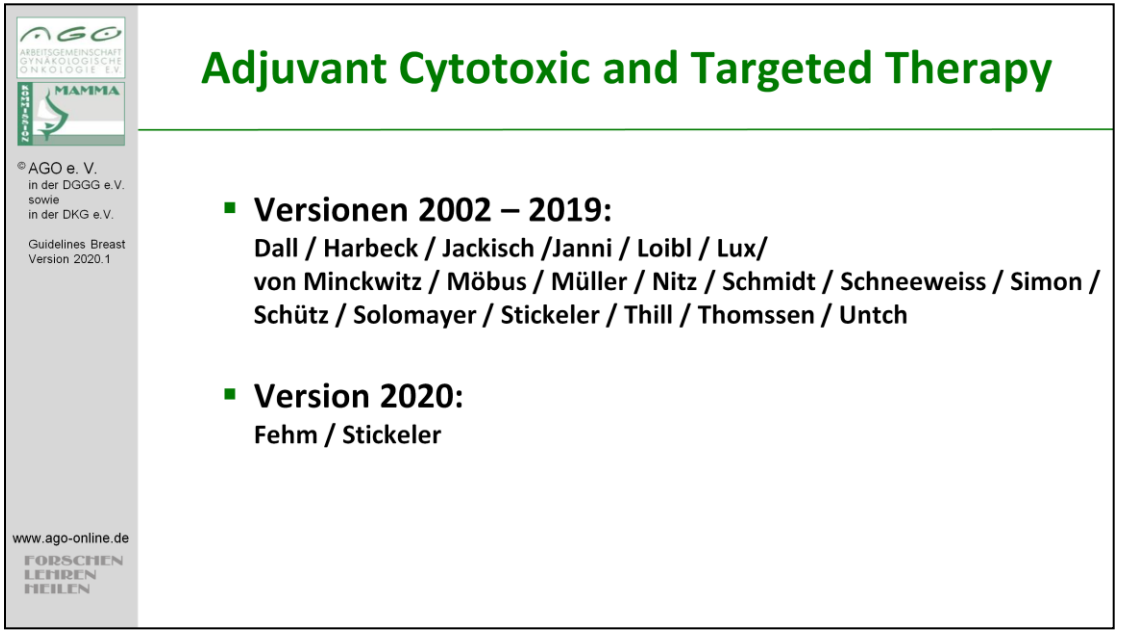
Guidelines Breast
Version 2020.1

Adjuvant Cytotoxic and Targeted Therapy



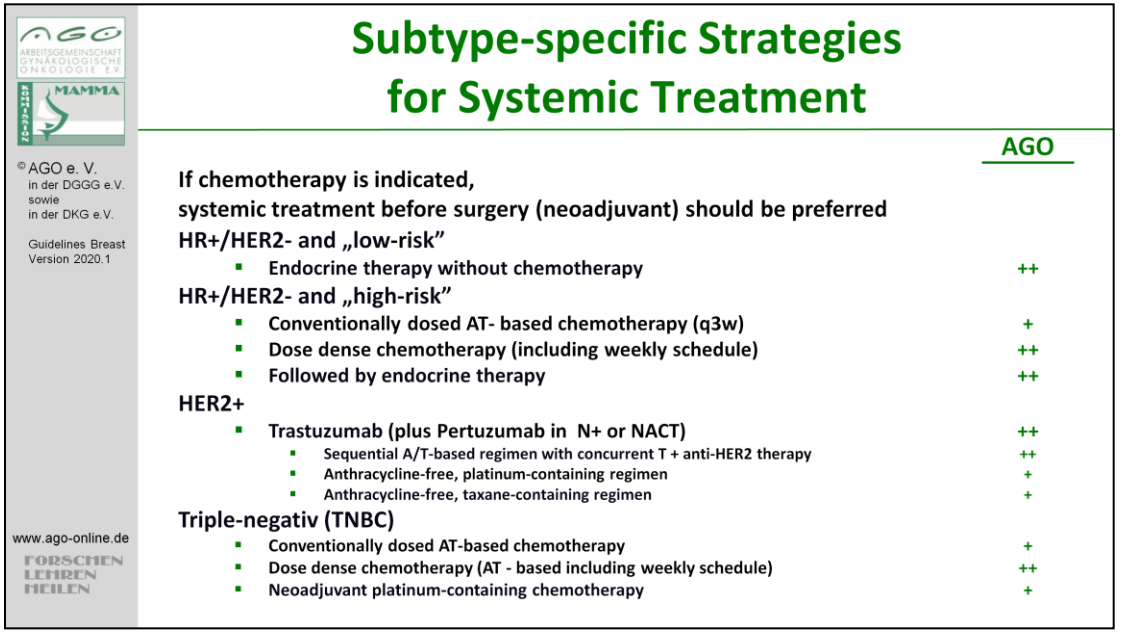
<u>Systematic review of published evidence</u>

PUBMED 1999-2019

ASCO 1999-2019

SABCS 1999-2019

ECCO/ESMO 1999-2019



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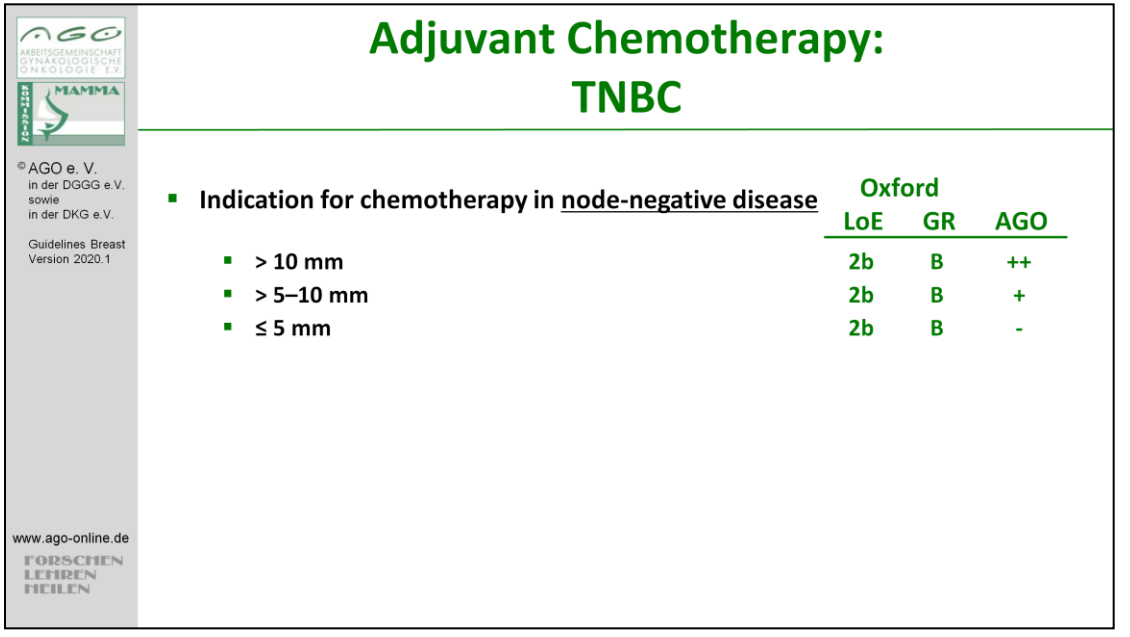
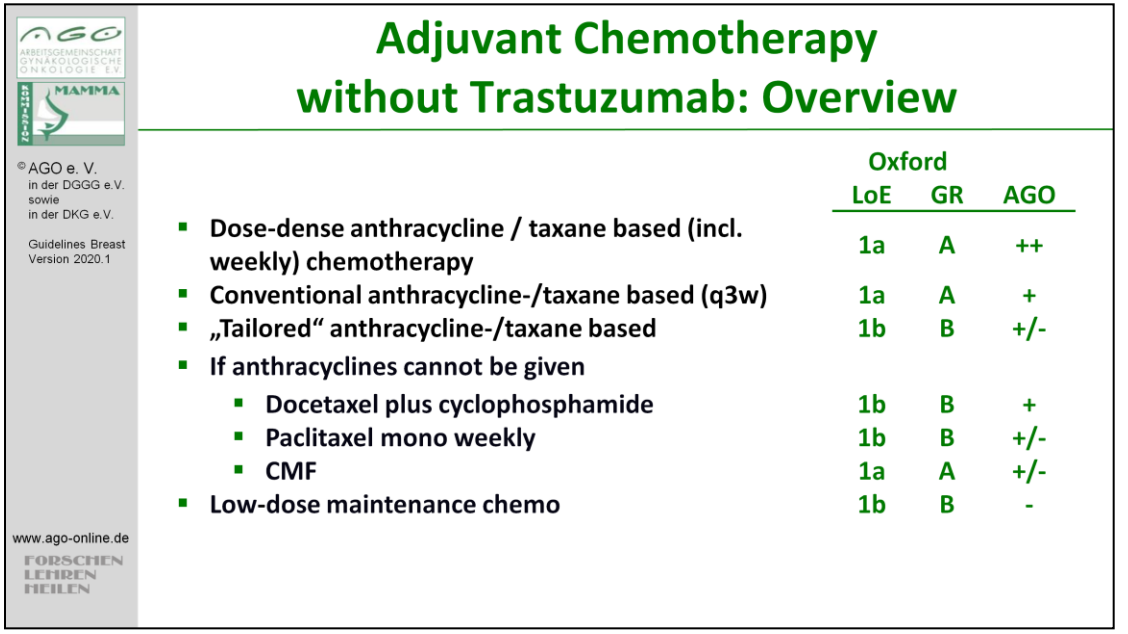


