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Comparison of Tru-Cut and Surgical Biopsy Specimens in Breast Carcinoma Cases Undergoing Neoadjuvant Chemotherapy

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Abstract

Background: Neoadjuvant chemotherapy (NACT) induces significant pathological changes in breast tumors, which are essential for assessing treatment response and informing postoperative management.

Objective: The present study aimed to evaluate the changes in hormone receptors and prognostic markers (ER, PR, HER2, Ki-67) in patients who underwent breast-conserving surgery or mastectomy after NACT regimens.

Methods: This retrospective study compared the expression of HER2, Ki-67, ER, and PR in tumor tissues from tru-cut biopsy samples and post-NACT resection materials using immunohistochemical analysis.

Results: Patients who underwent NACT between January 2021 and 2025 were evaluated. The distribution of patients based on receptor status and molecular subtypes in tru-cut biopsy material was as follows: 51.2% ER-positive, 51.2% PR-positive, 16.3% luminal A, 25.6% luminal B, 27.9% HER2-positive, and 13% triple-negative breast cancer. A small proportion (8%) of resection specimens from patients who received NACT showed post-treatment changes in hormone receptor status (ER and PR). A higher proportion (20%) of resection specimens from patients who received NACT exhibited a decrease in Ki-67 expression, shifting from high to low positivity.

Conclusion: Changes in receptor status after NACT cannot be attributed to treatment alone, but the shift from hormone receptor-positive to hormone receptor-negative and loss of HER2 are likely to be due to the effects of NACT. Conversely, shifts from negative to positive are more likely related to intratumoral heterogeneity. Clinically, positive receptor status is important because it can influence adjuvant treatment decisions. Thus, post-NACT reevaluation of biomarkers is essential for accurate therapeutic planning.

Keywords: Breast cancer, neoadjuvant chemotherapy, biomarker alteration, molecular subtypes.

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Neoadjuvan Kemoterapi Gören Meme Karsinomu Hastalarında Tru-Cut Biyopsi ve Cerrahi Rezeksiyon Örneklerinin Karşılaştırılması

Öz

Giriş: Neoadjuvan kemoterapi (NACT), meme tümörlerinde tedavi yanıtının değerlendirilmesi ve postoperatif yönetimin yönlendirilmesi için önemli olan önemli patolojik değişikliklere neden olur.

Amaç: Bu çalışmanın amacı, NACT rejimleri sonrasında meme koruyucu cerrahi veya mastektomi uygulanan hastalarda hormon reseptörleri ve prognostik belirteçlerdeki (ER, PR, HER2, Ki-67) değişiklikleri değerlendirmektir.

Yöntemler: Bu retrospektif çalışmada, tru-cut biyopsi örneklerinden ve NACT sonrası rezeksiyon materyallerinden alınan tümör dokularındaki HER2, Ki-67, ER ve PR ekspresyonu immünohistokimyasal analiz kullanılarak karşılaştırılmıştır.

Bulgular: Ocak 2021 ile 2025 tarihleri arasında NACT uygulanan hastalar değerlendirilmiştir. Tru-cut biyopsi materyalindeki hastaların reseptör durumu ve moleküler alt tiplerine göre dağılımı şu şekildeydi: %51,2 ER pozitif, %51,2 PR pozitif, %16,3 lüminal A, %25,6 lüminal B, %27,9 HER2 pozitif ve %13 Üçlü negatif meme kanseri. NACT ile tedavi edilen hastalardan alınan rezeksiyon örneklerinin küçük bir kısmında, tedaviden sonra hormon reseptör durumu değişti; %8'inde ER ekspresyonunda bir dönüşüm, %8'inde ise PR ekspresyonunda negatiften pozitife veya tam tersi bir dönüşüm görüldü. NACT uygulanan hastalardan alınan rezeksiyon örneklerinin daha yüksek bir oranında (%20), Ki-67 ekspresyonunda yüksek pozitiflikten düşük pozitifliğe doğru bir düşüş görüldü.

