

SUPPLEMENTARY MATERIAL

TITLE

Body mass index as a predictive factor for efficacy of adjuvant taxane-based chemotherapy in early-stage breast cancer patients. A pooled analysis from adjuvant GEICAM Spanish Breast Cancer Group and TRIO Translational Research in Oncology Group studies

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Supplementary Table 1. Patients' distribution by treatment scheme and BMI category

Treatment Scheme	Normal	Overweight	Obese	Severely Obese	Total
AC → T	1212 (20.7%)	885 (19.7%)	385 (18.4%)	190 (18.3%)	2672 (19.8%)
AC → TH	485 (8.3%)	344 (7.7%)	159 (7.6%)	80 (7.7%)	1068 (7.9%)
EC → T	278 (4.7%)	223 (5.0%)	106 (5.1%)	62 (6.0%)	669 (5.0%)
ET → X	288 (4.9%)	253 (5.6%)	114 (5.4%)	54 (5.2%)	709 (5.3%)
FAC	953 (16.2%)	751 (16.7%)	359 (17.1%)	160 (15.4%)	2223 (16.5%)
FAC + wP	396 (6.7%)	331 (7.4%)	158 (7.5%)	61 (5.9%)	946 (7.0%)
FEC	243 (4.1%)	208 (4.6%)	118 (5.6%)	56 (5.4%)	625 (4.6%)
FEC + wP	224 (3.8%)	241 (5.4%)	104 (5.0%)	42 (4.0%)	611 (4.5%)
TAC	1264 (21.5%)	953 (21.2%)	445 (21.3%)	248 (23.9%)	2910 (21.6%)
TCH	525 (8.9%)	296 (6.6%)	146 (7.0%)	86 (8.3%)	1053 (7.8%)

*A: doxorubicin, C: cyclophosphamide, E: epirubicin, F: fluorouracil, H: trastuzumab, T: docetaxel, wP: weekly paclitaxel, X: capecitabine.

Supplementary Table 2. Invasive disease-free survival (iDFS). First event description

	Total
Invasive Disease-Free Survival, n (%)	3897
Local-Regional Invasive Recurrence	569 (14.6%)
Local-Regional + Contralateral BC	13 (0.3%)
Local-Regional + Distant Recurrence	292 (7.5%)
Local-Regional + Distant Recurrence + Contralateral BC	12 (0.3%)
Second Primary BC	50 (1.3%)
Second Primary BC + Contralateral BC	2 (0.1%)
Contralateral BC	306 (7.9%)

Distant Recurrence	1873 (48.1%)
Distant Recurrence + Second Primary Invasive Cancer (non-breast)	3 (0.1%)
Distant Recurrence + Contralateral BC	21 (0.5%)
Second Primary Invasive Cancer (non-breast)	541 (13.9%)
Death	215 (5.5%)

Supplementary Table 3. Invasive Disease-free Survival (iDFS) per drug and BMI category (Sensitivity Analysis)

Normal	Overweight	Obese	Severely Obese
All patients			
71.4%	69.7%	67.9%	64.1%
	HR 1.05 (0.98-1.13)	HR 1.16 (1.06-1.28)	HR 1.30 (1.16-1.46)
	<i>P</i> -value=0.181	<i>P</i>-value=0.001	<i>P</i>-value <0.001
N=5,713	N=4,485	N=2,094	N=1,039
Adjuvant non-docetaxel-based chemotherapy patients			
61.8%	65.5%	62.4%	67.2%
	HR 0.89 (0.72-1.11)	HR 1.02 (0.79-1.33)	HR: 0.79 (0.54-1.14)
	<i>P</i> -value=0.297	<i>P</i> -value=0.855	<i>P</i> -value=0.200
N=492	N=442	N=206	N=97
Adjuvant docetaxel-based chemotherapy patients			
69.7%	67.4%	66.0%	63.5%
	HR 1.07 (0.97-1.18)	HR 1.15 (1.01-1.30)	HR 1.26 (1.08-1.48)
	<i>P</i> -value=0.189	<i>P</i>-value=0.035	<i>P</i>-value=0.004
N=3,378	N=2,478	N=1,135	N=604
Adjuvant non-paclitaxel-based chemotherapy patients			