1. Gamucci T, Vaccaro A, Ciancola F et. al. Recurrence risk in small, node-negative, early breast cancer: a multicenter retrospective analysis. J Cancer Res Clin Oncol. 2013;139(5):853-60. doi: 10.1007/s00432-013-1388-2. Epub 2013 Feb 15.
2. Kolben T, Harbeck N, Wuerstlein R et al. Endocrine sensitivity is decisive for patient outcome in small node-negative breast cancers (BC) (pT1a,b) - results from the Munich Cancer Registry. Breast. 2015;24(1):24-31. doi: 10.1016/j.breast.2014.10.007. Epub 2014 Nov 8.
3. Nonneville A, Goncalves C, Zemmour M et al. Adjuvant chemotherapy in pT1ab node-negative triple-negative breast carcinomas: Results of a national multi-institutional retrospective study . European J Cancer. 2017; (84):34-43.



Statement: Dosis-dicht Anthrazyklin-/ Taxan-basiert (inkl. weekly) LoE 1a A AGO ++

1. Moylan EJ, Connell LC, O'Reilly S et al. Are dose-dense and triplet chemotherapy regimens optimal adjuvant therapy in the majority of women with node-positive early breast cancer? J Clin Oncol. 2014;32(6):605-6.
2. Lemos Duarte I, da Silveira Nogueira Lima JP, Passos Lima CS et al. Dose-dense chemotherapy versus conventional chemotherapy for early breast cancer: a systematic review with meta-analysis. Breast. 2012;21(3):343-9.
3. Möbus V, Jackisch C, Lück HJ et al. Ten-year results of intense dose-dense chemotherapy show superior survival compared with a conventional schedule in high-risk primary breast cancer: final results of AGO phase III iddEPC trial. Ann Oncol. 2018 Jan 1;29(1):178-185.
4. Gray R, Bradley R, Braybrooke J et al. Increasing the dose density of adjuvant chemotherapy by shortening intervals between courses or by sequential drug administration significantly reduces both disease recurrence and breast cancer mortality: An EBCTCG meta-analysis of 21,000 women in 16 randomised trials. SABCS 2017, abstr. GS1-01
5. Budd GT, Barlow WE, Moore HC et al. SWOG S0221: A Phase III Trial Comparing Chemotherapy Schedules in High-Risk Early-Stage Breast Cancer. J Clin Oncol. 2015 Jan 1;33(1):58-64.
6. Zhou W, Chen S, Xu F, Zeng X. Survival benefit of pure dose-dense chemotherapy in breast cancer: a meta-analysis of randomized

controlled trials. World J Surg Oncol. 2018 Jul 14;16(1):144.

7. Goldvaser H, Majeed H, Ribnikar D et al. Influence of control group therapy on the benefit from dose-dense chemotherapy in early breast cancer: a systemic review and meta-analysis. Breast Cancer Res Treat. 2018 Jun;169(3):413-425.
8. Matikas A, Foukakis T, Moebus V et al. Dose tailoring of adjuvant chemotherapy for breast cancer based on hematologic toxicities: further results
   from the prospective PANTHER study with focus on obese patients. Ann Oncol. 2019 Jan 1;30(1):109-114.

Statement: Konventionell Anthrazyklin-/ Taxan-basiert (q3w) LoE 1a A AGO +

1. Budd GT, Barlow WE, Moore HC et al. SWOG S0221: A Phase III Trial Comparing Chemotherapy Schedules in High-Risk Early-Stage Breast Cancer. J Clin Oncol. 2015 Jan 1;33(1):58-64.
2. EBCTCG, Peto R, Davies C, Godwin J 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(9814):432-44
3. Denduluri N, Chavez-MacGregor M, Telli ML et al. Selection of Optimal Adjuvant Chemotherapy and Targeted Therapy for Early Breast Cancer: ASCO Clinical Practice Guideline Focused Update. J Clin Oncol. 2018 Aug 10;36(23):2433-2443.

Statement: „Tailored“ Anthrazyklin-/ Taxan-basiert LoE 1b B AGO +/-

1. Matikas A, Foukakis T, Moebus V, et al. Dose tailoring of adjuvant chemotherapy for breast cancer based on hematologic toxicities: further results from the prospective PANTHER study with focus on obese patients. Ann Oncol. 2019 Jan 1;30(1):109-114.

Statement: If anthracyclines cannot be given - Docetaxel plus cyclophosphamide

1. 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. Clin Oncol. 2009;27(8):1177-83.

Statement: If anthracyclines cannot be given - Paclitaxel mono weekly

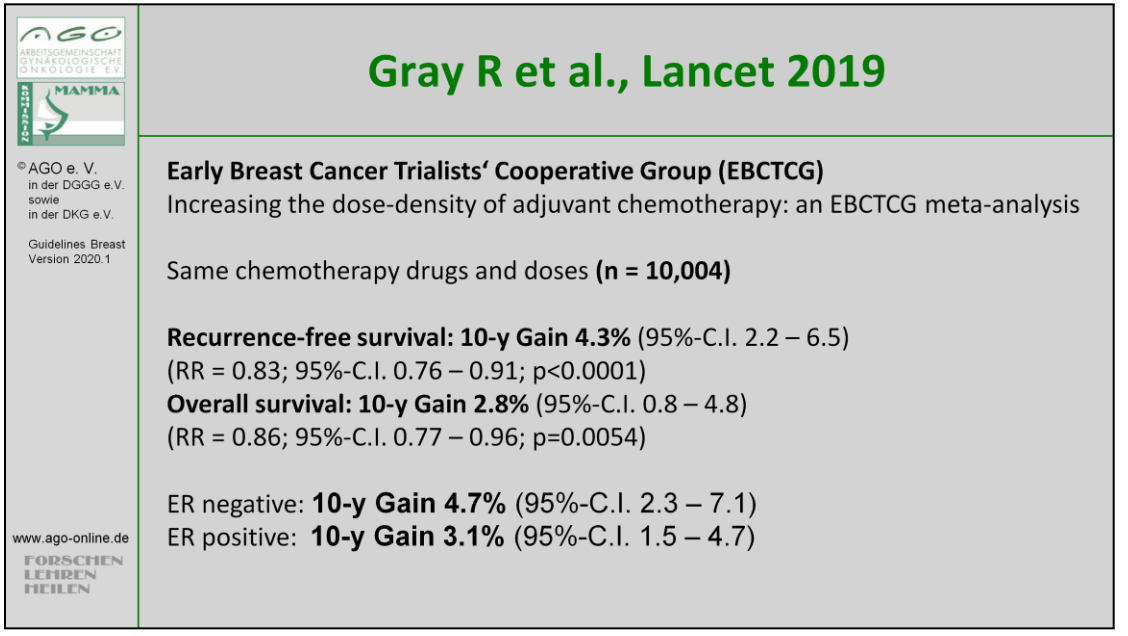
1. Amoroso V, Pedersini R, Sharratt P et al. Should adjuvant weekly Paclitaxel be considered less efficacious than anthracyclines plus cyclophosphamide for lower-risk patients with early-stage breast cancer? J Clin Oncol. 2015 Jan 20;33(3):290.
2. Shulman LN, Berry DA, Cirrincione CT et al. Comparison of doxorubicin and cyclophosphamide versus single-agent paclitaxel as adjuvant therapy for breast cancer in women with 0 to 3 positive axillary nodes: CALGB 40101 (Alliance). J Clin Oncol. 2014 Aug 1;32(22):2311-7.
3. Sparano JA, Wang M, Martino S et al. Weekly Paclitaxel in the Adjuvant Treatment of Breast Cancer. N Engl J Med. 2008 Apr 17;358(16):1663-71

Statement: If anthracyclines cannot be given - CMF

1. Perrone F, Nuzzo F, Di Rella F et al. Weekly docetaxel versus CMF as adjuvant chemotherapy for older women with early breast cancer: final results of the randomized phase III ELDA trial. Ann Oncol. 2015;26(4):675-82.