Sonuç: Ocak 2021 ile 2025 tarihleri arasında NACT uygulanan hastalar değerlendirilmiştir. Tru-cut biyopsi materyalindeki reseptör durumu ve moleküler alt tiplere göre hastaların dağılımı şu şekildeydi: %51,2 ER-pozitif, %51,2 PR-pozitif, %16,3 luminal A, %25,6 luminal B, %27,9 HER2-pozitif ve %13 üçlü-negatif meme kanseri. NACT uygulanan hastalardan alınan rezeksiyon örneklerinin küçük bir kısmında (%8), tedavi sonrası hormon reseptör durumunda (ER ve PR) değişiklikler görüldü. NACT uygulanan hastalardan alınan rezeksiyon örneklerinin daha yüksek bir kısmında (%20), Ki-67 ekspresyonunda yüksek pozitiflikten düşük pozitifliğe doğru bir düşüş görüldü.

Anahtar kelimeler: Meme kanseri, neoadjuvan kemoterapi, biyobelirteç değişikliği, moleküler alt tipi.

INTRODUCTION

Breast cancer (BC) has become the most prevalent malignancy among women worldwide. Neoadjuvant chemotherapy (NACT), which involves the administration of systemic treatments before surgical intervention, has become a cornerstone in the multidisciplinary management of BC[1]. Traditionally, systemic chemotherapy has been used as adjuvant therapy following breast and regional lymph node surgery in patients with operable BC. However, NACT has generally been reserved for managing advanced, non-metastatic BC, except in cases where surgery must be delayed[2]. Recently, the indications for preoperative therapy in early-stage BC have expanded. It is now routinely recommended for operable patients to reduce the need for extensive surgery to remove the tumor and to use the response of the breast and lymph nodes as a prognostic indicator[2,3]. However, established systems for handling and assessing such specimens are still lacking. Several assessment systems highlight the importance of a multidisciplinary approach to enhance the accuracy of BC assessments. Therefore, a comprehensive and systematic evaluation of clinical, radiological, and pathological findings is essential[1].

NACT for BC has become the standard of care, offering the chance to evaluate and measure the response in the tissue removed during surgery. Correlating this with radiology, macroscopic mapping, and histological review using a semi-quantitative reporting system like residual cancer burden provides valuable prognostic information that can guide further treatment decisions[3]. The precise definition of pathological complete response (pCR) and its prognostic impact on survival across different intrinsic BC subtypes remains unclear[1]. Neoadjuvant therapy can alter tumor biology and biomarker expression (e.g., ER, PR, HER2, Ki-67), which may affect prognosis and guide adjuvant treatment decisions. Evaluating both pre- and post-treatment specimens allows for more accurate risk stratification and personalized treatment planning. This study aimed to assess the alterations in hormone receptors and prognostic markers (ER, PR, HER2, Ki-67) in patients who underwent excisional surgery or mastectomy following NACT regimens.

METHODS

Patient Selection

We retrospectively reviewed the medical records of 43 patients with breast cancer (BC) who received neoadjuvant chemotherapy (NACT) and underwent surgery at our center between January 2021 and January 2025. Pathology reports and surgical slides of these patients were examined. Patients were categorized into three groups according to their response to NACT: non-responders, partial responders, and those who achieved pCR, defined as the absence of invasive tumor in the surgical specimen.

Ethical approval for the study was obtained from the İzmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (Date: 03.07.2024, Decision No: 1658).

Pathological Evaluation

Demographic data and tumor characteristics were obtained from patient medical records. The pCR rate in the study cohort was 41.9% (n = 18). Immunohistochemistry (IHC) results for estrogen receptor (ER), progesterone receptor (PR), HER2 status, and the Ki-67 proliferation index, along with histopathological features such as tumor type and grade, were obtained from original pathology reports of tru-cut biopsy specimens and postoperative residual tumors. IHC staining results were reassessed by two pathologists to ensure accuracy.

ER and PR status were classified as low positive when IHC staining appeared in 1-9% of cells. IHC staining for both hormone receptors was considered positive if ≥10% of cells showed staining. HER2 was considered positive with an IHC score of 2, accompanied by fluorescence in situ hybridization (FISH) positivity or an IHC score of 3. Cases with Ki67 of 20% and above were grouped as high, others as low[4,5].

