



18^{as} Jornadas **HITOS** **2023**
ONCOLÓGICOS: LO MEJOR DE

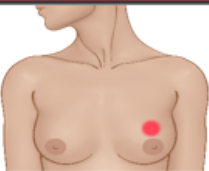
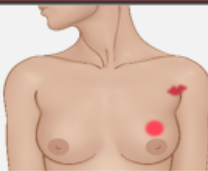
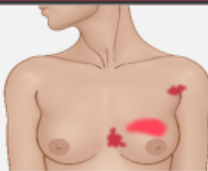
Madrid, 22 y 23 de noviembre de 2023

Ribociclib adyuvante en cáncer de mama HR+/HER2-: estudio NATALEE

Dr. Manuel Ruiz, Hospital Universitario Virgen del Rocío, Sevilla



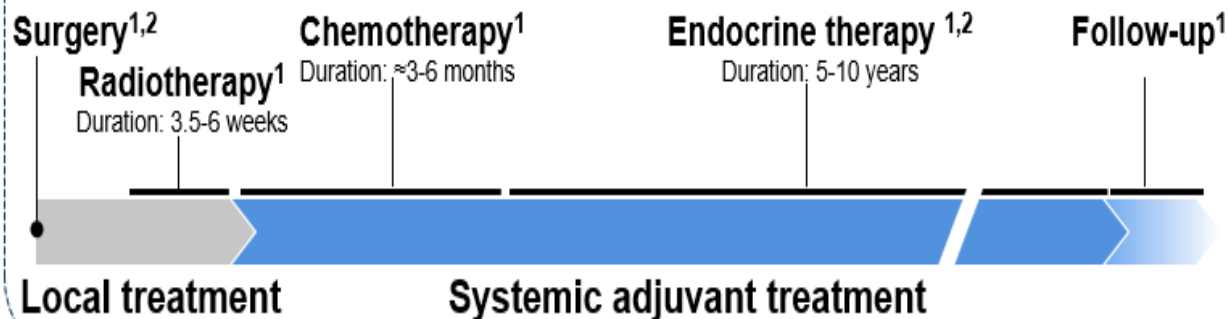
PORQUE ?

	Early breast cancer ¹		Locally advanced breast cancer ²
	Stage I	Stage II (IIA, IIB)	Stage III (IIIA, IIIB, IIIC)
Location of disease			
Patients Diagnosed with HR+/HER2- BC, % ³	54%	30%	10%
Risk of Recurrence, % ^{4,a}	18%	27-37%	46-57%



Treatment options for EBC
have not changed
in the last **two decades**

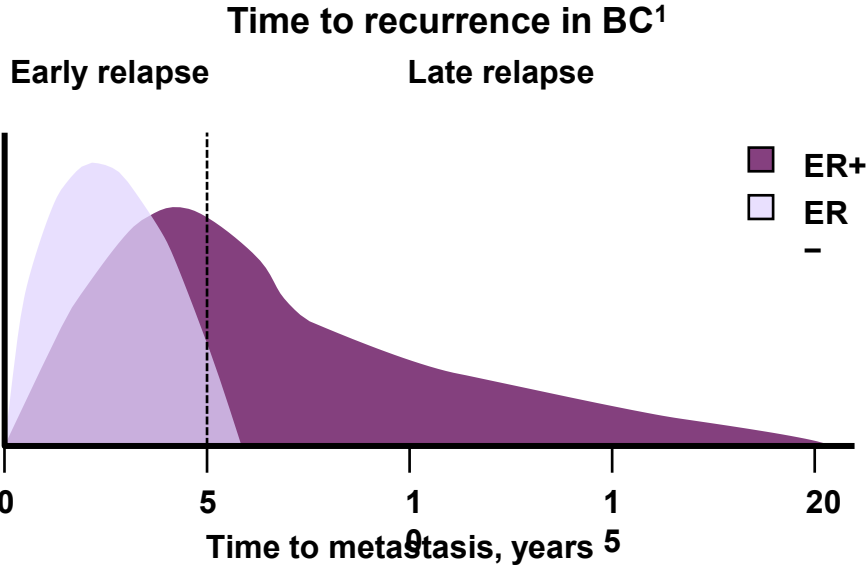
Treatment Journey: HR+, HER2- Early Breast Cancer



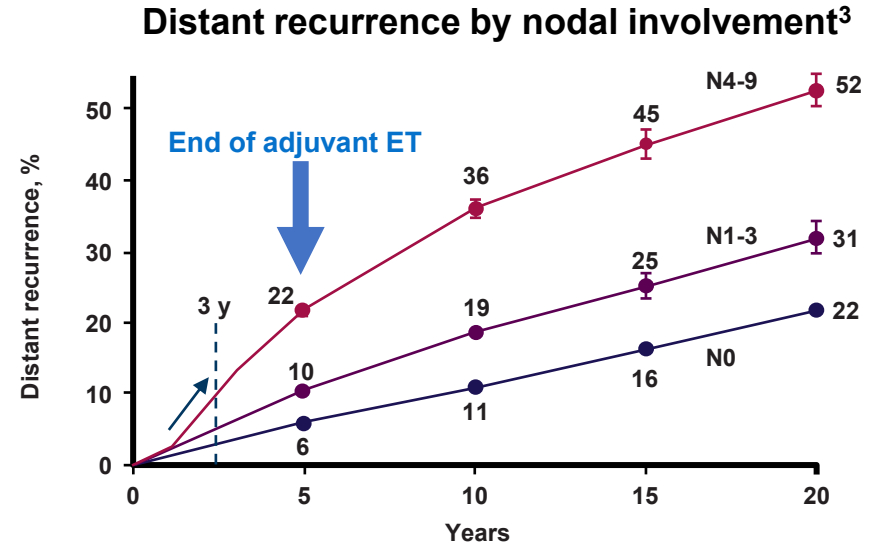
EBC

ABC

Risk of recurrence is high in HR+ EBC and continues after completion of adjuvant ET



- Unlike most solid tumors, ER+ breast cancer may recur 5–30 years after initial diagnosis²
- Longer treatment duration may be necessary to prevent early and late recurrences

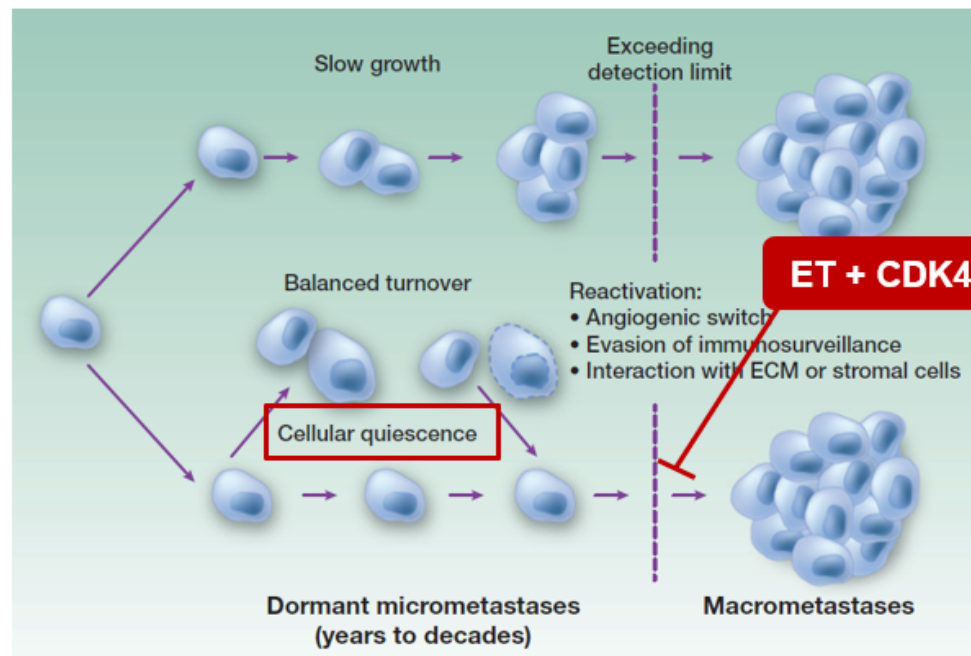


- >50% of recurrences occur after 5 years of adjuvant ET⁴
- Risk of recurrence remains with adjuvant ET and beyond 3 years³



Control of Micrometastatic Disease

Possible mechanisms underlying metastasis dormancy¹



- CDK4 inhibition has been previously demonstrated to lead to cell senescence (irreversible cell cycle arrest)²⁻⁴

