Guidelines Breast
Version 2018.1D

# Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

## Adjuvante endokrine Therapie bei prä- und postmenopausalen Patientinnen

FORSCHEN
LEHREN
HEILEN

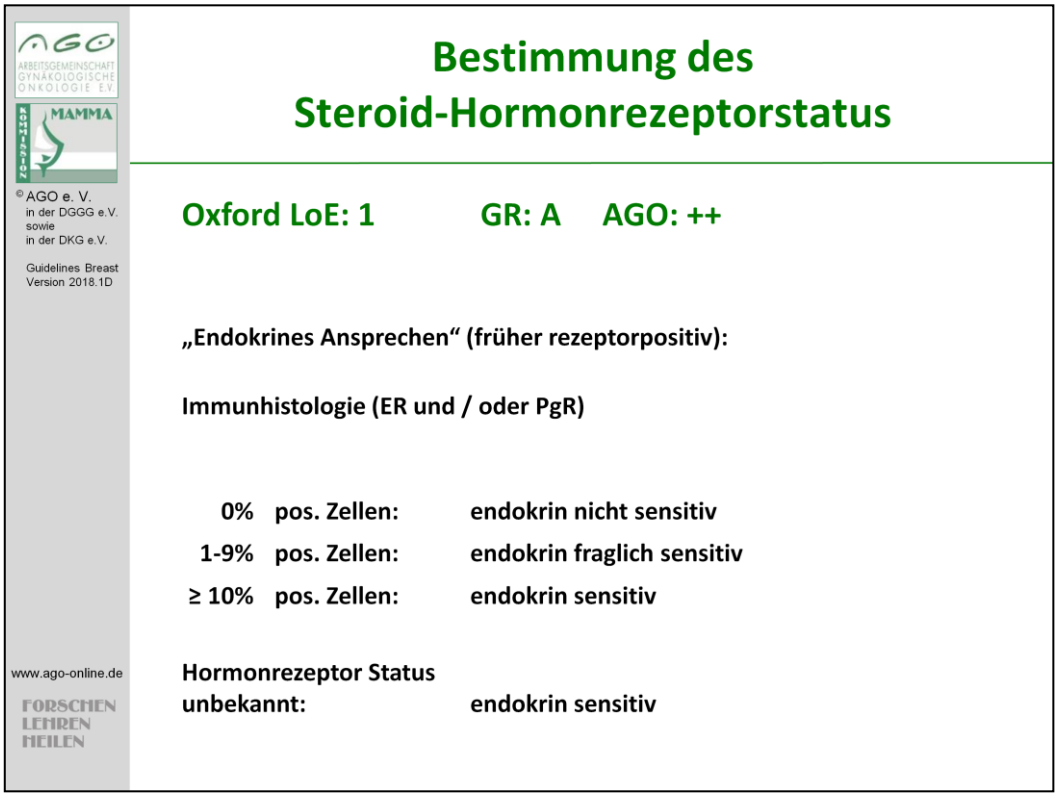
# Adjuvante endokrine Therapie bei prä- und postmenopausalen Patientinnen

- **Versionen 2002–2017:**
  **Bauerfeind / Dall / Diel / Fersis / Friedrichs / Gerber / Göring / Hanf/ Harbeck / Huober / Jackisch / Lisboa / Lück / Lux / Maass / von Minckwitz / Möbus / Müller / Oberhoff / Schaller / Scharl / Schneeweiss /Schütz / Solomeyer / Stickeler / Thomssen / Untch**

