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Mama localizada

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- **#ABSTRACT 512# Baseline (BL) characteristics and efficacy endpoints for patients (pts) with node-negative (N0) HR+/HER2– early breast cancer (EBC): NATALEE trial.**
- **#ABSTRACT LBA 500# A-BRAVE trial: A phase III randomized trial with avelumab in early triple-negative breast cancer with residual disease after neoadjuvant chemotherapy or at high risk after primary surgery and adjuvant chemotherapy.**
- **#ABSTRACT LBA 502# A randomized, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo) adjuvant therapy in patients with early triple-negative breast cancer: Korean Cancer Study Group BR 15-1 PEARLY trial.**
- **#ABSTRACT 516# Non-basal subtype defined by FOXC1 expression as an independent predictor of capecitabine efficacy in the triple negative breast cancer GEICAM/2003-11_CIBOMA/2004-01 trial.**
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- **#ABSTRACT 10503# Clinical behavior of breast cancer in young *BRCA* carriers and prognostic impact of the timing of genetic testing: Results from an international cohort study.**
- **#ABSTRACT 504# Impact of hormone receptor status and tumor subtypes on clinical behavior and outcomes of breast cancer in young *BRCA* carriers.**
- **#ABSTRACT 505# Correlation of serum anti-Müllerian hormone (AMH) levels on identification of premenopausal patients (pts) with hormone receptor positive (HR+), HER2-negative, node-positive breast cancer most likely to benefit from adjuvant chemotherapy in SWOG S1007 (RxPONDER).**
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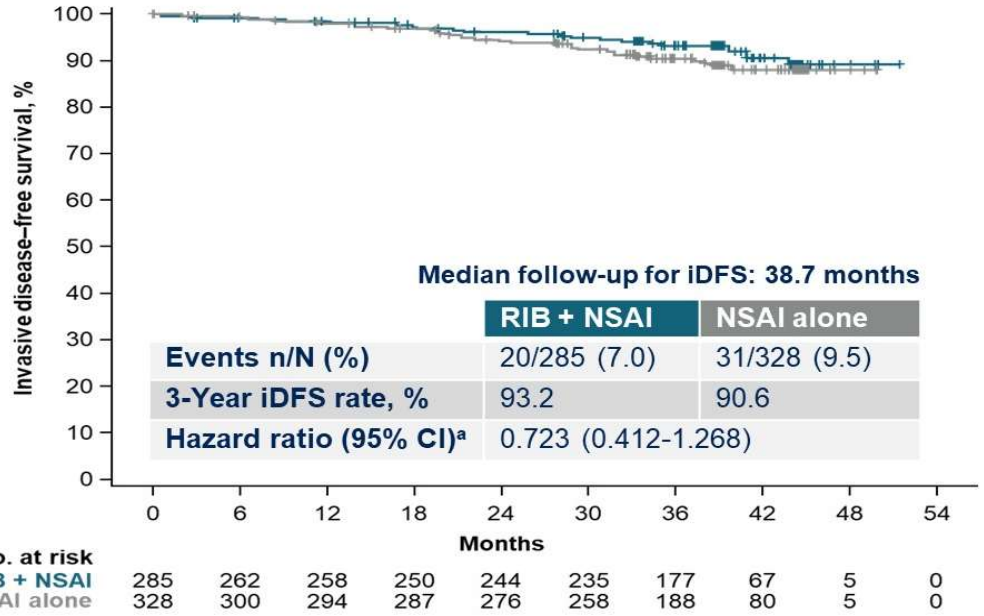
- **#ABSTRACT LBA 507# Prognostic utility of ctDNA detection in the monarchE trial of adjuvant abemaciclib plus endocrine therapy (ET) in HR+, HER2-, node-positive, high-risk early breast cancer (EBC).**
- **#ABSTRACT LBA 508# Development and validation of RSClin N+ tool for hormone receptor-positive (HR+), HER2-negative (HER2-), node-positive breast cancer.**

Ribociclib improved iDFS, DDFS, and DRFS in the NATALEE node-negative subgroup

- Patients with stage IIA N0 (T2N0) disease required additional specified high-risk features
- All patients with stage IIB N0 (T3N0) and IIIB N0 (T4N0) disease were included

iDFS in Node-Negative Subgroup



Median follow-up for iDFS: 38.7 months

	RIB + NSAI	NSAI alone
Events n/N (%)	20/285 (7.0)	31/328 (9.5)
3-Year iDFS rate, %	93.2	90.6
Hazard ratio (95% CI)[a]	0.723 (0.412-1.268)	

