A Review of the Impact of Neoadjuvant Chemotherapy on Breast Surgery Practice and Outcomes

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Abstract

Neoadjuvant chemotherapy facilitates breast conserving surgery and allows surgical treatment if patients are considered inoperable at baseline. The number of patients with breast cancer being treated with neoadjuvant chemotherapy is increasing, although mastectomy is still central to the surgical management of breast cancer.
Introduction: Neoadjuvant chemotherapy (NAC) is increasingly used in locally advanced breast cancer as it facilitates breast conserving surgery (BCS) and allows surgical treatment of patients considered inoperable at baseline. The aim of this study was to assess the trends in breast cancer management with regard to the administration of NAC and adjuvant chemotherapy and the effect this has on surgical practice, patient outcomes, and patterns of disease recurrence. **Patients and Methods:** Patients treated with chemotherapy from 2005 to 2014 were identified from a prospectively maintained database. Clinicopathologic details, timing of chemotherapy delivery, and surgical procedures carried out were analyzed. **Results:** A total of 1619 patients were included in the study. The NAC group (n = 383) had a higher T stage ($P < .001$) and higher grade disease than the adjuvant group ($P = .017$). Luminal A breast cancer was less likely to be treated by NAC. The proportion of patients treated with NAC has increased from 12.1% in 2005 to 48.3% in 2014 ($P < .001$). There was an increase in the BCS rate over time ($P = .002$); however, a higher proportion of the neoadjuvant group (55.5%) underwent mastectomy. Timing of chemotherapy influenced the type of reconstructive procedure carried out ($P = .003$). **Conclusion:** The number of patients with breast cancer being treated with NAC is increasing, which is influencing the increasing rate of BCS, though mastectomy is still central to the surgical management of those in receipt of NAC.

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Introduction

The treatment of breast cancer has evolved from Halsted's radical mastectomy to the current molecular-driven, subtype-specific rationale. Breast cancer surgery has changed from the routine removal of breast, chest wall muscles, and axillary lymph nodes to accurately selecting patients suitable for breast conserving surgery (BCS) and to skin- and often nipple-sparing mastectomy for those who still require complete removal of the breast.[1]

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Systemic chemotherapy is a well-established aspect of breast cancer treatment protocols that has traditionally been delivered in the adjuvant setting. There has been a move in the last decade towards neoadjuvant chemotherapy (NAC) for the treatment of breast cancer. In addition, chemotherapy regimens are often tailored towards specific breast tumor and patient characteristics, ever moving towards the concept of "personalized medicine."[2] The use of NAC has not been shown to convey survival benefit but is advantageous in other aspects of breast cancer management: it allows for tumor downsizing and BCS in patients who may previously have required mastectomy; it generates in vivo data on the tumor chemosensitivity, which in turn is a prognostic factor for recurrence and survival and potentially reduces the micro-metastatic component of the disease.[3]

Downsizing tumors, thus making the patient eligible for BCS, is a significant advantage of NAC. There is some evidence to show

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that this may be dependent on breast cancer subtype. Boughey et al demonstrated that patients with human epidermal growth factor receptor 2 (Her2)-overexpressing and triple-negative breast tumors were more likely to have a better pathologic response to treatment and had higher rates of BCS than luminal breast cancers.[4] On analysis by breast cancer subtype, pathologic complete response (pCR) does not always correlate with survival and outcomes. A study from the MD Anderson Cancer Center quoted a pCR rate of 9% in luminal A tumors; however, these patients had excellent locoregional recurrence-free survival regardless of the tumor response to neoadjuvant treatment, potentially as a reflection of overall favorable biology of luminal A disease and the efficacy of hormonal treatment.[5]

