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Impact of Race, Ethnicity and BMI on Achievement of Pathologic Complete Response Following Neoadjuvant Chemotherapy for Breast Cancer: A Pooled Analysis of Four Prospective Alliance Clinical Trials (A151426)

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Abstract

Purpose—Previous studies demonstrated poor response to neoadjuvant systemic therapy (NST) for breast cancer among black women and women who are overweight or obese but this may be due to chemotherapy under dosing. We assessed associations of race, ethnicity and body mass index (BMI) with pathologic complete response (pCR) in clinical trial populations.

Methods—1797 women enrolled in four NST trials (CALGB 40601, 40603; ACOSOG Z1041, Z1071) were included. Tumor subtypes were defined by estrogen receptor (ER) and HER2 status. Logistic regression generated odds ratios (OR) and 95% confidence intervals (CI) for the associations of race, ethnicity, and BMI with pCR adjusting for subtype, study arm, lymph node status, tumor size, and tumor grade.

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Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of Interests

The authors declare that they have no conflict of interests.

Results—253 (14.1%) were black, 199 (11.1%) Hispanic, 520 (28.9%) overweight, and 743 (41.4%) obese. Compared to whites, Blacks and Hispanics were more likely to be obese and Blacks were more likely to have triple-negative cancer. pCR rates differed significantly by tumor subtype. In multivariate analyses, neither race (black vs. white: OR: 1.18, 95% CI: 0.85–1.62) nor ethnicity (Hispanic vs. non-Hispanic: OR: 1.30, 95% CI: 0.67–2.53) were significant predictors of pCR overall or by subtype. Overweight and obese women had lower pCR rates in ER+/HER2+, but higher pCR rates in ER−/HER2+ cancers.

Conclusions—There was no difference in breast pCR according to race or ethnicity. Overall, there was no major difference in pCR rates by BMI. These findings suggest that pCR with optimally dosed NST is a function of tumor, rather than patient, biology.

Keywords

breast cancer; race; ethnicity; body mass index; pathologic complete response

Introduction

Obesity [1,2], and black race [3,4] have each been independently associated with poor breast cancer outcomes. The relationship of Hispanic ethnicity with breast cancer outcomes has been inconsistent with some studies suggesting equal or superior outcomes when compared to non-Hispanic whites, while others suggest worse outcomes [5,6,3]. Black race, Hispanic ethnicity, and obesity are each associated with a higher incidence of more aggressive tumor biology (high grade, hormone receptor negative, high proliferation fraction, more lymphovascular invasion) [5,7,8]. Differences in tumor subtype likely contribute to observed poorer outcomes, but residual disparities remain [9]. This could be due, at least in part, to differences in response to therapy [10]. In addition, differences in quality of chemotherapy, including treatment delays [11,12] and suboptimal dosing [13] may contribute to disparate breast cancer outcomes according to race, ethnicity, and body mass index (BMI). Given the high prevalence of overweight and obesity among black and Hispanic women in the US, it is possible that race and BMI may interact. In an effort to address these disparities, it is important to investigate whether, independent of their measurable tumor characteristics, and in a setting of standardized therapeutic regimens, overweight, obesity, or black race are associated with response to therapy.

Achievement of a pathologic complete response (pCR) to neoadjuvant systemic therapy (NST) can be defined in a number of ways, but all definitions include the absence of residual invasive cancer in the breast (in-breast pCR). Some definitions also require the absence of invasive *and* in-situ disease and include the axillary nodes [14]. While the absence of invasive and in-situ disease in the breast and the axillary nodes is most strongly associated with favorable prognosis [15], in-breast pCR is highly correlated with pCR in the axillary nodes [16]. Regardless of definition, pCR rates differ greatly across tumor subtypes with the highest rates observed among patients with triple negative or estrogen receptor (ER)-negative, human epidermal growth factor receptor-2 (HER2)-positive (ER−/HER2+) cancers while very low pCR rates are seen in patients with ER+/HER2− tumors [17]. In an era of personalized medicine, NST often allows women with locally advanced breast cancer to become candidates for breast conserving surgery[18] and permits *in vivo* assessment of

treatment response [19]. Women achieving pCR have better event-free and overall survival than those who do not, though this association is also subtype-dependent [15]. The greatest survival benefits of pCR appear to occur in patients with triple negative and ER−/HER2+ tumors [20]. Because of its demonstrated association with survival, the Food and Drug Administration allows pCR to be used as a surrogate endpoint for accelerated approval in pharmaceutical trials [21].