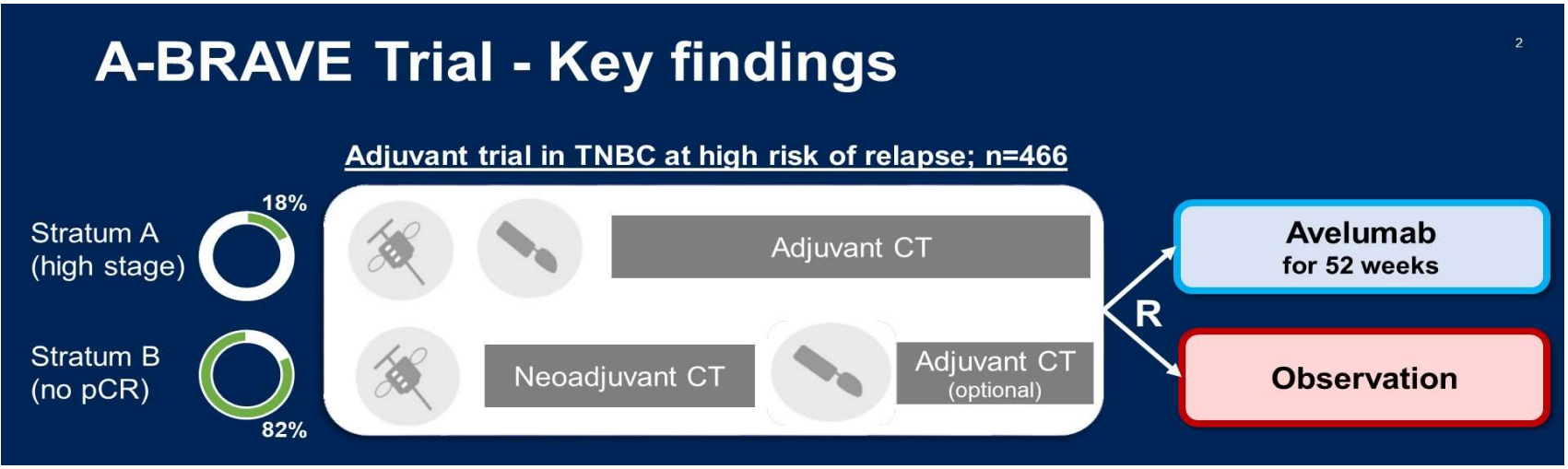
DDFS and DRFS in Node-Negative Subgroup

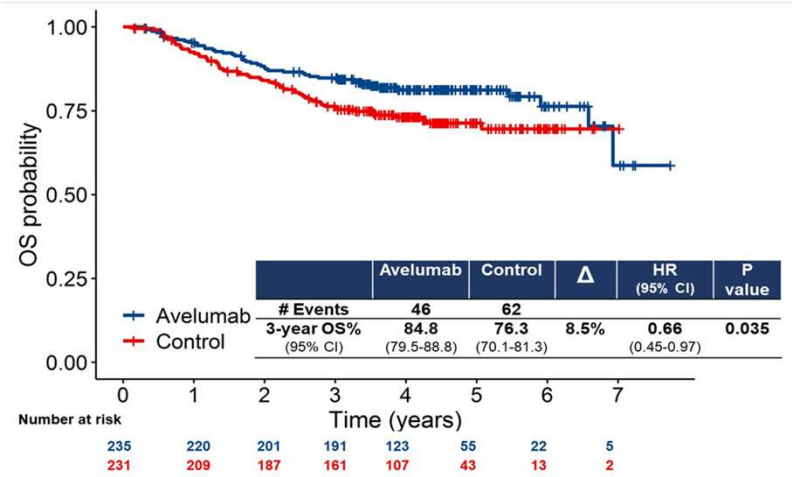
Efficacy outcome	RIB + NSAI n = 285	NSAI alone n = 328
DDFS		
Events, n	17	27
3-y rate (95% CI), %	94.3 (90.6-96.6)	91.5 (87.6-94.2)
Hazard ratio (95% CI)	0.703 (0.383-1.290)	
DRFS		
Events, n	12	23
3-y rate (95% CI), %	96.3 (93.0-98.1)	92.5 (88.8-95.1)
Hazard ratio (95% CI)	0.580 (0.289-1.170)	

[a] This was not a preplanned analysis and no formal *P* value was spent or tested.
DDFS, distant disease–free survival; DRFS, distant recurrence–free survival; iDFS, invasive disease–free survival; ITT, intention to treat; NSAI, nonsteroidal aromatase inhibitor; RIB, ribociclib.

These findings demonstrate the efficacy and tolerability of adding ribociclib to NSAI in select patients with node-negative HR+/HER2− EBC who are at high risk of recurrence despite current standard of care

A-BRAVE Trial - Key findings



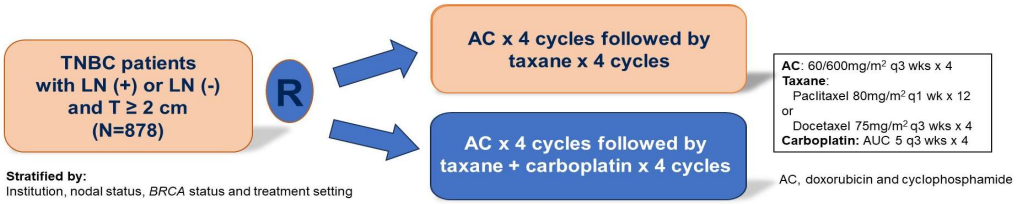


Endpoint and population			Δ 3-yr rate	HR (95% CI)
DFS	ITT	Co-primary	**+ 5.1%**	**0.81** (0.61-1.09)
	Post-neoadj	Co-primary	**+ 6.2%**	**0.80** (0.58-1.10)
OS	ITT	Secondary	**+ 8.5%**	**0.66** (0.45-0.97)
	Post-neoadj	Exploratory	**+ 8.6%**	**0.69** (0.46-1.03)
DDFS	ITT	Exploratory	**+ 7.5%**	**0.70** (0.50-0.96)

The 30% reduction in the risk of distant metastases and 34% reduction in the risk of death suggest that avelumab may have a role in early triple negative breast cancer patients at high risk after primary surgery or with invasive residual disease after NACT.

