Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix. List of collaborators

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eTable 1. Patient Demographic and Clinical Characteristics at Randomization

Characteristics	Total patients (N = 695) No.	%	P (N = 349) No.	%	nab-P (N = 346) No.	%
Stratification variables						
Cooperative Research Group						
Michelangelo	272	39	137	39	135	39
GEICAM	377	54	189	54	188	54
BCRC-WA	46	7	23	7	23	7
Disease stage						
Operable	525	76	261	75	264	76
Locally advanced	170	24	88	25	82	24
Tumor subtype						
Triple negative	219	32	110	32	109	32
Luminal-B like high	377	54	189	54	188	54
Luminal-B like intermediate	99	14	50	14	49	14
Other clinical characteristics						
cT stage						
1	3	<1	2	<1	1	<1
2	503	72	245	70	258	75
3	132	19	76	22	56	16
4a-c	42	6	18	5	24	7
4d	15	2	8	2	7	2
cN stage						
0	348	50	167	48	181	52
1	291	42	153	44	138	40
2	56	8	29	8	27	8
3	14	2	6	2	8	2

P: paclitaxel; nab-P: nab-paclitaxel; GEICAM: Grupo Español de Investigación en Cáncer de Mama; BCRC-WA: Breast Cancer Research Center- Western Australia

eTable 2. Multivariate analysis of pCR

Variable	Effect	Odds Ratio (95% CI)	P value
Treatment	P vs nab-P	0.76 (0.52-1.13)	0.17
Disease stage	Locally advanced vs early	0.74 (0.46-1.20)	0.23
Tumor subtype	Triple negative vs luminal B-like	4.85 (3.28-7.18)	< 0.0001
Age	≤ 50 yr vs > 50 yr	1.27 (0.86-1.88)	0.24

P: paclitaxel; nab-P: nab-paclitaxel; pCR: pathological complete response; CI: confidence interval

eTable 3. Clinical objective response

	End of Taxane		End of Chemotherapy	
	P	nab-P	P	nab-P
Objective clinical response (95% CI)	66.5% (61.3 – 71.4)	69.4% (64.2 – 74.2)	74.5% (69.6 – 79.0)	77.2% (72.4 – 81.5)
Complete Response	20.1%	20.8%	41.8%	42.2%
Partial Response	46.4%	48.6%	32.7%	35.0%
*Odds ratio (95% CI)	0.88 (0.64, 1.21)		0.87 (0.61, 1.23)	
*p-value	0.4392		0.4273	
Stable Disease	14.9%	11.3%	5.7%	2.6%
Progressive Disease	0.6%	2.3%	5.7%	5.5%

*Cochran-Mantel-Haenszel test, controlling for tumor subtype and disease stage and quantified by OR and rate difference

eTable 4. Percent frequency of selected treatment-emergent adverse events (TEAE)

	TEAE of any grade			Grade ≥ 3 TEAE		
	P # 335	**nab-P # 337**	**RD**	**P # 335**	**nab-P # 337**	**RD**
Peripheral neuropathy	53.7 (48.2-59.2)	62.9 (57.5-68.1)	-8.9* [0.016]	1.8 (0.7-3.9)	4.5 (2.5-7.2)	-2.7* [0.47]
Nausea	55.8 (50.3-61.2)	56.1 (50.6-61.5)	-0.3	3.9 (2.1-6.5)	3.6 (1.96.1)	0.3
Neutropenia	36.4 (31.3-41.8)	41.8 (36.5-47.3)	-5.4	19.7 (15.6-24.4)	30.6 (25.7-35.8)	-10.9* [0.001]
Asthenia	39.4 (34.1-44.9)	39.8 (34.5-45.2)	-0.4	1.8 (0.7-3.9)	2.7 (1.2-5.0)	-0.9
Fatigue	31.3 (26.4-36.6)	36.8 (31.6-42.2)	-5.5	1.2 (0.3-3.0)	2.4 (1.0-4.6)	-1.2
Vomiting	19.7 (15.6-24.4)	24.6 (20.1-29.6)	-4.9	2.4 (0.1-4.7)	4.2 (2.3-6.9)	-1.8
Diarrhea	23.9 (19.4-28.8)	23.4 (19.0-28.3)	0.5	0.9 (0.2-2.6)	2.1 (0.8-4.2)	-1.2
Leucopenia	20.6 (16.4-25.3)	22.3 (17.9-27.1)	-1.7	7.2 (4.6-10.5)	8.3 (5.6-11.8)	-1.1
Rash	13.4 (10.0-17.6)	13.9 (10.4-18.1)	-0.5	0.9 (0.2-3.0)	-	0.9
Alanine Aminotransferase increase	11.6 (8.4-15.6)	8.0 (5.3-11.4)	3.6	1.5 (0.5-3.4)	0.3 (0.0-1.6)	1.2
Lacrimation increase	3.3 (1.7-5.8)	8.6 (5.8-12.1)	-5.3* [0.004]	-	-	-
Aspartate Amino-Transferase increase	6.0 (3.7-9.1)	4.7 (2.7-7.6)	1.3	0.6 (0.1-2.1)	-	0.6
Hypersensitivity	6.0 (3.7-9.1)	1.8 (0.7-3.8)	4.2* [0.005]	0.6 (0.1-2.1)	0.3 (0.0-1.6)	0.3

