



## **OUTCOME DISPARITIES BY AGE AND 21-GENE RECURRENCE SCORE RESULT IN HORMONE RECEPTOR-POSITIVE (HR+) BREAST CANCER**

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## S. Shak Disclosures

- ◆ Employment: Genomic Health, Inc.
- ◆ Stock ownership: Genomic Health, Inc.

# Breast Cancer in the Elderly

- ◆ Women  $\geq 70$  years are the fastest growing segment of the female population in many countries, driving an unprecedented increase in breast cancer diagnoses in the elderly [1]
- ◆ Older women are under-represented in randomized clinical trials; relatively little is known about their breast cancer characteristics, treatment, and survival [2]
- ◆ Older women have been reported to be undertreated [3]
- ◆ Although breast cancer outcomes in older patients are generally believed to be favorable, the TEAM study in ER+ breast cancer (N=9,766) notably reported recently that disease-specific mortality was generally higher among patients  $\geq 65$  years [4].
- ◆ Unknown whether those worse outcomes are related to biology or treatment.

## Providing “Big Data” Insights into Quality Care and Outcomes Through A New Paradigm of Collaboration Between Government and Industry

- ◆ Multi-gene assays have been incorporated into breast cancer practice to identify patients for adjuvant chemotherapy treatment
- ◆ Recently, prospective outcomes in >50,000 patients treated based on the Oncotype DX Recurrence Score (RS) results have been reported — TAILORx (multinational), SEER (US), Clalit (Israel), and PlanB (Germany) [5-9] — and definitively confirm the clinical validation studies [10-15] and the assay’s value beyond traditional factors of age, tumor size, and grade
- ◆ The SEER program of the NCI [16], which collects data on 30% of US population, and Genomic Health are collaborating, and have committed to report annual updates of SEER patient outcomes
- ◆ Here, we report SEER results for the role of RS biology in older patients and also provide the first report of analyses with an additional year of follow-up beyond the first publication in *npj Breast Cancer* [6]

