After TAILORx: Are Clinical-Pathologic Features Enough?

Patrick I. Borgen, MD

Breast Cancer Program Director, Maimonides Medical Center

Christy A. Russell, MD

Senior Director Medical Affairs, Exact Sciences

CASE STUDY

NODE
[-]

AGE
41

Patient	41 year old
Tumor Size	2.5 cm
Menopausal	Premenopausal
Tumor Type	Invasive ductal carcinoma
ER Status (IHC)	Positive
PR Status (IHC)	Positive
HER2/NEU Status	Negative
Histologic Grade	3
Lymph Node Status	Negative
General Health	Good
Other Information	Patient would be considered high clinical risk by tumor size & grade

Would you assume this patient has a high Recurrence Score® result and recommend chemotherapy based on age, tumor size, & grade?

CASE STUDY

RESULTS

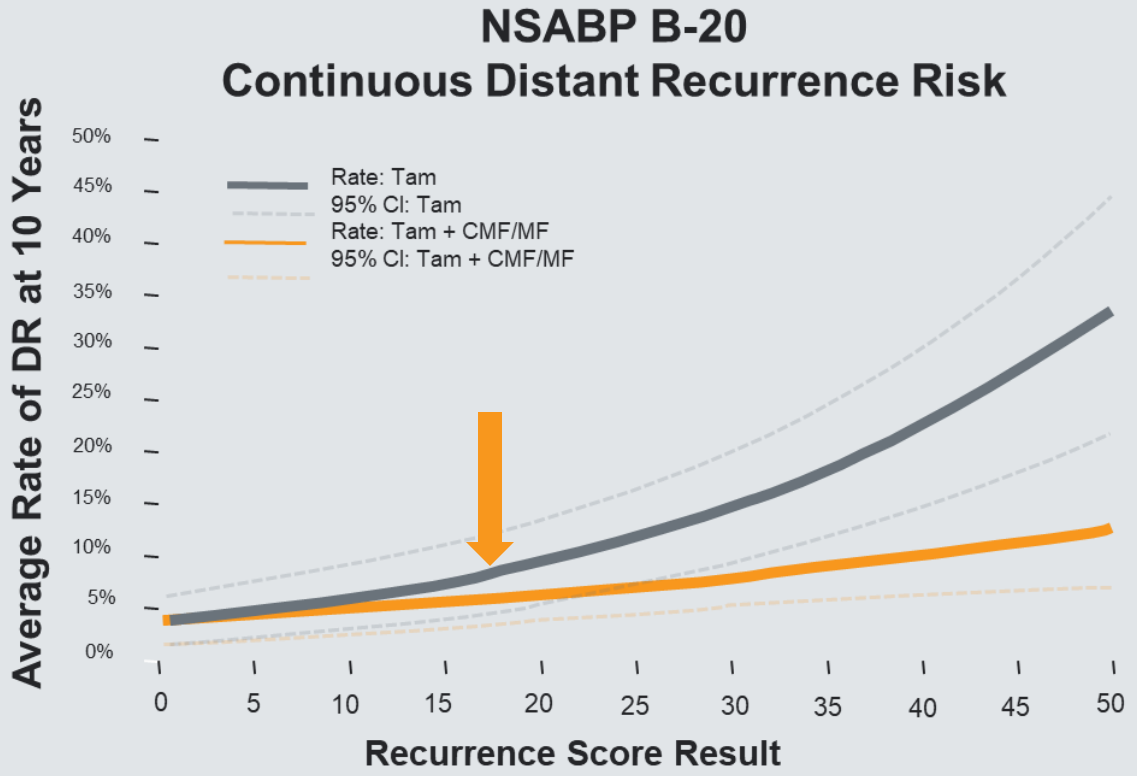
Recurrence Score® Result

17

Prediction for Node-Negative, ER-Positive Patients

In the TAILORx study, patients in Arm B with Recurrence Score results 11-25 had an average rate of distant recurrence at 9 years of 5% with endocrine therapy alone.

In NSABP B-20, patients with Recurrence Score results 0-17 receiving 5 years of endocrine therapy did not benefit from the addition of chemotherapy.

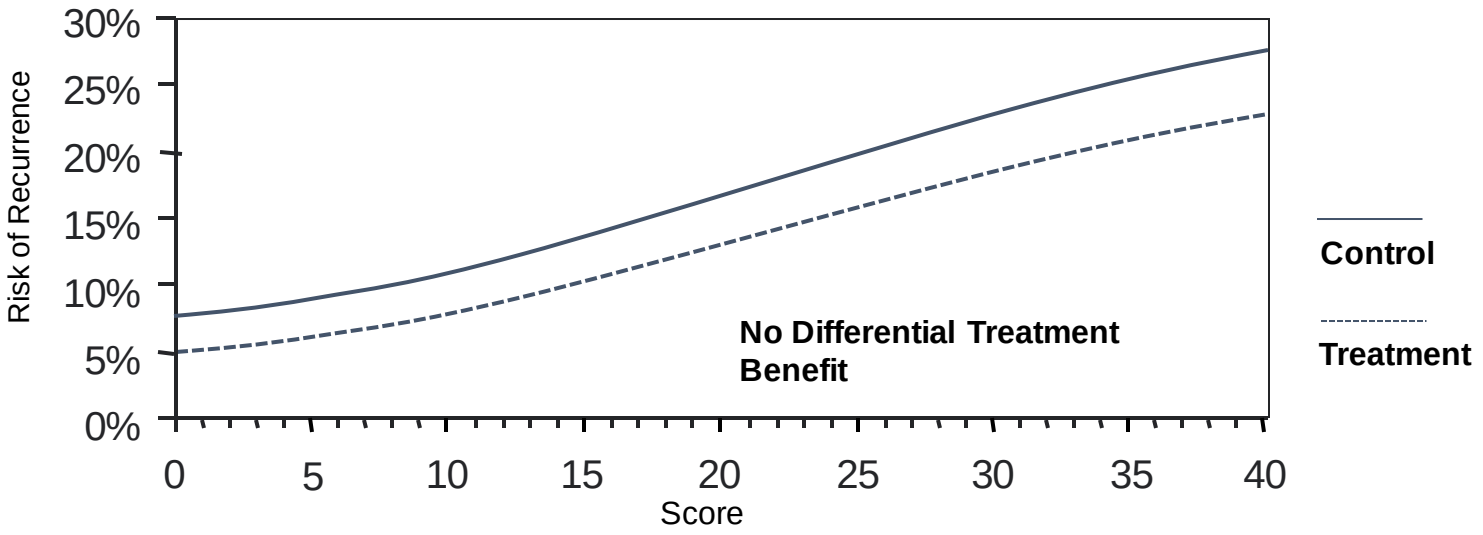


Sparano et al. *N Engl J Med.* 2018; Paik et al. *J Clin Oncol*. 2006.

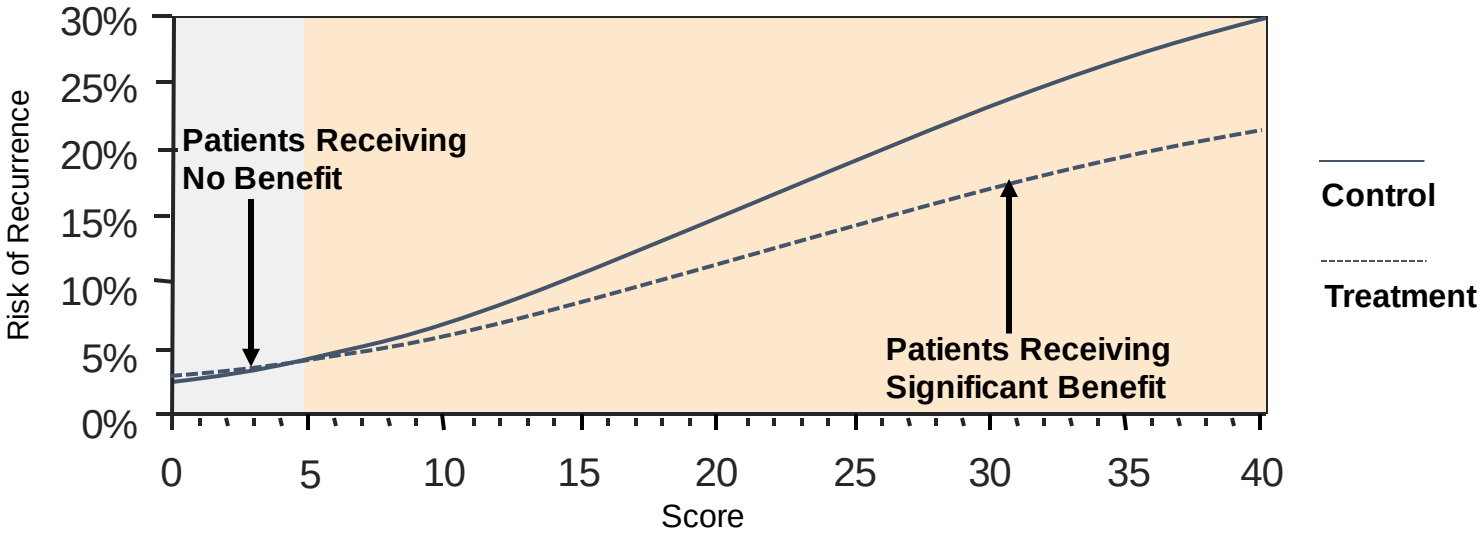
Clinicopathologic Factors and the Oncotype DX Breast Recurrence Score® Test

- Are clinical and/or pathologic factors (age, tumor grade, tumor size) predictive of chemotherapy benefit?
- Can the Recurrence Score® result be predicted based on clinical and pathologic factors?
- Should patients with high risk prognostic factors (i.e. high grade, large tumors, premenopausal) automatically be recommended chemotherapy without obtaining a Recurrence Score result?
- Should chemotherapy automatically be withheld in patients with low risk prognostic factors (i.e. low grade, small tumor, postmenopausal) without obtaining a Recurrence Score result?

Review of Prognosis Versus Prediction



Prognostic biomarkers are measured before treatment to indicate long-term outcome for patients untreated or receiving standard treatment



Predictive biomarkers are measured before treatment to identify who will or will not benefit from a particular treatment

Simon et al. *J Natl Cancer Inst.* 2009.

Patient Age, Tumor Size & Tumor Grade are Prognostic Only and Not Predictive of Chemotherapy Benefit

The Recurrence Score® Result is the Strongest and Only Statistically Significant Predictor of Chemotherapy Benefit

NSABP B-20

Variable	Assessable Patients (n = 651)			
	HR	Lower 95%	Upper 95%	*P**
Recurrence Score result	0.32	0.11	0.94	.038
Age ≥50 yrs	2.02	0.75	5.47	.162
Tumor size >2 cm	1.34	0.49	3.68	.569
Quantitative ER ≥50	1.96	0.73	5.30	.183
Quantitative PR ≥50	1.87	0.70	4.97	.214
Grade site				
Poor	0.27	0.02	3.01	.284
Moderate	0.60	0.06	6.42	.672
Grade, pathologist A				
Poor	0.73	0.19	2.89	.657
Moderate	1.04	0.23	4.58	.963
Grade, pathologist B				
Poor	0.32	0.06	1.77	.192
Moderate	0.36	0.06	2.03	.244

Age, tumor size & grade are not significant predictors of chemotherapy benefit

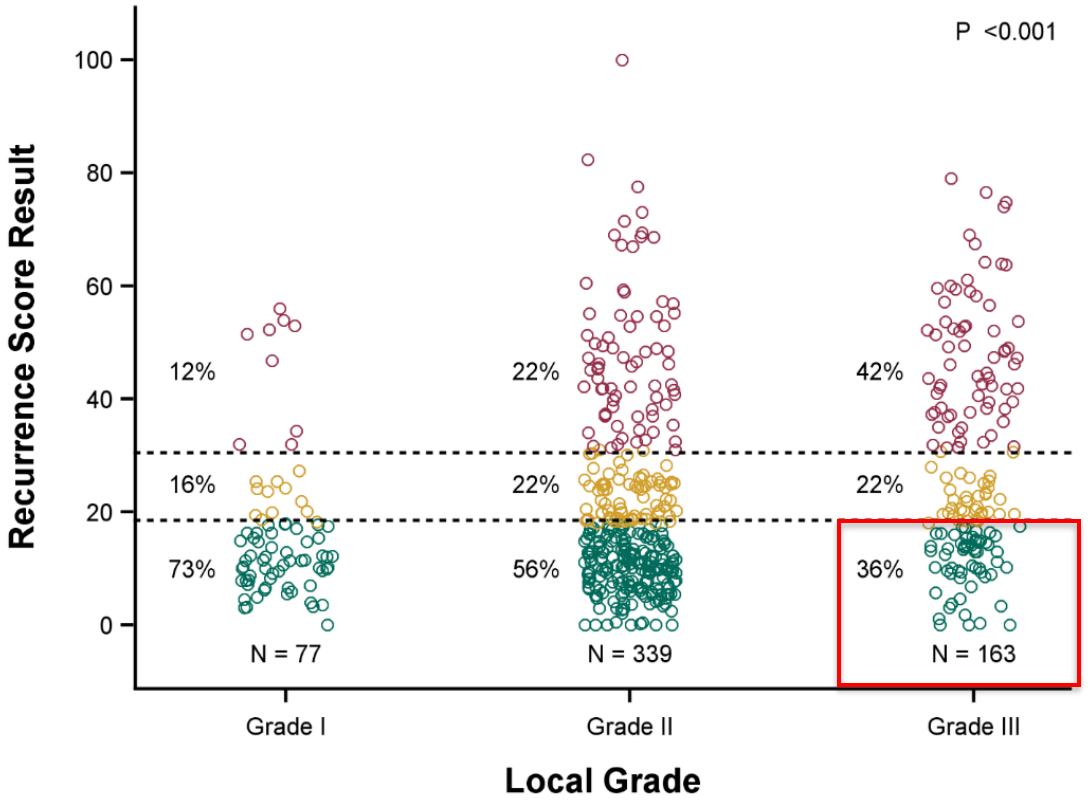
Paik et al. *J Clin Oncol*. 2006.

