How much TailorX and rXponder trials do change the treatment spectrum of HR positive breast cancer?

Safa najafi MD

Hematologist/oncologist

Motamed cancer institute

Associated professor

TailorX trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 12, 2018 VOL. 379 NO. 2

Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer

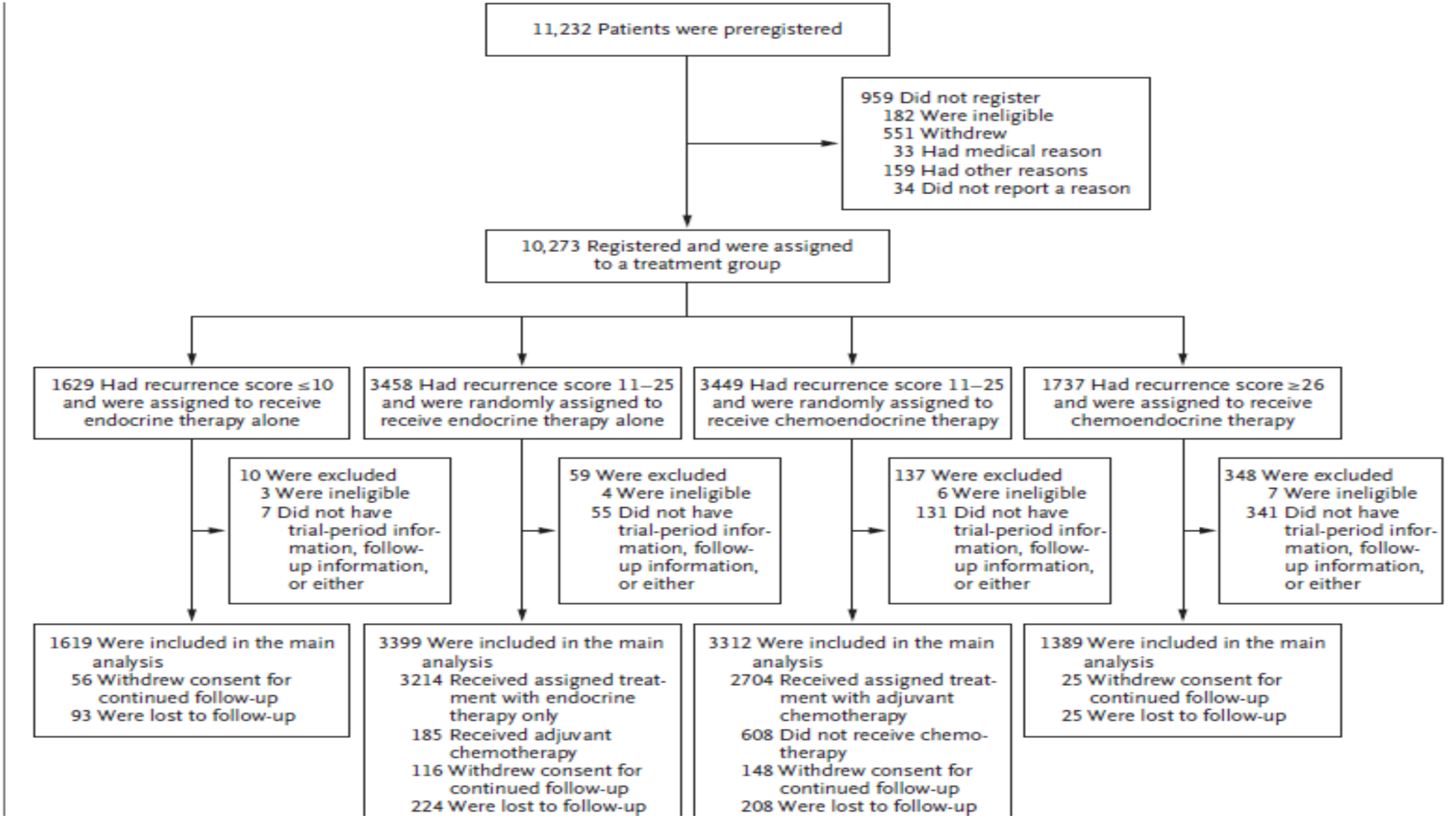
J.A. Sparano, R.J. Gray, D.F. Makower, K.I. Pritchard, K.S. Albain, D.F. Hayes, C.E. Geyer, Jr., E.C. Dees, M.P. Goetz, J.A. Olson, Jr., T. Lively, S.S. Badve, T.J. Saphner, L.I. Wagner, T.J. Whelan, M.J. Ellis, S. Paik, W.C. Wood, P.M. Ravdin, M.M. Keane, H.L. Gomez Moreno, P.S. Reddy, T.F. Goggins, I.A. Mayer, A.M. Brufsky, D.L. Toppmeyer, V.G. Kaklamani, J.L. Berenberg, J. Abrams, and G.W. Sledge, Jr.

The Trial Assigning Individualized Options for Treatment (TAILORx)

when the recurrence score is low (0 to 10), it is prognostic for a very low rate of distant recurrence (2%) at 10 years that is not likely to be affected by adjuvant chemotherapy.

The recurrence score based on the 21-gene assay ranges from 0 to 100 and is predictive of chemotherapy benefit when it is high, whether a high score is defined as 31 or higher, or 26 or higher.

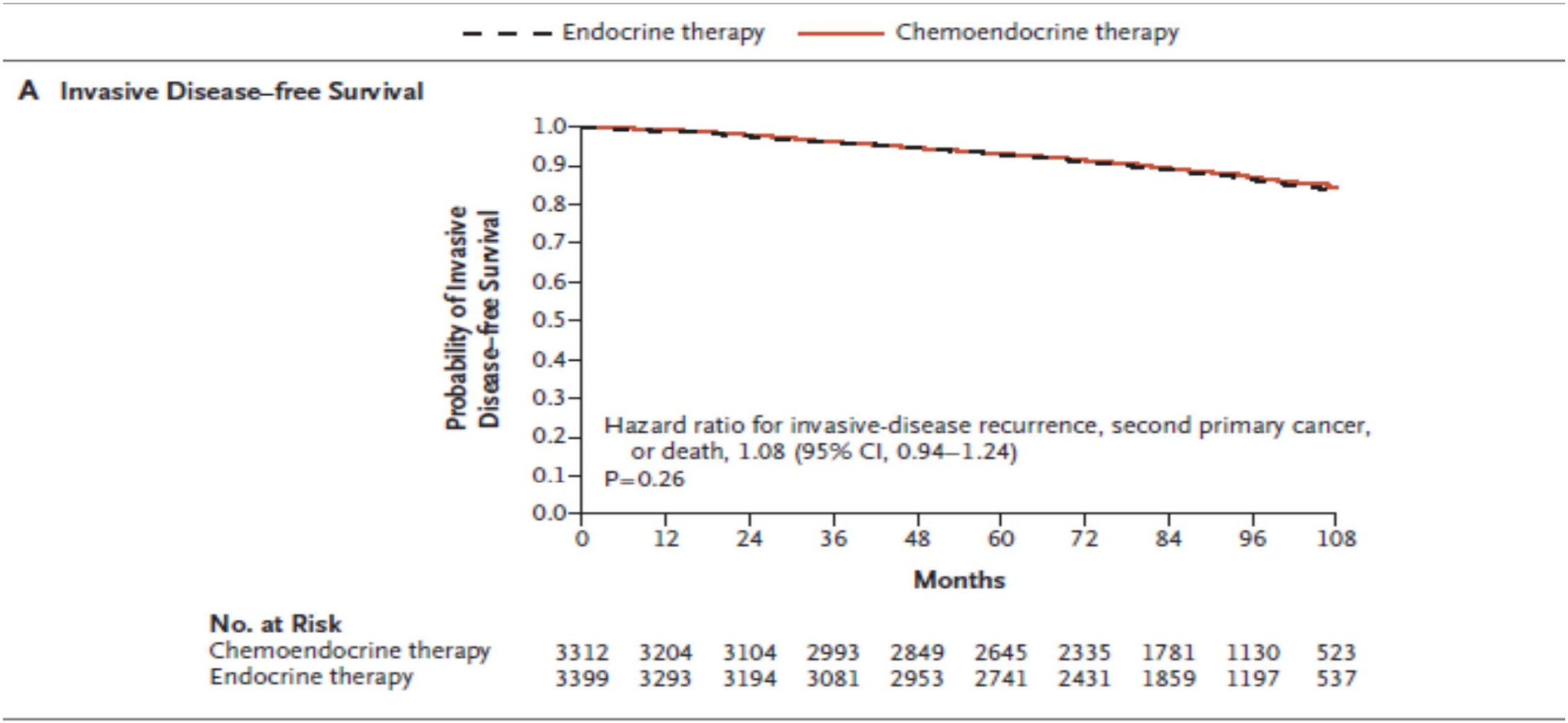
The Trial Assigning Individualized Options for Treatment (TAILORx) was designed to address these gaps in our knowledge by determining whether chemotherapy is beneficial for women with a mid-range recurrence score of 11 to 25.