Combination of ET + CDK4/6i is expected to achieve better control of micrometastatic disease



	NATALEE ^{1,2}	PALLAS ^{3,4}	PENELOPE-B ^{5,6}	monarchE ^{7,8}
N	5101	5796	1250	5637
Sex	Men and women	Men and women	Women	Men and women
Menopausal status	Pre- and postmenopausal	Pre- and postmenopausal	Pre- and postmenopausal	Pre- and postmenopausal
Disease severity	<ul style="list-style-type: none"> • Stage III (N0 and N1) • Stage IIB (N0 and N1) and IIA N1 • Stage IIA N0 G3 or N0 G2 with Ki-67 $\geq 20\%$ or high risk by genetic test • Stage II pts capped at 40% of enrollment 	<ul style="list-style-type: none"> • Stage II • Stage III • N0, N1, N2, N3 	<ul style="list-style-type: none"> • Residual invasive disease after neoadjuvant therapy ≥ 16 weeks (including 6 weeks of <u>taxane</u>) • CPS-EG ≥ 3 or score 2 if <u>ypN+</u> • N0, N1, N2, N3 	<ul style="list-style-type: none"> • Cohort 1: ≥ 4 ALN or 1-3 ALN + tumor size ≥ 5 cm and/or grade 3 • Cohort 2: 1-3 ALN + Ki-67 $\geq 20\%$
CDK4/6i, dose	RIB 400 mg QD (3 weeks on/1 week off)	PAL 125 mg QD (3 weeks on/1 week off)	PAL 125 mg QD (3 weeks on/1 week off)	ABE 150 mg BID
ET partner	LET or ANA	AI or TAM \pm LHRH agonist	Standard adjuvant ET	Standard adjuvant ET (eg, AI, TAM, LHRH agonist)
ET prior to randomization	≤ 12 months ([neo]adjuvant)	≤ 6 months (adjuvant)	Not specified	≤ 12 weeks (adjuvant)
Duration of CDK4/6i therapy	3 years	2 years	~13 months	Up to 2 years

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 \geq 20%
 - Oncotype DX Breast Recurrence Score \geq 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 \geq 5 y
+ goserelin in men
and premenopausal
women

NSAI

Letrozole or
anastrozole^d for \geq 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

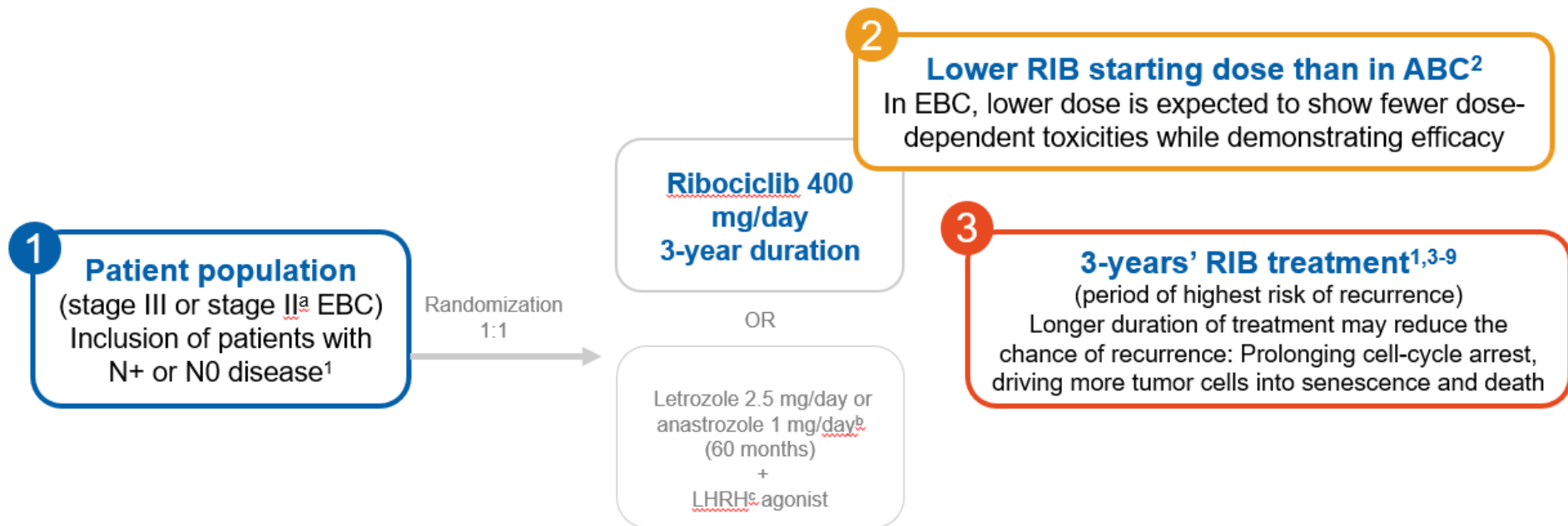
Anatomical stage: II vs III

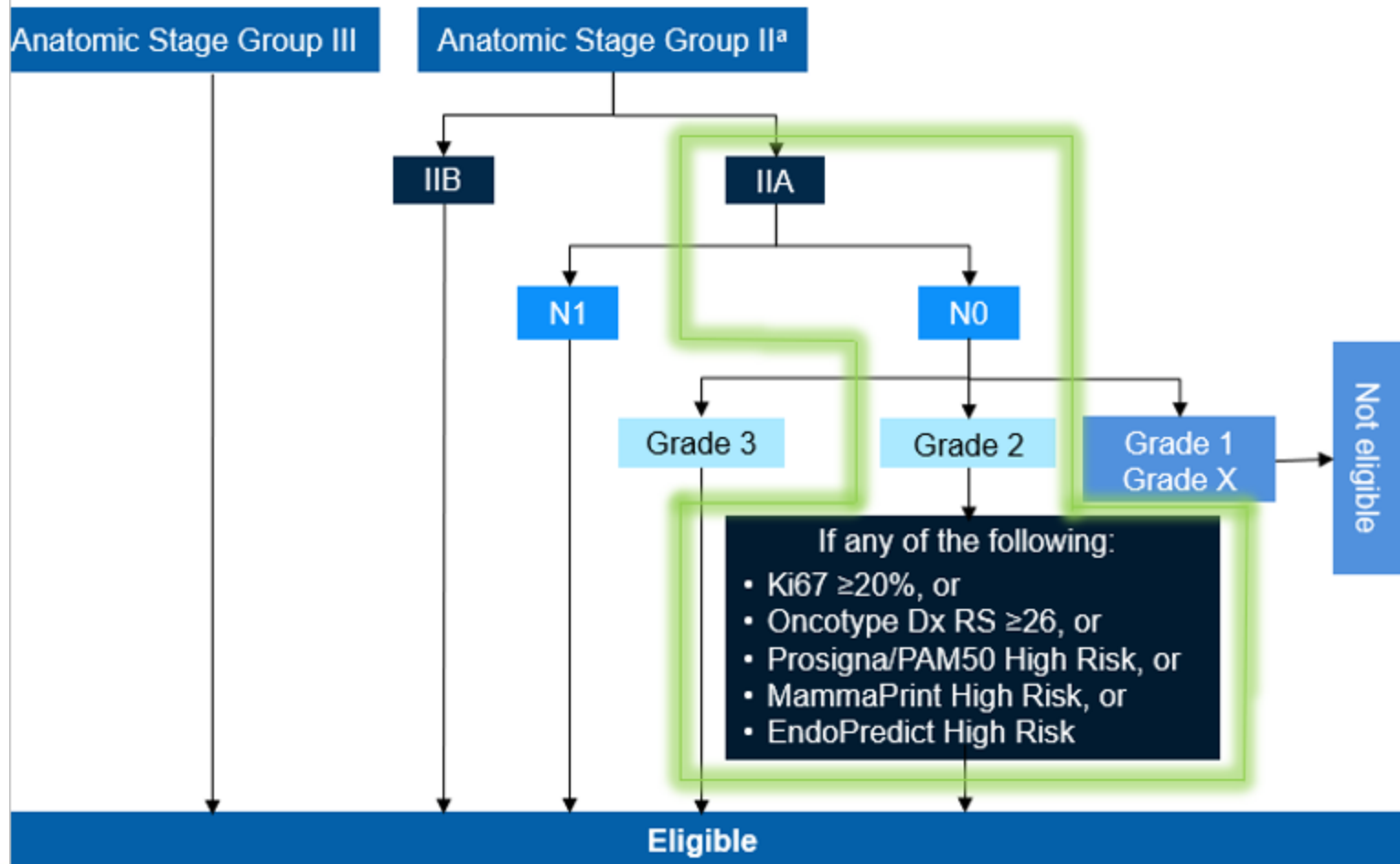
Menopausal status: men and premenopausal women vs postmenopausal women