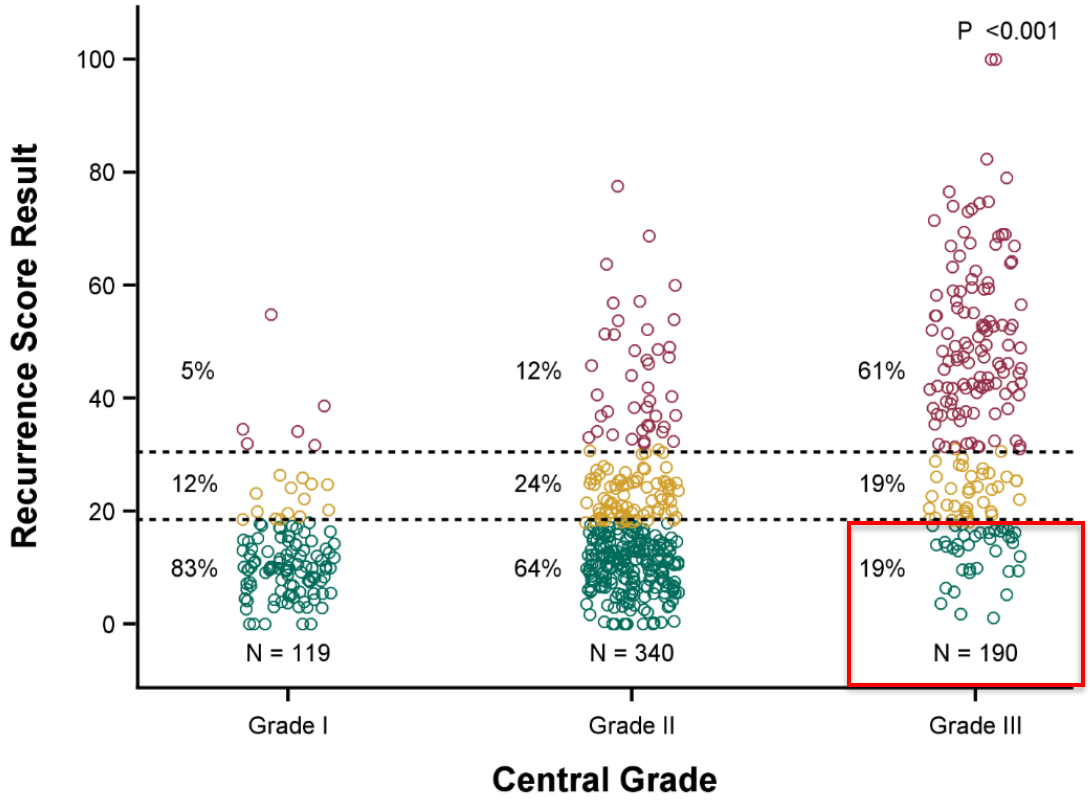
*P-value from the test of interaction with chemotherapy

Oncotype DX Breast Recurrence Score® Test and Tumor Grade

Many Patients With Grade 3 Tumors Have Low Recurrence Score® Results & Would Not Benefit From Chemotherapy

NSABP B-20





Paik et al. *J Clin Oncol*. 2006.

Many High Grade Tumors Have Low Recurrence Score® Results

TAILORx

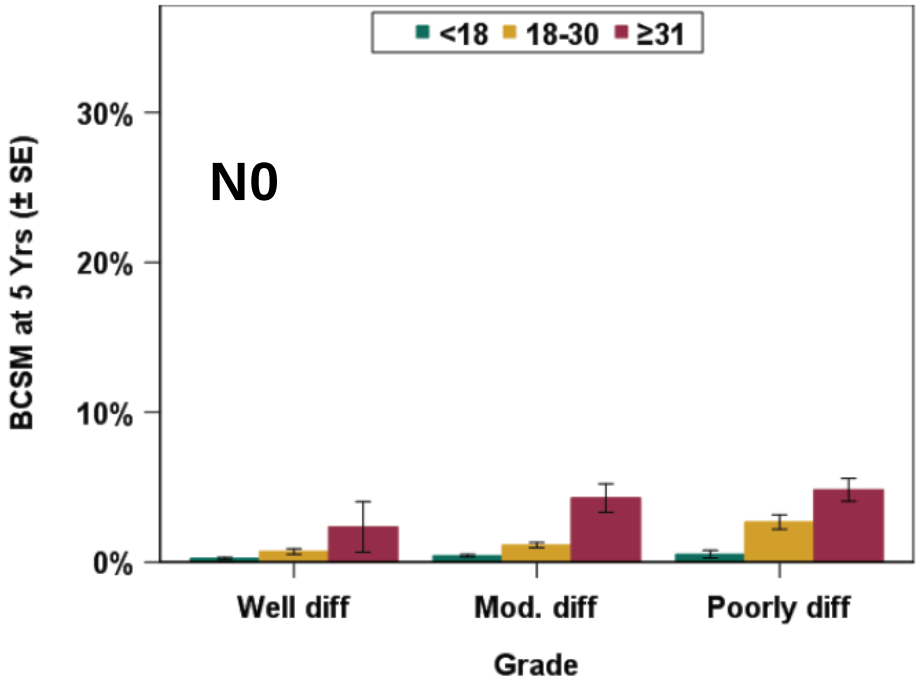
Tumor Grade Distribution – total no. (%)	RS Results 0-25	RS Results 26-100	All Patients
			9430 women
Low	2423 (96%)	89 (4%)	2512
Intermediate	4652 (89%)	590 (11%)	5242
High	995 (59%)	681 (41%)	1676

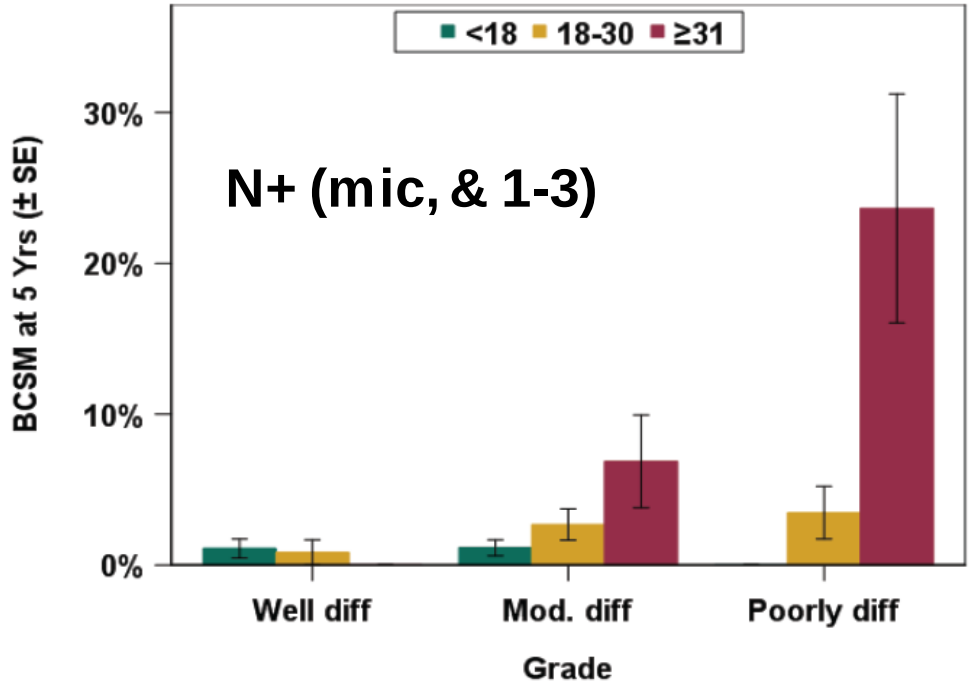
Of the 1676 (18%) TAILORx patients with high grade tumors, 995 (59%) had low Recurrence Score results (0-25)

Sparano et al. *N Engl J Med.* 2018.

RS: Recurrence Score result

SEER Subgroup Analysis: Regardless of Tumour Grade, N0 & N1 Patients With Recurrence Score® Results (0-17) had Excellent Outcomes





	N (% in each group known to have received chemotherapy)		
RS Result	Well differentiated	Moderately differentiated	Poorly differentiated
<18	7,521 (5%)	11,681 (8%)	1,860 (12%)
18-30	3,534 (25%)	8,174 (35%)	3,017 (46%)
≥31	153 (67%)	1,180 (69%)	1,827 (71%)

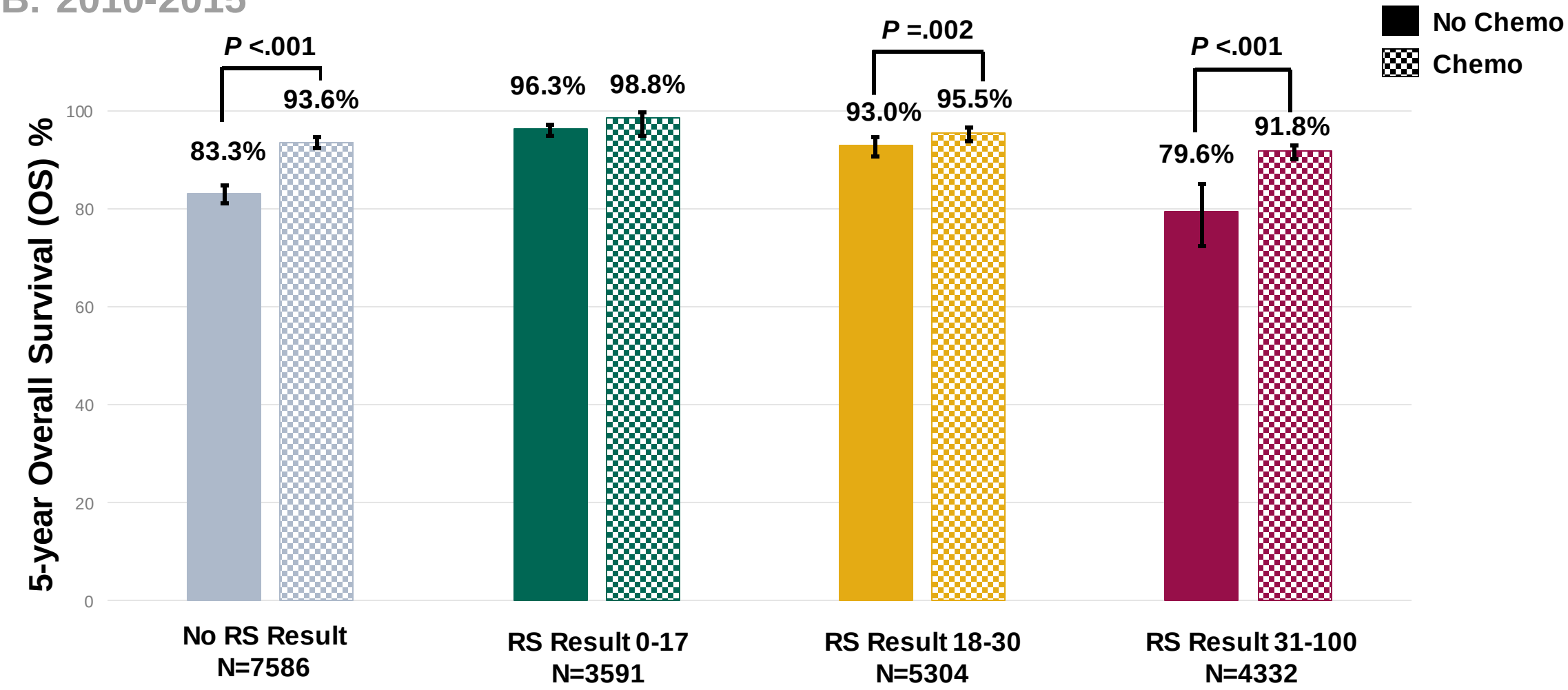
	N (% in each group known to have received chemotherapy)		
RS Result	Well differentiated	Moderately differentiated	Poorly differentiated
<18	938 (19%)	1,456 (25%)	239 (25%)
18-30	380 (41%)	932 (46%)	324 (57%)
≥31	15 (73%)	129 (79%)	179 (73%)

Petkov et al., *npj Breast Cancer*. 2016.

RS: Recurrence Score result; N0: node negative; N+: micrometastases & 1-3 positive lymph nodes; BCSM: breast cancer specific mortality

Node-Negative Patients With Grade 3 Lesions and Recurrence Score® Results

NCDB: 2010-2015



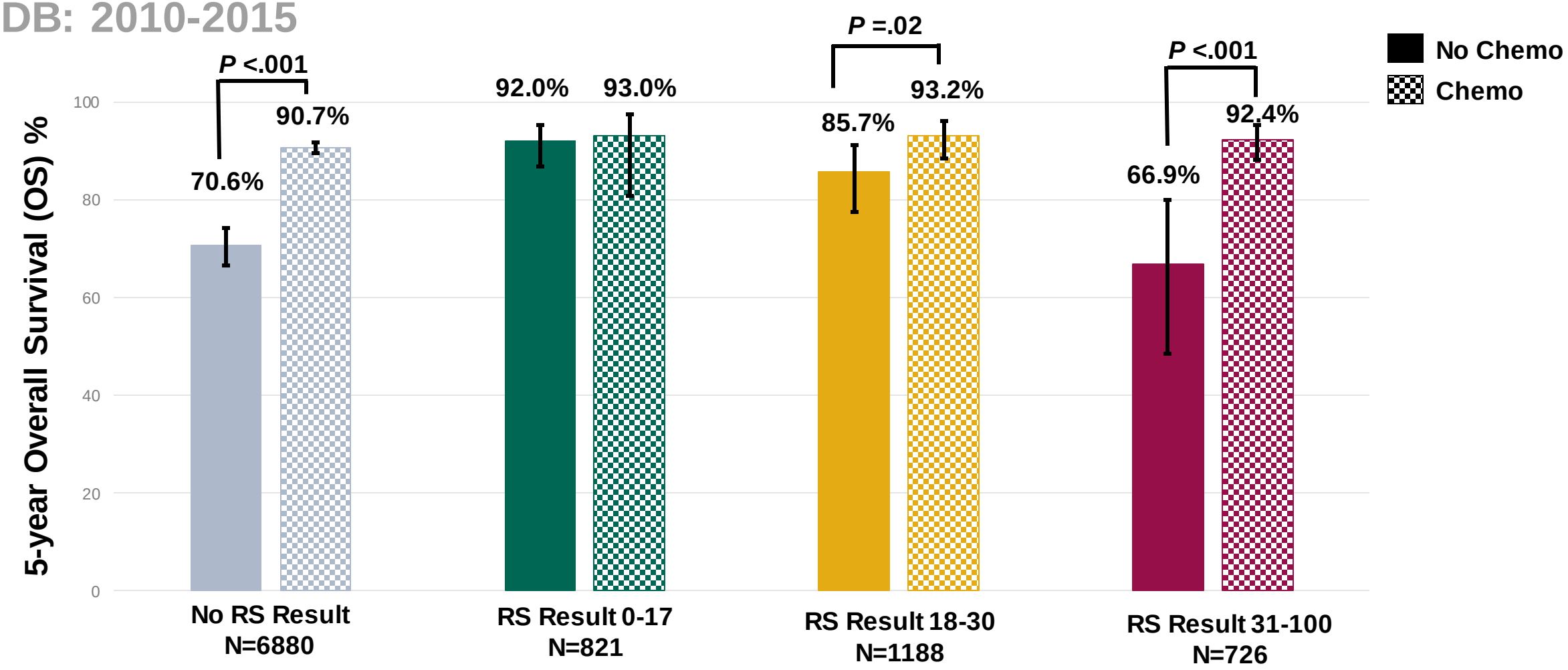
Patients with Recurrence Score results 0-17 and negative lymph nodes (pN0) had similar outcomes with or without chemotherapy

Iorgulescu et al. *JCO Precis Oncol*. 2019.

