# Neoadjuvant Systemic Therapy Use for Younger Patients with Breast Cancer Treated in Different Types of Cancer Centers Across the United States

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**BACKGROUND:** Multiple clinical trials have shown that neoadjuvant systemic therapy has a benefit in women who are borderline lumpectomy candidates and in those with locally advanced breast cancers by reducing the mastectomy rate and making inoperable tumors operable. The study aim was to examine the patterns of neoadjuvant chemotherapy and endocrine therapy use among younger women in the United States treated at different types of cancer centers.

**STUDY DESIGN:** Data from the National Cancer Data Base for 118,086 women younger than 65 years with clinical stage IIA (T2N0 only) to IIIC breast cancer. Following the National Comprehensive Cancer Network guideline categorization, patients were grouped into those who were borderline lumpectomy candidates (clinical stage IIA [T2N0 only], IIB, or IIIA [T3N1 only]) or those with locally advanced disease (clinical stage IIIA [T0-3N2 only], IIIB, or IIIC). The main outcome was the proportion of women who received neoadjuvant systemic therapy.

**RESULTS:** Use of neoadjuvant chemotherapy ranged from 17% (stage IIA) to 79% (stage IIIB). Across almost all stage and receptor subtypes, the use was lower in community vs academic centers. On multivariable analysis, use of neoadjuvant chemotherapy was decreased in community vs academic centers (borderline lumpectomy candidates: adjusted risk ratio = 0.73; 95% CI, 0.69−0.77; locally advanced disease: adjusted risk ratio = 0.78; 95% CI, 0.74−0.83).

**CONCLUSIONS:** Use of guideline-concordant neoadjuvant chemotherapy is significantly higher among women treated at academic vs community centers in young and healthy women who do not commonly have contraindications to this treatment. Our study identified a potential disparity in cancer care by type of center where patients receive treatment. (J Am Coll Surg 2016;223:717−728. © 2016 by the American College of Surgeons. Published by Elsevier Inc. All rights reserved.)

Neoadjuvant chemotherapy benefits two specific groups of breast cancer patients. The first group includes patients with inoperable locally advanced disease, as neoadjuvant chemotherapy can reduce the tumor burden and therefore make the tumor resectable with either a mastectomy or lumpectomy.[1,2] C7784, a phase 3 study from the Cancer and Leukemia Group B (now the Alliance for Clinical Trials in Oncology) found that of 113 stage III inoperable breast cancer patients, 81% were deemed operable after neoadjuvant chemotherapy.[2] The second group includes patients who desire breast conservation but have tumors too large for lumpectomy; for these patients, neoadjuvant chemotherapy can shrink the tumor enough to allow breast conservation. Long-term follow-up of the National Surgical Adjuvant Breast and Bowel Project B-18 and the European Organization for the Research and Treatment of Cancer 10902 trials showed that neoadjuvant vs adjuvant chemotherapy was associated with an absolute risk reduction for mastectomy of 7% and 13%, respectively.[3,4]

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Disclaimer: This study used the National Cancer Data Base. The interpretation and reporting of these data are the sole responsibility of the authors.

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**Abbreviations and Acronyms**

aRR = adjusted risk ratio
AUC = area under the receiver operating curve
NCCN = National Comprehensive Cancer Network
NCDB = National Cancer Data Base
pCR = pathologic complete response

Endocrine therapy can also be used neoadjuvantly to reduce tumor burden. Multiple clinical trials have shown that neoadjuvant endocrine therapy alone produces objective responses in up to 70% of women, and can also reduce the mastectomy rate and improve operability in these patients.[5-7]

Based on these data, published guidelines recommend neoadjuvant systemic therapy for patients with locally advanced breast cancers, as well as patients who are borderline lumpectomy candidates and desire breast conservation.[8] However, the patterns of use of neoadjuvant chemotherapy and endocrine therapy in younger women with breast cancer are unknown—and this was the main objective of this study. The primary focus of the study was to examine patterns of use of neoadjuvant systemic therapy across the United States for women with locally advanced (including inflammatory) breast cancers. In addition, we were interested in examining whether use of neoadjuvant systemic therapy differed by the type of cancer center where patients received care, that is, academic vs comprehensive community (treating >500 patients per year) vs smaller community centers. A secondary focus of the study was to examine patterns of neoadjuvant systemic therapy use in women with potentially borderline lumpectomy-eligible cancers. We focused on younger women because neoadjuvant therapy can be especially appropriate for this group, who might value breast preservation and are also less likely to have contraindications (such as comorbidities) to receiving neoadjuvant therapy. We examined data from the National Cancer Data Base (NCDB), a national cancer outcomes database that includes approximately 70% of all incident cancers in the United States.

## METHODS

### Data source

The NCDB is maintained jointly by the American College of Surgeons Commission on Cancer and the American Cancer Society.[9] All institutions accredited by the Commission on Cancer report data using standardized coding definitions as specified by the Commission on Cancer Facility Oncology Registry Data Standards. The NCDB contains information on patient demographics, comorbidity score (Charlson-Deyo), county-level socioeconomic attributes, facility characteristics, cancer diagnosis and tumor characteristics, and first course of treatment. Facilities are classified as academic/research, comprehensive community cancer program (defined as treating >500 new patients per year), or community cancer program (treating 100 to 500 patients per year).

### Patient cohort

In this study, we searched the NCDB for women younger than 65 years with incident breast cancers diagnosed from 2006 through 2012 (eFigure 1). Patients with earlier cancer diagnoses were excluded. This study focused on patients with clinical stage IIA (T2N0 only), IIB, IIIA, IIIB, and IIIC disease because these are the stages that the National Comprehensive Cancer Network (NCCN) guidelines consider eligible for neoadjuvant systemic therapy.[8] Patients with incomplete data on stage, receipt of systemic therapy, or primary surgery were excluded. Among patients who were excluded because they did not undergo surgery, 76% received chemotherapy, although it is not possible to know whether the intention was neoadjuvant. The study sample was limited to patients with ductal, lobular, mixed ductal and lobular, or inflammatory histologies (International Classification of Diseases for Oncology, 3rd edition, histology codes 8500-8508, 8520-8524, and 8530). This resulted in an analytic sample of 118,086 patients.

### Outcome definition and statistical analysis

Patients were stratified into two groups based on NCCN guideline categorization: locally advanced disease (stage IIIA [T0-3N2 only], IIIB, and IIIC) and stages that are borderline eligible for lumpectomy (IIA [T2N0 only], IIB, and IIIA [T3N1 only]). We used number of days from diagnosis to each modality of treatment to identify patients who received systemic therapy before surgery. Descriptive statistics summarized the proportion of patients who received no neoadjuvant therapy, neoadjuvant endocrine therapy alone, or neoadjuvant chemotherapy (with/without endocrine therapy), stratified by type of center (academic, comprehensive community, or community). Because NCDB did not systematically collect HER2 status until 2010, analysis of neoadjuvant therapy use based on HER2 status was limited to patients from 2010 through 2012.

Multivariable Poisson regression with a robust variance assessed the association between treatment facility type and receipt of neoadjuvant chemotherapy, and controlled for patient sociodemographic and diagnostic covariates. Separate models were constructed for patients with locally