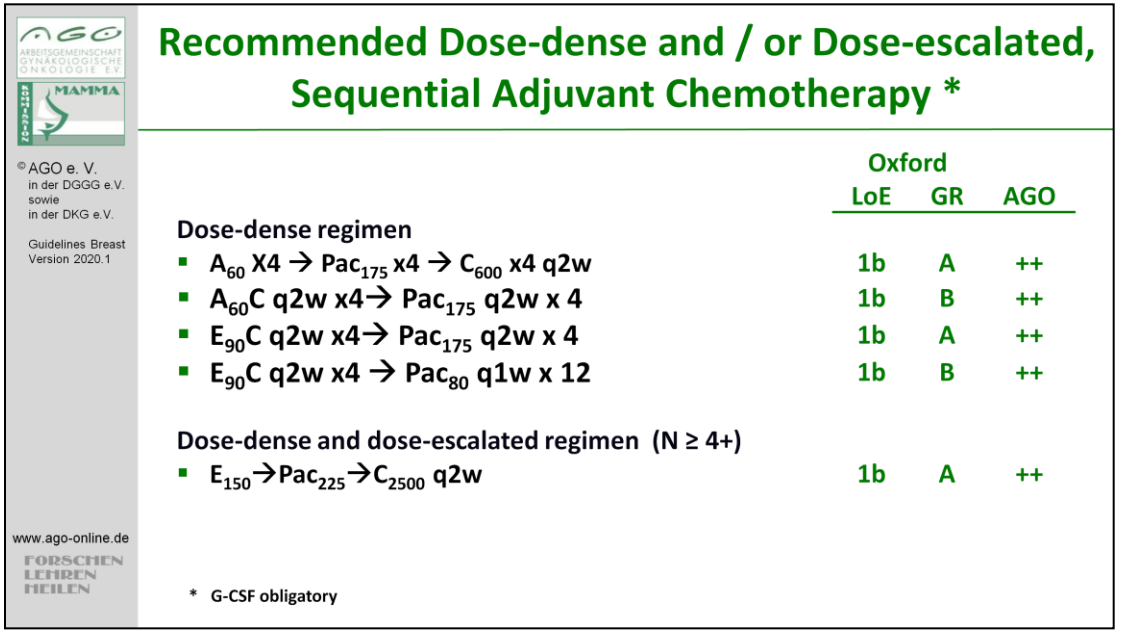
Statement: Low dose maintenance Chemotherapy

1. Colleoni, Viale G, Goldhirsch A. Low-dose oral cyclophosphamide and methotrexate maintenance for hormone receptor-negative early breast cancer: International Breast Cancer Study Group trial 22-00. J Clin Oncol 2016;34:3400-8



1. Gray R, Bradley R, Braybrooke J et al. 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(10179):1440-1452. doi: 10.1016/S0140-6736(18)33137-4. Epub 2019 Feb 8



Statement: Dose-dense regimen

A60x4 - Pac175x4 - C600x4 q2w / ACPac / AC-Pac q2w

1. Citron ML, Berry DA, Cirrincione C et al. 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 2003;21:1431-9.

Statement: Dose-dense regimen

AC /EC q2w x 4 Pac q2w x 4

1. Citron ML, Berry DA, Cirrincione C et al. 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 2003;21:1431-9.
2. Burnell M, Levine MN, Chapman JA et al. Cyclophosphamide, epirubicin, and fluorouracil versus dose-dense epirubicin and

cyclophosphamide followed by paclitaxel versus doxorubicin and cyclophosphamide followed by paclitaxel in node-positive or high-risk nodenegative breast cancer. J Clin Oncol 28:77-82, 2010.

3. Del Mastro L, De Placido S, Bruzzi P et al. Fluorouracil and dose-dense chemotherapy in adjuvant treatment of patients with early-stage breast cancer: an open-label, 2 × 2 factorial, randomised phase 3 trial. Lancet. 2015;385(9980):1863-72
4. Budd GT, Barlow WE, Moore HC et al. SWOG S0221: a phase III trial comparing chemotherapy schedules in high-risk early-stage breast cancer. J Clin Oncol. 2015 Jan 1;33(1):58-64.
5. Gray R, Bradley R, Braybrooke J et al. 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 Apr 6;393(10179):1440-1452. doi: 10.1016/S0140-6736(18)33137-4. Epub 2019 Feb 8

Statement: Dose-dense regimen

EC q2w / Pac q1w

EC q3w / Pac q1w

1. Sparano JA, Zhao, F Martino S et al. Long-Term Follow-Up of the E1199 Phase III Trial Evaluating the Role of Taxane and Schedule in Operable Breast Cancer. J Clin Oncol 2015;33:2353-60.
2. Jones RL, Walsh G, Ashley S et al. A randomized pilot phase II study of doxorubicin and cyclophosphamide (AC) or epirubicin and cyclophosphamide (EC) given 2 weekly with pegfilgrastim (accelerated) vs 3 weekly (standard) for women with early breast cancer. Br J Cancer 2009;100:305-10.
3. Budd GT, Barlow WE, Moore HC et al. SWOG S0221: a phase III trial comparing chemotherapy schedules in high-risk early-stage breast cancer. J Clin Oncol. 2015 Jan 1;33(1):58-64.

EBCTCG Metaanalyse

1. Gray R, Bradley R, Braybrooke J et al. 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 Apr 6;393(10179):1440-1452. doi: 10.1016/S0140-6736(18)33137-4. Epub 2019 Feb 8

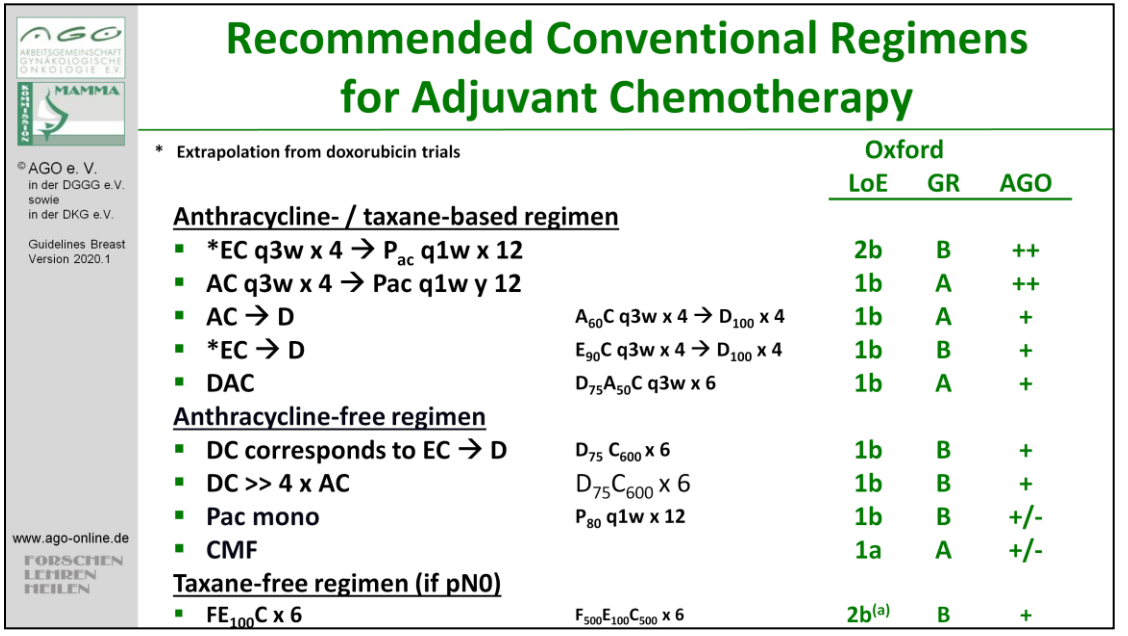
Statement: Dose-dense and dose-escalated regimen (N ≥ 4+)

E-Pac-C q2w

1. Möbus V, Jackisch C, Lück HJ et al. 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. 2010 Jun 10;28(17):2874-80.
2. Möbus V, Jackisch C, Lück HJ et al. AGO Breast Study Group (AGO-B) Ten-year Results of Intense Dose-dense chemotherapy show superior survival compared to a conventional schedule in High-risk Primary Breast Cancer: Final results of AGO Phase III iddEPC trial. Ann Oncol. 2017 Oct 24. doi: 10.1093/annonc/mdx690. [Epub ahead of print]

Negative Trial

1. Swain SM, Tang G, Geyer CE Jr et al. Definitive results of a phase III adjuvant trial comparing three chemotherapy regimens in women with operable, node-positive breast cancer: the NSABP B-38 trial. J Clin Oncol. 2013 Sep 10;31(26):3197-204.
2. Möbus V, von Minckwitz G, Jackisch C et al.German Breast Group (GBG), the AGO Breast Study Group (AGO-B) and NOGGO Study Groups. German Adjuvant Intergroup Node-positive Study (GAIN): a phase III trial comparing two dose-dense regimens (iddEPC versus ddEC-PwX) in high-risk early breast cancer patients. Ann Oncol. 2017 Aug 1;28(8):1803-1810.