NCDB: National Cancer Database; RS: Recurrence Score result

Node-Positive Patients With Grade 3 Lesions and Recurrence Score® Results

NCDB: 2010-2015



Patients with Recurrence Score results 0-17 and 1-3 positive lymph nodes (pN1) had similar outcomes with or without chemotherapy

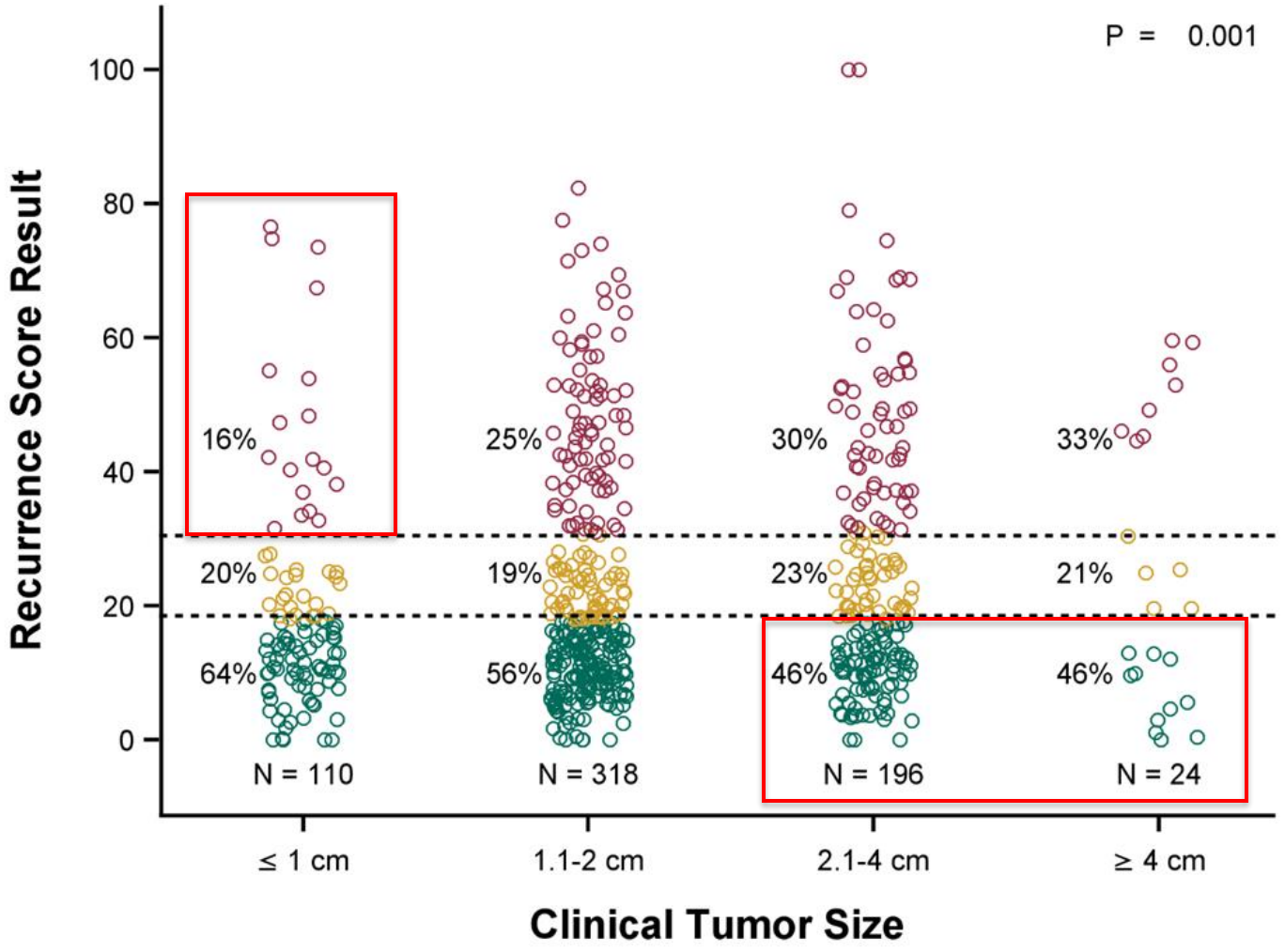
Iorgulescu et al. *JCO Precis Oncol*. 2019.

NCDB: National Cancer Database; RS: Recurrence Score result

Oncotype DX Breast Recurrence Score® Test and Tumor Size

Tumor Size Does Not Correlate With Recurrence Score® Result or Benefit From Chemotherapy

NSABP B-20



Paik et al. *J Clin Oncol*. 2006.

Many Large Tumors Have Low Recurrence Score® Results

TAILORx

Tumor Size Distribution – total no. (%)	RS Results 0-25	RS Results 26-100	All Patients
			9719 women
≤1 cm (grade 2/3)	1071 (13%)	188 (14%)	1259
1.1-2.0 cm	5271 (63%)	741 (53%)	6012
2.1-3.0 cm	1562 (19%)	348 (25%)	1910
3.1-4.0 cm	324 (4%)	91 (7%)	415
≥4.1 cm	100 (1%)	20 (1%)	120

Of the 2445 (25%) TAILORx patients with large tumors (2.1-≥4.1 cm), 1986 (81%) had low Recurrence Score results (0-25)

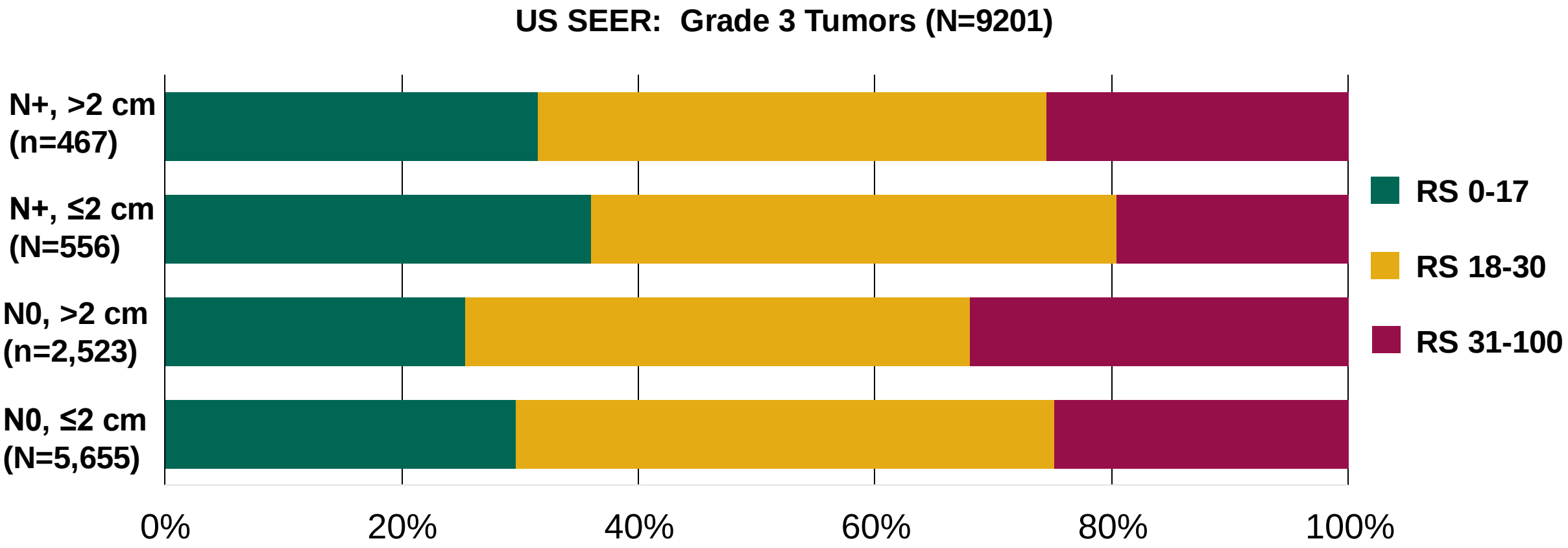
Sparano et al. *N Engl J Med.* 2018.

RS: Recurrence Score result

Combining Tumor Size & Tumor Grade With The Recurrence Score® Result

Low Recurrence Score® Results are Common in N- and N+ Patients With Grade 3 Breast Cancer Regardless of Tumor Size or Nodal Status

SEER Registry

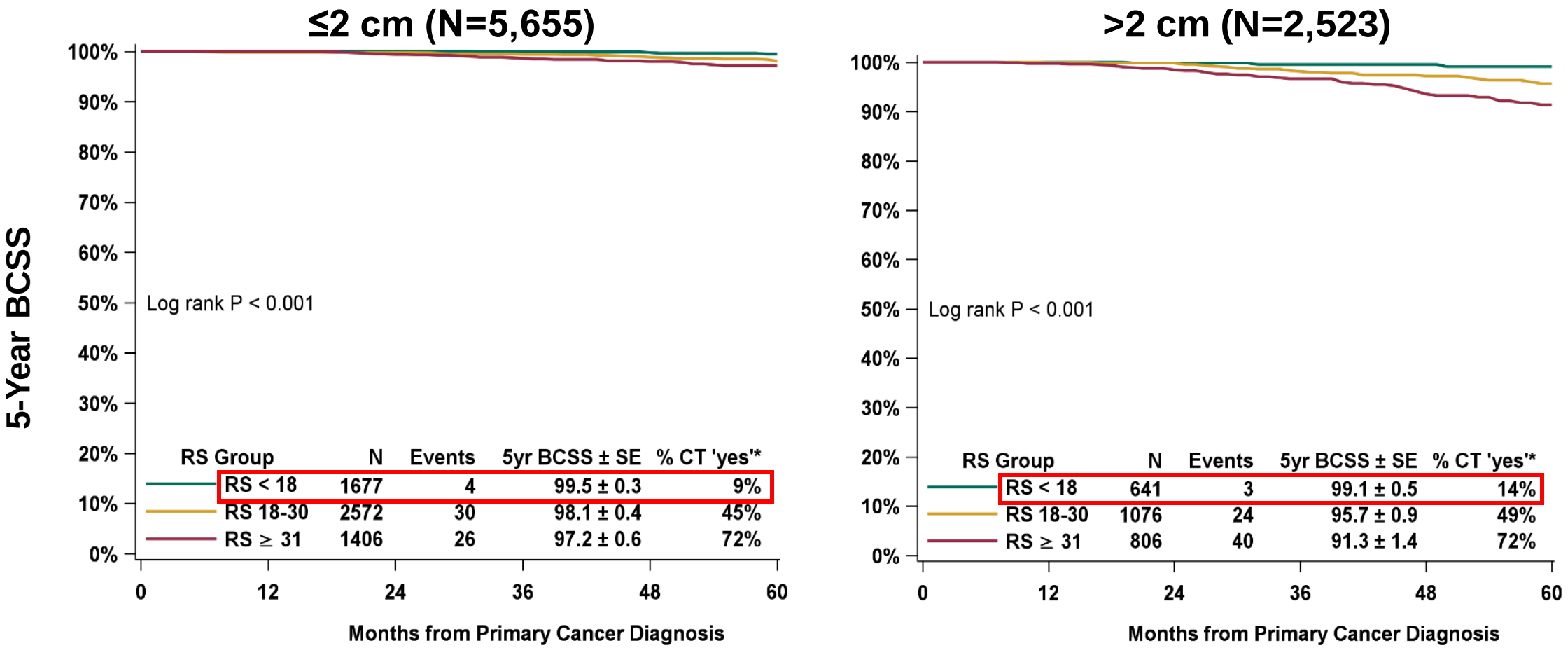


Petkov et al. SABCS 2016.

RS: Recurrence Score result

Patients With Recurrence Score® Results 0-17 Have Excellent Outcomes

SEER Registry: Node-Negative, Grade 3 Breast Cancer



Despite high tumor grade and low chemotherapy use, Recurrence Score results 0-17 were associated with excellent 5-year BCSS

Petkov et al. SABCS 2016.

BCSS: breast cancer-specific survival

Impact of Clinical Risk (Tumor Size & Grade) on Prognosis & Prediction of Chemotherapy Benefit With the Recurrence Score® Result

Can Genomic and Clinical Risk be Integrated for Prognosis in Early Stage Breast Cancer?

- Recurrence Score® results are independently prognostic (genomic risk) & predictive of chemotherapy benefit in women with ER-positive early-stage breast cancer
- Clinical & pathologic features (age, tumor size, grade) provide prognostic information only
- Clinical risk (tumor size & grade) does not always correlate with genomic risk
- Integration of genomic and clinical risk may provide greater precision in prognosis & potentially guide use of adjuvant therapy

Sparano et al. *N Engl J Med.* 2018.; Sparano et al. *J Clin Oncol*. 2008.; Paik et al. *J Clin Oncol*. 2006.

TAILORx 2019 Exploratory Analysis on Clinical Risk and Recurrence Score® Results

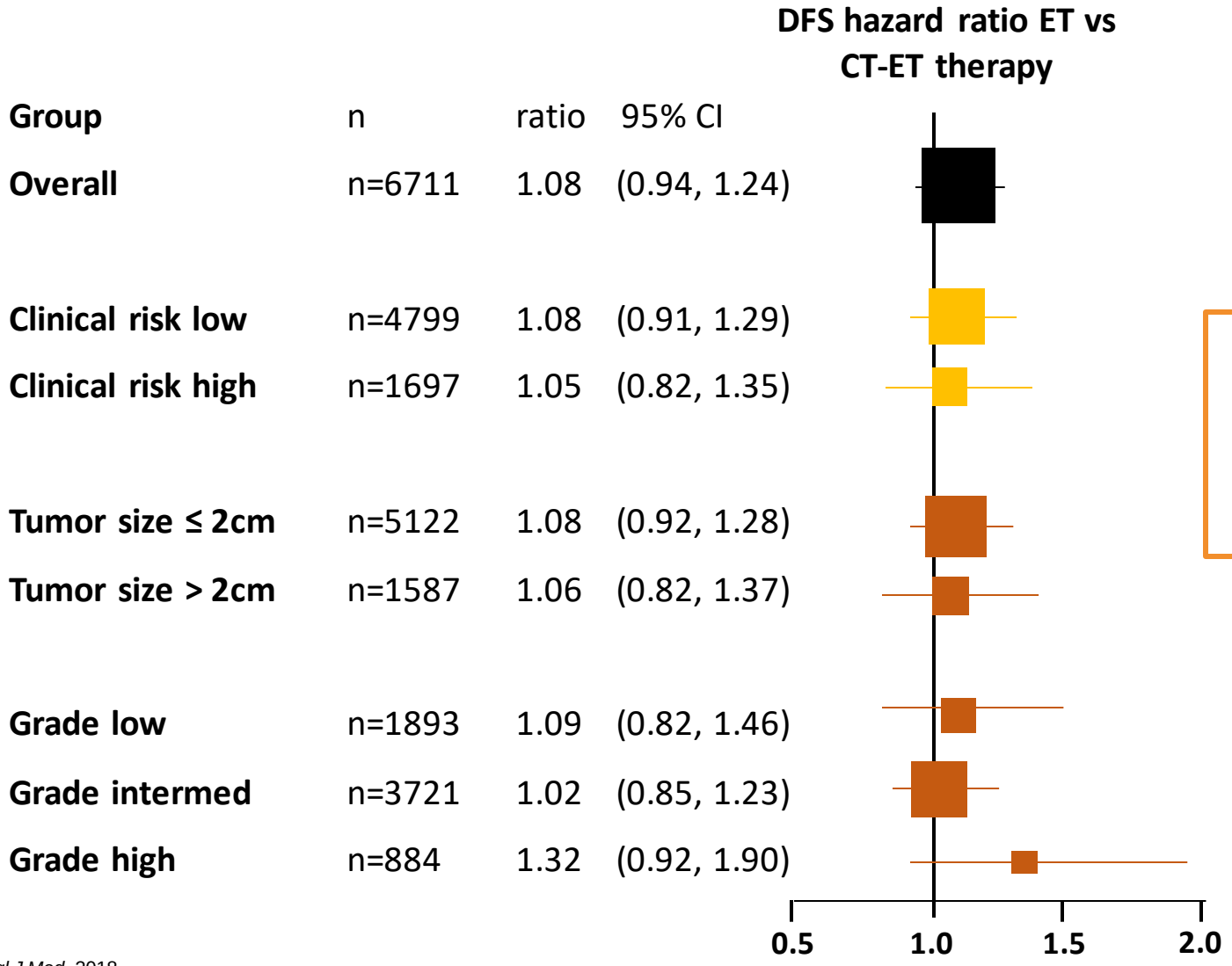
- Does adding clinical risk to Recurrence Score results refine prognosis for 9-year distant recurrence?
- Does adding clinical risk to Recurrence Score results refine which patients will and will not benefit from chemotherapy (prediction)?