Receipt of prior (neo)adjuvant chemotherapy: yes vs no

Geographic location: North America/Western Europe/Oceania vs rest of world

DIFERENCIAS EN EL ESTUDIO NATALEE





Baseline characteristics

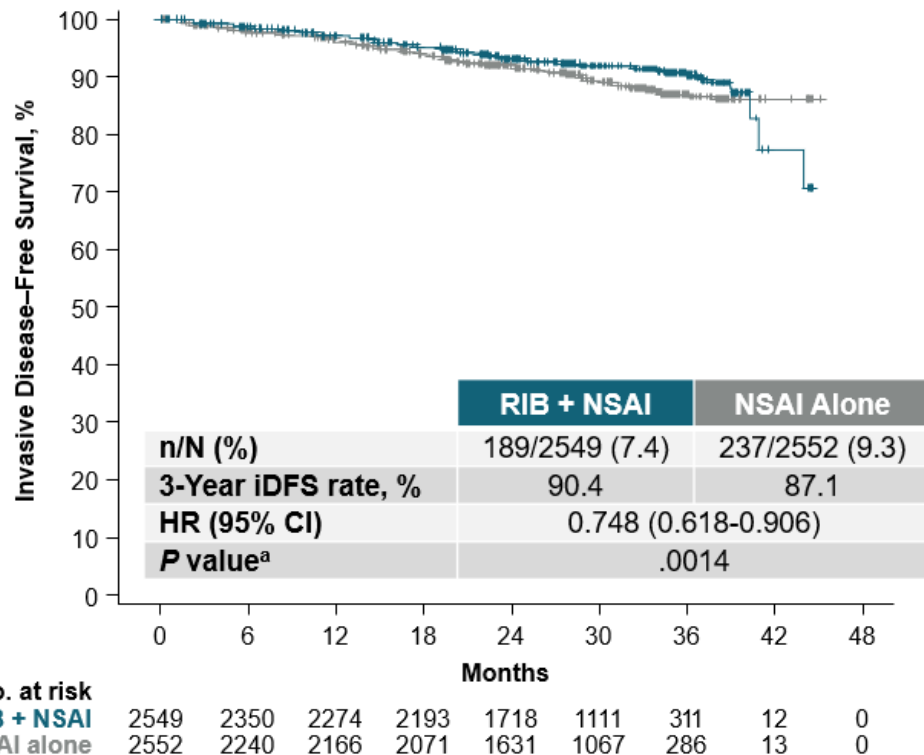
Parameter	RIB + NSAI n = 2549	NSAI Alone n = 2552	All Patients N = 5101
Age, median (min-max), years	52 (24-90)	52 (24-89)	52 (24-90)
Menopausal status, n (%)			
Men ^a and premenopausal women	1126 (44)	1132 (44)	2258 (44)
Postmenopausal women	1423 (56)	1420 (56)	2843 (56)
Anatomical stage,^{b,c} n (%)			
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)

Median follow-up of 34.0 months (minimum, 21 months)^a

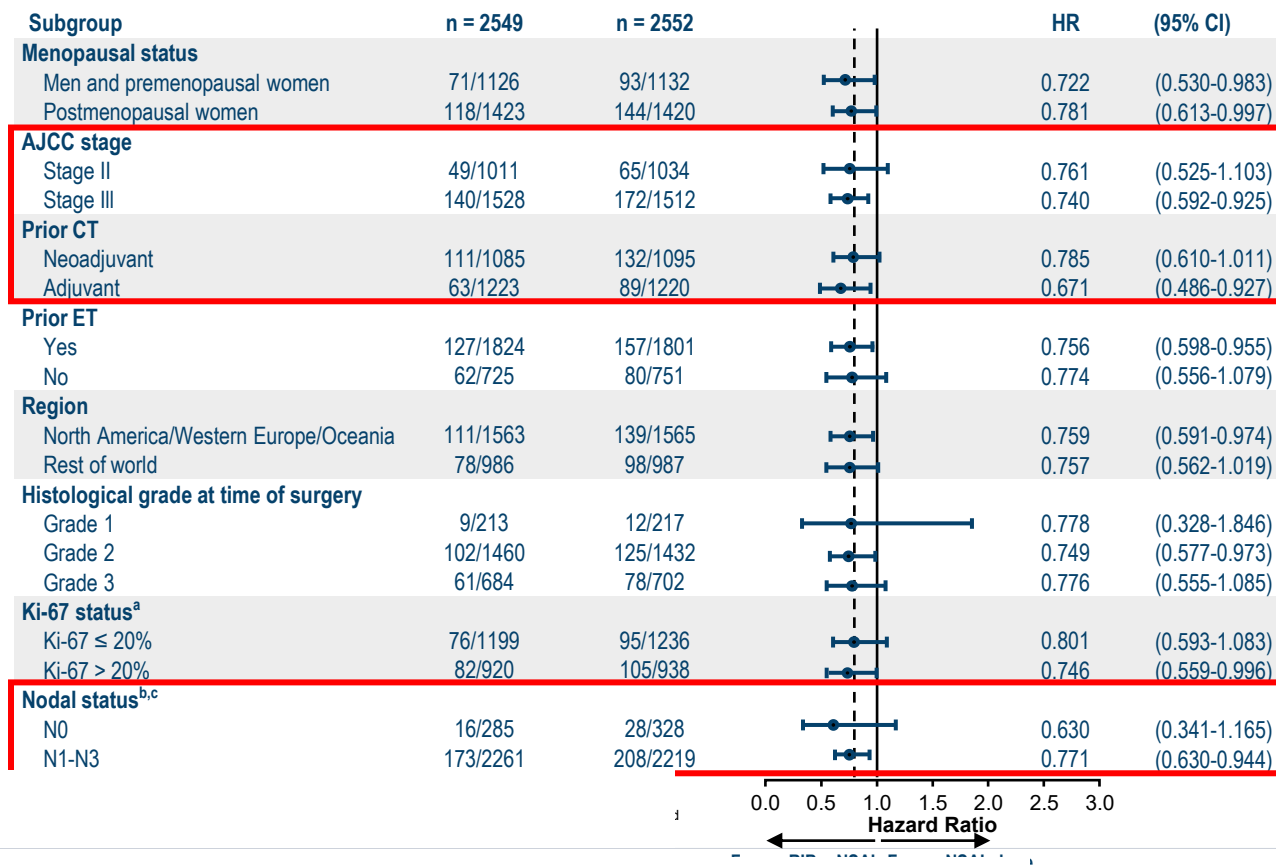
Parameter, n %	RIB + NSAI n = 2549	NSAI alone n = 2552
Patients treated	2526 (99)	2442 (96)
Patients with treatment ongoing ^b	1984 (78)	1826 (72)
Patients who discontinued NSAI	542 (21)	617 (24)
Primary reason for treatment discontinuation (NSAI)^c		
Adverse Event	118 (5)	105 (4)
Patient/Physician decision	256 (10)	296 (12)
Disease relapse	142 (6)	186 (7)
Other ^d	13 (0.5)	15 (0.6)
Lost to follow-up	8 (0.3)	12 (0.5)
Death ^e	5 (0.2)	3 (0.1)
Patients who completed ribociclib treatment		
≥2 years (including ongoing)	1449 (57)	-
Completed 3 years RIB	515 (20)	-
Primary reason for early discontinuation of RIB^f		
Adverse Event	477 (19)	-

