ORIGINAL ARTICLE

Does neoadjuvant chemotherapy provide any benefit for surgical de-escalation in luminal B, HER2(-) breast cancers?

¿La quimioterapia neoadyuvante proporciona algún beneficio para la desescalada quirúrgica en el cáncer de mama HER2(–) luminal B?

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Abstract

Background. *The use of neoadjuvant chemotherapy (NAC) in less aggressive breast cancer (BC) is controversial.* **Objective.** *To investigate the effect of neoadjuvant chemotherapy in HER2 negative luminal B breast cancer.* **Patients and methods.** *Patients between January 2016 and December 2021 were retrospectively evaluated.* **Results.** *A total of 128 patients were included in the study. Patients with pathological complete response (pCR) were younger and had higher ki67 levels. Cutoff levels for ki67 based on pCR and ypT status were ≤ 40% and ≤ 35%, respectively. According to pre-NAC magnetic resonance imaging findings, only mastectomy was viable in 90 patients, but after NAC breast-conserving surgery (BCS) was possible in 29 (32%). Moreover, 68.5% became eligible for sentinel lymph node biopsy (SLNB) after NAC. Since SLNB was positive in 45 (54.2%), axillary lymph node dissection (ALND) was performed and the remainder, 38 (31.4%), avoided ALND.* **Conclusion.** *In patients with Luminal B, HER2(-) BC a low pCR rate should not discourage the use of NAC. The ki67 level is a guide for individualizing treatment. Especially in young patients with high ki67 levels, NAC increases the chance of breast-conserving surgery and may spare patients from ALND.*

Keywords: *Breast cancer. Neoadjuvant chemotherapy. Pathological complete response. Surgical de-escalation.*

Resumen

Antecedentes. *El uso de quimioterapia neoadyuvante (QTN) en cáncer de mama (CB) menos agresivo es controversial.* **Objetivo:** *Investigar el efecto de la quimioterapia neoadyuvante en el cáncer de mama HER2 negativo luminal B.* **Método.** *Se evaluaron retrospectivamente pacientes entre enero de 2016 y diciembre de 2021.* **Resultados.** *Se incluyeron 128 pacientes. Los valores de corte para ki67 basados en el estado de respuesta patológica completa y el estadio tumoral tras la quimioterapia neoadyuvante fueron ≤ 40% y ≤ 35%, respectivamente. Según los hallazgos de la resonancia magnética previa a la quimioterapia neoadyuvante, la mastectomía solo fue viable en 90 pacientes, pero después de la quimioterapia neoadyuvante la cirugía conservadora de la mama fue posible en 29 (32%). Además, el 68.5% se volvieron elegibles para biopsia del ganglio linfático centinela después de la quimioterapia neoadyuvante, y se evitó la disección de ganglios linfáticos axilares en 38 pacientes (31.4%).* **Conclusiones.** *En las pacientes con cáncer de mama HER2 negativo luminal B, una tasa baja de respuesta patológica completa no debe desalentar el uso de quimioterapia neoadyuvante. En especial en pacientes*

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Date of reception: 11-05-2022
Date of acceptance: 04-08-2022
DOI: 10.24875/CIRU.22000277

Cir Cir. 2023;91(2):186-194
Contents available at PubMed
www.cirugiaycirujanos.com

jóvenes con niveles altos de ki67, la quimioterapia neoadyuvante aumenta la posibilidad de una cirugía conservadora de la mama y puede evitar que las pacientes sufran disección de ganglios linfáticos axilares.

Palabras clave: *Cáncer de mama. Quimioterapia neoadyuvante. Respuesta patológica completa. Desescalada quirúrgica.*

Introduction

Neoadjuvant chemotherapy (NAC) is the first-line treatment for locally advanced and inoperable breast cancer (BC). Its main purpose is to achieve a pathological complete response (pCR). Achieving pCR after NAC is associated with improved long-term survival outcomes[1-3].

NAC downstages the tumor and allows the de-escalation of breast and axillary surgery. It is increasingly used to allow the performance of breast-conserving surgery (BCS), thus avoiding mastectomy. Initially, biopsy-proven metastatic axillary lymph nodes may convert after NAC to become clinically negative and mean that axillary lymph node dissection (ALND) is not necessary[3,4]. NAC may provide a better prognosis while improving cosmetic outcomes and quality of life.

