Guidelines Breast
Version 2021.1D

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Adjuvante endokrine Therapie bei prä- und postmenopausalen Patientinnen

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- **Versionen 2002–2020:**
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- **Version 2021:**
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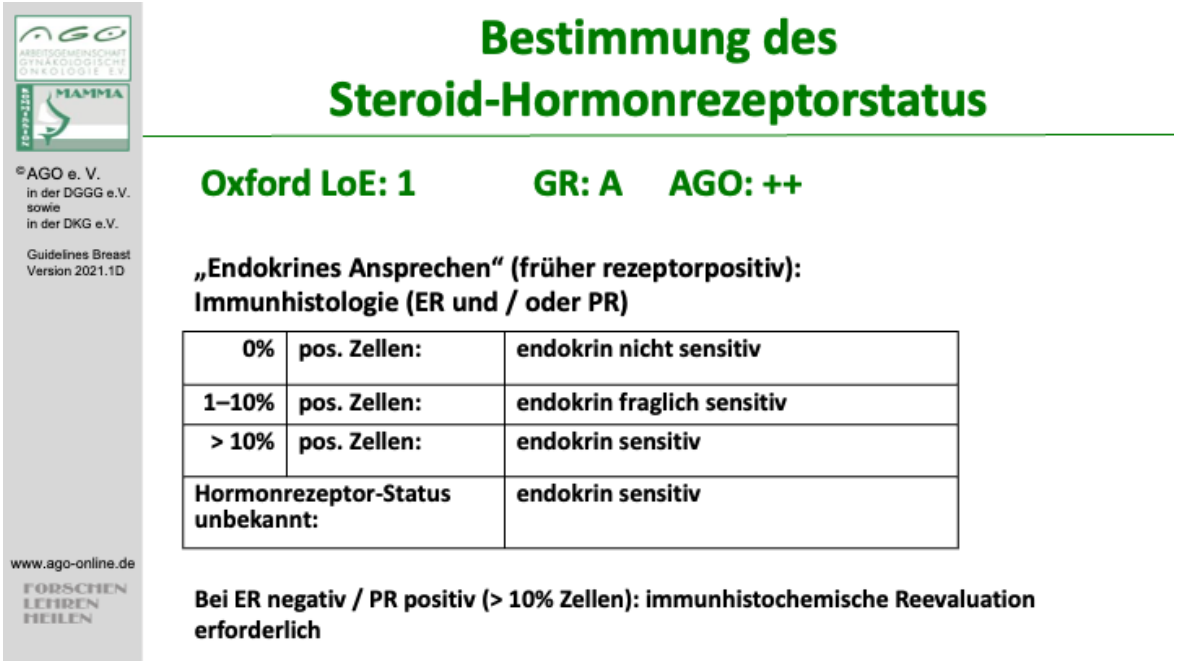


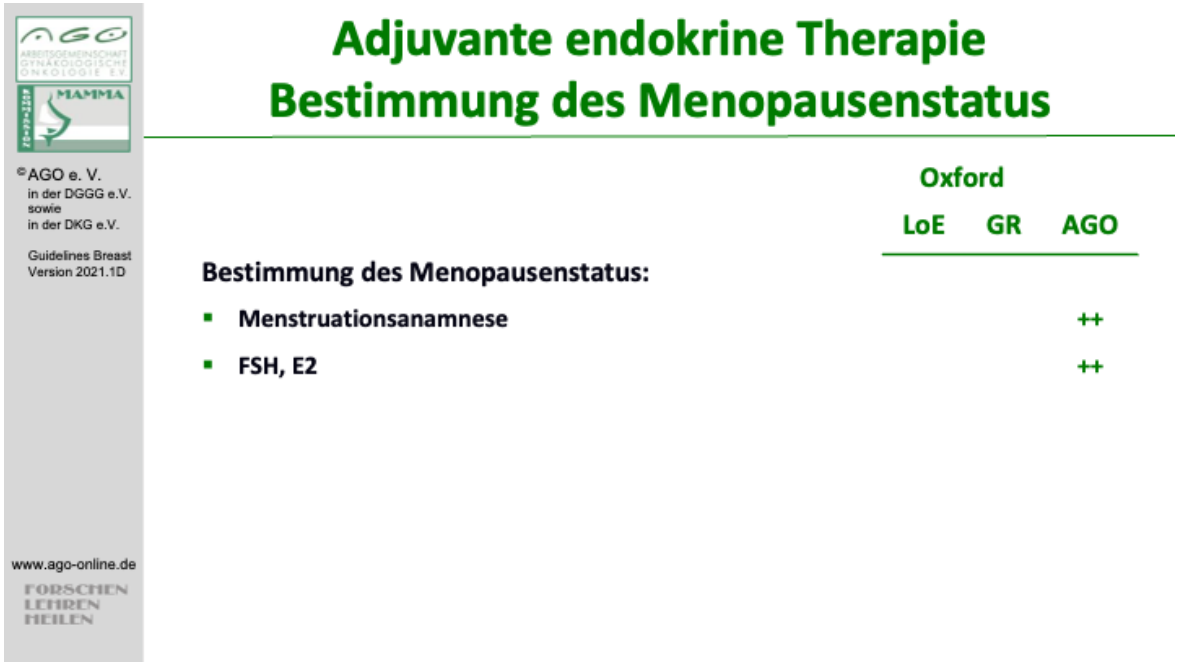
Endocrine responsiveness:

1. Hammond ME , Hayes DF, DowsettM et al. American Society of Clinical Oncology/College Of American Pathologists guideline recommendations for immunohistochemical testing of estrogen and progesterone receptors in breast cancer. J Clin Oncol. 2010 Jun 1;28(16):2784-95. Review. Erratum in: J Clin Oncol. 2010 Jul 20;28(21):3543.
2. 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.
3. Traub L, Thill M, Nitschmann S: 20-Jahres-Ergebnisse einer 5-jährigen Hormontherapie bei Mammakarzinom : Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Internist (Berl). Springer Medizin 2018;59(4):410–2.
4. Pan H, Gray R, Braybrooke J et al. 20-Year Risks of Breast-Cancer Recurrence after Stopping Endocrine Therapy at 5 Years. N Engl J Med. 2017;377(19):1836–46.

In case of ER negative / PR positive (>10% cells): consider immunohistochemical re-evaluation:

1. Viale G, Regan MM, Maiorano E et al. Prognostic and predictive value of centrally reviewed expression of estrogen and progesterone receptors in a randomized trial comparing letrozole and tamoxifen adjuvant therapy for postmenopausal early breast

cancer: BIG 1-98. J Clin Oncol 2007;25:3846-52.
2. Cserni G, Fracz M, Kalman E et al. Estrogen receptor negative and progesterone receptor positive breast carcinomas-how frequent are they? Pathol Oncol Res 2011;17:663-8.
3. Hefti MM, Hu R, Knblauch NW et al. Estrogen receptor negative/progesterone receptor positive breast cancer is not a reproducible subtype. Breast Cancer Res 2013;15:R68.
4. Yi M, Huo L, Koenig KB et al. Which threshold for ER positivity? a retrospective study based on 9639 patients. Ann Oncol 2014;25:1004-11.
5. Allison, K. H., et al. (2020). "Estrogen and Progesterone Receptor Testing in Breast Cancer: American Society of Clinical Oncology/College of American Pathologists Guideline Update." Arch Pathol Lab Med 144(5): 545-563.
6. Allison, K. H., et al. (2020). "Estrogen and Progesterone Receptor Testing in Breast Cancer: ASCO/CAP Guideline Update." J Clin Oncol 38(12): 1346-1366.



