2023 ASCO ANNUAL MEETING

Post-ASCO 2023 en sénologie

Dr Elise deluche
MCU-PH
Oncologie Médicale
Chu de limoges

CHU Centre hospitalier universitaire Limoges

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2023 ASCO ANNUAL MEETING

Ribociclib and endocrine therapy as adjuvant treatment in patients with HR+/HER2− early breast cancer: primary results from the Phase III NATALEE trial

Dennis Slamon,[1] Daniil Stroyakovskiy,[2] Denise A. Yardley,[3] Chiun-Sheng Huang,[4] Peter A. Fasching,[5] John Crown,[6] Aditya Bardia,[7] Stephen Chia,[8] Seock-Ah Im,[9] Miguel Martin,[10] Sherene Loi,[11] Binghe Xu,[12] Sara Hurvitz,[13] Carlos Barrios,[14] Michael Untch,[15] Rebecca Moroose,[16] Frances Visco,[17] Rodrigo Fresco,[18] Tetiana Taran,[19] Gabriel N. Hortobagyi[20]

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NATALEE study design[1,2]

- 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/day
3 weeks on/1 week 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

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

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

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Pratique clinique

- Adult patients with HR+/HER2− EBC
- Prior ET allowed up to 12 mo
- **Anatomical stage IIA**[a]
  - **N0** with:
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      - High risk via genomic risk profiling
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  - **N1**
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Randomization stratification
Anatomical stage: II vs III
Menopausal status: men and premenopausal women vs postmenopausal women
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Geographic location: North America/Western Europe/Oceania vs rest of world

Ribociclib
400 mg/day
3 weeks on/1 week off
for 3 y

Rationale for broad population of patients
Patients with stage II and III HR+/HER2− EBC, including those with no nodal involvement, are at risk of disease recurrence up to decades after initial diagnosis[3,4]

Rationale for 400 mg RIB
To improve tolerability while maintaining efficacy
Etude AMALEE

Rationale for 3-year treatment duration
Extended duration of treatment is crucial to prolong cell cycle arrest and drive more tumor cells into irreversible senescence[5-7]

tumor ctDNA/ctRNA samples

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Cardoso et al. SABCS 2022

Baseline characteristics

Parameter	RIB + NSAI n = 2549	NSAI Alone n = 2552	All Patients N = 5101
Age, median (min-max), years	52 (24-90)	52 (24-89)	52 (24-90)
Menopausal status, n (%)			
Men[a] and premenopausal women	1126 (44)	1132 (44)	2258 (44)
Postmenopausal women	1423 (56)	1420 (56)	2843 (56)
Anatomical stage,[b,c] n (%)			
Stage IIA	479 (19)	521 (20)	1000 (20)
Stage IIB	532 (21)	513 (20)	1045 (20)
Stage III	1528 (60)	1512 (59)	3040 (60)
Nodal status at diagnosis, n (%)			
NX	272 (11)	264 (10)	536 (11)
N0	694 (27)	737 (29)	1431 (28)
N1	1050 (41)	1049 (41)	2099 (41)
N2/N3	483 (19)	467 (18)	950 (19)
Prior ET, n (%)[d]			
Yes	1824 (72)	1801 (71)	3625 (71)
Prior (neo)adjuvant CT, n (%)			
Yes	2249 (88)	2245 (88)	4494 (88)
ECOG PS, n (%)			
0	2106 (83)	2132 (84)	4238 (83)
1	440 (17)	418 (16)	858 (17)

CT, chemotherapy; ECOG PS, Eastern Cooperative Oncology Group performance status; ET, endocrine therapy; N0, no nodal involvement; N1, 1-3 axillary lymph nodes; N2, 4-9 axillary lymph nodes; N3, ≥ 10 axillary lymph nodes or infra- or supraclavicular lymph nodes; NSAI, nonsteroidal aromatase inhibitor; NX, regional nodes were not assessed; OFS, ovarian function suppression; RIB, ribociclib.
[a] In the RIB + NSAI arm, there were 11 men (0.4%); in the NSAI alone arm, there were 9 men (0.4%). [b] A total of 14 patients with stage I disease were included: 9 (0.4%) in the RIB + NSAI arm and 5 (0.2%) in the NSAI alone arm. [c] Stage is derived using TNM from surgery for patients having not received (neo)adjuvant treatment or as worst stage derived using TNM at diagnosis and TNM from surgery for patients having received (neo)adjuvant treatment. [d] Prior OFS was received by 670 patients (26.3%) in the RIB + NSAI arm and 620 (24.3%) in the NSAI alone arm.

AJCC anatomical staging[1]	TN (M0)	NATALEE[2,3]	monarchE[4]
Stage IA	T1N0		
Stage IB	T0N1mi		
	T1N1mi		G3 or Ki67 ≥ 20%
Stage IIA	T0N1		
	T1N1		G3 or Ki67 ≥ 20%
	T2N0	G3, or G2 with Ki-67 ≥ 20% or high genomic risk[c]	
Stage IIB	T2N1		G3 or Ki67 ≥ 20%
	T3N0		
Stage IIIA	T0N2		
	T1N2		
	T2N2		
	T3N1		
	T3N2		
Stage IIIB	T4N0		
	T4N1		
	T4N2		
Stage IIIC	Any TN3		

- Pre- and postmenopausal women
- Men

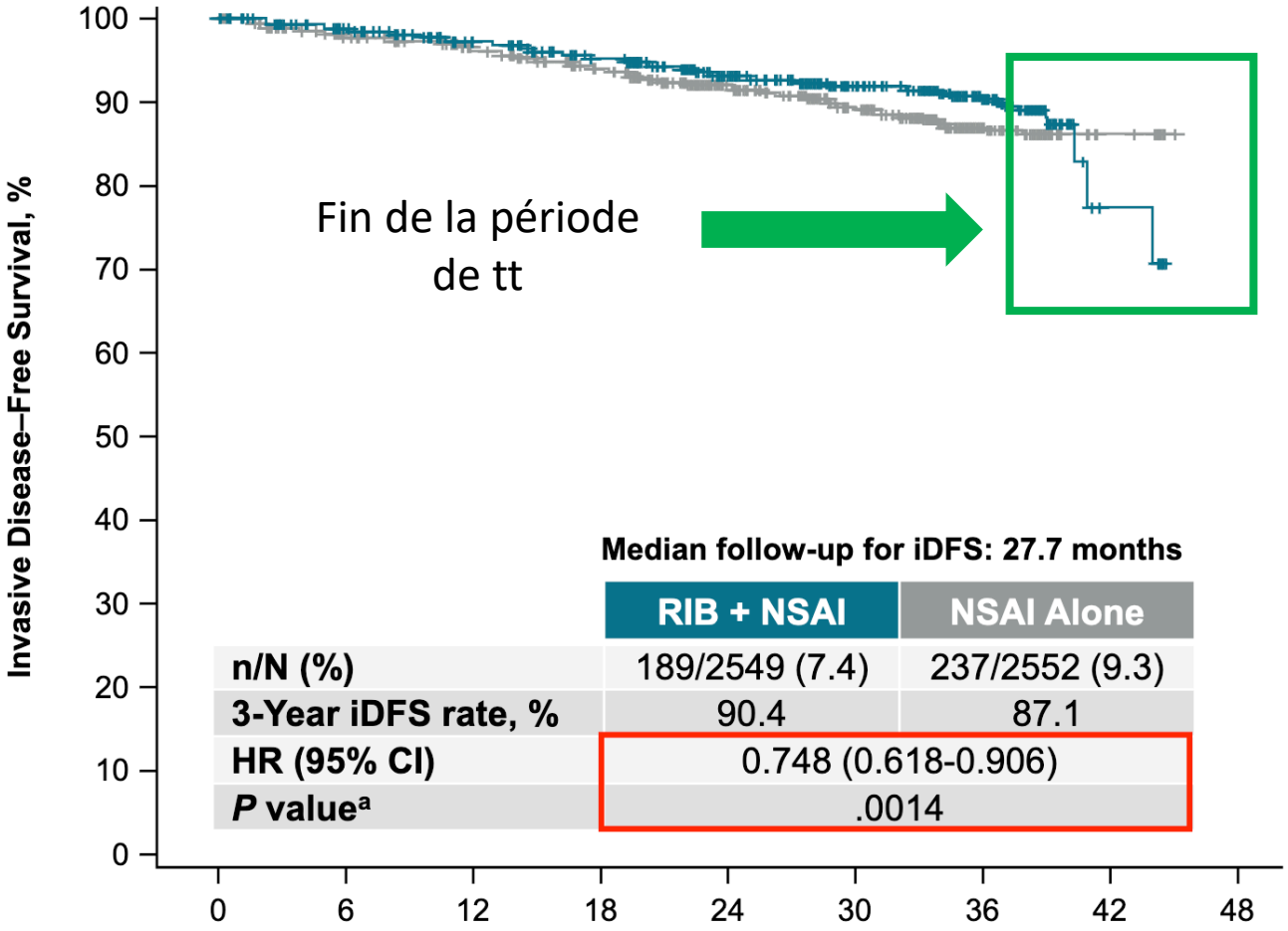
Choice of therapy will depend on approval, access, risk, long-term efficacy, safety profile, and patient preference

Not to forget: **gBRCA testing** in patients eligible for olaparib (OlympiA)

AJCC, American Joint Committee on Cancer; G, grade; M, metastasis; N0, no nodal involvement;; N1mi, nodal micrometastases; N1, 1-3 axillary lymph nodes; N2, 4-9 axillary lymph nodes; N3 ; RS, Recurrence Score; T, tumor; T0, no evidence of primary tumor; T1, tumor is 2cm or less; T2, Tumor is more than 2cm bu less than 5cm; T3, tumor is more than 5cm; T4, tumor of any size growi breast cancer. [a] Including stage IIIA (N1/N2), IIIB (N0/N1/N2), or IIIC (N3). [b] Capped at 40% (≈ 2000 patients). Simplified inclusion criteria are used in the illustration. [c] High risk as determined by Oncotype DX, P clin Risk Score.

