

Supplementary Files

Toxicity Index, patient-reported outcomes, and persistence of breast cancer chemotherapy-associated side effects in NRG Oncology/NSABP B-30

N. L. Henry, S. Kim, R. D. Hays, M. A. Diniz, M. Tighiouart, G. Gresham, M. Luu, R. S. Cecchini, G. Yothers, A. Rogatko, P. A. Ganz

Contents:

Supplementary Figure 1. Visual depiction of data timepoints that are included in the acute and subacute periods.

Supplementary Table 1. Comparison of baseline patient characteristics between participants with and without data in the subacute period.

Supplementary Table 2. Number of participants with one or more non-missing values for patient reported outcomes data, by cycle and study arm.

Supplementary Table 3. Multivariable Probabilistic Index Models (PIM) for the cumulative Toxicity Index (TI) for the pain domain during the acute and subacute time periods.

Supplementary Table 4. Multivariable PIM for the cumulative TI for pain domain individual items during the acute time period.

Supplementary Table 5. Multivariable PIM for the cumulative TI for pain domain individual items during the subacute time period.

Supplementary Table 6. Multivariable PIM for the cumulative TI for the cognitive domain during the acute and subacute time periods.

Supplementary Table 7. Multivariable PIM for the cumulative TI for cognitive domain individual items during the acute time period.

Supplementary Table 8. Multivariable PIM for the cumulative TI for cognitive domain individual items during the subacute time period.

Supplementary Table 9. Multivariable PIM for the cumulative TI for the vasomotor domain during the acute and subacute time periods.

Supplementary Table 10. Multivariable PIM for the cumulative TI for vasomotor domain individual items during the acute time period.

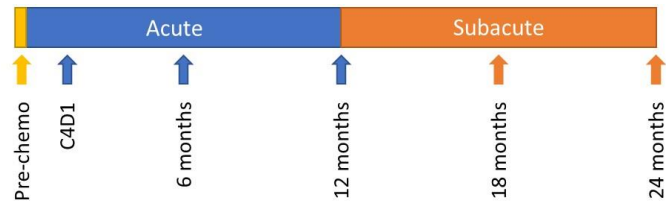
Supplementary Table 11. Multivariable PIM for the cumulative TI for vasomotor domain individual items during the subacute time period.

Supplementary Table 12. Multivariable PIM for the cumulative TI for the vaginal domain during the acute and subacute time periods.

Supplementary Table 13. Multivariable PIM for the cumulative TI for vaginal domain individual items during the acute time period.

Supplementary Table 14. Multivariable PIM for the cumulative TI for vaginal domain individual items during the subacute time period.

Supplementary Figure 1



Visual depiction of data timepoints that are included in the acute (blue) and subacute (orange) periods. Patient-reported outcomes were completed at the 5 timepoints designated in blue and orange, and reflected the symptoms in the 7 days prior to each assessment.

Supplementary Table 1. Comparison of baseline patient characteristics between participants with and without data in the subacute period. Bolded p values reflect those that are <0.05. NH: Non-Hispanic

Variable	All patients (N=2111)	Those with data in subacute period (N=1802)	Those without data in subacute period (N=309)	P-value
Age at surgery (Years), Median (IQR)	49 (43 - 57)	50 (44 - 57)	48 (42 - 56)	0.097
Age at surgery (Years)				0.292
[24, 43]	462 (21.89)	384 (21.31)	78 (25.24)	
[43, 50]	594 (28.14)	504 (27.97)	90 (29.13)	
[50, 57]	505 (23.92)	441 (24.47)	64 (20.71)	
[57, 80]	550 (26.05)	473 (26.25)	77 (24.92)	
Race/Ethnicity ¹				0.079
NH White	1817 (86.07)	1564 (86.79)	253 (81.88)	
Hispanic	59 (2.79)	44 (2.44)	15 (4.85)	
NH Black	174 (8.24)	142 (7.88)	32 (10.36)	
Other	60 (2.84)	51 (2.83)	9 (2.91)	
Unknown	1 (0.05)	1 (0.06)	0 (0)	
Body mass index (BMI; kg/m ²)				0.913
Underweight BMI < 18.5	24 (1.14)	20 (1.11)	4 (1.29)	
Normal weight 18.5 ≤ BMI < 25	771 (36.52)	663 (36.79)	108 (34.95)	
Overweight 25 ≤ BMI < 30	682 (32.31)	578 (32.08)	104 (33.66)	
Obesity BMI ≥ 30	634 (30.03)	541 (30.02)	93 (30.1)	
Type of surgery				0.825
Lumpectomy	1078 (51.07)	922 (51.17)	156 (50.49)	
Mastectomy	1033 (48.93)	880 (48.83)	153 (49.51)	
Hormonal therapy				<0.001
Yes	1672 (79.2)	1455 (80.74)	217 (70.23)	
No	439 (20.8)	347 (19.26)	92 (29.77)	
Data are presented as number of patients (column %) or median (IQR, interquartile range). P-value is calculated by Wilcoxon rank-sum test for the continuous variable and chi-square test for categorical variables as appropriate.				
¹ Unknown race/ethnicity is excluded from analyses.				