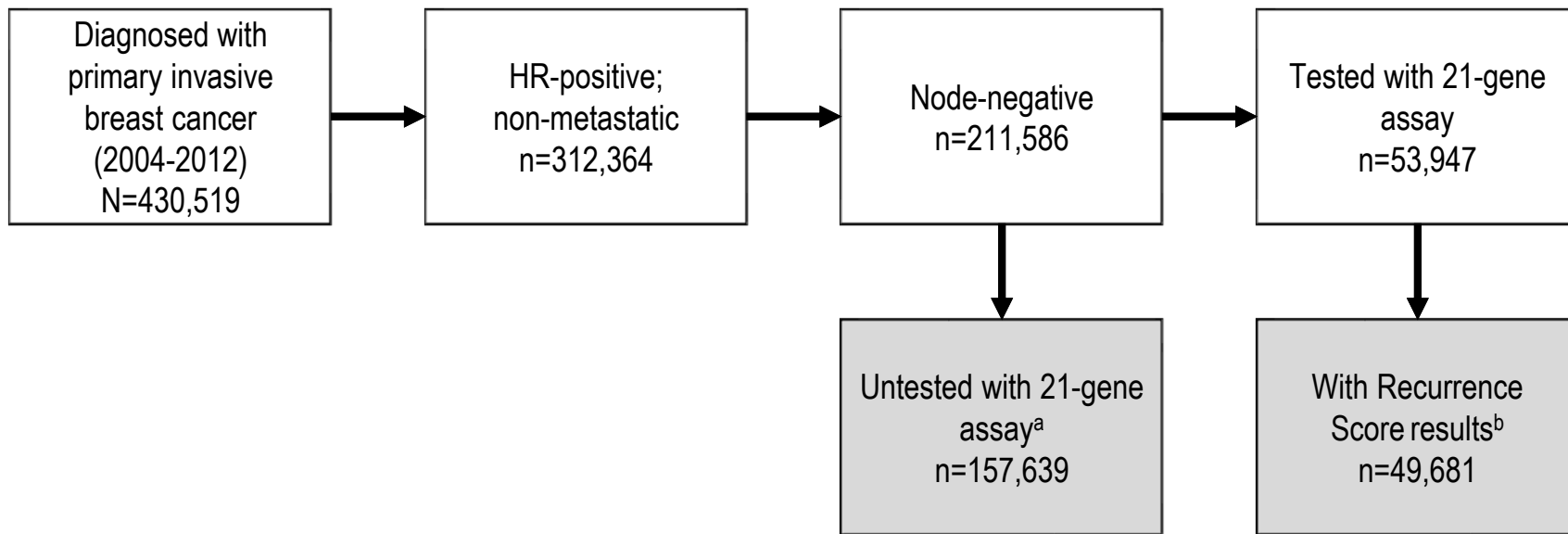
# Specific Objectives

- ◆ Evaluate population of newly diagnosed N0, HR+ invasive breast cancer:
  - ◆ 21-gene assay testing by age
  - ◆ Known chemotherapy (CT) use by age
  - ◆ Prospective breast cancer-specific mortality (BCSM) outcomes by RS results, patient age, and clinical-pathologic covariates

# Methods

- ◆ SEER demographics, tumor characteristics, reported CT use, and BCSM available through 2013
- ◆ Genomic Health provided RS electronically to SEER, per registry operations
- ◆ Analysis population: N0, HR+ (by SEER and RT-PCR), HER2-negative (by RT-PCR), diagnosed between January 2004 and December 2012
  - ◆ Excluded: N+, prior invasive tumors, or concurrent multiple tumors
- ◆ RS groups standard cutpoints (18, 31)
- ◆ Actuarial estimates of survival (cause-specific and overall) and BCSM computed through 5 years with 95% CI
- ◆ The log-rank test was used to compare the three RS groups

# SEER Population - STROBE Diagram



- a. Untested cohort without RS results includes patients with HER2+ breast cancer because HER2 status was not reported to SEER before 2010.
- b. Tested cohort with RS results excludes patients with HER2+ breast cancer, based on 21-gene assay quantitative single-gene HER2 result. Median follow-up for younger (<70 years) and older (≥70 years) patients were 45 and 40 months, respectively.

# Patient Testing and Demographics

		Age <70 years		Age ≥70 years	
		Tested (N=43,693)	Not Tested (N=100,519)	Tested (N=5,988)	Not Tested (N=57,120)
		%	%	%	%
Sex <sup>a</sup>	Female	99	99	99	99
Race	White	84	81	87	87
	Black	8	9	7	7
	Asian or Pacific Islander	8	10	5	6
	Am. Indian/Alaska Native	<1	<1	<1	<1
Socioeconomic status, quintile	Lowest SES	11	13	15	14
	Second lowest SES	15	17	17	18
	Middle SES	19	20	21	21
	Second highest SES	23	23	23	22
	Highest SES	32	28	25	25

- Testing occurred 3.2 times less frequently in patients ≥70 years
- Testing rates were similar by race and socioeconomic status