77.5%	74.0%	71.9%	65.0%
	HR 1.11 (0.88-1.39)	HR 1.35 (1.04-1.74)	HR 1.87 (1.37-2.57)
	<i>P</i> -value=0.382	<i>P</i>-value=0.024	<i>P</i>-value <0.001
N=677	N=517	N=271	N=119
Adjuvant paclitaxel-based chemotherapy patients			
79.0%	76.6%	77.8%	71.2%
	HR 1.10 (0.87-1.38)	HR 1.08 (0.81-1.45)	HR 1.45 (0.99-2.13)
	<i>P</i> -value=0.438	<i>P</i> -value=0.599	<i>P</i> -value=0.059
N=611	N=572	N=262	N=103
Adjuvant non-taxane-based chemotherapy patients			
70.9%	70.1%	67.8%	66.0%
	HR 0.99 (0.85-1.16)	HR 1.17 (0.98-1.41)	HR 1.23 (0.97-1.56)
	<i>P</i> -value=0.909	<i>P</i> -value=0.088	<i>P</i> -value=0.088
N=1,169	N=959	N=477	N=216
Adjuvant taxane-based chemotherapy patients			
71.5%	69.5%	67.7%	63.3%
	HR 1.07 (0.99-1.17)	HR 1.16 (1.04-1.29)	HR 1.32 (1.16-1.50)
	<i>P</i> -value=0.104	<i>P</i>-value=0.007	<i>P</i>-value <0.001
N=4,544	N=3,526	N=1,617	N=823

Supplementary Table 4. Comparison of Invasive Disease-free Survival (iDFS) by treatment regimens and BMI category (Sensitivity Analysis)

	Normal	Overweight	Obese	Severely obese
Docetaxel vs. non docetaxel	69.7% vs. 61.8%	67.4% vs. 65.5%	66.0% vs. 62.4%	63.5% vs. 67.2%
	HR 0.72	HR 0.83	HR 0.84	HR 1.12

	95% CI 0.58-0.89 P-value=0.002	95% CI 0.66-1.05 <i>P-value=0.124</i>	95% CI 0.61-1.16 <i>P-value=0.285</i>	95% CI 0.70-1.78 <i>P-value=0.646</i>
Paclitaxel vs. non paclitaxel	79.0% vs. 77.5% HR 0.92 95% CI 0.73-1.15 <i>P-value=0.444</i>	76.6% vs. 74.0% HR 0.89 95% CI 0.71-1.13 <i>P-value=0.347</i>	77.8 vs. 71.9% HR 0.72 95% CI 0.52-0.98 P-value=0.039	71.2% vs. 65.0% HR 0.70 95% CI 0.45-1.09 <i>P-value=0.113</i>
Taxane vs. non taxane	71.5% vs. 70.9% HR 0.81 95% CI 0.69-0.94 P-value=0.006	69.5% vs. 70.1% HR 0.86 95% CI 0.73-1.02 <i>P-value=0.079</i>	67.7% vs. 67.8% HR 0.78 95% CI 0.62-0.97 P-value=0.026	63.3% vs. 66.0% HR 0.87 95% CI 0.63-1.20 <i>P-value=0.397</i>

Supplementary Table 5. Comparison of Overall Survival (OS) by treatment regimens and BMI category

	Normal	Overweight	Obese	Severely obese
Docetaxel vs. non docetaxel	81.4% vs. 76.5% HR 0.70 95% CI 0.54-0.91 P-value=0.008	80.4% vs. 78.4% HR 0.72 95% CI 0.53-0.99 P-value=0.041	77.8% vs. 75.0% HR 0.73 95% CI 0.48-1.09 <i>P-value=0.125</i>	72.3% vs. 75.5% HR 1.22 95% CI 0.70-2.11 <i>P-value=0.482</i>
Paclitaxel vs. non paclitaxel	88.8% vs. 86.7% HR 0.89 95% CI 0.66-1.20 <i>P-value=0.426</i>	86.9% vs. 84.3% HR 0.87 95% CI 0.65-1.17 <i>P-value=0.372</i>	89.5 vs. 82.2% HR 0.62 95% CI 0.41-0.94 P-value=0.025	81.7% vs. 73.4% HR 0.72 95% CI 0.42-1.25 <i>P-value=0.244</i>
Taxane vs. non taxane	83.1% vs. 82.4% HR 0.77 95% CI 0.64-0.94 P-value=0.011	82.0% vs. 81.6% HR 0.80 95% CI 0.65-0.99 <i>P-value=0.039</i>	80.2% vs. 79.1% HR 0.67 95% CI 0.50-0.90 P-value=0.007	74.7% vs. 74.3% HR 0.93 95% CI 0.64-1.37 <i>P-value=0.726</i>

