

S3-Leitlinie Früherkennung, Diagnostik, Therapie und Nachsorge des Mammakarzinoms

Version 4.0 – Dezember 2017
AWMF-Registernummer: 032-045OL

4.7.3. Adjuvante Chemotherapie

4.55.	Evidenzbasierte Empfehlungen
Indikationen für eine adjuvante Chemotherapie	
Empfehlungsgrad B	<p>a.) Eine Indikation für eine adjuvante Chemotherapie sollte gestellt werden bei:</p> <ul style="list-style-type: none"> • HER2-positiven Tumoren (ab pT1b, N0; pT1a, N0 wenn weiteres Risiko: G3, ER/PR neg., Ki67 hoch) • Triple negative Tumoren (ER- und PgR-negativ, HER2-negativ) • Luminal-B-Tumoren mit hohem Rezidivrisiko (Ki-67 hoch, G 3, high risk multigen assay, junges Erkrankungsalter, Lymphknotenbefall)
Level of Evidence 1a	Quellen: (Reviews. 2003, 2005, Ferguson, Wilcken et al. 2007, NZGG 2009, Peto, Davies et al. 2012, Sparano, Zhao et al. 2015)
	Starker Konsens

4.55.	Evidenzbasierte Empfehlungen
	Indikationen für eine adjuvante Chemotherapie
Empfehlungsgrad	b.) Eine Chemotherapie soll in den empfohlenen Dosierungen verabreicht werden.
A	Bei Unterdosierung oder Reduktion der Zyklen droht ein Effektivitätsverlust.
Level of Evidence	Quellen: (Fisher, Anderson et al. 1997, Budman, Berry et al. 1998, 2001, Fumoleau, Kerbrat et al. 2003, Swain, Jeong et al. 2010, Peto, Davies et al. 2012)
1a	Starker Konsens

Quellen:

Reviews., E. (2003). "Multi-agent chemotherapy for early breast cancer." Cochrane Database of Systematic Review.

Ferguson, T., N. Wilcken, R. Vagg, D. Ghersi and A. K. Nowak (2007). "Taxanes for adjuvant treatment of early breast cancer." Cochrane Database Syst Rev(4): Cd004421.

NZGG. (2009). "Management of Early Breast Cancer - Evidence-based Best Practice Guideline." New Zealand Guidelines Group Retrieved 01.09.2016, from
<https://www.health.govt.nz/system/files/documents/publications/mgmt-of-early-breast-cancer-aug09.pdf>.

Peto, R., C. Davies, J. Godwin, R. Gray, H. C. Pan, M. Clarke, D. Cutter, S. Darby, P. McGale, C. Taylor, Y. C. Wang, J. Bergh, A. Di Leo, K. Albain, S. Swain, M. Piccart and K. Pritchard (2012). "Comparisons between different polychemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials." Lancet 379(9814): 432-444.

Sparano, J. A., F. Zhao, S. Martino, J. A. Ligibel, E. A. Perez, T. Saphner, A. C. Wolff, G. W. Sledge, Jr., W. C. Wood and N. E. Davidson (2015). "Long-Term Follow-Up of the E1199 Phase III Trial Evaluating the Role of Taxane and Schedule in Operable Breast Cancer." J Clin Oncol 33(21): 2353-2360.

Quellen:

Fisher, B., S. Anderson, D. L. Wickerham, A. DeCillis, N. Dimitrov, E. Mamounas, N. Wolmark, R. Pugh, J. N. Atkins, F. J. Meyers, N. Abramson, J. Wolter, R. S. Bornstein, L. Levy, E. H. Romond, V. Caggiano, M. Grimaldi, P. Jochimsen and P. Deckers (1997). "Increased intensification and total dose of cyclophosphamide in a doxorubicin-cyclophosphamide regimen for the treatment of primary breast cancer: findings from National Surgical Adjuvant Breast and Bowel Project B-22." J Clin Oncol 15(5): 1858-1869.