The oncologic safety of performing BCS over mastectomy in patients treated with NAC remains controversial. The National Surgical Adjuvant Breast and Bowel Project (NSABP)-B18 trial was set up in 1998 to compare disease-free survival and overall survival in patients treated with NAC or adjuvant chemotherapy. One of the secondary aims of this trial was to compare rates of BCS and mastectomy in the adjuvant and neoadjuvant groups. At the 9-year follow-up, patients in receipt of NAC were more likely to have undergone BCS over mastectomy, particularly those with a tumor of 5 cm or greater at time of entry to the study. BCS rates rose from 60% to 68% after administration of NAC. Additionally, rates of disease recurrence and survival in the BCS group were equivalent to those in the mastectomy group.[6] However, a meta-analysis of the long-term outcomes for NAC and adjuvant chemotherapy in breast cancer found that NAC with BCS had a higher rate of locoregional recurrence than adjuvant chemotherapy with BCS, with no difference in distant recurrence or survival.[7]

There has been some controversy surrounding the role of breast reconstruction in patients receiving chemotherapy as part of breast cancer treatment. In the adjuvant setting, chemotherapy does not cause an increase in the complication rate postoperatively or an increased length of time before administration of adjuvant radiotherapy.[8] The relationship between NAC and breast reconstruction is poorly described in the literature. A study by Hu et al reported that those in receipt of NAC have a 28% chance of undergoing an immediate breast reconstruction procedure compared with 40% in patients who have undergone adjuvant therapies only.[8]

The aim of this study is to assess what effect the use of NAC has had on surgical practice in a regional cancer center over a 10-year period. We examine the indications for and the trends in neoadjuvant chemotherapy use, response to treatment, the impact neoadjuvant chemotherapy has on breast surgery and reconstruction, patient outcomes, and its current role in the management of patients with breast cancer.

Patients and Methods

This study was undertaken at Galway University Hospital, a tertiary referral specialist breast cancer unit. Patients who were treated with chemotherapy for breast cancer were identified from a prospectively maintained institutional database including patient demographics, tumor clinicopathology, and surgical and medical therapeutic information. Patients were categorized as receiving NAC or adjuvant chemotherapy based on whether they had treatment before or after their curative surgery. Patients were also categorized by whether they underwent mastectomy or BCS. Those who underwent BCS as their primary tumor resection and then required a completion mastectomy were classified as "failed BCS."

Clinical decisions relating to surgical intervention and neoadjuvant/adjuvant local and systemic therapy are made by discussion and consensus at a multidisciplinary team meeting with medical, surgical, and radiation oncologists present. Breast reconstruction is offered to all suitable mastectomy patients at our institution, as per the 2009 National Institute for Health and Care Excellence guidelines.

Tumor size was assessed using postoperative pathology in the adjuvant chemotherapy group and using pre-treatment clinical and radiologic assessment in the NAC group.

Data analysis was carried out using IBM SPSS statistics 2.0. The association between categorical factors of interest and chemotherapy timing and surgical procedures was analyzed using the Pearson χ^2 test of association. A P-value of $< .05$ was assumed to represent statistical significance.

Results

Patient and Treatment Characteristics

A total of 1619 patients were included in the study from 2005 to 2014. Three hundred eighty-three patients were treated with NAC, and 1236 were treated with adjuvant chemotherapy. The average age at diagnosis within the NAC group was younger (48.67 $\pm$ 11.49 years) than the adjuvant chemotherapy group (54.5 $\pm$ 10.12 years) ($P < .001$) (Table 1). Patients in receipt of NAC had larger tumors (34.8 $\pm$ 15.7 mm) than those receiving adjuvant chemotherapy (22.8 $\pm$ 12.1 mm) ($P = .005$). Of the NAC group, 16.2% had T4 disease compared with 1.4% of the adjuvant group. The majority of patients treated with NAC were diagnosed with at least N1 disease at the time of presentation. Conversely, in the adjuvant chemotherapy group, 48% (n = 594) had no evidence of nodal disease at presentation ($P < .001$) (Table 1). Patients with higher grade disease were more likely to be treated with NAC. Of those treated with NAC, 46.4% had grade III disease compared with 39.0% of those treated with adjuvant chemotherapy ($P = .017$). A higher proportion of the adjuvant chemotherapy group was composed of the luminal A breast cancer subtype. NAC was more commonly administered in the treatment of luminal B, Her2-overexpressing, and triple-negative subtypes ($P < .001$) (Table 1).