*Clinical risk defined via modified Adjuvant! Online

- Low risk:
  - Tumor size ≤3 cm and Grade 1
  - Tumor size ≤2 cm and Grade 2
  - Tumor size ≤1 cm and Grade 3
- High risk: All other cases with known values for grade and tumor size

Sparano et al. *N Engl J Med.* 2018.; Sparano et al. *N Engl J Med.* 2019.

TAILORx Results: Exploratory Analysis of Chemotherapy Treatment Interactions in Recurrence Score® Results 11-25 Arms

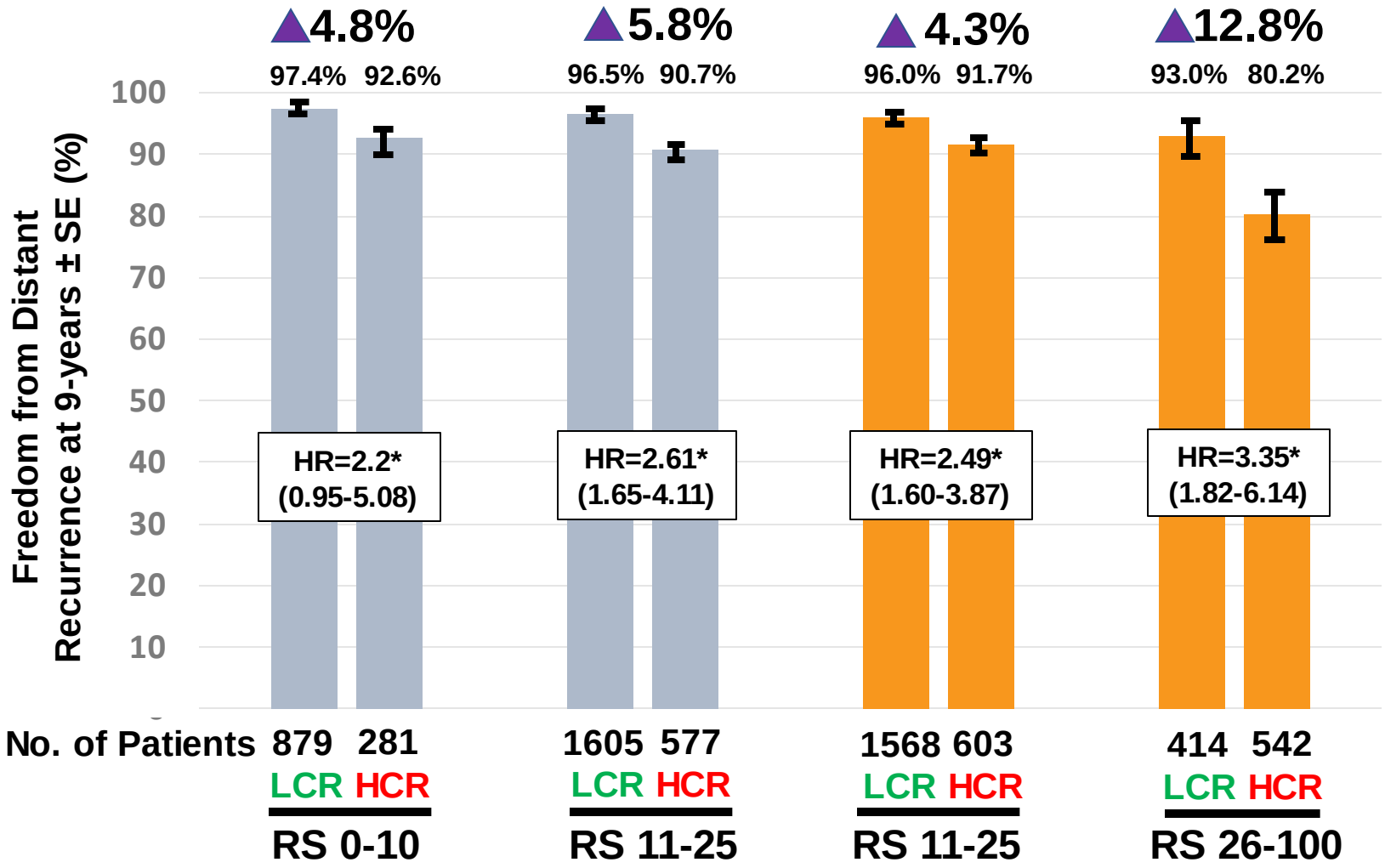


No statistically significant chemotherapy treatment interactions were found in any of these subgroups

*Low clinical risk defined by low grade and tumor size ≤ 3 cm, intermediate grade and tumor size ≤2 cm, and high grade and tumor size ≤1 cm; high clinical risk defined as all other cases with known values for grade and tumor size.

Sparano et al. *N Engl J Med.* 2018.

Clinical Risk Adds Significant Prognostic Information for Distant Recurrence to Recurrence Score® Results in Women >50 Years (N=6469)



Absolute Differences in Distant Recurrence Rates

ET

ET + CT

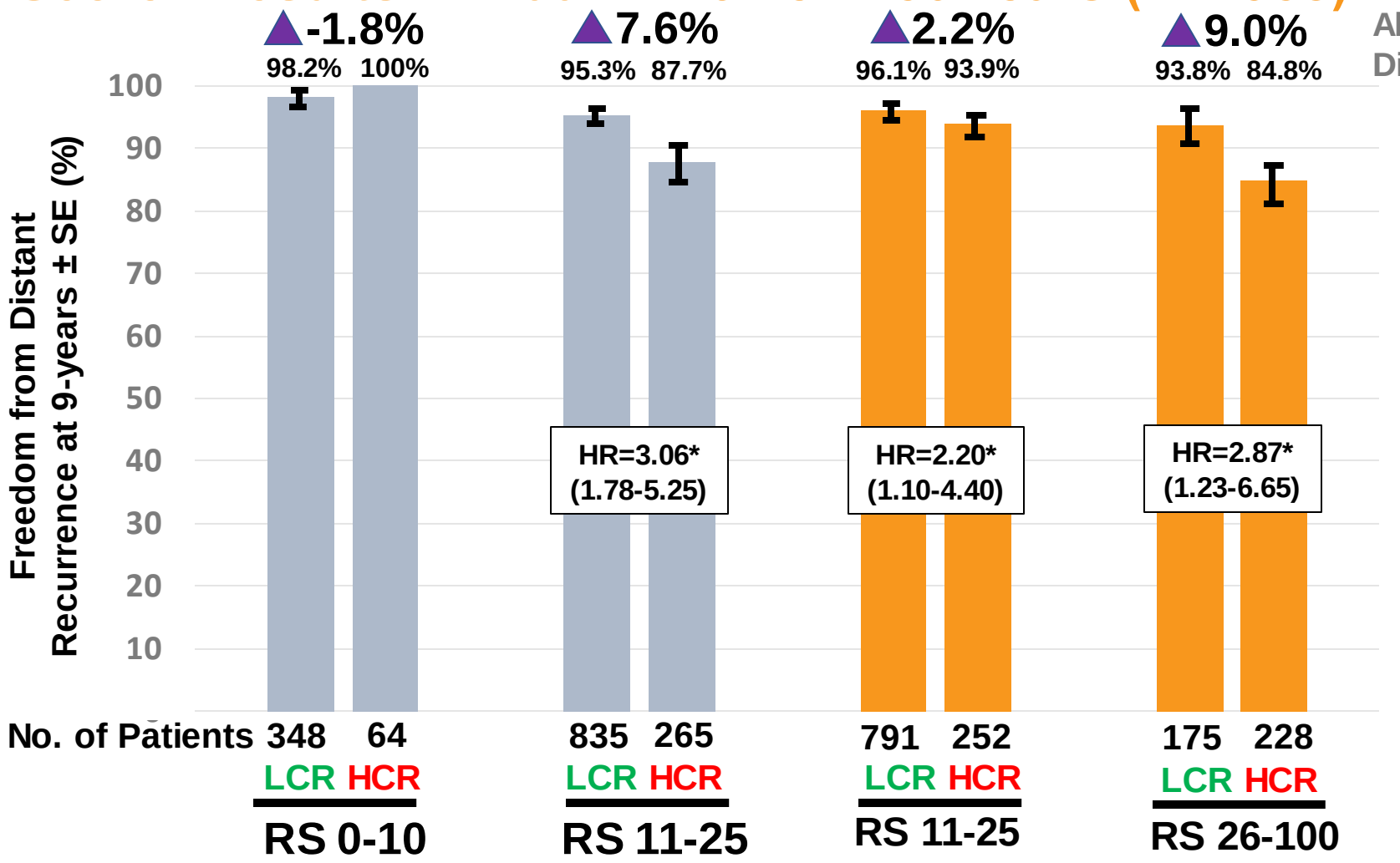
*HR >1 indicates a higher event rate with high compared to low clinical risk. 95% confidence intervals are in parentheses

High clinical risk is associated with a 2-3 fold higher distant recurrence rate across all Recurrence Score groups

LCR: Low clinical risk
HCR: high clinical risk
RS: Recurrence Score results
HR: hazard ratio
ET: endocrine therapy
ET + CT: chemoendocrine therapy

Sparano et al. *N Engl J Med.* 2019.

Clinical Risk Adds Significant Prognostic Information For Distant Recurrence to Recurrence Score® Results 11-100 in Women ≤50 Years (N=2958)



*HR >1 indicates a higher event rate with high compared to low clinical risk. 95% confidence intervals are in parentheses

High clinical risk is associated with a 2-3-fold higher distant recurrence rate for those with a Recurrence Score result of 11 or higher

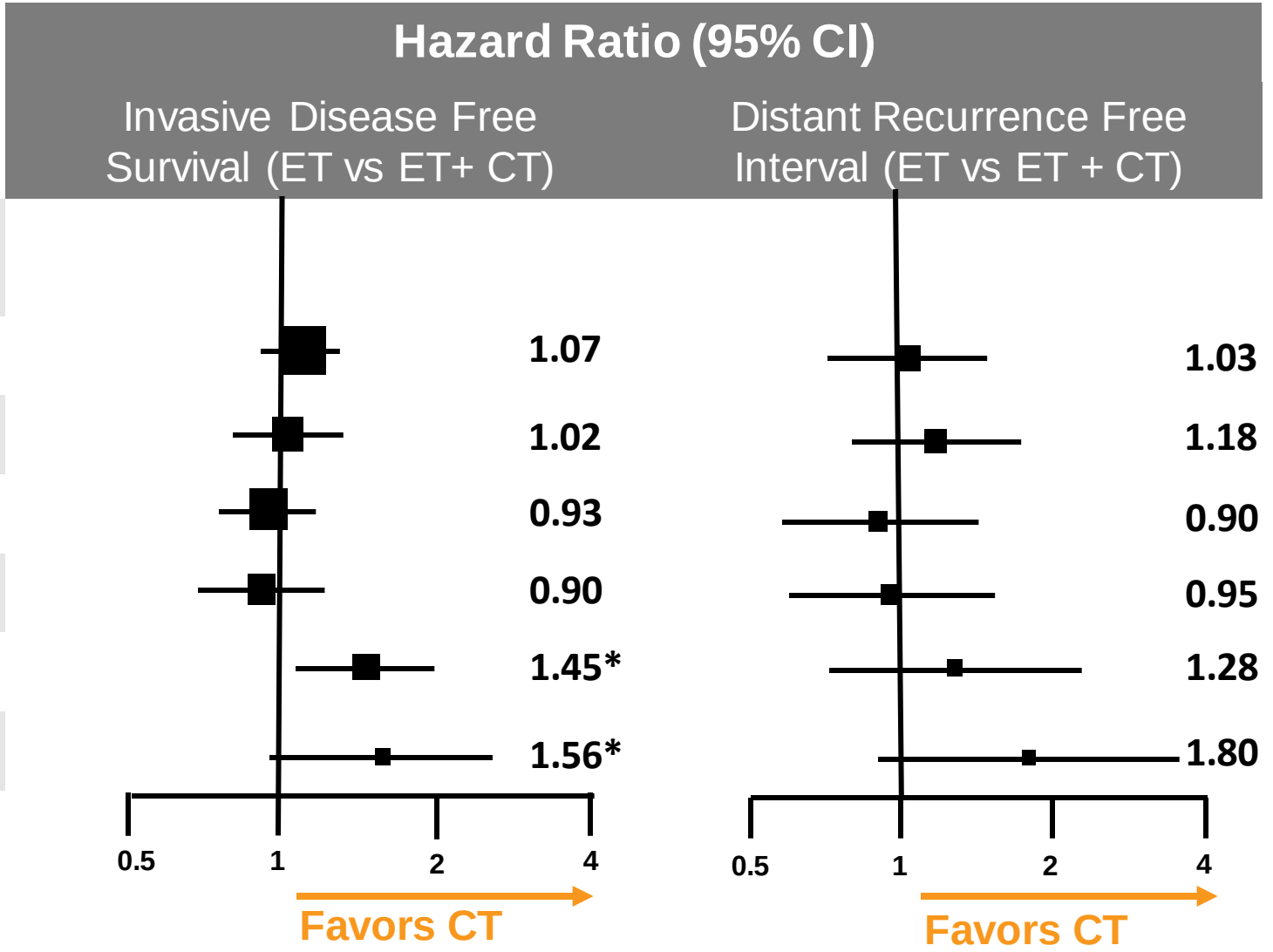
LCR: Low clinical risk
HCR: high clinical risk
RS: Recurrence Score results
HR: hazard ratio
ET: endocrine therapy
ET + CT: chemoendocrine therapy

Sparano et al. *N Engl J Med.* 2019.

Clinical/Pathologic Parameters Are Not Predictive of Chemotherapy Benefit in Women With Recurrence Score® Results 11-25

Subgroup	# of Patients	iDFS Events	DRFI Events
All Patients (RS 11-25)	6496		
LCR	4799	541	129
HCR	1697	270	111
Age >50, LCR	3173	361	80
Age >50, HCR	1180	204	73
Age ≤50, LCR	1626	180	49
Age ≤50, HCR	517	66	38

*Non-significant trend favoring CT consistent with treatment interaction previously reported between age/menopausal status, RS, & CT



Sparano et al. *N Engl J Med.* 2019.; Sparano et al. ASCO 2019.