References: 1. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual*. 8th ed. New York, NY: Springer; 2017:587-636. 2. Slamon DJ, et al. *J Clin Oncol*. 2019;37(suppl 15) [abs 2011O12301C (TRIO033). Clinical study protocol. V4.0. Novartis Pharmaceuticals Corp; August 27, 2020; [5]https://clinicaltrials.gov/ct2/show/NCT03155997

Ribociclib achieved highly significant iDFS benefit



Median follow-up for iDFS: 27.7 months

	RIB + NSAI	NSAI Alone
n/N (%)	189/2549 (7.4)	237/2552 (9.3)
3-Year iDFS rate, %	90.4	87.1
HR (95% CI)	0.748 (0.618-0.906)	
P value[a]	.0014	

No. at risk

RIB + NSAI	2549	2350	2274	2193	1718	1111	311	12	0
NSAI alone	2552	2240	2166	2071	1631	1067	286	13	0

- Based on the *P* value of .0014, the IDMC concluded that the results met the criteria to demonstrate statistically significant and clinically superior efficacy
  - **P < 0.025**
- Absolute iDFS benefit with RIB + NSAI at 3 years was 3.3%
- Risk of invasive disease was reduced by 25.2% with RIB + NSAI vs NSAI alone
- Ongoing patients will remain on treatment and follow-up will continue as prespecified

iDFS, invasive disease–free survival; IDMC, Independent Data Monitoring Committee; HR, hazard ratio; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.
[a] One-sided *P* value.

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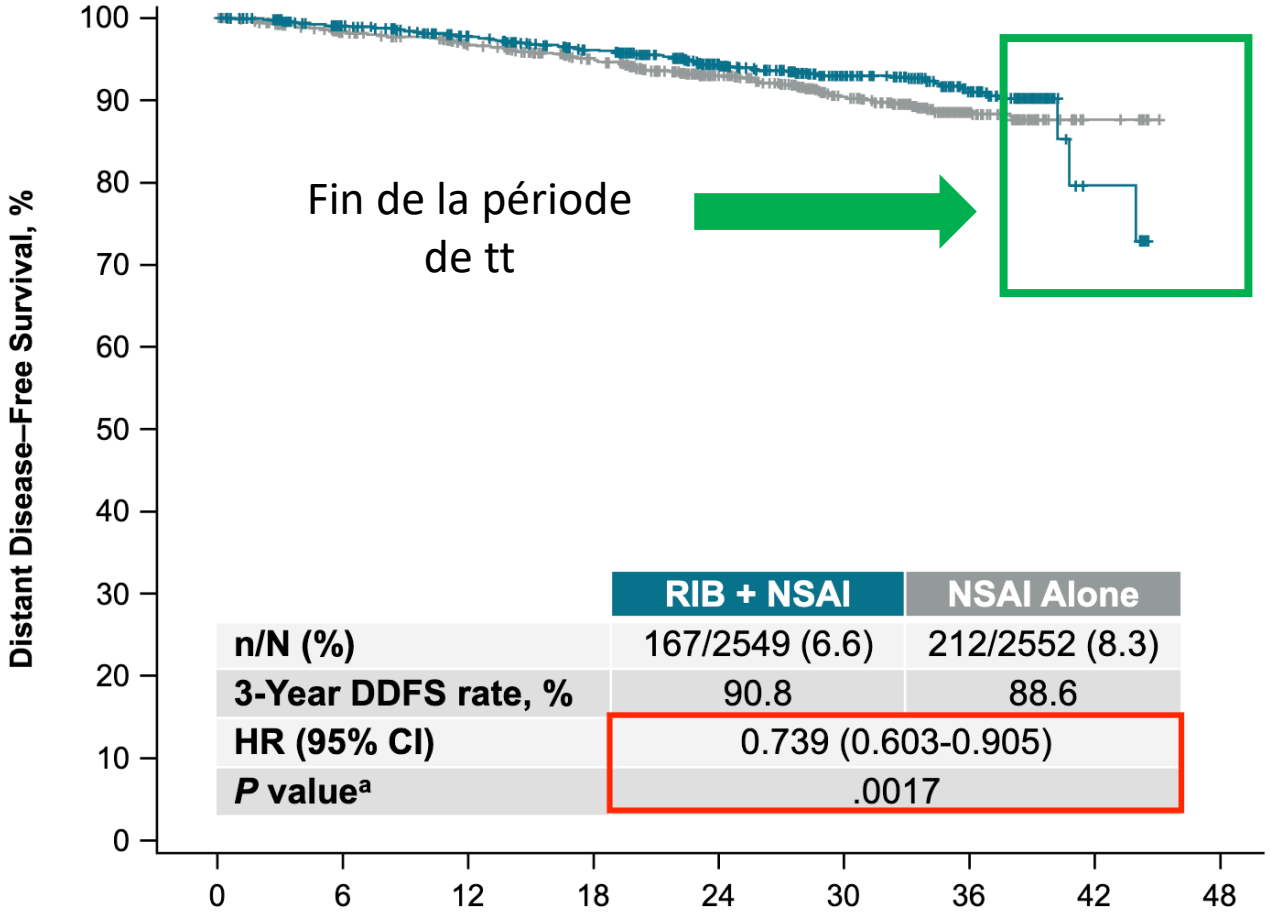
Consistent improvement in DDFS with ribociclib



	RIB + NSAI	NSAI Alone
n/N (%)	167/2549 (6.6)	212/2552 (8.3)
3-Year DDFS rate, %	90.8	88.6
HR (95% CI)	0.739 (0.603-0.905)	
P value[a]	.0017	

No. at risk									
RIB + NSAI	2549	2352	2280	2199	1729	1119	311	12	0
NSAI alone	2552	2244	2168	2080	1643	1076	288	13	0

- Distant disease–free survival is defined as the time from date of randomization to date of first event of distant recurrence, death (any cause), or second primary non-breast invasive cancer[b]
- The one-sided nominal *P* value was .0017
- Absolute distant disease–free survival benefit with RIB + NSAI at 3 years was 2.2%
- Risk of distant disease was reduced by 26.1% with RIB + NSAI vs NSAI alone

DDFS, distant disease–free survival; ET, endocrine therapy; HR, hazard ratio; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.
[a] One-sided *P* value. [b] Excluding basal and squamous cell carcinomas of the skin.