Temporal Trends in Systemic Chemotherapy and Breast Surgery

The proportion of patients being treated with NAC has increased over time, with 12.1% (n = 15) of all those in receipt of chemotherapy in 2005 being treated in the neoadjuvant setting and 48.3% (n = 58) of all patients being treated with chemotherapy in 2014 being treated in the neoadjuvant setting ($P < .001$). Delivery of chemotherapy to tumors of distinct breast cancer subtypes has also changed over time, with fewer luminal A cancers in receipt of chemotherapy toward the end of the study period ($P = .045$).

Trends in surgical procedures carried out in patients with breast cancer receiving chemotherapy were analyzed. Equal numbers of mastectomy and BCS were carried out at the start of the series (50.4% mastectomy rate in 2005), whereas BCS was more common

Table 1 Clinicopathologic Features

	Neoadjuvant Chemotherapy, n = 383 (23.7%)	Adjuvant Chemotherapy, n = 1236 (76.3%)	*P* Value
Age at diagnosis, y	48.67 ± 11.49	54.50 ± 10.12	<.001 Independent *t* test
T stage			<.001 χ^2 test
T1	23 (6.2)	436 (35.5)	
T2	145 (39.1)	659 (53.7)	
T3	143 (38.5)	115 (9.4)	
T4	60 (16.2)	17 (1.4)	
N stage			<.001 χ^2 test
N0	60 (17.0)	594 (48.3)	
N1	231 (65.4)	429 (34.9)	
N2	54 (15.3)	133 (10.8)	
N3	8 (2.3)	74 (6.0)	
M stage			.340 χ^2 test
M0	366 (24.9)	1104 (75.1)	
M1	1 (11.1)	8 (88.9)	
Grade			.017 χ^2 test
I	12 (3.2)	67 (5.5)	
II	188 (50.4)	678 (55.5)	
III	173 (46.4)	477 (39.0)	
Subtype			<.001 χ^2 test
Luminal A	202 (52.3)	855 (71.13)	
Luminal B	62 (16.4)	131 (10.9)	
Her2	44 (11.6)	74 (6.2)	
Triple negative	71 (18.7)	142 (11.8)	

Abbreviation: Her2 = human epidermal growth factor receptor 2.

towards the end of the study (69.2% BCS in 2014) ($P = .002$). Fifty-five patients underwent bilateral mastectomy, 33 (60%) of whom underwent adjuvant chemotherapy. Forty-six risk-reduction mastectomies were carried out during this study. A higher proportion (55.5%) of patients treated with NAC underwent mastectomy for the surgical treatment of breast cancer. In comparison, 66.8% of those in receipt of adjuvant chemotherapy underwent BCS ($P < .001$) (Table 2). However, there was an increase in NAC patients undergoing BCS over time (26.7% in 2005 vs. 63.8% in 2014). There was no difference in the rate of excision of margins post-BCS between the adjuvant chemotherapy and NAC groups ($P = .997$). However, there was a higher rate of BCS failure and patients requiring a completion mastectomy in the NAC group (21.8% neoadjuvant vs. 12.8% adjuvant; $P = .003$). The breast cancer subtype did not significantly influence whether patients had mastectomy or BCS ($P = .105$) (Table 3).