- **Version 2018:**
  **Jackisch / Lück**



Guidelines Breast
Version 2018.1D

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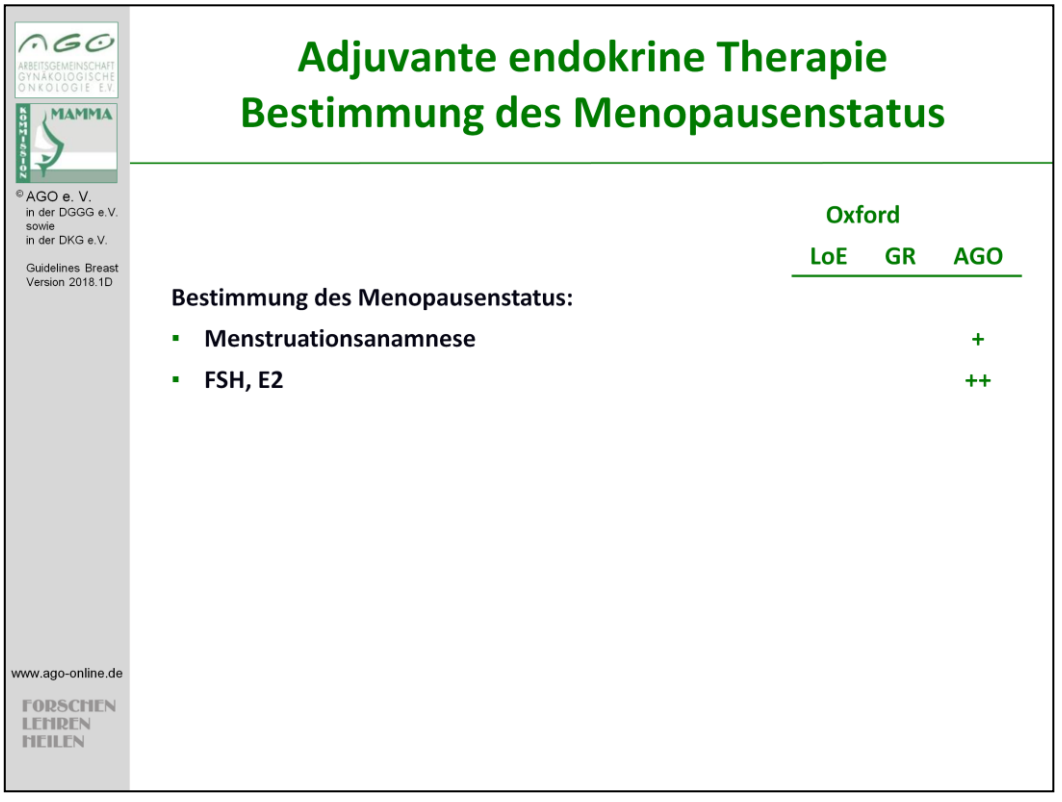



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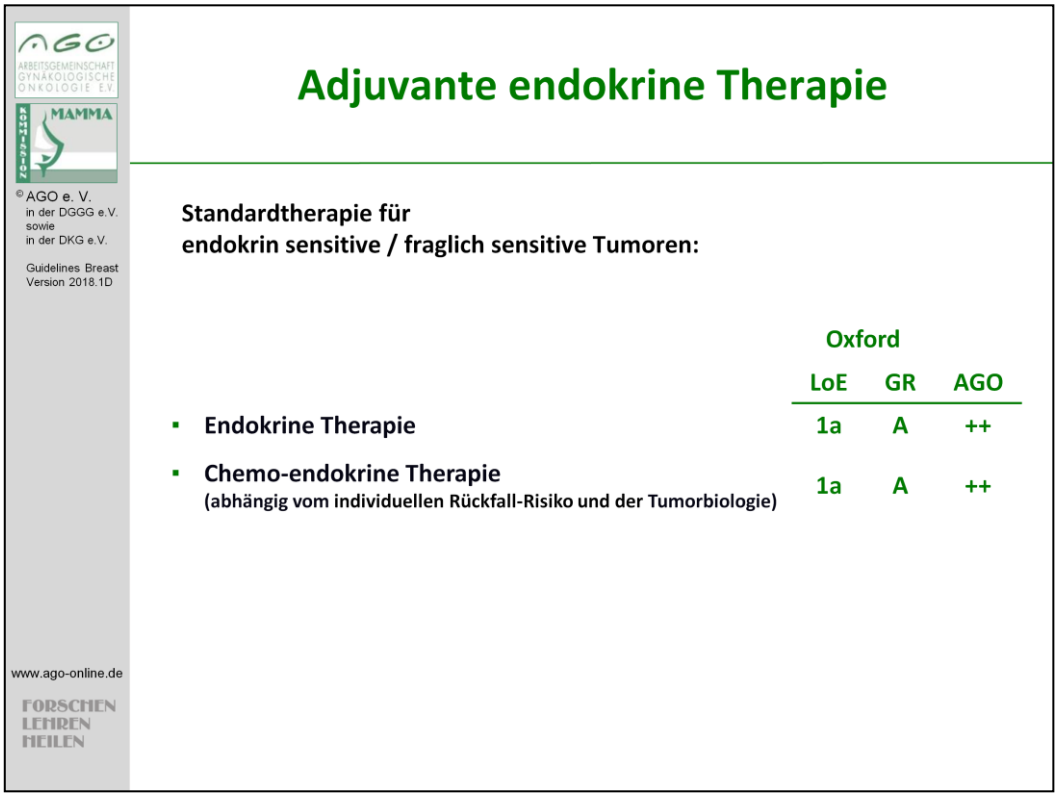