Supplementary Table 6. Overall Survival (OS) per drug and BMI category

Normal	Overweight	Obese	Severely Obese
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All patients			
83.0%	81.9% HR 1.09 95% CI 0.99-1.20 <i>P</i> -value=0.076	80.0% HR 1.24 95% CI 1.11-1.40 <i>P</i>-value <0.001	74.7% HR 1.46 95% CI 1.27-1.69 <i>P</i>-value <0.001
Adjuvant non-docetaxel-based chemotherapy patients			
76.5%	78.4% HR 0.91 95% CI 0.70-1.19 <i>P</i> -value=0.480	75.0% HR 1.09 95% CI 0.80-1.51 <i>P</i> -value=0.579	75.5% HR 0.87 95% CI 0.56-1.36 <i>P</i> -value=0.551
Adjuvant docetaxel-based chemotherapy patients			
81.4%	80.4% HR 1.09 95% CI 0.96-1.24 <i>P</i> -value=0.190	77.8% HR 1.22 95% CI 1.04-1.43 <i>P</i>-value=0.016	72.3% HR 1.44 95% CI 1.18-1.74 <i>P</i>-value <0.001
Adjuvant non-paclitaxel-based chemotherapy patients			
86.7%	84.3% HR 1.19 95% CI 0.89-1.59 <i>P</i> -value=0.241	82.2% HR: 1.43 95% CI 1.03-1.99 <i>P</i> -value=0.033	73.4% HR 2.17 95% CI 1.47-3.18 <i>P</i> -value <0.001
Adjuvant paclitaxel-based chemotherapy patients			
88.8%	86.9% HR 1.18 95% CI 0.87-1.60 <i>P</i> -value=0.290	89.5% HR 1.01 95% CI 0.68-1.51 <i>P</i> -value=0.946	81.7% HR 1.73 95% CI 1.07-2.80 <i>P</i>-value=0.026
Adjuvant non-taxane-based chemotherapy patients			
82.4%	81.6% HR 1.03 95% CI 0.84-1.25 <i>P</i> -value=0.784	79.1% HR 1.24 95% CI 0.98-1.56 <i>P</i> -value=0.067	74.3% HR 1.39 95% CI 1.04-1.85 <i>P</i> -value=0.026

Adjuvant taxane-based chemotherapy patients			
83.1%	82.0%	80.2%	74.7%
	HR 1.11	HR 1.24	HR: 1.48
	95% CI 1.00-1.24	95% CI 1.08-1.42	95% CI 1.26-1.75
	<i>P</i> -value=0.060	<i>P</i>-value=0.002	<i>P</i>-value <0.001

Supplementary Table 7. Comparison of Breast Cancer Overall Survival (BCOS) by treatment regimens and BMI category

	Normal	Overweight	Obese	Severely Obese
Docetaxel vs. non docetaxel	84.1% vs. 78.9% HR 0.62 95% CI 0.46-0.82 <i>P</i>-value=0.001	82.8% vs. 81.4% HR 0.74 95% CI 0.52-1.03 <i>P</i> -value=0.074	80.8% vs. 80.2% HR 0.89 95% CI 0.57-1.38 <i>P</i> -value=0.597	76.4% vs. 83.7% HR 1.48 95% CI 0.77-2.8 <i>P</i> -value=0.244
Paclitaxel vs. non paclitaxel	91.1% vs. 89.2% HR 0.88 95% CI 0.62-1.23 <i>P</i> -value=0.446	89.8% vs. 87.2% HR 0.81 95% CI 0.58-1.15 <i>P</i> -value=0.242	91.4 vs. 86.5% HR 0.64 95% CI 0.39-1.06 <i>P</i> -value=0.084	87.8% vs. 76.3% HR 0.68 95% CI 0.36-1.28 <i>P</i> -value=0.231
Taxane vs. non taxane	85.6% vs. 84.8% HR 0.71 95% CI 0.57-0.89 <i>P</i> -value=0.003	84.6% vs. 84.5% HR 0.77 95% CI 0.61-0.98 <i>P</i> -value=0.036	83.3% vs. 83.8% HR 0.77 95% CI 0.55-1.07 <i>P</i> -value=0.119	79.8% vs. 79.6% HR 0.98 95% CI 0.63-1.53 <i>P</i> -value=0.942

Supplementary Table 8. Breast Cancer Overall Survival (BCOS) per drug and BMI category

Normal	Overweight	Obese	Severely Obese
All patients			
85.5%	84.5%	83.5%	79.9%
	HR 1.07	HR 1.16	HR 1.33
	95% CI 0.96-1.18	95% CI 1.01-1.32	95% CI 1.13-1.56