Post-mastectomy breast reconstruction (immediate and delayed) post tumor excision was analyzed for patients in receipt of chemotherapy (Table 4). Overall, there was a reconstruction rate of

Table 2 Surgical Procedure Required by Timing of Chemotherapy Delivery

	Neoadjuvant Chemotherapy, n = 383 (23.7%)	Adjuvant Chemotherapy, n = 1236 (76.3%)	*P* Value
Surgery type			<.001
BCS	170 (44.5%)	818 (66.8%)	
Mastectomy	212 (55.5%)	406 (33.2%)	
BCS only (n = 988; 61.5% of all surgery)			
Excision of margins required			.977
No	152 (89.4%)	732 (89.5%)	
Yes	18 (10.6%)	86 (10.5%)	
Failed BCS			.003
No	133 (78.2%)	713 (87.2%)	
Yes	37 (21.8%)	105 (12.8%)	

Abbreviation: BCS = breast conserving surgery.

59.2% for those patients who underwent mastectomy. A latissimus dorsi flap with an implant was the most common breast reconstruction procedure carried out for those in receipt of mastectomy (57.8%). There was no significant difference in the rate of breast reconstruction post-mastectomy between patients receiving NAC or adjuvant chemotherapy ($P = .540$). However, NAC or adjuvant chemotherapy did influence the type of reconstruction procedure carried out ($P = .003$). Those in receipt of adjuvant chemotherapy were more likely to have a pedicled flap with or without an implant as their reconstruction procedure. There was a higher rate of free flaps in patients in receipt of NAC (14.6% NAC vs. 4.1% adjuvant). Forty-six prophylactic mastectomies were undertaken in this study with a reconstruction rate of 82.6%, and 56.5% of prophylactic mastectomies were carried out for patients in receipt of adjuvant chemotherapy ($P = .001$).

Disease Recurrence

Breast cancer recurrence rates were examined for patients in receipt of NAC or adjuvant chemotherapy (Table 5). A higher rate of disease recurrence was observed for the NAC group than the adjuvant therapy group (n = 87 vs. 138; 22.7% vs. 11.2%; $P < .001$). The NAC group had a local recurrence rate of 4.4% (n = 17) compared with 1.9% (n = 24) in the adjuvant chemotherapy group

Table 3 Surgical Procedure by Breast Cancer Subtype

	Breast Conserving Surgery, n = 968 (61.7%)	Mastectomy, n = 601 (38.3%)	*P* Value
Subtype			.105 χ^2 test
Luminal A	660 (68.2)	389 (64.7)	
Luminal B	114 (11.8)	77 (12.8)	
Her2	61 (6.3)	57 (9.5)	
Triple negative	133 (13.7)	78 (13.0)	

Abbreviation: Her2 = human epidermal growth factor receptor 2.

Table 4 Breast Reconstruction Practices in Patients in Receipt of Chemotherapy and Mastectomy

	Neoadjuvant Chemotherapy, n = 212 (34.3%)	Adjuvant Chemotherapy, n = 406 (65.7%)	*P* Value
Breast reconstruction			.540
Mastectomy alone	90 (42.5)	162 (39.9)	
Mastectomy and reconstruction	122 (57.5)	244 (60.1)	
Reconstruction type			.003
Implant only	24 (19.5)	46 (18.9)	
Pedicle flap + implant	68 (55.3)	144 (59.0)	
Pedicle flap	13 (10.6)	44 (18.0)	
Free flap	18 (14.6)	10 (4.1)	