1. Ortmann O, Cufer T, Dixon JM et al. Adjuvant endocrine therapy for perimenopausal women with early breast cancer. Breast 2009;18(1):2-7.
2. Clemons M, Simmons C: Identifying menopause in breast cancer patients: considerations and implications. Breast Cancer Res Treat 2007;104(2):115-20.
3. Su HI, Sammel MD, Green J et al. Antimullerian hormone and inhibin B are hormone measures of ovarian function in late reproductive-aged breast cancer survivors. Cancer 2010;116(3):592-9.
4. Partridge AH, Ruddy KJ, Gelber S et al. Ovarian reserve in women who remain premenopausal after chemotherapy for early stage breast cancer. Fertil Steril 2010;94(2):638-44.
5. Anders C, Marcom PK, Peterson B et al. A pilot study of predictive markers of chemotherapy-related amenorrhea among premenopausal women with early stage breast cancer. Cancer Invest 2008;26(3):286-95
6. Anderson RA, Cameron DA: Pretreatment serum anti-müllerian hormone predicts long-term ovarian function and bone mass after chemotherapy for early breast cancer. J Clin Endocrinol Metab 2011 96(5):1336-43.
7. Su HI, Chung K, Sammel MD et al. Antral follicle count provides additive information to hormone measures for determining ovarian function in breast cancer survivors. Fertil Steril 2011;95(5):1857-9.
8. Furlanetto J, Nekljudova V: Impact of chemotherapy-induced ovarian failure (CIOF) on disease –fee survival (dfs) and overall survival (osI in young women with early breast cancer, ESMO 2019 180 PD

Adjuvante endokrine Therapie

Endokrine Therapie:	Oxford LoE	GR	AGO
▪ Endokrin sensitiv	1a	A	++
▪ fraglich endokrin sensitiv	3b	D	+
▪ Endokrine Therapie sequentiell: nach einer adjuvanten Chemotherapie	5	D	+
▪ Endokrine Therapie simultan mit T-DM1/Anti-HER2-Therapie ohne Chemotherapie	5	D	+
▪ Nicht endokrin sensitiv: keine endokrine Therapie	1a	A	++

1. 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 randomised trials. Lancet 2005;365:1687-717.
2. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet 2011;378(9793):771-84.
3. Hackshaw A, Roughton M, Forsyth S et al. Long-term benefits of 5 years of tamoxifen: 10-year follow-up of a large randomized trial in women at least 50 years of age with early breast cancer. J Clin Oncol 2011;29(13): 1657-63.
4. Albain KS, Barlow WE, Ravdin PM, et al. Breast Cancer Intergroup of North America. Adjuvant chemotherapy and timing of tamoxifen in postmenopausal patients with endocrine-responsive, node-positive breast cancer: a phase 3, open-label, randomised controlled trial. Lancet 2009;374(9707):2055-63.
5. Bedognetti D, Sertoli MR, Pronzato P, et al. Concurrent vs sequential adjuvant chemotherapy and hormone therapy in breast cancer: a multicenter randomized phase III trial. J Natl Cancer Inst 2011;103(20):1529-39.
6. Fujii T, Kogawa T, Dong W et al. Revisiting the definition of estrogen receptor positivity in Her2-negative primary breast cancer. Ann Oncol 2017;28:2420-2428
7. Curigliano G, Burstein HJ, P Winer E et al. De-Escalating and escalating treatment for early-stage breast cancer: the St. Gallen International Expert Consensus Conference on the Primary Therapy of Early Breast Cancer. Ann Oncol 2017;28:1700-1712 .
8. Regan MM, Walley BA, Francis PA et al. Concurrent and sequential initiation of ovarian function suppression with chemotherapy in

premenopausal women with endocrine-responsive early breast cancer: an exploratory analysis of TEXT and SOFT. Ann Oncol 2017;28:2225-2232.
9. Villegas S, Lederer B: Similarities between low hormone receptor positive and hormone receptor negative breast cancer: an analysis of 4366 patients from multicenter clinical trials, SABCS 2018 P2-08-10
10. Chan, A., et al. (2016). "Neratinib after trastuzumab-based adjuvant therapy in patients with HER2-positive breast cancer (ExteNET): a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial." Lancet Oncol 17(3): 367-377.
11. von Minckwitz, G., et al. (2019). "Trastuzumab Emtansine for Residual Invasive HER2-Positive Breast Cancer." N Engl J Med 380(7): 617-628.
12. von Minckwitz, G., et al. (2017). "Adjuvant Pertuzumab and Trastuzumab in Early HER2-Positive Breast Cancer." N Engl J Med 377(2): 122-131
13. Early Breast Cancer Trialists' Collaborative, G. (2015). "Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials." Lancet 386(10001): 1341-1352.

Generelle Prinzipien der adjuvanten endokrinen Therapie AGO ++

- **Die adjuvante endokrine Therapie wird in die initiale Therapie (Jahre 1–5) und die erweiterte adjuvante Therapie (EAT, Jahre 6–10+) eingeteilt.**
- **Standard Therapiedauer der adjuvanten Therapie: 5 Jahre**
- **Erweiterte Therapiedauer nach individueller Nutzen-Risiko-Abwägung.**
- **Dauer, Wahl & Sequenz von AI oder Tam hängen v.a. von Menopausenstatus, Verträglichkeit und dem Rückfall-Risiko ab.**
- **Der Wechsel auf eine andere endokrine Therapie (Tam oder AI) ist besser, als die Therapie zu stoppen.**
- **Beginn mit AI insbesondere bei lobulären Karzinomen und/oder klar erhöhtem Rückfall-Risiko.**
- **Es existiert kein ausreichend validierter Biomarker für einen frühen versus einen späten Rückfall.**

1. Ingle JN: Overview of adjuvant trials of aromatase inhibitors in early breast cancer. Steroids 2011;76(8):765-7.
2. Higgins MJ, Liedke PE, Goss PE et al. Extended adjuvant endocrine therapy in hormone dependent breast cancer: the paradigm of the NCIC-CTG MA.17/BIG 1-97 trial. Crit Rev Oncol Hematol 2013;86(1):23-32.
3. Regan MM, Neven P, Giobbie-Hurder A et al. BIG 1-98 Collaborative Group; International Breast Cancer Study Group (IBCSG). Assessment of letrozole and tamoxifen alone and in sequence for postmenopausal women with steroid hormone receptor-positive breast cancer: the BIG 1-98 randomised clinical trial at 8·1 years median follow-up. Lancet Oncol 2011;12(12):1101-8.
4. 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):1341-52.
5. Rydén L, Heibert Arnlind M, Vitols S et al. Aromatase inhibitors alone or sequentially combined with tamoxifen in postmenopausal early breast cancer compared with tamoxifen or placebo - Meta-analyses on efficacy and adverse events based on randomized clinical trials. Breast 2016;26:106-140.
6. Goss PE, Ingle JN, Pritchard KI et al. Extending aromatase-inhibitor adjuvant therapy to 10 years. N Engl J Med 2016;375(3):209.
7. Pan H, Gray R, Braybrooke J et al. 20-year risks of breast recurrence after stopping endocrine therapy art 5 years. N Engl J Med 2017;1836-49.
8. Burstein HJ, Lacchetti C, Anderson H et al. Adjuvant endocrine therapy for women with hormone receptor–positive breast cancer: ASCO clinical practice guideline focused update. J Clin Oncol 2018 Nov 19:JCO1801160. doi: 10.1200/JCO.18.01160