	<i>P</i> -value=0.231	<i>P</i>-value=0.030	<i>P</i>-value=0.001
Adjuvant non-docetaxel-based chemotherapy patients			
78.9%	81.4 HR 0.85 95% CI 0.64-1.14 <i>P</i> -value=0.279	80.2% HR 0.94 95% CI 0.65-1.34 <i>P</i> -value=0.716	83.7% HR 0.63 95% CI 0.37-1.08 <i>P</i> -value=0.095
Adjuvant docetaxel-based chemotherapy patients			
84.1%	82.8% HR 1.11 95% CI 0.97-1.28 <i>P</i> -value=0.138	80.8% HR 1.21 95% CI 1.02-1.45 <i>P</i>-value=0.032	76.4% HR 1.41 95% CI 1.14-1.74 <i>P</i>-value=0.002
Adjuvant non-paclitaxel-based chemotherapy patients			
89.2%	87.2% HR 1.13 95% CI 0.81-1.57 <i>P</i> -value=0.473	86.5% HR 1.20 95% CI 0.81-1.76 <i>P</i> -value=0.366	76.3% HR 2.04 95% CI 1.32-3.15 <i>P</i>-value=0.001
Adjuvant paclitaxel-based chemotherapy patients			
91.1%	89.8% HR 1.05 95% CI 0.74-1.49 <i>P</i> -value=0.784	91.4% HR 0.89 95% CI 0.56-1.42 <i>P</i> -value=0.621	87.8% HR 1.54 95% CI 0.88-2.71 <i>P</i> -value=0.133
Adjuvant non-taxane-based chemotherapy patients			
84.8%	84.5% HR 0.96 95% CI 0.77-1.19 <i>P</i> -value=0.726	83.8% HR 1.04 95% CI 0.80-1.35 <i>P</i> -value=0.778	79.6% HR 1.16 95% CI 0.83-1.61 <i>P</i> -value=0.395
Adjuvant taxane-based chemotherapy patients			
85.6%	84.6% HR 1.10 95% CI 0.98-1.24	83.3% HR 1.19 95% CI 1.02-1.39	79.8% HR 1.38 95% CI 1.15-1.66

	<i>P</i> -value=0.121	<i>P</i>-value=0.023	<i>P</i>-value=0.001
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Supplementary Table 9. Dosing Patterns according to BMI