Supplementary Table 2. Number of participants with one or more non-missing values for patient reported outcomes data, by cycle and study arm A: doxorubicin; C: cyclophosphamide; QOL: quality of life; T: docetaxel

	Total	AC -> T	AT	ATC
Participants included in the QOL substudy	2156	717	718	721
Participants with follow-up questionnaires	2111	707	702	702
Baseline	2111 (100)	707 (100)	702 (100)	702 (100)
Day 1 of Cycle 4	1890 (89.5)	617 (87.3)	642 (91.5)	631 (89.9)
6-month follow-up	1764 (83.6)	595 (84.2)	587 (83.6)	582 (82.9)
12-month follow-up	1686 (79.9)	558 (78.9)	555 (79.1)	573 (81.6)
18-month follow-up	1551 (73.5)	523 (74.0)	507 (72.2)	521 (74.2)
24-month follow-up	1571 (74.4)	521 (73.7)	523 (74.5)	527 (75.1)
Data are presented as number of participants (%).				

Supplementary Table 3. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for the pain domain during the acute and subacute time periods Bolded p values reflect those that are <0.05. A: doxorubicin, BMI: body-mass index, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Acute Period (N=2075)		Subacute Period (N=1791)	
		Probability (95% CI) ²	P-value ²	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.505 (0.468, 0.541)	0.768	0.512 (0.471, 0.552)	0.489
	AT < AC -> T	0.637 (0.599, 0.673)	<0.001	0.572 (0.531, 0.613)	<0.001
	ATC < AC -> T	0.633 (0.595, 0.669)	<0.001	0.561 (0.519, 0.602)	0.001
TI at Baseline	1-unit increment	0.598 (0.587, 0.609)	<0.001	0.599 (0.587, 0.612)	<0.001
Age at surgery (Years)	1-year increment	0.501 (0.499, 0.502)	0.351	0.503 (0.502, 0.505)	<0.001
BMI (kg/m ²)	Obesity (BMI >= 30) < Underweight (BMI < 18.5)	0.48 (0.341, 0.623)	0.787	0.374 (0.236, 0.537)	0.128
	Obesity (BMI >= 30) < Normal (18.5 <= BMI < 25)	0.452 (0.42, 0.484)	0.004	0.406 (0.373, 0.441)	<0.001
	Obesity (BMI >= 30) < Overweight (25 <= BMI < 30)	0.475 (0.442, 0.507)	0.127	0.452 (0.418, 0.487)	0.007
Race/Ethnicity ⁵	NH White < NH Black	0.572 (0.52, 0.623)	0.007	0.537 (0.478, 0.595)	0.224
	NH White < Hispanic	0.543 (0.464, 0.621)	0.287	0.458 (0.359, 0.56)	0.421
	NH White < Other	0.512 (0.433, 0.59)	0.773	0.532 (0.446, 0.617)	0.462
Type of surgery	Lumpectomy < Mastectomy	0.503 (0.477, 0.529)	0.820	0.537 (0.509, 0.564)	0.009
Endocrine therapy	No < Yes	N/A		0.51 (0.474, 0.546)	0.585