9. Strasser-Weippl K, Sudan G, Ramjeesingh R et al. Outcomes in women with invasive ductal or invasive lobular early stage breast cancer treated with anastrozole or exemestane in CCTG (NCIC CTG) MA.27. Eur J Cancer 2018;90:19-25.
10. Goldvaser H, Barnes TA, Šeruga B, et al. Toxicity of extended adjuvant therapy with aromatase inhibitors in early breast cancer: a systematic review and meta-analysis. J Natl Cancer Inst. 2018;110(1)djx141.
11. van Hellemond I, Geurts SME, Tjan-Heijnen VCG: Current status of extended adjuvant endocrine therapy in early stage breast cancer. Curr Treat Options in Oncol 2018;19:26.
12. Regan MM, Walley BA, Francis PA et al. Concurrent and sequential initiation of ovarian function suppression with chemotherapy in premenopausal women with endocrine-responsive early breast cancer: an exploratory analysis of TEXT and SOFT. Ann Oncol 2017;28:2225-2232.
13. Blok EJ, Kroep JR, Meershoek-Klein Kranenbarg E et al. Treatment decisions and the impact of adverse events before and during extended endocrine therapy in postmenopausal early breast cancer. Eur J Cancer 2018;95:59-67.
14. Blok EJ, Kroep JR, Meershoek-Klein Kranenbarg E et al: Relevant factors for the optimal duration of extended endocrine therapy in early breast cancer. Breast Cancer Res Treat 2018;168:413-420.
15. Clement Z, Kollias J, Bingham J et al: Extended duration of adjuvant aromatase inhibitor in breast cancer: a meta-analysis of randomized controlled trials. Gland Surg 2018;7:449-457.

NEU:

- CTS-5
- BCI (H/I)

Tamoxifen 5-10 yrs:

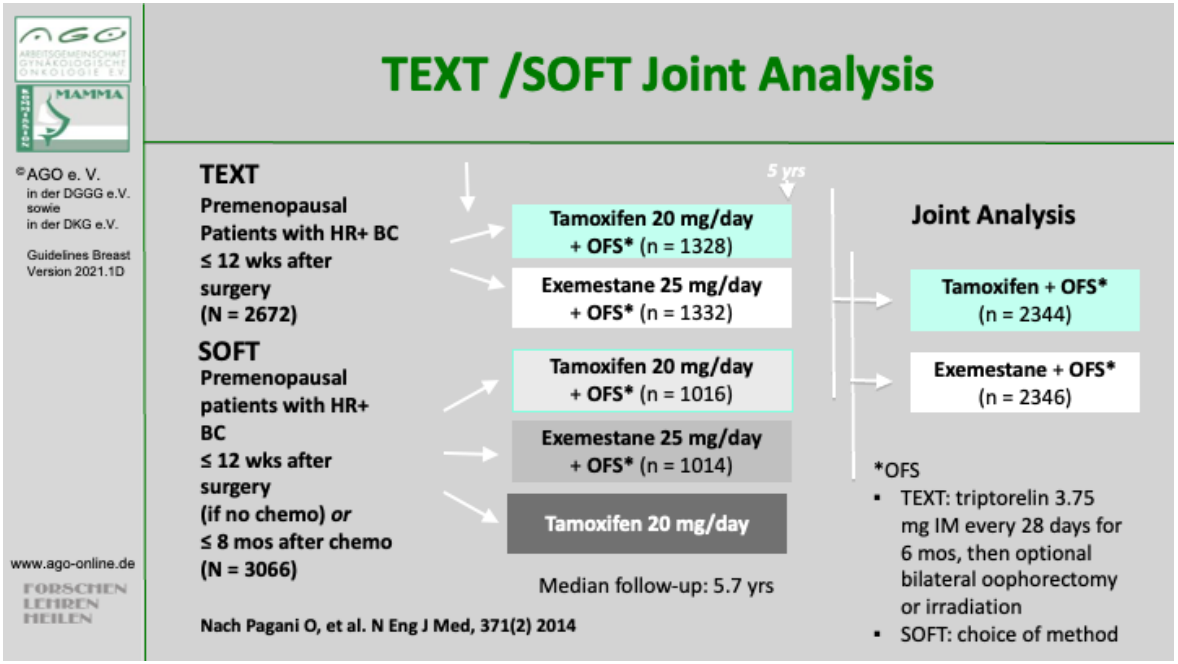
1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Effects of chemotherapy and hormonal therapy for early breast cancer on recurrence and 15-year survival: an overview of the randomised trials. Lancet 2005;365:1687-717.
2. Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet 2011;378:771-84.
3. Davies C, Pan H, Godwin J et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet 2013;381:805-806.
4. Tormey DC, Gray R, Falkson HC: Postchemotherapy adjuvant tamoxifen therapy beyond five years in patients with lymph node-positive breast cancer. Eastern Cooperative Oncology Group. J Natl Cancer Inst 1996;88:1828-33.
5. Goel S, Sharma R, Hamilton A et al: LHRH agonists for adjuvant therapy of early breast cancer in premenopausal women. Cochrane Database Syst Rev. 20097;(4):CD004562.
6. Ruhstaller T, Giobbie-Hurder A: Adjuvant Letrozole and Tamoxifen Alone or Sequentially for Postmenopausal Women With Hormone Receptor–Positive Breast Cancer: Long-Term Follow-Up of the BIG 1-98 Trial JCO 37:105-114

GnRH as monotherapy:

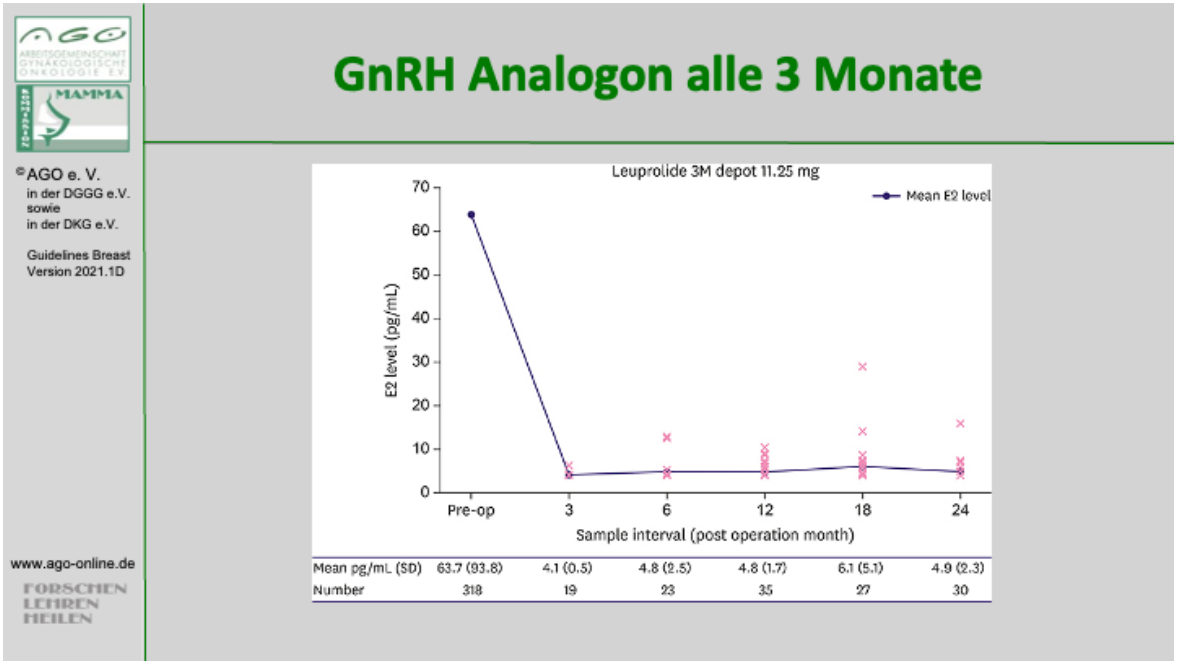
1. Cuzick J, Ambroisine L, Davidson N et al: Use of luteinising-hormone-releasing hormone agonists as adjuvant treatment in premenopausal patients with hormone-receptor-positive breast cancer: a meta-analysis of individual patient data from randomised adjuvant trials. Lancet 2007; 369:1711-23.