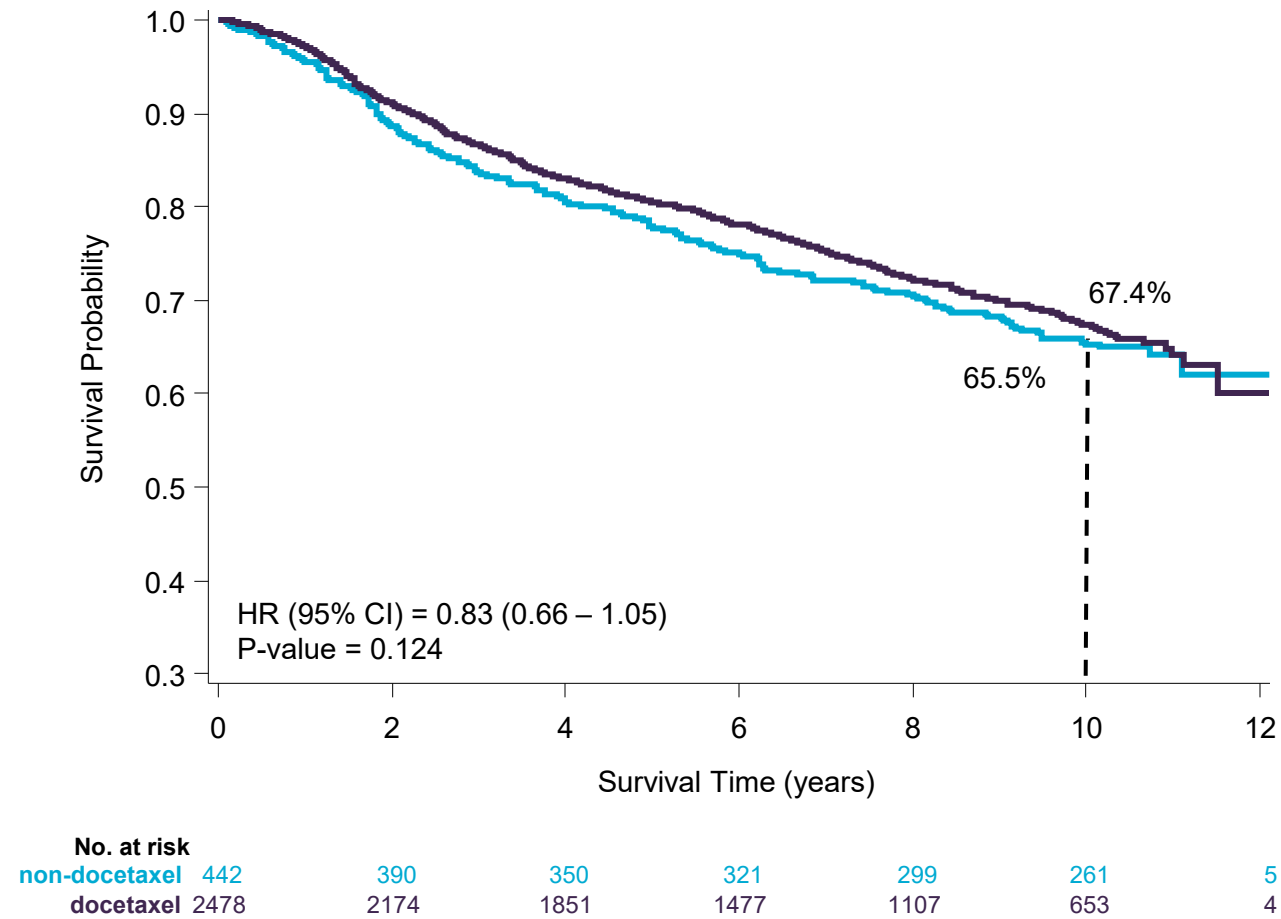
Under-treated	Normal	Overweight	Obese	Severely Obese	Total
Adjuvant non-docetaxel-based chemotherapy patients					
No	489 (95.9%)	425 (96.2%)	201 (97.6%)	87 (89.7%)	1202 (95.8%)
Yes	21 (4.1%)	17 (3.8%)	5 (2.4%)	10 (10.3%)	53 (4.2%)
Adjuvant docetaxel-based chemotherapy patients					
No	2997 (86.0%)	2114 (85.3%)	917 (80.8%)	465 (77.0%)	6493 (84.3%)
Yes	489 (14.0%)	364 (14.7%)	218 (19.2%)	139 (23.0%)	1210 (15.7%)
Adjuvant non-paclitaxel-based chemotherapy patients					
No	656 (95.6%)	487 (94.2%)	258 (95.2%)	112 (94.1%)	1513 (95.0%)
Yes	30 (4.4%)	30 (5.8%)	13 (4.8%)	7 (5.9%)	80 (5.0%)
Adjuvant paclitaxel-based chemotherapy patients					
No	562 (90.6%)	502 (87.8%)	213 (81.3%)	81 (78.6%)	1358 (87.2%)
Yes	58 (9.4%)	70 (12.2%)	49 (18.7%)	22 (21.4%)	199 (12.8%)
Adjuvant non-taxane-based chemotherapy patients					
No	1145 (95.7%)	912 (95.1%)	459 (96.2%)	199 (92.1%)	2715 (95.3%)
Yes	51 (4.3%)	47 (4.9%)	18 (3.8%)	17 (7.9%)	133 (4.7%)
Adjuvant taxane-based chemotherapy patients					
No	4012 (85.9%)	2984 (84.6%)	1302 (80.5%)	630 (76.5%)	8928 (83.9%)
Yes	660 (14.1%)	542 (15.4%)	315 (19.5%)	193 (23.5%)	1710 (16.1%)

Supplementary Figure 1. Kaplan-Meier curves for invasive disease-free survival in patients with overweight BMI category

