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Media Tip Sheet

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Additional Notable Research Presented at the 26th Annual Meeting of the American Society of Breast Surgeons

The following newsworthy abstracts presented at the 26th Annual Meeting of the American Society of Breast Surgeons (ASBrS) may be of particular interest, in addition to presentations during the Media Press Briefing. Researchers are available for telephone interviews. Onsite media is invited to attend all scientific sessions.

Abstracts

Impact of Time to Surgery Post Neoadjuvant Chemotherapy on Breast Cancer Outcomes: A Retrospective Study of Patients Enrolled in the I-SPY 2 Clinical Trial
Lead Author: Julie Van Hassel, MD
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Impact of Quality Improvement Interventions on Biopsy to Treatment Time in Breast Cancer: Results from the PROMPT Quality Collaborative of the National Accreditation Program for Breast Centers
Lead Author: Danielle Thompson, MD
University of Chicago
Chicago, IL

Impact of Neoadjuvant Chemotherapy on Surgical Outcomes and Conversion to Node-Negativity in Invasive Lobular Breast Cancer: Analysis of Molecularly High-Risk Tumors by Histologic Subtype on the I-SPY2 Clinical Trial
Lead Author: Rita Mukhtar, MD
Division of Surgical Oncology, Department of Surgery, University of California San Francisco
San Francisco, CA

Validation of the Performance of the Novel Prognostic Staging System for Overall Survival in De Novo Metastatic Breast Cancer and Demonstration of Performance for Cancer Specific Outcomes

Lead Author: Christopher Vetter, MD
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Disparities in the Surgical Management of the Axilla by Self-Identified Race in the Multicenter Neoadjuvant I-SPY2 Trial

Lead Author: Mandeep Kaur, MD
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ATTRIBUTION TO THE 26th ANNUAL MEETING OF THE AMERICAN SOCIETY OF BREAST SURGEONS IS REQUESTED IN ALL COVERAGE.

Abstract, Official Proceedings

Impact of Time to Surgery Post Neoadjuvant Chemotherapy on Breast Cancer Outcomes: A Retrospective Study of Patients Enrolled in the I-SPY 2 Clinical Trial

Authors: Julie Van Hassel[1], Katrina Dimitroff[2], Christina Yau[3], Rita Mukhtar[4], Marissa M. Howard-McNatt[5], Nora Jaskowiak[6], Jane Perlmutter[7], Angela DeMichele[8], Douglas Yee[9], Nola Hylton[10], W. Symmans[11], Laura van't veer[12], Hope Rugo[13], Laura Esserman[3], Rebecca Shatsky[14], Claudine Isaacs[15], Henry Kuerer[16], Anne Wallace[17], Nicolas Prionas[18], Judy Boughey[19], Jennifer Tseng[20], Chantal Reyna[21], Neil Taunk[22], Susan Kesmodel[23], Marie Lee[24], Jana Fox[25], Mara Piltin[26], Julia Tchou[27], Lauren Postlewait[28], Roshni Rao[29]

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Objective: Neoadjuvant chemotherapy (NCT) in the treatment of breast cancer allows for tumor downsizing, the ability to assess tumor response to NCT, and can increase surgical options. However, the optimal time to surgery (TTS) post NCT remains to be defined and surgeons typically operate between 4-6 weeks after completion of NCT. Existing studies are often single centered, of limited size, and do not delineate tumor receptor subtypes. Results may be conflicting, without a clear consensus. We thus aimed to investigate the impact of TTS following NCT on oncologic outcomes utilizing a large multi-institutional cohort within the I-SPY 2 Trial database.

Methods: A retrospective analysis of patients with breast cancer who were randomized on the I-SPY2 clinical trial to either the standard treatment arm (paclitaxel/anthracycline/cyclophosphamide) or to novel therapy treatment arms was performed. Patients were grouped based on TTS: 1-4 weeks, 5 weeks, 6-8 weeks, and 9+ weeks. We conducted subgroup analysis by tumor receptor subtypes (hormone receptor [HR]+/HER2-, HER2+, and triple negative breast cancer [TNBC]). Patient and clinical characteristics were analyzed between TTS groups using Chi-square and Kruskal-Wallis Rank Sum tests. The associations of TTS and local recurrence free interval (LRFI) and event free survival (EFS) were

examined with Kaplan-Meier, log-rank test, and univariate/multivariate Cox regression hazard models, adjusting for patient and clinical factors.