11,232 Patients were preregistered
959 Did not register
182 Were ineligible
551 Withdrew
33 Had medical reason
159 Had other reasons
34 Did not report a reason
10,273 Registered and were assigned to a treatment group
1629 Had recurrence score ≤10 and were assigned to receive endocrine therapy alone
3458 Had recurrence score 11–25 and were randomly assigned to receive endocrine therapy alone
3449 Had recurrence score 11–25 and were randomly assigned to receive chemoendocrine therapy
1737 Had recurrence score ≥26 and were assigned to receive chemoendocrine therapy
10 Were excluded
3 Were ineligible
7 Did not have trial-period information, follow-up information, or either
59 Were excluded
4 Were ineligible
55 Did not have trial-period information, follow-up information, or either
137 Were excluded
6 Were ineligible
131 Did not have trial-period information, follow-up information, or either
348 Were excluded
7 Were ineligible
341 Did not have trial-period information, follow-up information, or either
1619 Were included in the main analysis
56 Withdrew consent for continued follow-up
93 Were lost to follow-up
3399 Were included in the main analysis
3214 Received assigned treatment with endocrine therapy only
185 Received adjuvant chemotherapy
116 Withdrew consent for continued follow-up
224 Were lost to follow-up
3312 Were included in the main analysis
2704 Received assigned treatment with adjuvant chemotherapy
608 Did not receive chemotherapy
148 Withdrew consent for continued follow-up
208 Were lost to follow-up
1389 Were included in the main analysis
25 Withdrew consent for continued follow-up
25 Were lost to follow-up

e 1. Characteristics of the Patients in the Intention-to-Treat Population at Baseline.*

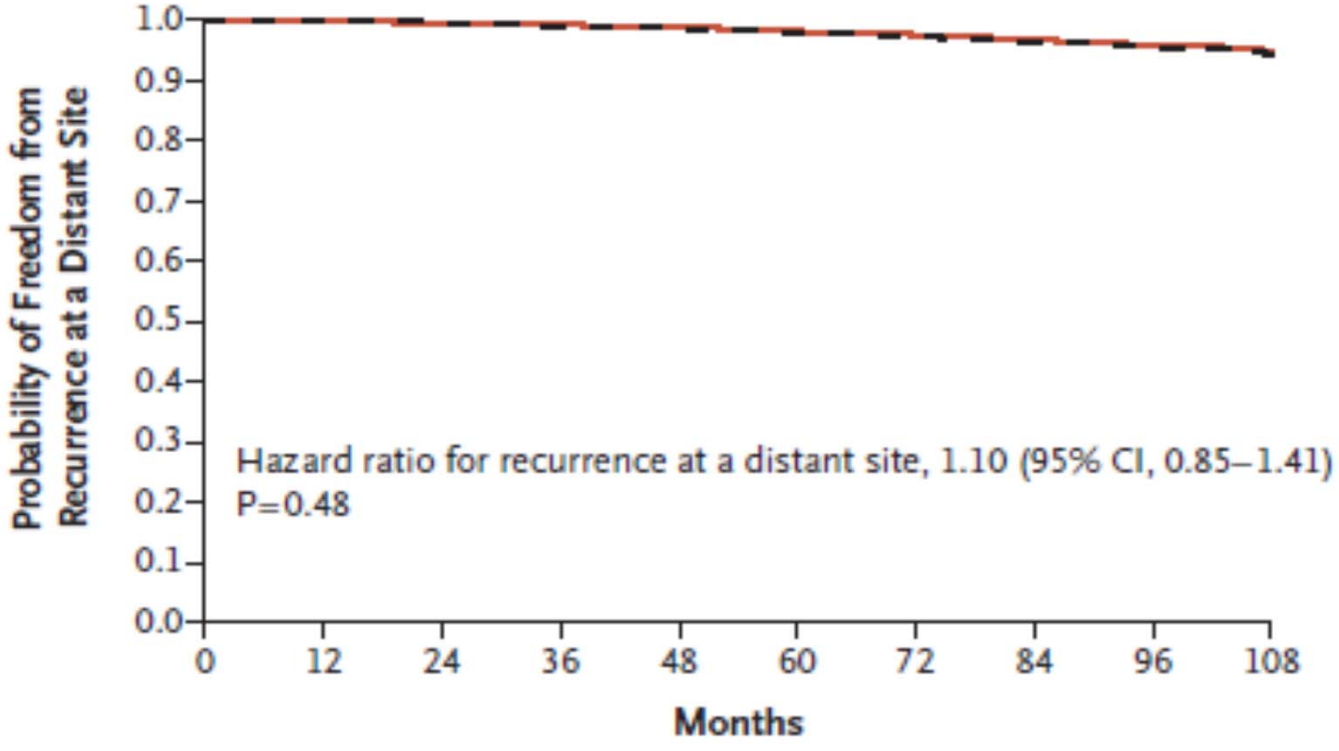
acteristic	Recurrence Score of ≤10	Recurrence Score of 11–25		Recurrence Score o
	Endocrine Therapy (N=1619)	Endocrine Therapy (N=3399)	Chemoendocrine Therapy (N=3312)	Chemoendocrin Therapy (N=1389)
ian age (range) — yr	58 (25–75)	55 (23–75)	55 (25–75)	56 (23–75)
≤50 yr — no. (%)	429 (26)	1139 (34)	1077 (33)	409 (29)
opausal status — no. (%)†				
remenopausal	478 (30)	1212 (36)	1203 (36)	407 (29)
ostmenopausal	1141 (70)	2187 (64)	2109 (64)	982 (71)
or size in the largest dimension — cm‡				
Median (IQR)	1.5 (1.2–2.0)	1.5 (1.2–2.0)	1.5 (1.2–2.0)	1.7 (1.3–2.3)
Mean	1.74±0.76	1.71±0.81	1.71±0.77	1.88±0.99
ologic grade of tumor — no./total no. (%)				
ow	530/1572 (34)	959/3282 (29)	934/3216 (29)	89/1363 (7)
ntermediate	931/1572 (59)	1884/3282 (57)	1837/3216 (57)	590/1363 (43)
High	111/1572 (7)	439/3282 (13)	445/3216 (14)	681/1363 (50)
gen-receptor expression — no. (%)				
Negative	5 (<1)	6 (<1)	3 (<1)	40 (3)
ositive	1614 (>99)	3393 (>99)	3309 (>99)	1349 (97)
esterone-receptor expression — no./total no. (%)				
Negative	28/1583 (2)	267/3339 (8)	251/3240 (8)	405/1353 (30)
ositive	1555/1583 (98)	3072/3339 (92)	2989/3240 (92)	948/1353 (70)
cal risk — no./total no. (%)§				
ow	1227/1572 (78)	2440/3282 (74)	2359/3214 (73)	589/1359 (43)
High	345/1572 (22)	842/3282 (26)	855/3214 (27)	770/1359 (57)
ary surgery — no. (%)				
Mastectomy	516 (32)	935 (28)	917 (28)	368 (26)
reast conservation	1103 (68)	2464 (72)	2395 (72)	1021 (74)
vant chemotherapy — no. (%)				
es	8 (0.5)	185 (5.4)	2704 (81.6)	1300 (93.6)
No	1611 (99.5)	3214 (94.6)	608 (18.4)	89 (6.4)

IDFS


Endocrine therapy
Chemoendocrine therapy
A Invasive Disease–free Survival
Probability of Invasive Disease–free Survival
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
Hazard ratio for invasive-disease recurrence, second primary cancer, or death, 1.08 (95% CI, 0.94–1.24)
P=0.26
0
12
24
36
48
60
72
84
96
108
Months
No. at Risk
Chemoendocrine therapy 3312 3204 3104 2993 2849 2645 2335 1781 1130 523
Endocrine therapy 3399 3293 3194 3081 2953 2741 2431 1859 1197 537

