

Bölüm 13

ERKEN EVRE MEME KANSERİNDE ADJUVAN SİSTEMİK TEDAVİ

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Erken evre meme kanseri evre I, IIA ve IIB'nin (T2N1) bir kısmını kapsar, lokal ileri evre ise evre IIB'nin diğer kısmı (T3N0) ile evre IIIA dan IIIC'ye kadar olan kısımları kapsar. Adjuvan sistemik tedavi ile mortalitede azalma meydana gelir. (1) Adjuvan sistemik tedavi sitotoksik kemoterapötik ajanların cerrahi sonrası kalan mikroskopik kanser odaklarını yok etmek için uygulanmasıdır. Genelde hormon reseptörü pozitif veya negatif olması farketmeksizin aynı ajanlar kullanılır ve eğer HER 2 pozitif ise anti HER 2 tedavi eklenir.

ENDİKASYON

Tedavi kararı multidisipliner takım tarafından hasta bazlı olarak planlanmalıdır. Tümörün yükü, büyülüğu, yerleşimi, hormon reesptör durumu, ki-67 proliferasyon indeksi, hastanın yaşı ve genel durumu göz önüne alınmalıdır. Herediter kanser riski göz önüne alınmalı ve gerekire genetik testler çalışılmalıdır.(2) Ayrıca genç hastalara fertilité koruyucu teknikler tedavi öncesi önerilmelidir.(3-6) The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta analizinde erken evre meme kanserinde adjuvan kemoterapinin hem nüksü hem de meme kanserine bağlı ölümleri azalttığı gösterilmiştir. (7-8) Fakat düşük risk skoruna sahip bir kısım hasta ile yaşlı ve komorbid hastalıkları olan hastalarda kemoterapi hem uygun değil hem de surviyeye katkısı yoktur. Kemoterapi cerrahiden sonraki 2-6 hafta içinde başlanmalıdır. Cerrahiden 12 hafta sonra KT başlanması etkinlik kaybına yol açtığı bilinmektedir. (9)

Hormon Reseptör Negatif(triple negatif) Hastalar

Adjuvan KT triple negatif hastalarda tümör boyutu >0.5 cm veya lenf nodu tutulumu durumunda endikedir. Bu hastalar hormon reesptörü negatif olduğundan adjuvan hormon terapi, HER 2 durumu negatif olduğundan anti HER 2 tedavi alamazlar.

endikasyonu mevcuttur. HER 2 negatif, hormon resptörü pozitif hastalarda KT kararı hastanın yaşı, lenfovasküler invazyon, grade, lenf nodu tutulumu ve risk skoruna göre karar verilir. Kemoterapi olarak doz dens AC sonrasında taksan bazlı rejimler kullanılır. Düşük riski hastalar ile kalp yetmezliği olanlar ve antrasiklin kullanmak istemeyen hastalarada dosetaksel siklofosfamid rejimi kullanılabilir. KT cerrahiden 4-6 hafta sonra başlanmalıdır.

KAYNAKLAR

1. Berry DA, Cronin KA, Plevritis SK, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005; 353:1784.
2. Pruthi S, Gostout BS, Lindor NM. Identification and management of women with BRCA mutations or hereditary predisposition for breast and ovarian cancer. *Mayo Clin Proc* 2010; 85: 1111–1120.
3. Senkus E, Gomez H, Dirix L et al. Young breast cancer patients' attitudes towardsthe risk of loss of fertility related to adjuvant therapies. EORTC study 10002 BIG3–98. *Psychooncology* 2014; 23: 173–182.41.
4. Lee SJ, Schover LR, Partridge AH et al. American Society of Clinical Oncologyrecommendations on fertility preservation in cancer patients. *J Clin Oncol* 2006;24: 2917–2931.42.
5. Partridge AH, Pagani O, Abulkhair O et al. First international consensus guidelinesfor breast cancer in young women (BCY1). *Breast* 2014; 23: 209–220.43.
6. Cardoso F, Loibl S, Pagani O et al. The European Society of Breast CancerSpecialists recommendations for the management of young women with breastcancer. *Eur J Cancer* 2012; 48: 3355–3377
7. Early Breast Cancer Trialists Collaborative Group. Polychemotherapy for early breast cancer: an overview of the randomised trials. *Lancet*. 1998;352:930-942.
8. Early Breast Cancer Trialists' Collaborative Group. Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. *Lancet*. 2005;365:1687-1717.
9. Lohrisch C, Paltiel C, Gelmon K et al. Impact on survival of time from definitivesurgery to initiation of adjuvant chemotherapy for early-stage breast cancer. *J ClinOncol* 2006; 24: 4888–4894
10. Harris LN, Ismail N, McShane LM, et al. Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 2016; 34:1134.
11. Paik S, Shak S, Tang G, et al. A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. *N Engl J Med* 2004;351:2817-2826. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/15591335>. 298. Dowsett M, Cuzick J, Wale C, et al.
12. Prediction of risk of distant recurrence using the 21-gene recurrence score in node-negative and node-positive postmenopausal patients with breast cancer treated with anastrozole or tamoxifen: a TransATAC study. *J Clin Oncol* 2010;28:1829-1834. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/20212256>.
13. Albain KS, Barlow WE, Shak S, et al. Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: a retrospective analysis of a randomised trial. *Lancet Oncol* 2010;11:55-65. Available at:
14. Paik S, Tang G, Shak S, et al. Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor- positive breast cancer. *J Clin Oncol* 2006;24:3726-3734. Available at: <http://www.ncbi.nlm.nih.gov/pubmed/16720680>.