LCR: low clinical risk; HCR: high clinical risk; ET: endocrine therapy; CT: chemotherapy; RS: Recurrence Score results; ET+CT: chemoendocrine therapy
iDFS: invasive disease free survival = recurrence, second primary cancer or death; DRFI: distant recurrence free interval

So…. If Clinical Risk, Grade, and Tumor Size Do Not Predict Chemotherapy Benefit, Let's Consider Patient Age in Clinical Decision-Making With the Recurrence Score® Result

CASE STUDY

NODE
[-]

AGE
41

Patient	41 year old
Tumor Size	2.5 cm
Menopausal	Premenopausal
Tumor Type	Invasive ductal carcinoma
ER Status (IHC)	Positive
PR Status (IHC)	Positive
HER2/NEU Status	Negative
Histologic Grade	3
Lymph Node Status	Negative
General Health	Good
Other Information	Patient would be considered high clinical risk by tumor size & grade

Would you assume this patient has a high Recurrence Score® result and recommend chemotherapy based on age, tumor size, & grade?

CASE STUDY

RESULTS

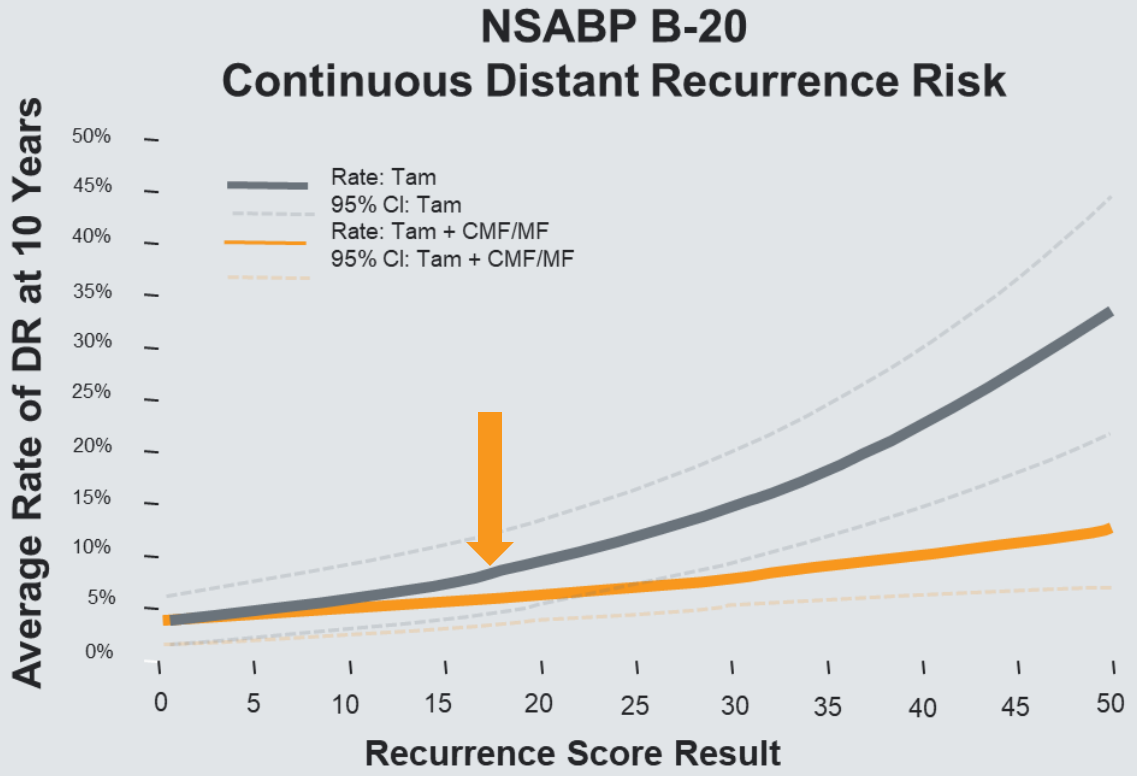
Recurrence Score® Result

17

Prediction for Node-Negative, ER-Positive Patients

In the TAILORx study, patients in Arm B with Recurrence Score results 11-25 had an average rate of distant recurrence at 9 years of 5% with endocrine therapy alone.

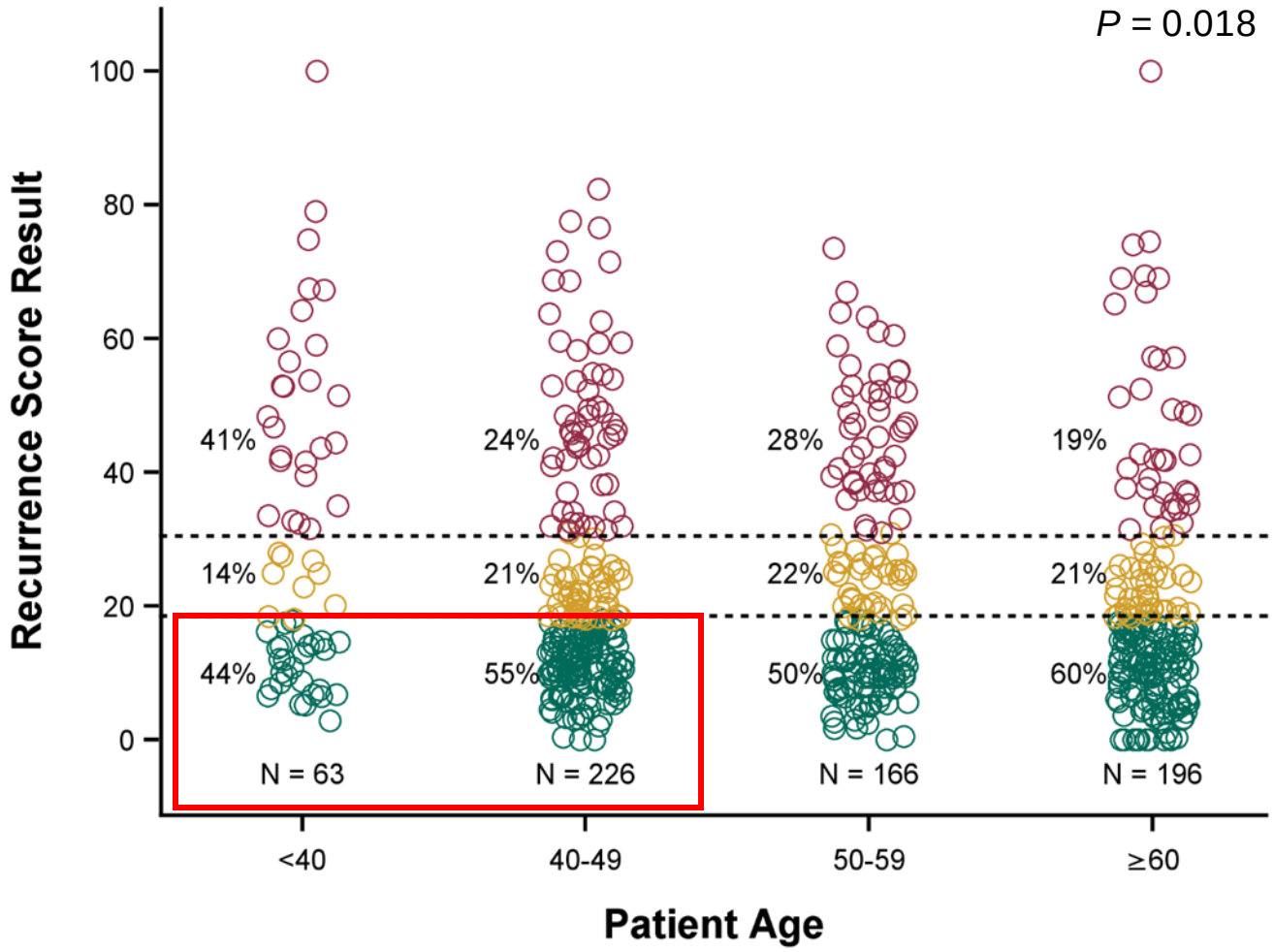
In NSABP B-20, patients with Recurrence Score results 0-17 receiving 5 years of endocrine therapy did not benefit from the addition of chemotherapy.



Sparano et al. *N Engl J Med.* 2018; Paik et al. *J Clin Oncol*. 2006.

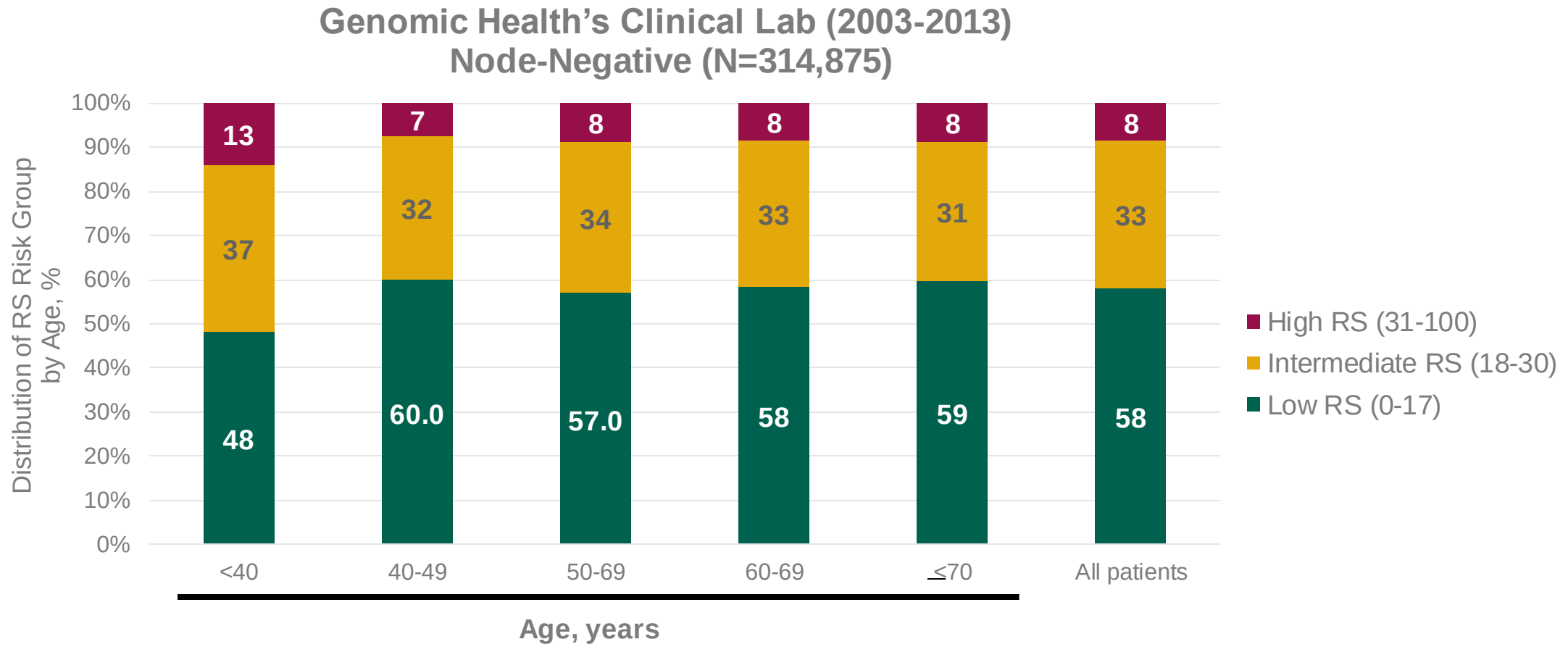
Majority of Patients <50 Years Have Low Recurrence Score® Results

NSABP B-20, <50 years N=289 (44%)



Paik et al. *J Clin Oncol*. 2006.

Majority of ER-positive, HER2-negative Women <40 Years Have Low Recurrence Score® Results



Even the youngest patients (<40 years) have a high percentage (48.3%) of low-risk (0-17) Recurrence Score results

Swain et al. *Adv Ther*. 2015.

RS: Recurrence Score result

Many Women ≤50 Years Have Low Recurrence Score® Results

TAILORx

	All Patients (N=9719)	Recurrence Score Result of 0-10	Recurrence Score Result of 11-25	Recurrence Score Result of 26-100
		Endocrine Therapy (N=1619)	Endocrine Therapy or Chemoendocrine Therapy (N=6711)	Chemoendocrine Therapy (N=1389)
Median Age (Range) – years	56 (23-75)	58 (25-75)	55 (23-75)	56 (23-75)
≤40 years total no. (%)	448 (5%)	58 (4%)	311 (5%)	79 (6%)
41-50 years total no. (%)	2606 (27%)	371 (23%)	1905 (28%)	330 (24%)

Of the 3054 (31%) TAILORx patients ≤50 Years, 2645 (87%) had low Recurrence Score results (0-25)

Sparano et al. *N Engl J Med* 2018; Genomic Health (data on file).

RS: Recurrence Score® result

TAILORx 2018 Exploratory Analysis of Chemotherapy Treatment Interactions in Recurrence Score® Result 11-25 Arms

Statistically significant chemotherapy treatment interactions

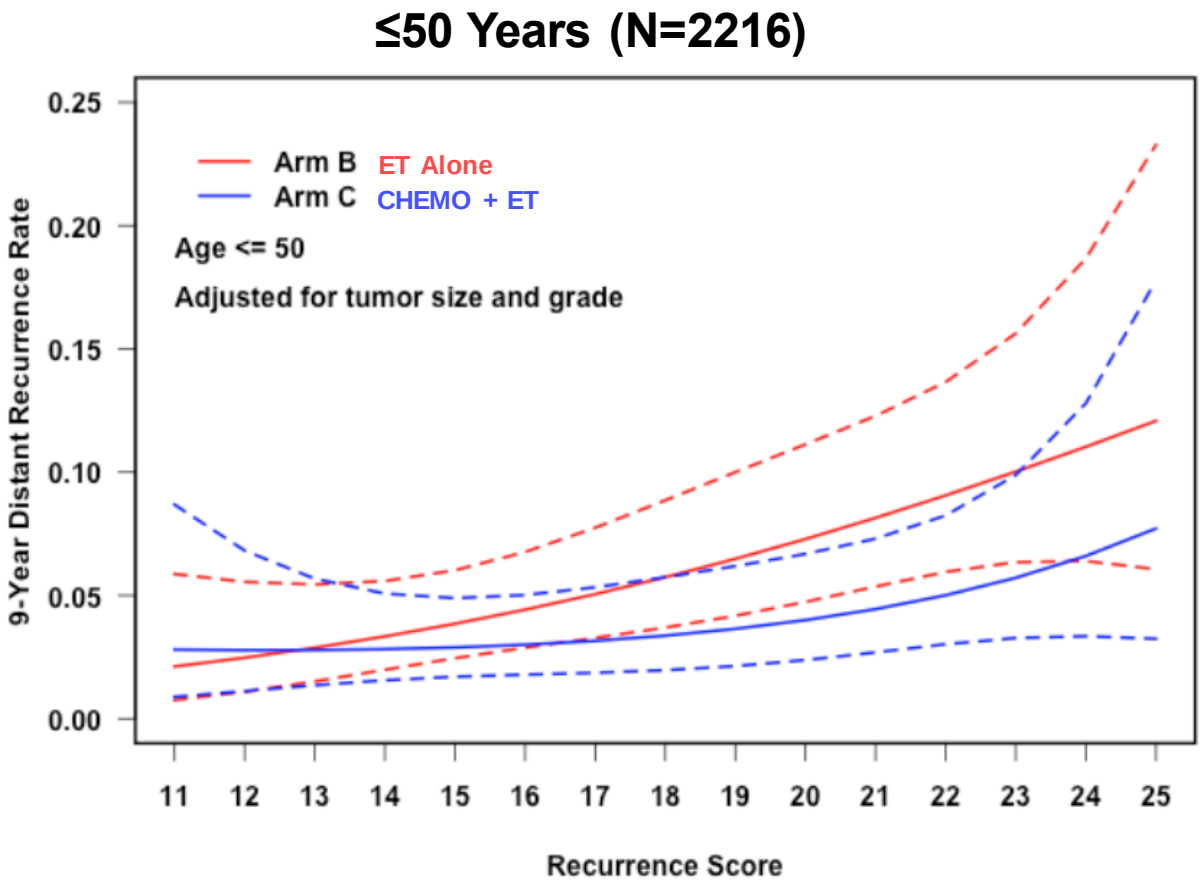
- Age (≤50, 51-65, >65) and chemotherapy benefit
  - IDFS (p=0.03)
  - RFI (p=0.02)
- Age (or menopause), Recurrence Score result (11-15, 16-20, 21-25), and chemotherapy benefit
  - IDFS - Age-Recurrence Score result (p=0.004)
  - IDFS - Menopause-Recurrence Score result (p=0.02)