Ovarian function suppression (OFS) with Tam/AI and Tam with or without OFS:

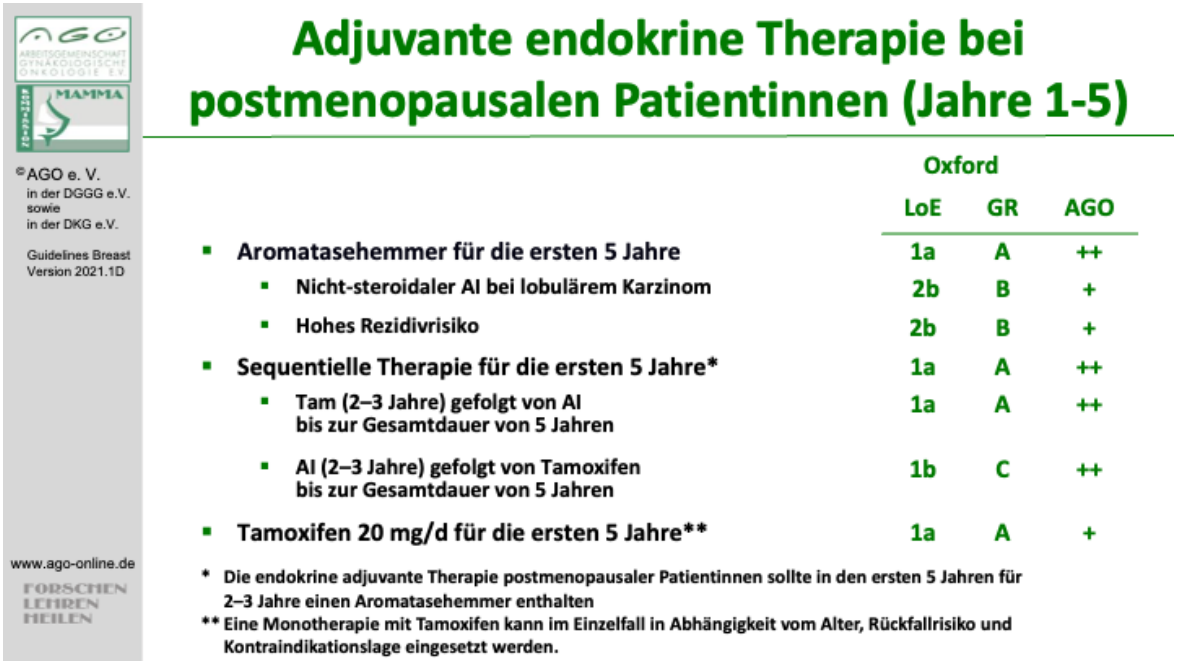
1. Goel S, Sharma R, Hamilton A et al: LHRH agonists for adjuvant therapy of early breast cancer in premenopausal women. Cochrane Database Syst Rev 20097;(4):CD004562.
2. Francis PA, Regan MM, Fleming GF et al. The SOFT Investigators and the International Breast Cancer Study Group. Adjuvant Ovarian Suppression in Premenopausal Breast Cancer. N Engl J Med 2015;372(5):436-46.
3. Pagani O, Regan MM, Walley BA et al. TEXT and SOFT Investigators; International Breast Cancer Study Group. Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. N Engl J Med 2014;371(2):107-18.
4. Gnant M, Mlineritsch B, Schippinger W et al: Endocrine therapy plus zoledronic acid in premenopausal breast cancer. N Engl J Med 2009;360(7):679-91.
5. Shiba E, Yamashita H, Kurebayashi J et al. A randomized controlled study evaluating safety and efficacy of leuprorelin acetate every-3-months depot for 2 versus 3 or more years with tamoxifen for 5 years as adjuvant treatment in premenopausal patients with endocrine-responsive breast cancer. Breast Cancer 2016;23(3):499-509.
6. JSaha P, Regan MM, Pagani O: Treatment efficacy, adherence, and quality of life among younger than 35 years in the International Breast Cancer Study Group TEXT and SOFT adjuvant endocrine therapy trial. J Clin Oncol 2017;35:3113-3122.
7. Francis PA, Pagani O, Fleming GF et al. Tailoring adjuvant endocrine therapy for premenopausal breast cancer. N Engl J Med 2018; 379: 122-137
8. Kim HA, Lee JW, Nam SJ et al. Adding Ovarian Suppression to Tamoxifen for Premenopausal Breast Cancer: A Randomized Phase III Trial. J Clin Oncol. 2019, https://doi.org/10.1200/JCO.19. 0012



1. Pagani O, Gelber S, Colleoni M, et al. Impact of SERM adherence on treatment effect: International Breast Cancer Study Group Trials 13-93 and 14-93. Breast Cancer Res Treat 2013;142(2):455-9.
2. Francis PA, Regan MM, Fleming GF et al. The SOFT Investigators and the International Breast Cancer Study Group. Adjuvant Ovarian Suppression in Premenopausal Breast Cancer. N Engl J Med 2015;372(5):436-46.



1. Schmid P, Untch M, Kossé V, Bondar G, Vassiljev L, Tarutinov V, et al. Leuprorelin acetate every-3-months depot versus cyclophosphamide, methotrexate, and fluorouracil as adjuvant treatment in premenopausal patients with node-positive breast cancer: the TABLE study. J Clin Oncol 2007;25:2509-15.
2. Masuda N, Iwata H, Rai Y, Anan K, Takeuchi T, Kohno N, et al. Monthly versus 3-monthly goserelin acetate treatment in pre-menopausal patients with estrogen receptor-positive early breast cancer. Breast Cancer Res Treat 2011;126:443-51.
3. Bellet M, Gray KP, Francis PA, Láng I, Ciruelos E, Lluch A, et al. Twelve-month estrogen levels in premenopausal women with hormone receptor-positive breast cancer receiving adjuvant triptorelin plus exemestane or tamoxifen in the Suppression of Ovarian Function Trial (SOFT): the SOFT-EST substudy. J Clin Oncol 2016;34:1584-93.
4. Young-Jin L et al. Change in estradiol levels among premenopausal patietn wiht breat cancer treated using leuprolide acetate 11.25mg 3months depot and tamoxifen. J Breast Cancer. 2020 Oct;23(5):553-559. https://doi.org/10.4048/jbc.2020.23.e57



<u>AI for first 5 years:</u>

1. 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):1341-52.
2. Rydén L, Heibert Arnlind M, Vitols S et al. Aromatase inhibitors alone or sequentially combined with tamoxifen in postmenopausal early breast cancer compared with tamoxifen or placebo - Meta-analyses on efficacy and adverse events based on randomized clinical trials. Breast 2016;26:106-14.
3. FACE Studie?

<u>Especially in case of lobular cancer</u>

1. Strasser-Weippl K et al. Outcomes in women with invasive ductal or invasive lobular early stage breast cancer treated with anastrozole or exemestane in CCTG (NCIC CTG) MA.27. Eur J Cancer 2018;90:19-25. doi: 10.1016/j.ejca.2017.11.014

<u>High risk of recurrence:</u>

1. 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):1341-52.