Results: 1,877 patients were included in the study. 526 (28.0%) underwent surgery between 1-4 weeks, 425 (22.6%) at 5 weeks, 490 (26.1%) between 6-8 weeks, and 436 (23.2%) 9+ weeks after NCT. On tumor receptor subgroup analysis, 27.5% of patients with TNBC had a TTS following NCT of 9+ weeks vs 22.4% of patients with HR+HER2- tumors and 18.7% of patients with HER2+ tumors. LRFI for each TTS group was 95% (1-4 weeks), 92% (5 week), 95% (6-8 weeks), and 87% (9+ weeks) ($p < 0.001$). On multivariate analysis, TTS >9 weeks was independently associated with worse LRFI (HR 2.20, $p = 0.003$). A similar trend was seen for 5-year EFS (86%, 81%, 80%, and 73%; $p < 0.001$, on multivariate analysis HR 1.70, $p < 0.001$). Statistically significant decreases in 5-year LRFI and EFS related to TTS were appreciated on tumor receptor subgroup analysis in patients with TNBC and HR+HER2- disease (Figure 1). No differences in 5-year LRFI and EFS were noted between TTS groups for patients with HER2+ disease (Figure 1). Additionally, a higher residual cancer burden (RCB) index was associated with longer TTS ($p < 0.001$).

Conclusions: Longer TTS (9+ weeks) after NCT is associated with worse local recurrence free interval and event-free survival outcomes in patients with breast cancer. On subgroup analysis, this relationship between TTS and survival remains in patients with HR+HER2- and TNBC tumor subtypes, but is not observed in patients with HER2+ tumor receptor subtypes, likely due to HER2 targeted agents. In the absence of contraindications, surgery should be considered within 8 weeks following NCT for improved survival outcomes.

Figure 1: Kaplan-Meier curves/log-rank test for local recurrence survival (A) and event free survival (B) in woman receiving NCT by TTS grouped by tumor receptor subtypes.