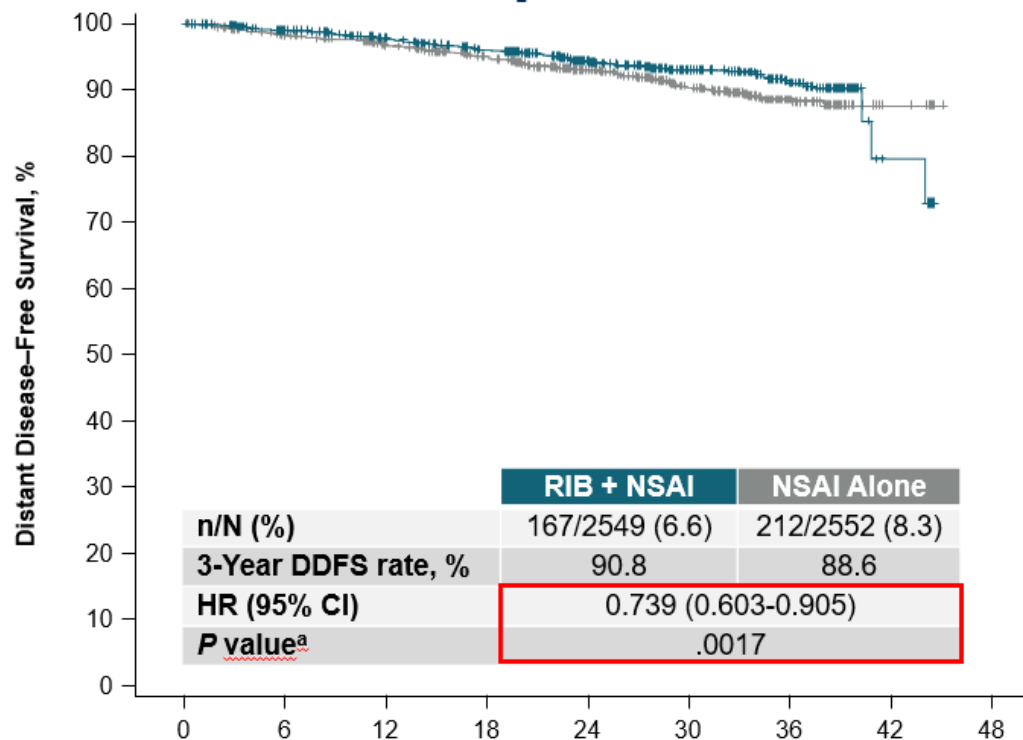
Ribociclib alcanza la significación estadística en iDFS

Primary endpoint of NATALEE met



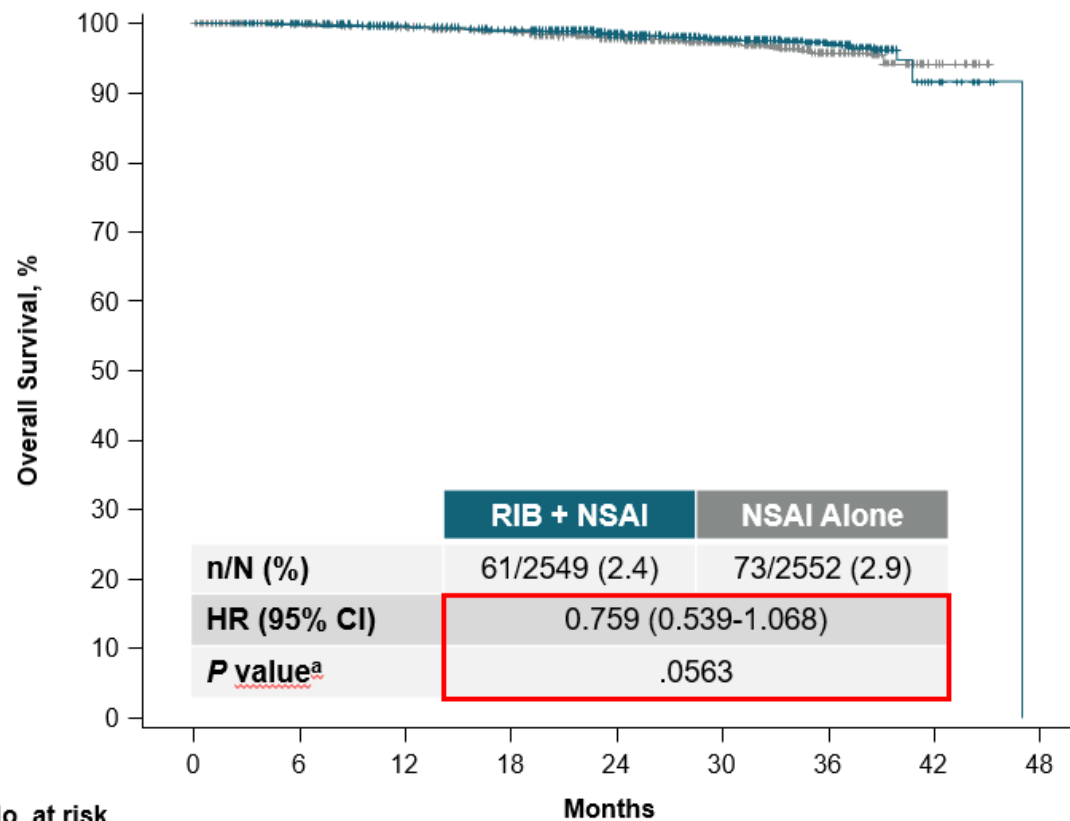
- Median follow-up for iDFS was 27.7 months
- Based on the *P* value of 0.0014, the IDMC concluded that the results met the criteria to demonstrate statistically significant and clinically superior efficacy
- Absolute iDFS benefit with RIB + NSA at 3 years was 3.3%
- Risk of invasive disease was reduced by 25.2% with RIB + NSA vs NSA alone
- Ongoing patients will remain on treatment and follow-up will continue as prespecified





- 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

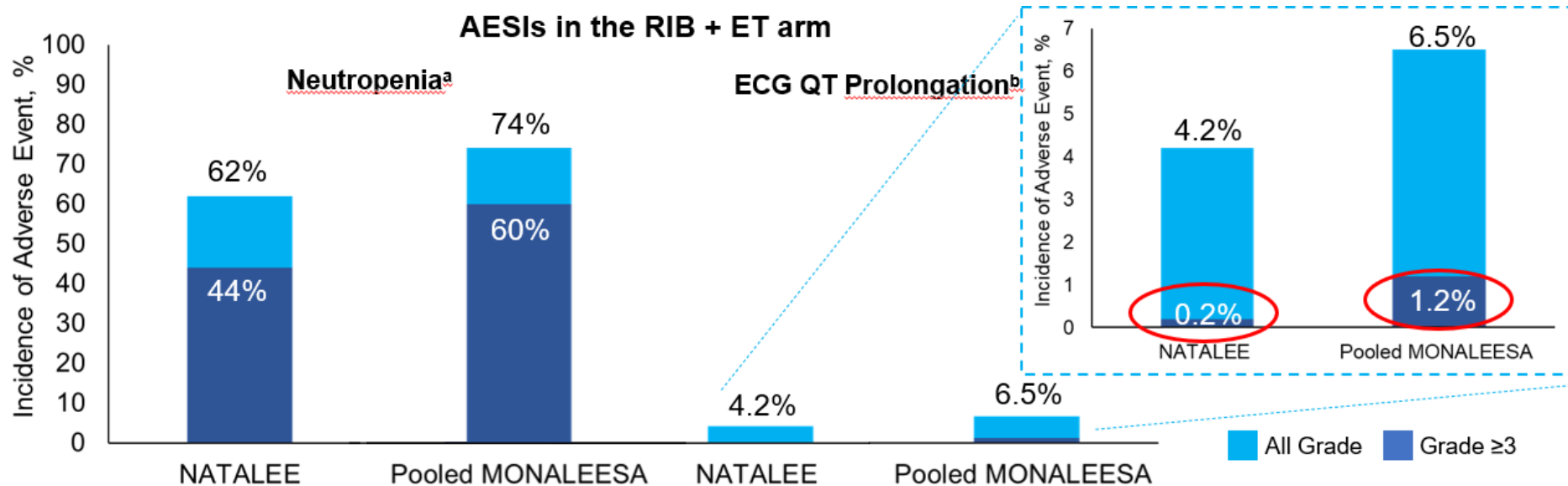
Ribociclib showed a trend for improved OS