Sequential therapy for first 5 years:

Tam (2-3 yrs.) followed by AI to complete 5 years

AI (2-3 yrs.) followed by Tam to complete 5 years

1. 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):1341-52.
2. Rydén L, Heibert Arnlind M, Vitols S et al. Aromatase inhibitors alone or sequentially combined with tamoxifen in postmenopausal early breast cancer compared with tamoxifen or placebo - Meta-analyses on efficacy and adverse events based on randomized clinical trials. Breast 2016;26:106-14.
3. Derks MGM, Blok EJ, Seynaeve C et al. Adjuvant tamoxifen and exemestane in women with postmenopausal early breast cancer (TEAM): 10-year follow-up of a multicentre, open-label, randomised, phase 3 trial. Lancet Oncol 2017;18:1211-1220.
4. Ruhstaller T, Giobbie-Hurder A, Colleoni M et al. Adjuvant letrozole and tamoxifen alone or sequentially for postmenopausal women with hormone receptor–positive breast cancer: long-term follow-up of the BIG 1-98 trial. J Clin Oncol 2019;37(2):105-114.
5. De Placido S, Gallo C, De Laurentiis M, et al. GIM Investigators. Adjuvant anastrozole versus exemestane versus letrozole, upfront or after 2 years of tamoxifen, in endocrine-sensitive breast cancer (FATA-GIM3): a randomised, phase 3 trial. Lancet Oncol. 2018 Apr;19(4):474-485.

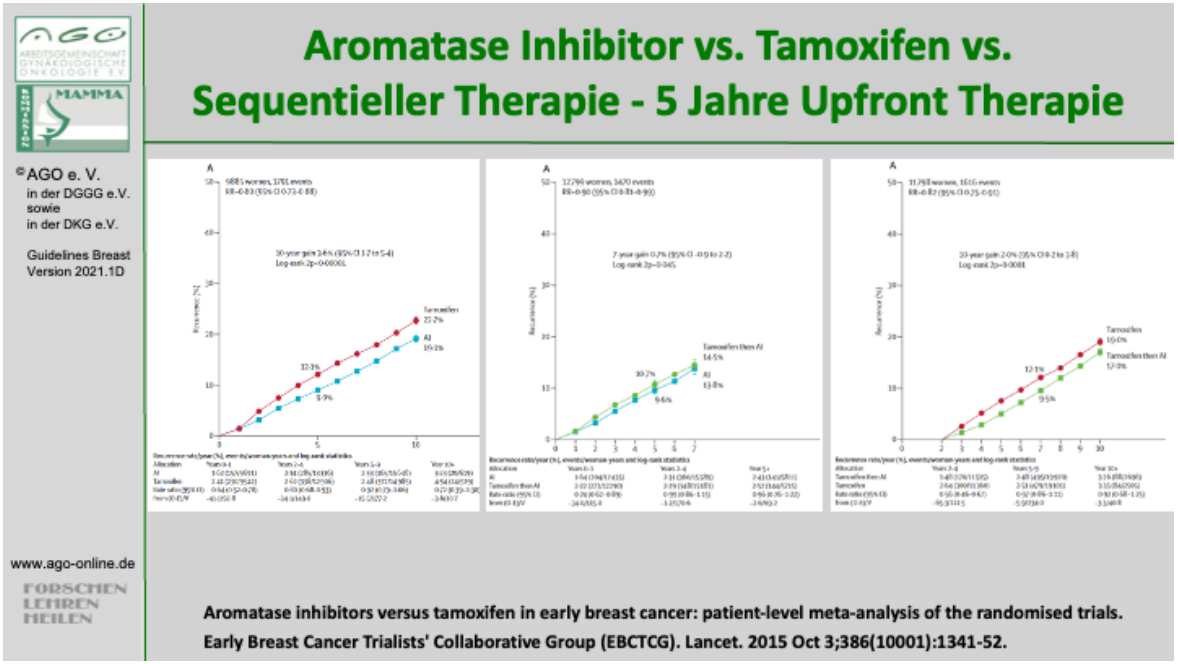
Tamoxifen 20 mg/d for first 5 yrs:

1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG), et al. Relevance of breast cancer hormone receptors and other factors to the efficacy of adjuvant tamoxifen: patient-level meta-analysis of randomised trials. Lancet 378:771-84, 2011
2. Early Breast Cancer Trialists' Collaborative Group (EBCTCG) et al. Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. Lancet 2015;386:1341-52.
3. Rydén L, Heibert Arnlind M, Vitols S et al. Aromatase inhibitors alone or sequentially combined with tamoxifen in postmenopausal

early breast cancer compared with tamoxifen or placebo - Meta-analyses on efficacy and adverse events based on randomized clinical trials. Breast. 2016;26:106-14.

Patient care/ adherence and side effects

1. Inwa ld EC, Koller M, Klinkhammer-Schalke M et al. Adjuvant endocrine therapy in pre- versus postmenopausal patients with steroid hormone receptor-positive breast cancer: results from a large population-based cohort of a cancer registry. J Cancer Res Clin Oncol 2015;141(12):2229-40.
2. Markopoulos C, Koukouras D, Venizelos V et al. Impact of chemotherapy followed by aromatase inhibitors on bone health of women with ER-positive early breast cancer in real world clinical settings in Greece: Results of the POCHARBI trial conducted by the Hellenic Society of Breast Surgeons. Breast 2016 ;27:27-34.
3. Kesmodel SB, Goloubeva OG, Rosenblatt PY et al. Patient-reported adherence to adjuvant aromatase inhibitor therapy using the Morisky Medication Adherence Scale: An evaluation of predictors. Am J Clin Oncol 2018;41(5):508-512.



1. Early Breast Cancer Trialists' Collaborative Group (EBCTCG) et l. Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomised trials. Lancet. 2015;386(10001):1341-52.

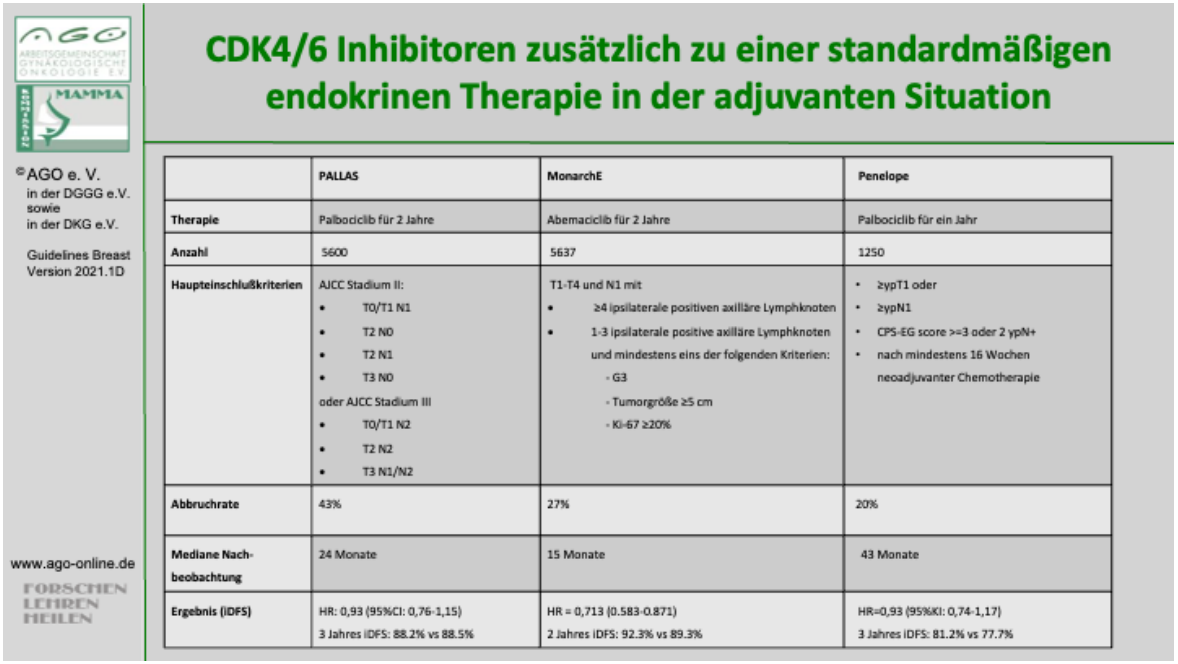
Adjuvante Therapie mit CDK4/6 Inhibitoren