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 4. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for pain domain individual items during the acute time period Bolded p values reflect those that are <0.05. A: doxorubicin, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Numbness (N=2067)		General Aches and Pains (N=2066)		Joint Pains (N=2064)		Swelling of Hands or Feet (N=2066)		Muscle Stiffness (N=2058)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.533 (0.499, 0.567)	0.022	0.502 (0.465, 0.539)	0.899	0.523 (0.486, 0.56)	0.263	0.508 (0.472, 0.543)	0.611	0.502 (0.465, 0.54)	0.877
	AT < AC -> T	0.691 (0.657, 0.722)	<0.001	0.556 (0.517, 0.593)	0.002	0.544 (0.506, 0.582)	0.018	0.585 (0.549, 0.621)	<0.001	0.587 (0.55, 0.623)	<0.001
	ATC < AC -> T	0.662 (0.626, 0.696)	<0.001	0.554 (0.515, 0.591)	0.002	0.521 (0.482, 0.559)	0.263	0.578 (0.541, 0.614)	<0.001	0.585 (0.548, 0.621)	<0.001
Symptom at Baseline	1-unit increment	0.598 (0.575, 0.62)	<0.001	0.636 (0.62, 0.65)	<0.001	0.658 (0.641, 0.674)	<0.001	0.641 (0.616, 0.665)	<0.001	0.609 (0.593, 0.624)	<0.001
Age at surgery (Years)	[57, 80] < [24, 43]	0.465 (0.430, 0.500)	0.051	0.488 (0.45, 0.525)	0.522	0.487 (0.45, 0.524)	0.478	0.496 (0.46, 0.533)	0.845	0.484 (0.448, 0.521)	0.395
	[57, 80] < [43, 50]	0.472 (0.439, 0.505)	0.097	0.517 (0.483, 0.551)	0.330	0.524 (0.489, 0.559)	0.177	0.508 (0.475, 0.541)	0.636	0.494 (0.46, 0.528)	0.737
	[57, 80] < [50, 57]	0.493 (0.458, 0.527)	0.685	0.513 (0.477, 0.549)	0.477	0.531 (0.495, 0.566)	0.092	0.525 (0.491, 0.559)	0.156	0.516 (0.482, 0.551)	0.358
BMI (kg/m ²)	Obesity < Underweight	0.476 (0.358, 0.597)	0.700	0.475 (0.345, 0.609)	0.722	0.448 (0.329, 0.574)	0.420	0.333 (0.25, 0.428)	0.001	0.505 (0.383, 0.627)	0.933
	Obesity < Normal	0.458 (0.429, 0.489)	0.007	0.456 (0.425, 0.488)	0.007	0.469 (0.437, 0.502)	0.064	0.387 (0.358, 0.418)	<0.001	0.473 (0.442, 0.505)	0.096
	Obesity < Overweight	0.48 (0.449, 0.512)	0.217	0.472 (0.439, 0.505)	0.092	0.484 (0.452, 0.517)	0.350	0.437 (0.406, 0.468)	<0.001	0.475 (0.443, 0.507)	0.120
Race/Ethnicity ⁵	NH White < NH Black	0.585 (0.538, 0.63)	<0.001	0.541 (0.492, 0.59)	0.101	0.522 (0.472, 0.573)	0.387	0.524 (0.473, 0.574)	0.363	0.535 (0.486, 0.583)	0.159
	NH White < Hispanic	0.519 (0.451, 0.586)	0.586	0.534 (0.446, 0.621)	0.451	0.562 (0.476, 0.644)	0.159	0.458 (0.386, 0.532)	0.265	0.457 (0.379, 0.537)	0.291
	NH White < Other	0.556 (0.484, 0.627)	0.128	0.474 (0.392, 0.556)	0.530	0.488 (0.41, 0.566)	0.759	0.467 (0.396, 0.538)	0.361	0.447 (0.376, 0.52)	0.156
Type of surgery	Lumpectomy < Mastectomy	0.517 (0.493, 0.541)	0.162	0.493 (0.467, 0.518)	0.585	0.502 (0.476, 0.527)	0.891	0.501 (0.477, 0.525)	0.942	0.496 (0.471, 0.521)	0.742