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

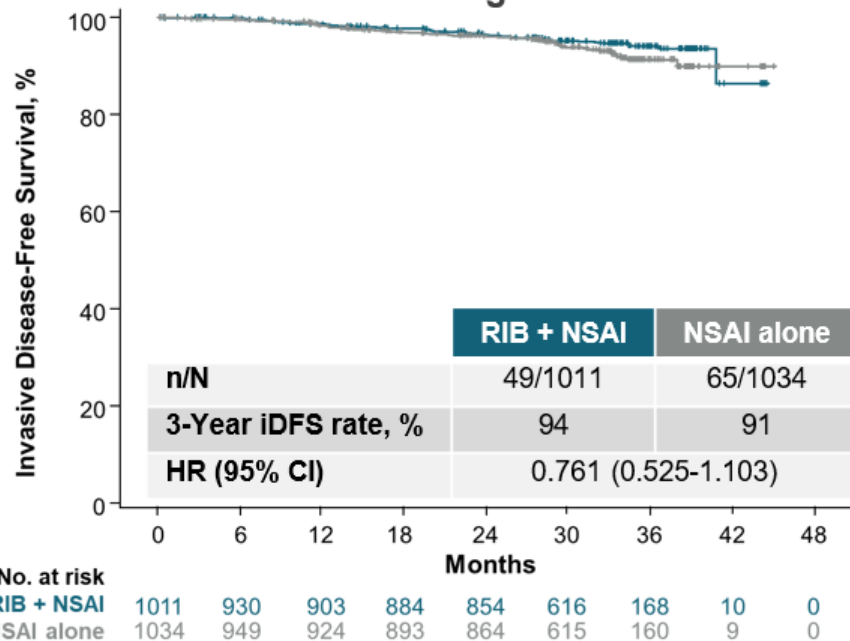


TOXICIDAD

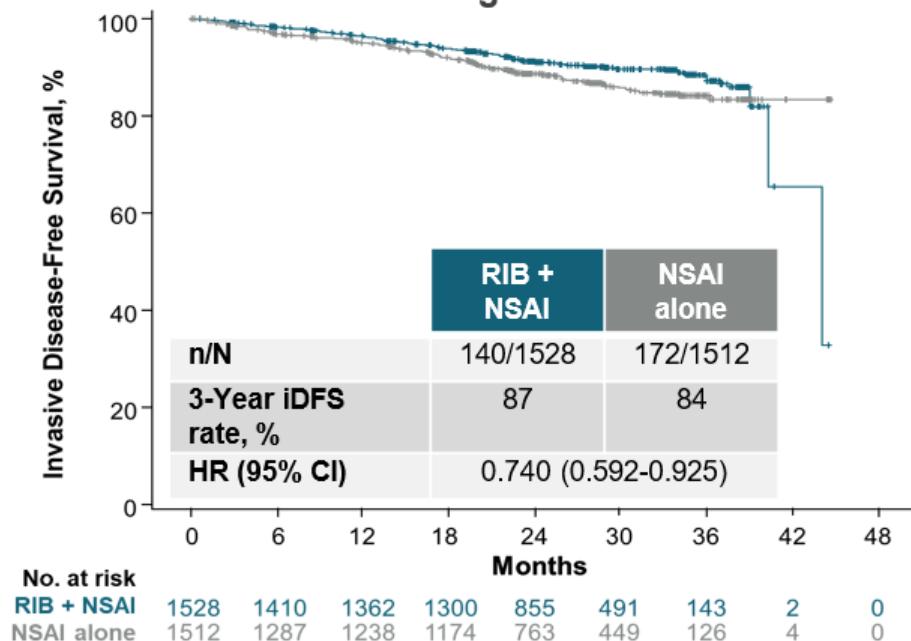




Stage II

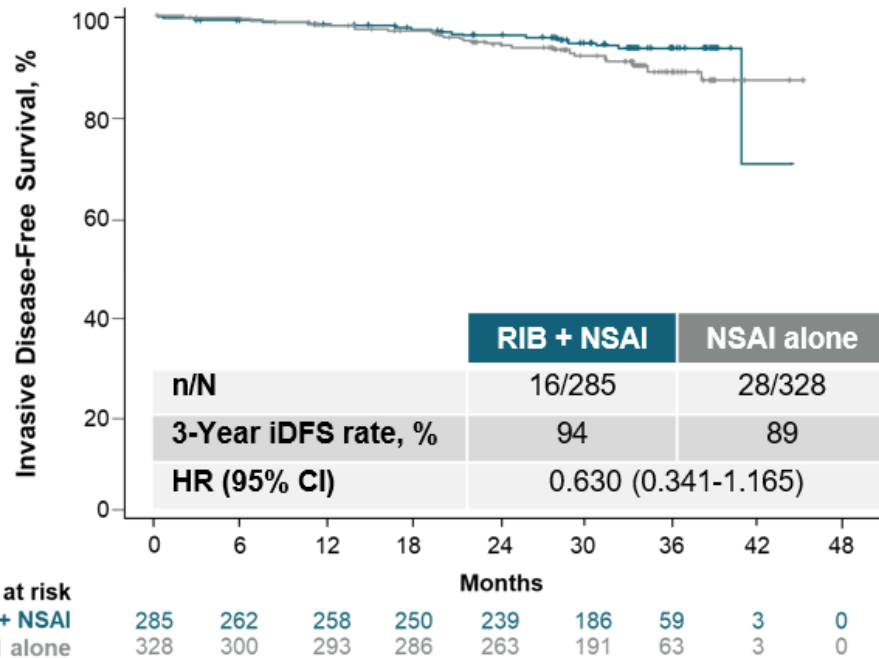


Stage III

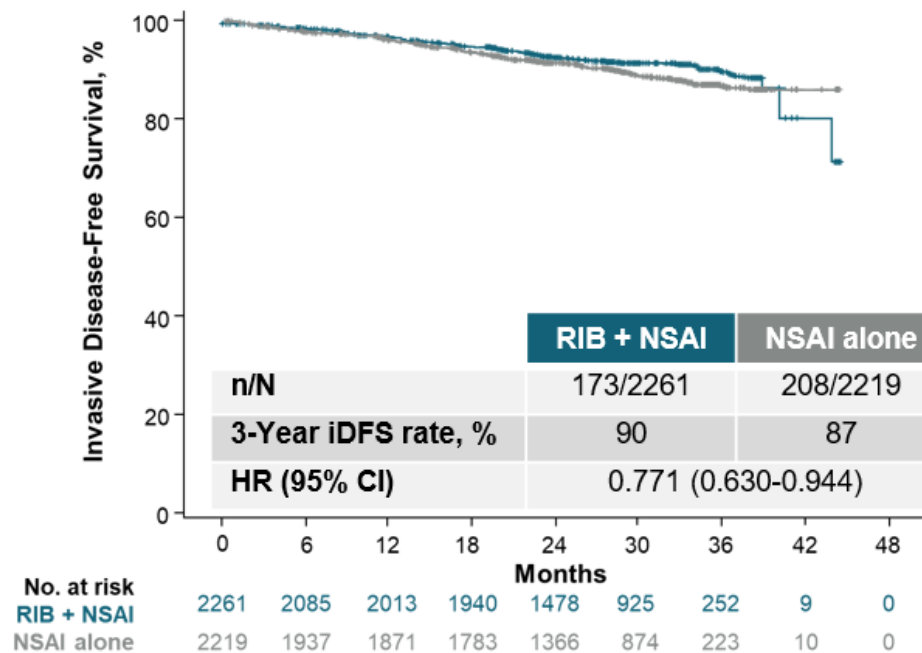




N0

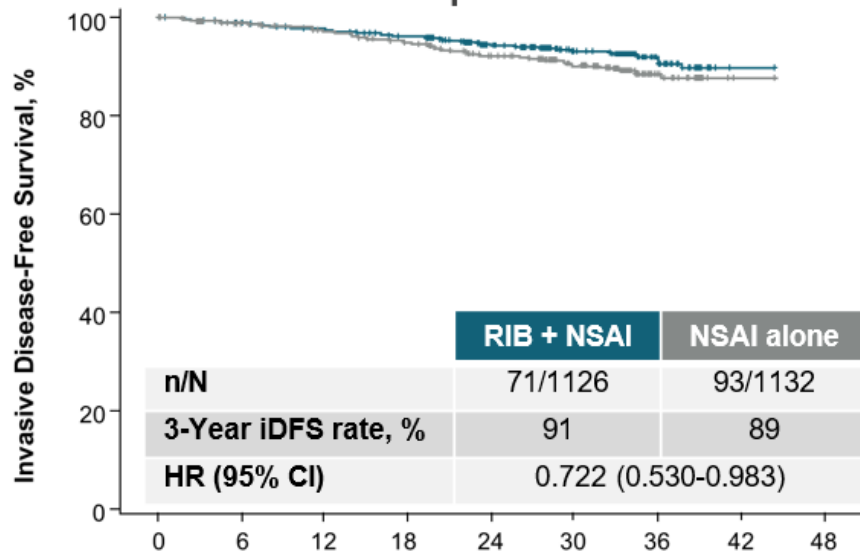


N1-N3



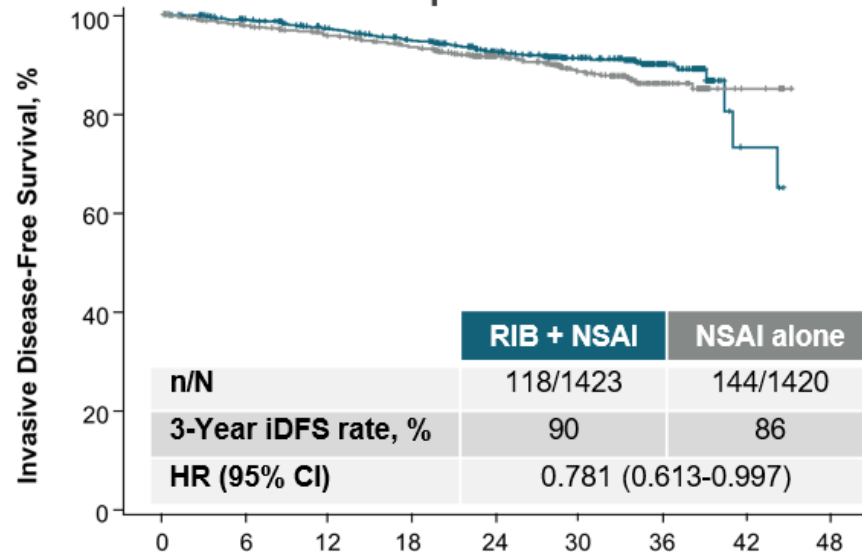


Premenopausal women



No. at risk									
Months									
RIB + NSAI	1126	1047	1022	990	755	470	125	3	0
NSAI alone	1132	1001	979	929	707	449	108	3	0

Postmenopausal women

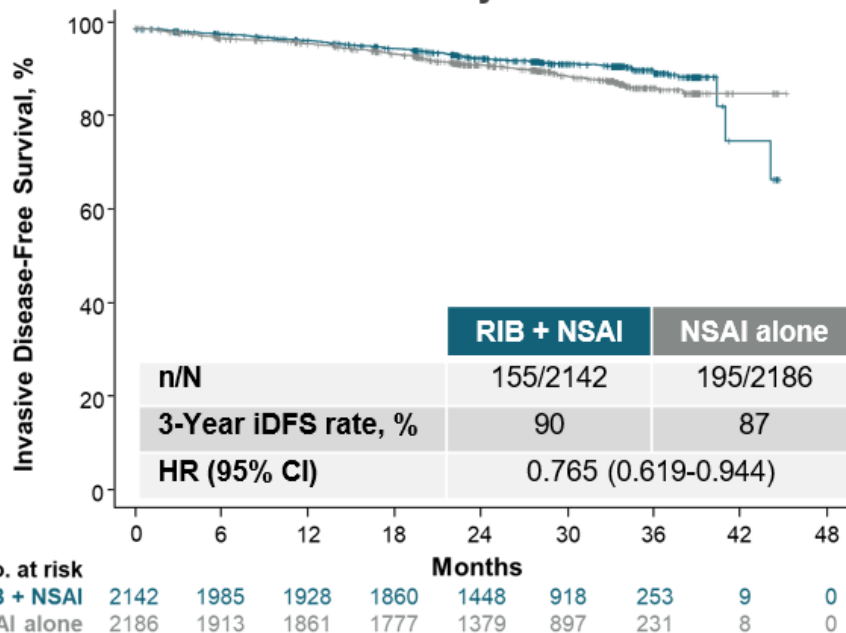


No. at risk									
Months									
RIB + NSAI	1423	1303	1252	1203	963	641	186	9	0
NSAI alone	1420	1239	1187	1142	924	618	178	10	0