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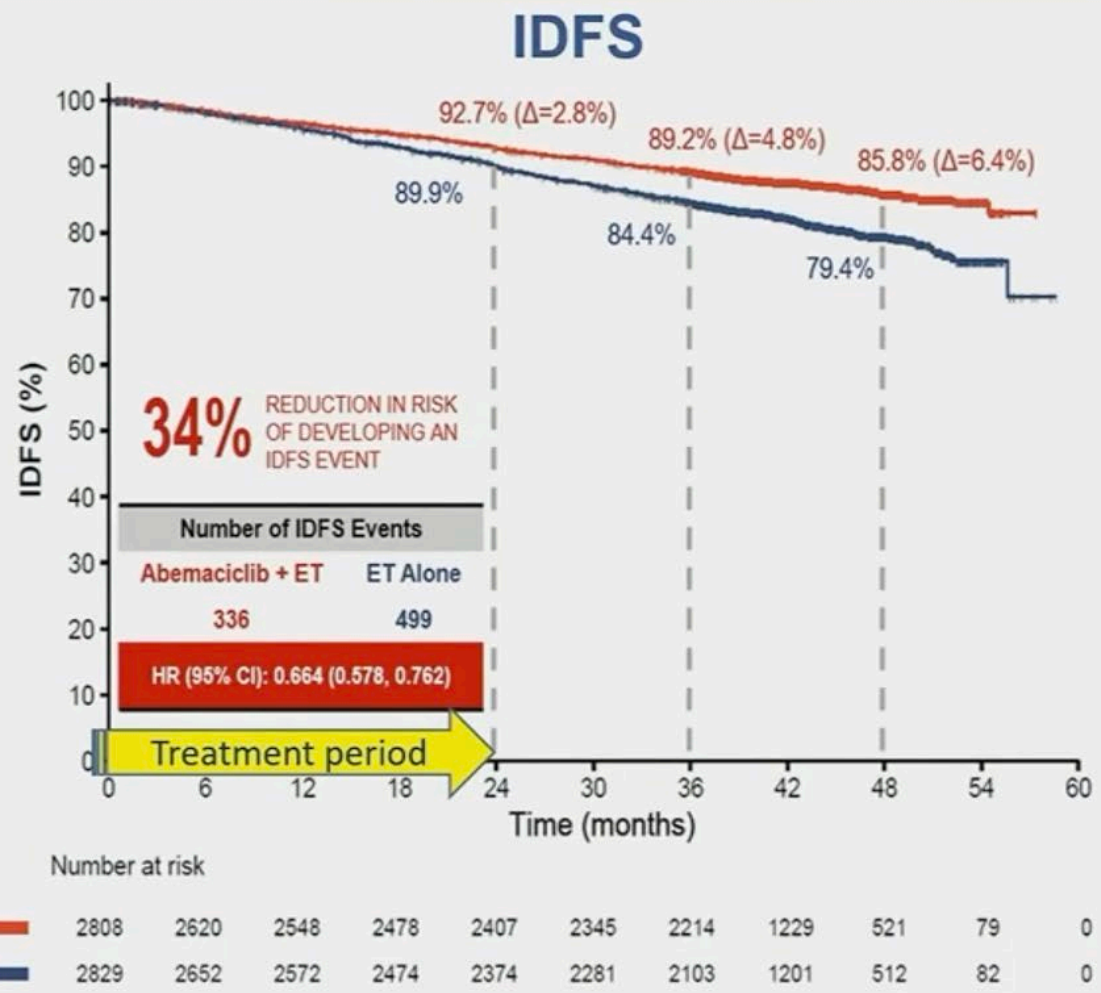
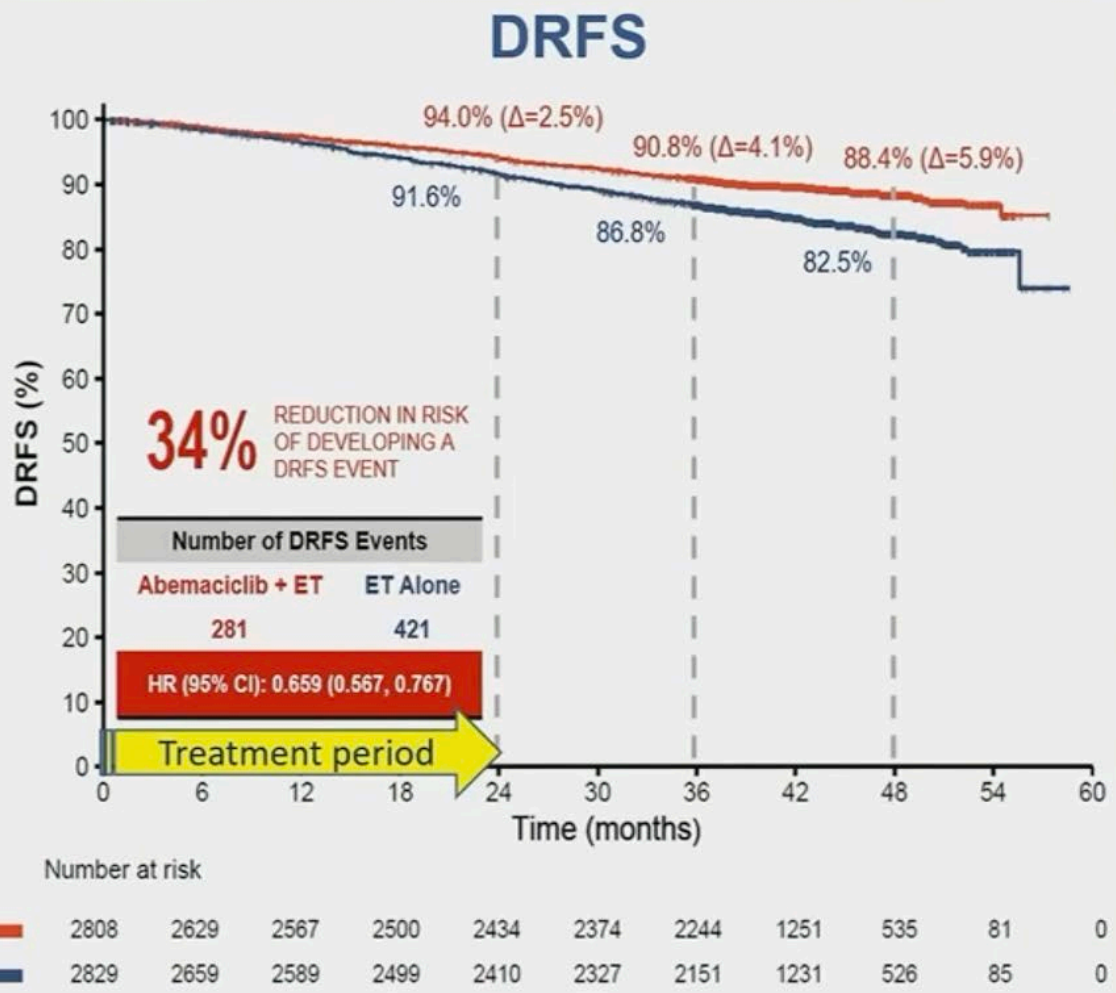
monarchE: IDFS and DRFS Benefit Persist and Deepen Beyond Completion of 2-Year Abemaciclib Treatment Period*[3]



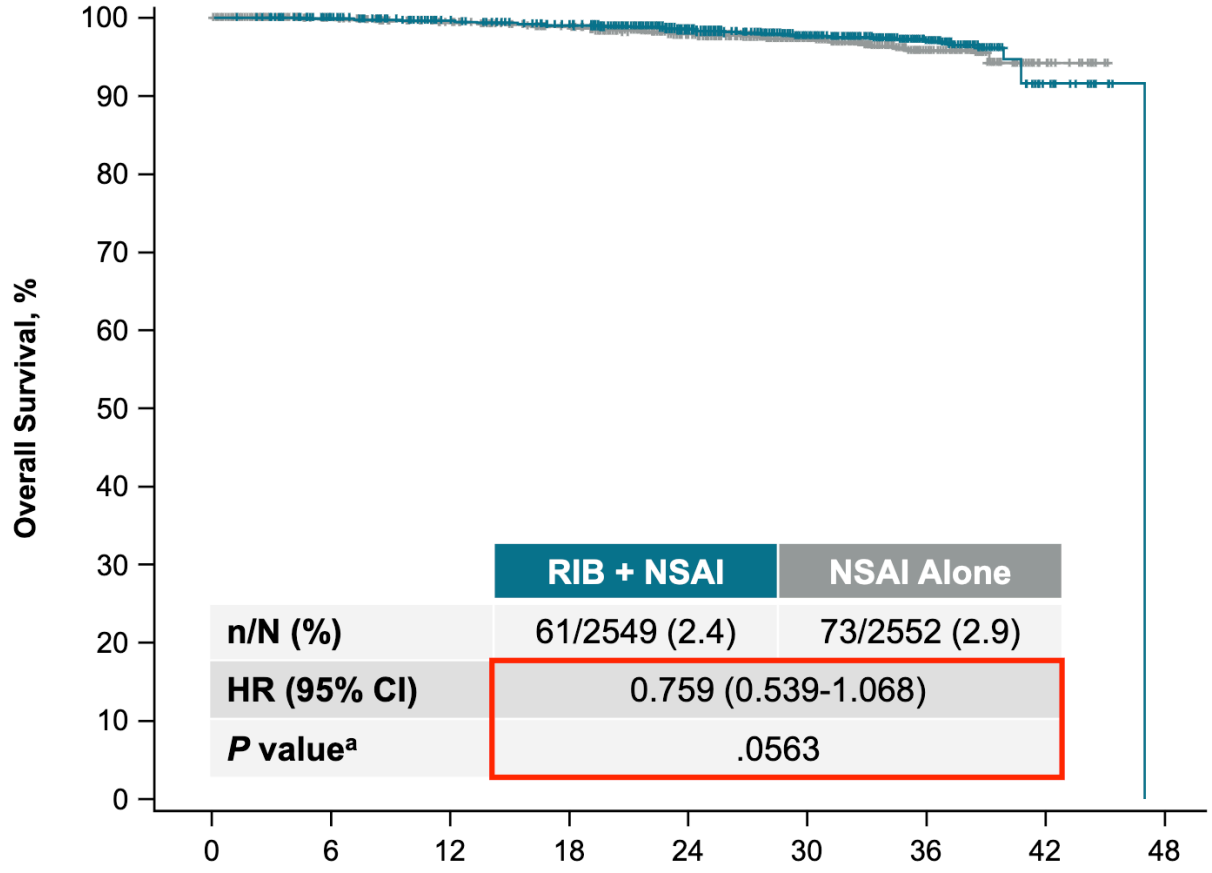


*From ITT analysis

[3]Johnston SRD et al. 2023 The Lancet Oncol;24(01):77-90

2023 ASCO

Ribociclib showed a trend for improved OS



- Median follow-up for OS was 30.4 months
- Additional follow-up for OS is planned

HR, hazard ratio; NSAI, nonsteroidal aromatase inhibitor; OS, overall survival; RIB, ribociclib.
[a] One-sided nominal *P* value.