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 5. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for pain domain individual items during the subacute time period Bolded p values reflect those that are <0.05. A: doxorubicin, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Numbness (N=1777)		General Aches and Pains (N=1780)		Joint Pains (N=1783)		Swelling of Hands or Feet (N=1782)		Muscle Stiffness (N=1776)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.519 (0.483, 0.555)	0.207	0.506 (0.466, 0.547)	0.910	0.528 (0.488, 0.567)	0.158	0.504 (0.467, 0.542)	0.780	0.522 (0.482, 0.562)	0.374
	AT < AC -> T	0.598 (0.561, 0.635)	<0.001	0.519 (0.478, 0.56)	0.815	0.558 (0.517, 0.598)	0.002	0.525 (0.487, 0.563)	0.352	0.542 (0.502, 0.582)	0.036
	ATC < AC -> T	0.58 (0.541, 0.618)	<0.001	0.513 (0.472, 0.553)	0.910	0.531 (0.489, 0.572)	0.158	0.52 (0.482, 0.559)	0.405	0.52 (0.48, 0.56)	0.374
Symptom at baseline	1-unit increment	0.596 (0.571, 0.62)	<0.001	0.636 (0.619, 0.652)	<0.001	0.642 (0.624, 0.66)	<0.001	0.62 (0.594, 0.646)	<0.001	0.591 (0.574, 0.607)	<0.001
Age at surgery (Years)	[57, 80] < [24, 43]	0.443 (0.406, 0.48)	0.003	0.434 (0.395, 0.473)	0.001	0.426 (0.387, 0.467)	<0.001	0.483 (0.446, 0.52)	0.361	0.408 (0.37, 0.446)	<0.001
	[57, 80] < [43, 50]	0.459 (0.424, 0.493)	0.019	0.479 (0.442, 0.516)	0.274	0.484 (0.447, 0.522)	0.412	0.499 (0.464, 0.534)	0.946	0.469 (0.433, 0.505)	0.090
	[57, 80] < [50, 57]	0.48 (0.444, 0.516)	0.270	0.501 (0.463, 0.539)	0.965	0.512 (0.474, 0.549)	0.540	0.538 (0.502, 0.573)	0.036	0.526 (0.49, 0.563)	0.159
BMI (kg/m ²)	Obesity < Underweight	0.475 (0.352, 0.601)	0.697	0.356 (0.238, 0.494)	0.041	0.428 (0.287, 0.582)	0.359	0.385 (0.28, 0.503)	0.056	0.386 (0.252, 0.539)	0.142
	Obesity < Normal	0.414 (0.383, 0.446)	<0.001	0.422 (0.388, 0.456)	<0.001	0.437 (0.403, 0.471)	<0.001	0.396 (0.365, 0.428)	<0.001	0.413 (0.38, 0.446)	<0.001
	Obesity < Overweight	0.471 (0.438, 0.504)	0.082	0.459 (0.424, 0.493)	0.020	0.471 (0.436, 0.506)	0.099	0.442 (0.409, 0.475)	0.001	0.449 (0.416, 0.483)	0.003
Race/Ethnicity ⁵	NH White < NH Black	0.509 (0.461, 0.557)	0.718	0.536 (0.48, 0.591)	0.212	0.493 (0.436, 0.549)	0.797	0.521 (0.468, 0.573)	0.441	0.505 (0.452, 0.559)	0.841
	NH White < Hispanic	0.512 (0.432, 0.591)	0.769	0.476 (0.379, 0.575)	0.632	0.488 (0.387, 0.59)	0.818	0.447 (0.37, 0.525)	0.183	0.407 (0.324, 0.495)	0.038
	NH White < Other	0.518 (0.436, 0.6)	0.664	0.511 (0.415, 0.606)	0.829	0.488 (0.404, 0.573)	0.786	0.444 (0.378, 0.512)	0.106	0.446 (0.374, 0.519)	0.149
Type of mastectomy	Lumpectomy < Mastectomy	0.549 (0.524, 0.574)	<0.001	0.513 (0.485, 0.54)	0.356	0.533 (0.506, 0.56)	0.018	0.527 (0.501, 0.552)	0.039	0.521 (0.494, 0.548)	0.134

Endocrine therapy	No < Yes	0.493 (0.461, 0.525)	0.683	0.491 (0.457, 0.525)	0.604	0.522 (0.488, 0.555)	0.209	0.533 (0.501, 0.564)	0.043	0.526 (0.492, 0.56)	0.128
--------------------------	----------	----------------------	-------	----------------------	-------	----------------------	-------	----------------------	--------------	---------------------	-------

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 6. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for cognitive domain during the acute and subacute time periods Bolded p values reflect those that are <0.05. A: doxorubicin, BMI: body-mass index, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Acute Period (N=2078)		Subacute Period (N=1793)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.51 (0.471, 0.548)	1.000	0.52 (0.48, 0.56)	0.694
	AT < AC -> T	0.516 (0.477, 0.555)	0.964	0.517 (0.475, 0.559)	0.694
	ATC < AC -> T	0.507 (0.468, 0.545)	1.000	0.497 (0.456, 0.539)	0.866
TI at Baseline	1-unit increment	0.627 (0.615, 0.639)	<0.001	0.609 (0.596, 0.621)	<0.001
Age at surgery (Years)	1-year increment	0.497 (0.495, 0.498)	<0.001	0.499 (0.497, 0.5)	0.118
BMI (kg/m ²)	Obesity (BMI >= 30) < Underweight (BMI < 18.5)	0.443 (0.319, 0.576)	0.402	0.446 (0.319, 0.58)	0.428
	Obesity (BMI >= 30) < Normal (18.5 <= BMI < 25)	0.487 (0.455, 0.519)	0.426	0.48 (0.446, 0.515)	0.261
	Obesity (BMI >= 30) < Overweight (25 <= BMI < 30)	0.497 (0.463, 0.53)	0.853	0.5 (0.465, 0.535)	0.989
Race/Ethnicity ⁵	NH White < NH Black	0.523 (0.472, 0.573)	0.374	0.524 (0.469, 0.579)	0.397
	NH White < Hispanic	0.547 (0.457, 0.633)	0.310	0.467 (0.367, 0.57)	0.530
	NH White < Other	0.435 (0.352, 0.521)	0.138	0.539 (0.444, 0.631)	0.424
Type of surgery	Lumpectomy < Mastectomy	0.507 (0.481, 0.533)	0.581	0.505 (0.477, 0.532)	0.733
Endocrine therapy	No < Yes	N/A		0.52 (0.485, 0.556)	0.263