($P < .001$). The NAC group had a distant recurrence rate of 18.3% (n = 70) compared with 9.2% (n = 114) in the adjuvant chemotherapy group ($P < .001$). The most common sites of disease recurrence were bone (30.7%), liver (18.2%), brain (15.6%), and lung (14.7%). Pre-NAC T stage was a positive predictor of recurrence, with larger tumors more commonly associated with disease recurrence (Table 6). Of those with T1 disease, 3 (14.3%) patients had a recurrence compared with 40 (28.2%) patients with T3 and 20 (37.7%) patients with pre-treatment T4 disease ($P = .007$). Post-NAC T stage was also predictive of disease recurrence. Of those patients with ypT0 disease after NAC, 10 (9.9%) had disease recurrence, compared with 31 (39.7%) of those with residual T3 disease or 3 (60.0%) of those who had residual T4 disease ($P < .001$). Pre-NAC N stage was not a predictor of disease recurrence ($P = .089$). However, N stage after NAC did predict recurrence ($P < .001$). Twenty (10.9%) patients with ypN0 disease had a recurrence of their disease compared with 26 (41.3%) patients with ypN2 disease or 15 (37.5%) patients with ypN3 disease. The Miller Payne response to NAC was also predictive of breast cancer recurrence ($P = .006$, χ^2 test). Five (7.2%) patients who had a pCR to NAC (Miller Payne grade 5) had a disease recurrence. Twelve (27.3%) patients with a Miller Payne grade 2 response and 29 (28.4%) patients with a Miller Payne grade 3 response had a recurrence of their breast cancer. Breast cancer subtype was also predictive of disease recurrence ($P = .002$, χ^2 test), with a smaller proportion of patients with luminal A disease (n = 135; 12.5%) having breast cancer recurrence compared with those with Her2-overexpressing tumors (n = 27; 22.9%) and triple-negative tumors (n = 38; 17.8%). Receipt of mastectomy or BCS did not have a significant influence on the rate of local recurrence ($P = .350$) or distant recurrence ($P = .121$).

Table 5 Disease Recurrence Pattern and Chemotherapy Timing

	Neoadjuvant Chemotherapy, n = 383 (23.7%)	Adjuvant Chemotherapy, n = 1236 (76.3%)	*P* Value
Recurrence			<.001
No	296 (77.3)	1098 (88.8)	
Yes	87 (22.7)	138 (11.2)	
Locoregional	17 (4.4)	24 (1.9)	<.001
Distant	70 (18.3)	114 (9.2)	

Table 6 Breast Cancer Recurrence Clinicopathologic Details

	No Recurrence, n = 1394 (86.1%)	Recurrence, n = 225 (13.9%)	*P* Value
Pre-neoadjuvant T			.007
T1	18 (85.7)	3 (14.3)	
T2	116 (83.5)	23 (16.5)	
T3	102 (71.8)	40 (28.2)	
T4	33 (62.3)	20 (37.7)	
Pre-neoadjuvant N			.089
N0	33 (80.5)	8 (19.5)	
N1	150 (74.6)	51 (25.4)	
N2	21 (56.8)	16 (14.3)	
N3	4 (66.7)	2 (33.3)	
Post-neoadjuvant T			<.001
ypT0	91 (90.1)	10 (9.9)	
ypT1	72 (80.0)	18 (20.0)	
ypT2	87 (77.0)	26 (23.0)	
ypT3	47 (60.3)	31 (39.7)	
ypT4	2 (40.0)	3 (60.0)	
Post-neoadjuvant N			<.001
ypN0	164 (89.1)	20 (10.9)	
ypN1	63 (68.5)	29 (31.5)	
ypN2	37 (58.7)	26 (41.3)	
ypN3	25 (62.5)	15 (37.5)	
Miller Payne response			.006
Grade 1	13 (92.9)	1 (7.1)	
Grade 2	32 (72.7)	12 (27.3)	
Grade 3	73 (71.6)	29 (28.4)	
Grade 4	45 (81.8)	10 (18.2)	
Grade 5	64 (92.8)	5 (7.2)	
Breast cancer subtype			.002
Luminal A	922 (87.2)	135 (12.8)	
Luminal B	174 (90.2)	19 (9.8)	
Her2	91 (77.1)	27 (22.9)	
Triple negative	175 (82.8)	38 (17.8)	

Abbreviation: Her2 = human epidermal growth factor receptor 2.