 # ABSTRACT LBA 500 # A randomized, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo) adjuvant therapy in patients with early triple-negative breast cancer: Korean Cancer Study Group BR 15-1 PEARLY trial

PEARLY Study Design (NCT02441933)



Stratified by:
Institution, nodal status, *BRCA* status and treatment setting

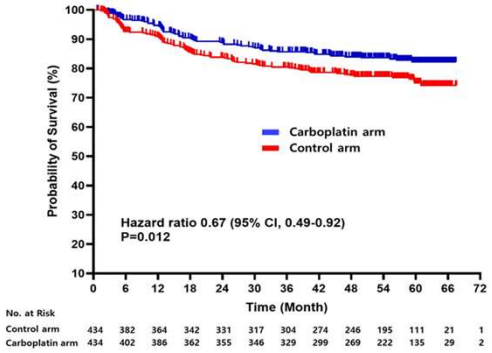
Primary Endpoint
– 5-year EFS (Event-Free Survival) rate

Disease progression or inoperable status for neoadjuvant group
Local or distant recurrence, second primary cancer, or death from any cause

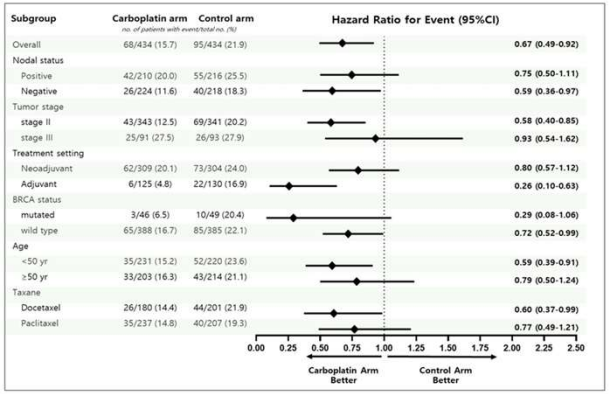
Secondary Efficacy Endpoints
Overall survival, OS
Distant recurrence-free survival, DRFS
Invasive disease-free survival, IDFS

Safety Endpoints
Safety and tolerability
QoL : EORTC-QLQ-CIPN20, EQ-5D

Characteristic	Carboplatin Arm (N=434)	Control Arm (N=434)
Age		
Median, yrs (range)	48 (21-77)	49 (23-76)
≥65, n (%)	33 (7.6)	22 (5.1)
ECOG PS, n (%)		
0	371 (85.5)	383 (88.2)
1	63 (14.5)	51 (11.8)
Germline *BRCA* status, n (%)		
Deleterious mutation	46 (10.6)	49 (11.3)
No deleterious mutation	388 (89.4)	385 (88.7)
Treatment setting, n (%)		
Neoadjuvant	309 (71.2)	304 (70.0)
Adjuvant	125 (28.8)	130 (30.0)
Tumor stage, n (%)		
T1 or T2	365 (84.1)	373 (85.9)
T3 or T4	69 (15.9)	61 (14.1)
Lymph node involvement, n (%)		
Negative	224 (51.6)	218 (50.2)
positive	210 (48.4)	216 (49.8)
TNM, n (%)		
Stage II	343 (79.0)	341 (78.6)
Stage III	93 (21.0)	91 (21.4)
Taxane, n (%)		
Docetaxel	180 (43.2)	201 (49.3)
Paclitaxel	237 (56.8)	207 (50.7)
Surgery, n (%)		
BCS	278 (67.1)	256 (62.9)
Mastectomy	136 (32.9)	151 (37.1)



ITT analysis	Carbo arm (n=434)	Control arm (n=434)
5-year EFS rate	82.3%	75.1%
Stratified HR (95% CI)	0.67 (0.49-0.92)	
Stratified Log Rank *P value*	0.012	



The PEARLY trial provides compelling evidence for including carboplatin in the treatment of early-stage TNBC, underscoring its value in the KN522 trial-based neoadjuvant setting and suggesting potential applicability in the adjuvant setting post-surgery

#ABSTRACT 516# Non-basal subtype defined by FOXC1 expression as an independent predictor of capecitabine efficacy in the triple negative breast cancer GEICAM/2003-11_CIBOMA/2004-01 trial.

GEICAM_CIBOMA clinical trial in early-stage TNBC (NCT00130533)

GEICAM spanish breast cancer group

- TNBC
- T1c-T3, N0-N3a, M0
- Prior standard neo/adjuvant CT with anthracyclines +/- taxanes

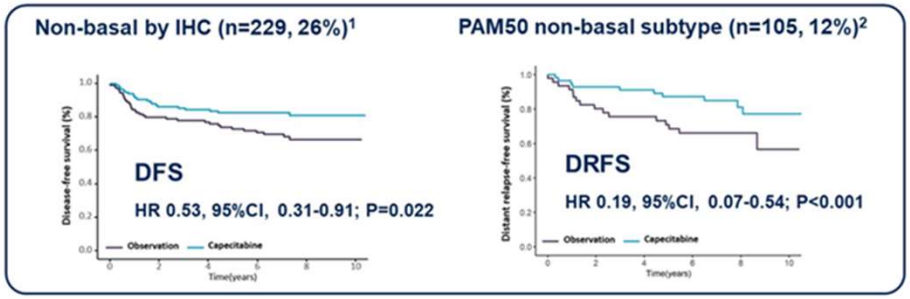
N= 876

R 1:1

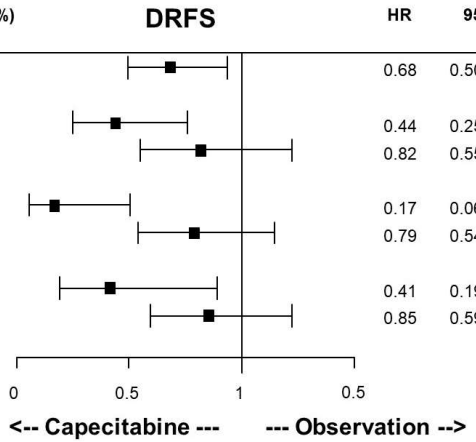
Capecitabine
1000 mg/m² p.o., b.i.d. x 14 days every 3 weeks x 8 cycles

Observation

Stratification factors:
Basal vs Non-basal
Prior taxane-based therapy
Involved axillary lymph nodes



Subgroup	No. of Patients (%)	HR	95%CI	P value
Overall	705 (100)	0.68	0.50 to 0.94	
VERESCA FOXC1 Score				
<4 (Non-Basal)	245 (35)	0.44	0.25 to 0.76	**0.003**
≥4 (Basal)	460 (65)	0.82	0.55 to 1.22	0.323
PAM50 Subtype				
PAM50 Non-basal	92 (15)	0.17	0.06 to 0.50	**0.002**
PAM50 Basal	511 (85)	0.79	0.54 to 1.14	0.207
IHC Subtype				
IHC Non-basal	178 (25)	0.41	0.19 to 0.89	**0.024**
IHC Basal	527 (75)	0.85	0.59 to 1.22	0.378



Non-basal breast cancer subtype defined by FOXC1 independently predicted capecitabine benefit after (neo)adjuvant chemotherapy (DRFS, DFS, OS)

#ABSTRACT 10503# Clinical behavior of breast cancer in young *BRCA* carriers and prognostic impact of the timing of genetic testing: Results from an international cohort study.