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Median follow-up of 34.0 months (minimum, 21 months)
78% des patients sont encore sous traitement
57 % sous ribociclib
19% d'arrêt du RIB pour tox
Uniquement 4% d'arrêt de l'HT

monarchE[1]: **6%** (180/2794) early discontinuations in abemaciclib arm due to AE

PenelopeB[2]: **5%** (33/628) early discontinuations in palbociclib arm due to AE

Ribociclib at the 400-mg dose was safe and well tolerated

	RIB + NSAI n = 2524		NSAI Alone n = 2444	
AESIs, %	**Any Grade**	**Grade ≥ 3**	**Any Grade**	**Grade ≥ 3**
Neutropenia[a]	62.1	43.8	4.5	0.8
Febrile neutropenia	0.3	0.3	0	0
Liver-related AEs[b]	25.4	8.3	10.6	1.5
QT interval prolongation[c]	5.2	1.0	1.2	0.5
ECG QT prolonged	4.2	0.2	0.7	0
ILD pneumonitis[d]	1.5	0	0.8	0.1
Other clinically relevant AEs,%				
Arthralgia	36.5	1.0	42.5	1.3
Nausea	23.0	0.2	7.5	0.04
Headache	22.0	0.4	16.5	0.2
Fatigue	21.9	0.7	12.7	0.2
Diarrhea	14.2	0.6	5.4	0.1
VTE	1.4	0.6	0.6	0.2

- The most frequent all-grade AEs (RIB + NSAI vs NSAI alone) leading to discontinuation were:
  - Liver-related AEs: 8.9% vs 0.1%
  - Arthralgia: 1.3% vs 1.9%
- Most of the AE discontinuations of RIB occurred early in treatment
  - Median time of these discontinuations was 4 months

Conclusion

- Etude positive mais il faut attendre les résultats au long cours
- Confirme intérêt des CDK4/6 en adjuvant
- Toxicités acceptables mais voir les données de qualité de vie
- Quid du positionnement par rapport à l'abémaciclib ?
  - **Avis favorable au remboursement « en association avec une hormonothérapie chez les patients adultes en traitement adjuvant du cancer du sein précoce RH+/HER2-, avec atteinte ganglionnaire et haut risque de rechute » juin 2023**
  - **Indication :**
    - ≥4 ganglions lymphatiques axillaires ipsilatéraux positif,
    - ou 1 à 3 ganglion(s) lymphatique(s) axillaire(s) ipsilatéral(aux) positif(s) avec au moins un des 2 critères suivants : grade histologique 3 ou taille de la tumeur primaire ≥5 cm.
  - **Choix entre les 2 inhibiteurs de CDK sera à discuter en fonction des caractéristiques des patientes, le profil de tolérance, l'ampleur du bénéfice attendu, la durée du traitement (2 contre 3 ans) et le coût**.

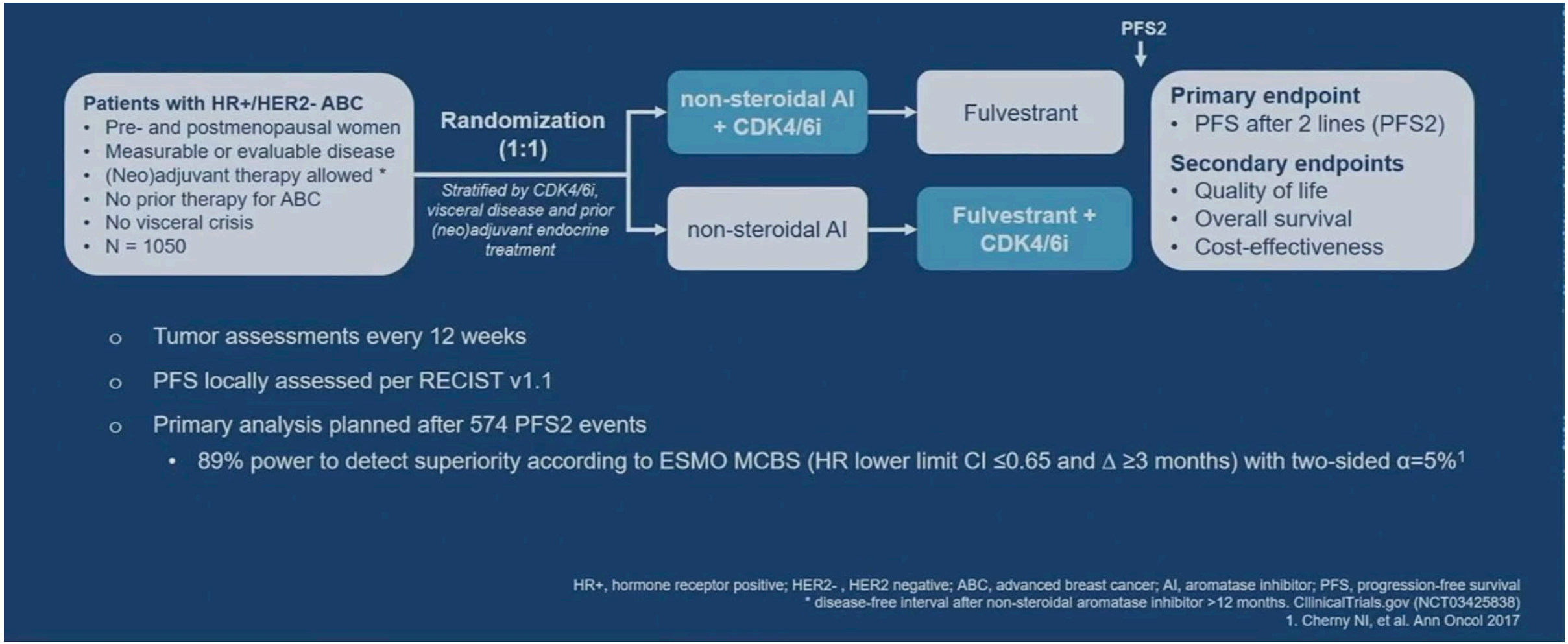
2023 ASCO ANNUAL MEETING

SONIA

Primary outcome of the phase 3 SONIA trial (BOOG 2017-03)

Gabe Sonke, Annemiek van Ommen - Nijhof, Noor Wortelboer, Vincent van der Noort, Astrid Swinkels, Hedwig Blommestein, Aart Beeker, Karin Beelen, Lisanne Hamming, Joan Heijns, Aafke Honkoop, Paul de Jong, Quirine van Rossum - Schornagel, Christa van Schaik - van de Mheen, Jolien Tol, Cathrien Tromp - van Driel, Suzan Vrijaldenhoven, Elise van Leeuwen - Stok, Inge Konings, Agnes Jager

PRESENTED BY: Prof. Gabe S. Sonke, MD, PhD



G.S. Sonke et al. ASCO® 2023, Abs. #LBA1000

Baseline characteristics

SONIA

		First-line CDK4/6i N=524	Second-line CDK4/6i N=526
Median age, years (range)		64 (24-88)	63 (25-87)
WHO PS, n (%)	0	257 (49)	257 (49)
	≥1	267 (51)	269 (51)
Menopausal status, n (%)	Pre- / perimenopausal	69 (13)	76 (14)
	Postmenopausal	455 (87)	450 (86)
Disease-free interval, n (%)	Newly diagnosed	182 (35)	182 (35)
	≤24 months	96 (18)	98 (19)
	>24 months	246 (47)	246 (47)
Prior (neo)adjuvant therapy, n (%)	Chemotherapy	212 (40)	210 (40)
	Endocrine therapy	258 (49)	254 (48)
Metastatic site, n (%)	Visceral disease	291 (56)	292 (56)
	Bone-only disease	91 (17)	91 (17)
Measurable disease, n (%)		315 (60)	312 (59)
Type of CDK4/6i, n (%)	Palbociclib	479 (91)	479 (91)
	Ribociclib	42 (8)	44 (8)
	Abemaciclib	3 (1)	3 (1)