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2. Goldhirsch A et al. Personalizing the treatment of women with early breast cancer: highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2013 Ann Oncol 2013;24:206-2223
3. Hackshaw A et al. Long-term 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 May 1;29(13):1657-63
4. Pagani O1,et al.Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. N Engl J Med. 2014 Jul 10;371(2):107-18.
5. Albain KS 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 Dec 19;374(9707):2055-63.
6. Bedognetti D et al. Concurrent vs sequential adjuvant chemotherapy and hormone therapy in breast cancer: a multicenter randomized phase III trial. J Natl Cancer Inst. 2011 Oct 19;103(20):1529-39.
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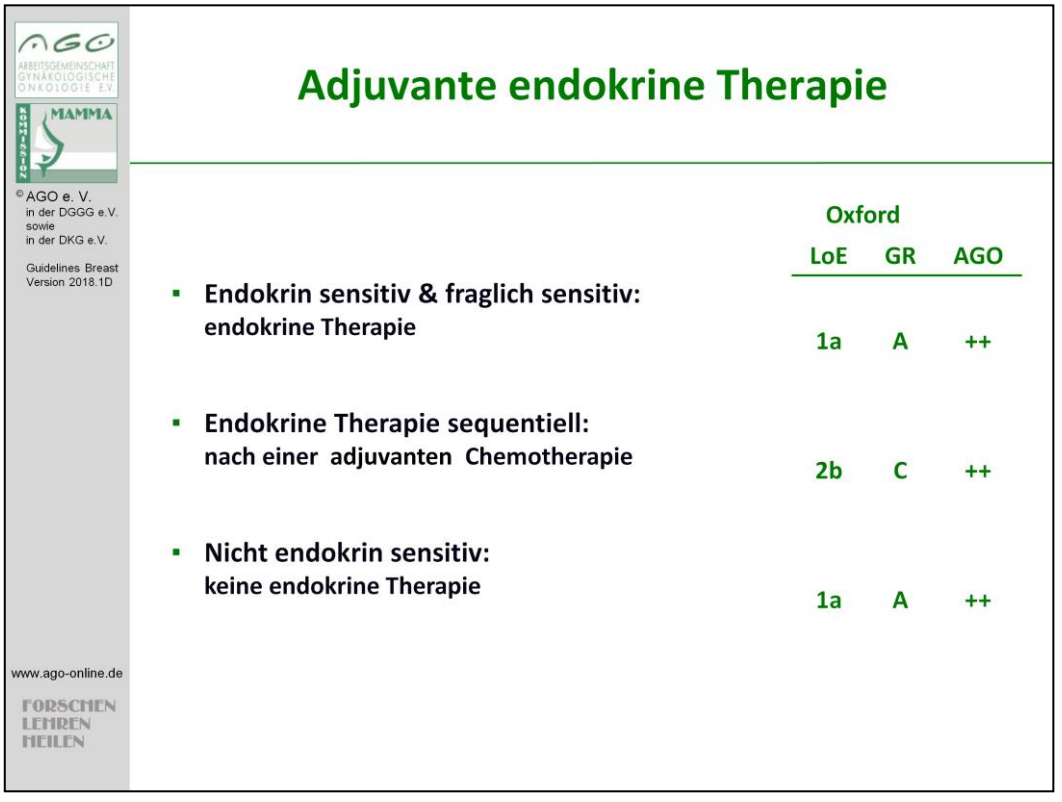