In luminal BC, NAC is less effective and has been reported to achieve lower pCR rates compared to the more aggressive subtypes[3]. Therefore, the decision to treat with NAC in patients with luminal BC remains controversial. Ki67, a nuclear protein associated with cell proliferation, is a well-established marker for predicting the outcome of patients with luminal BC[5]. Moreover, luminal tumors with high ki67 expression are reported to respond well to chemotherapy, possibly reflecting their high proliferative activity[6].

In this study, we investigated the clinicopathological features of tumors and the effect of NAC on breast and axillary surgical strategy in luminal B, HER2(-) BC patients.

Materials and methods

Study design and patient selection

Patients diagnosed with breast cancer and treated at the University of Health Sciences, Turkey, Istanbul Haydarpasa Numune Training and Research Hospital, between January 2016 and December 2021 were retrospectively evaluated. This study was approved by the local ethic committee. Estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2), and ki67 statuses were determined by immunohistochemistry (IHC). For HER2, patients with IHC scores of 0, 1+, or 2+ and who did not show gene amplification by fluorescence *in situ* hybridization (FISH) were considered HER2(-). Based on the percentage of tumor cells with nuclear ki67 expression, tumors were classified as ki67-low (< 20%) or ki67-high (≥ 20%). The receiver operating characteristics (ROC) curve analysis was used to determine the cutoff point for ki67 levels.

All patients underwent pre-operative staging with ultrasound (US) and mammography (MMG). US-guided fine-needle aspiration cytology (FNAC) was routinely performed in patients with radiological suspected axillary lymph nodes (ALNs). Magnetic resonance imaging (MRI) was used to evaluate the extent of disease. Patients with ER +, PR ±, HER2(-), and ki67 ≥ 20% were designated as Luminal B, HER2(-) BC and who underwent NAC were included in this study.

Patients with bilateral breast cancer, distant metastatic disease, supraclavicular lymph node and/or intramammary lymph node metastases, and inflammatory breast cancer were excluded from the study.

Age, tumor size, multifocality, multicentricity, ALNs size, pathologic ALNs number, histopathological type, histological grade (HG), and nuclear grade (NG) were obtained.

In this study, seven patients whose ALN-FNAC result showed atypical cells were not included in the evaluation of axillary pCR. Of the 14 patients with complete pCR, only one patient had atypical cells in the ALN-FNAC result.

Evaluation of NAC response and outcome

To evaluate the contribution of NAC to surgical de-escalation, the type of estimated breast surgery that could have been performed if NAC could not be given was determined and compared with the actual surgery performed post-NAC. To decide on the pre-NAC estimated type of surgeries, pre-NAC US, MMG, and MRI findings were evaluated regardless of the pre- and post-operative histopathological results and chemotherapy responses of the patients. Pre-NAC multifocality and multicentricity were evaluated according to their radiological images.

Pre-NAC estimated breast surgery was categorized into two groups: Group 1 Mastectomy – Patients for whom curative results could not have been obtained with BCS because of tumor size, tumor extent, and breast volume; Group 2 BCS/Mastectomy – No obvious features, patients who could undergo BCS.

MD Anderson residual cancer burden (RCB) was reported to evaluate the chemotherapy response of the tumor and axilla. The RCB index categorizes patients with breast cancer into four groups (RCB 0–III) based on the level of residual disease after NAC. These categories are: RCB-0, pathologic complete response; RCB-I, minimal burden; RCB-II, moderate burden; and RCB-III, extensive burden.

Post-NAC tumor stage (ypT) and lymph node stage (ypN), residual tumor diameter, multifocality, multicentricity, surgical margin, number of ALNs removed, number of metastatic ALNs, and metastases diameter of ALNs were evaluated according to the post-operative histopathological results; pCR was defined as both the absence of invasive tumors in the resected breast specimens and the absence of metastases in the sampled lymph nodes (ypT0, ypT *in situ* and ypN0).