Statement: Anthracycline/ taxane based regimen

*EC → Pw E90C q3w x 4 → P80 qw1 x 12

1. Sparano JA, Zhao, F Martino S et al. Long-Term Follow-Up of the E1199 Phase III Trial Evaluating the Role of Taxane and Schedule in Operable Breast Cancer. J Clin Oncol 2015;33:2353-60.

Statement: Anthracycline/ taxane based regimen

AC → Pw A60Cq3w x 4 → P80qw1 x 12

1. Mamounas EP, Bryant J, Lembersky B et al. Paclitaxel After Doxorubicin Plus Cyclophosphamide As Adjuvant Chemotherapy for Node-Positive Breast Cancer: Results From NSABP B-28 J Clin Oncol 2005;23:3686-3696.
2. Sparano JA, Zhao, F Martino S et al. Long-Term Follow-Up of the E1199 Phase III Trial Evaluating the Role of Taxane and Schedule in Operable Breast Cancer. J Clin Oncol 2015;33:2353-60

Statement: Anthracycline/ taxane based regimen

AC → D A60C q3w x 4 → D100 qw3 x 4

EC → D E90C q3w x 4 → D100 qw3 x 4

1. Denduluri N, Chavez-MacGregor M, Telli ML et al. Selection of Optimal Adjuvant Chemotherapy and Targeted Therapy for Early Breast Cancer: ASCO Clinical Practice Guideline Focused Update. J Clin Oncol. 2018 Aug 10;36(23):2433-2443.

Statement: Anthracycline/ taxane based regimen

DAC D75A50C q3w x 6

1. Swain SM, Tang G, Geyer CE Jr et al. Definitive results of a phase III adjuvant trial comparing three chemotherapy regimens in women with operable, node-positive breast cancer: the NSABP B-38 trial. J Clin Oncol. 2013;31(26):3197-204.
2. Blum JL, Flynn PJ, Yothers G et al. 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. 2017;35(23):2647-2655.

Statement: Anthracycline-free regimen

DC →D75 C600 x4 corresponds to EC → D

1. Harbeck N, Gluz O, Wuerstlein R et al. No age-related outcome disparities according to 21-gene recurrence score groups in early breast cancer patients treated by adjuvant chemotherapy in the prospective WSG PlanB trial. SABCS 2017, abstr.P1-06-06

Statement: Anthracykline-free regimen

DC >> 4 x AC

1. 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(8):1177-83.

Statement: Anthracycline-free regimen

Pac mono 80 mg q1w x 4-6

1. Shulman LN, Burstein HJ, Winer EP et al. Comparison of doxorubicin and cyclophosphamide versus single-agent paclitaxel as adjuvant therapy for breast cancer in women with 0 to 3 positive axillary nodes: CALGB 40101 (Alliance). J Clin Oncol. 2014;32:2311-7.

Statement: Anthracycline-free regimen

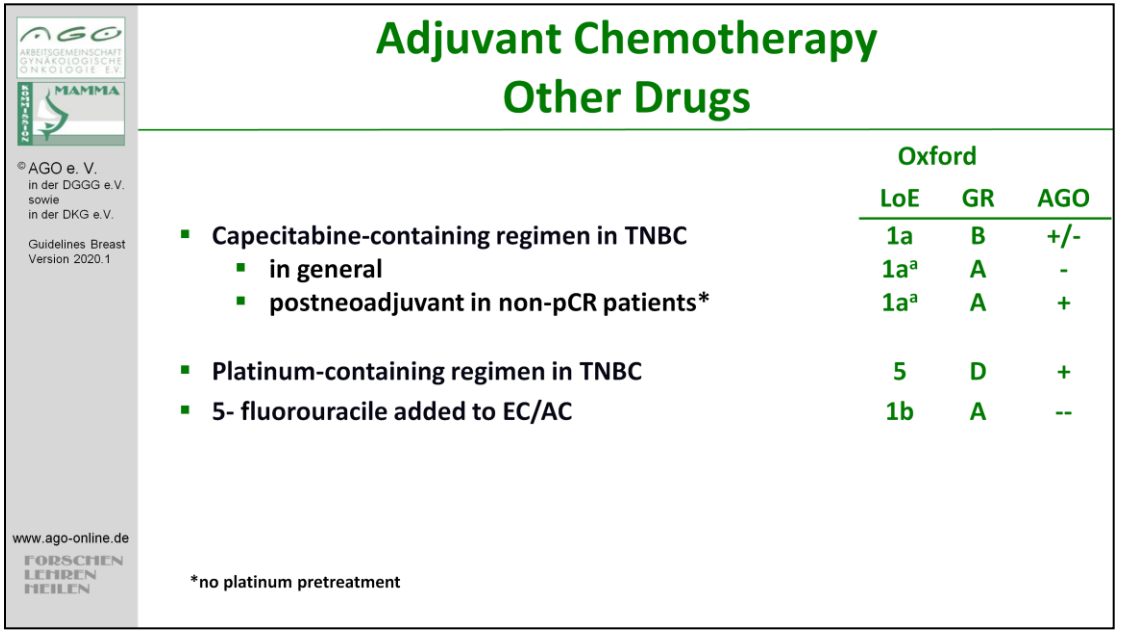
CMF 600/40/600 mg q3w x 6

1. Perrone F, Nuzzo F, Di Rella F et al. Weekly docetaxel versus CMF as adjuvant chemotherapy for older women with early breast cancer: final results of the randomized phase III ELDA trial. Ann Oncol. 2014;26:675-82

Statement: Taxan-freie Schemata (bei pN0)

FE100C x 6 q3w

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet. 2005 May 14-20;365(9472):1687-717.
2. Thomssen C, Vetter M, Kantelhardt EJ et al. on behalf of the NNBC-3 Study Group Adjuvant therapy with FEC and docetaxel in high risk node-negative breast cancer patients identified by tumor-biological (uPA/PAI-1) or clinico-pathological risk assessment. A joint trial of AGO-Breast Study Group, German Breast Group and EORTC Pathology and Biomarker Group (NNBC 3-Europe). Submitted



Statement: Capecitabine containing regimen in TNBC

1. O'Shaughnessy J, Koeppen H, Xiao Y et al. Patients with Slowly Proliferative Early Breast Cancer Have Low Five-Year Recurrence Rates in a Phase III Adjuvant Trial of Capecitabine. Clin Cancer Res. 2015;21:4305-11
2. Jiang Y, Yin W, Zhou L et al. First efficacy results of capecitabine with anthracycline-and taxane-based adjuvant therapy in high-risk early breast cancer: a meta-analysis. PLoS ONE 2012;7(3): e32474.
3. Joensuu H, Kellokumpu-Lehtinen PL, Huovinen R et al. Adjuvant Capecitabine in Combination With Docetaxel, Epirubicin, and Cyclophosphamide for Early Breast Cancer: The Randomized Clinical FinXX Trial. JAMA Oncol. 2017;3(6):793-800.
4. Martín M, Barrios CH, Torrecillas L et al. Efficacy results from CIBOMA/2004-01_GEICAM/2003-11 study: A randomized phase III trial assessing adjuvant capecitabine after standard chemotherapy for patients with early triple negative breast cancer. San Antonio Breast Cancer Symposium 2018, abstr. GS2-04.
5. Van Mackelenbergh M Seiter F, Möbus V et al. Effects of capecitabine as part of neo-/adjuvant chemotherapy. A meta-analysis of individual patient data from 12 randomized trials including 15,457 patients. SABCS 2019, abstr. GS1-07

Statement: Capecitabine containing regimen in TNBC in general:

1. Martín M, Barrios CH, Torrecillas L et al. Efficacy results from CIBOMA/2004-01_GEICAM/2003-11 study: A randomized phase III trial assessing adjuvant capecitabine after standard chemotherapy for patients with early triple negative breast cancer. San Antonio Breast Cancer Symposium 2018, abstr. GS2-04.

Statement: Capecitabine containing regimen in TNBC as postneoadjuvant therapy if non-pCR:

1. Masuda N, Lee SJ, Ohtani S et al. Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy. N Engl J Med. 2017 Jun 1;376(22):2147-59.