Key inclusion criteria

- Stage I - III invasive breast cancer
- Diagnosis between January 2000 and December 2020
- Age ≤ 40 years at diagnosis
- Known germline PV in the *BRCA1* or *BRCA2* genes

Key characteristics at breast cancer diagnosis

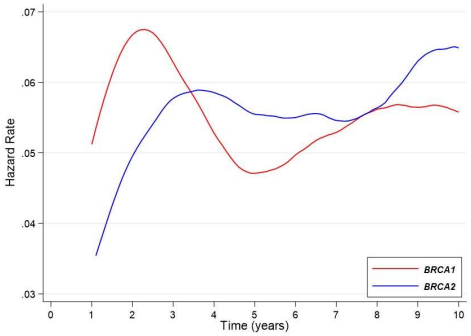
	BRCA1 carriers n = 3069, N (%)	*BRCA2* carriers n = 1683, N (%)
Age at diagnosis, median (IQR) years	34 (31 – 37)	35 (32 – 38)
Age at diagnosis		
≤ 30 years	**705 (23.0)**	**272 (16.2)**
31 – 35 years	1088 (35.4)	636 (37.8)
36 – 40 years	1276 (41.6)	775 (46.0)
Region		
Southern Europe	1278 (41.6)	810 (48.1)
Asia	539 (17.6)	235 (14.0)
Northern Europe	470 (15.3)	250 (14.8)
North America	324 (10.6)	193 (11.5)
Eastern Europe	239 (7.8)	70 (4.2)
Australia/Oceania	114 (3.7)	84 (5.0)
Latin/South America	105 (3.4)	41 (2.4)
Year at diagnosis		
2000 – 2005	485 (15.8)	275 (16.3)
2006 – 2010	745 (24.3)	391 (23.2)
2011 – 2015	891 (29.0)	462 (27.5)
2016 – 2020	948 (30.9)	555 (33.0)
Tumor grade		
G1	23 (0.7)	56 (3.3)
G2	395 (12.9)	602 (35.8)
G3	**2378 (77.5)**	**827 (49.1)**
Unknown	273 (8.9)	198 (11.8)
Tumor size		
T1 (≤ 2 cm)	1138 (37.1)	681 (40.5)
T2 (>2 – ≤ 5 cm)	1385 (45.1)	662 (39.3)
T3 (> 5 cm) - T4	396 (12.9)	244 (14.5)
Unknown	150 (4.9)	96 (5.7)
Nodal status		
N0	**1741 (56.7)**	**701 (41.6)**
N1	919 (29.9)	640 (38.0)
N2 – N3	196 (9.6)	258 (15.3)
Unknown	113 (3.7)	84 (5.0)
Hormone receptor status		
ER and/or PR positive	736 (24.0)	**1394 (82.8)**
ER and PR negative	**2282 (74.4)**	261 (15.5)
Unknown	51 (1.7)	28 (1.7)
HER2 status		
HER2 negative	2776 (90.4)	1398 (83.1)
HER2 positive	**147 (4.8)**	**188 (11.2)**
Unknown	146 (4.8)	97 (5.8)

Results: *BRCA1* vs. *BRCA2*

Type of disease-free survival (DFS) events

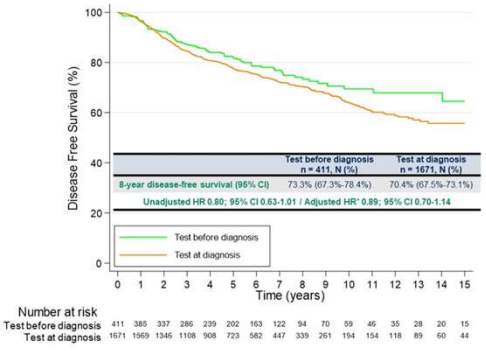
	BRCA1 carriers n = 3069, N (%)	*BRCA2* carriers n = 1683, N (%)
Loco-regional recurrence	235 (7.7)	124 (7.4)
Distant recurrence	**298 (9.7)**	**228 (13.6)**
Second primary malignancy	**139 (4.5)**	**50 (3.0)**
Ovary	**77 (2.5)**	**9 (0.5)**
Pancreas	5 (0.2)	5 (0.3)
Cervix	5 (0.2)	4 (0.2)
Colorectal-anus	4 (0.1)	5 (0.3)
Hematological	4 (0.1)	4 (0.2)
Skin cancer	10 (0.3)	8 (0.5)
Thyroid	5 (0.2)	2 (0.1)
Endometrium	7 (0.2)	1 (0.1)
Upper gastrointestinal	4 (0.1)	1 (0.1)
Others	18 (0.6)	11 (0.6)
Second primary breast cancer	**419 (13.7)**	**157 (9.3)**
Death without any DFS event	25 (0.8)	16 (0.1)