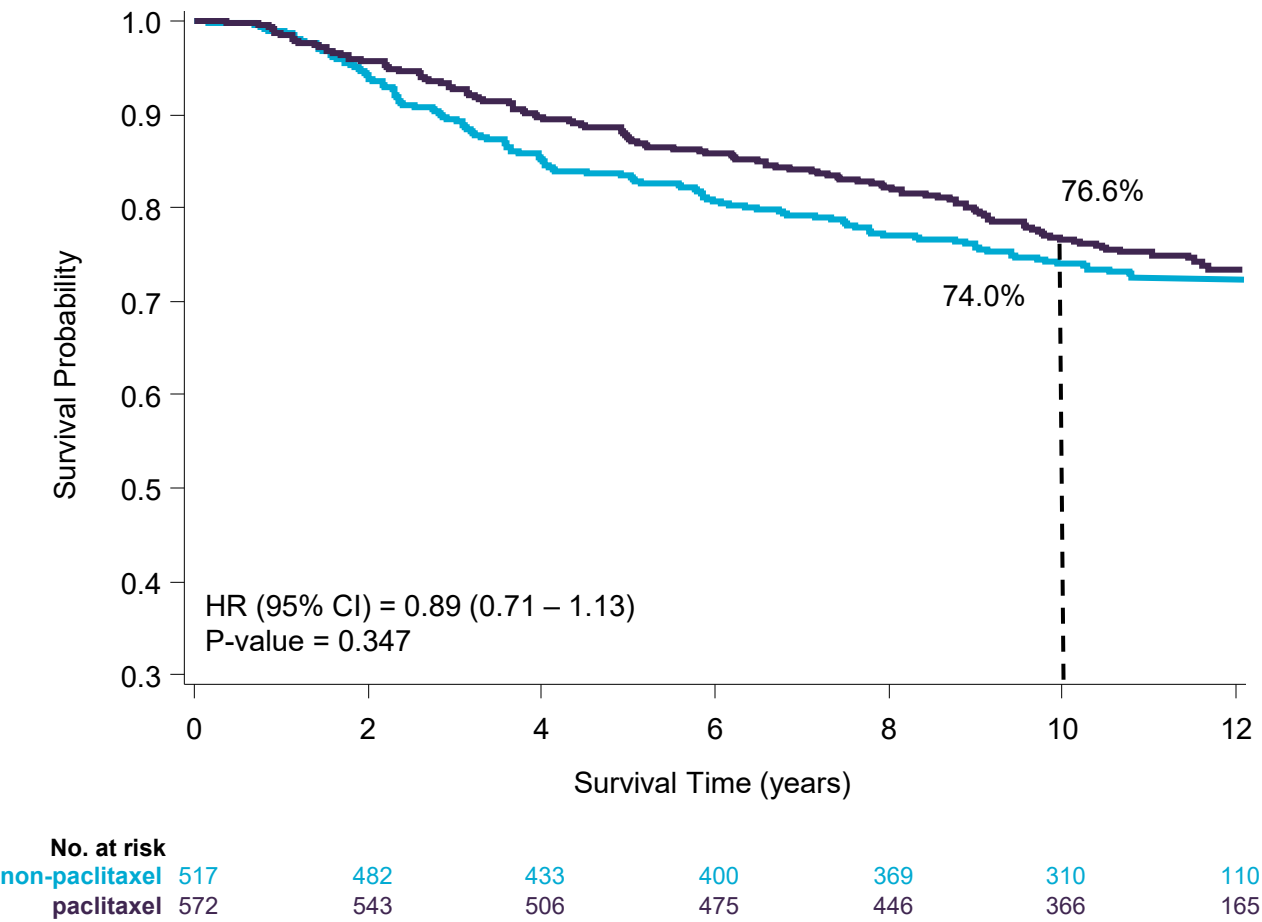
Supplementary Figure 2. Kaplan-Meier curves for invasive disease-free survival in patients with severely obese BMI category

Figure !