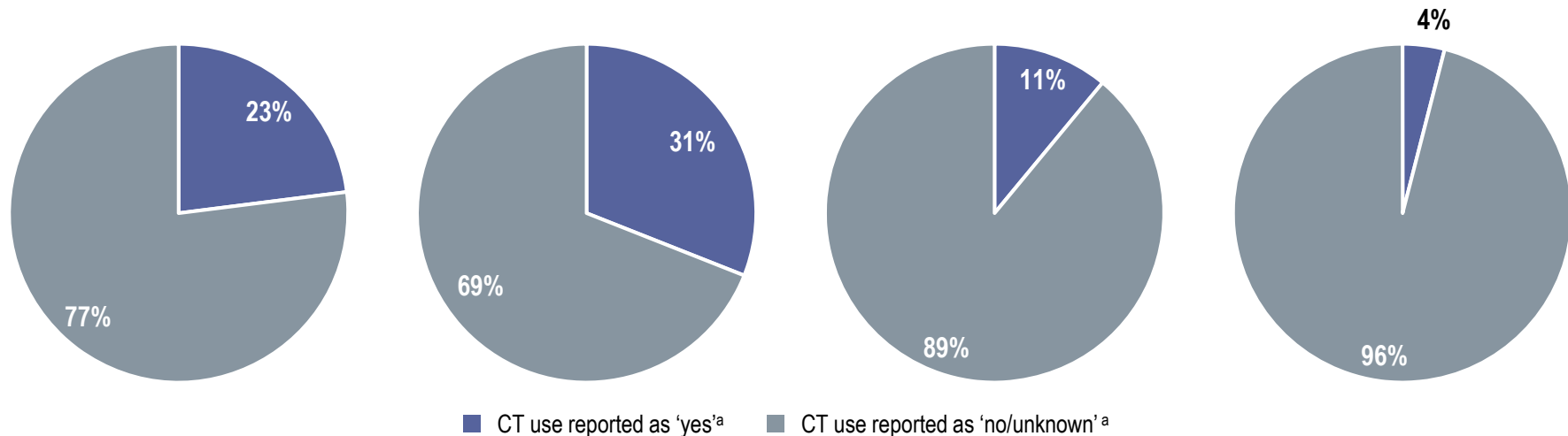
# Tumor Characteristics

		Age <70 years		Age ≥70 years	
		Tested (N=43,693)	Not Tested (N=100,519)	Tested (N=5,988)	Not Tested (N=57,120)
		%	%	%	%
Tumor grade	Well Differentiated	29	32	25	35
	Moderately Differentiated	54	44	55	49
	Poorly Differentiated	17	24	19	16
Tumor size, mm	≤5	3	17	2	11
	>5-10	22	25	17	26
	>10-20	53	34	49	39
	>20-40	19	19	27	19
	>40	2	5	4	5

- Testing was performed in a wide range of patients, consistent with guidelines
- In patients <70 y, testing higher in moderately differentiated tumors and tumors 10-20 mm
- In patients ≥70 y, testing lower in well differentiated tumors and tumors 10 mm or less

# Reported Chemotherapy (CT) Use

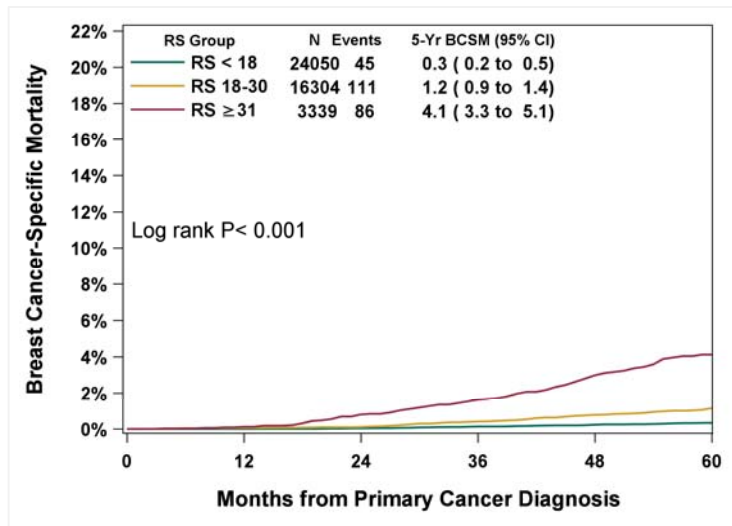
Age <70 years		Age ≥70 years	
Tested (N=43,693)	Not Tested (N=100,519)	Tested (N=5,988)	Not Tested (N=57,120)