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 7. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for cognition domain individual items during the acute time period Bolded p values reflect those that are <0.05. A: doxorubicin, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Mood Swings (N=2070)		Forgetfulness (N=2072)		Difficulty Concentrating (N=2072)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.508 (0.470, 0.546)	0.812	0.504 (0.466, 0.542)	1.000	0.485 (0.447, 0.522)	0.656
	AT < AC -> T	0.521 (0.484, 0.559)	0.523	0.511 (0.473, 0.549)	1.000	0.507 (0.469, 0.546)	0.656
	ATC < AC -> T	0.513 (0.475, 0.551)	0.812	0.508 (0.470, 0.545)	1.000	0.523 (0.485, 0.560)	0.445
Symptom at Baseline	1-unit increment	0.643 (0.629, 0.657)	<0.001	0.662 (0.646, 0.678)	<0.001	0.660 (0.644, 0.676)	<0.001
Age at surgery (Years)	[57, 80] < [24, 43)	0.596 (0.560, 0.632)	<0.001	0.547 (0.509, 0.585)	0.015	0.537 (0.499, 0.574)	0.054
	[57, 80] < [43, 50)	0.570 (0.536, 0.604)	<0.001	0.549 (0.515, 0.582)	0.005	0.543 (0.509, 0.577)	0.013
	[57, 80] < [50, 57)	0.515 (0.480, 0.551)	0.393	0.531 (0.496, 0.566)	0.083	0.546 (0.511, 0.581)	0.010
BMI (kg/m ²)	Obesity < Underweight	0.444 (0.313, 0.583)	0.427	0.536 (0.418, 0.651)	0.549	0.450 (0.327, 0.580)	0.451
	Obesity < Normal	0.471 (0.439, 0.503)	0.073	0.506 (0.474, 0.538)	0.711	0.505 (0.473, 0.537)	0.748
	Obesity < Overweight	0.483 (0.45, 0.515)	0.299	0.512 (0.479, 0.544)	0.487	0.512 (0.479, 0.545)	0.465
Race/Ethnicity ⁵	NH White < NH Black	0.552 (0.503, 0.6)	0.038	0.479 (0.430, 0.528)	0.397	0.455 (0.405, 0.506)	0.081
	NH White < Hispanic	0.504 (0.428, 0.581)	0.910	0.518 (0.435, 0.600)	0.667	0.527 (0.442, 0.611)	0.536
	NH White < Other	0.492 (0.414, 0.57)	0.840	0.436 (0.362, 0.513)	0.103	0.440 (0.366, 0.518)	0.13
Type of surgery	Lumpectomy < Mastectomy	0.497 (0.472, 0.523)	0.822	0.499 (0.474, 0.525)	0.959	0.510 (0.484, 0.535)	0.451

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 8. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for cognition domain individual items during the subacute time period Bolded p values reflect those that are <0.05. A: doxorubicin, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Mood Swings (N=1784)		Forgetfulness (N=1786)		Difficulty Concentrating (N=1790)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.518 (0.479, 0.557)	0.793	0.526 (0.487, 0.565)	0.346	0.503 (0.465, 0.542)	0.898
	AT < AC -> T	0.516 (0.476, 0.555)	0.793	0.521 (0.48, 0.562)	0.433	0.517 (0.477, 0.558)	0.898
	ATC < AC -> T	0.498 (0.458, 0.537)	0.886	0.495 (0.455, 0.536)	0.784	0.514 (0.474, 0.554)	0.898
Symptom at baseline	1-unit increment	0.601 (0.586, 0.617)	<0.001	0.633 (0.617, 0.649)	<0.001	0.646 (0.63, 0.662)	<0.001
Age at surgery (Years)	[57, 80] < [24, 43]	0.576 (0.537, 0.613)	<0.001	0.478 (0.439, 0.518)	0.279	0.494 (0.456, 0.532)	0.760
	[57, 80] < [43, 50]	0.544 (0.509, 0.579)	0.015	0.506 (0.47, 0.542)	0.748	0.535 (0.499, 0.57)	0.056
	[57, 80] < [50, 57]	0.525 (0.489, 0.561)	0.172	0.512 (0.475, 0.549)	0.514	0.525 (0.488, 0.561)	0.187
BMI (kg/m ²)	Obesity < Underweight	0.5 (0.362, 0.639)	0.998	0.452 (0.328, 0.582)	0.468	0.444 (0.341, 0.553)	0.316
	Obesity < Normal	0.474 (0.441, 0.507)	0.124	0.5 (0.466, 0.534)	1.000	0.487 (0.453, 0.521)	0.449
	Obesity < Overweight	0.497 (0.463, 0.53)	0.845	0.517 (0.483, 0.55)	0.337	0.496 (0.462, 0.531)	0.836
Race/Ethnicity ⁵	NH White < NH Black	0.527 (0.476, 0.579)	0.297	0.508 (0.454, 0.561)	0.780	0.49 (0.438, 0.542)	0.708
	NH White < Hispanic	0.497 (0.409, 0.584)	0.941	0.445 (0.357, 0.536)	0.237	0.458 (0.374, 0.546)	0.351
	NH White < Other	0.523 (0.438, 0.607)	0.596	0.513 (0.424, 0.6)	0.781	0.509 (0.439, 0.579)	0.804
Type of surgery	Lumpectomy < Mastectomy	0.499 (0.473, 0.525)	0.935	0.502 (0.475, 0.529)	0.866	0.505 (0.479, 0.532)	0.706
Endocrine therapy	No < Yes	0.482 (0.449, 0.516)	0.310	0.524 (0.489, 0.559)	0.171	0.521 (0.488, 0.555)	0.208