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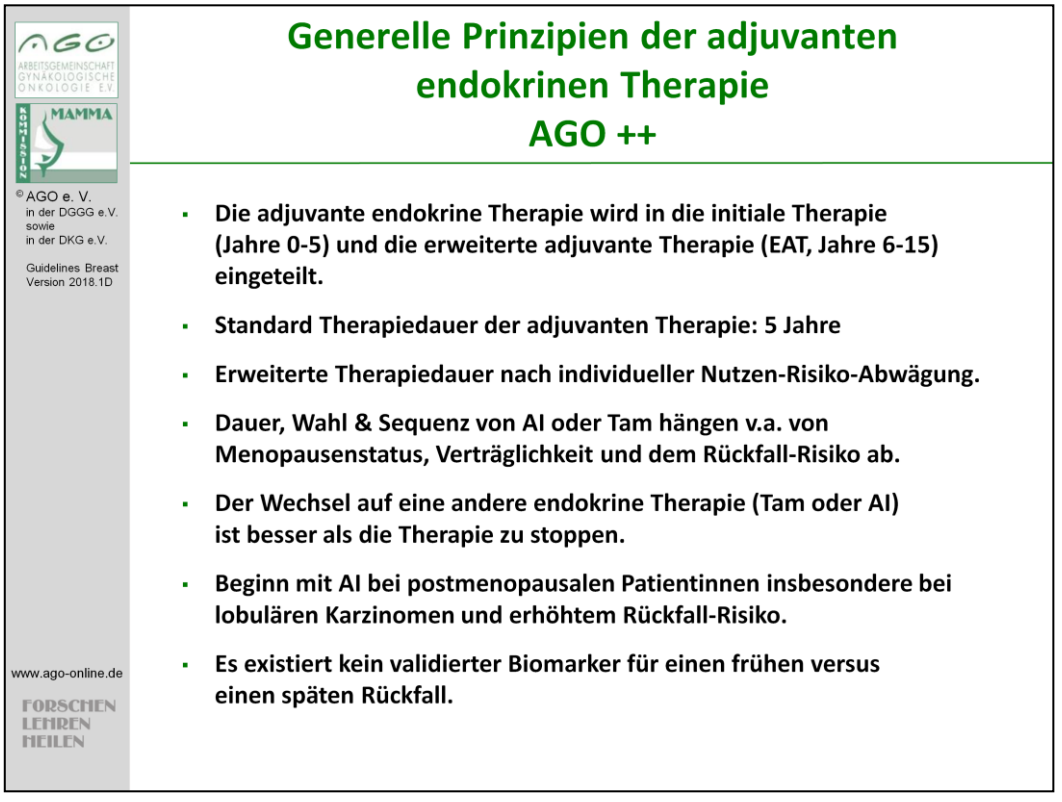
3. Hackshaw A et al.. Long-term benefits of 5 years of tamoxifen: 10-year follow-up of a large randomized trial in women at least 50 years of age with early breast cancer.J Clin Oncol. 2011;29(13): 1657-63.
4. Albain KS et al. Breast Cancer Intergroup of North America. Adjuvant chemotherapy and timing 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 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 et al. Revisiting the definition of estrogen receptor positivity in Her2-negative primary breast cancer. Ann Oncol 2017;28:2420-2428
7. Curigliano G. 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





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5. Regan MM 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 Nov;12(12):1101-8.
6. Ingle JN. Overview of adjuvant trials of aromatase inhibitors in early breast cancer. Steroids. 2011 Jul;76(8):765-7.
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8. 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.