Table 1. Pre-NAC demographic, biochemical, radiological, and pathological characteristics of the patients

(n = 128)	Characteristics	n	%
Age (years)	Median (range)	45 (18-77)	
Ki67 (%)	Median (range)	30 (20-90)	
Histological Grade	Grade 1	16	12.5
	Grade 2	63	49.2
	Grade 3	49	38.3
Nuclear Grade	Grade 1	6	4.7
	Grade 2	55	43
	Grade 3	67	52.3
Histopathological types	Ductal	102	79.7
	Lobular	5	3.9
	Mixed-Others	21	16.4
cT	1	10	7.8
	2	70	54.7
	3	15	11.7
	4	33	25.8
cN (n = 121)	1 (mobile)	113	93.4
	2 (fixed)	8	6.6
Tumor size (mm)	Median (range)	30 (9-88)	
Number of metastatic ALNs (n = 121)	1	48	39.7
	2	18	14.9
	3	24	19.8
	≥ 4	31	25.6
Size of metastatic ALNs (mm) (n = 121)	Median (range)	18 (6-53)	
Multicentricity	No	87	68
	Yes	41	32

NAC: neoadjuvant chemotherapy; n: number; cT: clinic tumor stage; cN: clinic lymph node stage; mm: millimeter; ALN: axillary lymph node.

NAC

A standard taxane plus anthracycline-based regimen was used. Our treatment protocol was 4 cycles of doxorubicin (60 mg/m^2) + cyclophosphamide (600 mg/m^2) followed by 12 weeks of paclitaxel (80 mg/m^2) or 4 cycles of docetaxel (75-100 mg/m^2). Over 90% of patients were able to complete the treatment regimen. Adjuvant endocrine therapy with tamoxifen or aromatase inhibitor was started postoperatively, taking into account menopausal status.

Statistical method

The Statistical Package for the Social Sciences (SPSS), version 23, was used for statistical analysis (IBM Inc., Armonk, NY, USA). Descriptive statistics reported included mean ± standard deviation (SD), median and range or interquartile range, and frequency and proportions (%) were used when evaluating the study data. The conformity of the quantitative data to the normal distribution was tested by Kolmogorov–Smirnov, Shapiro–Wilk test, Skewness–Kurtosis test, and graphical evaluations. Mann–Whitney U-test was used for the comparison of two groups of data that did not show normal distribution. Kruskal–Wallis test was used for comparisons of groups of three or more that did not show normal distribution, and the Bonferroni Dunn test was used for pairwise comparisons. Pearson Chi-square test and Fisher's exact test were used to comparing qualitative data. Diagnostic screening tests including receiver operator characteristic (ROC) curve analysis were used to determine the cutoffs for parameters. Significance was evaluated at $p < 0.05$ level.

Results

Patient characteristics

During the study period, 128 patients were identified as complying with the inclusion criteria. The median age of the patients was 45 years (range: 18-77 years). The median ki67 proliferation index in the cohort was of our patients was 30% (range: 20-90%) (Table 1).

When the tumor stages were evaluated clinically, 10 patients (7.8%) were cT1. NAC was planned for these patients because they had biopsy-proven ALN metastases. Tumor size and the number of metastatic ALNs were evaluated according to the results of pre-NAC ultrasound (Table 1).

The median residual tumor diameter was 14 mm (range: 0-85) (Table 2). According to the pre-NAC MRI findings, the rate of multicentric or extensive disease was 32% (n = 41). The axillary pCR (ypN0/ypN0i) was 37.2% (n = 45). When the number of metastatic ALNs were evaluated according to the pre-NAC US results, one of them was biopsy-proven N+, 48 patients (39.7%) had one metastatic ALN, 18 patients (14.9%) had two ALNs, three ALNs in 24 patients (19.8%) had three ALNs, and 31 patients (25.6%) had four or more metastatic ALNs. The median number of removed ALNs was 12 (range: 1-30) (Table 2). When the pCR was evaluated by RCB classification, 10.9% of the patients (n = 14) had pCR and 16.4% (n = 21) RCB Class-I, while 42.2% (n = 54) were RCB Class-II, and 30.5% (n = 39) were RCB Class-III.

Initially, mastectomy was judged to be necessary in 90 patients (70.3%). The actual surgical procedures performed after NAC for these patients is shown in table 2 and figure 1.

Of the 121 patients whose ALN-FNAC result was metastatic, 83 (68.6%) patients became eligible for SLNB after NAC. Since SLNB was positive in 45 of 83 (54.2%) patients, ALND was performed and the remaining 38 patients (31.4%) were spared ALND. It should be noted that ALND was not performed in two patients with micrometastatic SLNB results at their own request (Fig. 2).