Statement: 5- Fluorouracile added to EC/AC=>Pac

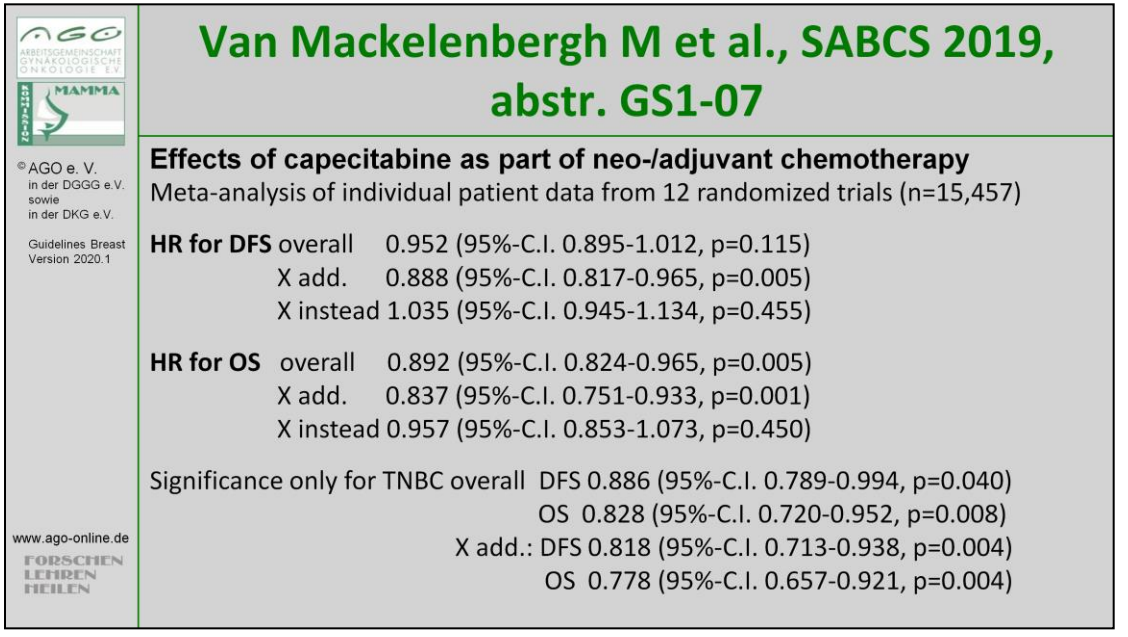
1. Del Mastro L, De Placido S, Bruzzi P et al. Fluorouracil and dose-dense chemotherapy in adjuvant treatment of patients with early-stage breast cancer: an open-label, 2 × 2 factorial, randomised phase 3 trial. Lancet. 2015;385(9980):1863-72.

Statement: Platinum containing regimen in TNBC

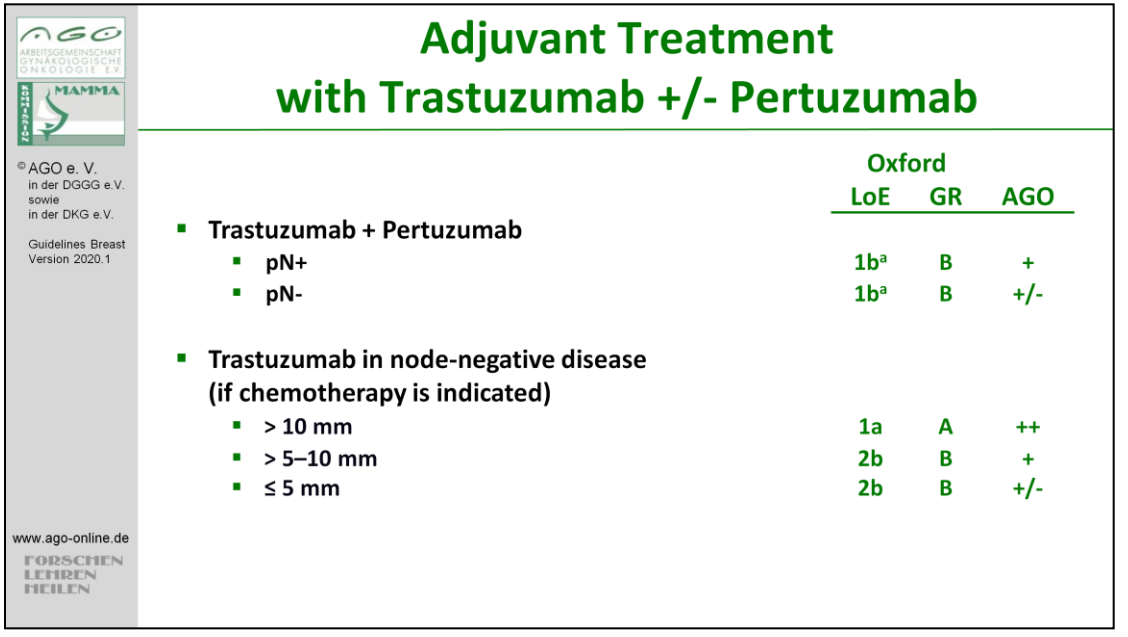
1. Joensuu H, Gligorov J. Adjuvant treatments for triple-negative breast cancers. Ann Oncol. 2012;23 Suppl 6:vi40-5.
2. Alba E, Chacon JI, Lluch A et al. A randomized phase II trial of platinum salts in basal-like breast cancer patients in the neoadjuvant setting. Results from the GEICAM/2006-03, multicenter study. Breast Cancer Res Treat 2012: 136; 487–493.
3. Von Minckwitz G, Schneeweiss A, Loibl S et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): a randomised phase 2 trial. Lancet Oncol 2014: 15; 747-56.
4. Ando M, Yamauchi H, Aogi K et al. Randomized phase II study of weekly paclitaxel with and without carboplatin followed by cyclophosphamide/epirubicin/5-fluorouracil as neoadjuvant chemotherapy for stage II/IIIA breast cancer without HER2 overexpression. Breast Cancer Res Treat 2014: 145; 401-09.
5. Petrelli F, Coinu A, Borgonova K et al. The value of platinum agents as neoadjuvant chemotherapy in triple-negative breast cancers: a

systematic review and meta-analysis. Breast Cancer Res Treat 2014: 144; 223-32.

6. Sikov WM, Berry DA, Perou CM et al. Impact of the Addition of Carboplatin and/or Bevacizumab to Neoadjuvant Once-per-Week Paclitaxel Followed by Dose-Dense Doxorubicin and Cyclophosphamide on Pathologic Complete Response Rates in Stage II to III Triple-Negative Breast Cancer: CALGB 40603 (Alliance). J Clin Oncol 2015: 33; 13-21.
7. Loibl S, O'Shaughnessy J, Untch M et al. Addition of the PARP inhibitor veliparib plus carboplatin or carboplatin alone to standard neoadjuvant chemotherapy in triple-negative breast cancer (BrighTNess): a randomised, phase 3 trial. Lancet Oncol. 2018 Apr;19(4):497-509.
8. Gluz O Nitz U, Liedtke C et al. Comparison of Neoadjuvant Nab-Paclitaxel+Carboplatin vs Nab-Paclitaxel+Gemcitabine in Triple-Negative Breast Cancer: Randomized WSG-ADAPT-TN Trial Results. J Natl Cancer Inst. 2018 Jun 1;110(6):628-637.

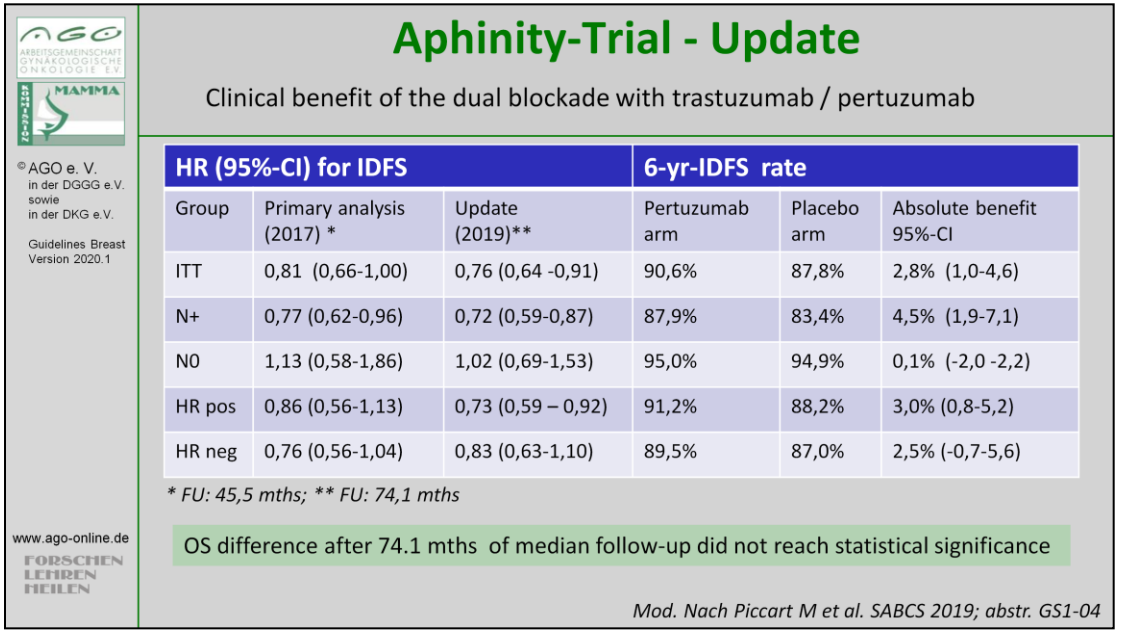


1. Van Mackelenbergh M Seiter F, Möbus V et al. Effects of capecitabine as part of neo-/adjuvant chemotherapy. A meta-analysis of individual patient data from 12 randomized trials including 15,457 patients. SABCS 2019, abstr. GS1-07