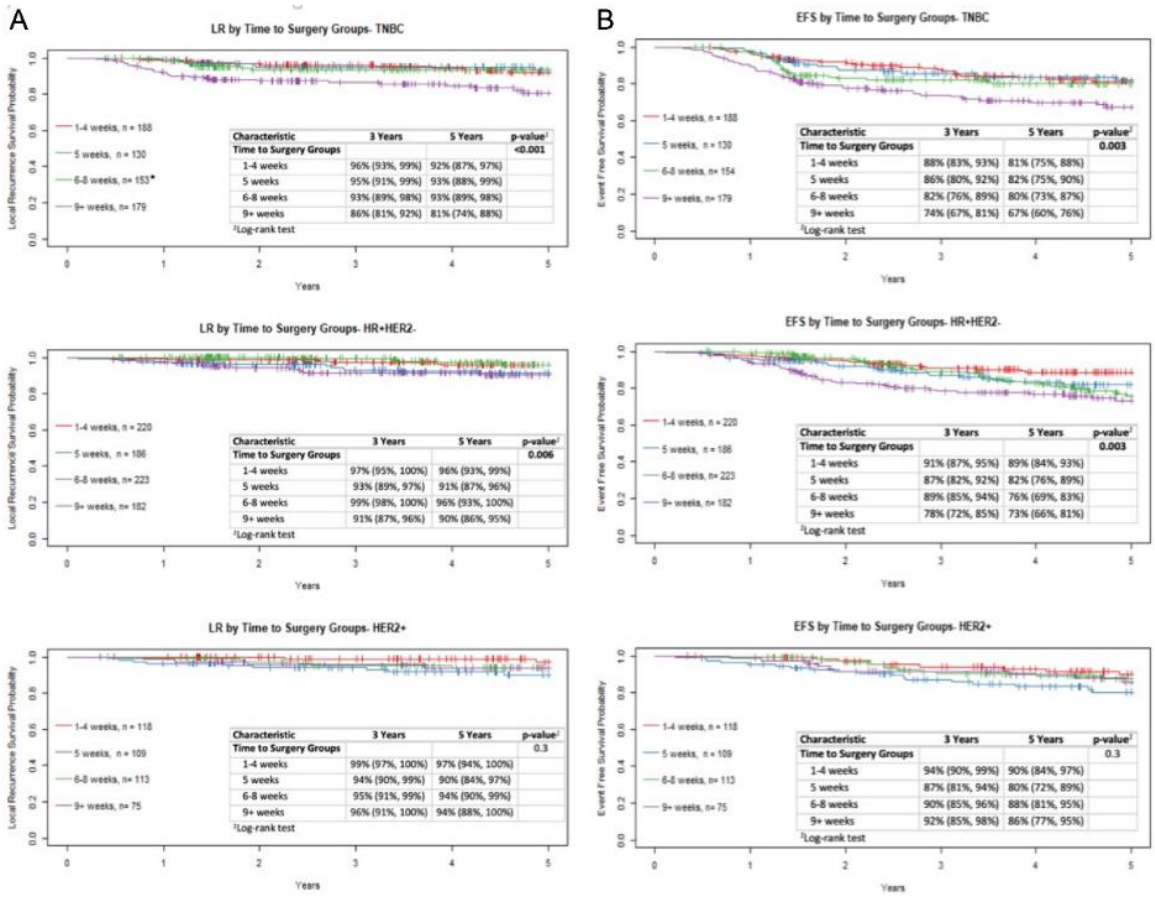

Figure 1. Kaplan-Meier curves/log-rank test for local recurrence survival (A) and event free survival (B) in woman receiving NCT by TTS grouped by tumor receptor subtypes.

Abstract, Official Proceedings

Impact of Quality Improvement Interventions on Biopsy to Treatment Time in Breast Cancer: Results from the PROMPT Quality Collaborative of the National Accreditation Program for Breast Centers

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Background/Objective: Timely care for breast cancer patients is an important quality metric. To address the time interval between biopsy and first treatment, the National Accreditation Program for Breast Centers (NAPBC) launched PROMPT, a network-wide quality collaborative that surveyed sites on times between mammographic exams, biopsy, and treatment. The objective of this study was to examine the time interval from biopsy to first treatment.

Methods: Participating PROMPT sites conducted quality improvement projects using the American College of Surgeons (ACS) quality framework. The main outcome measure was the number of days from biopsy to first treatment (either surgery or neoadjuvant treatment) before and after individual site interventions. We examined the association between facility and personnel factors and decreasing time intervals and successful interventions that decreased time intervals.

Results: Of 233 sites that participated in PROMPT, 103 (44.0%) sites chose the time interval of diagnosis to treatment. Sixty-one (59.2%) sites chose the time interval of biopsy to surgery and 42 (40.7%) sites chose biopsy to neoadjuvant therapy (NAC). Overall, from biopsy to treatment, 56 (54.4%) stated that their quality improvement projects were successful, meaning they were able to decrease the number of days between biopsy and treatment after their quality improvement project intervention. From biopsy to surgery, the average number of days before a successful intervention was 50.3 days compared to 38.8 days after intervention. From biopsy to NAC, the average number of days before a successful intervention was 40.7 days compared to 30.9 days after intervention. There were no facility or personnel factors that were found to be significantly associated with a site decreasing their time interval from biopsy to treatment. Out of 22 interventions listed, the top four most commonly used to decrease the time interval from biopsy to surgery were hiring a breast surgeon, increasing OR block time for either the breast surgeon or the breast surgeon and the plastic surgeon combined and enabling navigators to schedule appointments. Out of 17 interventions listed for time from biopsy to NAC, the top four most commonly used to decrease the time interval from biopsy to NAC were enabling navigators to schedule appointments especially for medical oncology, streamlining port placements, ordering staging studies prior to the medical oncology consult, and reserving echocardiogram slots.

Conclusions: PROMPT has demonstrated that monitoring and improving timely breast cancer treatment is feasible and resulted in improved time intervals for a majority of NAPBC sites. The type of interventions to improve timely care range from hiring of staff to process improvement which could be applicable to other disease sites.