The ages of the patients in whom pCR did not occur were significantly older (p = 0.022) whereas the ki67 levels were significantly higher in patients with pCR (p = 0.036) (Table 3).

Table 2. Post-NAC surgical and pathological characteristics of the patients

(n = 128)	Characteristics	n	%
RCB	0	14	10.9
	I	21	16.4
	II	54	42.2
	III	39	30.5
pCR	pCR	14	10.9
	non-pCR	114	89.1
ypT	ypT0	11	8.6
	ypTis	7	5.5
	ypT1mi	3	2.3
	ypT1a	16	12.5
	ypT1b	16	12.5
	ypT1c	23	18
	ypT2	37	28.9
	ypT3	13	10.2
	ypT4a	0	0
	ypT4b	2	1.6
	ypT0 (ypT0/ypTis)	18	14.1
	ypT+	110	85.9
ypN (n = 121)	ypN0/ypN0i	45	37.2
	ypN1mi	6	5
	ypN1a	35	28.9
	ypN2a	29	24
	ypN3a	6	5
	ypN0 (ypN0/ypN0i)	45	37.2
	ypN+	76	62.8
Residual tumor diameter (mm)	Median (range)	14 (0-85)	
pMultifocality	ypT0/ypTis	18	14.1
	Unifocal	79	61.7
	Bifocal	24	18.8
	Multifocal	7	5.5
pMulticentricity	No	120	93.8
	Yes	8	6.3
Surgical Margin (mm)	Median (range)	8.5 (0.5-30)	
Pre-NAC estimated breast surgery	BCS/Mastectomy	38	29.7
	Mastectomy	90	70.3

(*Continues*)

Table 2. Post-NAC surgical and pathological characteristics of the patients *(continued)*

(n = 128)	Characteristics	n	%
Applied post-NAC breast surgery	NSM	14	10.9
	SSM	9	7
	Mastectomy	53	41.4
	BCS	52	40.6
Axillary surgery (n = 121)	SLNB	38	31.4
	ALND	28	23.1
	ALND after SLNB	55	45.5
Number of ALNs removed	Median (range)	12 (1-30)	
Number of metastatic ALNs	Median (range)	1 (0-19)	
Metastases diameter of ALNs (mm)	Median (range)	4 (0-35)	

NAC: neoadjuvant chemotherapy; n: number; RCB: residual cancer burden; pCR: pathological complete response; ypT: Tumor stage after neoadjuvant chemotherapy; ypTis: *in situ*; ypT1mi: micro; ypN: lymph node stage after neoadjuvant chemotherapy; ypN0i: isolated cell; ypNmi: micrometastasis; mm: millimeter; pMultifocality: pathological multifocality; pMulticentricity: pathological multicentricity; BCS: breast-conserving surgery; NSM: nipple-sparing mastectomy; SSM: skin-sparing mastectomy; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection; ALNs: axillary lymph nodes.

Likewise, when ki67 levels and ypT status were compared, ki67 levels of ypT positive (ypT+) patients were found to be lower than those of ypT0. Based on this significant finding, cutoff points were calculated for ki67 levels according to pCR and ypT status. No statistically significant difference was found between ypN0 and ypN+ status and ki67 levels (Table 4).

According to the pCR status, the cutoff point ≤ 40% was determined for the ki67 levels. In cases with ki67 level of ≤ 40%, the risk of non-pCR was five times higher. According to the ypT status, the cutoff point ≤ 35% was determined for the ki-67 levels. In cases with ki-67 level of ≤ 35%, the risk of ypT+ was 3 times higher (Table 5 & Fig. 3A and B).

