

Abstract GS4-07

Race, ethnicity, and clinical outcomes in hormone receptor-positive, HER2-negative, node-negative breast cancer: results from the TAILORx trial

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Race, ethnicity and clinical outcomes in the TAILORx trial – Background (I)

- Black race is associated with worse outcomes in localized, hormone receptor (HR) positive, HER2-negative breast cancer
- Both population-based and clinical trial cohorts, using either:
 - Self-identified race (Albain et al. JNCI 2009, Sparano et al. JNCI 2012)
 - Genetically-identified race (Schneider et al. J Precision Oncol 2017)
- Disparity persists after adjusting for treatment delivery variables (Hershman et al. JCO 2009)

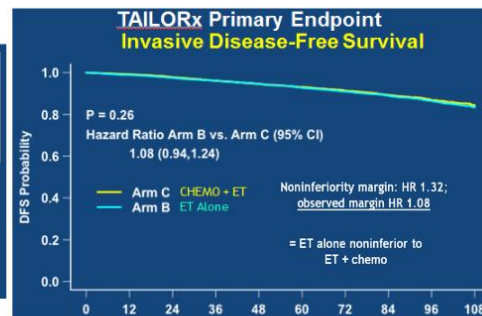
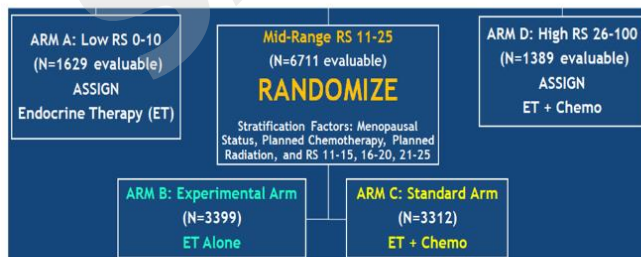
The **T**rial **A**ssigning **I**ndividualized **O**ptions for **T**reatment (TAILORx) is an ideal setting to assess clinical outcomes by race/ethnicity



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Race, ethnicity and clinical outcomes in the TAILORx trial – Background (II)

TAILORx: 9719 evaluable women with HR+, HER2-negative, node-negative tumors assigned or randomized to 4 arms (A-D) based on 21-gene Recurrence Score (RS) assay
(Sparano J, et al. NEJM 2018)



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Race, ethnicity and clinical outcomes in TAILORx – Objectives

- Evaluate the entire population and the combined randomized arms (B+C) for:
 - Clinicopathologic characteristics
 - Treatment delivered
- Assess if the reported lack of chemotherapy benefit in RS 11-25 is also true in race and ethnicity subsets
- Analyze clinical outcomes by race and ethnicity
- Determine if either race or ethnicity is independently prognostic

Race, ethnicity and clinical outcomes in TAILORx – Methods (I)

- Planned analysis of outcomes and treatment effects by race and ethnicity
- Not powered to look at race/ethnicity subsets, so no prospective statistical plan to interpret subset comparisons
- Examined associations between clinical outcomes and race or ethnicity
 - Race** - white, black, Asian, other/unknown
 - Ethnicity** - Hispanic, non-Hispanic
- Used 4 endpoints: invasive disease-free survival (iDFS), relapse-free interval (RFI), distant RFI (DRFI) and overall survival (OS)

Race, ethnicity and clinical outcomes in TAILORx – Methods (II)

- Compared by Wilcoxon, chi-square tests
- Estimated curves by Kaplan-Meier with log-rank p-values not adjusted for other factors
- Fit proportional hazards models in the overall and randomized (RS 11-25) populations, including:
 - Age (5 categories)
 - Tumor size (> or <= 2 cm)
 - Histologic grade (high, medium, low, unknown)
 - Continuous Recurrence Score
 - Race and ethnicity

Race, Ethnicity and Clinical Outcomes in TAILORx RESULTS

TAILORx distributions by race and ethnicity (all arms)