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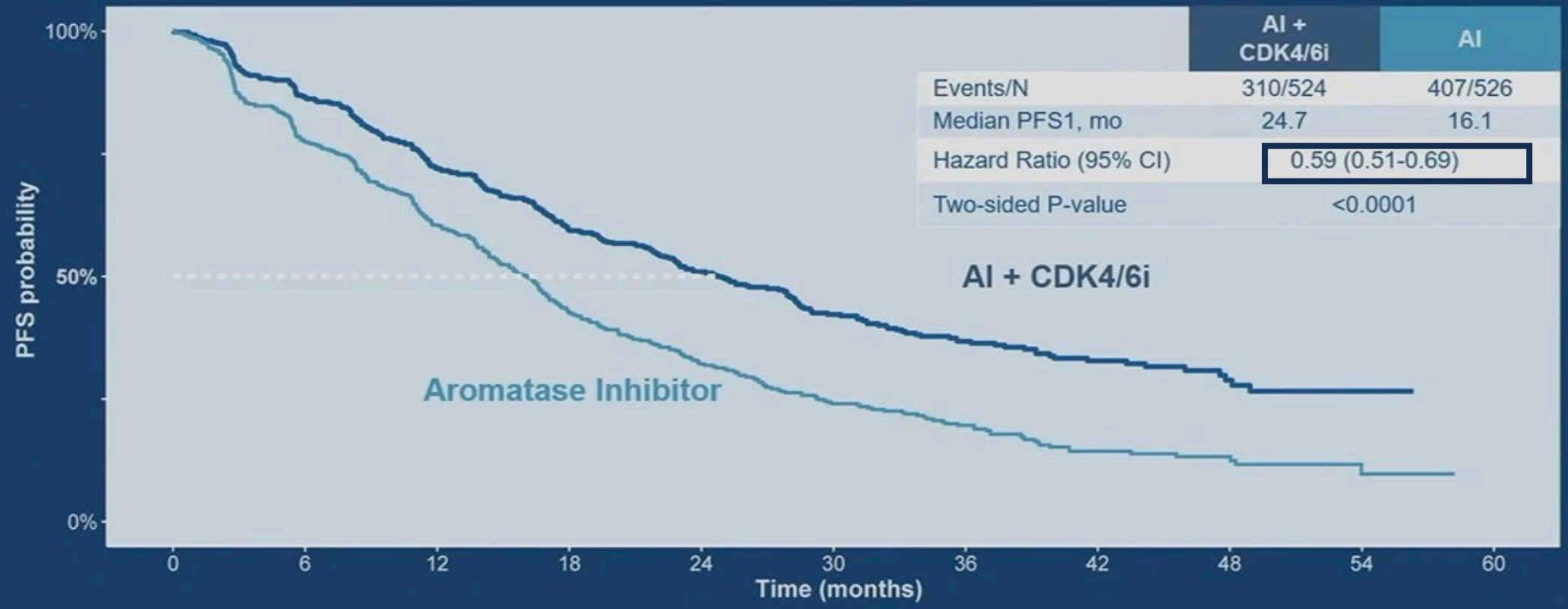
Progression-free survival in first line

SONIA



	AI + CDK4/6i	AI
Events/N	310/524	407/526
Median PFS1, mo	24.7	16.1
Hazard Ratio (95% CI)	0.59 (0.51-0.69)	
Two-sided P-value	<0.0001	

Numbers at risk (censored)

AI + CDK4/6i	524 (0)	451 (3)	374 (4)	285 (30)	202 (76)	137 (110)	101 (129)	63 (158)	27 (189)	4 (210)	0 (214)
AI	526 (0)	406 (2)	315 (4)	203 (25)	128 (54)	84 (68)	57 (81)	31 (93)	17 (105)	5 (114)	0 (119)

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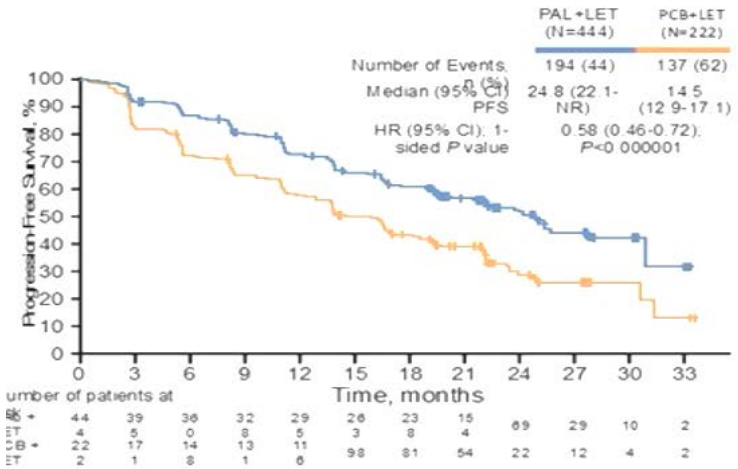
First line AI combination trials Primary endpoint PFS

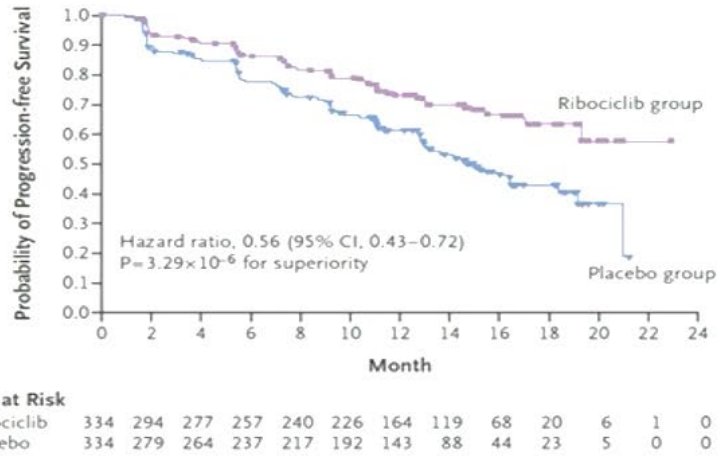
PALOMA2
palbociclib

HR 0.58, p<0.001



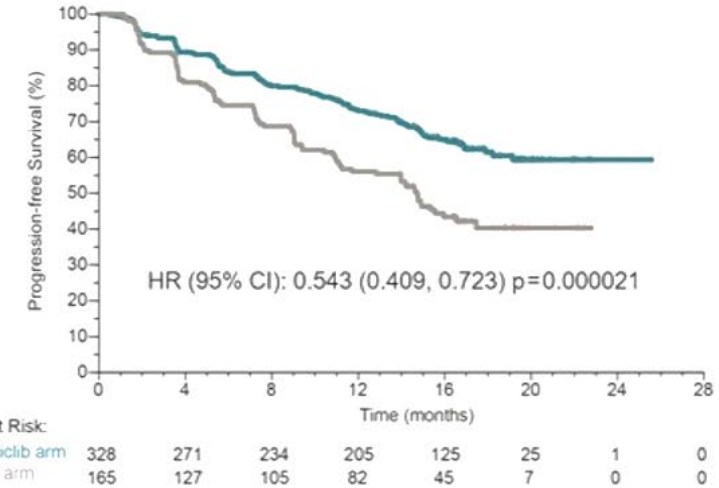
MONALEESA2
ribociclib

HR 0.56, p<0.001



MONARCH3
abemaciclib

HR 0.54, p<0.001



All inhibitors similar efficacy in PFS primary

First line AI plus CDK4/6 inihibitor is the standard of care

Finn *et al* NEJM 2016

Hortobagyi *et al* NEJM 2016

Di Leo *et al* JCO 2017

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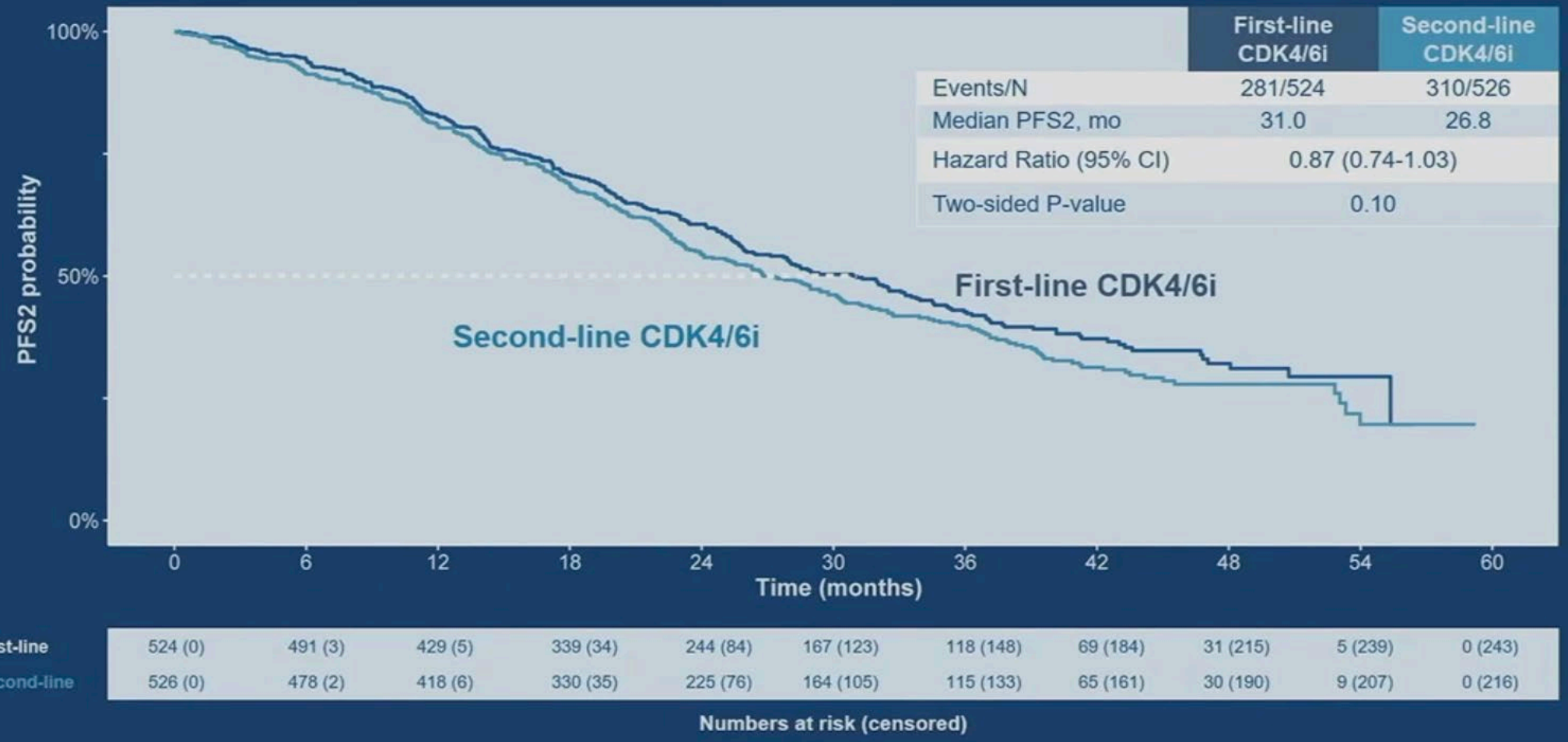
Primary endpoint: PFS2