Budman, D. R., D. A. Berry, C. T. Cirrincione, I. C. Henderson, W. C. Wood, R. B. Weiss, C. R. Ferree, H. B. Muss, M. R. Green, L. Norton and E. Frei, 3rd (1998). "Dose and dose intensity as determinants of outcome in the adjuvant treatment of breast cancer. The Cancer and Leukemia Group B." J Natl Cancer Inst 90(16): 1205-1211.

Fumoleau, P., P. Kerbrat, P. Romestaing, P. Fargeot, A. Bremond, M. Namer, S. Schraub, M. J. Goudier, J. Mihura, A. Monnier, P. Clavere, D. Serin, P. Seffert, C. Pourny, T. Facchini, J. P. Jacquin, J. F. Sztermer, J. Datchary, R. Ramos and E. Luporsi (2003). "Randomized trial comparing six versus three cycles of epirubicin-based adjuvant chemotherapy in premenopausal, node-positive breast cancer patients: 10-year follow-up results of the French Adjuvant Study Group 01 trial." J Clin Oncol 21(2): 298-305.

Swain, S. M., J. H. Jeong, C. E. Geyer, Jr., J. P. Costantino, E. R. Pajon, L. Fehrenbacher, J. N. Atkins, J. Polikoff, V. G. Vogel, J. K. Erban, P. Rastogi, R. B. Livingston, E. A. Perez, E. P. Mamounas, S. R. Land, P. A. Ganz and N. Wolmark (2010). "Longer therapy, iatrogenic amenorrhea, and survival in early breast cancer." N Engl J Med 362(22): 2053-2065.

4.56.	Evidenzbasierte Empfehlung
	Verabreichung der Zytostatika
Empfehlungsgrad B	Zytostatika können zeitlich simultan oder sequenziell verabreicht werden (entsprechend evidenzbasierter Protokolle). Bei hohem tumorbedingtem Mortalitätsrisiko und dafür geeigneten Patientinnen sollten dosisdichte Therapien eingesetzt werden.
Level of Evidence 1b	Quellen: (Bonadonna, Zambetti et al. 1995, Citron, Berry et al. 2003, Eiermann, Pienkowski et al. 2011) (Francis, Crown et al. 2008, Moebus, Jackisch et al. 2010, Del Mastro, De Placido et al. 2015)
	Starker Konsens

Quellen:

Bonadonna, G., M. Zambetti and P. Valagussa (1995). "Sequential or alternating doxorubicin and CMF regimens in breast cancer with more than three positive nodes. Ten-year results." Jama **273**(7): 542-547.

Citron, M. L., D. A. Berry, C. Cirrincione, C. Hudis, E. P. Winer, W. J. Gradishar, N. E. Davidson, S. Martino, R. Livingston, J. N. Ingle, E. A. Perez, J. Carpenter, D. Hurd, J. F. Holland, B. L. Smith, C. I. Sartor, E. H. Leung, J. Abrams, R. L. Schilsky, H. B. Muss and L. Norton (2003). "Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: first report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741." J Clin Oncol **21**(8): 1431-1439.

Eiermann, W., T. Pienkowski, J. Crown, S. Sadeghi, M. Martin, A. Chan, M. Saleh, S. Sehdev, L. Provencher, V. Semiglazov, M. Press, G. Sauter, M. A. Lindsay, A. Riva, M. Buyse, P. Drevot, H. Taupin and J. R. Mackey (2011). "Phase III study of doxorubicin/cyclophosphamide with concomitant versus sequential docetaxel as adjuvant treatment in patients with human epidermal growth factor receptor 2-normal, node-positive breast cancer: BCIRG-005 trial." J Clin Oncol **29**(29): 3877-3884.

Francis, P., J. Crown, A. Di Leo, M. Buyse, A. Balil, M. Andersson, B. Nordenskjold, I. Lang, R. Jakesz, D. Vorobiof, J. Gutierrez, G. van Hazel, S. Dolci, S. Jamin, B. Bendahmane, R. D. Gelber, A. Goldhirsch, M. Castiglione-Gertsch and M. Piccart-Gebhart (2008). "Adjuvant chemotherapy with sequential or concurrent anthracycline and docetaxel: Breast International Group 02-98 randomized trial." J Natl Cancer Inst **100**(2): 121-133.