Guidelines Breast
Version 2021.1D

	Oxford		
	LoE	GR	AGO
Bei erhöhtem Rückfallrisiko und Patientinnencharakteristika analog zu den Studien[1,2,3]			
▪ **Abemaciclib für 2 Jahre + endokrine Standardtherapie[1]**	2b	C	+/-
▪ **Palbociclib für 2 Jahre + endokrine Standardtherapie[2]**	2b	C	-
▪ **Palbociclib für 1 Jahr + endokrine Standardtherapie[3]**	1b	B	-

[1]MonarchE; [2]Pallas [3]PenelopeB

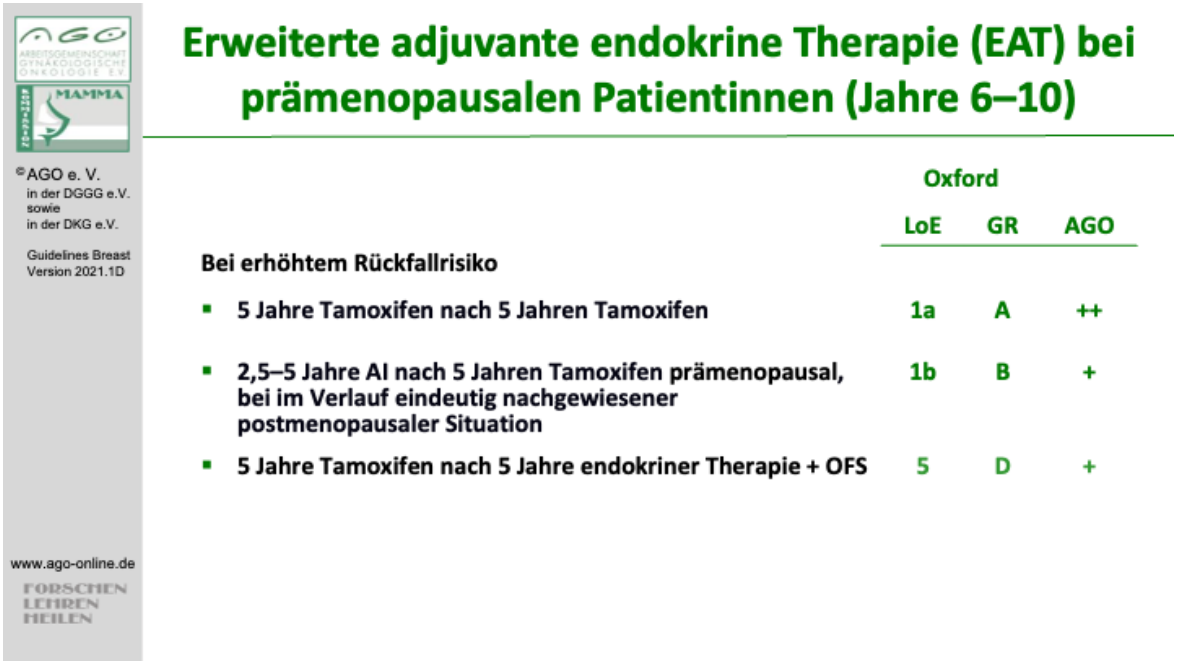
1. Johnston, S. R. D., et al. (2020). "Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2-, Node-Positive, High-Risk, Early Breast Cancer (monarchE)." J Clin Oncol: JCO2002514.
2. Mayer, E. L., et al. (2021). "Palbociclib with adjuvant endocrine therapy in early breast cancer (PALLAS): interim analysis of a multicentre, open-label, randomised, phase 3 study." Lancet Oncol.
3. Loibl, S., et al. (2020). "Phase III study of palbociclib combined with endocrine therapy (ET) in patients with hormone-receptor-positive (HR+), HER2-negative primary breast cancerand with high relapse risk after neoadjuvant chemotherapy (NACT): First results from PENELOPE-B." San



CDK4/6 Inhibitoren zusätzlich zu einer standardmäßigen endokrinen Therapie in der adjuvanten Situation

	PALLAS	MonarchE	Penelope
Therapie	Palbociclib für 2 Jahre	Abemaciclib für 2 Jahre	Palbociclib für ein Jahr
Anzahl	5600	5637	1250
Haupteinschlußkriterien	AJCC Stadium II: • T0/T1 N1 • T2 N0 • T2 N1 • T3 N0 oder AJCC Stadium III • T0/T1 N2 • T2 N2 • T3 N1/N2	T1-T4 und N1 mit • ≥4 ipsilaterale positiven axilläre Lymphknoten • 1-3 ipsilaterale positive axilläre Lymphknoten und mindestens eins der folgenden Kriterien: - G3 - Tumorgröße ≥5 cm - KI-67 ≥20%	• ≥ypT1 oder • ≥ypN1 • CPS-EG score >=3 oder 2 ypN+ • nach mindestens 16 Wochen neoadjuvanter Chemotherapie
Abbruchrate	43%	27%	20%
Mediane Nach-beobachtung	24 Monate	15 Monate	43 Monate
Ergebnis (IDFS)	HR: 0,93 (95%CI: 0,76-1,15) 3 Jahres iDFS: 88.2% vs 88.5%	HR = 0,713 (0.583-0.871) 2 Jahres iDFS: 92.3% vs 89.3%	HR=0,93 (95%KI: 0,74-1,17) 3 Jahres iDFS: 81.2% vs 77.7%

1. Johnston, S. R. D., et al. (2020). "Abemaciclib Combined With Endocrine Therapy for the Adjuvant Treatment of HR+, HER2-, Node-Positive, High-Risk, Early Breast Cancer (monarchE)." J Clin Oncol: JCO2002514.
2. Mayer, E. L., et al. (2021). "Palbociclib with adjuvant endocrine therapy in early breast cancer (PALLAS): interim analysis of a multicentre, open-label, randomised, phase 3 study." Lancet Oncol.
3. Loibl, S., et al. (2020). "Phase III study of palbociclib combined with endocrine therapy (ET) in patients with hormone-receptor-positive (HR+), HER2-negative primary breast cancerand with high relapse risk after neoadjuvant chemotherapy (NACT): First results from PENELOPE-B." San Antonio Breast Cancer Symposium 2020: GS1-02.



5 years Tamoxifen after 5 years Tamoxifen:

1. Davies C, Pan H, Godwin J et al. Adjuvant Tamoxifen: Longer Against Shorter (ATLAS) Collaborative Group. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet 2013;381(9869):805-16. Erratum in: Lancet. 2013;381(9869):804.
2. Gray RG, Rea D, Handley K et al. ATTom: long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6953 women with early breast cancer. J Clin Oncol 2013; 31 (18 suppl):5.
3. Petrelli F, Coinu A, Cabiddu M et al. Five or more years of adjuvant endocrine therapy in breast cancer: a meta-analysis of published randomised trials. Breast Cancer Res Treat 2013;140(2):233-40.
4. Burstein HJ, Temin S, Anderson H et al. Adjuvant endocrine therapy for women with hormone receptor-positive breast cancer: american society of clinical oncology clinical practice guideline focused update. J Clin Oncol 2014;32(21):2255-69.