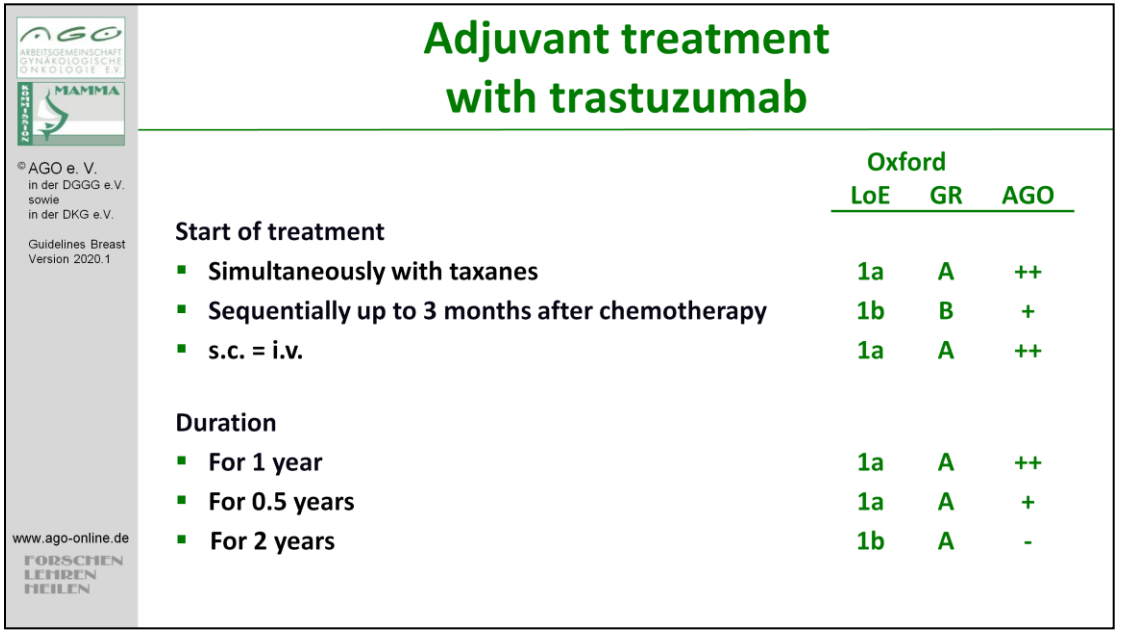


Statement Trastuzumab + Pertuzumab (pN+/-)

1. von Minckwitz G, Procter M, de Azambuja E et al; APHINITY Steering Committee and Investigators. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med. 2017;377(2):122-131.
2. Piccart M , Procter M, Fumagalli D et al. Interim overall survival analysis of APHINITY (BIG 4-11): A randomized multicenter, double-blind, placebo-controlled trial comparing chemotherapy plus trastuzumab plus pertuzumab versus chemotherapy plus trastuzumab plus placebo as adjuvant therapy in patients with operable HER2-positive early breast cancer. SABCS 2019; abstr. GS 01-04



Piccart M , Procter M, Fumagalli D et al. Interim overall survival analysis of APHINITY (BIG 4-11): A randomized multicenter, double-blind, placebo-controlled trial comparing chemotherapy plus trastuzumab plus pertuzumab versus chemotherapy plus trastuzumab plus placebo as adjuvant therapy in patients with operable HER2-positive early breast cancer. SABCS 2019; abstr. GS 01-04



Statement: Start of treatment simultaneously with taxanes

1. Smith I, Procter M, Gelber RD et al.; HERA study team. 2-year follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive breast cancer: a randomised controlled trial. Lancet. 2007;369(9555):29-36.
2. Goldhirsch A, Gelber RD, Piccart-Gebhart, MJ et al.; Herceptin Adjuvant (HERA) Trial Study Team. 2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): an open-label, randomised controlled trial. Lancet. 2013;382(9897):1021-8.
3. Cameron D, Piccart-Gebhart MJ, Gelber RD, et al.; Herceptin Adjuvant (HERA) Trial Study Team. 11 years' follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive early breast cancer: final analysis of the HERceptin Adjuvant (HERA) trial. Lancet. 2017;389(10075):1195-1205.
4. Perez EA, Romond EH , Suman VJ et al. Trastuzumab plus adjuvant chemotherapy for human epidermal growth factor receptor 2-positive breast cancer: planned joint analysis of overall survival from NSABP B-31 and NCCTG N9831.J Clin Oncol. 2014;32(33):3744-52.
5. Joensuu H, Bono P, Kataja V et al. Fluorouracil, epirubicin, and cyclophosphamide with either docetaxel or vinorelbine, with or without trastuzumab, as adjuvant treatments of breast cancer: final results of the FinHer Trial. J Clin Oncol. 2009;27(34):5685-92.
6. Yin W, Jiang Y, Shen Z et al. Trastuzumab in the adjuvant treatment of HER2-positive early breast cancer patients: a meta-analysis

of published randomized controlled trials. PLoS One. 2011;6(6):e21030.

7. Perez EA, Suman VJ, Davidson NE et al. Sequential Versus Concurrent Trastuzumab in Adjuvant Chemotherapy for Breast Cancer. J Clin Oncol 2011;29:4491-4497
8. Slamon D, Eiermann W, Robert N et al.; Breast Cancer International Research Group. Adjuvant trastuzumab in HER2-positive breast cancer. N Engl J Med. 2011;365(14):1273-83.

Statement s.c.

1. Gligorov J, Ataseven B, Verrill M et al.; SafeHer Study Group. Safety and tolerability of subcutaneous trastuzumab for the adjuvant treatment of human epidermal growth factor receptor 2-positive early breast cancer: SafeHer phase III study's primary analysis of 2573 patients. Eur J Cancer. 2017;82:237-246.
2. Pivot X, Verma S, Fallowfield L et al.; PrefHer Study Group. Efficacy and safety of subcutaneous trastuzumab and intravenous trastuzumab as part of adjuvant therapy for HER2-positive early breast cancer: Final analysis of the randomised, two-cohort PrefHer study. Eur J Cancer. 2017;86:82-90.
3. Jackisch C, Stroyakovskiy D, Pivot X et al. Subcutaneous vs Intravenous Trastuzumab for Patients With ERBB2-Positive Early Breast Cancer: Final Analysis of the HannaH Phase 3 Randomized Clinical Trial. JAMA Oncol. 2019;5(5):e190339. doi: 10.1001/jamaoncol.2019.0339.

Statement: Duration

Duration Trastuzumab 1 year

Duration Trastuzumab 2 year

Duration Trastuzumab 0.5 years

1. Goldhirsch A, Gelber RD, Piccart-Gebhart, MJ et al.; Herceptin Adjuvant (HERA) Trial Study Team. 2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): an open-label, randomised controlled trial. Lancet. 2013;382(9897):1021-8.
2. Cameron D, Piccart-Gebhart MJ, Gelber RD, et al.; Herceptin Adjuvant (HERA) Trial Study Team. 11 years' follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive early breast cancer: final analysis of the HERceptin Adjuvant (HERA) trial. Lancet. 2017;389(10075):1195-1205.
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3. Niraula S, Gyawali B. Optimal duration of adjuvant trastuzumab in treatment of early breast cancer: a meta-analysis of randomized controlled trials. Breast Cancer Res Treat. 2019;173(1):103-109. doi: 10.1007/s10549-018-4967-8..