SONIA



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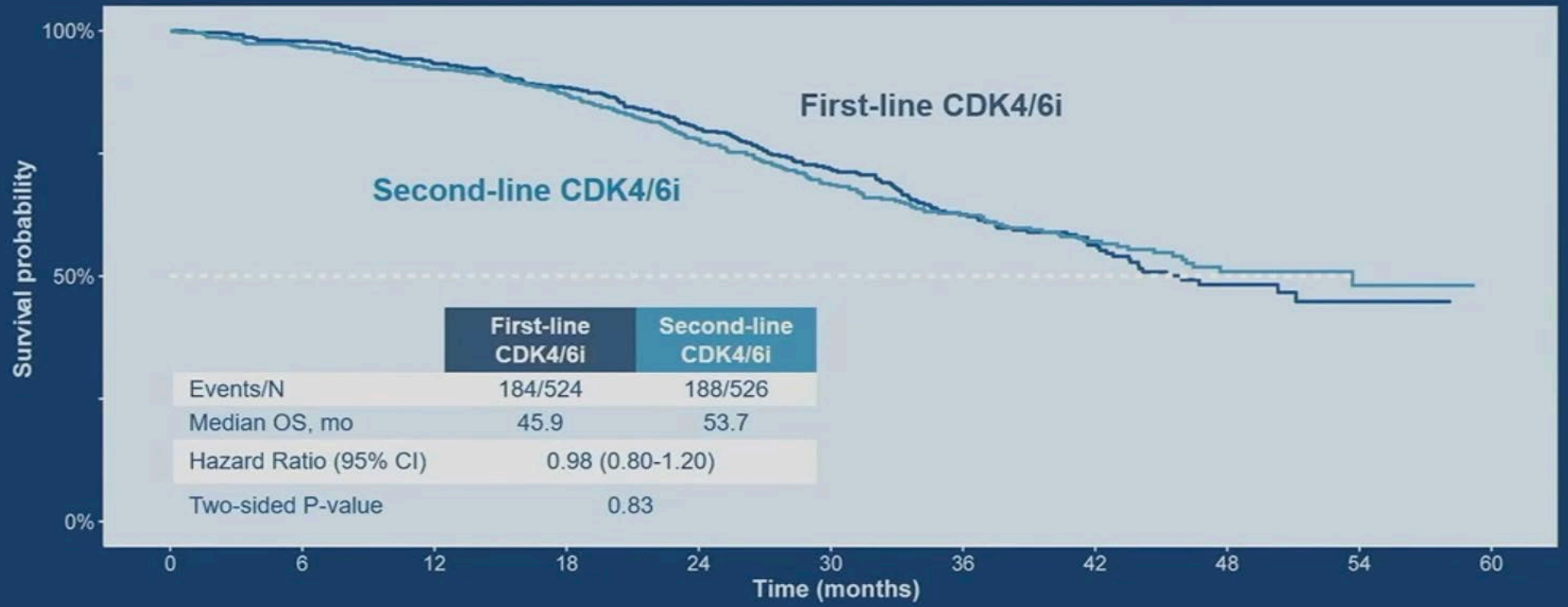
Overall survival

SONIA



	First-line CDK4/6i	Second-line CDK4/6i
Events/N	184/524	188/526
Median OS, mo	45.9	53.7
Hazard Ratio (95% CI)	0.98 (0.80-1.20)	
Two-sided P-value	0.83	

Numbers at risk (censored)

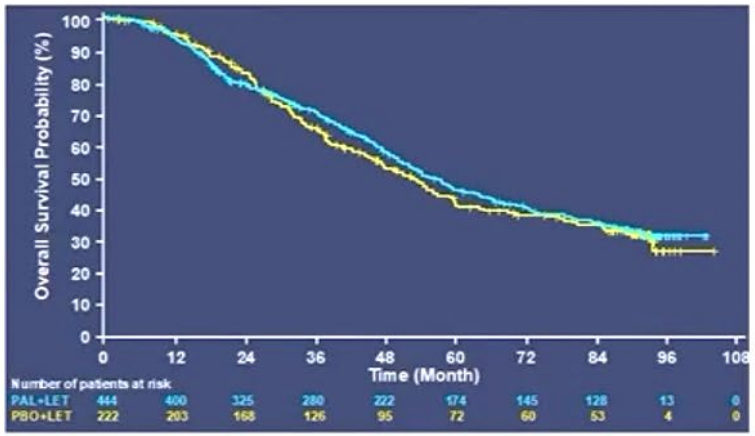
First-line	524 (0)	510 (3)	485 (4)	427 (37)	324 (103)	240 (157)	171 (197)	104 (250)	42 (300)	7 (333)	0 (340)
Second-line	526 (0)	506 (2)	483 (2)	426 (32)	328 (89)	242 (139)	175 (186)	112 (236)	52 (287)	16 (322)	0 (338)

G.S. Sonke et al. ASCO® 2023, Abs. #LBA1000

First line AI combination trials Secondary endpoint OS

PALOMA2
palbociclib

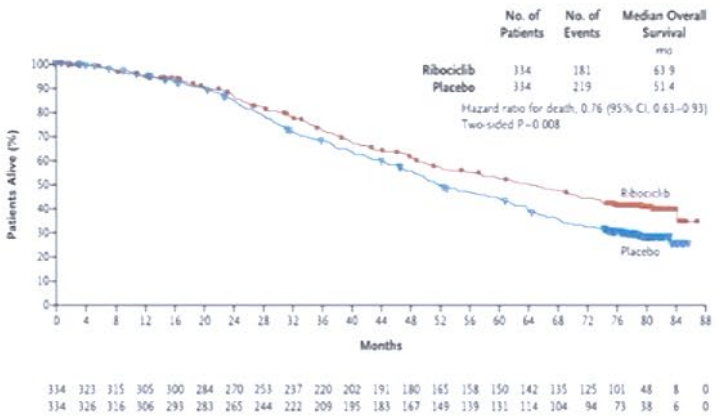
HR 0.96, p=0.3



Finn *et al* ASCO 2022

MONALEESA2
ribociclib

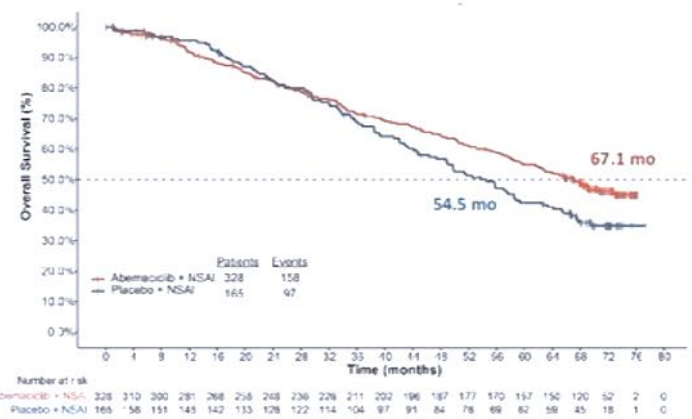
HR 0.76, p=0.008



Hortobagyi *et al* NEJM 2022

MONARCH3
abemaciclib

HR 0.754, p=0.03 NS



Goetz *et al* ESMO 2022

Quality of life

SONIA

- Quality of life was assessed using validated questionnaires
- Up to 11 timepoints
- FACT-B and EQ-5D-5L
- Completion rate 87% for FACT-B in both arms
- FACT-B subscores and cost-effectiveness analyses will follow

No difference in FACT-B total score between the study arms (p=0.4)

G.S. Sonke et al. ASCO® 2023, Abs. #LBA1000

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Conclusion

Etude de stratégie importante

L'administration d'un iCDK 4/6 en première ligne, par rapport à sa prescription en deuxième ligne

- N'améliore pas la survie sans progression SSP2
- N'améliore pas la survie globale
- N'améliore pas la qualité de vie

Conclusion de l'auteur :

- Augmente la durée de prescription de l'iCDK 4/6 de 16,5 mois
- Augmente l'incidence des toxicités de grade 3-4 de 42 %
- Augmente le prix du traitement par patient de 200 000 dollars

Remise de l'intérêt des iCDK4/6 en 1ère ligne ou de l'intérêt du Palbociclib en 1ère ligne ?

