

BÖLÜM II

NEOADJUVAN KEMOTERAPİ SONRASI CERRAHİ TEDAVİ

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GİRİŞ

Lokal ileri meme kanserli (T3N0 evre IIb, evre IIIa-IIIc) hastalarda kesin tedavi neoadjuvan kemoterapi olmakla birlikte; operasyona uygun ve sonrasında adjuvan kemoterapi uygulanabilecek olan daha erken evre (T1-2N0-1, evre 2IIa-b) seçilmiş tümör biyolojisi agresif triple negatif veya HER2(+) hastalara da günümüzde neoadjuvan kemoterapi uygulanmaya başlanmıştır (1,2). Her iki hasta grubunda neoadjuvan tedaviden (NAT) beklenen fayda farklıdır. İlk grup meme kanseri hastalarında kanser boyutu ve aksilla pozitifliğinde sağlanan gerileme ile hasta daha konservatif cerrahiye aday hale getirilir. Bu tedavideki temel amaç ise hastayı mastektomiden ve/veya aksiller diseksiyondan kurtarıp meme koruyucu cerrahi (MKC) veya onkoplastik rekonstruktif cerrahi ve/veya sentinel lenf nodu (SLN) diseksiyonu imkanı sağlamaktır. İkinci grup hastada ise ek olarak tümörün kemoterapiye cevabını görmek ve buna göre ek sistemik tedavi gereksimini ortaya koymaktır. HER2 pozitif rezidüel hastalıkta adjuvan TDM-1 (transtuzumab-emtansine) verilmesi ve triple negatif meme kanserinde ise adjuvan kape-sitabin uygulanmasının sürviye ek katkısı gösterilmiştir (3,4). Bu tür erken evre vakalarda sağlanan yüksek tam cevap oranları nedeniyle cerrahinin deeskaledilmesi prospektif çalışmalarda araştırılmış, ancak bu konuda bir konsensüs sağlanamamıştır(5).

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KAYNAKLAR

- 1- Rubens RD, Sexton S, Tong D, et al. Combined chemotherapy and radiotherapy for locally advanced breast cancer. *Eur J Cancer*.1980; 16:351-356.
- 2- Kaufmann M, von Minckwitz G, Bear HD, et al. Recommendation from an international expert panel on the use of neoadjuvant (primary) systemic treatment of operable breast cancer: new perspectives, *Ann Oncol* .2007; 18: 1927–34
- 3- von Minckwitz G, Huang CS, Mano MS, et al. Trastuzumab emtansine for residual invasive HER2-Positive breast cancer. *N Engl J Med*. 2019; 380(7):617-628 Doi: 10.1056/NEJMoa1814017
- 4- Masuda N, Lee SJ, Ohtani S, et al. Adjuvant capecitabine for breast cancer after preoperative chemotherapy. *N Engl J Med* 2017; 376: 2147–2159.
- 5- Heil J,Kuerer H.M, Pfof A, et al. Eliminating the breast cancer surgery paradigm after neoadjuvant systemic therapy: current evidence and future challenges. *Annals of Oncology*. 2020; 31:61-71. Doi:10.1016/j.annonc.2019.10.012