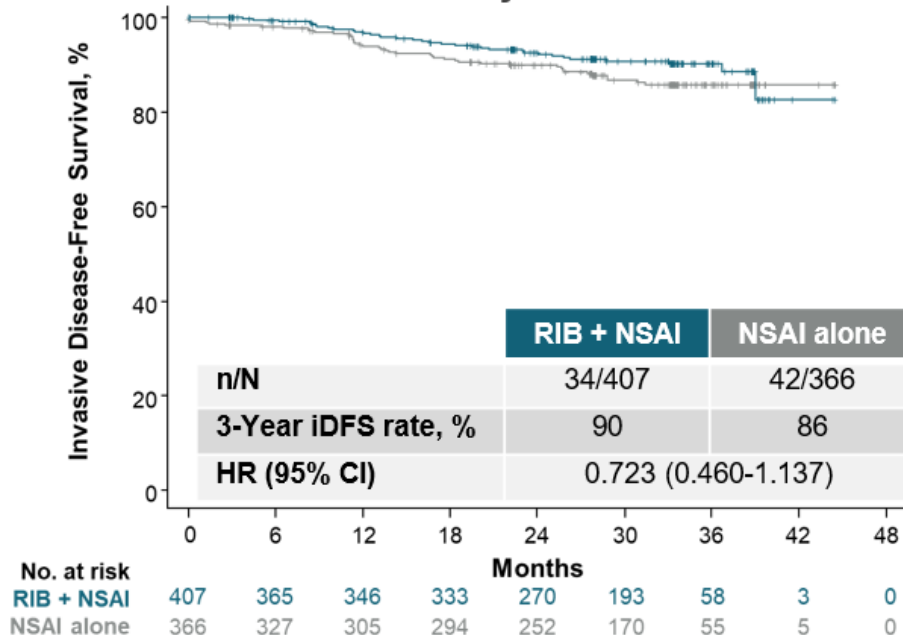


iDFS benefit with ribociclib + NSAI across age groups

<65 years

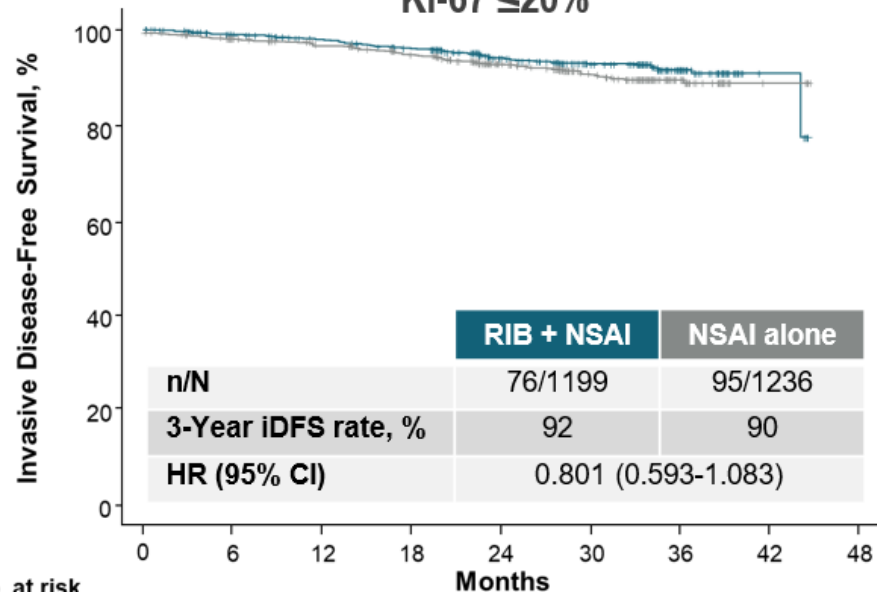


≥65 years

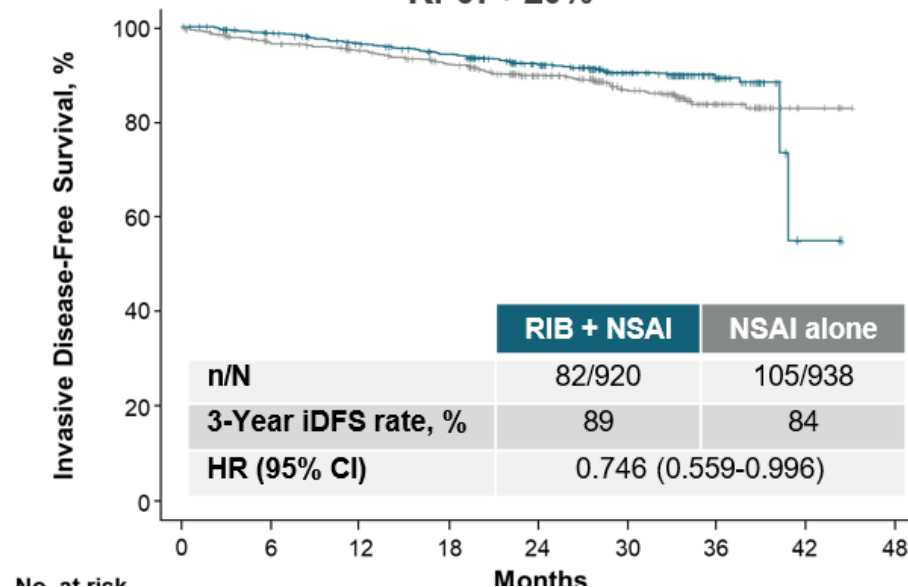




Ki-67 $\leq 20\%$



Ki-67 $> 20\%$

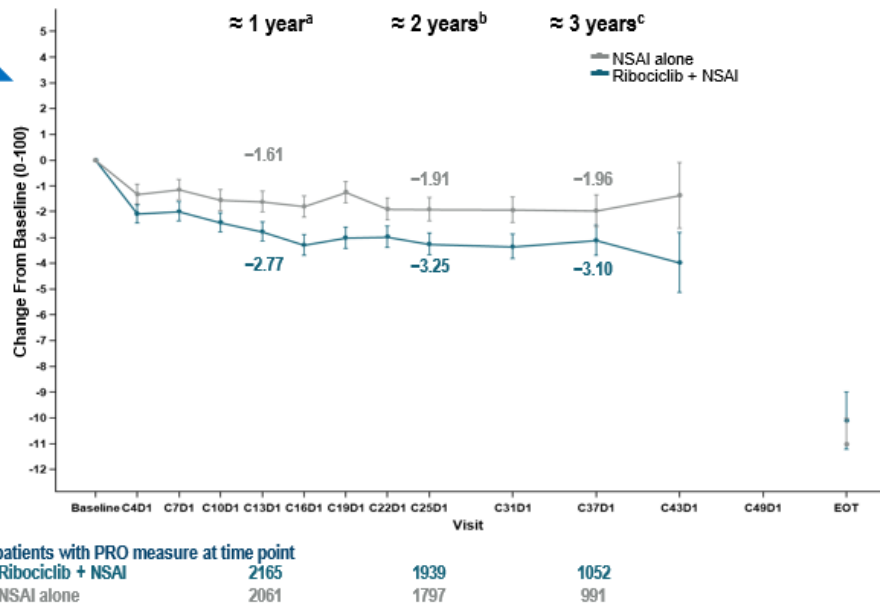