Given the observed disparities in survival according to race, ethnicity, and BMI and the association of pCR with survival, the purpose of this study was to examine the association of race, ethnicity and BMI with pCR in clinical trial populations. Our sample includes multiple trials in which chemotherapy dosing, which may vary considerably between patient populations outside of trials [22,23], was standardized and rigorously accounted for. Using data on 1,797 women participating in four Alliance for Clinical Trials in Oncology (Alliance) clinical trials we evaluated the proportion of women achieving in-breast pCR according to race, ethnicity, and BMI. We examine these factors overall, and stratified by subtypes defined by ER status and HER2.

Methods

Study population

This analysis pools data from four neoadjuvant chemotherapy clinical trials conducted by the members of the Alliance (Table 1), Cancer and Leukemia Group B (CALGB) and American College of Surgeons Oncology Group (ACOSOG) are now part of the Alliance. Two trials (CALGB 40601 and ACOSOG Z1041) were limited to patients with HER2+ cancers, while one (CALGB 40603) enrolled only patients with triple-negative cancers [24–26]. The fourth trial (ACOSOG Z1071) included all breast cancer subtypes of breast cancer; it was designed to evaluate the false-negative rate for sentinel lymph node surgery following neoadjuvant chemotherapy in women initially presenting with biopsy-proven node-positive breast cancer [27]. All trials were approved by the appropriate medical ethics committees. All patients gave written informed consent for study participation and data collection.

Data collection and statistical analysis

Data collection and statistical analyses were conducted by the Alliance Statistics and Data Center. Race and ethnicity were self-reported and BMI was collected by institutional study coordinators from chemotherapy orders. Breast cancer tumor subtypes were assigned on the basis of clinical estrogen receptor (ER) and HER2 status as determined locally. ER was assessed by standard criteria using immunohistochemical (IHC) staining. HER2 was assessed using either IHC or fluorescence in situ hybridization (FISH). Pathologic complete response was defined as the absence of residual invasive disease in the breast (ypT0/is). This was the primary endpoint for all trials except Z1071, which as noted previously, evaluated a nodal question but collected breast and nodal pCR rates on participants.

Analyses included 1797 women from the four trials. We used logistic regression models to examine the relationship between race, ethnicity BMI and response to neoadjuvant chemotherapy. We evaluated the association between race (Black or White), ethnicity

(Hispanic or Non-Hispanic) and BMI (<20, 20–24, 25–29, ≥30 kg/m^2) with pCR in the breast following NST. We tested for potential interaction between race and BMI using a cross product term. We present models overall and stratified by subtypes defined by ER status and HER2 (ER+/HER2−, ER+/HER2+, ER−/HER2+, and triple negative). Models are adjusted for subtype (overall model only), study arm, lymph node status, and tumor grade. Tumor size was not collected in Z1041. We performed a sensitivity analysis by running models with and without tumor size included (using a missing indicator). As results did not materially differ, we present results without adjustment for tumor size. Statistical tests were two-sided, and $p < 0.05$ was considered significant. Statistical analyses were performed by Alliance statisticians at the Alliance Statistics and Data Center using SAS version 9.3 (SAS Institute, Cary, NC) on a dataset frozen on January 13, 2016.

Results

Patient Characteristics (Table 2)

Of the 1797 women included in analyses, 1177 (83.1%) were white, 253 (14.1%) were black, 127 (7.1%) were listed as 'other', 199 (11.1%) were Hispanic, and 520 (28.9%) were overweight (BMI 25–29) and 743 (41.3%) were obese (BMI ≥ 30 kg/m^2). Information on ER, PR, and HER2 status was available for 1784 (99.3 %) patients. The mean age of overweight and obese women (50.5 years) was higher than for normal weight women (47.4 years) ($p < 0.0001$). Compared to white women, a higher percentage of black women had triple-negative cancers (49.8% vs. 34.1%), with consequent reductions in the percentage of black women with ER+ and HER2+ cancers (p=0.0001). A slightly higher percentage of black women had clinically node-positive disease at study entry (24.9%, vs. 18.8% for white women; p=0.05). Compared to white women, black women had a higher mean BMI (31.9 kg/m^2 vs. 29.1 kg/m^2; $p < 0.0001$) and were more likely to be obese (60.1% vs. 38.9%; $p < 0.0001$). Hispanic women were also more likely to be obese than non-Hispanic women (49.2% vs. 41.2%; p=0.0003). Aside from a slight increase in the percentage of patients with triple-negative cancers who were obese (43.8% vs. 40.2% for other subtypes), there were no major differences in the distribution of BMI among the subtypes (p=0.68).