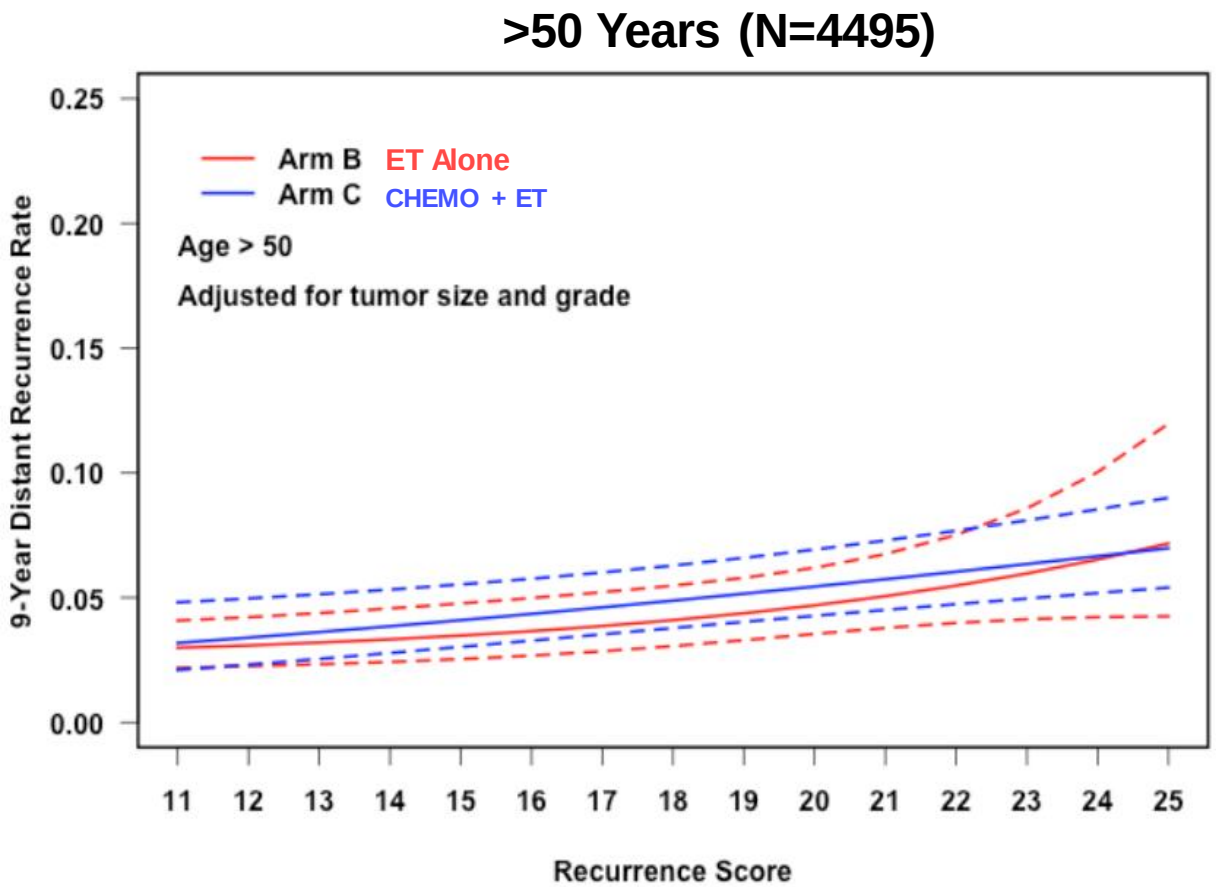
There was no statistically significant chemotherapy treatment interaction seen with patient age and Recurrence Score result for distant recurrence–free interval

Sparano et al. *N Engl J Med.* 2018.

IDFS: invasive disease free survival
RFI: recurrence free interval

TAILORx 2018: Association Between Continuous Recurrence Score® Results 11-25 and 9-Year Distant Recurrence Rate by Treatment Arms Stratified by Age





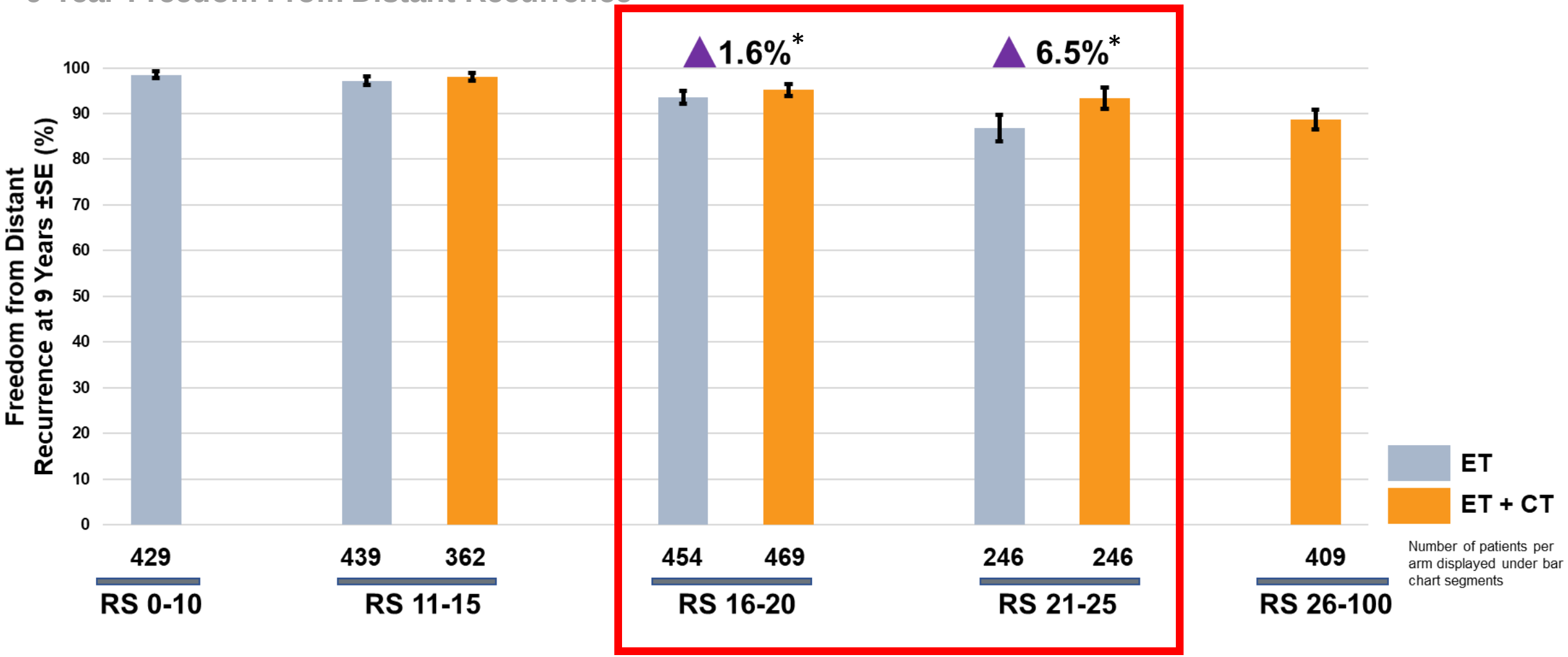
The magnitude of chemotherapy benefit in patients ≤50 years increases with increasing Recurrence Score result, but was not statistically significant

Sparano et al. *N Engl J Med.* 2018.

ET: endocrine therapy

TAILORx Results: A Small Chemotherapy Benefit is Seen in Women ≤50 Years (N = 3054) With Recurrence Score® Results 16-20 and 21-25

9-Year Freedom From Distant Recurrence

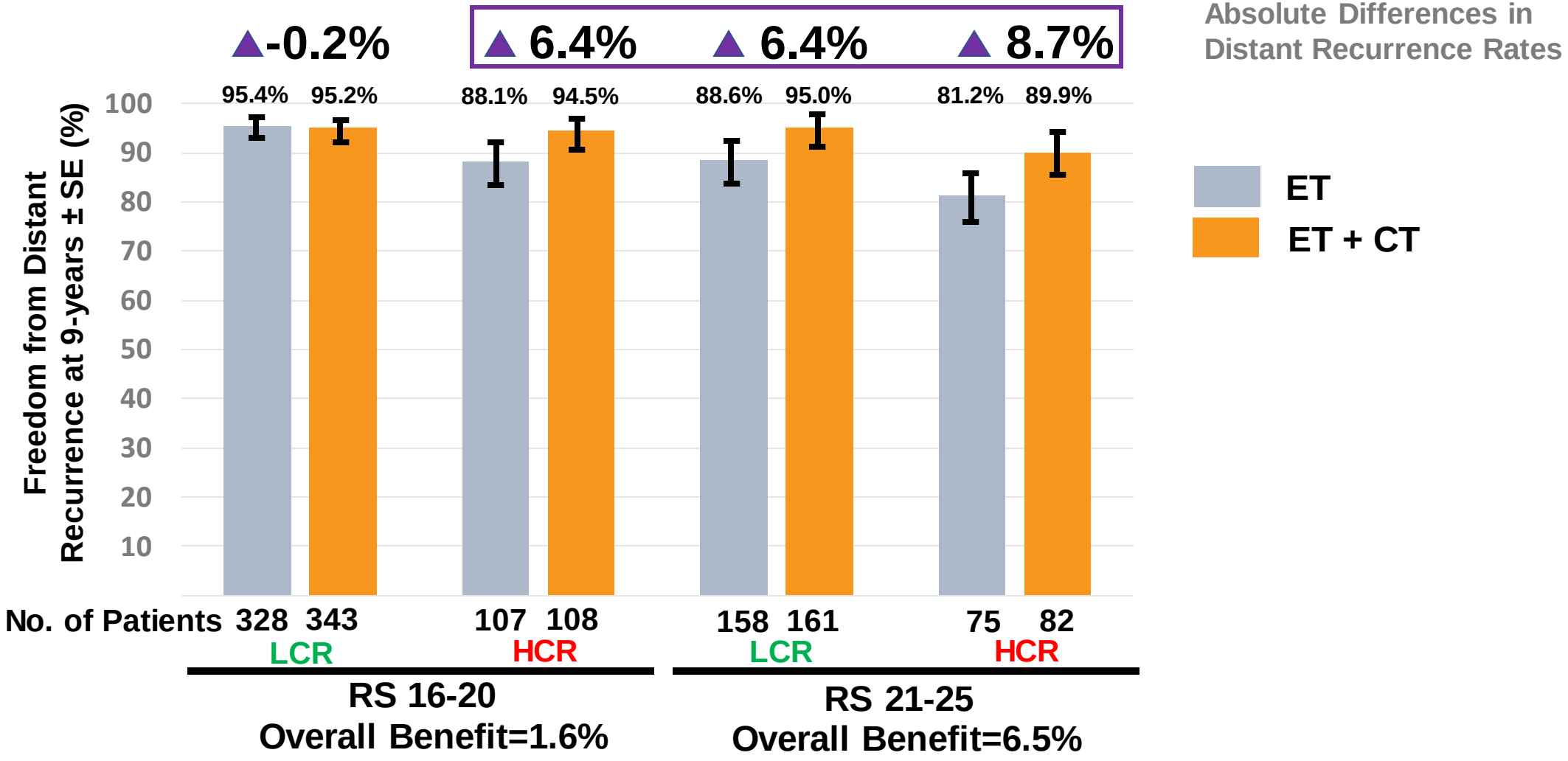


*These differences in distant recurrences, while not statistically significant, may be clinically significant.

ET: endocrine therapy
CT: chemotherapy
RS: Recurrence Score results

Sparano et al. *N Engl J Med.* 2018.

Chemotherapy Benefit Observed in Women ≤50 Years With Recurrence Score® Results 16-20 & High Clinical Risk or RS Results 21-25 Regardless of Clinical Risk



No CT benefit observed in women ≤50 years with RS Results 16-20 & low clinical risk

LCR: low clinical risk
HCR: high clinical risk

RS: Recurrence Score results; ET: endocrine therapy; CT: chemotherapy; ET + CT: chemoendocrine therapy

Sparano et al. *N Engl J Med.* 2019.