Table 1: Successful QI Project Interventions from Most Successful to Least Successful

Successful QI Project Interventions from Most Successful to Least Successful	
Biopsy to Surgery	**Biopsy to NAC**
Hired a breast surgeon	Navigator scheduled appts
Navigator scheduled appts	Ordered staging studies prior to medical oncology appt
Increased OR block time for breast surgeons	Expedited port placements
Increased OR block time for combination breast/plastic surgery cases	Offered concurrent medical oncology and breast surgery appts
Special scheduling process for combination breast/plastic surgery cases	Reserved echo slots
Hired a plastic surgeon	Standardized eligibility for NAC
Hired a navigator	Identified SDOH factors
Increased breast surgery clinic slots	Monitored time intervals in real time
Increased plastic surgery clinic slots	Scheduled more infusion slots
Standardized who gets a breast MRI	Hired a med oncologist
Presence of a dedicated surgery scheduler	Hired a navigator
Increased MRI slots	Increased medical oncology clinic slots
Monitored time intervals in real time	Increased MRI slots
Hired a radiologist	Streamlined first chemo treatment
Streamlined cardiac clearance	Streamlined ordering of genomic tests
Increased medical oncology clinic slots	Added a tumor board
Ordered staging studies prior to medical oncology appt	Read echo's same day
Expedited port placements	-
Process to get outside imaging and slides ahead of appt	-
Navigators educated patients on time to surgery	-
Dedicated breast OR team lead	-
Surgeon placed genetic testing orders	-

Abstract, Official Proceedings

Impact of Neoadjuvant Chemotherapy on Surgical Outcomes and Conversion to Node-Negativity in Invasive Lobular Breast Cancer: Analysis of Molecularly High-Risk Tumors by Histologic Subtype on the I-SPY2 Clinical Trial

Authors: Rita Mukhtar[1], Katrina Dimitroff[2], Christina Yau[3], Jo Chien[4], Eileen Connolly[5], Marissa M. Howard-McNatt[6], Roshni Rao[7], Velle Ladores[8], Mehra Golshan[9], Candice Sauder[10], Kamran Ahmed[11], Rachael Lancaster[12], Jana Fox[13], Lily Gutnik[14], Marie Lee[15], Julia Tchou[16], Nicolas Prionas[17], Cletus Arciero[18], Chantal Reyna[19], Henry Kuerer[20], Kayla Switalla[8], Neil Taunk[21], Todd Tuttle[22], Meena Moran[23], Lauren Postlewait[24], Jane Perlmutter[25], Angela DeMichele[26], Douglas Yee[27], Nola Hylton[28], W. Symmans[29], Hope Rugo[30], Rebecca Shatsky[31], Claudine Isaacs[32], Laura Esserman[3], Laura van't veer[33], Judy Boughey[34]

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Background/Objective: Invasive lobular carcinoma (ILC) represents 10-15% of all breast cancers and has significant treatment challenges compared to invasive ductal carcinoma. ILC tumors typically have poor response to neoadjuvant chemotherapy (NAC), require more extensive surgery, and have more positive margins. While many lobular tumors have low-risk biology by gene expression assays, there is significant heterogeneity within ILC, and the subset with high-risk biology may have different treatment response. We compared surgical treatment and outcomes by lobular versus non-lobular histology among patients with high genomic risk on I-SPY2, a prospective, multicenter NAC trial.

Methods: We evaluated 1,329 patients with stage II-III breast cancer and high-risk 70 gene assay (MammaPrint, Agendia) who completed treatment on I-SPY2 between 2011-2021. I-SPY2 tests novel NAC agents, with patients randomized by subtype (hormone receptor [HR]+/HER2-, triple negative, or HER2+) and monitored with serial breast magnetic resonance imaging. Patients with classic, pleomorphic, or mixed lobular/ductal histology were included in the lobular cohort and compared to the non-lobular cohort. We evaluated rates of mastectomy, positive margins, axillary dissection, and conversion from clinical node positive (cN+, defined as biopsy proven positive lymph node pre-NAC,) to pathologic node negative (ypN-) status.