pCR rates, Race, Ethnicity (Tables 3 & 4)

Overall, the pCR rate was significantly higher in patients with ER+/HER2+ (38.1%; OR: 2.16, 95% CI: 1.32–3.51), ER−/HER2+ (62.7%; 5.48: 3.40–8.85) and triple-negative (46.6%; 2.56: 1.75–3.75) cancers than in patients with ER+/HER2− cancers (15.9%). In total, 40.4% (99/245) of black women achieved pCR as compared to 39.8% (550/1381) of white women. Adjusting for subtype and other potential confounders, we observed no significant association between black race and pCR (OR: 1.18, 95% CI: 0.85–1.62). In analyses stratified by tumor subtype, we also saw no significant differences in pCR rates between black and white women (Table 4). Hispanic ethnicity was also not associated with pCR, either overall (Table 3) or when stratified by tumor subtype (Table 4). Overall, 46.4% (90/194) of Hispanic women achieved pCR compared to 39.6% (570/1441) of non-Hispanic women. Adjusting for subtype and other potential confounders, we found no significant association between Hispanic ethnicity and pCR (OR: 1.22, 95% CI 0.86–1.72). In analyses

stratified by tumor subtype, we also saw no significant differences in pCR rates between Hispanic and non-Hispanic women (Table 4).

BMI and pCR (Tables 3 & 4)

Compared to normal weight women (BMI 20–24), in whom the overall pCR rate was 43.6%, the small cohort (n= 66, 3.7% of the study population) of underweight women (BMI <20) had a non-significantly higher pCR rate of 51.6% (OR 1.60: 95% CI 0.89–2.86), while overweight (38.8%; OR 0.86: 0.64–1.16) and obese (38.4%; OR 0.82: 0.62–1.08) had non-significantly lower pCR rates. In multivariable adjusted models, there was a statistically non-significant, inverse association between BMI and pCR (p-trend=0.09; Table 4). In adjusted models there was a significant inverse association between BMI and pCR in ER+/HER2+ patients (p-trend=0.01); in this subtype, overweight and obese women had pCR rates of 25.9% (30/116) and 39.4% (61/155) compared to 47.7% (52/109) and 47.4% (9/19) for normal and underweight women, respectively. In contrast, in ER−/HER2+ patients pCR rates were higher in overweight (71.3%; 62/87), obese women (60.7%; 74/122) and underweight women (83.3%; 10/12) women compared to normal weight women (54.4%; 49/90), resulting in a non-significant positive association between BMI and pCR (p-trend=0.82) for that subtype. We saw no significant differences in pCR rates according to BMI among women with ER+/HER2− or triple negative tumors. There was no interaction between race and BMI (p=0.91).

Discussion

In this large pooled analysis of four randomized clinical trials including 1797 patients, we examined whether race, Hispanic ethnicity and/or BMI were associated with in-breast pathologic complete response to neoadjuvant chemotherapy and HER2−targeted therapy in patients with HER2+ cancers. We observed no difference in pCR rates according to race or ethnicity overall or when stratified by tumor subtype. We observed no overall differences according to BMI, but did see trends associating increasing BMI with lower pCR rates in ER +/HER2+ patients and higher pCR rates in ER−/HER2+ patients.

In our study pCR rates were similar in black and white women as well as in Hispanics and non-Hispanics. Several previous studies have examined the association between race and pCR with some finding no difference by race [28,10], while others found lower pCR rates among black women.[29,30] Chavez-MacGregor and colleagues found no differences in pCR rates between blacks, whites and Hispanics, overall or within tumor subtypes, in a retrospective analysis of 2074 patients treated at the M.D. Anderson Cancer Center between 1994 and 2008, in which the reported pCR rates (overall = 12.5%, HER2+ 22.6%, triple-negative 19.4%, hormone receptor-positive 5%) were much lower than in our population. [28] This lower observed pCR rates is at least in part because of differences in pCR definition (in-breast vs. breast and axilla) and use of combination therapy (i.e., trastuzumab) in our trials. In a more recent paper, Killelea and colleagues, using data from the National Cancer Data Base (NCDB), found similar pCR rates across racial groups overall, but when stratified by tumor subtype non-Hispanic black women had a non-significantly lower pCR rate for ER −/HER2+ tumors (42.6% vs. 53.9%; OR: 0.72, 95% CI: 0.46–1.14) and a significantly lower