Metastatic free survival

B **Freedom from Recurrence at a Distant Site**



No. at Risk										
Chemoendocrine therapy	3312	3215	3142	3059	2935	2734	2432	1866	1197	554
Endocrine therapy	3399	3318	3239	3147	3033	2833	2537	1947	1267	581

Table 2. Estimated Survival Rates According to Recurrence Score and Assigned Treatment in the Intention-to-Treat Population.*

End Point and Treatment Group	Rate at 5 Yr	Rate at 9 Yr
	percent	
Invasive disease–free survival†		
Score of ≤10, endocrine therapy	94.0±0.6	84.0±1.3
Score of 11–25, endocrine therapy	92.8±0.5	83.3±0.9
Score of 11–25, chemoendocrine therapy	93.1±0.5	84.3±0.8
Score of ≥26, chemoendocrine therapy	87.6±1.0	75.7±2.2
Freedom from recurrence of breast cancer at a distant site		
Score of ≤10, endocrine therapy	99.3±0.2	96.8±0.7
Score of 11–25, endocrine therapy	98.0±0.3	94.5±0.5
Score of 11–25, chemoendocrine therapy	98.2±0.2	95.0±0.5
Score of ≥26, chemoendocrine therapy	93.0±0.8	86.8±1.7
Freedom from recurrence of breast cancer at a distant or local–regional site		
Score of ≤10, endocrine therapy	98.8±0.3	95.0±0.8
Score of 11–25, endocrine therapy	96.9±0.3	92.2±0.6
Score of 11–25, chemoendocrine therapy	97.0±0.3	92.9±0.6
Score of ≥26, chemoendocrine therapy	91.0±0.8	84.8±1.7
Overall survival		
Score of ≤10, endocrine therapy	98.0±0.4	93.7±0.8
Score of 11–25, endocrine therapy	98.0±0.2	93.9±0.5
Score of 11–25, chemoendocrine therapy	98.1±0.2	93.8±0.5
Score of ≥26, chemoendocrine therapy	95.9±0.6	89.3±1.4

Table 3. Estimated Survival Rates According to Recurrence Score and Assigned Treatment among Women 50 Years of Age or Younger in the Intention-to-Treat Population.*

End Point and Treatment Group	Rate at 5 Yr	Rate at 9 Yr
	percent	
Invasive disease–free survival†		
Score of ≤10, endocrine therapy	95.1±1.1	87.4±2.0
Score of 11–15, endocrine therapy	95.1±1.1	85.7±2.2
Score of 11–15, chemoendocrine therapy	94.3±1.3	89.2±1.9
Score of 16–20, endocrine therapy	92.0±1.3	80.6±2.5
Score of 16–20, chemoendocrine therapy	94.7±1.1	89.6±1.7
Score of 21–25, endocrine therapy	86.3±2.3	79.2±3.3
Score of 21–25, chemoendocrine therapy	92.1±1.8	85.5±3.0
Score of ≥26, chemoendocrine therapy	86.4±1.9	80.3±2.9
Freedom from recurrence of breast cancer at a distant site		
Score of ≤10, endocrine therapy	99.7±0.3	98.5±0.8
Score of 11–15, endocrine therapy	98.8±0.6	97.2±1.0
Score of 11–15, chemoendocrine therapy	98.5±0.7	98.0±0.8
Score of 16–20, endocrine therapy	98.1±0.7	93.6±1.4
Score of 16–20, chemoendocrine therapy	98.9±0.5	95.2±1.3
Score of 21–25, endocrine therapy	93.2±1.7	86.9±2.9
Score of 21–25, chemoendocrine therapy	96.4±1.2	93.4±2.3
Score of ≥26, chemoendocrine therapy	91.1±1.6	88.7±2.1
Freedom from recurrence of breast cancer at a distant or local–regional site		
Score of ≤10, endocrine therapy	98.4±0.6	95.4±1.3
Score of 11–15, endocrine therapy	97.5±0.8	93.3±1.6
Score of 11–15, chemoendocrine therapy	97.2±0.9	94.4±1.5
Score of 16–20, endocrine therapy	95.7±1.0	89.6±1.9
Score of 16–20, chemoendocrine therapy	97.2±0.8	93.0±1.5
Score of 21–25, endocrine therapy	89.8±2.0	82.0±3.2
Score of 21–25, chemoendocrine therapy	94.2±1.6	90.7±2.5
Score of ≥26, chemoendocrine therapy	88.6±1.8	86.1±2.2
Overall survival		
Score of ≤10, endocrine therapy	100.0	98.6±0.9
Score of 11–15, endocrine therapy	99.3±0.4	96.8±1.0
Score of 11–15, chemoendocrine therapy	98.9±0.6	97.5±0.9
Score of 16–20, endocrine therapy	98.6±0.6	95.8±1.2
Score of 16–20, chemoendocrine therapy	99.8±0.2	96.1±1.2
Score of 21–25, endocrine therapy	98.2±0.9	92.7±2.0
Score of 21–25, chemoendocrine therapy	98.3±0.8	93.9±1.9
Score of ≥26, chemoendocrine therapy	95.6±1.1	92.4±1.9

Take home message for Premenopausal patients with score 16 to 25

- Exploratory analyses indicated that chemotherapy was associated with some benefit for women 50 years of age or younger who had a recurrence score of 16 to 25 (a range of scores that was found in 46% of women in this age group). A greater treatment effect from adjuvant chemotherapy has been noted in younger women,7 which may be at least partly explained by an antiestrogenic effect associated with premature menopause induced by chemotherapy.

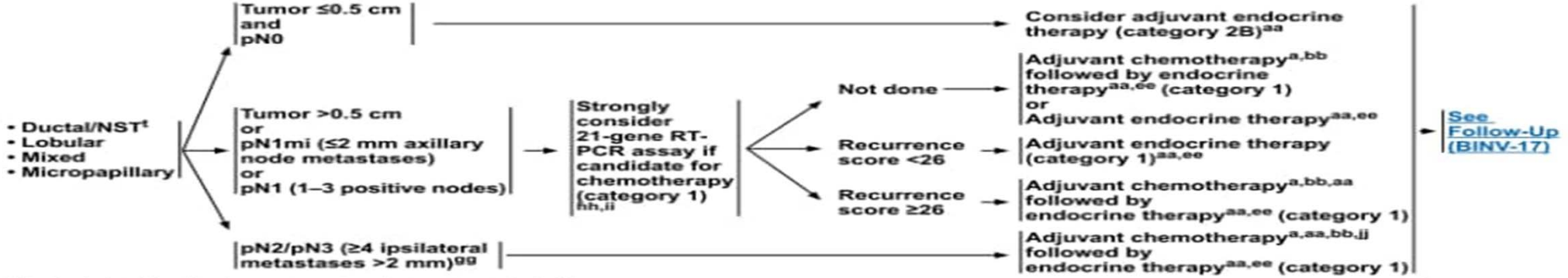
Premenopausal with score 0 to15

- Conversely, in the 40% of women 50 years of age or younger who had a recurrence score of 0 to 15, the rate of distant recurrence was approximately 2% at 9 years among those who had been assigned (either randomly or nonrandomly) to endocrine therapy alone.

Postmenopausal scores;

- . When all recurrence score cohorts (≤10, 11 to 25, and ≥26) and treatment-group assignments were considered, there were significant differences in the rates of invasive disease–free survival, recurrence, and death .