Results: Of 1,329 patients, 124 (9.3%) had lobular histology, with most lobular tumors being HR+/HER2- (69%) and grade 2 (64%). Histologic subtype of lobular tumors was mixed lobular/ductal in 62%, classic ILC in 24%, and pleomorphic ILC in 14%; average age was 59.9 years, and 53% were cN+. There was no difference in mastectomy rate by histology (57.2% for lobular versus 55.8% for non-lobular cases, p=0.8). The ILC cohort had a significantly higher positive margin rate than the non-ILC cohort (13.1% versus 4.8%, p=0.005), including in the lumpectomy setting (21.2% versus 7.9%, p=0.023), and nearly significantly in the mastectomy setting (7.8% versus 2.4%, p=0.058). Within the cN- subset (n=630), axillary dissection was significantly more common among the lobular cases compared to non-lobular (24.1% [n=14/58] versus 14.0% [n=80/572], p=0.039). In the cN+ subset (n=699), axillary dissection rates were similar (62.1% [n=41/66 lobular] versus 61.5% [n=389/633 non-lobular], p>0.9). Notably, conversion from cN+ to ypN- status did not differ statistically between lobular and non-lobular cases (40.1% [n=27/66] versus 51.2% [n=324/633] respectively, p=0.11). The rate of conversion from positive to negative nodal status among lobular tumors was high at 30.6% in HR+/HER2-, 72.7% in HER2+, and 66.7% in triple negative cases.

Conclusions: Relative to prior reports in ILC, we found a high rate of nodal response after NAC in this cohort of genomically high-risk lobular tumors in the I-SPY2 trial, as well as higher positive margin and axillary dissection rates. Overall, our data underscore the challenges of surgical management for ILC, but also hold promise that molecular classification can improve treatment selection. While genomically high-risk status is less common in ILC tumors in general, our findings suggest that gene expression assay testing in cN+ ILC patients can identify a subset who may benefit from NAC and potentially be spared axillary dissection. Further work on ILC specific predictors of therapy benefit is needed.

Abstract, Official Proceedings

Validation of the Performance of the Novel Prognostic Staging System for Overall Survival in De Novo Metastatic Breast Cancer and Demonstration of Performance for Cancer Specific Outcomes

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Background/Objective: A novel prognostic staging system was developed by Plichta et al. to differentiate among patients with de novo metastatic breast cancer using data from the National Cancer Database (NCDB). We aimed to validate this staging system within a more contemporary cohort using individual patient specific data and to assess model performance with respect to cancer specific outcomes.

Methods: A retrospective review was conducted of all patients diagnosed with AJCC 8th edition clinicopathologic stage IV breast cancer in our institutional cancer registry from 2010-2022. Primary outcome was overall survival (OS). Secondary outcomes were disease-specific survival (DSS), progression-free survival (PFS), time to progression (TTP), and distant progression-free survival (DPFS). Progression was defined according to the RECIST 1.1 criteria. With more granular individual patient level data available in our dataset than the NCDB model-development cohort, we expanded the possible metastatic sites from the four in the NCDB (bone, brain, liver, and lung) to all possible metastatic sites. Statistical analysis was performed used Kaplan-Meier curves with log-rank tests; model discrimination was estimated using the C-statistic.

Results: 425 patients met inclusion criteria. Median age 59 (IQR 49-69), 99.5% female, 88% non-Hispanic white, 78% ductal histology, 3.3% cT0/is, 13.2% cT1, 35.1% cT2, 21.2% cT3, 25.9% cT4, 1.4% missing clinical T category, 64.7% HR positive/HER2 negative, 22.4% HER2 positive, 12.5% triple negative. Compared to the model-development cohort, our cohort had a slightly lower percentage of HER2 positive (22.4% vs 25.9%), triple negative cancers (12.5% vs 14.8%), and lung metastases (22.4% vs 29.6%). Applying the Plichta algorithm with granular clinical data resulted in a stage distribution of 6% IVA, 46% IVB, 31% IVC, and 15% IVD. Ten patients (2%) did not have sufficient information for stage grouping. Application of the staging system using granular data showed fair discrimination at 3 years for OS (C-statistic 0.64, 95% CI: 0.60-0.68). Furthermore, the staging system had fair discrimination for DSS (0.64), PFS (0.60), TTP (0.60), and DPFS (0.60). With a median follow-up of 41 months, stage IVA-D overall survival was 84%, 79%, 59%, and 47% at 3 years and 73%, 66%, 42%, and 28% at 5 years (Figure 1a); this differed significantly across groups ($p< 0.001$) and was higher than seen in the Plichta NCDB data. Stage groups also discriminated patients for all cancer specific outcomes: DSS, PFS, DPFS (Figure 1b), and TTP (each $p< 0.001$). DSS was 88%, 81%, 62%, 52% at 3 years, 81%, 70%, 44%, and 32% at 5 years for stage groups A-D respectively, PFS was 60%, 44%, 26%, and 14% at 3 years, and DPFS was 63%, 46%, 30%, and 15% at 3 years. The median TTP was 45 months for IVA, 28 months for IVB, 17 months for IVC, and 12 months for IVD ($p< 0.001$).