- 6- Fisher B, Brown A, Mamounas E, et al. Effect of preoperative chemotherapy on local-regional disease in women with operable breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-18. *Journal of Clinical Oncology : Official Journal of the American Society of Clinical Oncology*. 1997;15(7):2483-2493. Doi: 10.1200/jco.1997.15.7.2483.
- 7- Mamounas EP. NSABP Protocol B-27. Preoperative doxorubicin plus cyclophosphamide followed by preoperative or postoperative docetaxel. *Oncology (Williston Park)*. 1997;11(6 Suppl 6):37-40.
- 8- Van Nes JG, Putter H, Julien JP, et al. Preoperative chemotherapy is safe in early breast cancer, even after 10 years of follow-up; clinical and translational results from the EORTC trial 10902. *Breast Cancer Res Treat*. 2009;115(1):101-13
- 9- Spring LM, Gupta A, Reynolds KL, et al: Neoadjuvant endocrine therapy for estrogen receptor-positive breast cancer: A systematic review and meta-analysis. *JAMA Oncol* 2016;2:1477-1486
- 10- Rouzier R, Perou CM, Symmans WF, et al. Breast cancer molecular subtypes respond differently to preoperative chemotherapy. *Clin Cancer Res*. 2005;11(16):5678-85
- 11- Cortazar P, Zhang L, Untch M, et al. Pathological complete response and long-term clinical benefit in breast cancer: the CTNeoBC pooled analysis. *Lancet* 2014; 384: 164–72.
- 12- Wimmer K, Bolliger M, Bago-Horvath Z,et al. Impact of surgical margins in breast cancer after preoperative systemic chemotherapy on local recurrence and survival. *Ann Surg Oncol*. 2020;27:1700
- 13- Loibl S, Poortmans P, Morrow M, et al. Breast cancer. *Lancet*. 2021;397:1750-1769
- 14- Lee JS, Yost SE, Yuan Y. Neoadjuvant Treatment for Triple Negative Breast Cancer: Recent Progresses and Challenges. *Cancers (Basel)*. 2020;12(6):1404. doi: 10.3390/cancers12061404.
- 15- Korde LA, Somerfield MR, Carey LA,et al. Neoadjuvant Chemotherapy, Endocrine Therapy, and Targeted Therapy for Breast Cancer: ASCO Guideline, *J Clin Oncol*. 2021;39(13):1485.
- 16- Schmid P, Cortes J, Pusztai L, et al. Pembrolizumab for Early Triple-Negative Breast Cancer. *New England Journal of Medicine*. 2020;382(9):810-821. doi: 10.1056/NEJMoa1910549.
- 17- Liu Q, Wang C, Li P,et al. The role of (18) F-FDG PET/CT and MRI in assessing pathological complete response to neoadjuvant chemotherapy in patients with breast cancer: a systematic review and meta-analysis. *Biomed Res Int* 2016;2016:3746232
- 18- Fowler AM, Mankoff DA, Joe BN. Imaging neoadjuvant therapy response in breast cancer. *Radiology* 2017;285:358-375
- 19- Buchholz TA, Mittendorf EA, Hunt KK. Surgical Considerations After Neoadjuvant Chemot-