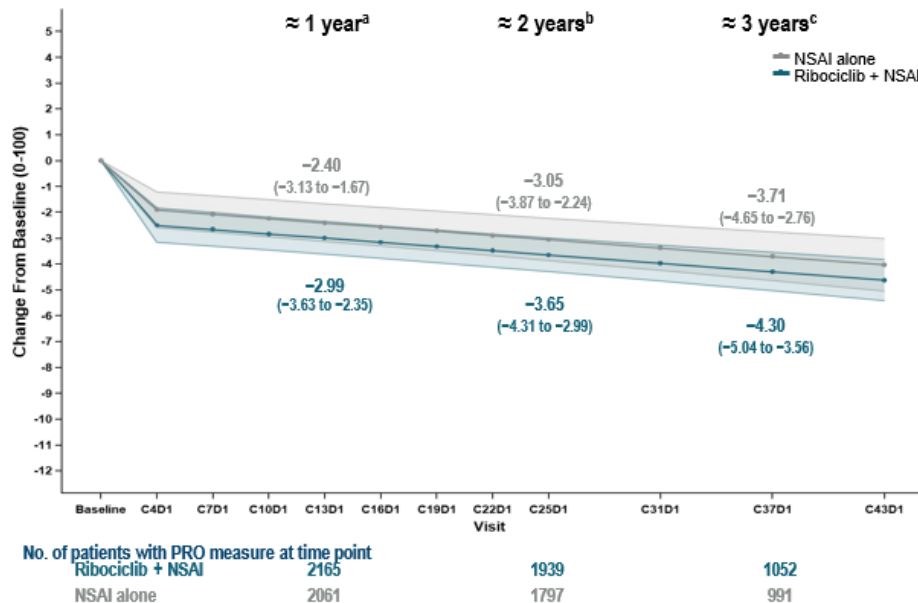
EORTC QLQ-C30: GLOBAL HEALTH STATUS

Descriptive Analysis

Better QOL



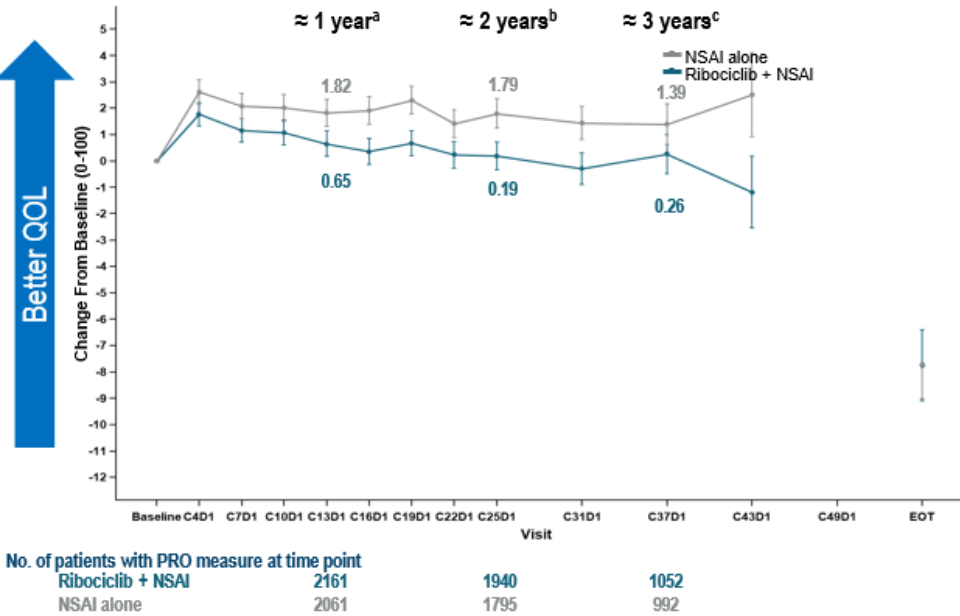
Model-Based Analyses



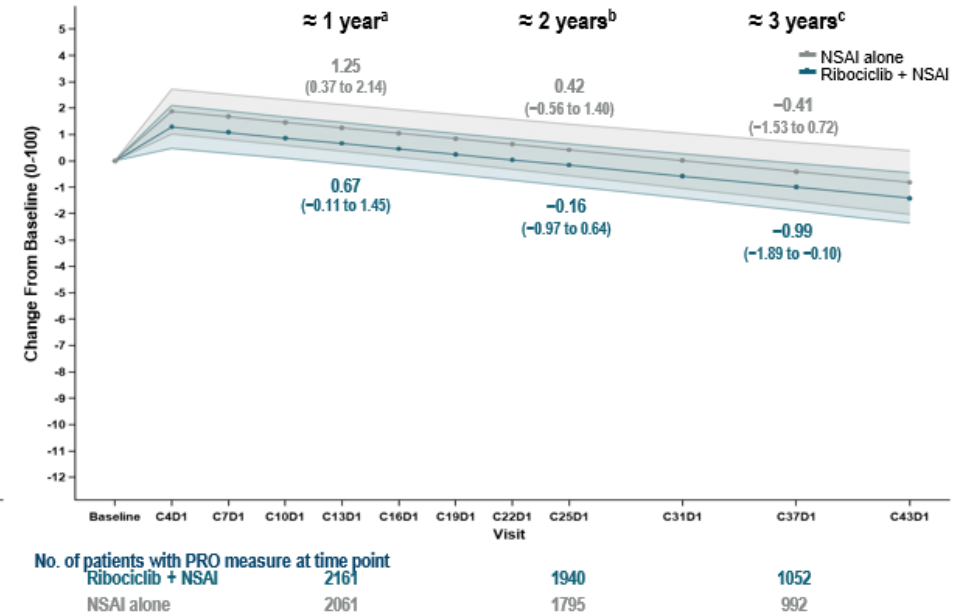
Global health status was not impacted over time in both arms^{1,d,e}