Luminal A (LA) tumors were characterized by the presence of ER and/or PR, absence of HER2, and low expression of Ki-67 (less than 20%). Luminal B (LB) tumors, on the other hand, were defined by the presence of PR and/or ER and high Ki-67 expression (more than 20%). HER2-positive tumors were characterized by HER2 overexpression, irrespective of ER or PR status. Triple-negative (TNBC) tumors were defined as ER, PR, and HER2 negative. Residual tumors were categorized according to their response to NACT: complete responders had no residual tumor in the resection specimen; partial responders showed evidence of regression with residual tumor fragments; and non-responders exhibited no significant histopathological reduction in tumor size.

Statistical Analysis

Concordance and discordance rates for hormone receptors (ER, PR), HER2, and the Ki-67 proliferation index were calculated by comparing their status in tru-cut biopsy specimens and residual tumors. To evaluate chemosensitivity, tumor characteristics of partially responsive (chemotherapy-sensitive) and non-responsive (chemotherapy-resistant) cases were analyzed. Changes in ER and PR expression (%), tumor grade, and Ki-67 index were assessed separately within each group.

Statistical analyses were performed using IBM® SPSS® Statistics version 22.0. Pearson's chi-square test was used to analyze categorical variables. When more than 20% of the expected cell frequencies were below 5, Fisher's exact test was applied instead. Agreement between categorical data obtained from two different methods on the same samples was evaluated using Cohen's kappa coefficient. A p-value of ≤0.05 was considered statistically significant.

RESULTS

Forty-three cases undergoing tru-cut biopsy followed by neoadjuvant chemotherapy at our hospital were included in this study. The patients' ages ranged from 28 to 78 years, with a mean age of 50.11 years. Patients aged 51 years and older showed a statistically significant association with right breast tumor localization (p=0.037). Among cases with tru-cut biopsy, the tumor grade was predominantly grade 2 (55.8%). Classification of clinicopathological features of breast carcinoma tru-cut biopsy materials according to age groups is summarized in Table 1.

Table I: Classification of clinicopathological features of breast carcinoma tru-cut biopsy materials by age group

	Age			p
	50 years and under	51 years and over	Total	
Localization				
Right	10	15	25	0.037
	23.3%	34.9%	58.1%	
Left	13	5	18	
	30.2%	11.6%	41.9%	
Tumor type				
No special type (NST)	21	13	34	0.04
	48.8%	30.2%	79.1%	
Invasive	2	7	9	
	4.7%	16.3%	20.9%	
Tumor grade				
2	11	13	24	>0.05
	25.6%	30.2%	55.8%	
3	12	7	19	
	27.9%	16.3%	44.2%	
DCIS				
(+)	5	2	7	>0.05
	11.6%	4.7%	16.3%	
(-)	18	18	36	
	41.9%	41.9%	83.7%	
DCIS grade				
2	1	2	3	>0.05
	2.3%	4.7%	7.0%	
3	4	0	4	
	9.3%	0.0%	9.3%	
DCIS morphology				
Comedo	4	0	4	>0.05
	9.3%	0.0%	9.3%	
Cribriform+/-Solid	1	2	3	
	2.3%	4.7%	7.0%	
DCIS necrosis				
(+)	4	1	5	>0.05
	9.3%	2.3%	11.6%	
(-)	1	1	2	
	2.3%	2.3%	4.7%	
DCIS calcification				
(+)	0	0	0	>0.05
(-)	5	2	7	
	11.6%	4.7%	16.3%	

DCIS: Ductal Carcinoma in-situ

Most cases (76.7%) involved breast and sentinel lymph node excision specimens. Skin involvement was absent in all cases. There was no relationship between lymphovascular and perineural invasion and age group (<0.05). There was no lymph node invasion in any case. 76.7% of the resection materials were excision, the rest were modified radical mastectomy. The tumor was a nonspecific type invasive carcinoma (NST) in 21 cases. Four of the resections had mixed (NST and lobular) carcinoma. In resection specimens, lymphovascular invasion (LVI) was observed in 13 cases (30.2%) and perineural invasion (PNI) in 3 cases (7%). Classification of clinicopathological features of breast carcinoma resection materials according to age groups is summarized in Table 2.