SYSTEMIC ADJUVANT TREATMENT: HR-POSITIVE - HER2-NEGATIVE DISEASE[d,q,y] POSTMENOPAUSAL[z] PATIENTS with pT1–3 AND pN0 or pN+ TUMORS



[a] For tools to aid optimal assessment and management of older adults, see NCCN Guidelines for Older Adult Oncology.
[d] See Principles of Biomarker Testing (BINV-A).
[q] See Special Considerations for Breast Cancer in Males (Sex Assigned at Birth) (BINV-J).
[t] According to WHO, carcinoma of NST encompasses multiple patterns including medullary pattern, cancers with neuroendocrine expression, and other rare patterns.
[y] Although patients with cancers with 1%–100% ER IHC staining are considered ER-positive and eligible for endocrine therapies, there are more limited data on the subgroup of cancers with ER-low–positive (1%–10%) results. The ER-low–positive group is heterogeneous with reported biologic behavior often similar to ER-negative cancers; thus individualized consideration of risks versus benefits of endocrine therapy and additional adjuvant therapies should be incorporated into decision-making. See Principles of Biomarker Testing (BINV-A).
[z] See Definition of Menopause (BINV-O).
[aa] See Adjuvant Endocrine Therapy (BINV-K).
[bb] See Preoperative/Adjuvant Therapy Regimens (BINV-L).
[ee] Consider adjuvant bisphosphonate therapy for risk reduction of distant metastasis for 3–5 years in postmenopausal patients (natural or induced) with high-risk node-negative or node-positive tumors.
[gg] There are few data regarding the role of gene expression assays in those with ≥4 ipsilateral axillary lymph nodes. Decisions to administer adjuvant chemotherapy for this group should be based on clinical factors.
[hh] Other prognostic gene expression assays may be considered to help assess risk of recurrence but have not been validated to predict response to chemotherapy. See Gene Expression Assays for Consideration of Adjuvant Systemic Therapy (BINV-N).
[ii] Patients with T1b tumors with low-grade histology and no lymphovascular invasion should be treated with endocrine monotherapy as the TAILORx trial did not include patients with such tumors.
[jj] Addition of 1 year of adjuvant olaparib is an option for select patients with germline *BRCA1/2* mutation after completion of adjuvant chemotherapy. See BINV-L (1 of 8).

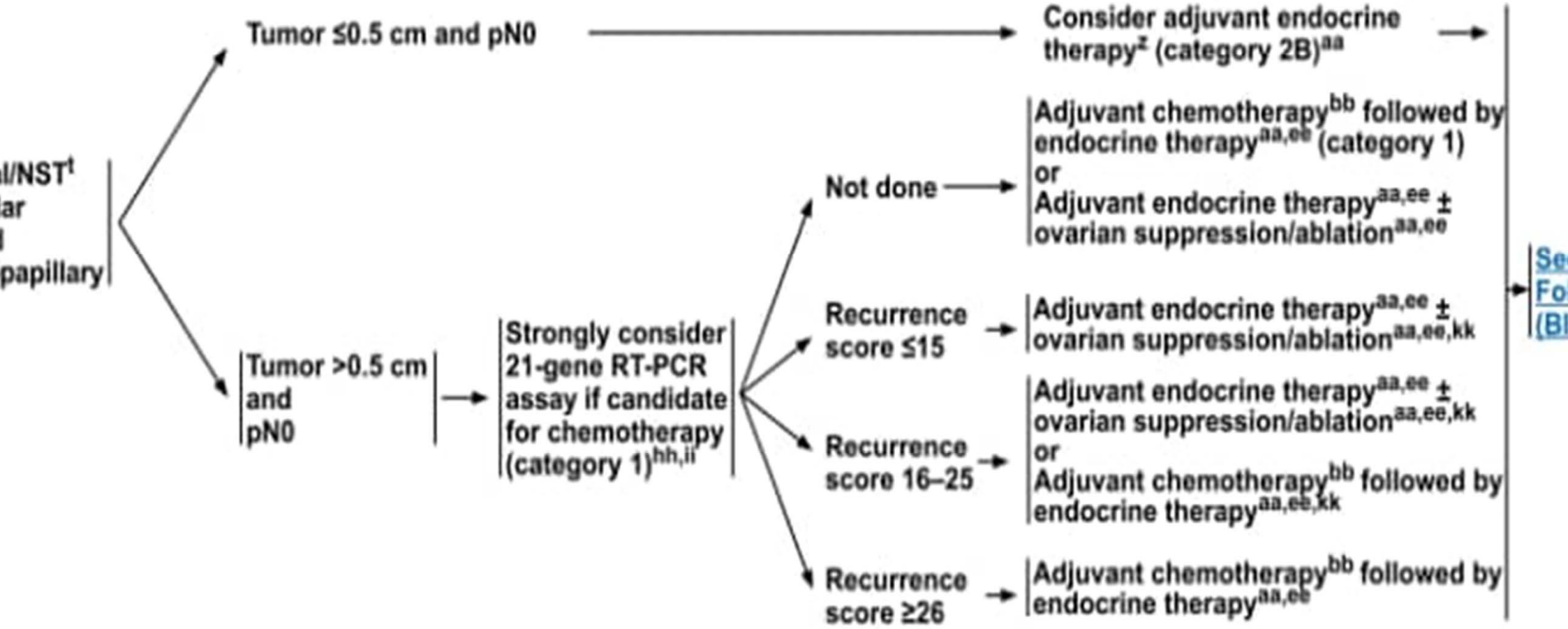
Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

National Comprehensive Cancer Network®

NCCN Guidelines Version 2.2022
Invasive Breast Cancer

NCCN Guidelin
Table of
Di

EMIC ADJUVANT TREATMENT: HR-POSITIVE - HER2-NEGATIVE DISEASE[d,q,y]
ENOPAUSAL[z] PATIENTS with pT1–3 AND pN0 TUMORS



Are we dare enough to extend this to N+??

This article was published on December 1, 2021, at NEJM.org. N Engl J Med 2021;385:2336-47. DOI: 10.1056/NEJMoa2108873

ORIGINAL ARTICLE

21-Gene Assay to Inform Chemotherapy Benefit in Node-Positive Breast Cancer

K. Kalinsky, W.E. Barlow, J.R. Gralow, F. Meric-Bernstam, K.S. Albain, D.F. Hayes, N.U. Lin, E.A. Perez, L.J. Goldstein, S.K.L. Chia, S. Dhesy-Thind, P. Rastogi, E. Alba, S. Delaloge, M. Martin, C.M. Kelly, M. Ruiz-Borrego, M. Gil-Gil, C.H. Arce-Salinas, E.G.C. Brain, E.-S. Lee, J.-Y. Pierga, B. Bermejo, M. Ramos-Vazquez, K.-H. Jung, J.-M. Ferrero, A.F. Schott, S. Shak, P. Sharma, D.L. Lew, J. Miao, D. Tripathy, L. Pusztai, and G.N. Hortobagyi