(A) Docetaxel vs. non-docetaxel



(B) Paclitaxel vs. non-paclitaxel



(C) Taxane vs. non-taxane

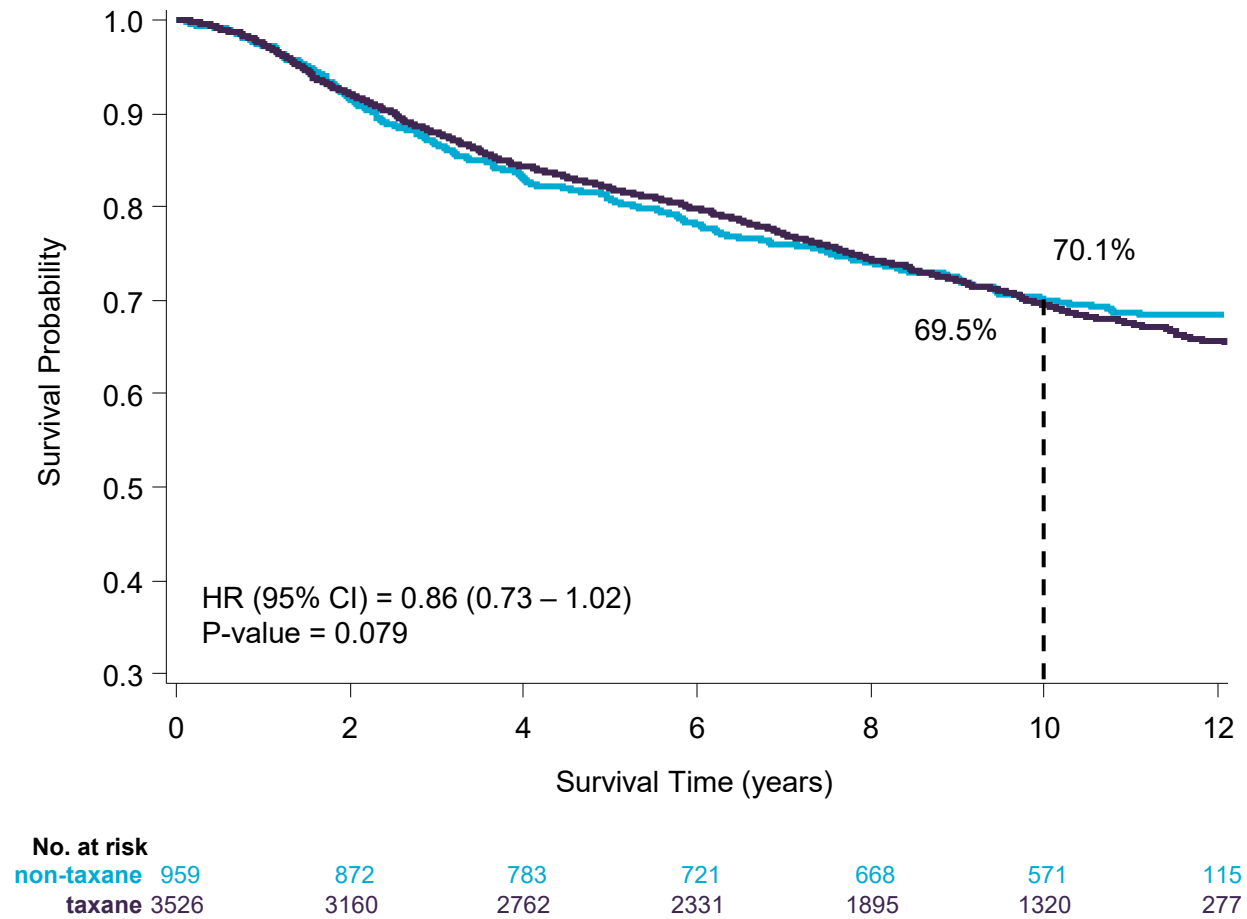
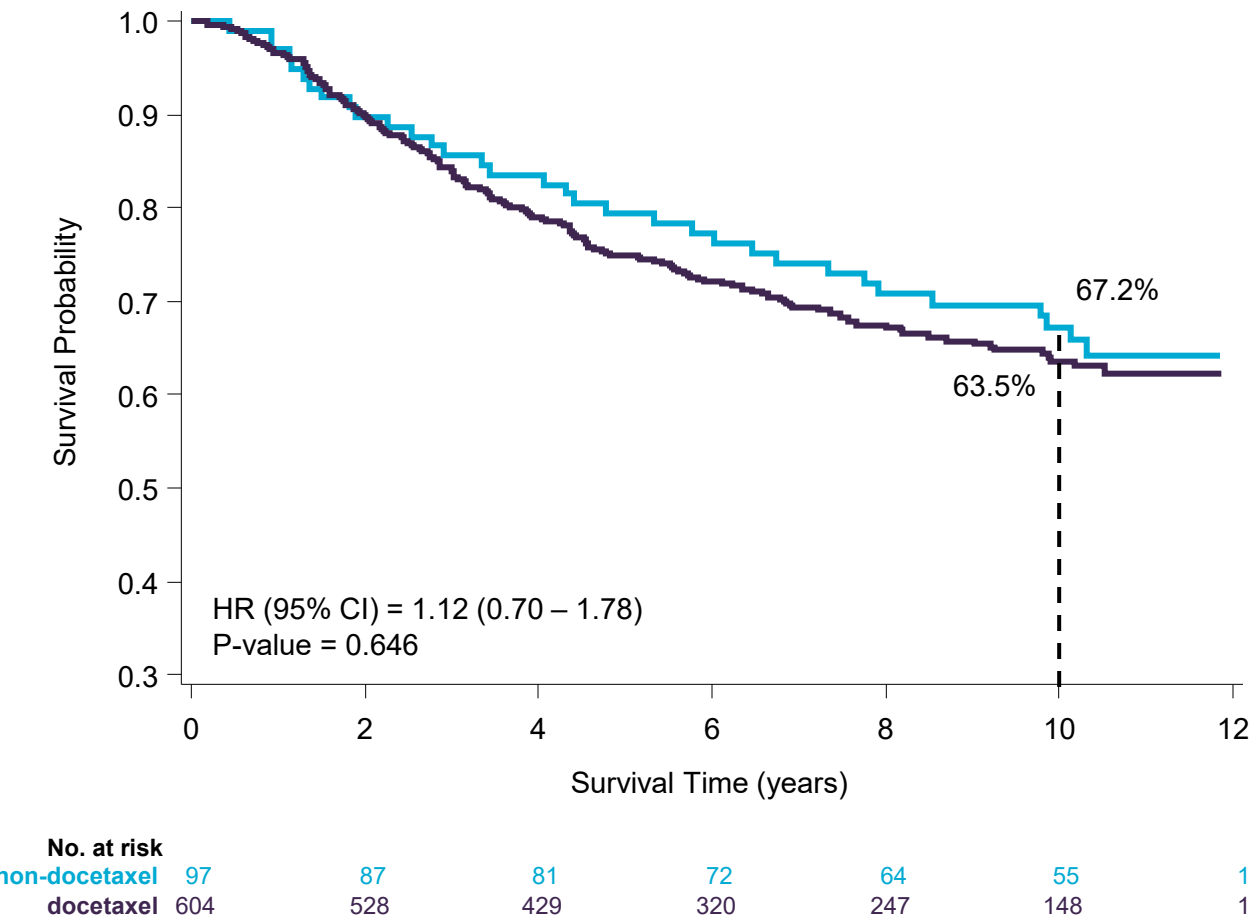