Quellen:

Moebus, V., C. Jackisch, H. J. Lueck, A. du Bois, C. Thomssen, C. Kurbacher, W. Kuhn, U. Nitz, A. Schneeweiss, J. Huober, N. Harbeck, G. von Minckwitz, I. B. Runnebaum, A. Hinke, R. Kreienberg, G. E. Konecny and M. Untch (2010). "Intense dose-dense sequential chemotherapy with epirubicin, paclitaxel, and cyclophosphamide compared with conventionally scheduled chemotherapy in high-risk primary breast cancer: mature results of an AGO phase III study." J Clin Oncol **28**(17): 2874-2880.

Del Mastro, L., S. De Placido, P. Bruzzi, M. De Laurentiis, C. Boni, G. Cavazzini, A. Durando, A. Turletti, C. Nistico, E. Valle, O. Garrone, F. Puglisi, F. Montemurro, S. Barni, A. Ardizzone, T. Gamucci, G. Colantuoni, M. Giuliano, A. Gravina, P. Papaldo, C. Bighin, G. Bisagni, V. Forestieri and F. Cognetti (2015). "Fluorouracil and dose-dense chemotherapy in adjuvant treatment of patients with early-stage breast cancer: an open-label, 2 x 2 factorial, randomised phase 3 trial." Lancet **385**(9980): 1863-1872.

4.57.	Evidenzbasierte Empfehlung
	Anthrazyklin/Taxanhaltige adjuvante Standard-Chemotherapie
Empfehlungsgrad	
B	Die adjuvante Chemotherapie sollte ein Taxan und ein Anthrazyklin enthalten.
	Starker Konsens
O	6 Zyklen TC (Docetaxel/Cyclophosphamid) können bei einem mittleren klinischen Risiko (≤ 3 befallene Lymphknoten) eine Alternative darstellen.
	Konsens
A	Eine adjuvante Standard-Chemotherapie soll 18-24 Wochen dauern.
	Konsens
Level of Evidence 1a	Quellen: (Citron, Berry et al. 2003, Henderson, Berry et al. 2003, Mamounas, Bryant et al. 2005, Bria, Nistico et al. 2006, Clavarezza, Del Mastro et al. 2006, Roche, Fumoleau et al. 2006, Estevez, Munoz et al. 2007, Ferguson, Wilcken et al. 2007, Blum, Flynn et al. 2017, Ejlertsen, Tuxen et al. 2017, Harbeck, Gluz et al. 2017)

Quellen:

Citron, M. L., D. A. Berry, C. Cirrincione, C. Hudis, E. P. Winer, W. J. Gradishar, N. E. Davidson, S. Martino, R. Livingston, J. N. Ingle, E. A. Perez, J. Carpenter, D. Hurd, J. F. Holland, B. L. Smith, C. I. Sartor, E. H. Leung, J. Abrams, R. L. Schilsky, H. B. Muss and L. Norton (2003). "Randomized trial of dose-dense versus conventionally scheduled and sequential versus concurrent combination chemotherapy as postoperative adjuvant treatment of node-positive primary breast cancer: first report of Intergroup Trial C9741/Cancer and Leukemia Group B Trial 9741." J Clin Oncol **21**(8): 1431-1439.

Henderson, I. C., D. A. Berry, G. D. Demetri, C. T. Cirrincione, L. J. Goldstein, S. Martino, J. N. Ingle, M. R. Cooper, D. F. Hayes, K. H. Tkaczuk, G. Fleming, J. F. Holland, D. B. Duggan, J. T. Carpenter, E. Frei, 3rd, R. L. Schilsky, W. C. Wood, H. B. Muss and L. Norton (2003). "Improved outcomes from adding sequential Paclitaxel but not from escalating Doxorubicin dose in an adjuvant chemotherapy regimen for patients with node-positive primary breast cancer." J Clin Oncol **21**(6): 976-983.