pCR rate for triple-negative (36.6%; 416/1138) tumors (36.6% vs. 42.8%; OR 0.73, 95% CI: 0.59–0.89) compared to white women [29]. There were no significant differences according to Hispanic ethnicity. The different results in the present study and that by Killelea et al. may be due to our use of clinical trial populations. The setting of randomized clinical trials provides several important advantages including standardized enrollment requirements, uniform assessment of disease characteristics such as stage, tumor phenotype and other factors associated with prognosis. Treatment is also standardized, carefully monitored, and facilitated, eliminating variation in care that may occur outside of a trial. While the NST regimen for patients enrolled on Z1071 was not specified in the protocol, most received an anthracycline and a taxane in the neoadjuvant setting, and since the treating physicians at the participating institutions were familiar with treatment guidelines from other cooperative group trials, we considered it highly likely that the treatment plans utilized followed similar guidelines (standard chemotherapy dosing using actual rather than ideal body weight to calculate body surface area, for example).

Though most of the available data is from the adjuvant setting, there is evidence that black women with early stage breast cancer start chemotherapy later, are more likely to receive a lower than standard dose and lower relative dose intensity, and are more likely to have dose reductions in the first and subsequent treatment cycles compared to whites [31,32]. These differences could not be explained by racial differences in BMI, comorbid conditions or hematological factors [33]. There is also little evidence of greater levels of acute toxicity in black women receiving neoadjuvant or adjuvant chemotherapy [34]. It is possible that the lower pCR rates among black women in the NCDB are due to dose reductions, treatment delays, or differences in chemotherapy regimens received. Taken together, our results suggest that racial differences in pCR identified in retrospective studies may not be caused by biology.

Our results suggest that, overall, in-breast pCR rates are not significantly affected by BMI in appropriately dosed patients, though there was a non-significant trend towards lower pCR rates with a higher BMI (p-trend=0.094). In another retrospective analysis from the M. D. Anderson database, Litton and colleagues found that overweight (OR = 0.59, 95% CI: 0.37–0.95) or the combination of overweight and obese (OR = 0.67, 95% CI: 0.45–0.99) women had significantly lower pCR rates compared to normal/underweight women.[35] Results were not stratified by tumor subtype [35]. Among Chinese women, patients with BMI ≥ 25 kg/m^2 were 55% less likely to achieve pCR compared to those with BMI <25 kg/m^2. Differences were largest among postmenopausal and HR− patients [36]. Several other studies have associated lower BMI with higher rates of pCR [37]. Weight gain during neoadjuvant chemotherapy has not been associated with pCR [38], except perhaps in subgroups of women who were normal/underweight or postmenopausal at baseline, where it was associated with higher pCR rates [39].

In our study, the impact of BMI on pCR appeared to differ by tumor subtype. Specifically, in overweight and obese women we saw lower pCR rates in ER+/HER2+ cancers and higher pCR rates in ER−/HER2+ cancers. However confidence intervals were wide and it is possible that result was due to chance. Potential mechanisms relating overweight and obesity to lower pCR rates and poorer survival include: 1) higher circulating estrogen levels among

obese postmenopausal women as compared to leaner women and higher estrogen levels when on aromatase inhibitor therapy [40], 2) higher levels of circulating insulin, adiponectin, c-peptide, leptin and other metabolic hormones [41], and 3) higher circulating inflammatory cytokines which may reduce apoptosis and increase proliferation among obese women [42,43]. In some settings chemotherapy may not be dosed appropriately leading to under dosing of obese women, and this would have a greater impact on black women where we observed higher rates of obesity compared to whites [44,45]. Chemotherapy under dosing is less of a concern in our clinical trials because weight-based dosing is required [26,25,24].