Epanechnikov Kernel-Smoothed annual hazard of DFS events



Results: *BRCA* Test Before vs. At Diagnosis

Disease-free survival

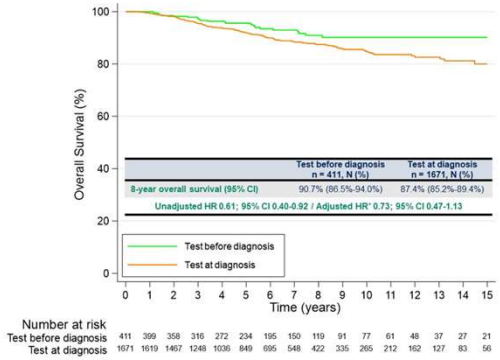


	Test before diagnosis n = 411, N (%)	Test at diagnosis n = 1671, N (%)
8-year disease-free survival (95% CI)	73.3% (67.3%-78.4%)	70.4% (67.5%-73.1%)

Unadjusted HR 0.80; 95% CI 0.63-1.01 / Adjusted HR* 0.89; 95% CI 0.70-1.14

Number at risk																
Test before diagnosis	411	385	337	286	239	202	163	122	94	70	59	46	35	28	20	15
Test at diagnosis	1671	1569	1346	1108	908	723	582	447	339	261	194	154	118	89	60	44

Overall survival



	Test before diagnosis n = 411, N (%)	Test at diagnosis n = 1671, N (%)
8-year overall survival (95% CI)	90.7% (86.5%-94.0%)	87.4% (85.2%-89.4%)

Unadjusted HR 0.61; 95% CI 0.40-0.92 / Adjusted HR* 0.73; 95% CI 0.47-1.13

Number at risk																
Test before diagnosis	411	399	358	316	272	234	195	150	119	91	77	61	48	37	27	21
Test at diagnosis	1671	1619	1467	1248	1036	849	695	548	422	335	265	212	162	127	83	56

* Adjusted for country, specific *BRCA* gene, grade, tumor size, nodal status axillary surgery and chemotherapy use

#ABSTRACT 504# Impact of hormone receptor status and tumor subtypes on clinical behavior and outcomes of breast cancer in young *BRCA* carriers.

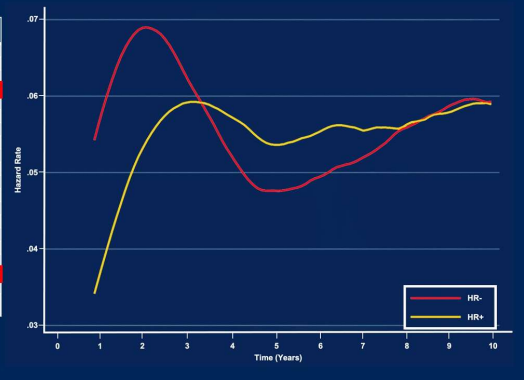
Results: Analyses by Hormone Receptor Status

Pattern of first Disease-Free Survival event

	HR+ cohort n = 2,143, N (%)	HR- cohort n = 2,566, N (%)	P value*
Loco-regional recurrence	150 (7.0)	211 (8.2)	0.14
Distant recurrence	280 (13.1)	245 (9.6)	0.01
Second primary malignancy	72 (3.4)	115 (4.5)	0.07
Ovaries	25 (1.2)	60 (2.3)	
Pancreas	6 (0.3)	4 (0.2)	
Cervix	3 (0.1)	6 (0.2)	
Colon-rectal-anal	3 (0.1)	6 (0.2)	
Haematological	3 (0.1)	4 (0.2)	
Skin	8 (0.4)	10 (0.4)	
Thyroid	2 (0.1)	5 (0.2)	
Endometrial	5 (0.2)	3 (0.1)	
Upper-gastrointestinal	2 (0.1)	3 (0.1)	
Others	15 (0.7)	14 (0.6)	
Second primary breast cancer	195 (9.1)	378 (14.7)	<0.0001
Death without any disease-free survival event	23 (1.1)	17 (0.7)	0.13

*P values for time-dependent events estimated by means of the Log-rank test

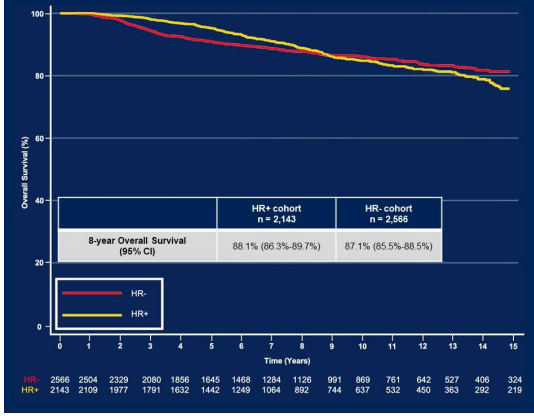
Smoothed annual hazard rate of Disease-Free Survival



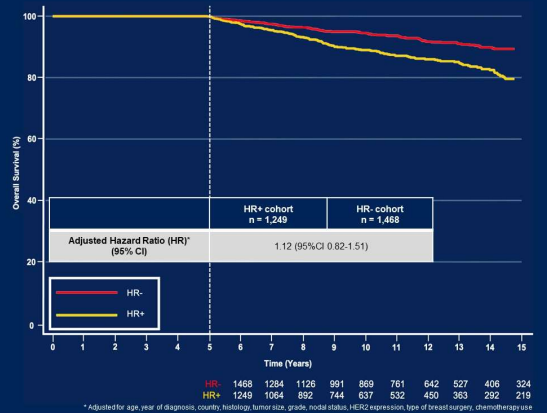
- Hormone receptor positivity did not seem to have a strong positive prognostic value in young *BRCA* carriers affected by early breast cancer
- Young *BRCA* carriers with luminal A-like disease showed a relatively worse prognosis (in terms of DFS) compared to the other breast cancer subtypes

