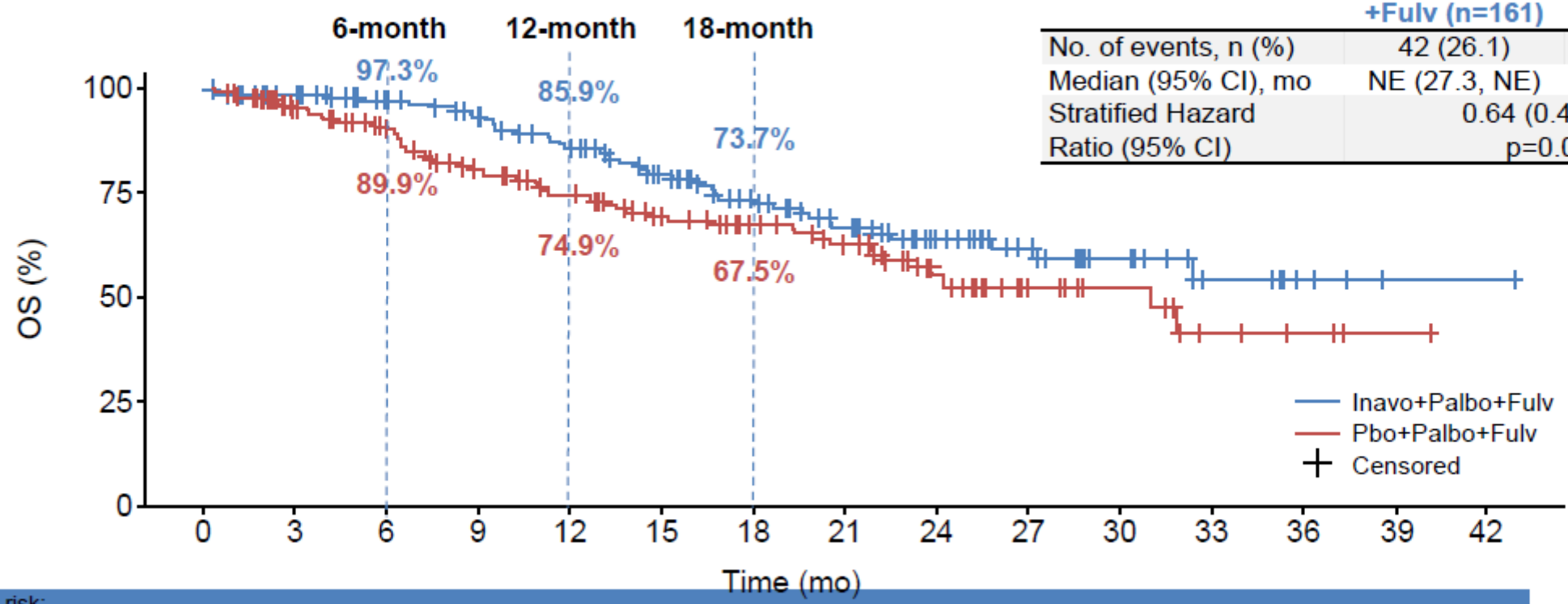
Patients at risk:													
Inavo+Palbo+Fulv	161	134	111	92	66	48	41	31	22	13	11	5	1
Pbo+Palbo+Fulv	164	113	77	59	40	23	19	16	12	6	3	3	1

Median follow-up:
21.3 months

CCOD: 29th September 2023
CI, confidence interval; Fulv, fulvestrant; Inavo, inavolisib; mo, months; Palbo, palbociclib; Pbo, placebo; PFS, progression-free survival.

Key secondary endpoint: Overall survival (interim analysis)

	Inavo+Palbo +Fulv (n=161)	Pbo+Palbo +Fulv (n=164)
No. of events, n (%)	42 (26.1)	55 (33.5)
Median (95% CI), mo	NE (27.3, NE)	31.1 (22.3, NE)
Stratified Hazard Ratio (95% CI)	0.64 (0.43, 0.97) p=0.0338	



Patients at risk:															
Inavo+Palbo+Fulv	161	143	127	114	101	85	69	56	38	26	17	8	4	1	1
Pbo+Palbo+Fulv	164	139	120	98	87	72	61	52	33	19	11	5	3	1	0

Median follow-up: **21.3 months**

The pre-specified boundary for OS (p of 0.0098 or HR of 0.592) was not crossed at this interim analysis

CI, confidence interval; Fulv, fulvestrant; Inavo, inavolisib; mo, months; NE, not estimable; OS, overall survival; Palbo, palbociclib; Pbo, placebo.

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Adverse events with any grade AEs ≥20% incidence in either treatment group

Adverse Events	Inavo+Palbo+Fulv (N=162)		Pbo+Palbo+Fulv (N=162)	
	All Grades	Grade 3–4	All Grades	Grade 3–4
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/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%)	<2%	14 (8.6%)	<2%
Fatigue	38 (23.5%)	<2%	21 (13.0%)	<2%
COVID-19	37 (22.8%)	<2%	17 (10.5%)	<2%
Headache	34 (21.0%)	<2%	22 (13.6%)	<2%
Leukopenia	28 (17.3%)	11 (6.8%)	40 (24.7%)	17 (10.5%)
Ocular Toxicities	36 (22.2%)	0	21 (13.0%)	0

Key AEs are shown in **bold.** AES were assessed per CTCAE V5. Neutropenia, thrombocytopenia, stomatitis/mucosal inflammation, anemia, hyperglycemia, diarrhea, nausea and rash were assessed as medical concepts using grouped terms

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Fulv, fulvestrant; Inavo, inavolisib; Palbo, palbociclib; Pbo, placebo.

6.8% stopped inavolisib due to toxicity
70% had dose interruption and/or reduction

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New Results from Endocrine Therapy Trials

- 3 yrs of ribociclib in high/intermediate risk pts improves iDFS and DRFS
- Adjuvant abemaciclib effective regardless of intrinsic subtype or RS
- LHRH agonist + AI most effective therapy for premenopausal pts – Responder to preop ET with Ki67 < 10% and RS < 26, ER/PR+++ and 0/1 N+ -- avoid chemoRx
- 1L MBC abemaciclib did not improve OS (13 mo additional OS vs AI alone) – likely due to smaller sample size
- Capivasertib effective in *PIK3CA, AKT or PTEN*-altered HR+ HER2- MBCs
- Elacestrant effective in CDKi-sensitive *ESR1*- and *PIK3CA*- or *p53*-mutant MBC regardless of metastatic site
- PI3K inhibitor inavolisib + fulvestrant + palbociclib in ET-resistant MBC is promising