Conclusions: Using granular patient level data, the novel prognostic staging system for de novo metastatic breast cancer provided meaningful discrimination in overall survival. Furthermore, the novel prognostic staging system performed well for DSS, PFS, DPFS, and TTP. This supports use of this staging system for Stage IV breast cancer.

Figure 1. (A) Overall survival among stage groups A-D and (B) distant progression-free survival among stage groups A-D

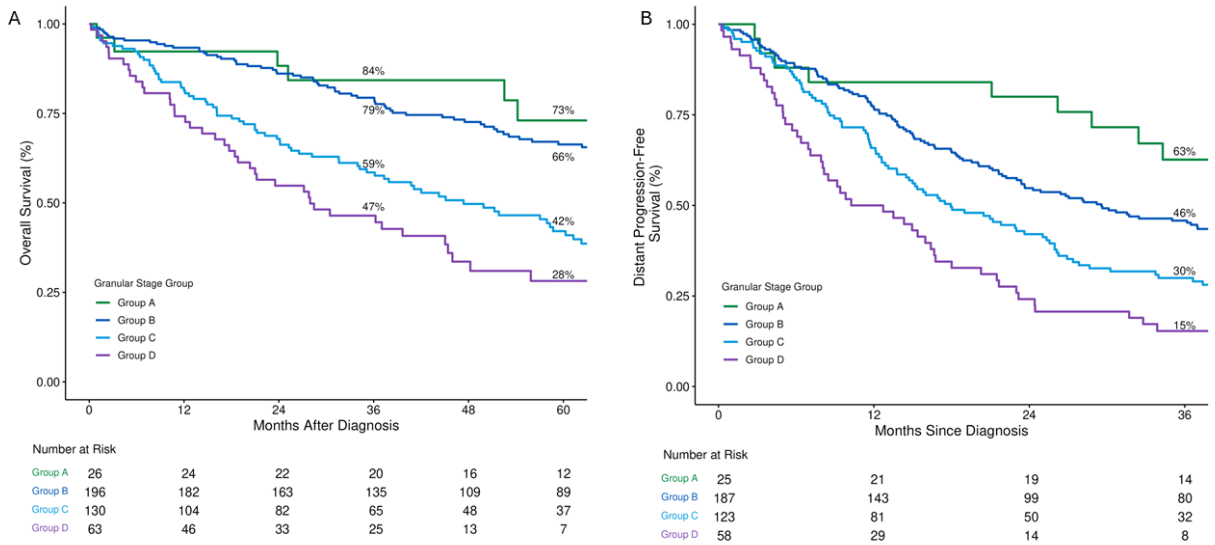

Figure 1. (A) Overall survival among stage groups A-D and (B) distant progression-free survival among stage groups A-D

Abstract, Official Proceedings

Disparities in the Surgical Management of the Axilla by Self-Identified Race in the Multicenter Neoadjuvant I-SPY2 Trial

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Background/Objective: Axillary dissection (ALND) confers significant morbidity and its use in breast cancer management has been shown to vary by patient race, with higher rates of ALND reported for Black-identifying patients. Neoadjuvant chemotherapy (NAC) may allow for omission of ALND by facilitating nodal downstaging. Whether disparities in ALND use persist in this context is not well described. We therefore compared ALND rates after NAC by self-identified race in a multicenter NAC trial.