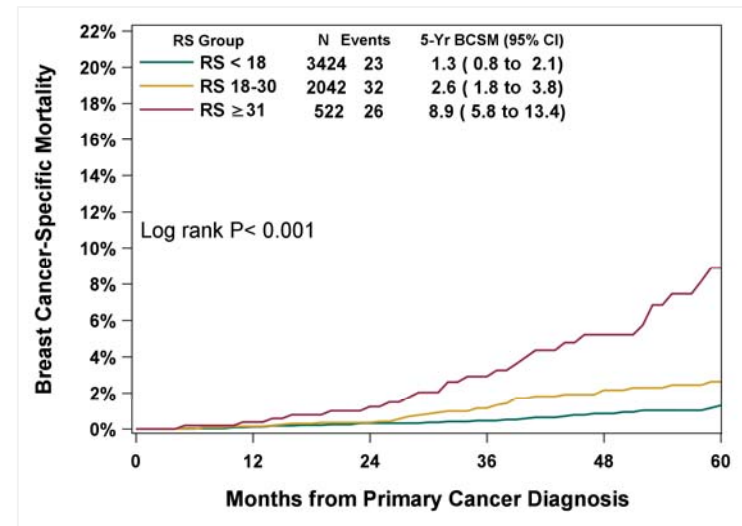
- CT use was lower in patients ≥70 years, in both RS-tested and untested cohorts

# 5-year BCSM by Age and RS Group

Age <70 y



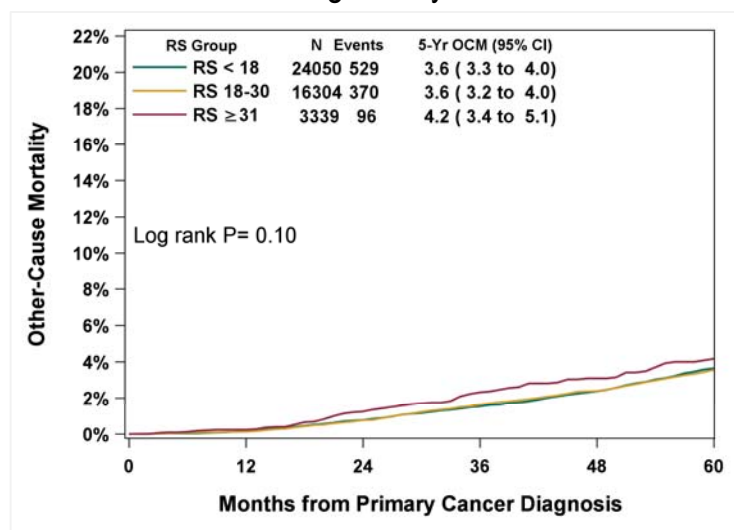
Age ≥70 y



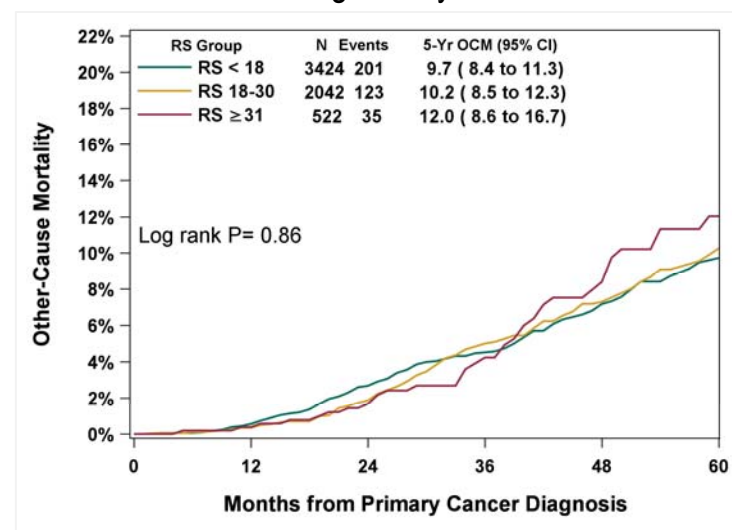
- RS predicts BCSM in both age groups ( $p < 0.001$ )
- Low 5-y BCSM was observed with RS <18 in both age groups
- Higher 5-y BCSM was observed with RS 18-30 and RS  $\geq 31$  in older patients