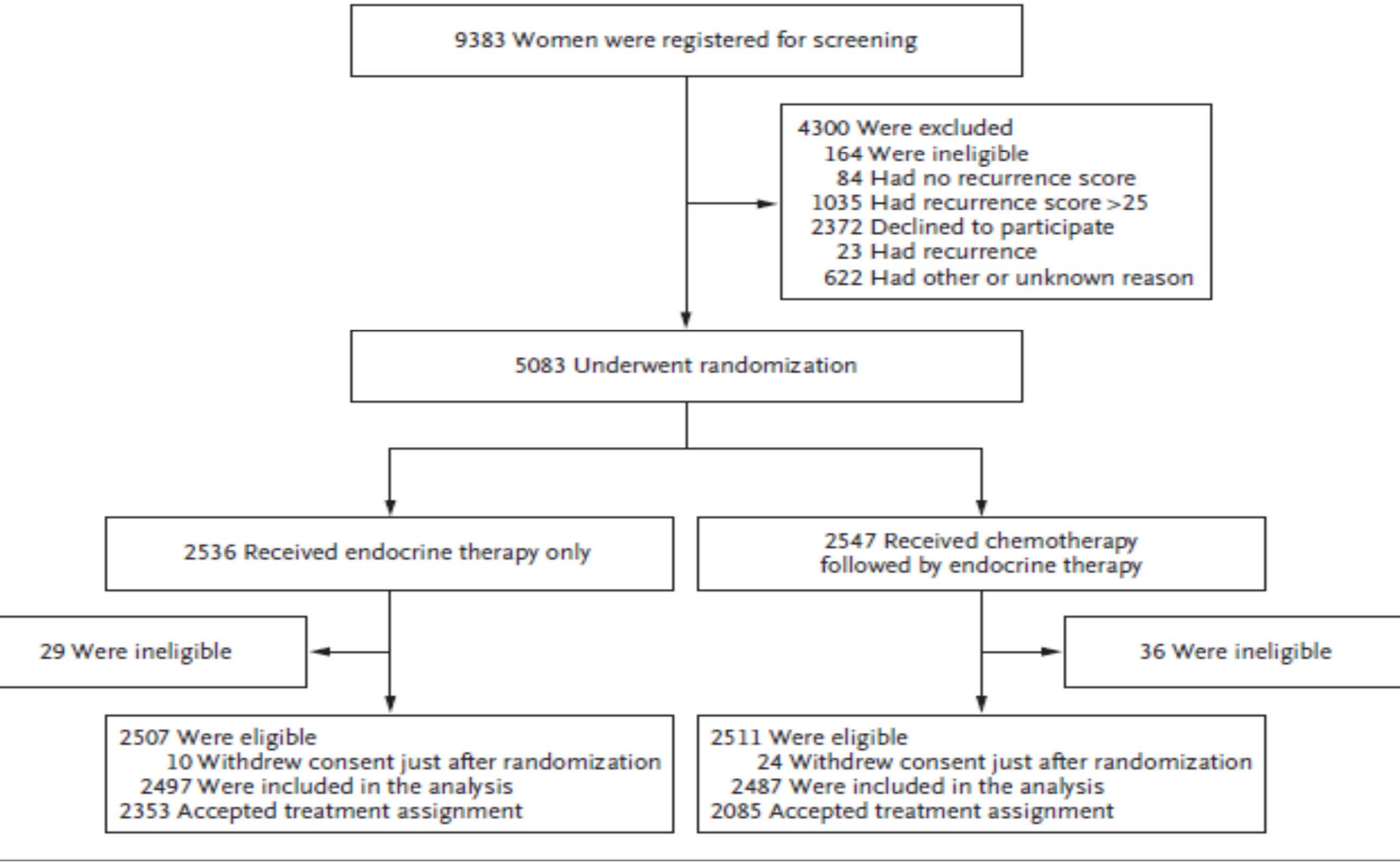
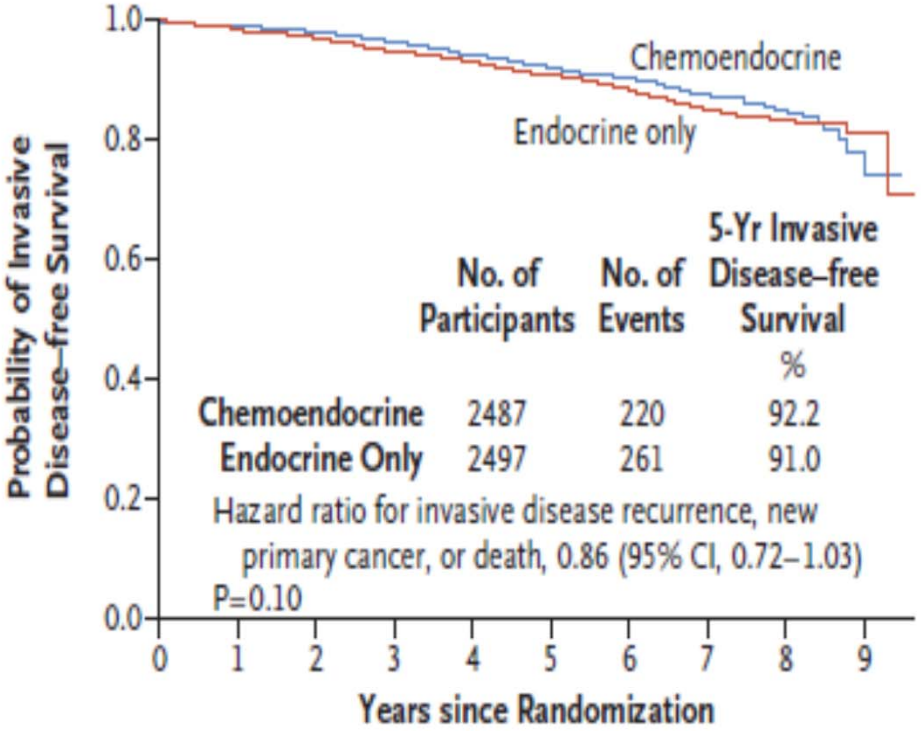

9383 Women were registered for screening
4300 Were excluded
164 Were ineligible
84 Had no recurrence score
1035 Had recurrence score >25
2372 Declined to participate
23 Had recurrence
622 Had other or unknown reason
5083 Underwent randomization
2536 Received endocrine therapy only
2547 Received chemotherapy followed by endocrine therapy
29 Were ineligible
36 Were ineligible
2507 Were eligible
10 Withdrew consent just after randomization
2497 Were included in the analysis
2353 Accepted treatment assignment
2511 Were eligible
24 Withdrew consent just after randomization
2487 Were included in the analysis
2085 Accepted treatment assignment

Table 1. Baseline Characteristics of the Participants.*

Characteristic	Endocrine-Only Group (N=2507)	Chemoendocrine Group (N=2511)	All Participants (N=5018)
Median age (range) — yr	57.2 (18.3–86.0)	57.9 (28.0–87.6)	57.5 (18.3–87.6)
Age category — no. (%)			
<40 yr	80 (3.2)	67 (2.7)	147 (2.9)
40–49 yr	547 (21.8)	530 (21.1)	1077 (21.5)
50–59 yr	838 (33.4)	837 (33.3)	1675 (33.4)
60–69 yr	761 (30.4)	777 (30.9)	1538 (30.6)
≥70 yr	281 (11.2)	300 (12.0)	581 (11.6)
Menopausal status — no. (%)			
Premenopausal	831 (33.1)	834 (33.2)	1665 (33.2)
Postmenopausal	1676 (66.9)	1677 (66.8)	3353 (66.8)
Recurrence score — no. (%)†			
0–13	1071 (42.7)	1076 (42.9)	2147 (42.8)
14–25	1436 (57.3)	1435 (57.1)	2871 (57.2)
Axillary surgery — no. (%)			
Axillary lymph-node dissection, with or without sentinel-node mapping	1571 (62.7)	1569 (62.5)	3140 (62.6)
Sentinel-node biopsy without axillary lymph-node dissection	936 (37.3)	942 (37.5)	1878 (37.4)
Positive nodes — no. (%)			
1 node	1647 (65.7)	1628 (64.8)	3275 (65.3)
2 nodes	623 (24.8)	643 (25.6)	1266 (25.2)
3 nodes	229 (9.1)	231 (9.2)	460 (9.2)
Not reported	8 (0.3)	9 (0.4)	17 (0.3)

A Invasive Disease–free Survival, All Participants



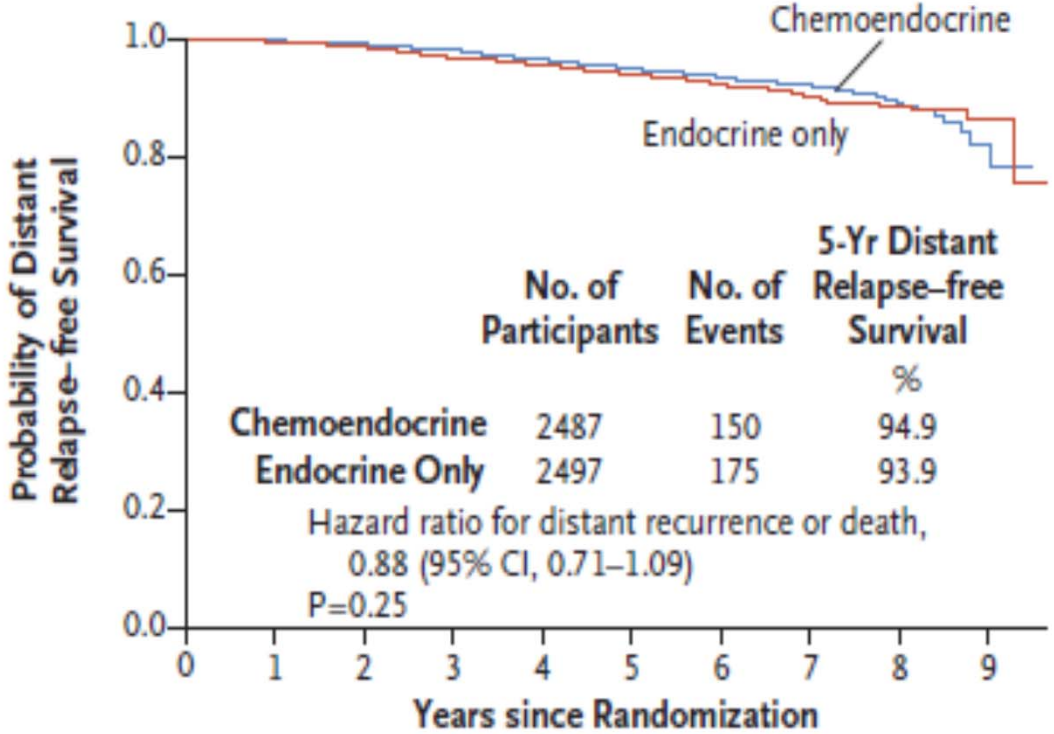
	No. of Participants	No. of Events	5-Yr Invasive Disease–free Survival %
Chemoendocrine	2487	220	92.2
Endocrine Only	2497	261	91.0