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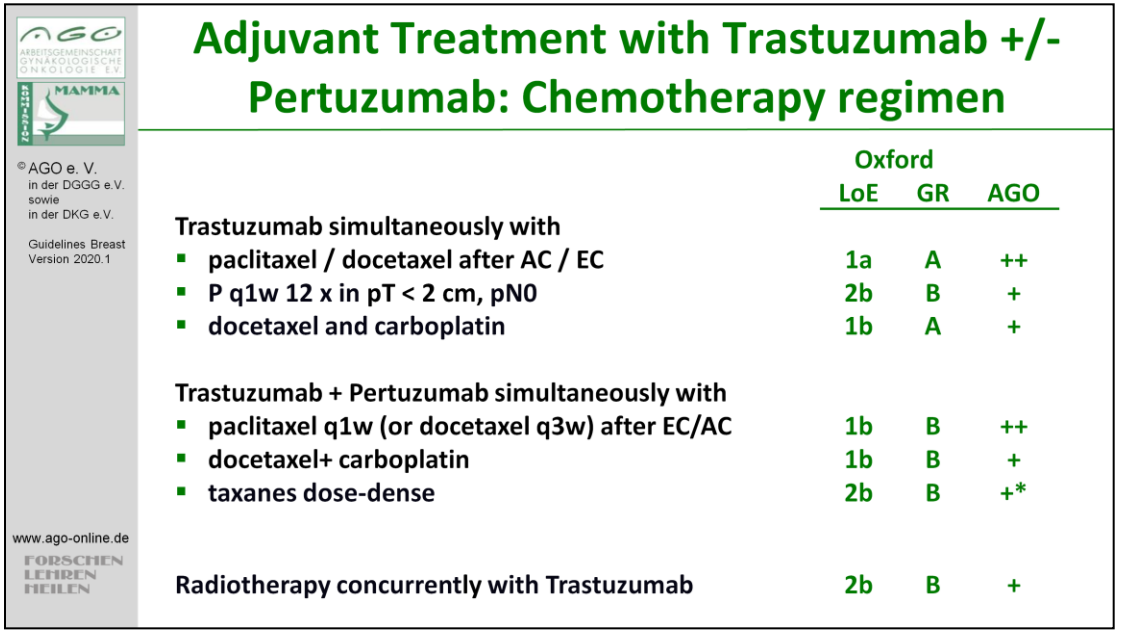

Statement: with paclitaxel/docetaxel after AC/EC

1. Perez EA, Suman VJ, Davidson NE et al. Sequential Versus Concurrent Trastuzumab in Adjuvant Chemotherapy for Breast Cancer. J Clin Oncol 2011;29:4491-4497
2. Cameron D, Piccart-Gebhart MJ, Gelber RD, et al.; Herceptin Adjuvant (HERA) Trial Study Team. 11 years' follow-up of trastuzumab after adjuvant chemotherapy in HER2-positive early breast cancer: final analysis of the HERceptin Adjuvant (HERA) trial. Lancet. 2017;389(10075):1195-1205.
3. Papakonstantinou A, Matikas A, Bengtsson NO et al. Efficacy and Safety of Tailored and Dose-Dense Adjuvant Chemotherapy and Trastuzumab for Resected HER2-Positive Breast Cancer: Results From the Phase 3 PANTHER Trial. Cancer 2019 doi: 10.1002/cncr.32653. [Epub ahead of print]

Statement: P q1w12 in pT < 2 cm pN0

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Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer. J Clin Oncol. 2019;37(22):1868-1875. doi: 10.1200/JCO.19.00066.

Statement: with docetaxel and carboplatin

1. Valero V, Forbes J, Pegram MD et al. Multicenter phase III randomized trial comparing docetaxel and trastuzumab with docetaxel, carboplatin, and trastuzumab as first-line chemotherapy for patients with HER2-gene-amplified metastatic breast cancer (BCIRG 007 study): two highly active therapeutic regimens. J Clin Oncol. 2011;29(2):149-56.
2. Burstein HJ, Piccart-Gebhart MJ, Perez EA et al. Choosing the Best Trastuzumab-Based Adjuvant Chemotherapy Regimen: Should We Abandon Anthracyclines? Journal of Clinical Oncology 2012;18(30):2179-2182

Statement: Trastuzumab + Pertuzumab simultaneously with Paclitaxel q1w or Docetaxel q3w (after EC or AC)

1. von Minckwitz G, Procter M, de Azambuja E et al; APHINITY Steering Committee and Investigators. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med. 2017;377(2):122-131.

Statement: Trastuzumab + Pertuzumab simultaneously with Docetaxel and Carboplatin q3w

1. von Minckwitz G, Procter M, de Azambuja E et al; APHINITY Steering Committee and Investigators. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med. 2017;377(2):122-131.
2. Schneeweiss A, Chia S, Hickish T et al. Long-term efficacy analysis of the randomised, phase II TRYPHAENA cardiac safety study: Evaluating pertuzumab and trastuzumab plus standard neoadjuvant anthracycline-containing and anthracycline-free chemotherapy regimens in patients with HER2-positive early breast cancer. Eur J Cancer 89:27-35, 2017

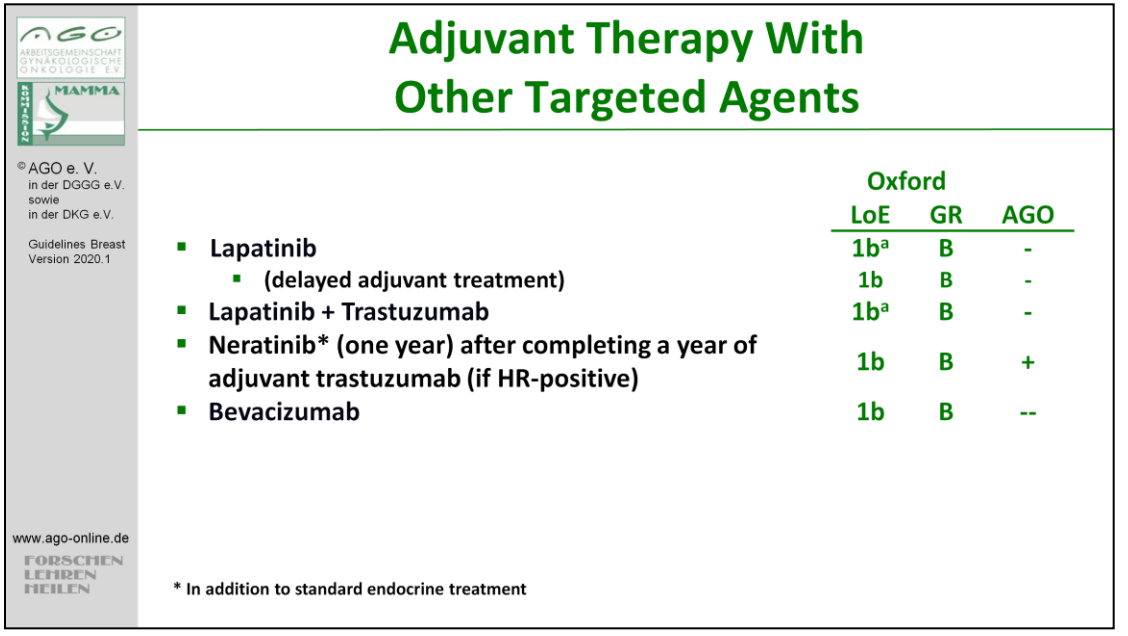
Statement: Trastuzumab + Pertuzumab simultaneously with taxanes dose-dense

1. von Minckwitz G, Procter M, de Azambuja E et al; APHINITY Steering Committee and Investigators. Adjuvant Pertuzumab and

Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med. 2017;377(2):122-131.

Statement: radiotherapy concurrent with trastuzumab

1. M. Y. Halyard, T. M. Pisansky, L. J. Solin et al. Trastuzumab can be administered concurrent to adjuvant radiotherapy of the breast or thoracic wall. Adjuvant radiotherapy (RT) and trastuzumab in stage I-IIA breast cancer: Toxicity data from North Central Cancer Treatment Group Phase III trial N9831 J Clin Oncol. 2009;27(16):2638-44



Statement: Lapatinib

Delayed adjvuvant treatment

1. Moreno-Aspitia A, Dueck AC, Ghanem-Cañete I et al. RC0639: phase II study of paclitaxel, trastuzumab, and lapatinib as adjuvant therapy for early stage HER2-positive breast cancer. Breast Cancer Res Treat. 2013;138(2):427-35.
2. Goss PE, Smith IE, O'Shaughnessy J.; TEACH investigators. Adjuvant lapatinib for women with early-stage HER2-positive breast cancer: a randomised, controlled, phase 3 trial. Lancet Oncol. 2013;14(1):88-96.
3. Perez EA, Holmes E, De Azambuja E et al. Disease-free survival (DFS) in the lapatinib alone arm and expanded results of the phase III ALTTO trial (BIG 2-06; NCCTG [Alliance] N063D) in the adjuvant treatment of HER2-positive early breast cancer (EBC). Ann Oncol 2014;25(5):1-41