	White n=8189 (84%)	Black n=693 (7%)	Asian n=405 (4%)	Oth/Unk n=432 (4%)	Total n=9719
Ethnicity: Hispanic	770 (11%)	12 (2%)	4 (1%)	103 (47%)	889 (9%)
Not Hispanic	6508 (89%)	632 (98%)	379 (99%)	116 (53%)	7635(79%)
Unk	911	49	22	213	1195(12%)
ARMS A, RS 0-10: ET	1361 (17%)	107 (15%)	82 (20%)	69 (16%)	1619
B, RS 11-25: ET	2883 (35%)	236 (34%)	140 (35%)	140 (32%)	3399
C, RS 11-25: ET+CT	2783 (34%)	235 (34%)	132 (33%)	162 (38%)	3312
D, RS 26-100: ET+CT	1162 (14%)	115 (17%)	51 (13%)	61 (14%)	1389
Adj Chemo: No	4666 (57%)	389 (56%)	241 (60%)	226 (52%)	
Yes	3523 (43%)	304 (44%)	164 (40%)	206 (48%)	

TAILORx distributions all arms (A+B+C+D) combined: clinicopathologic characteristics and RS by race and ethnicity

Significant (p<.01)*

- **Race: black vs. white comparison**
 - Blacks younger (39% vs. 30%, <= 50)
 - More premenopausal (39% vs 33%)
 - Larger tumor size (31% vs. 24% > 2 cm)
 - More poor histologic grade (24% vs. 17%)
 - Higher clinical risk (37% vs. 29%)

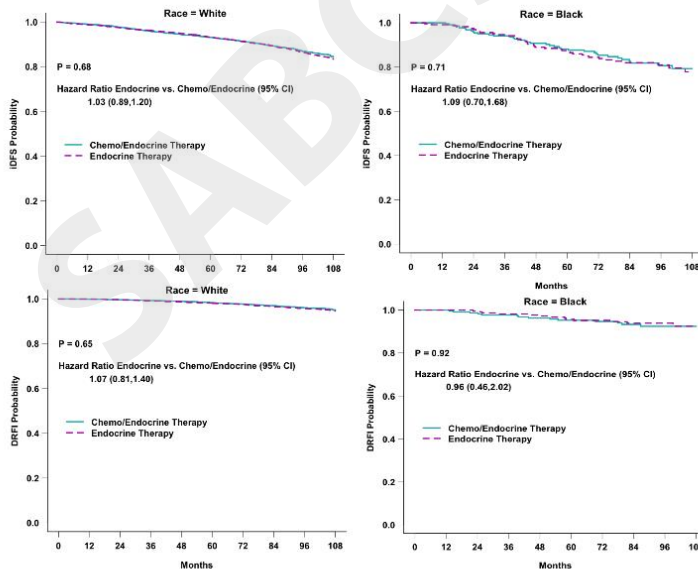
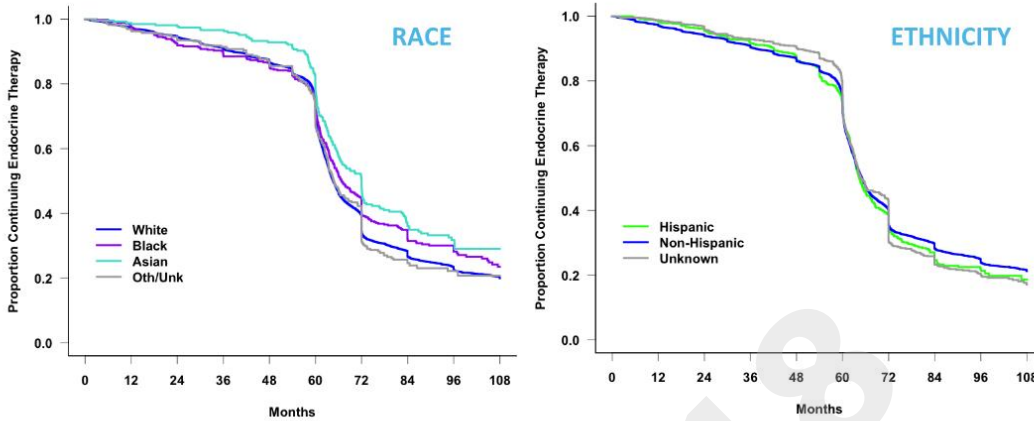
- **Ethnicity: Hispanic vs non-Hispanic**

Hispanics younger (39% vs 30%, <=50)

Not Significant*

- **Continuous RS distribution, median RS and mean RS**
 - Blacks vs. whites
 - Hispanic vs. non-Hispanic
- **Treatment by race or ethnicity**
 - type of chemotherapy
 - type of endocrine therapy (ET)
 - duration of ET (self-report)