TEAE: treatment emergent adverse event; P: paclitaxel; nab-P: nab-paclitaxel; RD: risk difference, i.e. frequency in P arm - frequency in nab-P arm; 95% confidence intervals in parenthesis; *statistically significant, P value in brackets

eTable 5 Extent of exposure and dose modifications during taxane treatment in the safety population*

	P # 335	nab-P # 337
Median treatment duration in weeks (range) Mean treatment duration in weeks (SD)	16 (4-19.7) 15.7 (2.2)	16 (4-21) 15.9 (1.8)
Median number of cycles (range) Mean number of cycles (SD)	4 (1-4) 3.9 (0.5)	4 (1-4) 3.9 (0.4)
Patients with dose omitted	20 (6%)	24 (7.1%)
Patients with dose reduction Due to any adverse event	32 (9.6%) 28 (8.4%)	39 (11.6%) 37 (11%)
Patients with dose delay Due to any adverse event	104 (31%) 49 (15%)	123 (36.5%) 69 (20.5%)
Median days of delay due to adverse events Median days of delay due to other reasons (e.g. logistics)	7 (1-20) 2 (1-12)	7 (1-20) 2 (1-7)
Patients who discontinued taxanes Due to adverse events Patient's refusal to continue on taxane Progressive disease Others	27 (8.1%) 12 (3.4%) 1 (0.3%) 10 (2.9%) 4 (1.1%)	32 (9.5%) 12 (3.5%) - 16 (4.6%) 4 (1.2%)
Relative dose intensity** Median Mean (SD)	 99.53% 97.30 (12.39)	 99.35% (96.42 (8.55)

* Patient who received at least one dose of either taxane; P: paclitaxel; nab-P; nab-paclitaxel; SD: standard deviation)
**The relative dose intensity (%) is the ratio between the absolute and the intended dose intensity (mg/m^2/week) multiplied by 100

eTable 6 Extent of exposure and dose modifications during anthracycline treatment and frequency of Grade ≥ 3 treatment-emergent adverse events (TEAE) in the safety population*

	P # 312	nab-P # 322
Received regimen		
AC (doxorubicin and cyclophosphamide)	87 (27.9%)	117 (36.3%)
ED (epirubicin and cyclophosphamide)	108 (34.6%)	95 (29.5%)
FEC (fluorouracil, epirubicin, cyclophosphamide)	117 (37.5%)	110 (34.2%)
Median number of cycles (range)	4 (1-4)	4 (1-4)
Mean number of cycles (SD)	3.9 (0.5)	3.9 (0.4)
Median treatment duration in weeks (range)	12 (3-15.1)	12 (3.16.6)
Mean treatment duration in weeks (SD)	12.1 (1.3)	12 (1.7)
Patients with dose reduction due to any drug	19 (6.1%)	29 (9.0%)
Due to any adverse event	16 (5.1%)	27 (8.4%)
Patients with dose delay	88 (28.2%)	89 (27.6%)
Due to any adverse event	68 (21.8%)	71 (22.9%)
Grade ≥ 3 TEAE		
Peripheral neuropathy	2 (0.6%)	3 (0.9%)
Neutropenia	58 (18.6%)	79 (24.5%)
Leucopenia	22 (7.1%)	22 (6.8%)
Nausea	13 (4.2%)	17 (5.3%)
Vomiting	8 (2.6%)	13 (4.0%)
Fatigue	2 (0.6%)	7 (2.2%)

* Patient who received at least one dose of anthracyclines after taxanes; P: received paclitaxel before anthracyclines; nab-P; received nab-paclitaxel before anthracyclines; SD: standard deviation)