CASE STUDY

NODE
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Patient	41 year old
Tumor Size	2.5 cm
Menopausal	Premenopausal
Tumor Type	Invasive ductal carcinoma
ER Status (IHC)	Positive
PR Status (IHC)	Positive
HER2/NEU Status	Negative
Histologic Grade	3
Lymph Node Status	Negative
General Health	Good
Other Information	Patient would be considered high clinical risk by tumor size & grade

CASE STUDY

41 year old patient, high clinical risk (HCR)

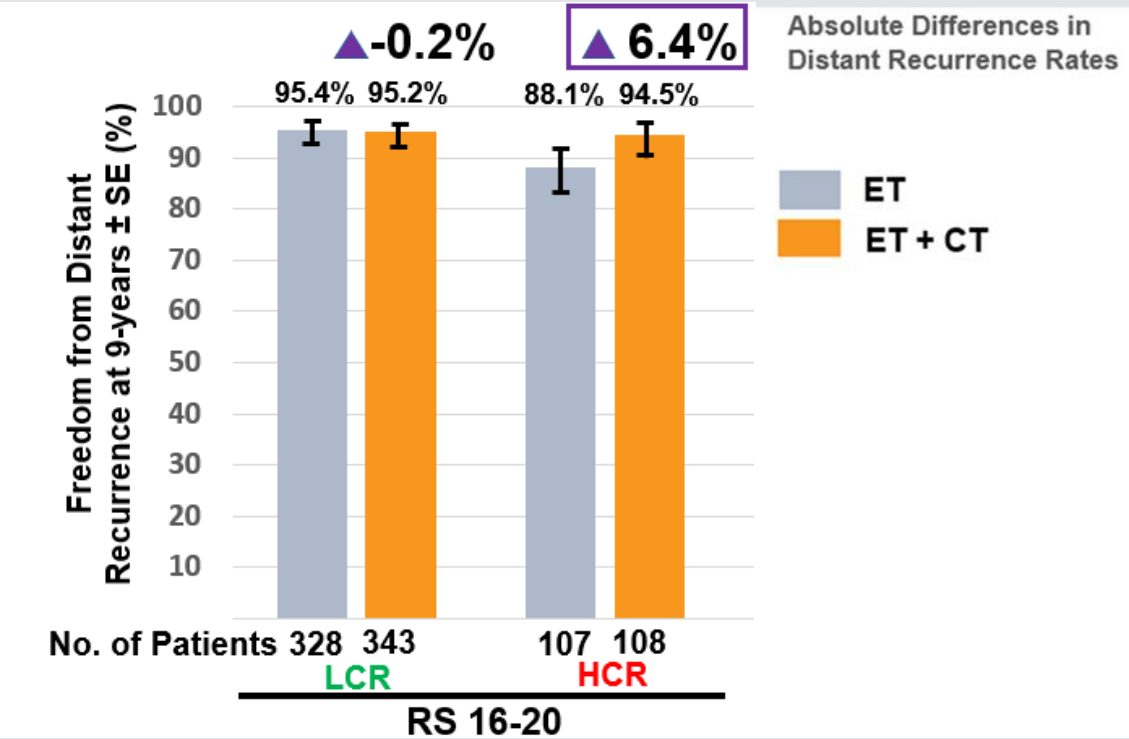
RESULTS

Recurrence Score® Result

17

Subgroup Age ≤50 Years

RS 0-10	RS 11-15	RS 16-20	RS 21-25	RS 26-100
No CT Benefit	No CT Benefit	~1.6% CT Benefit	~6.5% CT Benefit	CT Benefit



Overall CT benefit in patients ≤50 years with Recurrence Score results 16-20 is 1.6%:

- If LCR = no CT benefit
- If HCR, CT benefit = 6.4%

CT: chemotherapy
RS: Recurrence Score results
LCR: low clinical risk
HCR: high clinical risk

Sparano et al. *N Engl J Med.* 2018.; Sparano et al. *N Engl J Med.* 2019.

CASE STUDY

NODE
[-]

AGE
41

Patient	41 year old
Tumor Size	1 cm
Menopausal	Premenopausal
Tumor Type	Invasive ductal carcinoma
ER Status (IHC)	Positive
PR Status (IHC)	Positive
HER2/NEU Status	Negative (2+ by IHC, 1.0 by FISH)
Histologic Grade	2
Lymph Node Status	Negative
General Health	Good
Other Information	Patient would be considered low clinical risk by tumor size & grade

CASE STUDY

41 year old patient, low clinical risk (LCR)

RESULTS

Recurrence Score® Result

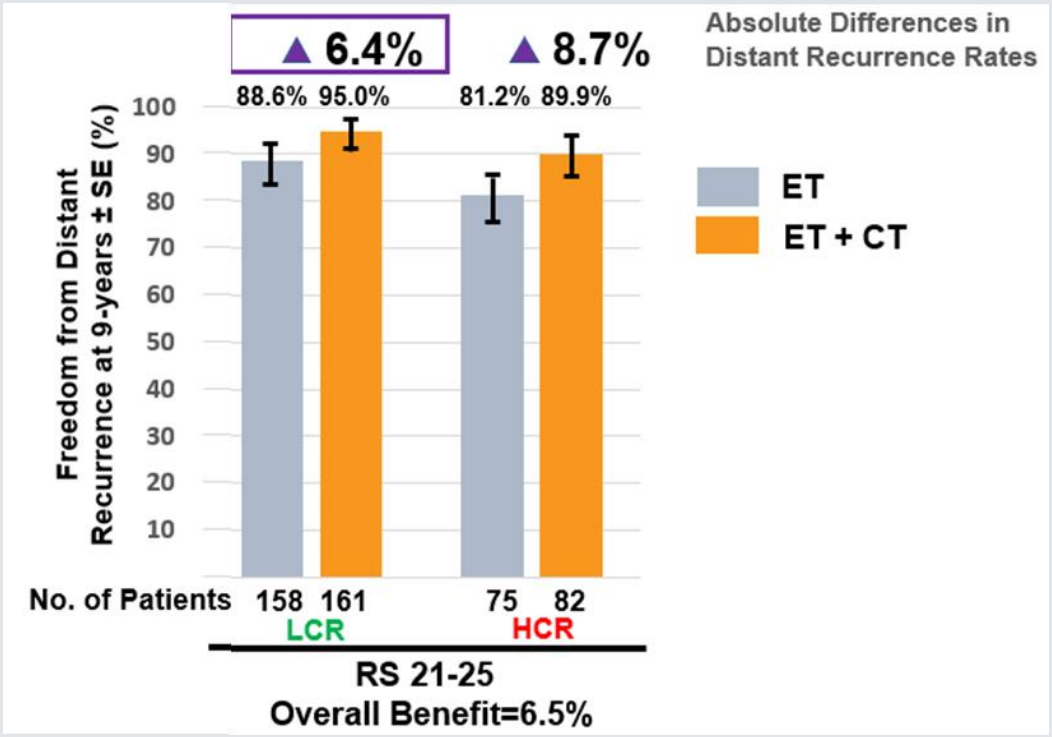
22

Subgroup Age ≤50 Years

RS 0-10	RS 11-15	RS 16-20	RS 21-25	RS 26-100
No CT Benefit	No CT Benefit	~1.6% CT Benefit	~6.5% CT Benefit	CT Benefit

Overall CT benefit in patients ≤50 years with Recurrence Score results 21-25 is 6.5%:

- If LCR, CT benefit = 6.4%
- If HCR, CT benefit = 8.7%



CT: chemotherapy
RS: Recurrence Score results
LCR: low clinical risk
HCR: high clinical risk

Sparano et al. *N Engl J Med.* 2018.; Sparano et al. *N Engl J Med.* 2019.

TAILORx Exploratory Subgroup Analysis Reinforces Evidence to Predict With Precision Which Patients Are More Likely to Benefit From Chemotherapy

Total patients N=9719	RS 0-10 N=1619	RS 11-15 N=2373	RS 16-20 N=2712	RS 21-25 N=1626	RS 26-100 N=1389
Age >50 years N=6665 (68.6%)	No CT Benefit N=1190 (12.2%)	No CT Benefit N=1572 (16.2%)	No CT Benefit N=1789 (18.4%)	No CT Benefit N=1134 (11.7%)	**CT Benefit** **N=980 (10.1%)**
Age ≤50 years N=3054 (31.4%)	No CT Benefit N=429 (4.4%)	No CT Benefit N=801 (8.2%)	**1.6% CT Benefit** **N=923 (9.5%)**	**6.5% CT Benefit** **N=492 (5.1%)**	**CT Benefit** **N=409 (4.2%)**

% out of total patients.

Patients ≤50 years

Low clinical risk	No CT benefit N=671*	**~6.4% CT benefit** **N=319***
High clinical risk	**~6.5% CT benefit** **N=215***	**~8.7% CT benefit** **N=157***

*Clinical risk data were not available for 3% of patients enrolled in TAILORx. The patient count (N = *) reflects those with available clinical risk parameters.

Sparano et al. *N Engl J Med.* 2018; Paik et al. *J Clin Oncol*. 2006; Sparano and Paik. *J Clin Oncol*. 2008; Sparano et al. *N Engl J Med* 2019.

RS: Recurrence Score® result

Conclusions

- **Tumor grade, tumor size and patient age are prognostic only and do not predict chemotherapy (CT) benefit**
- Wide distribution of Recurrence Score results found in all patient subgroups, reinforcing that clinical/pathologic features alone are not sufficient to determine CT benefit or predict the Recurrence Score® result
- Clinical risk category (tumor size & grade) provides additional prognostic information but does not provide predictive information for CT benefit observed with Recurrence Score results 11-25
- TAILORx exploratory analyses suggest women ≤50 years with Recurrence Score results 16-25 can derive some benefit from chemotherapy
  - Chemotherapy benefit is observed with Recurrence Score results 16-20 and high clinical risk or Recurrence Score results 21-25 regardless of clinical risk

Oncotype DX Breast Recurrence Score® Test is the only biomarker proven to be prognostic & predictive of CT benefit for ER-positive, HER2-negative patients

Consistent Inclusion of 21-Gene Assay (Oncotype DX Breast Recurrence Score® Test) in National Treatment Guidelines

Node-Negative, Hormone Receptor-Positive, HER2-Negative Invasive Breast Cancer

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)

(pT1-3, pN0) → Tumor >0.5 cm → Strongly consider 21-gene assay

RS* 0-25	Adjuvant endocrine therapy*
RS 26-30	Adjuvant endocrine therapy or Adjuvant chemotherapy followed by endocrine therapy
RS 31-100	Adjuvant endocrine therapy + adjuvant chemotherapy

***In the TAILORx study, exploratory analyses of patients ≤50 years with RS results 16-25 revealed lower distant recurrence rates for those randomized to chemoendorine therapy; adjuvant chemotherapy may be considered for these patients.**

ASCO® Guidelines

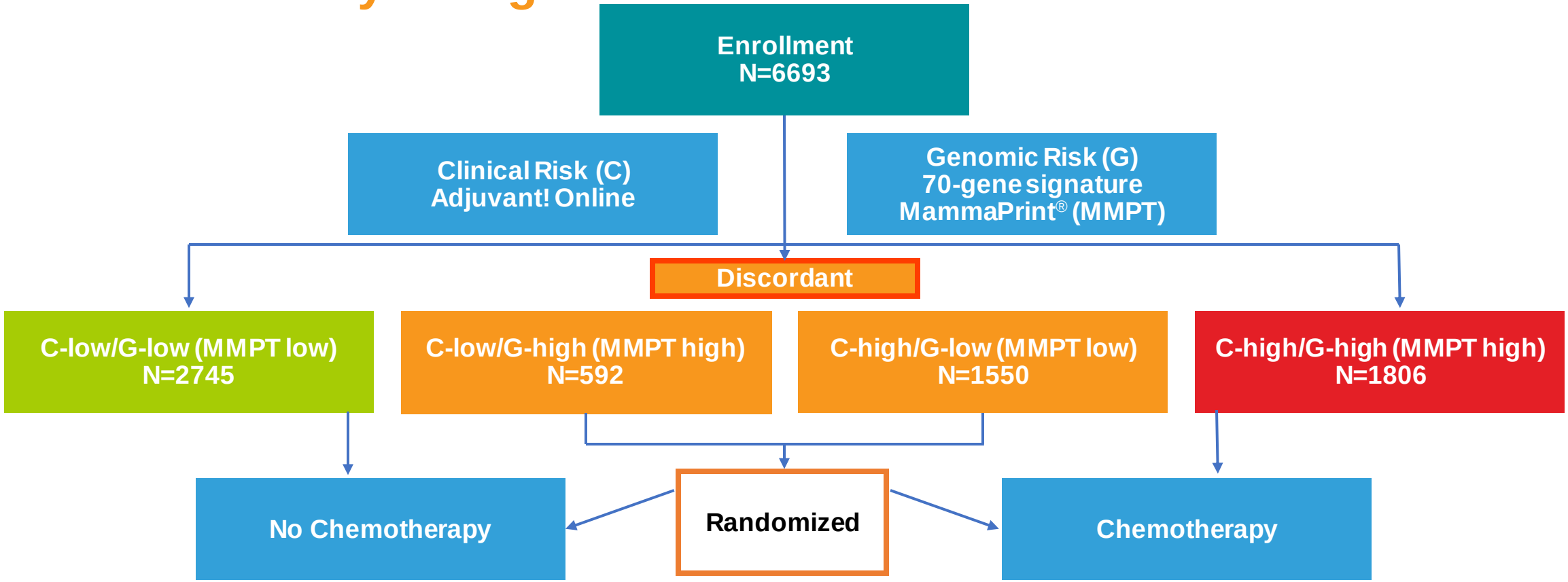
Patients	Recommendation
RS 0-25, Age >50 RS 0-15, Age ≤50	May offer endocrine therapy alone
RS 16-25, Age ≤50	May offer chemoendocrine therapy
RS 31-100, All Ages	Should be considered for chemoendocrine therapy
RS 26-30, All Ages	May offer chemoendocrine therapy

*RS: Recurrence Score® result

Andre et al. *J Clin Oncol.* 2019.

MINDACT – MammaPrint® in Patients <50 Years

MINDACT: Study Design



"We sought to provide prospective evidence of the clinical utility of the addition of the 70-gene signature to standard clinical–pathological criteria in selecting patients for adjuvant chemotherapy."

Modified from Cardoso et al. *N Engl J Med.* 2016.

MINDACT: Primary Objective Was Met

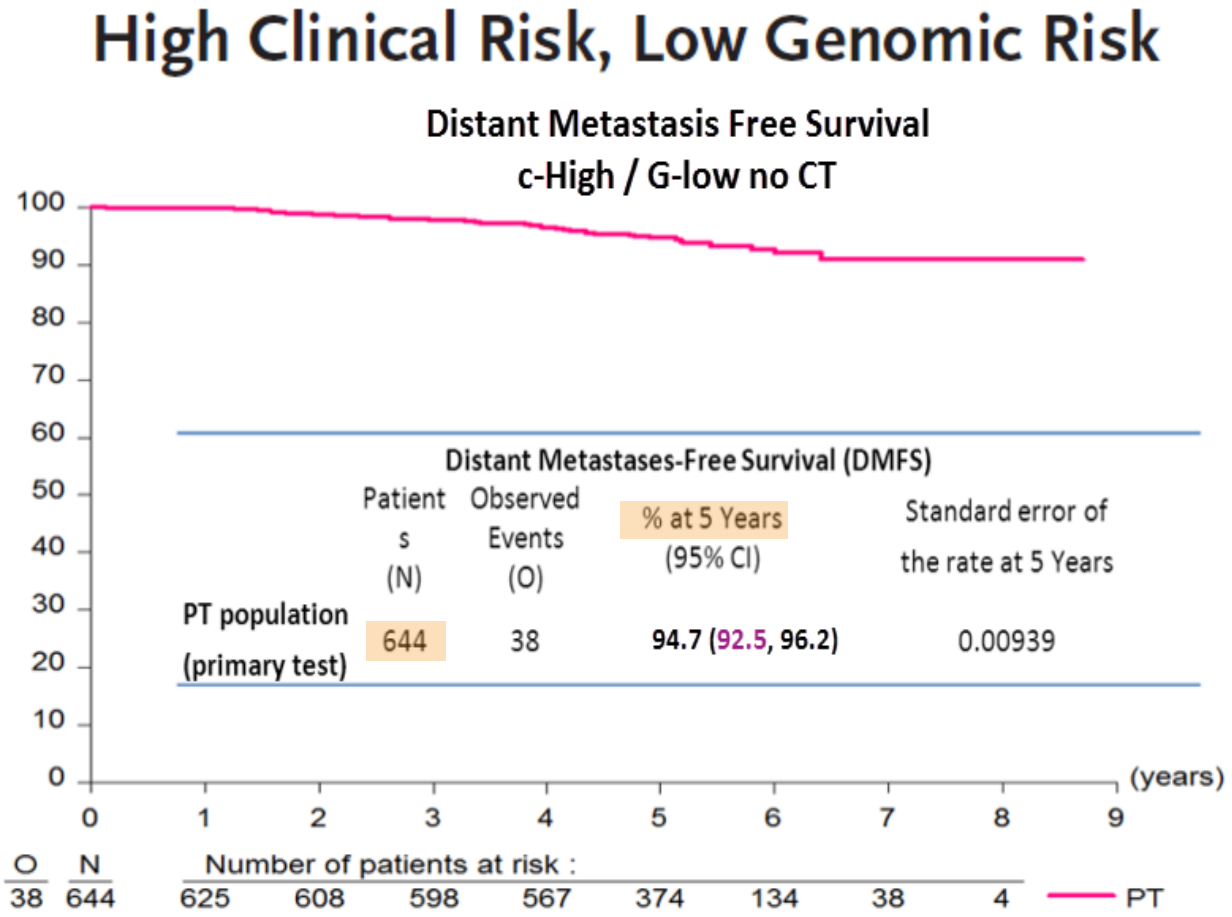
5-Year Rate of Distant Metastasis–Free Survival (DMFS)

Primary Objective:
In patients with high clinical risk, low genomic risk (no chemotherapy), is the lower boundary of the 95% confidence interval (CI) for the rate of 5-year DMFS 92% or higher?

