Table 5

Cox proportional hazards univariate modeling for time to treatment failure and overall survival

Variable	Time to treatment failure		Overall survival	
	Hazard ratio (95% CI)	*P* value[a]	Hazard ratio (95% CI)	*P* value[a]
Univariate modeling				
Age >50 years	0.59 (0.42–0.83)	0.0051	0.64 (0.46–0.89)	0.041
Performance status: 0 versus 1 or 2	1.30 (0.95–1.78)	0.11	1.41 (1.03–1.94)	0.031
ER positive	0.78 (0.56–1.08)	0.13	0.61 (0.43–0.84)	0.0029
PR positive	0.72 (0.51–1.00)	0.53	0.71 (0.51–1.00)	0.049
ER/PR positive	0.72 (0.51–1.00)	0.53	0.62 (0.44–0.86)	0.0048
Number of metastatic sites: 0 to 2 versus 3+	1.72 (1.03–2.88)	0.37	1.10 (0.66–1.82)	0.72
Disease-free interval: ≤2 years versus >2 years	0.72 (0.52–1.00)	0.49	0.81 (0.59–1.12)	0.20
Prior adjuvant chemotherapy	0.87 (0.63–1.20)	0.39	0.93 (0.68–1.29)	0.67
HER2 positive by CB11	1.44 (0.97–2.15)	0.68	1.34 (0.91–1.99)	0.41
HER2 positive by FISH	1.22 (0.85–1.76)	0.29	1.24 (0.86–1.79)	0.25
HER2 by HercepTest: 0–1 versus 2–3	1.02 (0.73–1.43)	0.90	1.04 (0.74–1.46)	0.83
HER2 by HercepTest: 0–2 versus 3	1.34 (0.91–1.98)	0.14	1.11 (0.76–1.64)	0.59
Multivariate modeling				
Age >50 years	0.99 (0.97–1.00)	0.045	0.99 (0.97–1.00)	0.10
ER/PR positive	1.28 (0.89–1.82)	0.18	1.55 (1.08–2.22)	0.017
HER2 negative on HercepTest: 0–1 versus 2–3	0.97 (0.68–1.40)	0.88	0.93 (0.65–1.35)	0.71

[a]*P* values were calculated using the log-rank test. CI, confidence interval; ER, estrogen receptor; FISH, fluorescence *in situ* hybridization; PR, progesterone receptor.

Triple-negative phenotype

Of the 136 patients in this study for whom complete biomarker data were available, 44 had tumors that were found to carry the triple-negative phenotype (ER negative, PR negative, and HER2 negative). There was a higher proportion of triple-negative tumors with over-expression of p53 on IHC, but this result did not reach statistical significance (53% versus 36%; $P = 0.088$). We conducted an exploratory analysis to determine the objective response rate, TTF, and OS in patients with the triple-negative phenotype. We found that neither the response rate nor TTF differed in the triple-negative subgroup as compared with all other patients (response rate: 26% versus 23%, $P = 0.70$; TTF: 2.8 months versus 4.5 months, $P = 0.092$). However, the triple-negative phenotype was associated with a significant decrement in OS (8.6 months versus 12.8 months; $P = 0.008$; Figure 2). The results were similar when FISH was used to determine HER2 negativity in this subgroup (8.8 months versus 11.7 months; $P = 0.038$).

Outcomes and biomarkers according to race

A total of 105 (22%) of the participants in CALGB 9342 identified themselves as African-American. An exploratory analysis showed that the response rate and TTF were similar in African-American women and Caucasian women. However, the median OS was significantly shorter among African-American women (10.1 months versus 13.1 months; $P = 0.0005$); the difference persisted in a multivariate analysis (hazard ratio 1.44, 95% CI 1.13 to 1.84).

The proportion of African-American women in the subset of patients with biomarker data (20.6%; $n = 34$) was similar to the proportion in the overall group. Tumors were HER2 positive, according to the CB11 assay, in 9% of African-American women, as compared with 22% of Caucasian women ($P = 0.08$). The percentage of African-American women presenting with tumors that were negative for ER, PR, and HER2 expression was more than twice that of Caucasian women (47% versus 21%; $P = 0.003$; Table 7). Both TTF and OS were significantly worse among African-American women than among Caucasian women ($P = 0.038$ and $P = 0.045$, respectively), a difference that persisted in a multivariate analysis (hazard ratio 1.44, 95% CI 1.13 to 1.84). However, when evaluating disease-free survival and OS in triple-negative tumors, survival did not differ by race, suggesting that the negative outcome of African-American women in this cohort is attributable to the greater proportion of triple-negative tumors and not other race-related variables (Figure 2). Of note, there were no significant differences between the proportions of African-American