Table II: Classification of clinicopathological features of tumors in resection materials according to age groups

	Age			p
	50 years and under	51 years and over	Total	
Tumors in Resection Materials				
Number of tumor focuses				
Single	8	9	17	>0.05
	32%	36%	68%	
Multiple	6	2	8	
	24	8%	32%	
Chemotherapy response				
Partial	11	7	18	>0.05
	25.6%	16.3%	41.9%	
Unresponsive	3	4	7	
	7.0%	9.3%	16.3%	
pT				
1mi	2	0	2	>0.05
	4.7%	0.0%	4.7%	
1a	1	1	2	
	2.3%	2.3%	4.7%	
1b	1	1	2	
	2.3%	2.3%	4.6%	
1c	3	5	8	
	7.0%	11.6%	18.6%	
2	7	3	10	
	16.3%	7.0%	23.3%	
3	0	1	1	
	0.0%	2.3%	2.3%	
DCIS in Resection Materials				
DCIS				
(+)	10	5	15	>0.05
	23.3%	11.6%	34.9%	
(-)	13	15	28	
	30.2%	34.9%	65.1%	
DCIS Grade				
2	4	4	8	>0.05
	9.3%	9.3%	18.6%	
3	6	1	7	
	14.0%	2.3%	16.3%	
DCIS Morphology				
Comedo	3	1	4	>0.05
	7.0%	2.3%	9.3%	
Cribriform+/-Solid	6	4	10	
	14.0%	9.3%	23.3%	
Solid	1	0	1	
	2,3%	0,0%	2.3%	
DCIS Necrosis				
(+)	3	2	5	>0.05
	7.0%	4.7%	11.6%	
(-)	7	3	10	
	16.3%	7.0%	23.3%	
DCIS Calcification				
(+)	1	0	1	>0.05
	2.3%	0.0%	2.3%	
(-)	9	5	14	
	20.9%	11.6%	32.6%	

Concordance was found between tumor grade in resection specimens and tru-cut biopsy tumor grade (p=0.038). Higher tumor grades in resection specimens were associated with the presence of DCIS (p=0.022). Tumor grade in resection specimens also correlated with the number of tumor foci (p<0.001), presence of tumor (p<0.001), and LVI (p=0.002). Additionally, concordance was observed between morphology in resection specimens and tru-cut DCIS (p<0.001), as well as necrosis in resection and tru-cut DCIS (p=0.017). The relationship between tumor grade and clinicopathological parameters in the resection material is summarized in Table 3.

Table III: Relationship between tumor grade and clinicopathological parameters in resection material

	Tumor Grade			**Total**	**P**
	1	**2**	**3**		
LVI					
(+)	1	6	6	13	**0.002**
	4%	24%	24%	52%	
(-)	3	4	5	12	
	12%	16%	2%	48%	
Chemotherapy Response					
Partial	2	8	8	18	**<0.001**
	8%	32%	32%	72%	
Unresponsive	2	2	3	7	
	8%	8%	12%	28%	
pT					
1mi	0	1	1	2	**<0.001**
	0.0%	4%	4%	8%	
1a	0	2	0	2	
	0.0%	8%	0.0%	8%	
1b	1	0	1	2	
	4%	0.0%	4%	8%	
1c	0	3	5	8	
	0.0%	12%	20%	32%	
2	2	4	4	10	
	8%	16%	16%	40%	
3	1	0	0	1	
	4%	0.0%	0.0%	4%	
ER (%)					
Negative	1	4	6	11	
	4%	16%	24%	44%	**<0.001**
1-10	1	0	0	1	
	4%	0.0%	0.0%	2%	
11-100	2	6	5	13	
	8%	24%	20%	52%	
PR (%)					
Negative	1	4	8	13	**<0.001**
	4%	16%	32%	52%	
1-10	1	1	1	3	
	4%	8%	8%	20%	
11-100	2	5	2	9	
	8%	40%	8%	56%	
HER2 Score					
Negative	4	8	7	19	**<0.001**
	16%	32%	28%	76%	
Positive	0	2	4	6	
	0.0%	8%	16%	12%	
Ki67					
Low	2	6	3	11	**<0.001**
	8%	12%	24%	44%	
High	2	4	8	14	
	8%	16%	32%	56%	
Molecular subtype					
Luminal A	**1**	**4**	**2**	**7**	**<0.001**
	4%	16%	8%	28%	
Luminal B	**2**	**2**	**3**	**7**	
	8%	8%	12%	28%	
HER2	**0**	**2**	**4**	**6**	
	0%	8%	16%	24%	
Tripple Negative	**1**	**2**	**2**	**5**	
	4%	8%	8%	20%	

LVI: Lymphovascular invasion, pT: Pathologic T stage

In patients aged 50 and younger, the NST tumor count was significantly higher in tru-cut biopsy specimens (p=0.04). Furthermore, ER and PR positivity were significantly higher in patients aged 50 and under (p=0.028 and p=0.01, respectively). Concordance was observed between ER and PR positivity, tumor subtype, and findings in tru-cut biopsy and excision specimens.