Second-line endocrine therapy with or without palbociclib maintenance in patients with HR[+]/HER2[-] advanced breast cancer: PALMIRA trial

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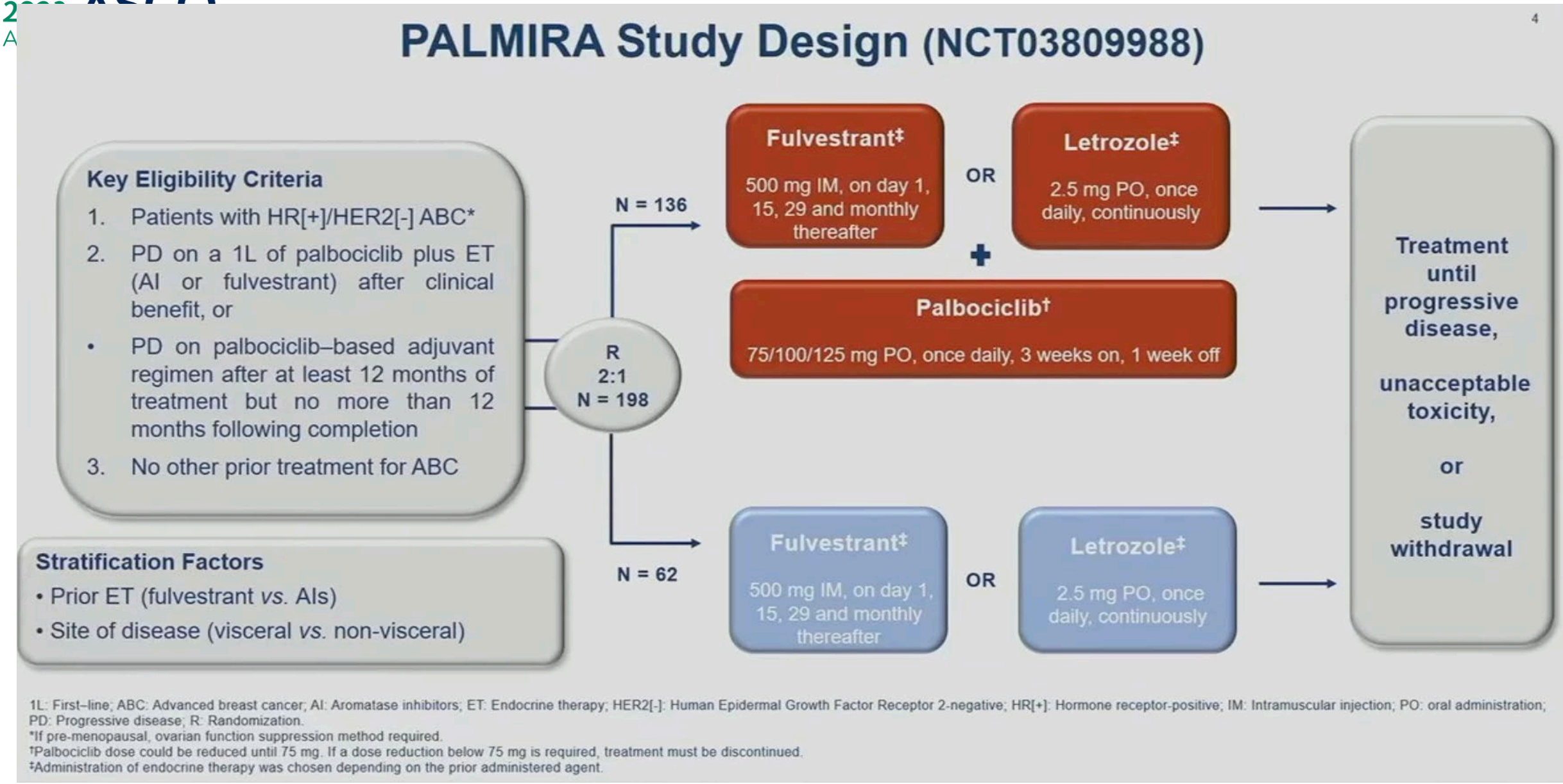
PRESENTED BY: Dr. ANTONIO LLOMBART CUSSAC, MD PhD

palmira

PALMIRA Study Design (NCT03809988)



1L: First–line; ABC: Advanced breast cancer; AI: Aromatase inhibitors; ET: Endocrine therapy; HER2[-]: Human Epidermal Growth Factor Receptor 2-negative; HR[+]: Hormone receptor-positive; IM: Intramuscular injection; PO: oral administration; PD: Progressive disease; R: Randomization.
*If pre-menopausal, ovarian function suppression method required.
†Palbociclib dose could be reduced until 75 mg. If a dose reduction below 75 mg is required, treatment must be discontinued.
‡Administration of endocrine therapy was chosen depending on the prior administered agent.

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Study Endpoints

Primary Endpoint

- Investigator-assessed progression-free survival (PFS) determined by RECIST v.1.1

Secondary Endpoints

- Objective response rate (ORR), clinical benefit rate (CBR), overall survival (OS), duration of response (DoR), time to response (TTR), and time to progression (TTP)
- ORR, DoR, TTR, CBR, TTP, OS, and PFS by prior endocrine therapy, site of disease, and HER2 expression status
- Overall change from baseline in patient reported global quality of life (QoL), functioning, symptoms and general health status
- Time to deterioration in global QoL
- Time to deterioration in pain
- Time to first chemotherapy
- Safety and tolerability

Exploratory Endpoints

- Molecular subtypes
- Predictive biomarkers

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Baseline Characteristics (ITT population)

Baseline characteristics, n (%)	ET + Palbociclib (N = 136)	ET (N = 62)
Age in years, Median (Min; Max)	59 (33; 85)	61 (34; 83)
Menopausal status		
Premenopausal	18 (13.2%)	6 (9.7%)
Postmenopausal	118 (86.8%)	56 (90.3%)
ECOG PS score		
0	90 (66.2%)	31 (50.0%)
1*	45 (33.1%)	31 (50.0%)
Measurable disease at baseline		
Yes	94 (69.1%)	44 (71.0%)
No	42 (30.9%)	18 (29.0%)
Visceral involvement		
Yes	84 (61.8%)	37 (59.7%)
No	52 (38.2%)	25 (40.3%)

ECOG PS: Eastern Cooperative Oncology Group performance status; ITT: Intention to treat.

*One patient in ET + Palbociclib group had ECOG 2.

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Baseline Characteristics cont. (ITT population)

Baseline characteristics, n (%)	ET + Palbociclib (N = 136)	ET (N = 62)
Number of metastatic sites		
<3	92 (67.6%)	38 (61.3%)
≥3	44 (32.4%)	24 (38.7%)
Prior endocrine therapy used in combination with palbociclib		
Fulvestrant	16 (11.8%)	4 (6.5%)
Aromatase Inhibitor	120 (88.2%)	58 (93.5%)
Duration of first-line palbociclib (6-12; ≥12 months)		
6-12 months	18 (13.2%)	10 (16.1%)
≥ 12 months	118 (86.8%)	52 (83.9%)
Last dose of first-line palbociclib		
125 mg	83 (53.2%)	33 (61.0%)
100 mg	45 (43.5%)	27 (33.1%)
75 mg	8 (3.2%)	2 (5.9%)

ITT: Intention to treat.

