

# 19. BÖLÜM

## NEOADJUVAN KEMOTERAPİ SONRASI AKSİLLAYA YAKLAŞIM

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### GİRİŞ

Günümüzde neoadjuvan sistemik kemoterapi (NAK) sadece lokal ileri evre meme kanserinde değil aynı zamanda lokalize erken evre meme kanserinde de giderek daha fazla kullanılır hale gelmiştir. İnflamatuvar meme kanseri olan, N2-N3 düzey aksiller lenf nodu tutulumu olan, T4 tümörü olan lokal ileri veya inoperabl meme kanserli hastalar ile operabl olsa bile üçlü negatif meme kanseri ve HER2 protein aşırı ekspresyonu gösteren meme kanserinde NAK önerilmektedir (1). NAK yalnızca tümör boyutunda küçülmeyi ve tümörde “downstaging”i sağlamakla kalmaz, patolojik tam yanıtı (PTY) da sağlayabilir. Böylece meme ya da aksillada daha az cerrahi uygulanmasına olanak sağlar. Oluşan PTY özellikle üçlü negatif ve HER2 pozitif meme kanserinde, daha iyi genel sağ kalım ve hastalısız sağ kalım için güçlü bir prognostik faktördür. NAK sonrası patolojik tam yanıtı (ypT0/is ypN0) meme kanserinin subtiplerine bağlı olarak %20-40 oranında erişilebilir (2-5). NAK sonrası küçülen tümörün cerrahisi, sağlam cerrahi sınırlarda güvenle uygulanabilirken, aksiller cerrahi ile ilgili tartışmalar halen devam etmektedir.

Aksiller lenf nodu tutulumu meme kanserinde en önemli prognostik faktördür. Nodal tutulum, cerrahi ve sistemik tedavi kararlarını etkiler. Sentinel lenf nodu biyopsisi (SLNB) aksillaya yönelik cerrahiye şekillendirir. Ancak SLNB'nin güvenle uygulanabilmesi için sentinel lenf nodunun (SLN) saptanma oranının yüksek olması, yanlış negatiflik oranının düşük olması önemlidir. NAK lenfatik

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ji, patolojik tam yanıtın elde edildiği durumlarda ALND'den güvenli bir şekilde kaçınma potansiyelidir. Daha düşük yanlış negatiflik oranları elde etmek için en az üç SLN çıkarılmalı, SLN saptanma oranlarını arttırmak için aksiller haritalamayı ikili ajan ile yapmalı ve immünohistokimyasal analiz yapılmalıdır. NAK sonrası nod pozitif hastalığı olan hastalar için ALND en iyi cerrahi yaklaşımdır ancak bu hastalarda adjuvan RT lokorejyonel tedavi alternatifi olma yolunda ilerlemeye devam etmektedir. NAK uygulanan hastalarda aksilla yönetimi Şekil-2'de şematize edilmiştir (32).

### KAYNAKÇA

1. Gradishar WJ, Anderson BO, Balassanian R, Blair SL, Burstein HJ, Cyr A, et al. Breast cancer, version 1.2016. *J Natl Compr Cancer Netw JNCCN*. 2015;13(12):1475–85.
2. Esserman LJ, Berry DA, DeMichele A, Carey L, Davis SE, Buxton M, et al. Pathologic complete response predicts recurrence-free survival more effectively by cancer subset: results from the I-SPY 1 TRIAL--CALGB 150007/150012, ACRIN 6657. *J Clin Oncol Off J Am Soc Clin Oncol*. 2012;30(26):3242–9.
3. Gianni L, Pienkowski T, Im YH, Roman L, Tseng LM, Liu MC, et al. Efficacy and safety of neoadjuvant pertuzumab and trastuzumab in women with locally advanced, inflammatory, or early HER2-positive breast cancer (NeoSphere): a randomised multicentre, open-label, phase 2 trial. *Lancet Oncol*. 2012;13(1):25–32.
4. Alvarado R, Yi M, Le-Petross H, Gilcrease M, Mittendorf EA, Bedrosian I, et al. The role for sentinel lymph node dissection after neoadjuvant chemotherapy in patients who present with node-positive breast cancer. *Ann Surg Oncol*. 2012;19(10):3177–84.
5. Boileau JF, Poirier B, Basik M, Holloway CM, Gaboury L, Sideris L, et al. Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. *J Clin Oncol Off J Am Soc Clin Oncol*. 2015;33(3):258–64.
6. Hunt KK, Yi M, Mittendorf EA, Guerrero C, Babiera GV, Bedrosian I, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy is accurate and reduces the need for axillary dissection in breast cancer patients. *Ann Surg*. 2009;250(4):558–66.
7. Xing Y, Foy M, Cox DD, Kuerer HM, Hunt KK, Cormier JN. Meta-analysis of sentinel lymph node biopsy after preoperative chemotherapy in patients with breast cancer. *Br J Surg*. 2006;93(5):539–46.
8. Kelly AM, Dwamena B, Cronin P, Carlos RC. Breast cancer sentinel node identification and classification after neoadjuvant chemotherapy-systematic review and meta analysis. *Acad Radiol*. 2009;16(5):551–63.
9. Classe JM, Bordes V, Campion L, Mignotte H, Dravet F, Leveque J, et al. Sentinel lymph node biopsy after neoadjuvant chemotherapy for advanced breast cancer: results of Ganglion Sentinelle et Chimiotherapie Neoadjuvante, a French prospective multicentric study. *J Clin Oncol Off J Am Soc Clin Oncol*. 2009;27(5):726–32.
10. Lyman GH, Temin S, Edge SB, Newman LA, Turner RR, Weaver DL, et al. Sentinel lymph node biopsy for patients with early-stage breast cancer: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol*. 2014;32(13):1365–1383.
11. Network NCC. NCCN Clinical Practice Guidelines in Oncology, Version 2.2016 Invasive Breast Cancer.
12. Zetterlund L, Celebioglu F, Axelsson R, de Boniface J, Frisell J. Swedish prospective multicenter trial on the accuracy and clinical relevance of sentinel lymph node biopsy before neoadjuvant systemic therapy in breast cancer. *Breast Cancer Res Treat*. 2017;163(1):93-101.
13. Rouzier R, Extra JM, Kljanienco J, et al. Incidence and prognostic significance of complete axillary downstaging after primary chemotherapy in breast cancer patients with T1 to T3