Yes, patients not treated with chemotherapy (CT) had a **5-year DMFS rate** of: 94.7% (95% CI, **92.5** to 96.2)

Heterogeneous primary test population:

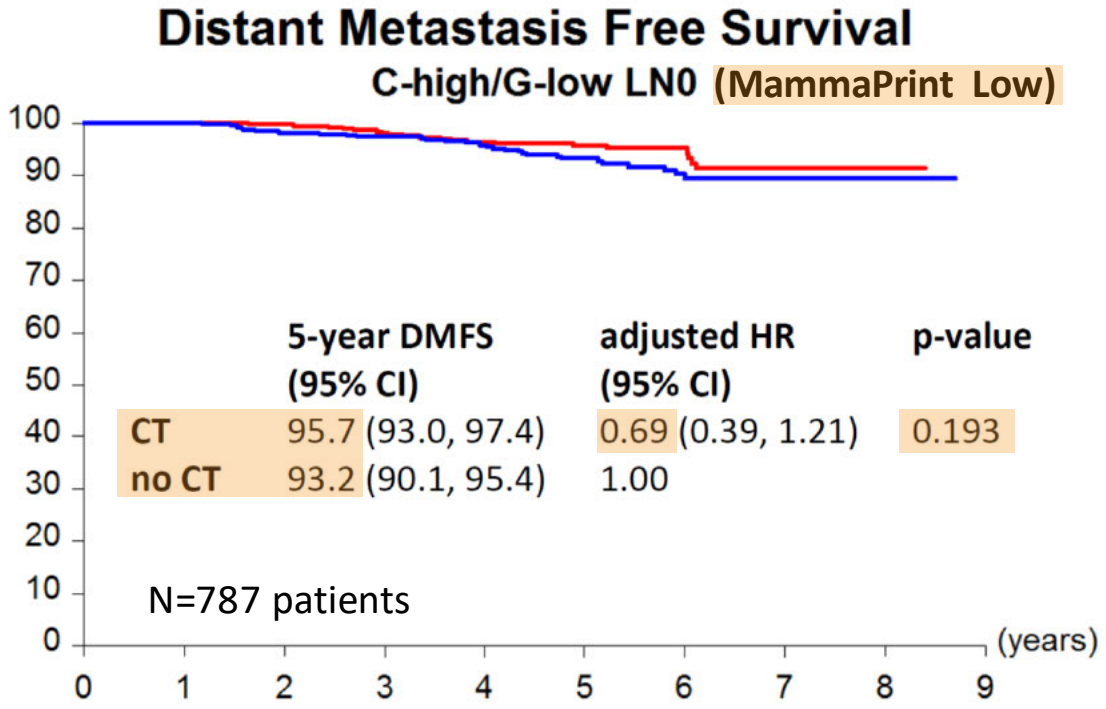
- N0, N1, N2
- ER/PR+, ER-/PR-
- HER2+ & HER2-



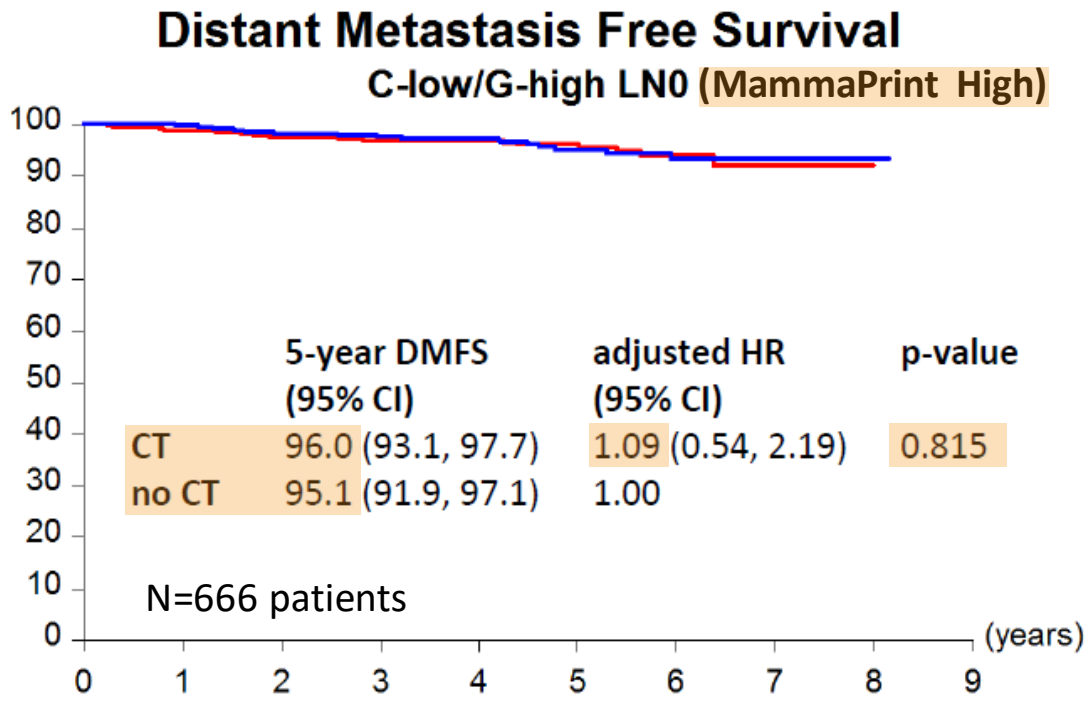
ER: estrogen receptor
HER2: human epidermal growth factor receptor 2
PR: progesterone receptor
CI: confidence interval

Cardoso et al. *N Engl J Med.* 2016.; Piccart et al. AACR. 2016.

MINDACT: MammaPrint® Has Not Been Show to be Predictive of Chemotherapy Benefit in Node-Negative Patients – ITT Population



Despite low-risk MammaPrint results, patients show a trend towards chemotherapy benefit (31% risk reduction)



Despite high-risk MammaPrint results, patients receive no benefit from chemotherapy

DMFS: distant metastasis–free survival
ITT: intent-to-treat population
CT: chemotherapy
CI: confidence interval

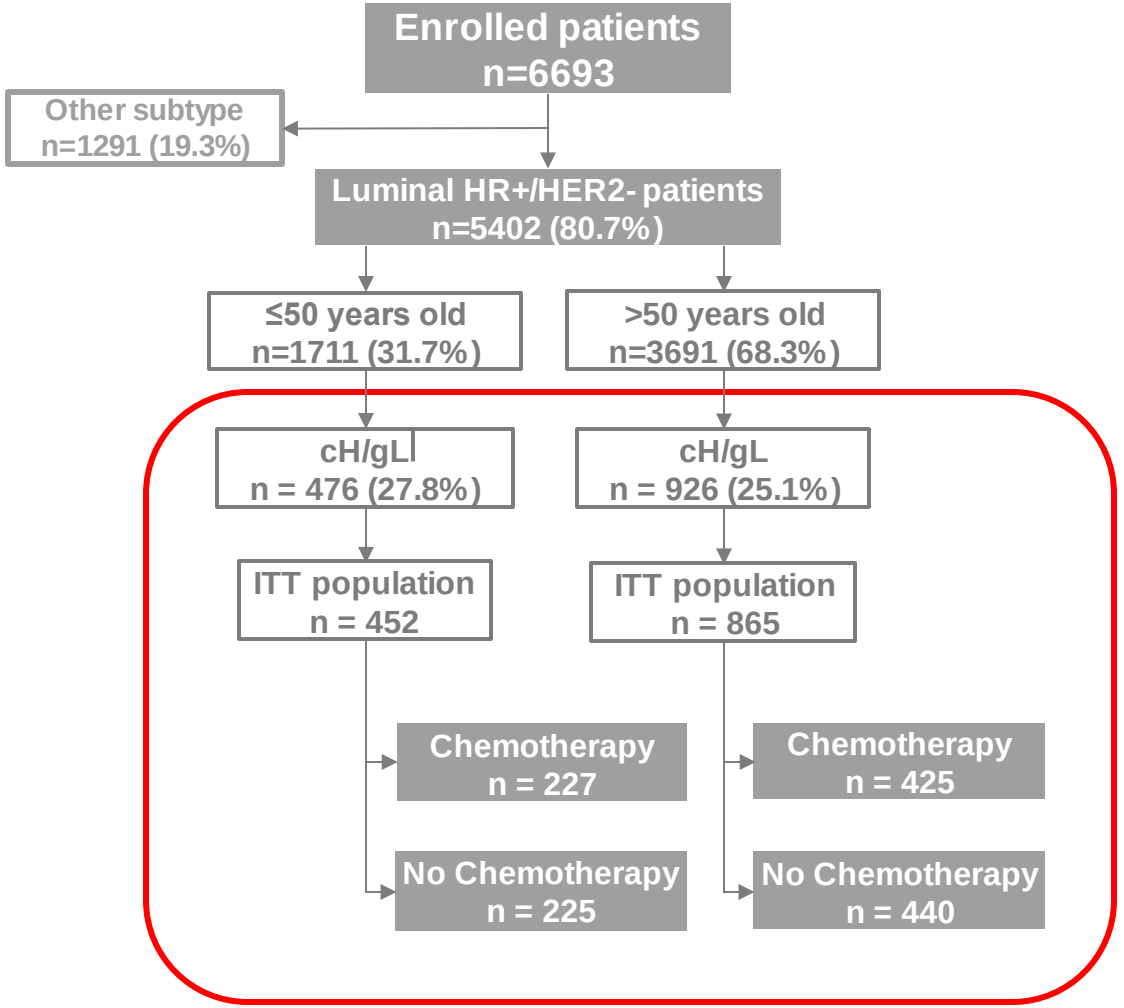
Cardoso et al. *N Engl J Med.* 2016.

MINDACT Luminal Breast Cancer Age Analysis

SABCS 2019

- **Analysis ITT population (1317 pts):**

- C-High/G-Low (452 and 865 pts)
- Chemotherapy vs no chemotherapy analyzed for both age cohorts:
  - ≤50 years
  - >50 years



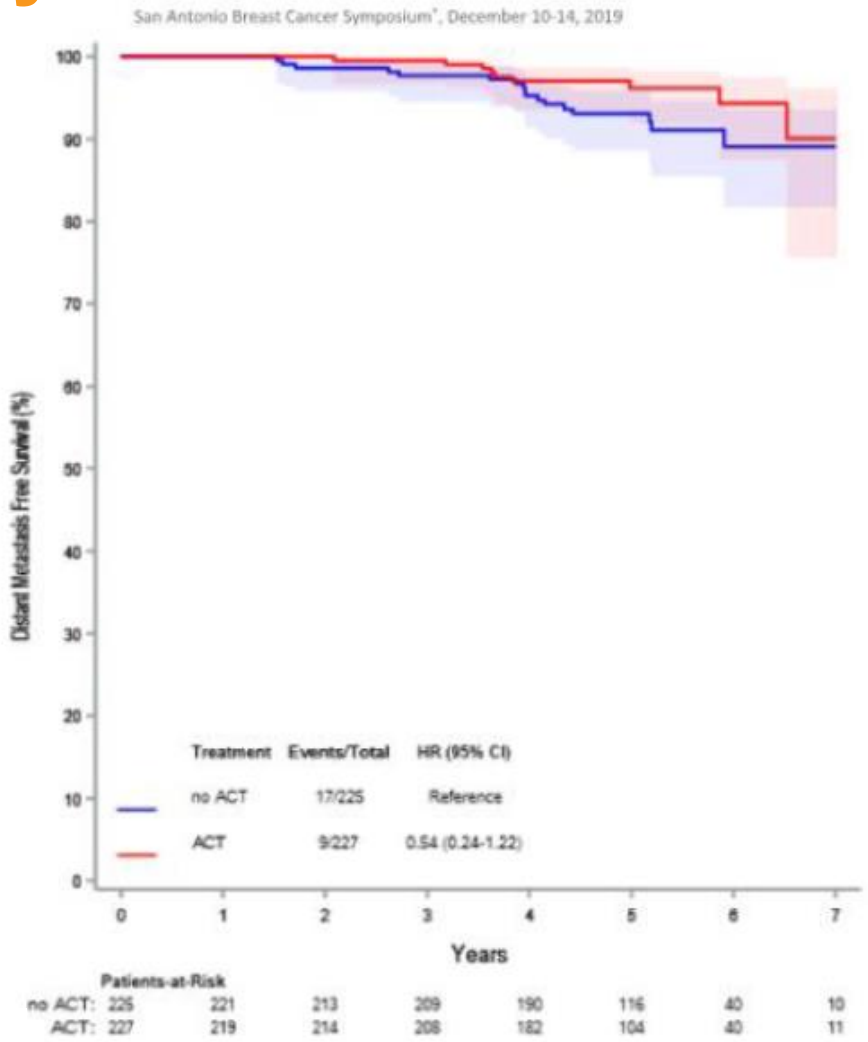
Piccart et al. SABCS 2019.

MammaPrint® Has No Clinical Utility for Patients ≤50 Years

Patients ≤50 Years

Treatment	Event/Total	Hazard Ratio (95% CI)	5-Year DMFS (95% CI)
No ACT	17/225	Ref	93.1 (88.6-95.8%)
ACT	9/227	0.54 (0.24-1.22)	96.1 (91.9-98.2%)

Despite having low MammaPrint results, patients saw **3% reduction in DMFS** with chemotherapy



Piccart et al. SABCS 2019.

CI: confidence interval
ACT: adjuvant chemotherapy; DMFS: distant metastasis-free survival

Conclusions

- **TAILORx data have allowed greater confidence in ordering the Oncotype DX® test in young women. However, with any landmark study, more questions are asked:**
  - Is it really safe to avoid chemotherapy in young women with early breast cancer? What about node +?
  - Is a different multigene assay superior in helping make the decision regarding chemotherapy?
  - What is the impact of clinical risk (tumor size, grade, and node status) on the use and benefit from chemotherapy?
  - What is the distribution of Recurrence Score® results in young women – don't they all have a high score?
- **These data presented today help to answer some, but not all of these questions**
  - However, there is no better assay out there that can provide the prediction of chemotherapy benefit, nor the guidance as to best systemic therapy than the Oncotype Dx Breast Recurrence Score® test, regardless of age

Thank You