15. Sparano JA, Gray RJ, Makower DF, et al. Adjuvant Chemotherapy Guided by a 21-Gene Expression Assay in Breast Cancer. *N Engl J Med* 2018; 379:111.
16. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), Peto R, Davies C, et al. Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. *Lancet* 2012; 379:432.
17. Sparano JA, Wang M, Martino S, et al. Phase III study of doxorubicin-cyclophosphamide followed by paclitaxel or docetaxel given every 3 weeks or weekly in patients with axillary node positive or high risk node negative breast cancer [abstract]. San Antonio Breast Cancer Symposium 2005:Abstract 48. Available at:
18. Sparano JA, Wang M, Martino S, et al. Phase III study of doxorubicin-cyclophosphamide followed by paclitaxel or docetaxel given every 3 weeks or weekly in operable breast cancer: Results of Intergroup Trial E1199 [abstract]. *J Clin Oncol* 2007;25 (Suppl_18)Abstract 516..
19. Sparano J, Wang M, Martino S, et al. Weekly paclitaxel in the adjuvant treatment of breast cancer. *N Engl J Med* 2008;358:1663-1671. Available at
20. Nitz U, Gluz O, Clemens M, et al. West German Study PlanB Trial: Adjuvant Four Cycles of Epirubicin and Cyclophosphamide Plus Docetaxel Versus Six Cycles of Docetaxel and Cyclophosphamide in HER2-Negative Early Breast Cancer. *J Clin Oncol* 2019; 37:799.
21. Jones S, Holmes FA, O'Shaughnessy J, et al. Docetaxel with cyclophosphamide is associated with an overall survival benefit compared with doxorubicin and cyclophosphamide: 7-year follow-up of US Oncology Research trial 9735. *J Clin Oncol* 2009;27:1177-1183.
22. Samuel JA, Wilson JW, Bandos H, et al. Abstract S3-02: NSABP B-36: A randomized phase III trial comparing six cycles of 5-fluorouracil (5-FU), epirubicin, and cyclophosphamide (FEC) to four cycles of adriamycin and cyclophosphamide (AC) in patients (pts) with node-negative breast cancer. *Cancer Research* 2015;75:S3-02.
23. Swain SM, Jeong J-H, Geyer CE, et al. NSABP B-30: definitive analysis of patient outcome from a randomized trial evaluating different schedules and combinations of adjuvant therapy containing doxorubicin, docetaxel and cyclophosphamide in women with operable, node-positive breast cancer [abstract]. *Cancer Research* 2009;69
24. Zaheed M, Wilcken N, Willson ML, et al. Sequencing of anthracyclines and taxanes in neoadjuvant and adjuvant therapy for early breast cancer. *Cochrane Database Syst Rev* 2019; 2:CD012873.
25. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Increasing the dose intensity of chemotherapy by more frequent administration or sequential scheduling: a patient-level meta-analysis of 37 298 women with early breast cancer in 26 randomised trials. *Lancet* 2019; 393:1440.
26. Citron ML. Dose-Dense Chemotherapy: Principles, Clinical Results and Future Perspectives. *Breast Care (Basel)* 2008; 3:251.