Results: Analyses by Hormone Receptor Status

Overall Survival



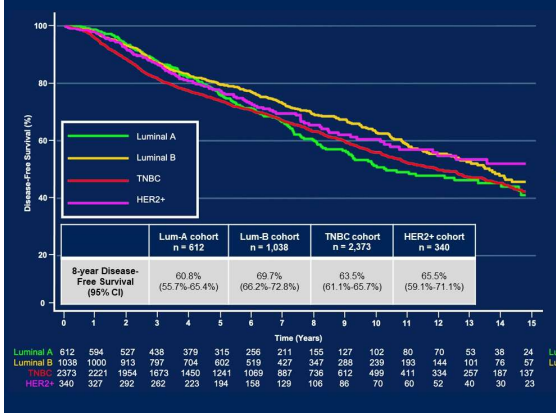
Overall Survival (years >5)



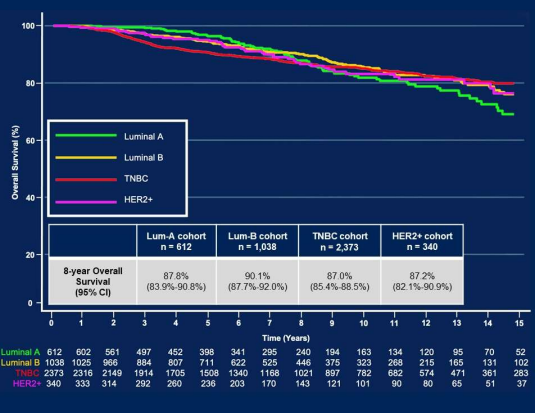
* Adjusted for age, year of diagnosis, country, histology, tumor size, grade, nodal status, HER2 expression, type of breast surgery, chemotherapy use

Results: Analyses by Tumor Subtype

Disease-Free Survival

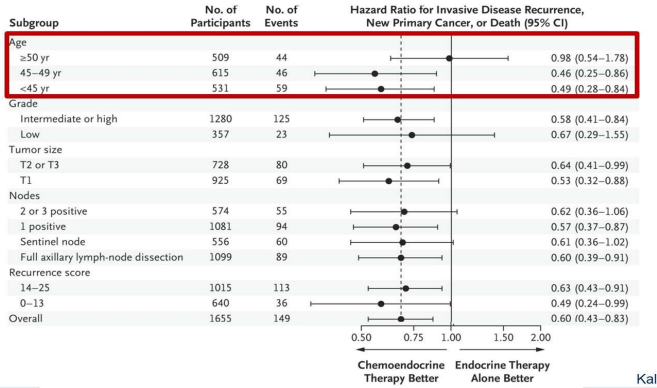


Overall Survival



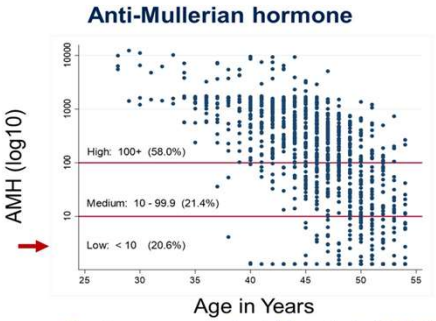
#ABSTRACT 505# Correlation of serum anti-Müllerian hormone (AMH) levels on identification of premenopausal patients (pts) with hormone receptor positive (HR+), HER2-negative, node-positive breast cancer most likely to benefit from adjuvant chemotherapy in SWOG S1007 (RxPONDER).

Chemotherapy benefit lower in older "premenopausal" in RxPONDER



Kalinsky, et al. NEJM 2021

21% of "premenopausal" women < 55 years had serum AMH in postmenopausal range



Postmenopausal: < 10 pg/mL (20.6%)

Category (AMH)	Menstrual Category (Final Menstrual Period)	picoAMH (pg/mL)
Low	At FMP or Later	< 10
Medium	< 5 years from FMP	10-99.9
High	> 5 years from FMP	≥ 100

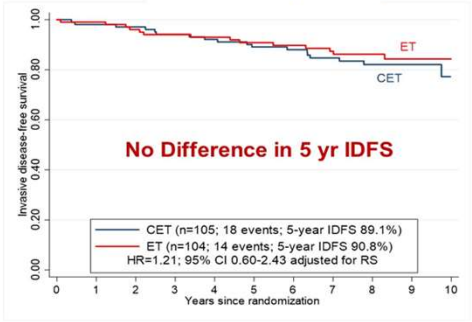
Category	Age < 45	Age 45-49	Age 50-54
Low AMH	10/348 (2.9%)	58/397 (14.6%)	141/270 (52.2%)

10 pg/ML = 0.01 ng/ML

picoAMH package insert (ELISA) 2023

"Premenopausal" < 55 years with low AMH have no IDFS benefit with chemotherapy

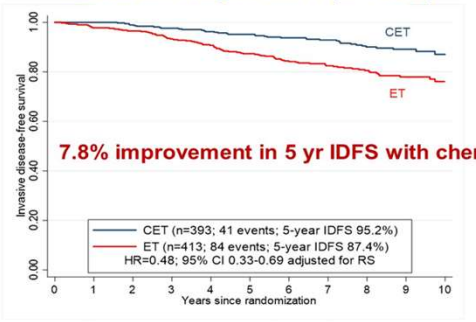
Low AMH (n=209)



No Difference in 5 yr IDFS

Postmenopausal: < 10 pg/mL

Medium/High AMH (n=806)