Of the 43 patients who underwent tru-cut biopsy, a tumor was detected in only 25 of the resection material after NAC. In NACT-treated cases, ER and PR status changed in 8% of resection specimens. One case with ER negative in tru-cut biopsy was observed as low positive after NAC. 1 case with ER low positive in tru-cut biopsy was observed as negative after NAC. 2 positive and 1 negative PR cases in tru-cut biopsy were observed as low positive after NAC. 1 positive and 2 low positive in tru-cut biopsy PR cases were observed as negative after NAC. HER2 status conversion was observed in 12% of NACT-treated cases. Two positive HER2 cases in tru-cut biopsy were detected as negative after NAC, and 1 negative case was detected as positive after NAC.

In five cases, high Ki-67 expression in tru-cut biopsy decreased after NACT. The age-based distribution of prognostic parameters in tru-cut and resection specimens is presented in Table 4. After NACT, two HER2-positive cases in tru-cut biopsy converted to luminal B, one triple-negative case became HER2-positive, three luminal B cases became luminal A, and one luminal A case converted to luminal B.

Table IV: Distribution of prognostic parameters of Tru-cut and resection materials according to age

	TRU-CUT TM				**RESECTION TM**			
	Age				**Age**			
	50 and below	**51 and above**	**Total**	**p**	**50 and below**	**51 and above**	**Total**	**p**
ER								
Negative	7	14	21		3	7	10	
	16,3%	32,6%	48,8%		7,0%	16,3%	23,3%	
Low positive	1	1	2	**0.028**	1	1	2	<0.05
	2,3%	2,3%	4,7%		2,3%	2,3%	4,7%	
	15	5	20		9	4	13	
Positive	34,9%	11,6%	46,5%		20,9%	9,3%	30,2%	
PR								
Negative	7	14	21		5	7	12	
	16,3%	32,6%	48,8%		11,6%	16,3%	27,9%	
Low positive	6	0	6	**0.01**	3	1	4	<0.05
	14,0%	0,0%	14,0%		7,0%	2,3%	9,3%	
	10	6	16		5	4	9HER	
Positive	23,3%	14,0%	37,2%		11,6%	9,3%	20,9%	
HER2								
Negative	17	13	30		11	9	20	
	39,5%	30,3%	69,8%	<0.05	44%	36%	80%	<0.05
	6	7	13		2	3	5	
Positive	14,0%	16,3%	30,2%		8%	12%	20%	
Ki67								
High ≥20	19	16	35		9	6	15	
	44,2%	37,2%	81,4%	<0.05	20,9%	14,0%	34,9%	<0.05
Low ≤19	4	4	8		5	6	11	
	9,3%	9,3%	18,6%		11,6%	14,0%	25,6%	

DISCUSSION

NACT has been extensively used in clinical trials because it allows for the evaluation of tumor response to therapeutic agents. This approach has contributed to improved survival rates and increased opportunities for breast-conserving surgery. Current neoadjuvant therapy protocols include chemo-immunotherapy for patients with TNBC, chemotherapy combined with HER2-targeted therapy for HER2-positive tumors, and chemotherapy or endocrine therapy for hormone receptor-positive, HER2-negative tumors6. NACT has been shown to be effective in aggressive TNBC and HER2-positive breast cancers, with high rates of pCR reported[1]. NACT has become a standard treatment for locally advanced and large breast cancers and is increasingly used even in early-stage disease[6]. The relatively small sample size (n=43) represents a limitation of this study, as it may restrict the statistical power and the robustness of subgroup analyses. Future research with larger and more diverse cohorts is warranted to validate these findings and enhance their generalizability.