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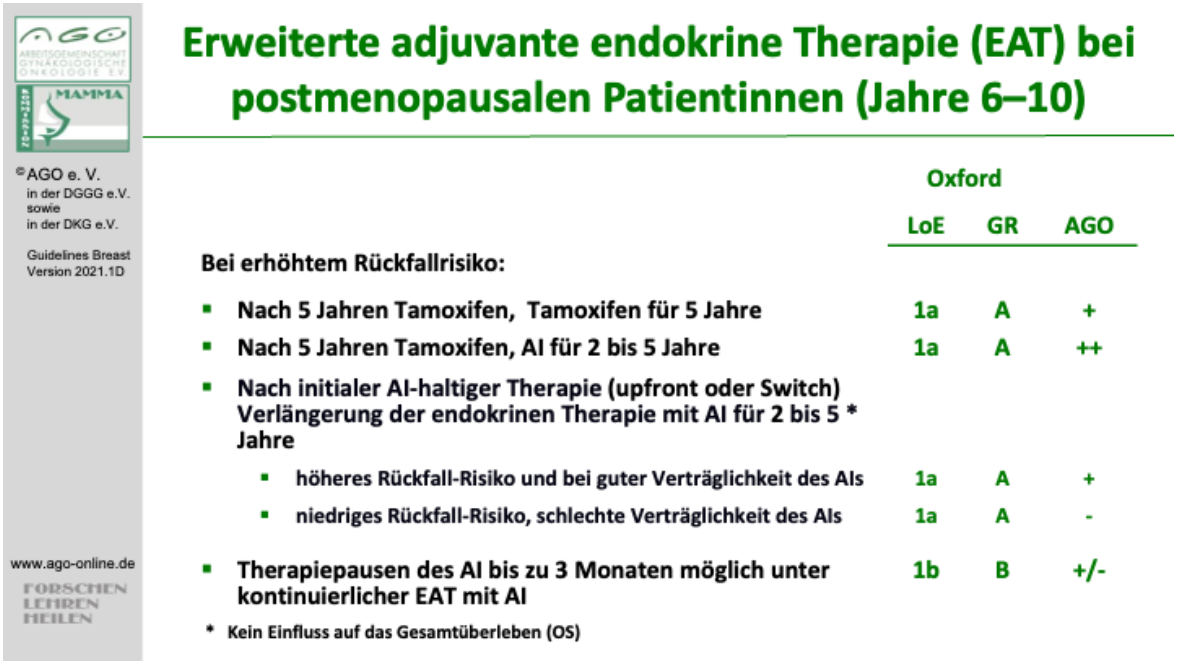

Erweiterte adjuvante endokrine Therapie (EAT) bei postmenopausalen Patientinnen (Jahre 6–10)

	Oxford		
	LoE	GR	AGO
Bei erhöhtem Rückfallrisiko:			
▪ Nach 5 Jahren Tamoxifen, Tamoxifen für 5 Jahre	1a	A	+
▪ Nach 5 Jahren Tamoxifen, AI für 2 bis 5 Jahre	1a	A	++
▪ Nach initialer AI-haltiger Therapie (upfront oder Switch) Verlängerung der endokrinen Therapie mit AI für 2 bis 5 * Jahre			
▪ höheres Rückfall-Risiko und bei guter Verträglichkeit des AIs	1a	A	+
▪ niedriges Rückfall-Risiko, schlechte Verträglichkeit des AIs	1a	A	-
▪ Therapiepausen des AI bis zu 3 Monaten möglich unter kontinuierlicher EAT mit AI	1b	B	+/-

* Kein Einfluss auf das Gesamtüberleben (OS)

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1. Davies C, Pan H, Godwin J et al. Adjuvant Tamoxifen: Longer Against Shorter (ATLAS) Collaborative Group. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. Lancet 2013;381(9869):805-16. Erratum in: Lancet. 2013;381(9869):804.
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2–5 years AI after 5 years Tamoxifen

1. Goss PE, Ingle JN, Martino S et al. Randomized trial of letrozole following tamoxifen as extended adjuvant therapy in receptor-positive breast cancer: updated findings from NCIC CTG MA.17. J Natl Cancer Inst 2005;97(17):1262-71.

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7. Gray R (EBCTCG) et al. Extended aromatase inhibitor treatment following 5 or more years of endocrine therapy: a metaanalysis of 22192 women in 11 randomised trials. SABCS 2018;GS3-03
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low risk, poor tolerabilty of the AI

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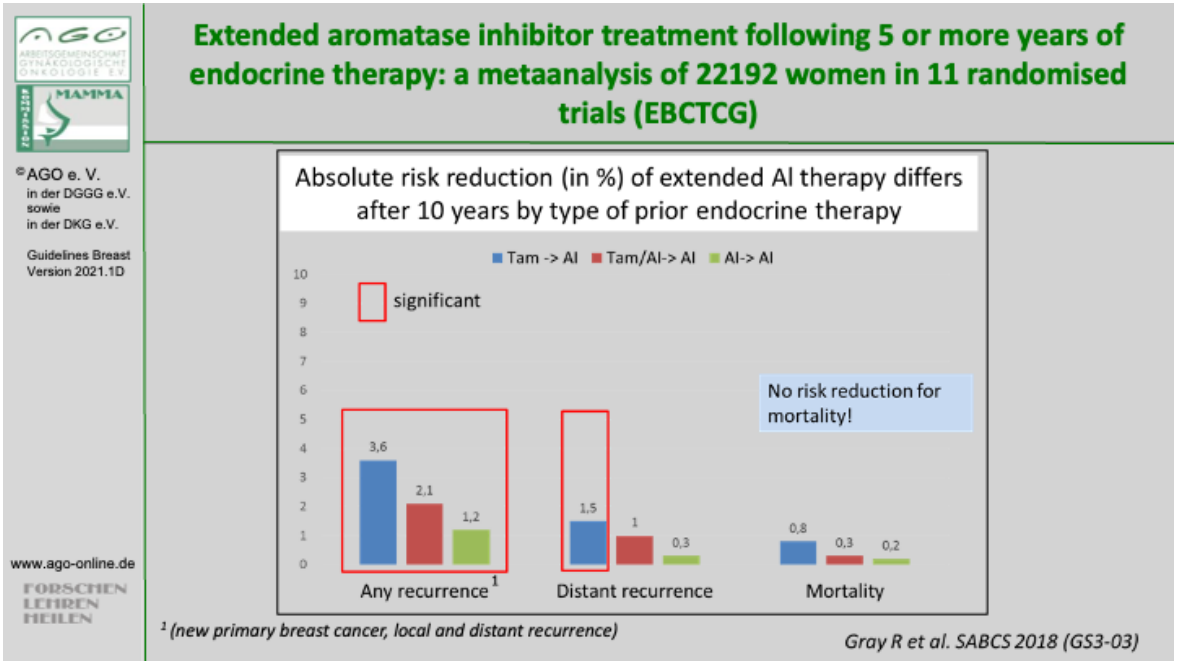


1. Gray R (EBCTCG) et al. Extended aromatase inhibitor treatment following 5 or more years of endocrine therapy: a metaanalysis of 22192 women in 11 randomised trials. SABCS 2018;GS3-03

Erweiterte, adjuvante endokrinen Therapie im Überblick

Studie	Therapien											De-facto-Vergleiche (Jahre)	HR für DFS	AI-Therapie Jahre 0-5 (%)
Jahre nach Diagnose	1	2	3	4	5	6	7	8	9	10	15			
Studien mit Tamoxifen nach 5 Jahren Tamoxifen														
ATLAS					*							5 vs 10	0,75 – 0,99	0
ATTOM					*							5 vs 10	0,75 – 0,99	0
Studien mit AI nach 5 Jahren Tamoxifen														
MA. 17					*							5 vs 10	0,57	0
NSAPB B-33					*							5 vs 10	0,68	0
ABCSG 6a					*							5 vs 8	0,62	0
Studien mit erweiterter AI-Th. nach 5 Jahren endokrin inkl. AI														
DATA			*									6 vs 9	0,79	100
NSABP B-42					*							5 vs 10	0,85	100
MA.17R										§		10 vs 15	0,66	100
Studien bzgl. optimaler Dauer in Jahr 5-10														
BOOG 2006-05 IDEAL					*							7,5 vs 10	0,92	88
ABCSG 16					*							7 vs 10	1,007	49
SOLE												Cont vs unterbr	1,08	81