Discussion

Modern breast cancer management is multidisciplinary, involving surgery, systemic chemotherapy, and radiotherapy, to improve outcomes for patients. Over the past decades, the use of systemic chemotherapy in particular has becomes subtype-dependent and moved in the direction of NAC rather than adjuvant chemotherapy to utilize the therapeutic window to assess its ability to shrink tumor size for facilitation of BCS and assess chemosensitivity in vivo.[9]

In this study, NAC was more commonly used for luminal B, Her2-overexpressing, and triple-negative breast cancer subtypes, with luminal A breast tumors being administered adjuvant chemotherapy. Traditionally, node-negative luminal A breast cancer was managed surgically, whereas node-positive luminal A breast cancer was administered systemic chemotherapy regardless of tumor size or grade. The realization that few of these patients benefit from this treatment has seen in a decline in the number of these patients with breast cancer being treated with chemotherapy. Analysis of the Collaborative Trials in Neoadjuvant Breast Cancer (CTNeoBC) data showed that a pCR to NAC was more common in more aggressive breast cancer subtypes such as triple-negative and Her2-overexpressing disease.[10] Luminal A breast cancer has been shown to be somewhat more resistant to NAC, despite its more positive outcomes in terms of survival than its more aggressive counterparts.[11]

Pathologic response to NAC has been proposed as a predictor of disease-free survival and overall survival and a predictor of long-term clinical benefit.[10] Results from the Investigation of Serial Studies to Predict Your Therapeutic Response (I-SPY) 1 trial demonstrated that hormone receptor-positive, Her2-negative tumors were the least sensitive to NAC and that those patients who achieved a pCR after neoadjuvant chemotherapy had a greater 3-year recurrence-free survival.[12] This has been reflected in the results of our study, with fewer patients with luminal A disease being treated with chemotherapy, adjuvantly or neoadjuvantly, over time. However, the timeline in our study has coincided with the introduction of Oncotype, a 21 gene panel capable of predicting disease recurrence in patients with node-negative estrogen receptor-positive tumors. Those patients with a recurrence score of less than 18 are known to receive no benefit from adjuvant chemotherapy, therefore reducing the numbers of patients with luminal A breast cancer being treated with adjuvant chemotherapy during this time.[13]

More patients were treated with NAC in this institution over time, with 12.1% of patients treated with chemotherapy receiving treatment neoadjuvantly in 2005 compared with 48.3% in 2014, in keeping with international trends. Indications for NAC appear to be expanding. Graham et al identified factors such as younger age, higher T stage, tumor palpability, multifocality, multicentricity, molecular subtype, Her2 status, clinical lymph node status, and year of treatment that are predictive of treatment with NAC.[14] Additionally, data from the I-SPY 1 trial suggests that those tumors with a high Ki67 also respond favorably to neoadjuvant chemotherapy with higher rates of pCR.[12] The timing of delivery of NAC also facilitates other aspects of care, such as genetic testing, fertility preservation, and immediate breast reconstruction.[14]

Several studies have demonstrated an increased use of BCS compared with mastectomy in patients treated with NAC; the NSABP-B18 trial demonstrated an increased rate of BCS from 60% to 68% post-neoadjuvant therapy; trials from the Royal Marsden reported an increase from 78% to 89% and trials from the Curie Institute reported an increased BCS rate of 82% from 77%.[15-17] The use of BCS in patients receiving chemotherapy increased from 49.6% in 2005 to 69.2% in 2014 in our institution. However, 55.5% of patients receiving NAC underwent mastectomy, although the rate of BCS did increase over the study period. Graham et al similarly found that those treated with NAC were more likely to undergo mastectomy.[14] This may reflect the finding reported in the Neoadjuvant Lapatinib and/or Trastuzumab Treatment Optimisation (Neo-ALLTO) trial that preoperative tumor characteristics were more likely to influence the surgical procedure carried out than the rate of response to NAC.[18] This finding of an increased use of mastectomy in patients who underwent NAC and the higher rate of BCS failure in patients treated with NAC demonstrated clearly the difficulty in assessing, clinically and radiologically, the pathologic response to NAC in patients who have an unpredictable, honeycomb pattern response to treatment.[3] Achieving clear margins at time of resection is paramount for the prevention of disease recurrence and thus, an audit of the oncologic safety of BCS for large breast tumors that have been shrunk by NAC and relapse pattern is important.