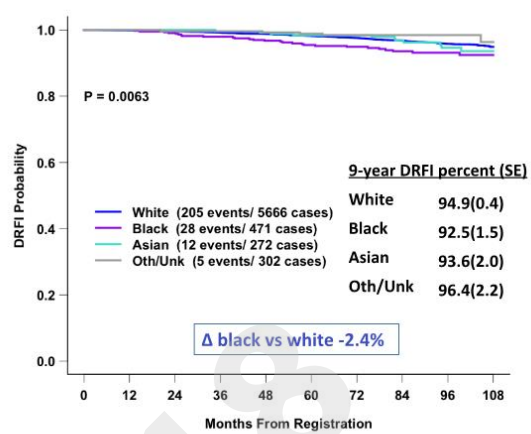
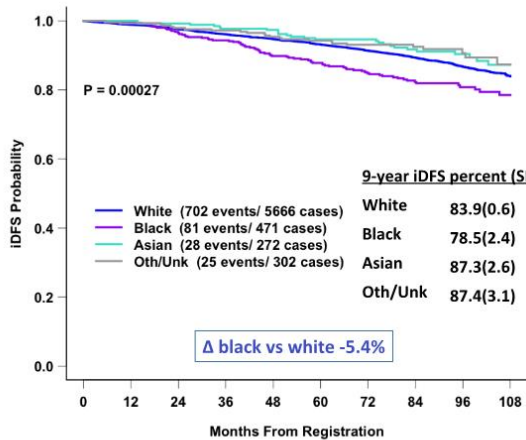
TAILORx - no difference in reported endocrine therapy duration by race or ethnicity (arms B+C combined)



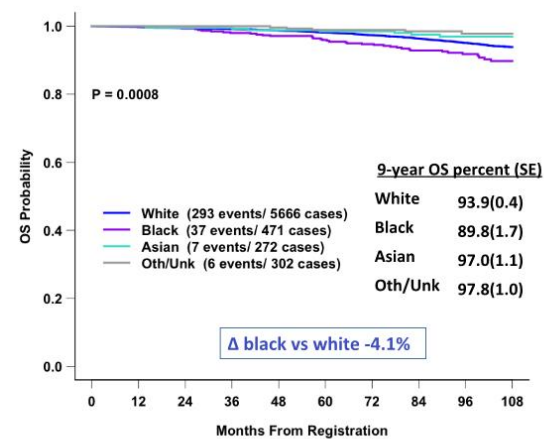
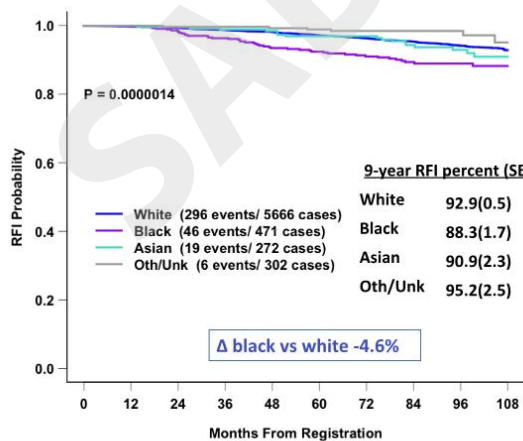
TAILORx trial Randomized arms (B+C) RS 11-25

- No chemotherapy benefit iDFS (top panels) or DRFI (bottom panels) in whites or in blacks
- Same results RFI, OS (not shown)
- Lack of chemotherapy benefit all 4 endpoints, in Hispanics and non-Hispanics (not shown)