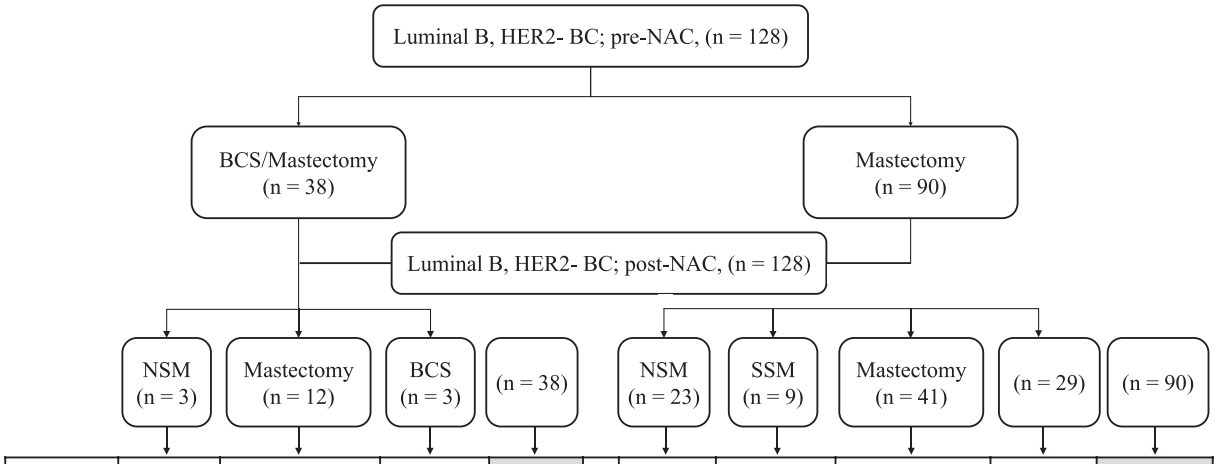
Discussion

In this study, the effect of NAC on the choice of a surgical method for breast and axilla in patients with Luminal B, HER2(-) BC was investigated. NAC has the benefit of downsizing the primary tumor, thereby making the feasibility of BCS more likely and may downstage axillary disease and spare the patients from ALND, especially in patients with HER2 positive and triple-negative BC. However, controversy remains regarding the benefit of neoadjuvant therapy in luminal BCs[7]. We found that patient age and ki67 level were the most significant variables when assessing NAC response in luminal B, HER-2 negative patients.

The ki67 status is not only of important prognostic value, it may also help make treatments for breast cancer more individualized. The clinical implication of ki67 levels is of critical importance in hormone receptor (HR) positive and HER2(-) tumors. In the study of Horimoto et al. Luminal, HER2(-) patients were evaluated and the pCR rate was 10% while the cutoff value for ki67 to distinguish pCR from non-pCR luminal breast cancer cases was 35%[5]. Other studies have also reported that ki67 cutoff values > 35% were found to predict pCR to NAC for the HR-positive and HER2(-) BC cases[8,9]. In our study, the cutoff value of ki67 for pCR was found to be 40%. According to ypT results, our cutoff value was found to be 35%. There was no significant association between ypN status and ki67 levels. In a study, the cutoff level of ki67 for ypN0 was found to be 30%, but they included all molecular subtypes in their study[10].

In the prospective study of Mamtani et al., 85% of 155 biopsy-proven N+ patients with potential for downstaging became eligible for SLNB after NAC. The morbidity of ALND was avoided in 48% of cases, and this was in N+ patients, particularly in HER2 positive and TN BC. In ER+/HER2(-) patients, a higher rate of differential pCR was observed in the axilla than in the breast, with more than 20% of this group achieving nodal pCR[11]. In our study, 68.5% of patients became eligible for SLNB after NAC and more than 30% were spared ALND.

The most clearly established advantage of NAC is to convert patients who were initially ineligible for BCS. NAC has the potential benefit of reducing the size of the tumor, thus allowing BCS performance in patients initially requiring total mastectomy pre-NAC. The proportion of patients who underwent BCS after NAC ranged from 13% to 83%[4]. This wide range is probably due to different patient selection criteria in studies. Kim et al. found a BCS conversion rate of 16.3% in Luminal, HER2(-) BC, with no significant difference from rates in other subtypes[4]. According to pre-NAC MRI findings, the only option was mastectomy in 90 patients, but after NAC, 32% of these



ypT0	1	1	2	4	2		1	4	7
ypTis		1	3	4	2			1	3
ypT1mi		1		1			2		2
ypT1a	1	2	3	6	1	3	5	1	10
ypT1b		3	4	7	1		5	3	9
ypT1c	1	1	5	7	1	1	6	8	16
ypT2		3	6	9	2	3	12	11	28
ypT3					2	2	8	1	13
ypT4a									
ypT4b							2		2