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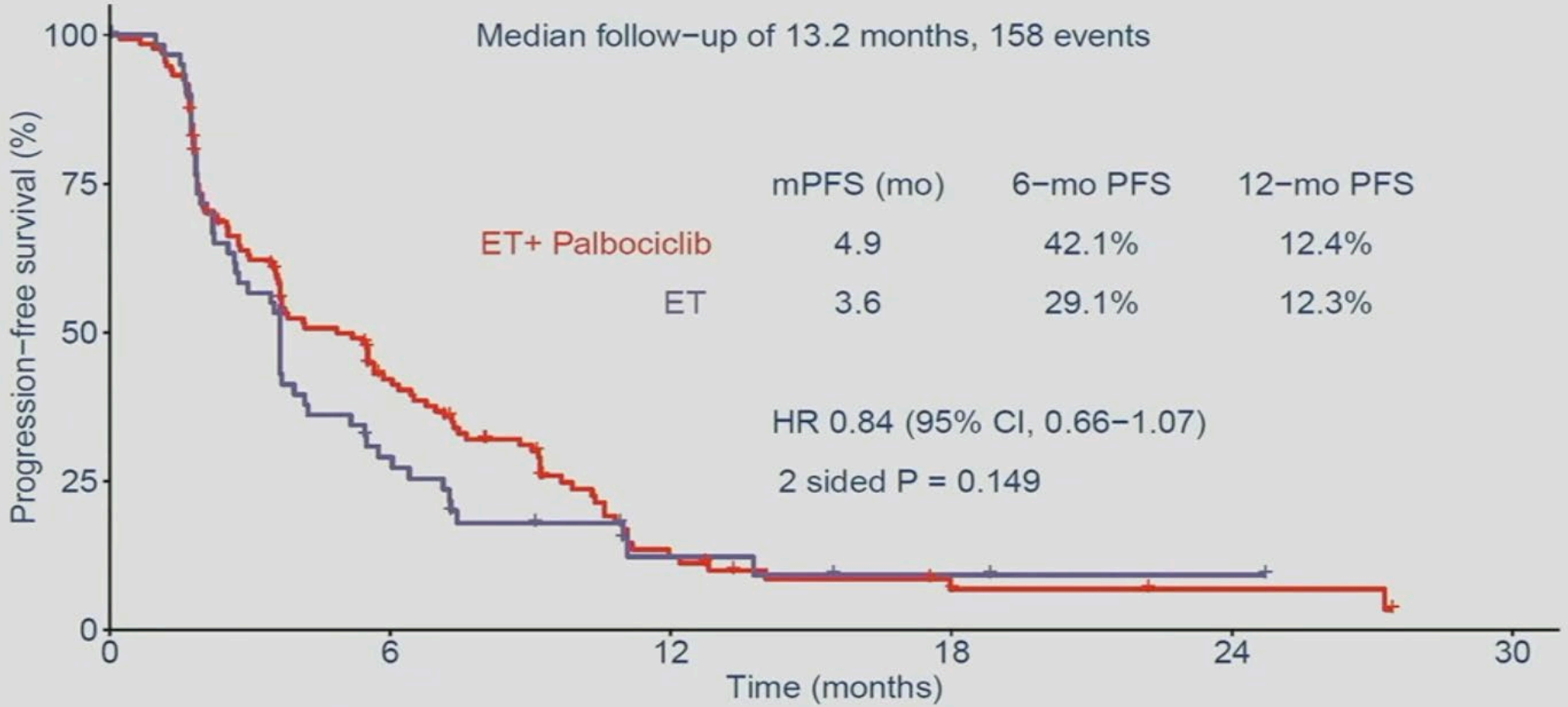
Primary Objective: Investigator-assessed PFS (ITT Population)



Patients at risk, n (%)

ET+Palbociclib	136 (100)	47 (35)	11 (8)	4 (3)	2 (1)	0 (0)
ET	62 (100)	16 (26)	4 (6)	2 (3)	1 (2)	0 (0)

CI: Confidence interval; HR: Hazard ratio; ITT: Intention to treat; mo: Months; mPFS: Median progression-free survival; PFS: Progression-free survival.

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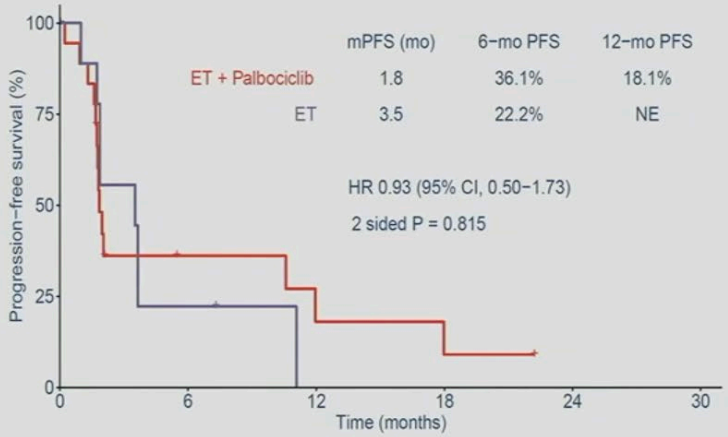
PFS by prior duration of palbociclib treatment (ITT Population)

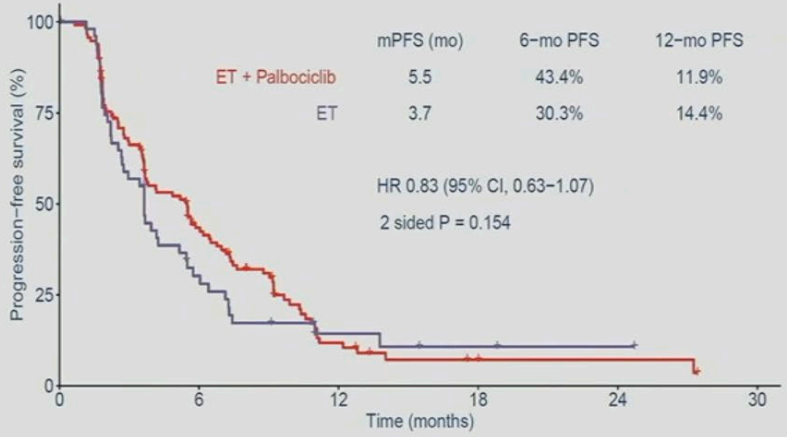
6-12 months (N = 28)



Patients at risk, n (%)

ET+Palbociclib	18 (100)	4 (22)	2 (11)	1 (6)	0 (0)	0 (0)
ET	10 (100)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)

≥ 12 months (N = 170)



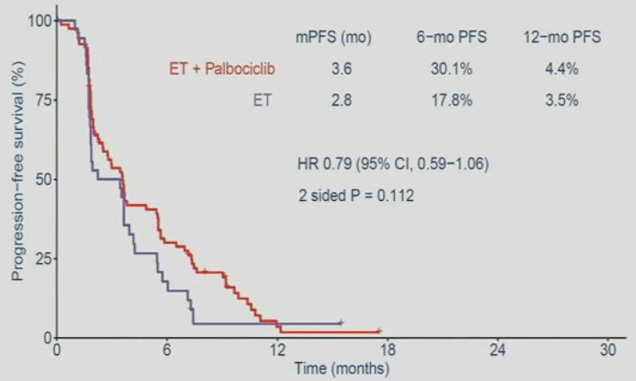
Patients at risk, n (%)

ET+Palbociclib	118 (100)	43 (36)	9 (8)	3 (3)	2 (2)	0 (0)
ET	52 (100)	14 (27)	4 (8)	2 (4)	1 (2)	0 (0)

CI: Confidence interval; HR: Hazard ratio; ITT: Intention to treat; mo: Months; mPFS: Median progression-free survival; PFS: Progression-free survival.

PFS by Visceral Disease (ITT Population)

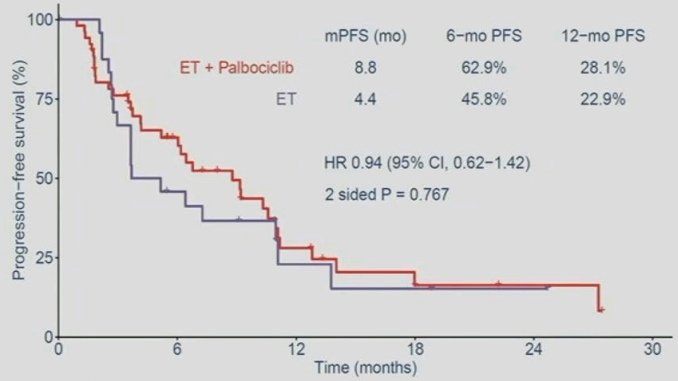
Visceral involvement (N = 121)



Patients at risk, n (%)

ET+Palbociclib	84 (100)	23 (27)	2 (2)	0 (0)	0 (0)	0 (0)
ET	37 (100)	6 (16)	1 (3)	0 (0)	0 (0)	0 (0)

Without visceral involvement (N = 77)



Patients at risk, n (%)

ET+Palbociclib	52 (100)	24 (46)	9 (17)	4 (8)	2 (4)	0 (0)
ET	25 (100)	10 (40)	3 (12)	2 (8)	1 (4)	0 (0)

CI: Confidence interval; HR: Hazard ratio; ITT: Intention to treat; mo: Months; mPFS: Median progression-free survival; PFS: Progression-free survival.

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Conclusion

- Etude de stratégie importante +++
- Pas de poursuite du CDK4/6 systématique
- Rôle du palbociclib ?

	MAINTAIN	PACE	PALMIRA
Patients (n)	120	166	198
1st line CDK4/6i	Palbociclib (84%)	Palbociclib (90%)	Palbociclib (100%)
% 1st line CDK4/6i >12mo	67%	75%	86%
Endocrine therapy	Fulvestrant (83%) or exemestane	Fulvestrant (100%)	Fulvestrant (90%) or letrozole
'Continuation' CDK4/6i	Ribociclib	Palbociclib	Palbociclib
PFS ET only	**2.8mo**	**4.8mo**	**3.6mo**
PFS Fulv + CDK4/6i	**5.3mo**	**4.6mo**	**4.9mo**

alinsky *JCO* 2023; Mayer *SABCS* 2022; Llombart-Cussac *ASCO* 2023

- Intérêt du fulvestrant ? Place des nouveaux SERDS ?