9. Rydén L 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 Apr;26:106-140
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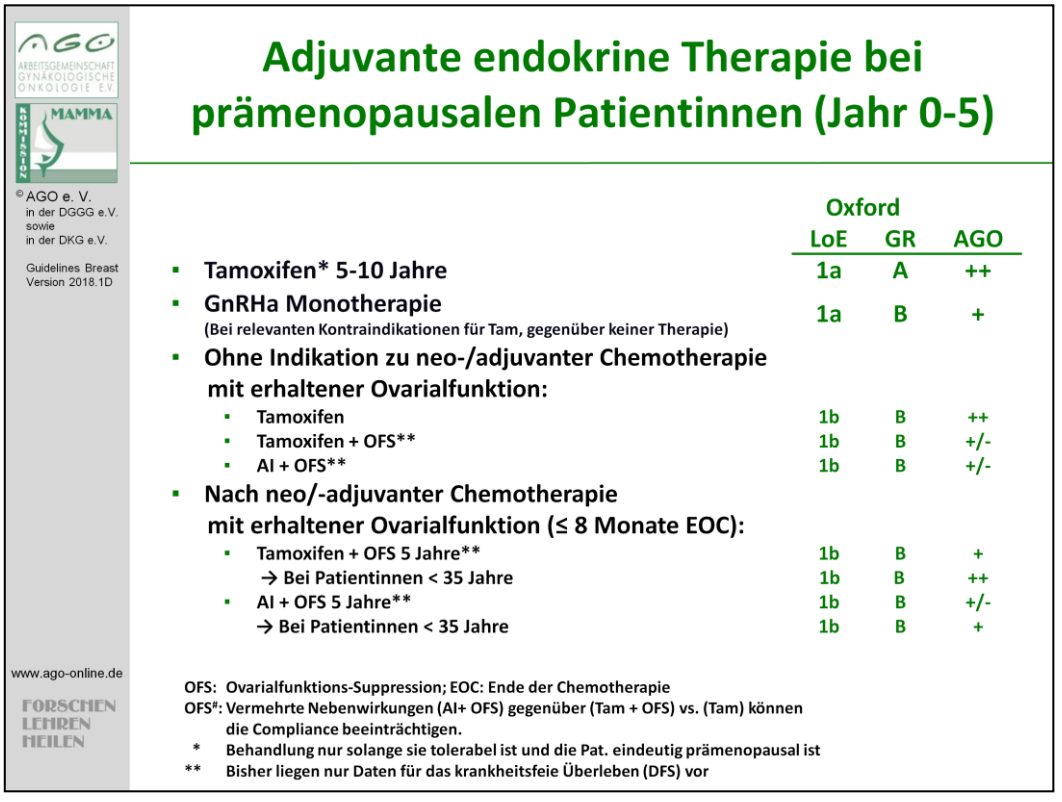



Tamoxifen 5-10 yrs.

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 365 (9472): 1687-717, 2005.
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 Aug 27;378(9793):771-84.
3. Davies C 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 et al. 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. Mathew A et al. Adjuvant endocrine therapy for premenopausal women with hormone-responsive breast cancer. Breast. 2015 Nov;24 Suppl 2:S120-5. doi: 10.1016/j.breast.2015.07.027.
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7. 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 365 (9472): 1687-

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9. Cuzick J 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.

In patients with ovarian function (within 8 mon.) after adjuvant chemotherapy:
OFS (ovarian function suppression) 5 years + Tam 5 years - OFS 5 years + AI 5 years

- in patients < 35 y.