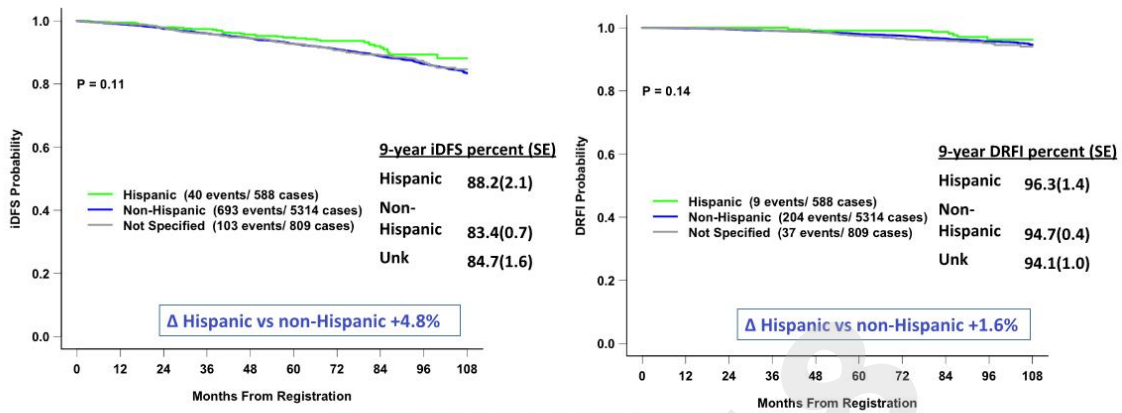
TAILORx iDFS and DRFI rates by race Randomized arms (B+C) combined (RS 11-25: ET +/- CT)



TAILORx RFI and OS rates by race Randomized arms (B+C) combined (RS 11-25: ET +/- CT)

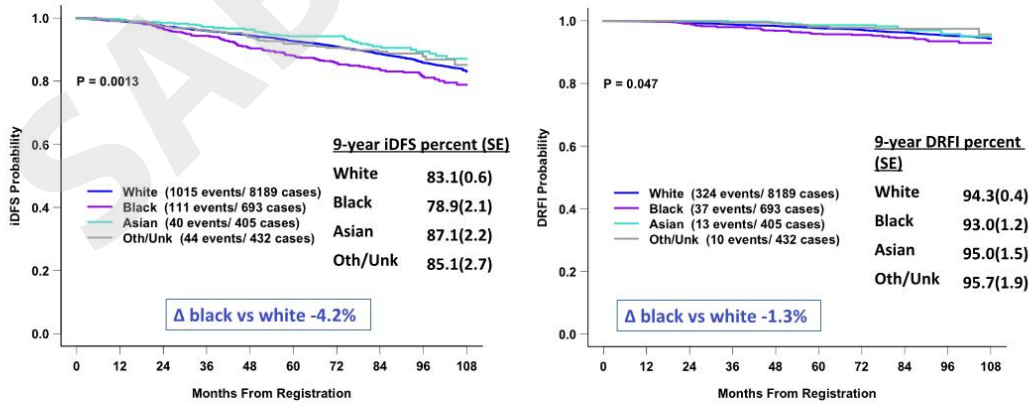


TAILORx iDFS and DRFI rates* by ethnicity Randomized arms (B+C) combined (RS 11-25: ET +/- CT)



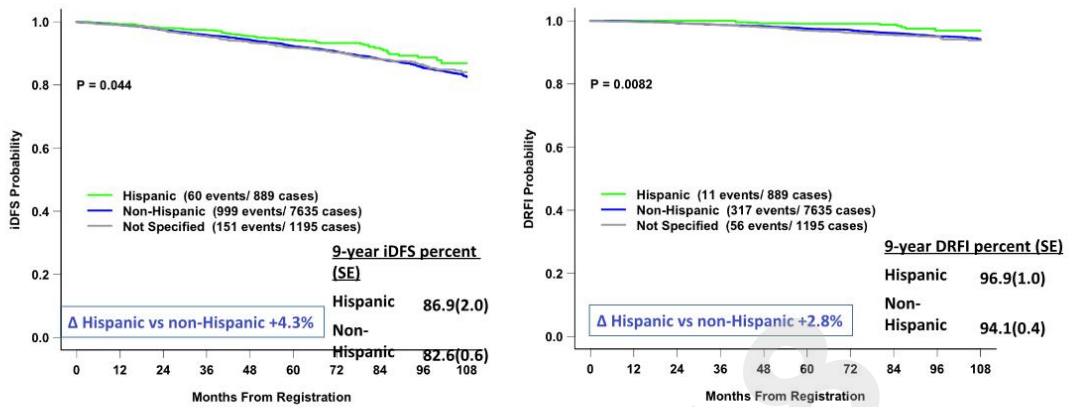
*Similar nonsignificant results for RFI and OS

TAILORx iDFS and DRFI rates* by race All arms (A+B+C+D combined)