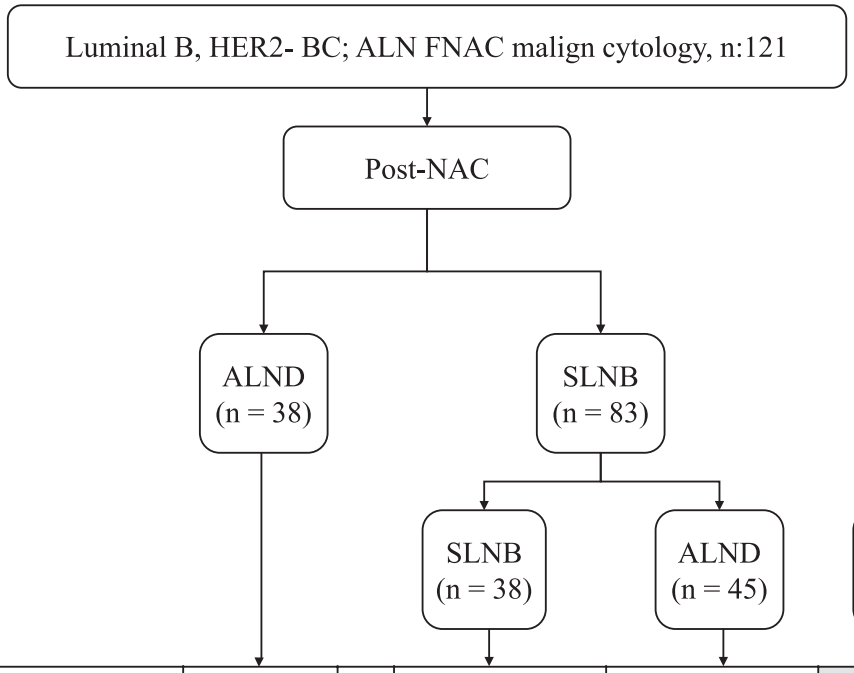
HER2- human epidermal growth factor receptor 2 negative, *BC* breast cancer, *NAC* neoadjuvant chemotherapy, *n* number, *BCS* breast-conserving surgery, *NSM* nipple-sparing mastectomy, *SSM* skin-sparing mastectomy, *ypT* Tumor stage after neoadjuvant chemotherapy, *ypTis* in situ, *ypT1mi* micro

Figure 1. *Evaluation of pre-neoadjuvant chemotherapy (NAC) estimated breast surgery, applied post-NAC breast surgery and tumor stage after NAC.*

Table 3. Evaluation according to pathological complete response status

n	Variables	pCR		p
		pCR	non-pCR	
		14	114	
Age (years)	Median (Q1-Q3)	41.5 (37.8-43.8)	46 (38.8-56)	[c]0.022*
Ki67 (%)	Median (Q1-Q3)	50 (25-70)	30 (20-40)	[c]0.036*
Histological grade; n (%)	Grade 1	0 (0)	16 (14)	[b]0.070
	Grade 2	5 (35.7)	58 (50.9)	
	Grade 3	9 (64.3)	40 (35.1)	
Nuclear grade; n (%)	Grade 1	0 (0)	6 (5.3)	[b]0.274
	Grade 2	4 (28.6)	51 (44.7)	
	Grade 3	10 (71.4)	57 (50)	
Histopathological type, n (%)	IDC	12 (85.7)	90 (78.9)	[a]0.486
	ILC	1 (7.1)	4 (3.5)	
	Others	1 (7.1)	20 (17.5)	
Multicentricity, *n* (%)	no	11 (78.6)	76 (66.7)	[b]0.368
	yes	3 (21.4)	38 (33.3)	
Pre-NAC ALN number, *n* (%)	1	7 (53.8)	41 (38)	[a]0.232
	2	2 (15.4)	16 (14.8)	
	3	0 (0)	24 (22.2)	
	≥ 4	4 (30.8)	27 (25)	

[a]Fisher Freeman Halton exact test. [b]Pearson Chi-squrare test. [c]Mann–Whitney U-test. *p < 0.05.
pCR: pathological complete response; n: number; Q1: quartile 1; Q3: quartile 3; IDC: invasive ductal carcinoma; ILC: invasive lobular carcinoma; NAC: neoadjuvant chemotherapy; ALN: axillary lymph node.