LVI has been reported at varying rates in BC resection specimens. We found a higher rate of LVI (30.2%) in the resection material compared to the data reported in the previous literature[6]. LVI is considered a resistant component of BC following NACT. Consequently, in some cases, the only remaining evidence of disease after NACT may be tumor emboli within lymphatic and vascular spaces, even when no residual tumor is present in the breast parenchyma[7].

Various guidelines suggest different approaches based on core biopsy results, as biomarker status after NACT is primarily determined by pretreatment core biopsy. However, no consensus exists on this matter, and HER2 status should be reassessed in BC patients undergoing NACT. When ER, PR, and HER2 are positive on pretreatment core biopsy, their status generally remains unchanged, and reassessment is usually not necessary. Conversely, if the core biopsy is negative or indeterminate, these markers should be reassessed in the surgical specimen[1]. In our study, an 8–12% change in these markers in resection specimens highlighted the importance of reassessment following NACT. Previous studies have shown that pCR is associated with favorable outcomes in patients with luminal B, HER2-positive, and triple-negative breast cancer subtypes. However, this association was not observed in patients with LA tumors[8]. In our study, no correlation was found between tumor subtypes on tru-cut biopsy and pCR. Two cases with HER2-positivity in tru-cut biopsy were LB after NACT. One case with TN in tru-cut biopsy was HER2-positive after NACT, three cases with LB in biopsy were LA after NAC, and one case with LA in biopsy was LB after NACT.

The evaluation of sentinel lymph nodes was performed using the same method as in non-neoadjuvant cases[7]. In our study, no lymph node metastases were detected following NACT. Although each system for assessing response to NACT defines pCR differently, all systems document the presence of invasive carcinoma and whether it is located in the breast parenchyma. The main differences between these systems relate to the inclusion or exclusion of ductal carcinoma in situ (DCIS) and the evaluation of axillary lymph node status. Therefore, because response assessment systems may vary between institutions, clear definitions of in-situ carcinoma and sentinel lymph node status should be provided in pathological reports[7]. Previous study have shown that the relationship between pathological complete response and long-term results was most significant in cases with TNBC and in patients with HER2-positive, hormone receptor-negative tumors who received trastuzumab[9-12].

In the present study, ER and PR positivity were notably higher in patients aged 50 and under. Higher tumor grades in resection specimens were associated with the presence of in-situ carcinoma. Additionally, tumor grade in resection specimens correlated with both the number of tumor foci and the presence of LVI. Concordance was also observed between ER and PR positivity, tumor subtypes, and the findings in both tru-cut biopsy and excision specimens. Our findings are consistent with previously reported data in the literature[13-18].

Previous study reported that about 3-5% of HR and about 10% of HER2 inconsistency can be observed in BC after the NACT regimens are used. They stated that discordances may be bidirectional and that their causes are multifactorial[19]. In our study, both 8% of ER and PR showed a change in the resection materials of cases receiving NACT. The rate of change for HER2 was 12%. Ki67 changed from high to low positivity in 20% of cases. While the effects of NACT alone cannot fully explain these discordances, it likely contributes to changes in biomarker expression. Transitions from negative to positive receptor status are mainly attributable to intratumoral heterogeneity, whereas conversions from positive to negative are largely driven by the effects of NACT. Clinically, the acquisition of positive receptor status is particularly important because it may influence adjuvant therapy decisions.

CONCLUSION

Among the histological responses to NACT, evaluating residual disease is paramount, as it directly impacts prognosis and recurrence risk. Post-NACT biomarker assessment should be routinely incorporated into standard pathology protocols. Loss of hormone receptor expression typically reflects treatment-induced tumor regression or clonal selection, whereas conversion from negative to positive status usually results from intratumoral heterogeneity, revealing subclones undetected in the pretreatment biopsy. Clinically, newly positive receptor status is significant, as it may influence adjuvant therapy decisions, including the initiation of hormone or HER2-targeted treatments. Thus, repeated biomarker evaluation after NACT is crucial for accurate risk stratification and personalized therapy planning.

Ethical approval: Ethical approval for the study was obtained from the İzmir Bakırçay University Non-Interventional Clinical Research Ethics Committee (Date: 03.07.2024, Decision No: 1658).

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