*Similar results for RFI and OS

TAILORx iDFS and DRFI rates* by ethnicity All arms (A+B+C+D) combined



*Similar results for RFI and OS

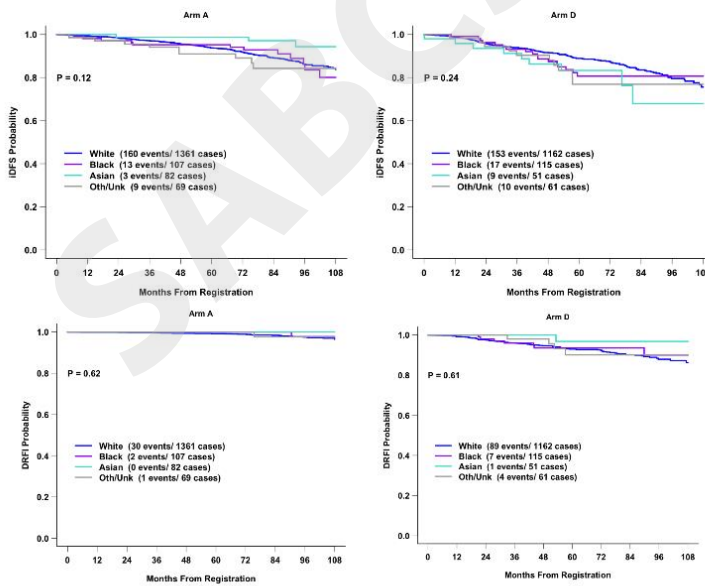
Significant independent variables across proportional hazards models for all 4 endpoints: effects of race and ethnicity, adjusting for other factors within randomized TAILORx cohort (combined arms B+C)*

- Younger age worse
- Smaller tumors better
- Higher (continuous) RS worse (significant for DRFI, RFI, OS)
- Lowest grade better
- Blacks worse than whites
- Hispanics had better outcomes (significant for iDFS and OS)

*Similar results in arms A-D combined, with all endpoints significant for Hispanics

Black race significantly worse outcomes compared with white race independent of other factors in proportional hazards models overall and in randomized arms

Outcome endpoint	Entire population (n = 693 black) Hazard ratio for event	RS 11-25 (n = 471 black) Hazard ratio for event
iDFS	1.33 (p=0.005)	1.49 (p=0.001)
DRFI	1.21 (p=0.28)	1.60 (p=0.02)
RFI	1.39 (p=0.02)	1.80 (p<0.001)
OS	1.52 (p=0.005)	1.67 (p=0.003)



TAILORx Trial

- Blacks similar iDFS and DRFI as other races in Arm A (favorable biology, RS 0-10, only ET-treated)
- Blacks similar outcomes as other races in Arm D (aggressive biology, RS 26-100, all chemotherapy-treated)

Race, ethnicity and clinical outcomes in TAILORx – caveats and future plans

- **Disparity in black vs. white outcomes less pronounced in overall population compared with randomized cohort (RS 11-25, arms B+C)**
 - Lack of significant difference by race in arms A, D
 - Actual ET adherence by race and ethnicity arms B+C unknown
- **Relatively greater benefit from ET in mid-range RS; racial differences in actual ET adherence, sensitivity to antiestrogen therapy, or both may contribute to more pronounced disparities for RS 11-25**
- **Tumor biology (such as individual proliferation genes) in RS 11-25 may differ by race**
- **Future analyses planned of single genes and gene groups by race in TAILORx**

Race, ethnicity and clinical outcomes in the TAILORx trial – Conclusions

- **Main message of TAILORx – that chemotherapy in HR(+) HER2(-) N0 breast cancer can be safely avoided if RS <26 – is true for all races/ethnicities analyzed**
- **Higher recurrence and overall mortality rates observed for blacks vs. whites, others**
- **All enrolled in same trial, treated identically with contemporary cancer care**
- **Disparity not explained by differences in RS, reported ET duration, use or type of adjuvant chemotherapy, or clinicopathologic factors**
- **Careful attention to monitoring adherence to ET for all races/ethnicities necessary**
- **These findings add to emerging evidence that a biologic basis (with or without other factors) may contribute to racial outcomes disparities in HR+ breast cancer**

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10,273 TAILORx
Volunteers
Pioneers
in Pink

Also supported by:



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