Statement: Lapatinib + Trastuzumab

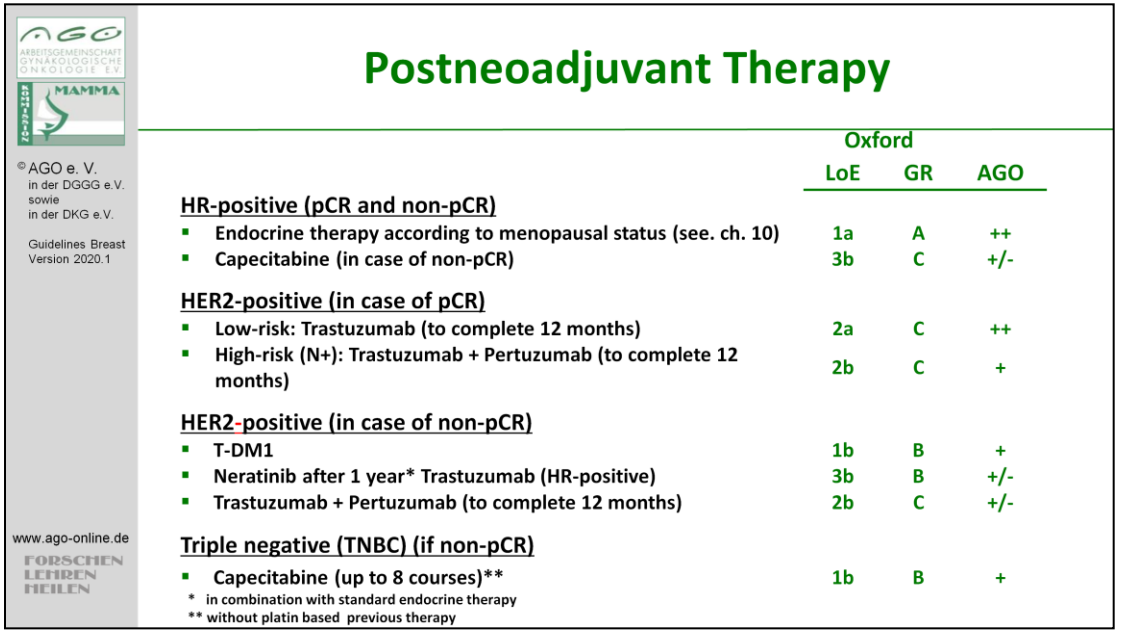
1. Piccart-Gebhart M, Holmes E, Baselga J et al. Adjuvant Lapatinib and Trastuzumab for Early Human Epidermal Growth Factor Receptor 2-Positive Breast Cancer: Results From the Randomized Phase III Adjuvant Lapatinib and/or Trastuzumab Treatment Optimization Trial. J Clin Oncol. 2016 1;34(10):1034-42.

Statement: Neratinib

1. Martin M, Holmes FA, Ejlertsen B et al.; ExteNET Study Group. Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2017;18(12):1688-1700

Statement: Bevacizumab

1. Cameron D, Brown J, Dent R et al. Adjuvant bevacizumab-containing therapy in triple-negative breast cancer (BEATRICE): primary results of a randomised, phase 3 trial. Lancet Oncol. 2013;14(10):933-42.
2. Slamon D et al.. BETH: A Randomized Phase III Study Evaluating Adjuvant Bevacizumab Added to Trastuzumab/Chemotherapy for Treatment of HER2+ Early Breast Cancer. SABCS 2013
3. Miller KD, O'Neill A, Gradishar W et al. Double-Blind Phase III Trial of Adjuvant Chemotherapy With and Without Bevacizumab in Patients With Lymph Node-Positive and High-Risk Lymph Node-Negative Breast Cancer (E5103). J Clin Oncol. 2018;36(25):2621-2629.



Statement ER and/or PgR positiv (pCR und non-pCR) Endokrine Therapie nach Menopausenstatus (s. Kap. 10)

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). 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(9472):1687-717.
2. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. Lancet. 2015;386(10001):1341-1352.

Statement HER2 positiv (bei pCR): Low risk: Trastuzumab (bis 12 Mon. komplett)

1. Goldhirsch A, Gelber RD, Piccart-Gebhart, MJ et al.; Herceptin Adjuvant (HERA) Trial Study Team. 2 years versus 1 year of adjuvant trastuzumab for HER2-positive breast cancer (HERA): an open-label, randomised controlled trial. Lancet. 2013;382(9897):1021-8.

Statement HER2 positiv (bei pCR): pN+ Trastuzumab + Pertuzumab (bis 12 Mon. komplett)

1. von Minckwitz G, Procter M, de Azambuja E, et al. APHINITY Steering Committee and Investigators. Adjuvant Pertuzumab and

Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med. 2017 Jul 13;377(2):122-131.

2. Piccart M , Procter M, Fumagalli D et al. Interim overall survival analysis of APHINITY (BIG 4-11): A randomized multicenter, double-blind, placebo-controlled trial comparing chemotherapy plus trastuzumab plus pertuzumab versus chemotherapy plus trastuzumab plus placebo as adjuvant therapy in patients with operable HER2-positive early breast cancer. SABCS 2019; abstr. GS 01-04

Statement HER2 positiv (bei non-pCR) T-DM1 (bis 12 Mon. anti-HER2-Therapie komplett)

1. 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

Statement HER2 positiv (bei non-pCR) Neratinib (1 Jahr) nach 1 Jahr Trastuzumab (nur bei HR-positiv)

1. Martin M et al.; ExteNET Study Group. Neratinib after trastuzumab-based adjuvant therapy in HER2-positive breast cancer (ExteNET): 5-year analysis of a randomised, double-blind, placebo-controlled, phase 3 trial. Lancet Oncol. 2017;18(12):1688-1700

Statement HER2 positiv (bei non-pCR): Trastuzumab + Pertuzumab (bis 12 Mon. komplett)

1. von Minckwitz G, Procter M, de Azambuja E, et al. APHINITY Steering Committee and Investigators. Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer. N Engl J Med. 2017 Jul 13;377(2):122-131.
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Statement Tripel negativ (TNBC) (bei non-pCR) Capecitabine (8 Kurse)

1. Masuda N, Lee SJ, Ohtani S, et al. Adjuvant Capecitabine for Breast Cancer after Preoperative Chemotherapy. N Engl J Med. 2017;376(22):2147-2159.
2. Lluch A, Barrios CH, Torrecillas L, et al. Phase III Trial of Adjuvant Capecitabine After Standard Neo-/Adjuvant Chemotherapy in Patients With Early Triple-Negative Breast Cancer (GEICAM/2003-11_CIBOMA/2004-01). J Clin Oncol. 2020;38(3):203–213. doi:10.1200/JCO.19.00904
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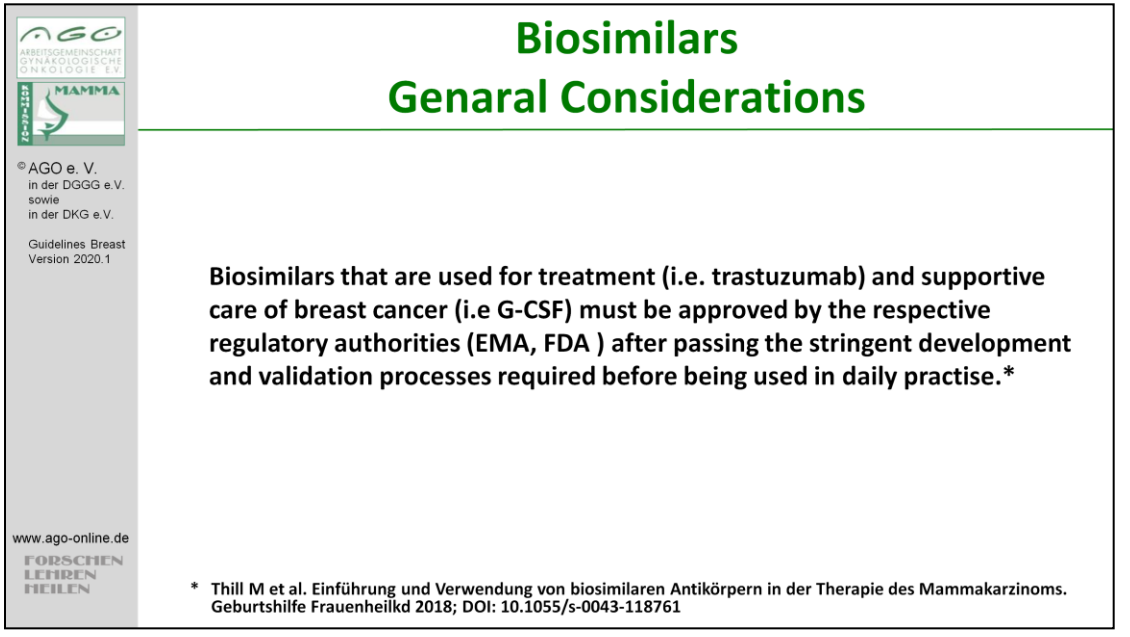

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4. Jacobs I, Ewesuedo R, Lula S et al. Biosimilars for the Treatment of Cancer: A Systematic Review of Published Evidence. BioDrugs. 2017;31(1):1-36.