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 9. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for the vasomotor domain during the acute and subacute time periods Bolded p values reflect those that are <0.05. A: doxorubicin, BMI: body-mass index, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Acute Period (N=2075)		Subacute Period (N=1791)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.568 (0.53, 0.606)	<0.001	0.577 (0.537, 0.616)	<0.001
	AT < AC -> T	0.508 (0.469, 0.547)	0.617	0.545 (0.503, 0.585)	0.019
	ATC < AC -> T	0.439 (0.402, 0.478)	<0.001	0.467 (0.426, 0.508)	0.057
TI at Baseline	1-unit increment	0.595 (0.585, 0.604)	<0.001	0.584 (0.573, 0.594)	<0.001
Age at surgery (Years)	1-year increment	0.491 (0.489, 0.492)	<0.001	0.497 (0.496, 0.499)	0.001
BMI (kg/m ²)	Obesity (BMI >= 30) < Underweight (BMI < 18.5)	0.442 (0.345, 0.544)	0.262	0.317 (0.213, 0.443)	0.005
	Obesity (BMI >= 30) < Normal (18.5 <= BMI < 25)	0.514 (0.482, 0.546)	0.398	0.498 (0.464, 0.532)	0.917
	Obesity (BMI >= 30) < Overweight (25 <= BMI < 30)	0.54 (0.507, 0.572)	0.018	0.528 (0.493, 0.562)	0.117
Race/Ethnicity ⁵	NH White < NH Black	0.494 (0.443, 0.546)	0.826	0.519 (0.462, 0.575)	0.522
	NH White < Hispanic	0.444 (0.362, 0.529)	0.197	0.412 (0.315, 0.516)	0.095
	NH White < Other	0.445 (0.368, 0.525)	0.174	0.517 (0.433, 0.599)	0.697
Type of surgery	Lumpectomy < Mastectomy	0.504 (0.479, 0.53)	0.735	0.515 (0.487, 0.542)	0.302
Endocrine therapy	No < Yes	N/A		0.656 (0.622, 0.688)	<0.001

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 10. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for vasomotor domain individual items during the acute time period Bolded p values reflect those that are <0.05. A: doxorubicin, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Hot Flashes (N=2072)		Night Sweats (N=2069)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.573 (0.535, 0.61)	<0.001	0.571 (0.533, 0.608)	<0.001
	AT < AC -> T	0.515 (0.476, 0.553)	0.354	0.523 (0.484, 0.561)	0.160
	ATC < AC -> T	0.442 (0.404, 0.479)	<0.001	0.451 (0.414, 0.489)	0.004
Symptom at Baseline	1-unit increment	0.602 (0.59, 0.614)	<0.001	0.623 (0.609, 0.637)	<0.001
Age at surgery (Years)	[57, 80] < [24, 43]	0.673 (0.638, 0.706)	<0.001	0.68 (0.646, 0.713)	<0.001
	[57, 80] < [43, 50]	0.722 (0.692, 0.75)	<0.001	0.72 (0.691, 0.748)	<0.001
	[57, 80] < [50, 57]	0.636 (0.603, 0.669)	<0.001	0.639 (0.606, 0.671)	<0.001
BMI (kg/m ²)	Obesity < Underweight	0.501 (0.378, 0.624)	0.989	0.463 (0.363, 0.566)	0.483
	Obesity < Normal	0.518 (0.485, 0.55)	0.279	0.532 (0.5, 0.564)	0.050
	Obesity < Overweight	0.541 (0.508, 0.573)	0.015	0.537 (0.504, 0.57)	0.026
Race/Ethnicity ⁵	NH White < NH Black	0.503 (0.452, 0.554)	0.894	0.493 (0.443, 0.543)	0.780
	NH White < Hispanic	0.469 (0.388, 0.553)	0.474	0.442 (0.365, 0.521)	0.150
	NH White < Other	0.444 (0.364, 0.527)	0.188	0.415 (0.347, 0.486)	0.019
Type of surgery	Lumpectomy < Mastectomy	0.502 (0.477, 0.528)	0.857	0.503 (0.477, 0.529)	0.821