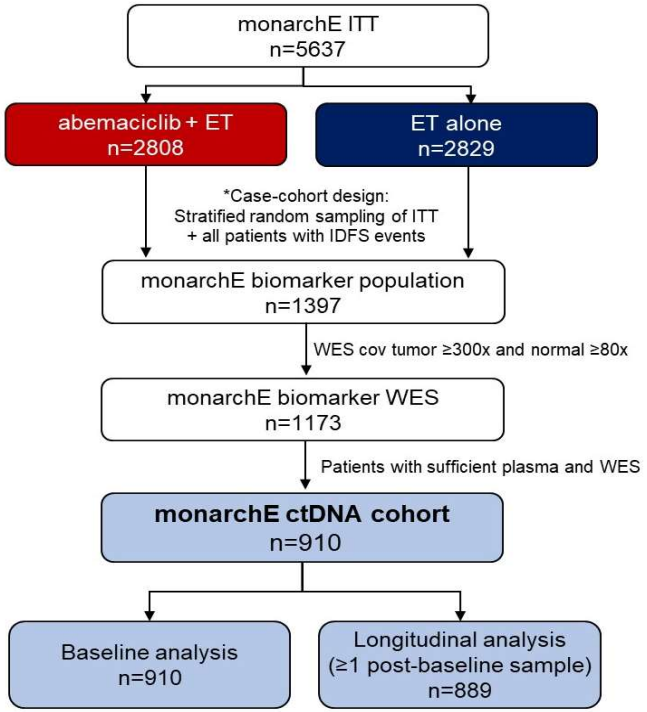
7.8% improvement in 5 yr IDFS with chemo

Premenopausal: ≥ 10 pg/mL

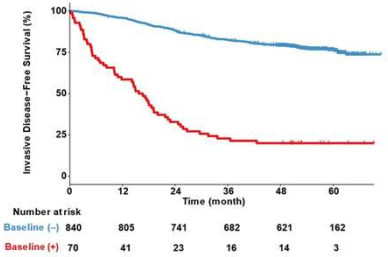
Significant interaction p=0.019, adjusting for RS

In RxPONDER, "premenopausal" women < 55 years with 1-3 LN+ and RS ≤ 25, 20.6% have low pre-treatment serum AMH levels < 10 pg/ML by traditional ELISA assay and did not benefit from adding chemotherapy to ET

#ABSTRACT LBA 507# Prognostic utility of ctDNA detection in the monarchE trial of adjuvant abemaciclib plus endocrine therapy (ET) in HR+, HER2-, node-positive, high-risk early breast cancer (EBC).



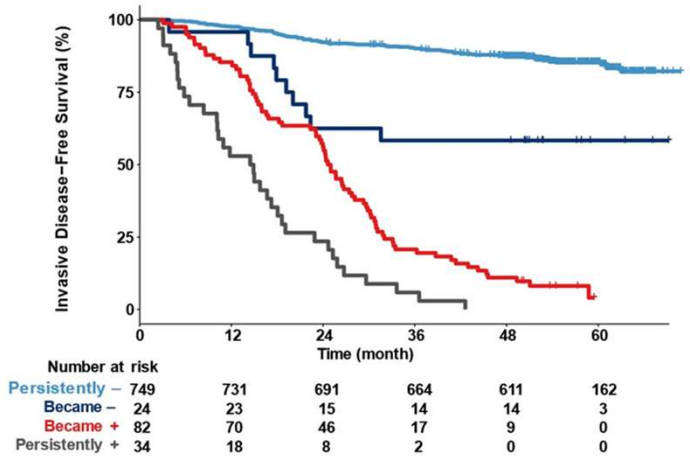
Baseline ctDNA Detection is Associated with Worse Outcomes



	Baseline Analysis* N=910	
	Baseline (–), undetected N=840	Baseline (+), detected N=70
IDFS event, n (%)	191 (23)	56 (80)
4-year IDFS rate, % (95% CI)	79.1 (76.4-82.0)	20.0 (12.5-32.0)
Log-rank test	Nominal p-value < 0.0001	

*The ctDNA subset was enriched by patients with IDFS events within 24 months; therefore, the estimated IDFS rates in each subgroup are not reflective of that in the overall population