Braun: Tamoxifen

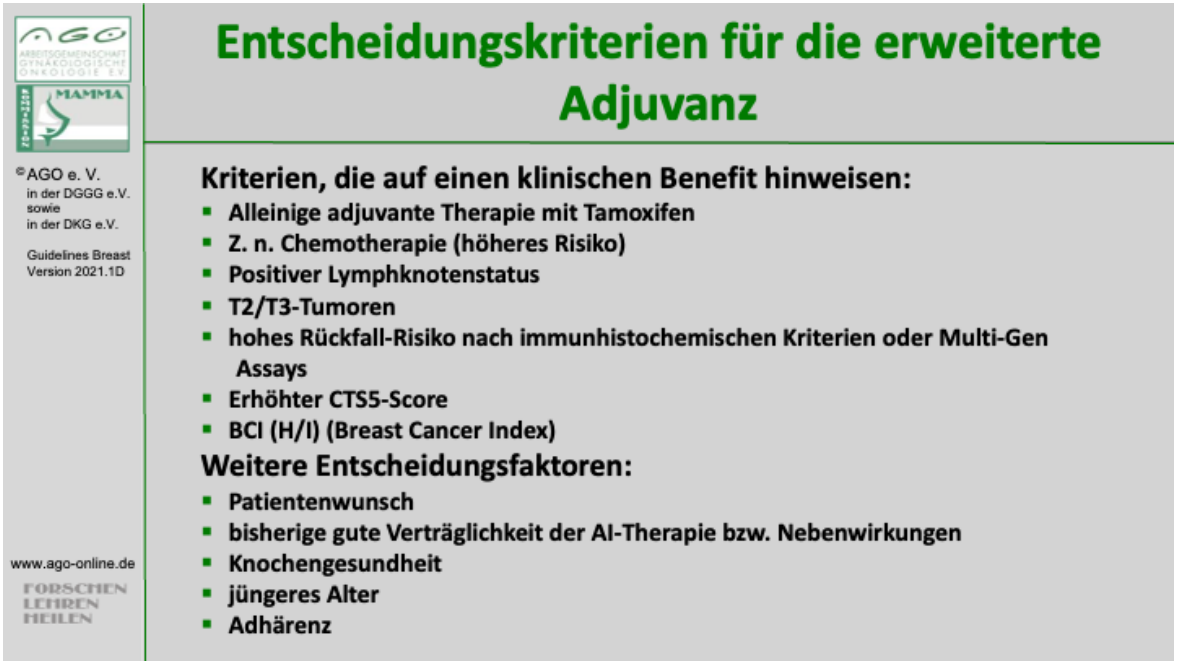
Grün: Tamoxifen oder AI

Blau: AI

Gestreift: Zeit der randomisierten Intervention vs keine Therapie od. Placebo

*: Randomisierungs-zeitpunkt

§ : MA17R nach 5 Jahren AI mit /ohne Tam zuvor



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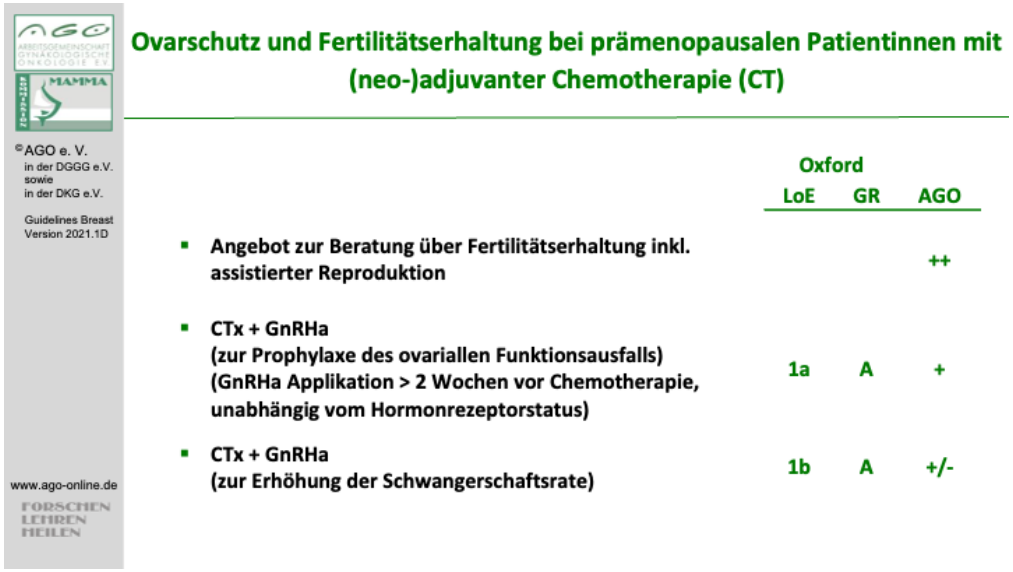

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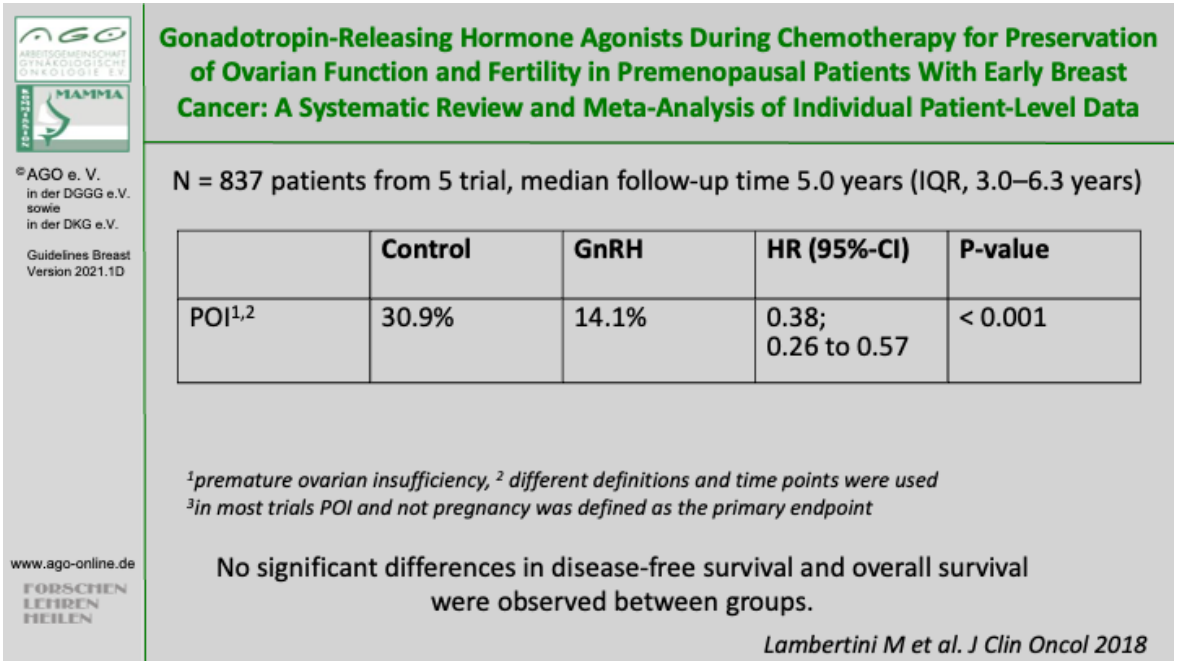

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