Mamounas, E. P., J. Bryant, B. Lembersky, L. Fehrenbacher, S. M. Sedlacek, B. Fisher, D. L. Wickerham, G. Yothers, A. Soran and N. Wolmark (2005). "Paclitaxel after doxorubicin plus cyclophosphamide as adjuvant chemotherapy for node-positive breast cancer: results from NSABP B-28." J Clin Oncol **23**(16): 3686-3696.

Bria, E., C. Nistico, F. Cuppone, P. Carlini, M. Ciccarese, M. Milella, G. Natoli, E. Terzoli, F. Cognetti and D. Giannarelli (2006). "Benefit of taxanes as adjuvant chemotherapy for early breast cancer: pooled analysis of 15,500 patients." Cancer **106**(11): 2337-2344.

Quellen:

Clavarezza, M., L. Del Mastro and M. Venturini (2006). "Taxane-containing chemotherapy in the treatment of early breast cancer patients." Ann Oncol **17 Suppl 7**: vii22-26.

Roche, H., P. Fumoleau, M. Spielmann, J. L. Canon, T. Delozier, D. Serin, M. Symann, P. Kerbrat, P. Soulie, F. Eichler, P. Viens, A. Monnier, A. Vindevoghel, M. Campone, M. J. Goudier, J. Bonneterre, J. M. Ferrero, A. L. Martin, J. Geneve and B. Asselain (2006). "Sequential adjuvant epirubicin-based and docetaxel chemotherapy for node-positive breast cancer patients: the FNCLCC PACS 01 Trial." J Clin Oncol **24**(36): 5664-5671.

Estevez, L. G., M. Munoz, I. Alvarez, Y. Fernandez, J. Garcia-Mata, M. Ruiz-Borrego, I. Tusquets, M. A. Segui, A. Rodriguez-Lescure, E. Adrover and A. Lluch (2007). "Evidence-based use of taxanes in the adjuvant setting of breast cancer. A review of randomized phase III trials." Cancer Treat Rev **33**(5): 474-483.

Ferguson, T., N. Wilcken, R. Vagg, D. Ghersi and A. K. Nowak (2007). "Taxanes for adjuvant treatment of early breast cancer." Cochrane Database Syst Rev(4): Cd004421.

Blum, J. L., P. J. Flynn, G. Yothers, L. Asmar, C. E. Geyer, Jr., S. A. Jacobs, N. J. Robert, J. O. Hopkins, J. A. O'Shaughnessy, C. T. Dang, H. L. Gomez, L. Fehrenbacher, S. J. Vukelja, A. P. Lyss, D. Paul, A. M. Brufsky, J. H. Jeong, L. H. Colangelo, S. M. Swain, E. P. Mamounas, S. E. Jones and N. Wolmark (2017). "Anthracyclines in Early Breast Cancer: The ABC Trials-USOR 06-090, NSABP B-46-I/USOR 07132, and NSABP B-49 (NRG Oncology)." J Clin Oncol: Jco2016714147.

Quellen:

Ejlertsen, B., M. K. Tuxen, E. H. Jakobsen, M. B. Jensen, A. S. Knoop, I. Hojris, M. Ewertz, E. Balslev, H. Dano, P. M. Vestlev, J. Kenholm, D. L. Nielsen, T. Bechmann, M. Andersson, S. Cold, H. M. Nielsen, E. Maae, D. Carlsen and H. T. Mouridsen (2017). "Adjuvant Cyclophosphamide and Docetaxel With or Without Epirubicin for Early TOP2A-Normal Breast Cancer: DBCG 07-READ, an Open-Label, Phase III, Randomized Trial." *J Clin Oncol*: Jco2017723494.

Harbeck, N., O. Gluz, M. R. Clemens, W. Malter, T. Reimer, B. Nuding, B. Aktas, A. Stefek, A. Pollmanns and F. Lorenz-Salehi (2017). Prospective WSG phase III PlanB trial: Final analysis of adjuvant 4xEC→ 4x doc vs. 6x docetaxel/cyclophosphamide in patients with high clinical risk and intermediate-to-high genomic risk HER2-negative, early breast cancer, American Society of Clinical Oncology.