Dynamics of ctDNA Detection on Treatment is Associated with Outcomes

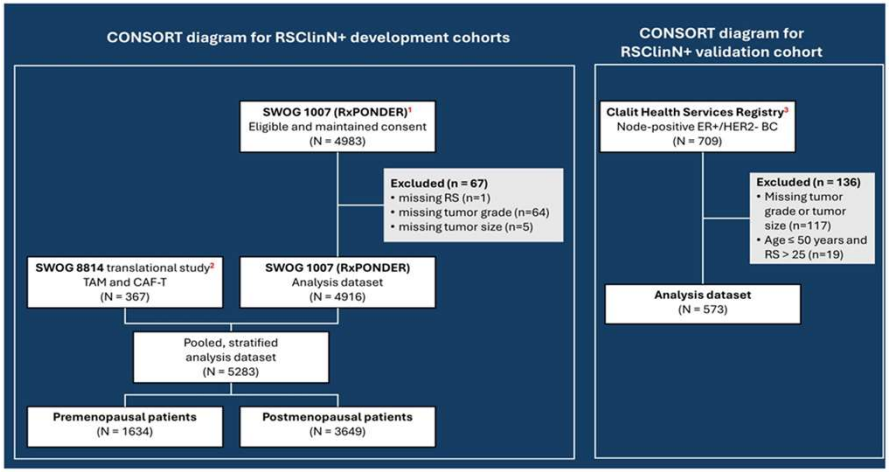


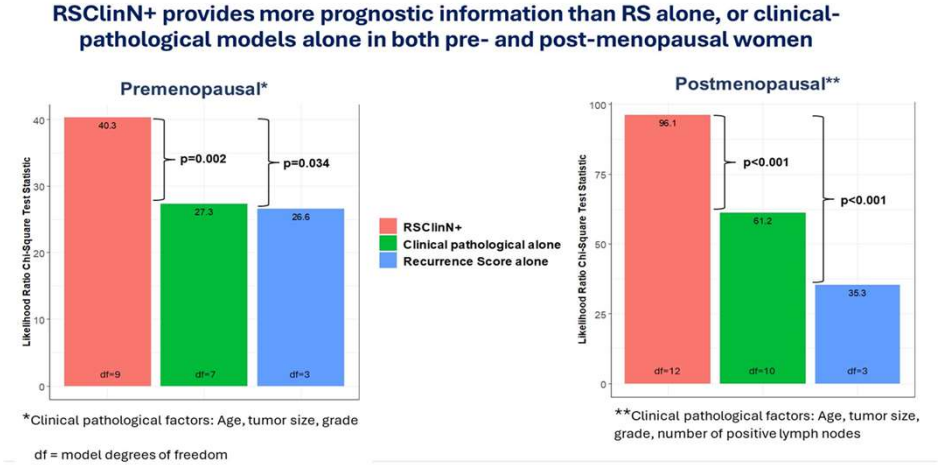
	Longitudinal Analysis (N=889)*			
	Baseline (–), undetected N=831		Baseline (+), detected N=58	
	Persistently –	Became +	Persistently +	Became – (undetected)
N	749 (90)	82 (10)	34 (60)	24 (40)
IDFS event, n (%)	107 (14)	76 (93)	34 (100)	10 (42)
4-year IDFS rate, % (95% CI)	87.5 (85.1-89.9)	11.0 (5.9-20.3)	NA	58.3 (41.6-81.8)

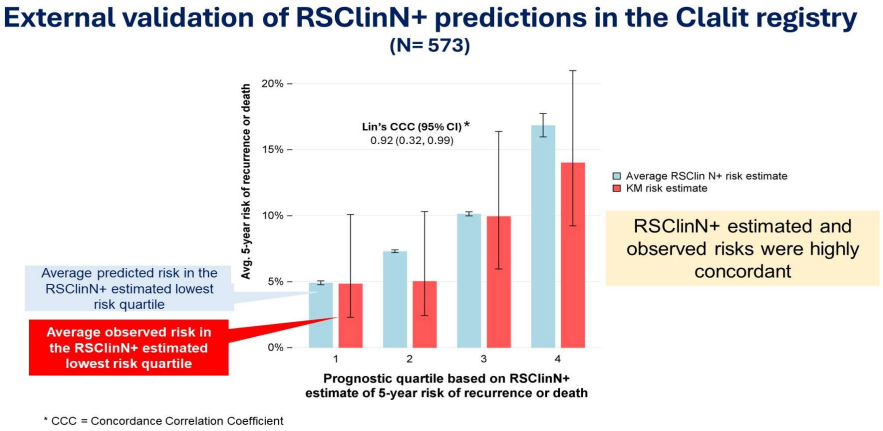
*The ctDNA subset was enriched by patients with IDFS events within 24 months; therefore, the estimated IDFS rates in each subgroup are not reflective of that in the overall population. Robust assessment was limited in 194 patients with <3 post-baseline timepoints and there may be differences in IDFS; total events 227.

Patients who remained Persistently + or Became + on treatment were more likely to experience an IDFS event compared to those who Became – (undetected) or remained Persistently – on treatment

#ABSTRACT LBA 508# Development and validation of RSClin N+ tool for hormone receptor-positive (HR+), HER2-negative (HER2-), node-positive breast cancer.







- RSClinN+ provides more prognostic information than either the RS alone, or clinical-pathological factors alone in both pre- and postmenopausal women.
- In **postmenopausal** patients, RS showed interaction with chemotherapy benefit; absolute benefit from chemotherapy increased as RS increased above 25.
- In **premenopausal** patients, with RS ≤25, there was no interaction between RS and chemotherapy benefit, chemotherapy benefit was seen at all RS levels.
- In external validation, RSClinN+ risk estimates were prognostic and concordant with observed risk.

What to do tomorrow?

- **#ABSTRACT 512# Baseline (BL) characteristics and efficacy endpoints for patients (pts) with node-negative (N0) HR+/HER2− early breast cancer (EBC): NATALEE trial.**
- **#ABSTRACT LBA 500# A-BRAVE trial: A phase III randomized trial with avelumab in early triple-negative breast cancer with residual disease after neoadjuvant chemotherapy or at high risk after primary surgery and adjuvant chemotherapy.**
- **#ABSTRACT LBA 502# A randomized, multicenter, open-label, phase III trial comparing anthracyclines followed by taxane versus anthracyclines followed by taxane plus carboplatin as (neo) adjuvant therapy in patients with early triple-negative breast cancer: Korean Cancer Study Group BR 15-1 PEARLY trial.**

  -> I will use platin in the adjuvant treatment of CMTN
- **#ABSTRACT 516# Non-basal subtype defined by FOXC1 expression as an independent predictor of capecitabine efficacy in the triple negative breast cancer GEICAM/2003-11_CIBOMA/2004-01 trial.**

  -> I will ask to my pathologist if he can do the FOXC1 IHQ

- **#ABSTRACT 10503# Clinical behavior of breast cancer in young *BRCA* carriers and prognostic impact of the timing of genetic testing: Results from an international cohort study.**
- **#ABSTRACT 504# Impact of hormone receptor status and tumor subtypes on clinical behavior and outcomes of breast cancer in young *BRCA* carriers.**

  -> Be careful with luminal breast cancer in BRCA 1 / 2 carriers
- **#ABSTRACT 505# Correlation of serum anti-Müllerian hormone (AMH) levels on identification of premenopausal patients (pts) with hormone receptor positive (HR+), HER2-negative, node-positive breast cancer most likely to benefit from adjuvant chemotherapy in SWOG S1007 (RxPONDER).**

  -> If I am not sure about menopausal status, I will measure AMH level.

- **#ABSTRACT LBA 507# Prognostic utility of ctDNA detection in the monarchE trial of adjuvant abemaciclib plus endocrine therapy (ET) in HR+, HER2-, node-positive, high-risk early breast cancer (EBC).**
- **#ABSTRACT LBA 508# Development and validation of RSClin N+ tool for hormone receptor-positive (HR+), HER2-negative (HER2-), node-positive breast cancer.**

  -> I will keep taking into account the clinical and pathologic factors to better understand the prognosis.