# 5-year Other-Cause Mortality by Age and RS Group

Age <70 y



Age ≥70 y



- As expected, RS group does not predict other-cause mortality (p=NS)
- As expected, higher other-cause mortality was observed in older patients

## 5-year BCSM (95% CI) by Age in Tested and Untested Patients

	RS < 18			RS 18-30			RS ≥31			Untested		
	N	CT Use <sup>a</sup> (% of N)	5-y BCSM (95% CI)	N	CT Use <sup>a</sup> (% of N)	5-y BCSM (95% CI)	N	CT Use <sup>a</sup> (% of N)	5-y BCSM (95% CI)	N	CT Use <sup>a</sup> (% of N)	5-y BCSM (95% CI)
<70 y	24050	7%	0.3% (0.2%, 0.5%)	16304	37%	1.2% (0.9%, 1.4%)	3339	73%	4.1% (3.3%, 5.1%)	100519	31%	2.3% (2.2%, 2.4%)
≥70 y	3424	2%	1.3% (0.8%, 2.1%)	2042	14%	2.6% (1.8%, 3.8%)	522	52%	8.9% (5.8%, 13.4%)	57120	4%	5.5% (5.2%, 5.7%)
70-74 y	2116	2%	1.1% (0.6%, 2.0%)	1245	17%	2.4% (1.4%, 3.9%)	320	61%	6.2% (3.2%, 11.9%)	17647	8%	2.8% (2.6%, 3.2%)
75-79 y	968	2%	1.9% (0.9%, 4.0%)	590	11%	2.4% (1.1%, 5.2%)	142	43%	11.6% (5.5%, 23.8%)	16445	4%	4.3% (4.0%, 4.7%)
≥80 y	340	1%	1.0% (0.2%, 4.5%)	207	6%	4.8% (2.3%, 9.9%)	60	32%	20.5% (9.6%, 40.6%)	23028	2%	8.6% (8.2%, 9.1%)

- Notably, 5-y BCSM is relatively high in untested patients at all ages; this deserves further study

# Limitations

- ◆ Follow-up time has been relatively short to date; however, since most of the benefit of chemotherapy, if any, is observed in the first five years, and 5-year BCSS predicts 10- and 15-year BCSS [17], these results are highly relevant to the chemotherapy decision at diagnosis
- ◆ Longer follow-up is needed to address questions on duration of hormonal therapy
- ◆ Chemotherapy use is under-reported to SEER
- ◆ Other molecular signatures for breast recurrence risk were not included in this analysis
  - ◆ 21-gene assay majority (>93%) of tests in manually reported SEER data (2010-2012)

# Summary

- ◆ The 21-gene Recurrence Score assay significantly predicts prospective 5-year BCSM outcomes in a population-based study of >49,000 patients with N0, HR+ breast cancer
- ◆ Low 5-year BCSM was observed for patients with RS results <18, regardless of age and despite only a small proportion reporting chemotherapy use as 'yes'
- ◆ 5-year BCSM was higher for patients  $\geq 70$  years, especially for those with RS results  $\geq 31$
- ◆ Older patients were less frequently tested than younger patients

# Conclusions

- ◆ This population-based SEER analysis of N0, HR+, HER-negative breast cancer represents the largest report of prospective outcomes in patients 70+ years of age treated based on the 21-gene assay and provides additional evidence that the assay predicts prospective outcomes
- ◆ The study highlights poor outcomes for older patients with intermediate and high RS disease, consistent with the TEAM report and contrary to a societal perception that older women tend to have low-risk disease
- ◆ Global action needs to be taken to understand and address higher breast cancer mortality in older patients and disparities in treatment



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