ypN0/ypN0i	8	36		45
ypNmi	1	2	4	6
ypN1a	4		31	35
ypN2a	19		10	29
ypN3a	6			6

HER2- human epidermal growth factor receptor 2 negative, *BC* breast cancer, *ALN* axillary lymph node, *FNAC* fine needle aspiration cytology, *n* number, *NAC* neoadjuvant chemotherapy, *ALND* axillary lymph node dissection, *SLNB* sentinel lymph node biopsy, *ypN* lymph node stage after neoadjuvant chemotherapy, *ypN0i* isolated cell, *ypNmi* micro metastasis

Figure 2. *Evaluation of applied post-neoadjuvant chemotherapy (NAC) axillary surgery and lymph node stage after NAC.*

Table 4. Evaluation of ki67 levels according to pCR, ypT and ypN status

Variables	Parameter	n	Ki67
pCR			
pCR	Median (Q1-Q3)	14	50 (25-70)
non-pCR	Median (Q1-Q3)	114	30 (20-40)
	p		0.036*
ypT			
ypT0	Median (Q1-Q3)	18	40 (28.8-62.5)
ypT+	Median (Q1-Q3)	110	30 (20-40)
	p		0.017*
ypN (n = 121)			
ypN0	Median (Q1-Q3)	45	30 (20.5-50)
ypN+	Median (Q1-Q3)	76	30 (20-40)
	p		0.186

Mann–Whitney U Test. *p < 0.05.
n: number; pCR: pathological complete response; Q1: quartile 1; Q3: quartile 3; ypT: tumor stage after neoadjuvant chemotherapy; ypN: lymph node stage after neoadjuvant chemotherapy.

patients became eligible for BCS, exactly twice the rate reported by Kim et al. In our study, we evaluated not only BCS, but also patients who underwent reconstruction with NSM and SSM as a good cosmetic outcome. Among the patients who underwent mastectomy after NAC, three patients were ypT0 and 25 patients were ypT1, and BCS could be performed on these patients. However, the surgical preference of the patients and the fact that the marker was not placed at the beginning affected the post-NAC surgical treatment strategy.

In the study of King et al., it was reported that a surgical margin of no ink tumor is probably adequate for Stage I-III invasive breast cancer treated with NAC and BCS, in the absence of multiple scattered microscopic tumor foci[12]. In our study, pre-NAC these were 32% bifocal tumors and 25.8% multifocal by radiological assessment but post-NAC these proportions regressed to