- herapy: Breast Conservation Therapy. *J Natl Cancer Inst Monogr.* 2015;2015(51):11-4.
- 20- Buchholz TA, Hunt KK, Whitman GJ, et al. Neoadjuvant chemotherapy for breast carcinoma: multidisciplinary considerations of benefits and risks. *Cancer.* 2003;98(6):1150-60.
 - 21- Morrow M, Harris JR, Schnitt SJ. Surgical margins in lumpectomy for breast cancer—bigger is not better. *New Engl J Med.* 2012;367(1):79–82
 - 22- Untch M, Huober J, Jackisch C, et al. Initial treatment of patients with primary breast cancer: evidence, controversies, consensus: spectrum of opinion of German specialists at the 15th International St. Gallen Breast Cancer Conference (Vienna 2017). *Geburtshilfe und Frauenheilkunde.* 2017;77(6):633–44.
 - 23- Chen AM, Meric-Bernstam F, Hunt KK, et al. Breast conservation after neoadjuvant chemotherapy. *Cancer.* 2005 ;103(4):689-95. doi: 10.1002/cncr.20815.
 - 24- Mamounas EP, Anderson SJ, Dignam JJ, et al. Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27. *J Clin Oncol.* 2012;30(32):3960-6. doi: 10.1200/JCO.2011.40.8369.
 - 25- Tsai RJ, Dennis LK, Lynch CF, et al. The risk of developing arm lymphedema among breast cancer survivors: a meta-analysis of treatment factors. *Ann Surg Oncol.* 2009;16(7):1959–72.
 - 26- Wong SM, Weiss A, Mittendorf EA, et al. Surgical Management of the Axilla in Clinically Node-Positive Patients Receiving Neoadjuvant Chemotherapy: A National Cancer Database Analysis. *Ann Surg Oncol.* 2019;26(11):3517-3525. doi: 10.1245/s10434-019-07583-6.
 - 27- Samiei S, Simons JM, Engelen SME, et al. EUBREAST Group. Axillary Pathologic Complete Response After Neoadjuvant Systemic Therapy by Breast Cancer Subtype in Patients With Initially Clinically Node-Positive Disease: A Systematic Review and Meta-analysis. *JAMA Surg.* 2021;156(6):e210891. doi: 10.1001/jamasurg.2021.0891.
 - 28- Kilbride KE, Lee MC, Nees AV, et al. Axillary staging prior to neoadjuvant chemotherapy for breast cancer: predictors of recurrence. *Ann Surg Oncol.* 2008;15(11):3252-8. doi: 10.1245/s10434-008-0136-3.
 - 29- Gradishar WJ, Anderson BO, Balassanian R, et al. Breast Cancer, version 4.2017, NCCN Clinical Practice Guidelines in Oncology. *J Natl Compr Canc Netw.* 2018;16(3):310-20
 - 30- Al-Hilli Z, Hoskin TL, Day CN, et al. Impact of Neoadjuvant Chemotherapy on Nodal Disease and Nodal Surgery by Tumor Subtype. *Ann Surg Oncol* 2018, 25: 482-93.
 - 31- Nguyen TT, Hoskin TL, Day CN, et al. Decreasing Use of Axillary Dissection in Node-Positive Breast Cancer Patients Treated with Neoadjuvant Chemotherapy. *Ann Surg Oncol.* 2018; 25:2596-2602.
 - 32- Ozmen V, Unal ES, Muslumanoglu ME, et al. Axillary sentinel node biopsy after neoadjuvant chemotherapy. *Eur J Surg Oncol.* 2010;36(1):23-9. doi: 10.1016/j.ejso.2009.10.015.
 - 33- Boughey JC, Suman VJ, Mittendorf EA, et al. Alliance for Clinical Trials in Oncology. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. *JAMA.* 2013; 310:1455-61. doi: 10.1001/jama.2013.278932
 - 34- Kuehn T, Bauerfeind I, Fehm T, et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. *Lancet Oncol.* 2013; 14:609-618. doi: 10.1016/S1470-2045(13)70166-9.
 - 35- Donker M, Straver ME, Wesseling J, et al. Marking axillary lymph nodes with radioactive iodine seeds for axillary staging after neoadjuvant systemic treatment in breast cancer patients: the MARI procedure. *Ann Surg.* 2015;261(2):378-82. doi: 10.1097/SLA.0000000000000558.
 - 36- Caudle A.S, Yang W.T, Krishnamurthy S, et al. Improved Axillary Evaluation Following Neo-