- tumors and cytologically proven axillary metastatic lymph nodes. *J Clin Oncol* 2002; 20: 1304–10.
14. Van Deurzen CH, Vriens BE, Tjan-Heijnen VC, et al. Accuracy of sentinel node biopsy after neoadjuvant chemotherapy in breast cancer patients: a systematic review. *Eur J Cancer* 2009; 45: 3124–30.
  15. Kuehn T, Bauerfeind I, Fehm T, Fleige B, Hausschild M, Helms G, 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(7):609–18.
  16. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. *JAMA*. 2013;310(14):1455–61.
  17. Gradishar WJ, Anderson BO, Balassanian R, Blair SL, Burstein HJ, Cyr A, et al. Breast cancer version 2.2015. *J Natl Compr Cancer Netw JNCCN*. 2015;13(4):448–75.
  18. Kirova YM, Carroll S, Fourquet A, Offersen B, Aristei C, Chen JY. The St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2017: the point of view of an International Panel of Experts in Radiation Oncology. *Ann Oncol*. 2018 Jan 1;29(1):280–281.
  19. Boughey JC, Suman VJ, Mittendorf EA, Ahrendt GM, Wilke LG, Taback B, et al. Factors affecting sentinel lymph node identification rate after neoadjuvant chemotherapy for breast cancer patients enrolled in ACOSOG Z1071 (Alliance). *Ann Surg*. 2015;261(3):547–52.
  20. Fu JF, Chen HL, Yang J, Yi CH, Zheng S. Feasibility and accuracy of sentinel lymph node biopsy in clinically node-positive breast cancer after neoadjuvant chemotherapy: a meta-analysis. *PLoS One*. 2014;9(9):e105316.
  21. Caudle AS, Yang WT, Mittendorf EA, Black DM, Hwang R, Hobbs B, et al. Selective surgical localization of axillary lymph nodes containing metastases in patients with breast cancer: a prospective feasibility trial. *JAMA Surg*. 2015;150(2):137–43.
  22. Rubio IT. Sentinel lymph node biopsy after neoadjuvant treatment in breast cancer: work in progress. *Eur J Surg Oncol J Eur Soc Surg Oncol Br Assoc Surg Oncol*. 2016;42(3):326–32.
  23. Kuerer HM, Sahin AA, Hunt KK, Newman LA, Breslin TM, Ames FC, et al. Incidence and impact of documented eradication of breast cancer axillary lymph node metastases before surgery in patients treated with neoadjuvant chemotherapy. *Ann Surg*. 1999;230(1):72–8.
  24. Kishan AU, McCloskey SA. Postmastectomy radiation therapy after neoadjuvant chemotherapy: review and interpretation of available data. *Ther Adv Med Oncol*. 2016;8(1):85–97.
  25. Chapman CH, Jaggi R. Postmastectomy radiotherapy after neoadjuvant chemotherapy: a review of the evidence. *Oncology (Williston Park)*. 2015;29(9):657–66.
  26. Cain H, Macpherson IR, Beresford M, Pinder SE, Pong J, Dixon JM. Neoadjuvant therapy in early breast Cancer: treatment considerations and common debates in practice. *Clin Oncol (R Coll Radiol)*. 2017;29(10):642–52.
  27. Huang EH, Tucker SL, Strom EA, McNeese MD, Kuerer HM, Buzdar AU, et al. Postmastectomy radiation improves local-regional control and survival for selected patients with locally advanced breast cancer treated with neoadjuvant chemotherapy and mastectomy. *J Clin Oncol*. 2004;22(23):4691–9.
  28. McGuire SE, Gonzalez-Angulo AM, Huang EH, Tucker SL, Kau SW, Yu TK, et al. Postmastectomy radiation improves the outcome of patients with locally advanced breast cancer who achieve a pathologic complete response to neoadjuvant chemotherapy. *Int J Radiat Oncol Biol Phys*. 2007;68(4):1004–9.
  29. Klein J, Tran W, Watkins E, Vesprini D, Wright FC, Look Hong NJ, Ghandi S, Kiss A, Czarnota GJ. Locally advanced breast cancer treated with neoadjuvant chemotherapy and adjuvant radiotherapy: a retrospective cohort analysis. *BMC Cancer*. 2019;19(1):306.
  30. Sautter-Bihl ML, Sedlmayer F, Budach W, Dunst J, Feyer P, Fietkau R, et al. DEGRO practical guidelines: radiotherapy of breast cancer III- radiotherapy of the lymphatic pathways. *Strahlenther Onkol Organ der Deutschen Röntgengesellschaft [et al]*. 2014;190(4):342–51.

31. Donker M, van Tienhoven G, Straver ME, Meijnen P, van de Velde CJ, Mansel RE, et al. Radiotherapy or surgery of the axilla after a positive sentinel node in breast cancer (EORTC 10981-22023 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncol.* 2014;15(12):1303–10.
32. Wyld LM, Leidenius C, Senkus-Konefka ME, editors (2017). *Breast Cancer Management for Surgeons. A European Multidisciplinary Textbook.* Berlin: Springer.