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 11. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for vasomotor domain individual items during the subacute time period Bolded p values reflect those that are <0.05. A: doxorubicin, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Hot Flashes (N=1787)		Night Sweats (N=1786)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.582 (0.542, 0.621)	<0.001	0.56 (0.521, 0.599)	0.001
	AT < AC -> T	0.559 (0.518, 0.6)	0.001	0.536 (0.496, 0.575)	0.059
	ATC < AC -> T	0.477 (0.436, 0.518)	0.183	0.476 (0.436, 0.516)	0.145
Symptom at baseline	1-unit increment	0.592 (0.579, 0.604)	<0.001	0.602 (0.588, 0.617)	<0.001
Age at surgery (Years)	[57, 80] < [24, 43]	0.515 (0.473, 0.556)	0.483	0.542 (0.503, 0.58)	0.034
	[57, 80] < [43, 50]	0.648 (0.613, 0.682)	<0.001	0.641 (0.606, 0.673)	<0.001
	[57, 80] < [50, 57]	0.615 (0.578, 0.651)	<0.001	0.635 (0.6, 0.669)	<0.001
BMI (kg/m ²)	Obesity < Underweight	0.378 (0.25, 0.526)	0.106	0.303 (0.203, 0.426)	0.002
	Obesity < Normal	0.509 (0.475, 0.543)	0.617	0.515 (0.481, 0.549)	0.386
	Obesity < Overweight	0.534 (0.499, 0.568)	0.056	0.523 (0.489, 0.557)	0.185
Race/Ethnicity ⁵	NH White < NH Black	0.522 (0.467, 0.576)	0.428	0.523 (0.471, 0.575)	0.384
	NH White < Hispanic	0.439 (0.347, 0.536)	0.215	0.45 (0.358, 0.546)	0.307
	NH White < Other	0.499 (0.414, 0.584)	0.982	0.454 (0.378, 0.532)	0.245
Type of surgery	Lumpectomy < Mastectomy	0.51 (0.482, 0.537)	0.497	0.518 (0.491, 0.545)	0.190
Endocrine therapy	No < Yes	0.66 (0.628, 0.691)	<0.001	0.625 (0.594, 0.656)	<0.001

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 12. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for the vaginal domain during the acute and subacute time periods. Bolded p values reflect those that are <0.05. A: doxorubicin, BMI: body-mass index, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Acute (N=2068)		Subacute (N=1791)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.483 (0.447, 0.519)	0.642	0.521 (0.484, 0.558)	0.349
	AT < AC -> T	0.502 (0.465, 0.538)	0.919	0.534 (0.497, 0.572)	0.085
	ATC < AC -> T	0.519 (0.483, 0.554)	0.642	0.513 (0.475, 0.551)	0.405
TI at Baseline	1-unit increment	0.635 (0.614, 0.655)	<0.001	0.626 (0.607, 0.645)	<0.001
Age at surgery (Years)	1-year increment	0.497 (0.495, 0.498)	<0.001	0.498 (0.496, 0.499)	<0.001
BMI (kg/m ²)	Obesity (BMI >= 30) < Underweight (BMI < 18.5)	0.503 (0.368, 0.637)	0.971	0.433 (0.311, 0.564)	0.318
	Obesity (BMI >= 30) < Normal (18.5 <= BMI < 25)	0.554 (0.524, 0.584)	<0.001	0.544 (0.513, 0.576)	0.006
	Obesity (BMI >= 30) < Overweight (25 <= BMI < 30)	0.544 (0.513, 0.574)	0.005	0.529 (0.497, 0.56)	0.074
Race/Ethnicity ⁵	NH White < NH Black	0.488 (0.442, 0.535)	0.613	0.44 (0.396, 0.485)	0.009
	NH White < Hispanic	0.502 (0.429, 0.575)	0.950	0.469 (0.392, 0.548)	0.446
	NH White < Other	0.433 (0.374, 0.495)	0.033	0.508 (0.436, 0.579)	0.833
Type of surgery	Lumpectomy < Mastectomy	0.504 (0.48, 0.528)	0.770	0.5 (0.475, 0.525)	0.997
Endocrine therapy	No < Yes	N/A		0.525 (0.494, 0.557)	0.119