In this study, there was a post-mastectomy breast reconstruction rate of 59.2% in the overall chemotherapy cohort. There has been apprehension regarding immediate breast reconstruction (IBR) in patients treated with NAC owing to a fear of delaying subsequent adjuvant therapy and increased rates of complications.[8] A meta-analysis by Song et al showed that NAC does not increase complication rates post-IBR and that there is no association between NAC and hematomas, seroma, or infection postoperatively. There was also no significant increase in the rate of expander implant loss or total flap loss in implant and autologous reconstruction, respectively, after NAC.[19]

NAC in the treatment of breast cancer has been shown to be associated with a higher rate of locoregional recurrence than adjuvant chemotherapy.[20] In this study, the rate of local recurrence was 4.4% (n = 17) in the NAC group, and 1.9% (n = 24) in the adjuvant group. This is in keeping with international trends, with a meta-analysis published by the Early Breast Cancer Trialists' Collaborative Group (EBCTCG) reporting a local recurrence rate of 21.4% in patients receiving NAC compared with 15.9% for those receiving adjuvant chemotherapy.[7] The decreased rate of recurrence in our study reflects improvements in treatments delivered over time and the more careful selection of patients to be treated with systemic cytotoxic therapy. A significant difference in rates of distant recurrence between NAC and adjuvant chemotherapy was observed in our study, which is not in keeping with that reported in the EBCTCG meta-analysis. The data included in these studies pertains to patients entered into trials from 1983 to 2002 and so is older than data included in our study; therefore, our results, though in a smaller population, may be more in keeping with modern image-guided surgery and better assessment of imaging and may be a better reflection of tumor biology.

Pre-neoadjuvant N stage was not predictive of disease recurrence in this study; however, N stage after NAC did predict recurrence. This suggests that response to NAC has greater prognostic value than disease stage at presentation. A negative nodal status after completion of NAC appears to be protective against breast cancer recurrence, according to our data. Analysis of the CTNeoBC pooled data showed that those patients with ypT0 ypN0 after NAC have a greater event-free and overall survival than those patients who had a complete response in the breast but residual nodal disease. The prognostic value of pCR in the breast and axilla was also greater in Her2-overexpressing and triple-negative breast cancer subtypes than luminal subtypes.[10]

Patterns of disease recurrence by tumor subtype in our study revealed that those with luminal breast cancer were less likely to

experience disease recurrence than those patients with Her2 overexpression or triple-negative tumors. Her2-overexpressing and triple-negative tumors are known to be associated with a greater rate of locoregional and distant disease recurrence.[21] Luminal A disease has been shown to have a lower rate of recurrence and greater survival despite its poor pathologic response to NAC, and therefore it has been recommended that pCR is not used as a surrogate endpoint for disease recurrence or survival in a luminal A population.[22]

Conclusion

Trends in the timing of chemotherapy delivery have changed dramatically in recent years, with NAC becoming the standard of care in breast cancer management. Patients treated with NAC are more likely to undergo BCS than those in receipt of adjuvant chemotherapy. NAC is associated with increased rates of disease recurrence, thought this could be as a result of NAC being prescribed for those patients with a higher disease stage at presentation. NAC has been shown to not be a contraindication to IBR. Pathologic response appears to be influenced by breast cancer subtype, with doubt cast over the effectiveness of administering chemotherapy in the case of luminal A tumors. More accurate selection of those patients who are likely to respond to NAC is required to avoid administering this high morbidity treatment to those patients who will not gain benefit. Longer term follow-up of patients with luminal A breast cancer will also allow us to better understand the recurrence pattern in this breast cancer subtype.

Clinical Practice Points

- The number of patients with breast cancer being treated with NAC is increasing, which is influencing the increasing rate of breast conserving surgery, although mastectomy is still central to the surgical management of those in receipt of NAC.

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Disclosure

The authors have stated that they have no conflicts of interest.

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