Hazard ratio for invasive disease recurrence, new primary cancer, or death, 0.86 (95% CI, 0.72–1.03)
P=0.10

No. at Risk

Chemoendocrine group	2487	2279	2123	1940	1691	1477	971	511	175	19
Endocrine-only group	2497	2328	2177	1965	1738	1493	969	502	181	23

D Distant Relapse–free Survival, All Participants



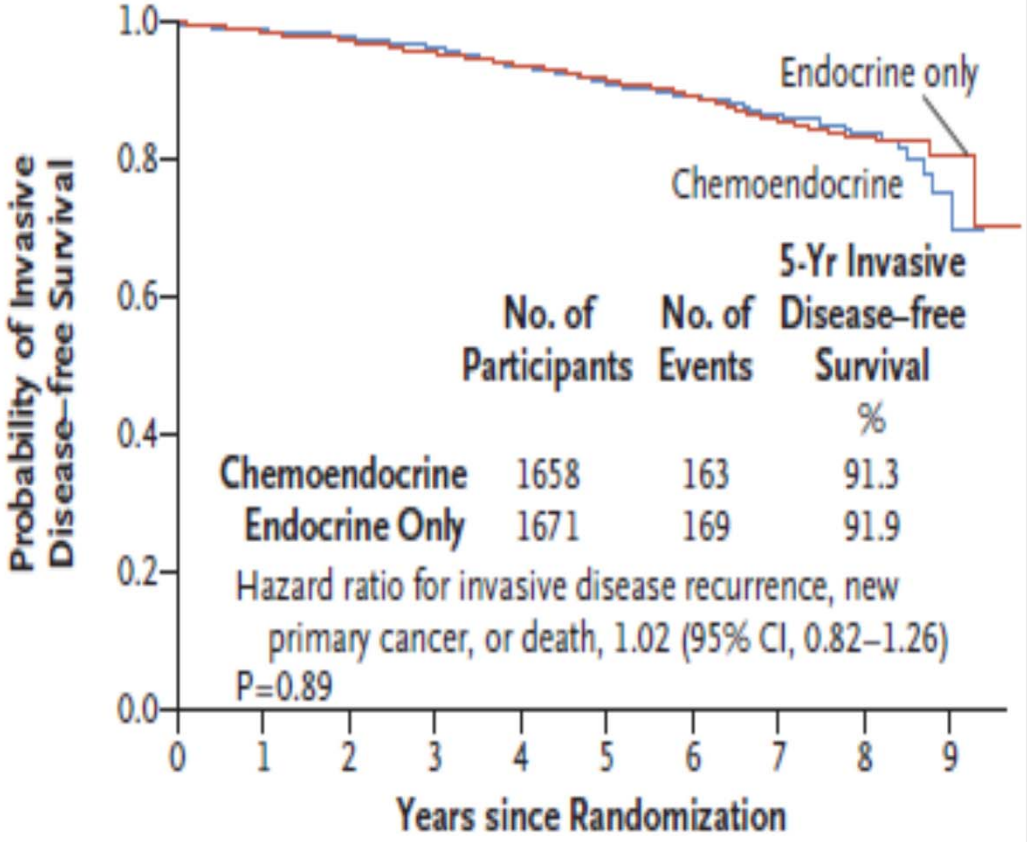
	No. of Participants	No. of Events	5-Yr Distant Relapse–free Survival %
Chemoendocrine	2487	150	94.9
Endocrine Only	2497	175	93.9

Hazard ratio for distant recurrence or death, 0.88 (95% CI, 0.71–1.09)
P=0.25

No. at Risk

Chemoendocrine group	2487	2292	2145	1970	1729	1522	1008	542	188	21
Endocrine-only group	2497	2348	2207	2002	1784	1540	1013	533	190	24

B Invasive Disease–free Survival, Postmenopausal Participants



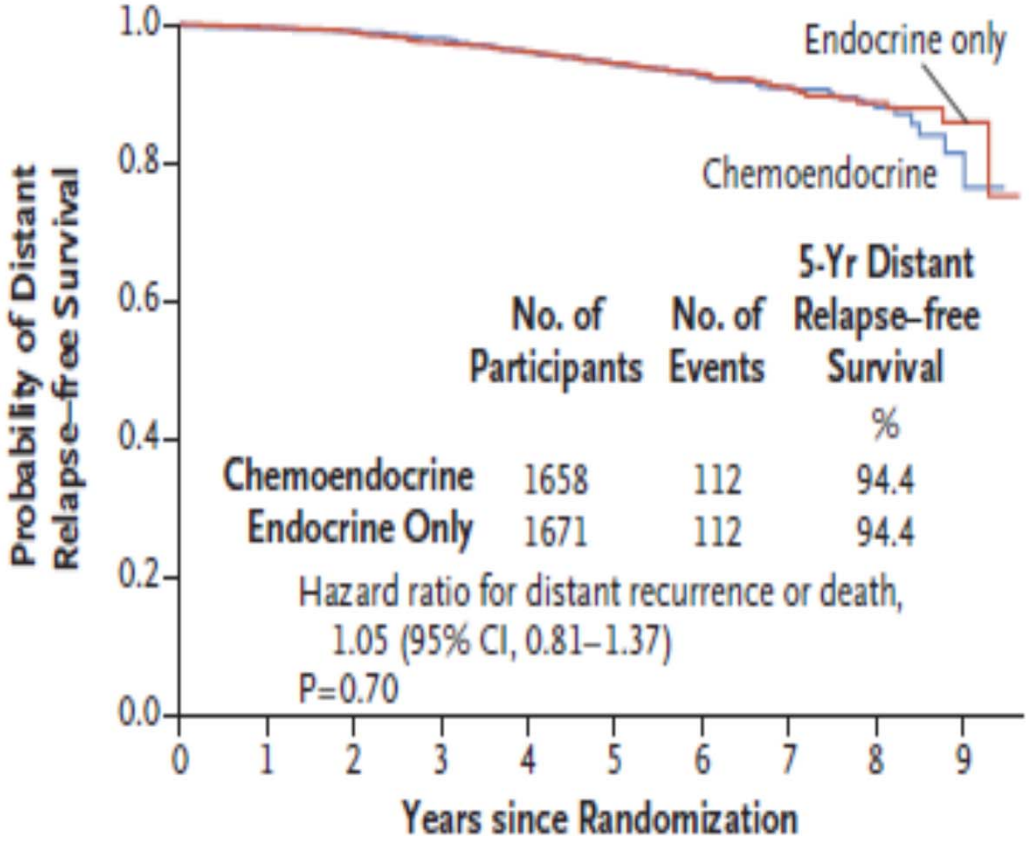
	No. of Participants	No. of Events	5-Yr Invasive Disease–free Survival %
Chemoendocrine	1658	163	91.3
Endocrine Only	1671	169	91.9

Hazard ratio for invasive disease recurrence, new primary cancer, or death, 1.02 (95% CI, 0.82–1.26)
P=0.89

No. at Risk

Chemoendocrine group	1658	1515	1413	1298	1145	993	659	358	129	14
Endocrine-only group	1671	1568	1474	1343	1196	1030	679	364	137	21