Our study has several important strengths and limitations. While our analysis included almost 1800 women, dividing the population by tumor subtype, race, ethnicity and BMI limited our statistical power. Our outcome was in-breast pCR (ypT0/Tis), while many other studies have used pCR in the breast and axillary nodes (ypT0/Tis ypN0) pCR as their endpoint, as it has a stronger association with disease-free survival [46,20]. However, in order to explain the difference in results between our study and those using ypT0/Tis ypN0 race or BMI would have to only affect the likelihood of achieving pCR in the axilla, but not in the breast. This seems unlikely since most women that achieve pCR in-breast also do so in the axilla [15]. Assigning subtype by ER and HER status alone ignores certain molecular heterogeneity within those subtypes that may have a major impact on tumor response and achievement of pCR [47,48]. While the treatment regimens received across our included trials were not uniform, within each trial with the exception of Z1071, patients received standardized therapy. Clinical trial participants may not be representative of the general population. For example, clinical trial participants are generally younger than patients in the community [49]. Lack of racial and ethnic diversity is problematic in many clinical trials; however, our sample was 14% black and 11% Hispanic, reasonably similar to their distribution in the United States. Lastly, we did not look at long-term outcomes associated with pCR according to race, ethnicity or BMI. Studies that have done this suggest that among women that achieve pCR outcomes such as disease-free survival and overall survival are similar, but disparities persist among women that do not [28,50]. Further research is necessary to tease apart the molecular characteristics and post-neoadjuvant treatment and behavioral/environmental exposures that contribute to these disparities among non-responders.

In conclusion, our study found no differences in breast pCR according to race or Hispanic ethnicity and no significant impact of BMI on the overall pCR rate. These findings suggest that achievement of pCR with optimally dosed NST is largely a function of tumor, rather than patient, biology. It further suggests that yet-to-be-defined biologic factors that may influence which patients within each subtype achieve a pCR are also little influenced by race, ethnicity and BMI; if these patient characteristics determined those factors we would expect to see more substantial differences in the pCR rates among our subgroups. Analysis of other studies utilizing similarly effective NST regimens are warranted to see if they also demonstrate lower pCR rates in ER+/HER2+ and higher pCR rate in ER−/HER2+ overweight and obese women that could generate hypotheses for the etiology of these observations.

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Table 1

Trials included in pooled analysis

Study Number	Title	Accrual	Subtype	Study Open Date	Study Close Date	Reference
CALGB 40603	Paclitaxel With or Without Carboplatin and/or Bevacizumab Followed By Doxorubicin and Cyclophosphamide in Treating Patients With Breast Cancer That Can Be Removed by Surgery	454	Triple Negative	May 2009	August 2013	Sikov WM et al. (2014) JCO [26]
CALGB 40601	Paclitaxel and Trastuzumab With or Without Lapatinib in Treating Patients With Stage II or Stage III Breast Cancer That Can Be Removed by Surgery	305	HER2+	December 2008	January 2014	Carey LA et al. (2015) JCO [25]
ACOSOG Z1041	Definitive analysis of randomized neoadjuvant trial comparing 5-fluorouracil, epirubicin and cyclophosphamide (FEC) followed by paclitaxel plus trastuzumab with paclitaxel plus trastuzumab followed by FEC plus trastuzumab in HER2+ operable breast cancer	282	HER2+	September 2007	December 2011	Buzdar AU et al. (2013) Lancet Oncol [24]
ACOSOG Z1071	A Phase II Study Evaluating The Role of Sentinel Lymph Node Surgery and Axillary Lymph Node Dissection Following Preoperative Chemotherapy in Women with Node Positive Breast Cancer (T1–4, N1–2, M0) at Initial Diagnosis	756	Any	July 2009	July 2011	Boughey JC et al., (2013) JAMA [51]