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 13. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for vaginal domain individual items during the acute time period Bolded p values reflect those that are <0.05. A: doxorubicin, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Vaginal Dryness (N=2064)		Pain with Intercourse (N=1861)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.491 (0.456, 0.527)	1.000	0.486 (0.453, 0.519)	0.379
	AT < AC -> T	0.496 (0.46, 0.531)	1.000	0.518 (0.485, 0.552)	0.379
	ATC < AC -> T	0.504 (0.469, 0.54)	1.000	0.533 (0.499, 0.566)	0.063
Symptom at Baseline	1-unit increment	0.642 (0.618, 0.665)	<0.001	0.669 (0.634, 0.702)	<0.001
Age at surgery (Years)	[57, 80] < [24, 43)	0.555 (0.52, 0.59)	0.002	0.583 (0.551, 0.615)	<0.001
	[57, 80] < [43, 50)	0.55 (0.518, 0.581)	0.002	0.569 (0.54, 0.598)	<0.001
	[57, 80] < [50, 57)	0.544 (0.511, 0.577)	0.008	0.564 (0.532, 0.594)	<0.001
BMI (kg/m ²)	Obesity < Underweight	0.526 (0.397, 0.652)	0.692	0.597 (0.474, 0.709)	0.120
	Obesity < Normal	0.554 (0.524, 0.583)	<0.001	0.545 (0.517, 0.572)	0.001
	Obesity < Overweight	0.538 (0.508, 0.568)	0.012	0.543 (0.516, 0.57)	0.002
Race/Ethnicity ⁵	NH White < NH Black	0.499 (0.453, 0.545)	0.955	0.462 (0.424, 0.5)	0.051
	NH White < Hispanic	0.504 (0.431, 0.577)	0.912	0.489 (0.423, 0.555)	0.736
	NH White < Other	0.404 (0.347, 0.465)	0.002	0.477 (0.414, 0.541)	0.475
Type of surgery	Lumpectomy < Mastectomy	0.504 (0.48, 0.527)	0.768	0.488 (0.466, 0.511)	0.307

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis

Supplementary Table 14. Multivariable Probabilistic Index Models for the cumulative Toxicity Index (TI) for vaginal domain individual items during the subacute time period Bolded p values reflect those that are <0.05. A: doxorubicin, C: cyclophosphamide, CI: confidence interval, NH: non-Hispanic, T: docetaxel.

Variable	Comparison A < B ¹	Vaginal Dryness (N=1775)		Pain with Intercourse (N=1563)	
		Probability (95% CI) ²	P-value ³	Probability (95% CI) ²	P-value ³
Treatment ⁴	AT < ATC	0.529 (0.493, 0.565)	0.140	0.521 (0.486, 0.556)	0.231
	AT < AC -> T	0.53 (0.494, 0.566)	0.140	0.545 (0.509, 0.58)	0.008
	ATC < AC -> T	0.501 (0.464, 0.538)	0.940	0.524 (0.487, 0.561)	0.231
Symptom at baseline	1-unit increment	0.623 (0.601, 0.645)	<0.001	0.645 (0.61, 0.678)	<0.001
Age at surgery (Years)	[57, 80] < [24, 43)	0.508 (0.473, 0.543)	0.644	0.564 (0.529, 0.598)	<0.001
	[57, 80] < [43, 50)	0.552 (0.518, 0.585)	0.002	0.568 (0.535, 0.6)	<0.001
	[57, 80] < [50, 57)	0.538 (0.504, 0.572)	0.029	0.535 (0.501, 0.567)	0.042
BMI (kg/m ²)	Obesity < Underweight	0.462 (0.342, 0.586)	0.550	0.528 (0.418, 0.635)	0.619
	Obesity < Normal	0.545 (0.514, 0.575)	0.004	0.548 (0.519, 0.578)	0.001
	Obesity < Overweight	0.527 (0.497, 0.558)	0.080	0.527 (0.498, 0.555)	0.072
Race/Ethnicity ⁵	NH White < NH Black	0.447 (0.404, 0.491)	0.019	0.427 (0.389, 0.465)	<0.001
	NH White < Hispanic	0.475 (0.405, 0.547)	0.495	0.485 (0.408, 0.563)	0.711
	NH White < Other	0.472 (0.402, 0.544)	0.446	0.516 (0.443, 0.588)	0.674
Type of surgery	Lumpectomy < Mastectomy	0.503 (0.478, 0.527)	0.829	0.479 (0.455, 0.503)	0.090
Endocrine therapy	No < Yes	0.515 (0.484, 0.545)	0.343	0.543 (0.513, 0.572)	0.004

¹ Comparison A < B denotes the probability that the cumulative TI for B is higher than that for A

² Probability of 0.5 indicates no difference between comparisons (i.e., A=B)

³ P values are calculated using the Wald statistic

⁴ CI are adjusted for multiple tests for treatment using the Bonferroni procedure; p-values are adjusted for multiple tests for treatment using the Holm procedure

⁵ Unknown race/ethnicity was excluded from analysis