E Distant Relapse–free Survival, Postmenopausal Participants



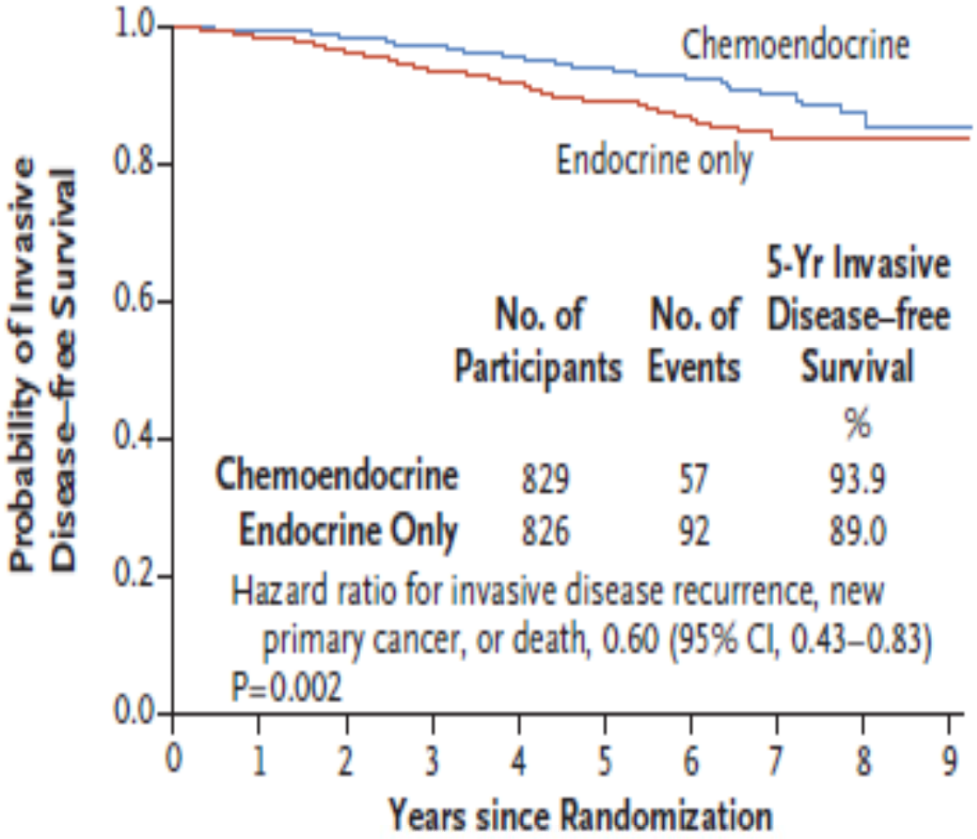
	No. of Participants	No. of Events	5-Yr Distant Relapse–free Survival %
Chemoendocrine	1658	112	94.4
Endocrine Only	1671	112	94.4

Hazard ratio for distant recurrence or death, 1.05 (95% CI, 0.81–1.37)
P=0.70

No. at Risk

Chemoendocrine group	1658	1525	1429	1320	1175	1026	686	382	139	16
Endocrine-only group	1671	1583	1492	1368	1226	1059	706	386	144	22

C Invasive Disease–free Survival, Premenopausal Participants

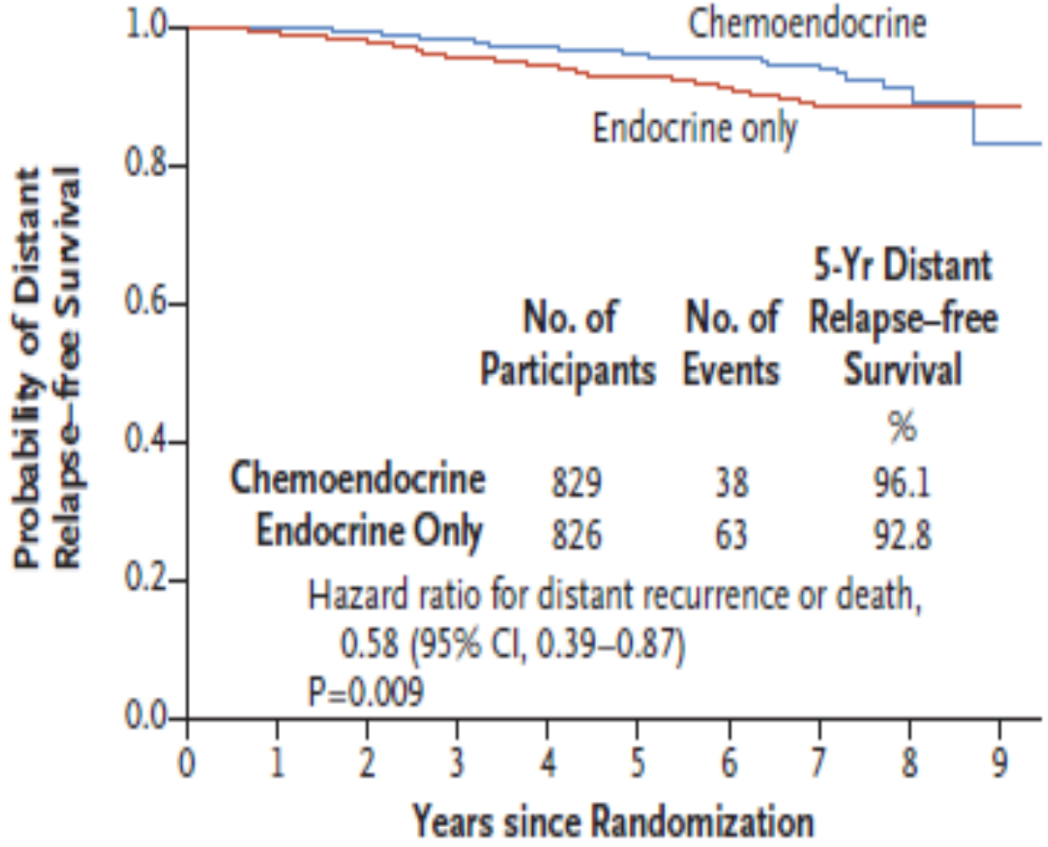


	No. of Participants	No. of Events	5-Yr Invasive Disease–free Survival %
Chemoendocrine	829	57	93.9
Endocrine Only	826	92	89.0

Hazard ratio for invasive disease recurrence, new primary cancer, or death, 0.60 (95% CI, 0.43–0.83)
P=0.002

No. at Risk										
Chemoendocrine group	829	764	710	642	546	484	312	153	46	5
Endocrine-only group	826	760	703	622	542	463	290	138	44	2

F Distant Relapse–free Survival, Premenopausal Participants



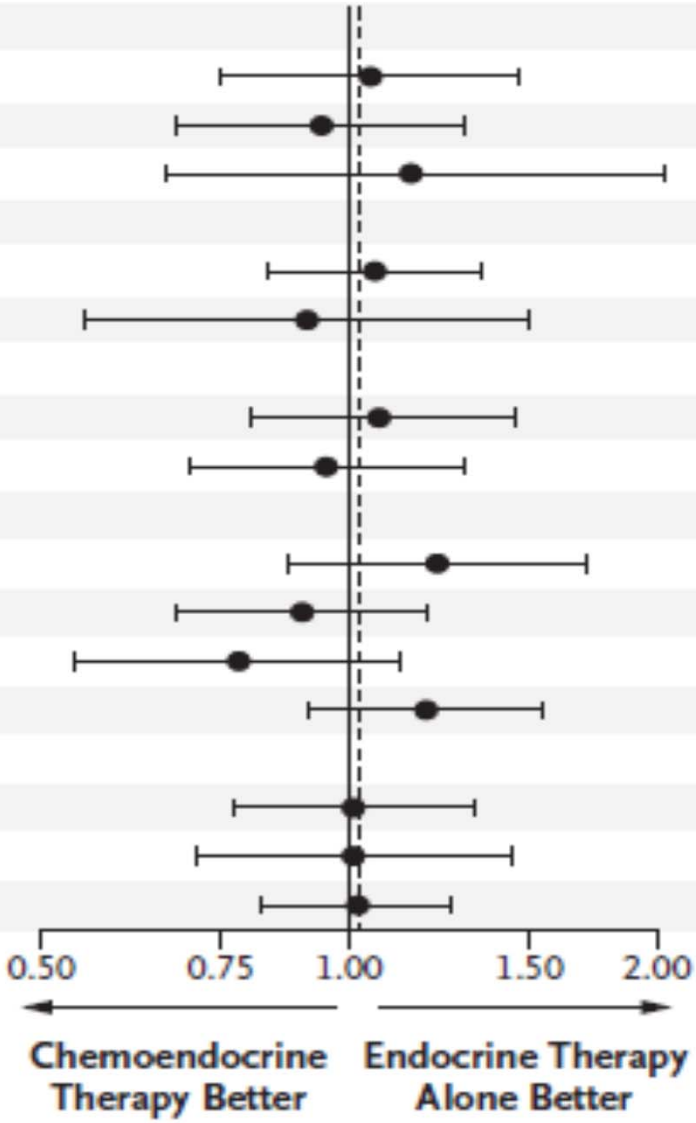
	No. of Participants	No. of Events	5-Yr Distant Relapse–free Survival %
Chemoendocrine	829	38	96.1
Endocrine Only	826	63	92.8