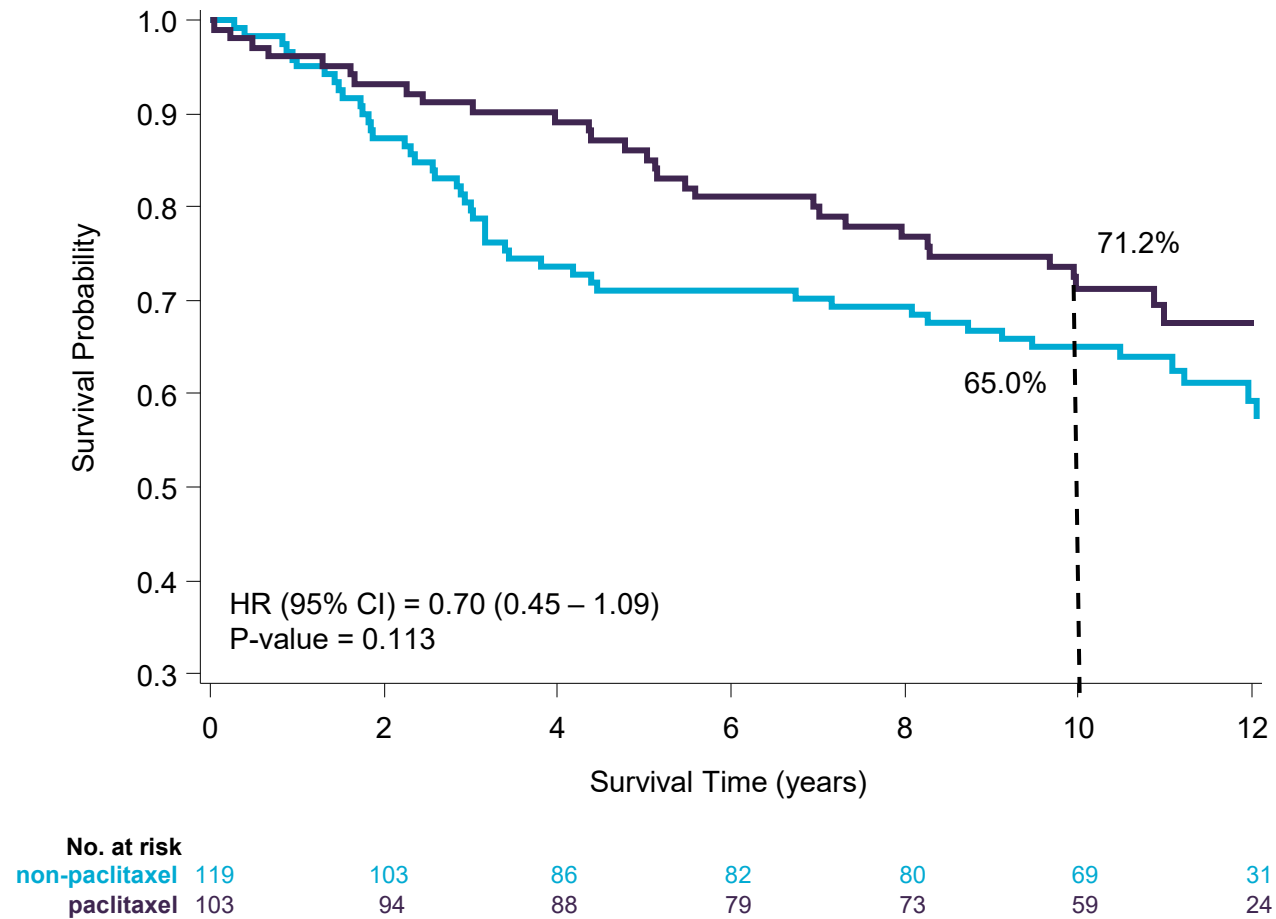


Figure 2

(A) Docetaxel vs. non-docetaxel



(B) Paclitaxel vs. non-paclitaxel



(C) Taxane vs. non-taxane