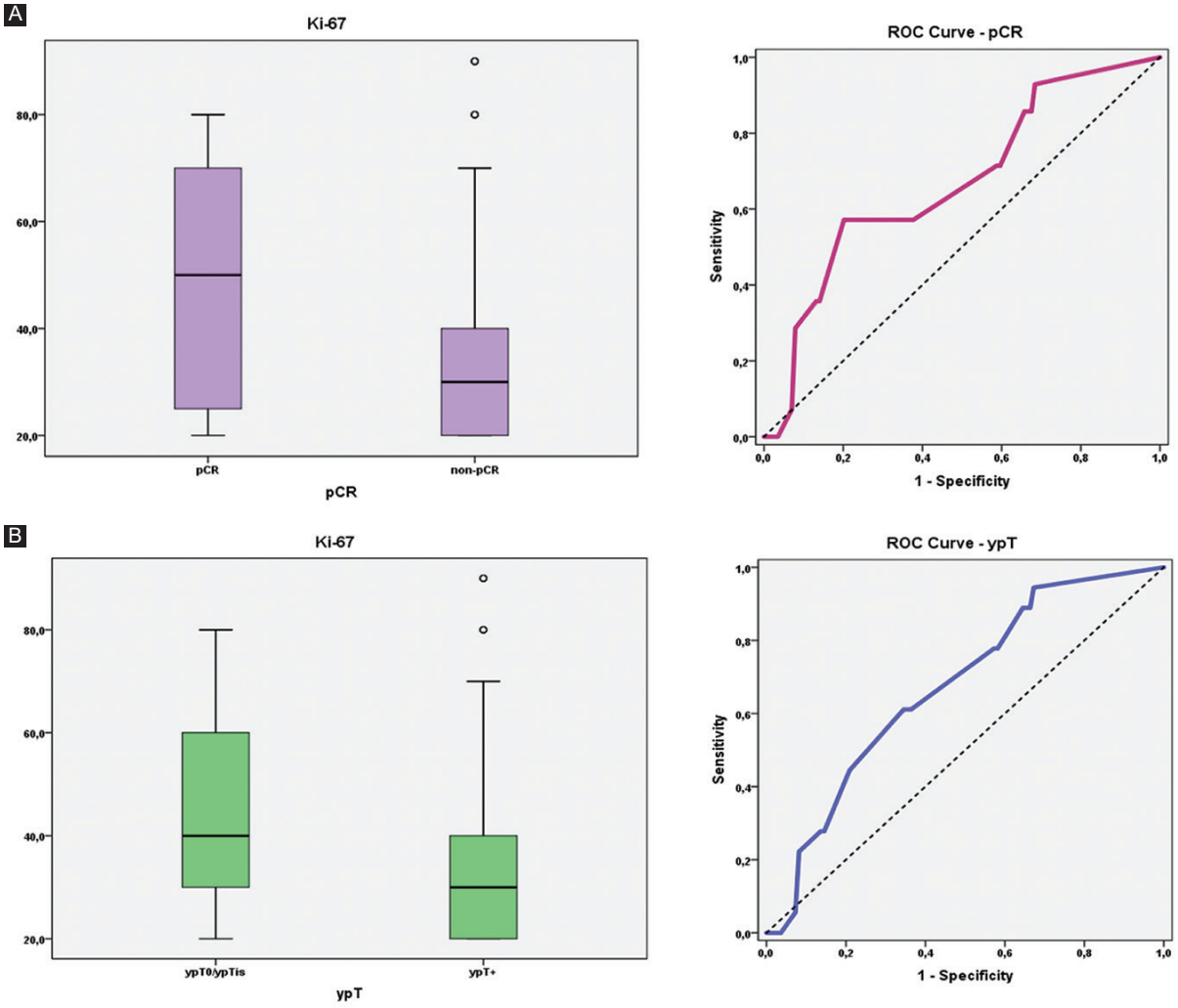


Figure 3. A: *Receiver operating characteristics (ROC) curve of ki67 levels by pathological complete response (pCR) status.* **B:** *ROC curve for ki67 levels by tumor stage after neoadjuvant chemotherapy (ypT) status (ypT is in situ).*

Table 5. Diagnostic screening tests and ROC curve analyses for ki67 levels according to pCR and ypT values, and the relationship between pCR and ypT status and ki67 levels (cut-off values)

Variables		Diagnostic scan	ROC curve		p
		Cut-off	Area	95% confidence interval	
pCR	Ki67	≤ 40	0.669	0.518-0.820	0.040*
ypT	Ki67	≤ 35	0.672	0.549-0.796	0.019*

*p < 0.05

Variables		pCR		non-pCR		p
		n	%	n	%	
Ki67	> 40	8	57.1	23	20.2	0.005**
	≤ 40	6	42.9	91	79.8	

Fisher's exact test. **p < 0.01

Variables		ypT0/ypTis		ypT+		p
		n	%	n	%	
Ki67	> 35	11	61.1	38	34.5	0.032*
	≤ 35	7	38.9	72	65.5	

Pearson Chi-square test. *p < 0.05. ROC: receiver operating characteristics; pCR: pathological complete response; ypT: tumor stage after neoadjuvant chemotherapy; ypTis: *in situ.*

18.8% bifocal and 5.5% multifocal histopathologically. The mean surgical margin of 110 patients with ypT+ was 11.46 mm. NAC facilitated safe surgical margins.

Our study has some limitations. It has a retrospective design. It was not always possible to determine whether a patient would be a candidate for BCS or total mastectomy before and after NAC. Patient preference after NAC also affected surgical decisions.

Conclusion

In patients with luminal B, HER2(-) BC a low pCR rate should not discourage the use of NAC. The ki67 level is a guide for individualizing treatment. Especially in young patients with high ki67 levels, NAC increases the chance of BCS and may spare patients from ALND.

Funding

The authors declare that they have not received funding for this study.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. Right to privacy and informed consent. The authors have obtained approval from the Ethics Committee for analysis and publication of routinely acquired clinical data and informed consent was not required for this retrospective and observational study.

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