Hazard ratio for distant recurrence or death, 0.58 (95% CI, 0.39–0.87)
P=0.009

No. at Risk										
Chemoendocrine group	829	767	716	650	554	496	322	160	49	5
Endocrine-only group	826	765	715	634	558	481	307	147	46	2

A Postmenopausal Women

Subgroup	No. of Participants	No. of Events	Hazard Ratio for Invasive Disease Recurrence, New Primary Cancer, or Death (95% CI)
Age			
>65 yr	1180	138	1.05 (0.75–1.47)
55–65 yr	1637	145	0.94 (0.68–1.30)
<55 yr	511	49	1.15 (0.66–2.03)
Grade			
Intermediate or high	2433	265	1.06 (0.83–1.35)
Low	850	62	0.91 (0.55–1.50)
Tumor size			
T2 or T3	1360	173	1.07 (0.80–1.45)
T1	1966	159	0.95 (0.70–1.30)
Nodes			
2 or 3 positive	1146	133	1.22 (0.87–1.71)
1 positive	2181	199	0.90 (0.68–1.19)
Sentinel node	1306	118	0.78 (0.54–1.12)
Full axillary lymph-node dissection	2022	214	1.19 (0.91–1.55)
Recurrence score			
14–25	1837	206	1.01 (0.77–1.33)
0–13	1492	126	1.01 (0.71–1.44)
Overall	3328	332	1.02 (0.82–1.26)



B Premenopausal Women

Subgroup	No. of Participants	No. of Events	Hazard Ratio for Invasive Disease Recurrence, New Primary Cancer, or Death (95% CI)
Age			
≥50 yr	509	44	0.98 (0.54–1.78)
45–49 yr	615	46	0.46 (0.25–0.86)
<45 yr	531	59	0.49 (0.28–0.84)
Grade			
Intermediate or high	1280	125	0.58 (0.41–0.84)
Low	357	23	0.67 (0.29–1.55)
Tumor size			
T2 or T3	728	80	0.64 (0.41–0.99)
T1	925	69	0.53 (0.32–0.88)
Nodes			
2 or 3 positive	574	55	0.62 (0.36–1.06)
1 positive	1081	94	0.57 (0.37–0.87)
Sentinel node	556	60	0.61 (0.36–1.02)
Full axillary lymph-node dissection	1099	89	0.60 (0.39–0.91)
Recurrence score			
14–25	1015	113	0.63 (0.43–0.91)
0–13	640	36	0.49 (0.24–0.99)
Overall	1655	149	0.60 (0.43–0.83)

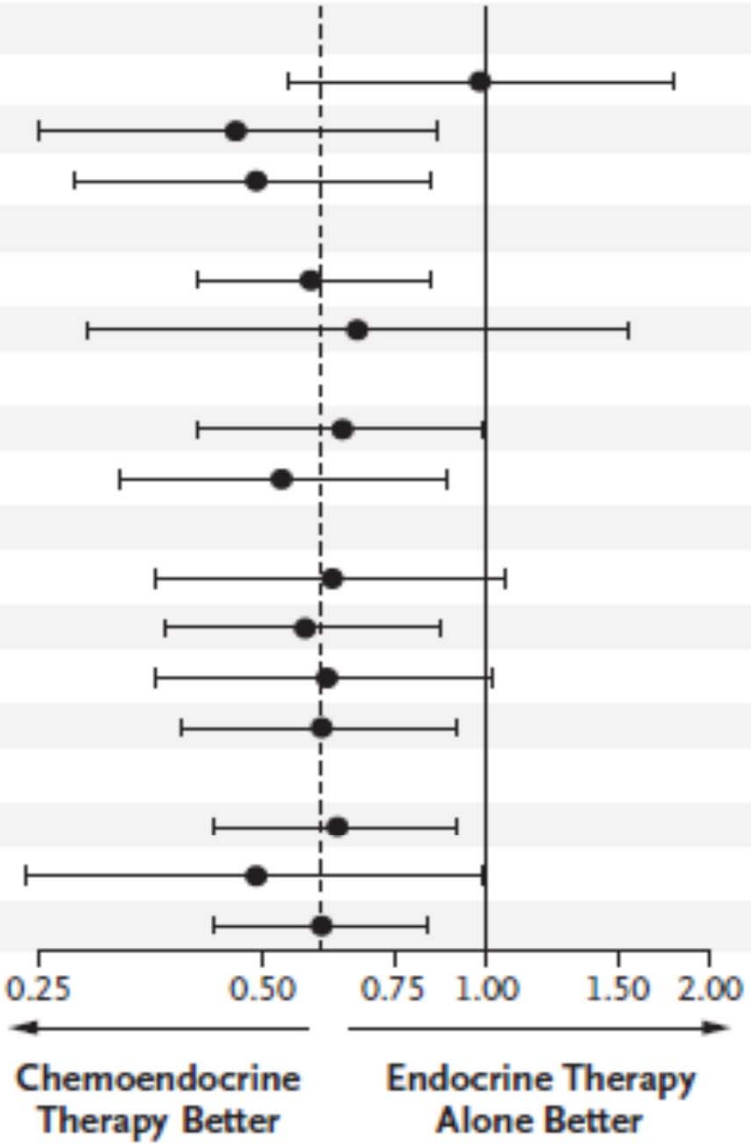


Table 2. Invasive Disease–free Survival, According to Recurrence Score and Treatment (Intention-to-Treat Population).*

Recurrence-Score Category and Type of Therapy	No. of Participants	Invasive Disease–free Survival at 5 Yr	Hazard Ratio for Recurrence (95% CI)†
		percent	
Premenopausal women			
≤10, endocrine only	174	92.4±2.2	0.47 (0.18–1.20)
≤10, chemoendocrine	151	96.6±1.7	
11–15, endocrine only	277	93.3±1.7	0.68 (0.33–1.37)
11–15, chemoendocrine	287	95.5±1.4	
16–20, endocrine only	254	83.8±2.6	0.57 (0.35–0.94)
16–20, chemoendocrine	269	91.5±1.9	
21–25, endocrine only	118	85.2±3.6	0.63 (0.30–1.31)
21–25, chemoendocrine	121	92.4±2.8	
Women ≤50 yr			
≤10, endocrine only	145	91.0±2.6	0.31 (0.10–0.94)
≤10, chemoendocrine	135	97.9±1.5	
11–15, endocrine only	247	93.1±1.8	0.71 (0.33–1.51)
11–15, chemoendocrine	235	95.4±1.6	
16–20, endocrine only	227	85.1±2.6	0.58 (0.33–1.00)
16–20, chemoendocrine	224	92.2±2.0	
21–25, endocrine only	107	80.0±4.3	0.56 (0.27–1.17)
21–25, chemoendocrine	98	90.0±3.6	

Postmenopausal women			
≤10, endocrine only	434	92.7±1.4	0.72 (0.44–1.18)
≤10, chemoendocrine	434	92.7±1.4	
11–15, endocrine only	454	95.8±1.0	1.30 (0.88–1.92)
11–15, chemoendocrine	524	93.5±1.2	
16–20, endocrine only	525	90.8±1.5	0.91 (0.57–1.43)
16–20, chemoendocrine	454	93.2±1.3	
21–25, endocrine only	451	93.2±1.3	1.13 (0.75–1.70)
21–25, chemoendocrine	255	84.8±2.5	
Women >50 yr			
≤10, endocrine only	463	93.1±1.3	0.78 (0.48–1.26)
≤10, chemoendocrine	472	95.5±1.0	
11–15, endocrine only	554	93.6±1.1	1.22 (0.83–1.79)
11–15, chemoendocrine	577	91.2±1.4	
16–20, endocrine only	481	92.1±1.3	0.86 (0.56–1.32)
16–20, chemoendocrine	496	92.8±1.3	
21–25, endocrine only	266	86.9±2.3	1.17 (0.77–1.76)
21–25, chemoendocrine	246	81.8±2.7	