Table 2

Patient characteristics according to race and body mass index

	Race[a]				Ethnicity			BMI (kg/m^2)[b]				
	White n=1417	**Black n=253**	**Other n=127**	**p-value**	**Hispanic**	**Non-Hispanic n=1476**	**p-value**	**<20 n=66**	**20–24 n=468**	**25–29 n=520**	**≥30 n=743**	**p-value**
Age				0.03			0.04					<0.0001
Mean (SD)	49.7 (10.8)	49.4 (9.6)	47.2 (10.8)		48.4 (11.8)	49.8 (10.4)		45.9 (10.4)	47.4 (10.9)	50.5 (10.4)	50.5 (10.4)	
BMI				<0.0001			0.002					
Mean (SD)	29.1 (6.8)	31.9 (6.0)	27.2 (5.5)		30.6 (7.1)	29.3 (6.6)						
Race, n (%)							<0.0001					<0.0001
White					166 (83.4)	1177 (79.7)		54 (3.8)	398 (28.1)	414 (29.2)	551 (38.9)	
Black					8 (4.0)	226 (15.3)		2 (0.8)	32 (12.6)	67 (26.5)	152 (60.1)	
Other					25 (12.6)	73 (4.9)		10 (7.9)	38 (29.9)	39 (30.7)	40 (31.5)	
Ethnicity, n (%)				<0.00001								0.003
Non-Hispanic	1177 (83.1)	226 (89.3)	73 (57.5)					54 (3.7)	389 (26.4)	425 (28.8)	608 (41.2)	
Hispanic	166 (11.7)	8 (3.2)	25 (19.7)					2 (1.0)	44 (22.1)	55 (27.6)	98 (49.2)	
Unknown	74 (5.2)	19 (7.5)	29 (22.8)					10 (8.2)	35 (28.7)	40 (32.8)	37 (30.3)	
HER2+, n (%)	589 (41.6)	74 (29.2)	64 (50.4)	0.0006	108 (54.3)	572 (38.8)	0.0003	31 (4.3)	205 (28.2)	209 (28.7)	282 (38.8)	0.08
ER+, n (%)	671 (47.7)	96 (37.9)	56 (44.8)	0.02	97 (48.7)	674 (45.9)	0.6	31 (5.9)	217 (41.5)	242 (46.3)	333 (6.3)	0.88
Subtype, n (%)				0.0001			<0.0001					0.68
ER+/HER2−	343 (24.4)	53 (20.9)	21 (16.8)		38 (19.2)	361 (24.6)		12 (2.9)	105 (25.2)	124 (29.7)	176 (42.2)	
ER+/HER2+	328 (23.3)	43 (17.0)	35 (28.0)		59 (29.8)	313 (21.4)		19 (4.7)	112 (27.6)	118 (29.1)	157 (38.7)	
ER−/HER2+	255 (18.1)	31 (12.3)	27 (21.6)		49 (24.7)	252 (17.2)		12 (3.8)	90 (28.8)	87 (27.8)	124 (39.6)	
Triple	480 (34.1)	126 (49.8)	42 (33.6)		52 (26.3)	540 (36.8)		23 (3.5)	155 (23.9)	186 (28.7)	284 (43.8)	
Negative												
Node pos, n (%)	266 (18.8)	63 (24.9)	34 (26.8)	0.05	35 (17.6)	291 (19.7)	0.006	11 (3.0)	96 (26.4)	107 (29.5)	149 (41.0)	0.92
Grade 3, n (%)	859 (60.6)	166 (65.6)	94 (74.0)	0.03	126 (63.3)	910 (61.7)	0.1	43 (3.8)	304 (27.2)	317 (28.3)	455 (40.7)	0.37
Tumor Size[c]				0.06			0.05					0.09
Mean (SD)	3.3 (2.3)	3.1 (2.4)	3.8 (2.5)		3.1 (1.9)	3.3 (2.3)		3.9 (3.5)	3.1 (2.1)	3.4 (2.4)	3.3 (2.3)	
Trial, n (%)				<0.0001			<0.0001					0.13

	Race[a]				Ethnicity			BMI (kg/m^2)[b]				
	White n=1417	**Black n=253**	**Other n=127**	**p-value**	**Hispanic**	**Non-Hispanic n=1476**	**p-value**	**<20 n=66**	**20–24 n=468**	**25–29 n=520**	**≥30 n=743**	**p-value**
40601	243 (17.1)	27 (10.7)	35 (27.6)		23 (11.6)	249 (16.9)		15 (4.9)	94 (30.8)	92 (30.2)	104 (34.1)	
40603	331 (23.4)	89 (35.2)	34 (26.8)		36 (18.1)	373 (25.3)		11 (2.4)	115 (25.3)	132 (29.1)	196 (43.2)	
Z1041	232 (16.4)	31 (12.3)	19 (15.0)		64 (32.2)	212 (14.4)		10 (3.5)	78 (27.7)	72 (25.5)	122 (43.3)	
Z1071	611 (43.1)	106 (41.9)	39 (30.7)		76 (38.2)	642 (43.5)		30 (4.0)	181 (23.9)	224 (29.6)	321 (42.5)	