Methods: I-SPY2 is a prospective, adaptive trial for patients with molecularly high-risk clinical stage II-III breast cancer who are randomized to novel NAC agents. We retrospectively analyzed data from ISPY-2 patients across 19 participating centers who completed NAC and surgical treatment. Type of axillary

surgery is not mandated by the trial and was categorized as sentinel lymph node surgery (SLN)-only or ALND (+/- SLN). We compared ALND rates by self-identified race and clinical/pathologic nodal status (cN and ypN, respectively) using chi-square and Kruskal-Wallis rank sum tests. cN+ status required pre-treatment needle biopsy demonstrating nodal disease, and analyses were performed by nodal stage (0-3) and categorically (N+/N-). To adjust for confounders such as regional variations in practice, we used a multivariable regression model including race, age, region of treatment, receptor subtype, cN, cT, ypN, and ypT stage to identify factors associated with undergoing ALND.

Results: Among 1,394 patients, 849 (60.9%) underwent SLN-only and 545 (39.1%) underwent ALND. Self-identified race was Black in 156 (11.2%), Asian/Other in 131 (9.4%), and White in 1,107 (79.4%). Overall, 52.5% of the study population was cN+ and 66.9% was ypN-, with no difference in cN or ypN stage or category by race. Among cN+ patients the rate of conversion to ypN- status did not differ by race (32.1%, 19.1%, and 26.6% for Black, Asian/other, and White, respectively, p=0.3). On univariate analysis, Black patients had significantly higher rates of ALND compared to those identifying as Asian/other or White (50.6%, 38.9%, and 37.5%, respectively, p=0.007, Table). When stratified by nodal status, Black patients were more likely to undergo ALND specifically among cN+ and ypN- subgroups (Table). Notably, among those that converted from cN+ to ypN-, Black patients had significantly higher rates of ALND than Asian/other or White patients (62.0% vs. 40.0% and 41.2%, respectively, p=0.021). On multivariable analysis accounting for age, stage, region, and receptor subtype, Black patients still had significantly higher odds of undergoing ALND compared to White patients (OR 1.64, 95% CI 1.03-2.59, p=0.035).

Conclusions: In this prospective, multicenter NAC trial, we identified significant disparities in surgical management of the axilla, with Black-identifying patients experiencing higher rates of ALND surgery compared to other groups. This finding persisted both in the subgroup who converted to ypN- status and after adjusting for region and clinical/pathologic nodal stage, suggesting disparities in surgical treatment that are not solely driven by extent of disease or regional practice patterns. This underscores the need for further analysis of underlying causes, treatment standardization, and continuous improvement in the context of clinical trials to enhance the quality of cancer care for diverse populations.

Table 1: Type of Axillary Surgery by Self-Identified Race, Clinical Nodal Status, and Pathologic Nodal Status

Table. Type of Axillary Surgery by Self-Identified Race, Clinical Nodal Status, and Pathologic Nodal Status

Overall (N=1,394)				
	Self-Reported Race			
Axillary Surgery	Black (n=156)	Asian/other (n=131)	White (n=1,107)	p-value
SLN-Only	77 (49.4)	80 (61.1)	692 (62.5)	0.007
ALND	79 (50.6)	51 (38.9)	415 (37.5)	
Clinically Node Negative Patients (N=662)				
	Self-Reported Race			
Axillary Surgery	Black (n=65)	Asian/other (n=70)	White (n=527)	p-value
SLN-Only	54 (83.1)	56 (80.0)	455 (86.3)	0.3
ALND	11 (16.9)	14 (20.0)	72 (13.7)	
Clinically Node Positive Patients (N=732)				
	Self-Reported Race			
Axillary Surgery	Black (n=91)	Asian/other (n=61)	White (n=580)	p-value
SLN-Only	23 (25.3)	24 (39.3)	237 (40.9)	0.018
ALND	68 (74.7)	37 (60.7)	343 (59.1)	
Pathologic Node Negative Patients (N=932)				
	Self-Reported Race			
Axillary Surgery	Black (n=105)	Asian/other (n=84)	White (n=743)	p-value
SLN-Only	70 (66.7)	67 (79.8)	600 (80.8)	0.004
ALND	35 (33.3)	17 (20.2)	143 (19.2)	
Pathologic Node Positive Patients (N=462)				
	Self-Reported Race			
Axillary Surgery	Black (n=51)	Asian/other (n=47)	White (n=364)	p-value
SLN-Only	7 (13.7)	13 (27.7)	92 (25.3)	0.2
ALND	44 (86.3)	34 (72.3)	272 (74.7)	

Data reported n (%). P-values reported from Pearson's chi-square tests.