adjuvant Therapy for Patients With Node-Positive Breast Cancer Using Selective Evaluation of Clipped Nodes: Implementation of Targeted Axillary Dissection. *J. Clin. Oncol.* 2016; 34, 1072–1078

- 37- Cabioğlu N, Karanlık H, Kangal D, et al. Improved False-Negative Rates with Intraoperative Identification of Clipped Nodes in Patients Undergoing Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy. *Ann Surg Oncol.* 2018;25(10):3030-3036. doi: 10.1245/s10434-018-6575-6.
- 38- Reinisch M, Heil J, Rüländ A, et al. Prospective, multicenter registry trial to evaluate the clinical feasibility of targeted axillary dissection (TAD) in patients (pts) with breast cancer (BC) and core biopsy proven axillary involvement (cN+). *Ann. Oncol.* 2019; 30: v56.
- 39- Boughey J.C, Ballman K.V, Le-Petross H.T, et al. Identification and Resection of Clipped Node Decreases the False-negative Rate of Sentinel Lymph Node Surgery in Patients Presenting With Node-positive Breast Cancer (T0-T4, N1-N2) Who Receive Neoadjuvant Chemotherapy: Results From ACOSOG Z1071 (Alliance). *Ann. Surg.* 2016 ;263, 802–807
- 40- Simons J, Nijnatten T.J.V, Koppert L.B, et al. Radioactive Iodine Seed placement in the Axilla with Sentinel lymph node biopsy after neoadjuvant chemotherapy in breast cancer: Results of the prospective multicenter RISAS trial. *Gen. Sess. Abstr.* 2021; 81, GS1-10.
- 41- Hartmann S, Stachs A, Kühn T, et al. Target Lymph Node Biopsy (TLNB) nach Kohlenstoffmarkierung bei Mammakarzinom-Patientinnen im Rahmen der primären Systemtherapie—Ergebnisse der TATTOO-Studie. *Geburtshilfe Frauenheilkd.* 2020; 80(10): e112. Doi: 10.1055/s-0040-1717893
- 42- ASCO. Guideline Recommendations for Sentinel lymph Node Biopsy in Early-Stage Breast Cancer: Guideline Summary. *J Oncol Pract.* 2005;1(4):134-6.
- 43- Morigi C. Highlights from the 15th St Gallen International Breast Cancer Conference 15-18 March, 2017, Vienna: tailored treatments for patients with early breast cancer. *Ecancermedical-science.* 2017;11:732. doi: 10.3332/ecancer.2017.732.
- 44- Henke G, Knauer M, Ribi K, et al. Tailored axillary surgery with or without axillary lymph node dissection followed by radiotherapy in patients with clinically node-positive breast cancer (TAXIS): study protocol for a multicenter, randomized phase-III trial. *Trials.* 2018;19(1):667. doi: 10.1186/s13063-018-3021-9.
- 45- van Loevezijn AA, van der Noordaa MEM, Stokkel MPM, et al. Three-year follow-up of de-escalated axillary treatment after neoadjuvant systemic therapy in clinically node-positive breast cancer: the MARI-protocol. *Breast Cancer Res Treat.* 2022 ;193(1):37-48. doi: 10.1007/s10549-022-06545-z.
- 46- Wong SM, Basik M, Florianova L, et al. Oncologic Safety of Sentinel Lymph Node Biopsy Alone After Neoadjuvant Chemotherapy for Breast Cancer. *Ann Surg Oncol.* 2021;28(5):2621-2629. doi: 10.1245/s10434-020-09211-0.
- 47- Cabioğlu N, Karanlık H, Yıldırım N, et al. Favorable outcome with sentinel lymph node biopsy alone after neoadjuvant chemotherapy in clinically node positive breast cancer at diagnosis: Turkish Multicentric NEOSENTI-TURK MF-18-02-study. *Eur J Surg Oncol.* 2021;47(10):2506-2514. doi: 10.1016/j.ejso.2021.06.024.
- 48- Barys-Paluchowski M, Gasparri ML, Boniface J.D, et al. The Axsana Study Group. Surgical Management of the Axilla in Clinically Node-Positive Breast Cancer Patients Converting to Clinical Node Negativity through Neoadjuvant Chemotherapy: Current Status, Knowledge Gaps, and Rationale for the EUBREAST-03 AXSANA Study. *Cancers (Basel).* 2021;13(7):1565. doi: 10.3390/cancers13071565. PMID: 33805367; PMCID: PMC8037995

- 49- Barrio AV, Montagna G, Mamtani A, et al. Nodal Recurrence in Patients With Node-Positive Breast Cancer Treated With Sentinel Node Biopsy Alone After Neoadjuvant Chemotherapy-A Rare Event. *JAMA Oncol.* 2021;7(12):1851-1855. doi: 10.1001/jamaoncol.2021.4394.
- 50- NCI Community Oncology Research Program. CTSU Alliance A011202 - "A Randomized Phase III Trial Evaluating the Role of Axillary Lymph Node Dissection in Breast Cancer Patients (CT1-3 N1) Who Have Positive Sentinel Lymph Node Disease After Neoadjuvant Chemotherapy". 2014. (26/04/2022 tarihinde <http://www.kccop.org/cancer-trials/breast/index.cgi/summary?iID=110> adresinden ulařılmıştır).
- 51- Mamounas EP, White JR, Bandos H ,et al. NSABP B-51/RTOG 1304: Randomized phase III clinical trial evaluating the role of postmastectomy chest wall and regional nodal XRT (CWR-NRT) and post-lumpectomy RNRT in patients (pts) with documented positive axillary (Ax) nodes before neoadjuvant chemotherapy (NC) who convert to pathologically negative Ax nodes after NC. *Journal of Clinical Oncology.* 2014;32, No. 15 Suppl. Doi: 10.1200/jco.2014.32.15_suppl.tps1141
- 52- Cabiođlu N, Karanlık H, İđci A, et al. Is Sentinel Lymph Node Biopsy with Radiotherapy Alone Safe in Clinically Node-Positive Breast Cancer After Neoadjuvant Chemotherapy?: Turkish Multicentric Neosentitürk-Trial/MF-18-03. *Annals of Surgical Oncology.* 2021;28:163-400