EORTC QLQ-C30: SOCIAL FUNCTIONING

Descriptive Analysis



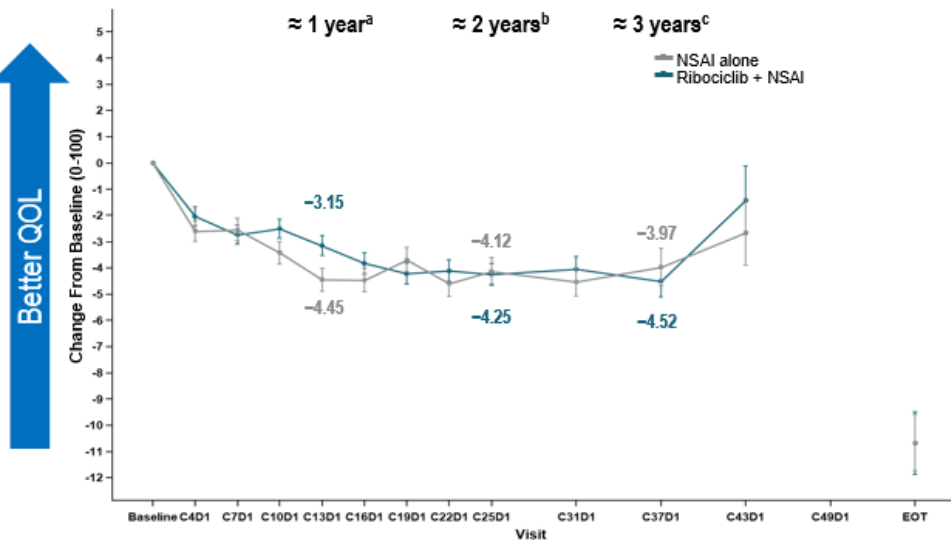
Model-Based Analyses



No difference in social functioning from baseline was observed in both arms^{1,d,e}

EORTC QLQ-C30: EMOTIONAL FUNCTIONING

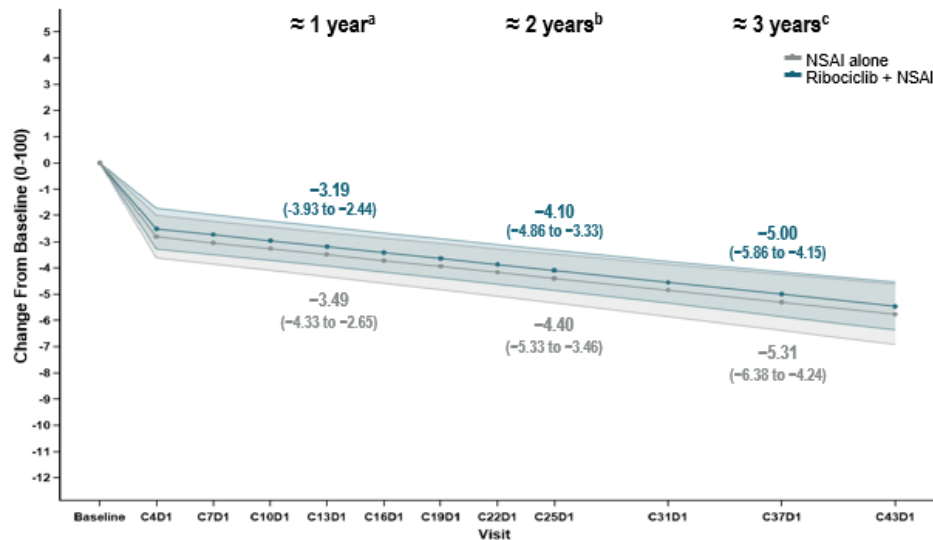
Descriptive Analysis



No. of patients with PRO measure at time point

Time Point	Ribociclib + NSAI	NSAI alone
Baseline	2164	2062
C43D1	1941	1797
EOT	1053	992

Model-Based Analyses



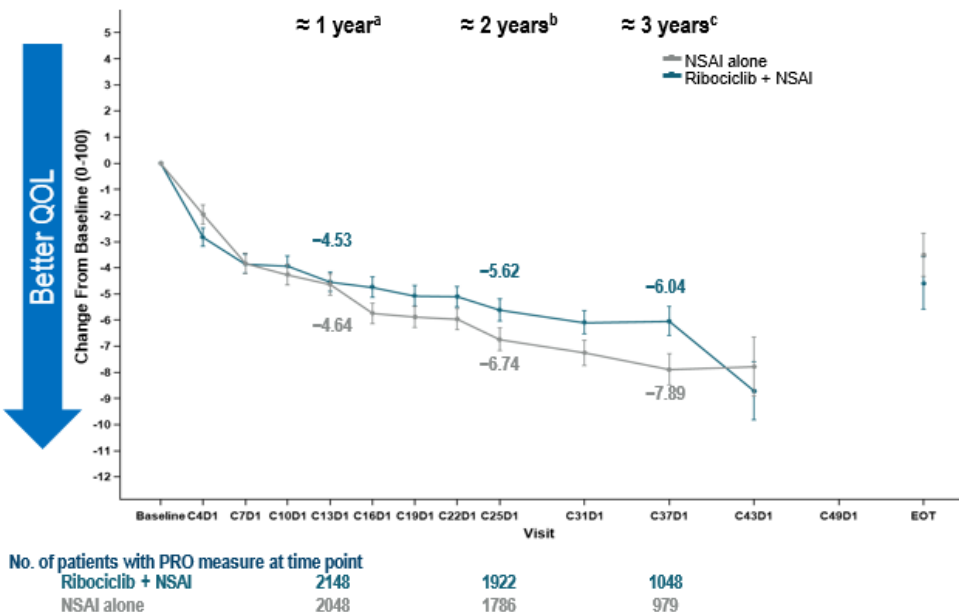
No. of patients with PRO measure at time point

Time Point	Ribociclib + NSAI	NSAI alone
Baseline	2164	2062
C43D1	1941	1797
EOT	1053	992

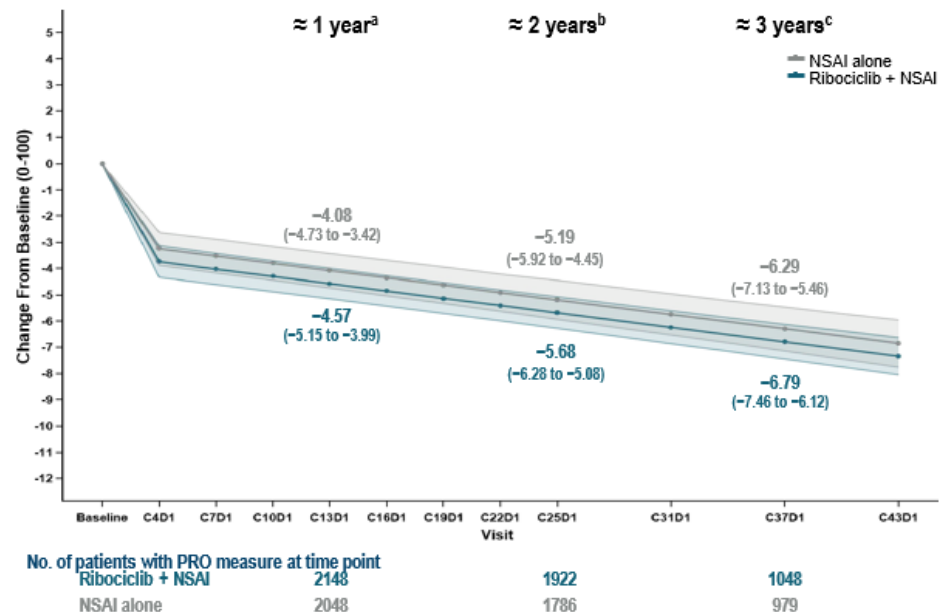
A small deterioration in emotional functioning from baseline was observed in both arms^{1,d,e}
No difference was observed between patients treated with ribociclib + NSAI vs NSAI alone

EORTC QLQ-BR23: BREAST CANCER SYMPTOMS

Descriptive Analysis



Model-Based Analyses



Breast cancer symptoms were reduced quickly and then improved at a slower rate over the study^d



18^{as} Jornadas HITOS
ONCOLÓGICOS: LO MEJOR DE 2023

Madrid, 22 y 23 de noviembre de 2023

En definitiva...

EL FUTURO DEL TRATAMIENTO ADYUVANTE PARA EL CÁNCER DE MAMA LUMINAL(INCLUIDAS PACIENTES DE “RIEGO INTERMEDIO”) ES PRESENTE.



18^{as} Jornadas HITOS LO MEJOR DE 2023
ONCOLÓGICOS:

Madrid, 22 y 23 de noviembre de 2023

GRACIAS