[a] Column percents presented.;

[b] Row percents presented;

[c] Tumor size not collected in Z1041

Table 3

Pathologic complete response in four Alliance clinical trials according to race, ethnicity and BMI (N=1672)

	N[a]	%pCR	OR (95% CI)[b]
Race			
White	1381	550 (39.8)	1.0 (reference)
Black	245	99 (40.4)	1.18 (0.85, 1.62)
Ethnicity			
Non-Hispanic	1441	570 (39.6)	1.0 (reference)
Hispanic	194	90 (46.4)	1.22 (0.86, 1.72)
BMI (kg/m^2)			
<20	64	33 (51.6)	1.60 (0.89, 2.86)
20–24	454	198 (43.6)	1.0 (reference)
25–29	510	198 (38.8)	0.86 (0.64, 1.16)
≥30	722	277 (38.4)	0.82 (0.62, 1.08)
p-trend [c]			0.094
Subtype			
ER+/HER2−	416	66 (15.9)	1.0 (reference)
ER+/HER2+	399	152 (38.1)	2.16 (1.32, 3.51)
ER−/HER2+	311	195 (62.7)	5.48 (3.40, 8.85)
Triple Negative	611	285 (46.6)	2.56 (1.75, 3.75)

[a] 125 women excluded due to missing values of variables;

[b] mutually adjusted for all variables in table plus trial arm, tumor grade, lymph node status, tumor size, and subtype;

[c] p-trend is from a test of linear trend of an ordinal variable defined by the median of each category.

Table 4

Pathologic complete response according to breast cancer subtype in four Alliance clinical trials

	ER+/HER2− (N=416)			ER+/HER2+ (N=406)			ER−/HER2+ (N=313)			Triple Negative (N=648)		
	N	**% pCR**	**OR (95% CI)[a]**	**N**	**% pCR**	**OR (95% CI)[a]**	**N**	**% pCR**	**OR (95% CI)[a]**	**N**	**% pCR**	**OR (95% CI)[a]**
Race												
White	343	51 (14.9)	1.0 (reference)	323	125 (38.7)	1.0 (reference)	254	156 (61.4)	1.0 (reference)	450	211 (46.9)	1.0 (reference)
Black	52	9 (17.3)	1.04 (0.41, 2.66)	42	18 (42.9)	1.42 (0.66, 3.08)	30	18 (60.0)	0.65 (0.27, 1.59)	121	54 (44.6)	1.09 (0.70, 1.72)
Ethnicity												
Non-Hispanic	361	53 (14.7)	1.0 (reference)	307	120 (39.1)	1.0 (reference)	250	153 (61.2)	1.0 (reference)	513	238 (46.4)	1.0 (reference)
Hispanic	38	7 (18.4)	1.24 (0.45, 3.38)	59	26 (44.1)	1.30 (0.67, 2.53)	49	32 (65.3)	0.97 (0.47, 2.03)	47	24 (51.1)	1.32, (0.68, 2.54)
BMI (kg/m^2)												
<20	12	3 (25.0)	1.75 (0.32, 9.52)	19	9 (47.4)	1.03 (0.34, 3.13)	12	10 (83.3)	4.49 (0.84, 24.1)	21	11 (52.4)	1.32 (0.50, 3.48)
20–24	104	18 (17.3)	1.0 (reference)	109	52 (47.7)	1.0 (reference)	90	49 (54.4)	1.0 (reference)	145	74 (51.0)	1.0 (reference)
25–29	124	20 (16.1)	1.27 (0.54, 2.98)	116	30 (25.9)	0.36 (0.19, 0.67)	87	62 (71.3)	2.24 (1.09, 4.62)	178	83 (46.6)	0.81, (0.50, 1.31)
≥30	176	25 (14.2)	0.97 (0.43, 2.18)	155	61 (39.4)	0.68 (0.38, 1.22)	122	74 (60.7)	1.35 (0.72, 2.54)	267	117 (43.8)	0.72 (0.46, 1.14)
p-trend [b]			0.88			0.010			0.082			0.40

[a] mutually adjusted for all variables in table plus trial arm, tumor grade, and lymph node status

[b] p-trend is from a test for linear trend of an ordinal variable defined by the median of each category