1. Pagani O. 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 Nov;142(2):455-9
2. Ganz PA, et al. Menstrual history and quality-of-life outcomes in women with node-positive breast cancer treated with adjuvant therapy on the NSABP B-30 trial. J Clin Oncol. 2011 Mar 20;29(9):1110-6
3. Goel S et al: LHRH agonists for adjuvant therapy of early breast cancer in premenopausal women. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD004562.
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5. Pagani O 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 Jul 10;371(2):107-18
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8. Shiba E 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 May;23(3):499-509.
9. Del Mastro L et al. New insights on the role of luteinizing hormone releasing hormone agonists in premenopausal early breast cancer patients. Cancer Treat Rev. 2016 Jan;42:18-23.10
10. Kim HA et al. The role of the addition of ovarian suppression to tamoxifen in young women with hormone-sensitive breast cancer who remain premenopausal or regain menstruation after chemotherapy (ASTRRA): study protocol for a randomized controlled trial and progress. BMC Cancer. 2016 May 19;16:319.
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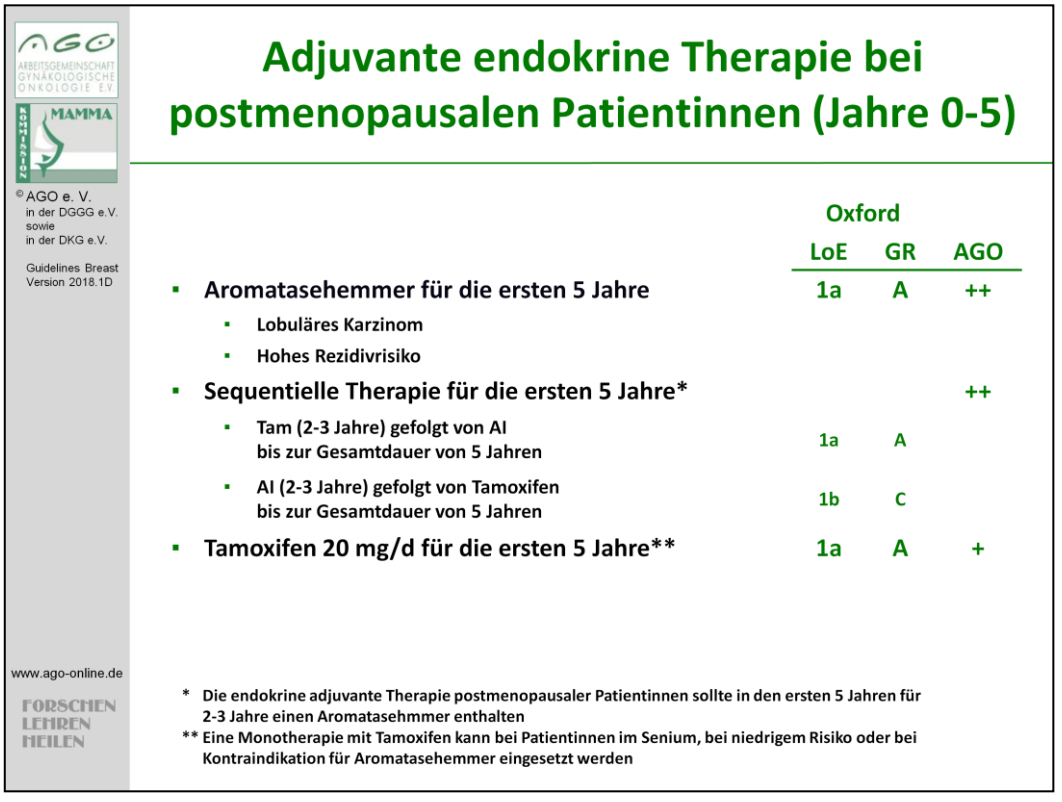
younger than 35 years in the International Breast Cancer Study Group TEXT and SOFT adjuvant endocrine therapy trial. J Clin Oncol 2017;35:3113-3122




<u>AI for first 5 years</u>
<u>Especially in case of lobular cancer</u>
<u>High risk of recurrence</u>


1. Cuzick J et al. Effect of anastrozole and tamoxifen as adjuvant treatment for early-stage breast cancer: 10-year analysis of the ATAC trial. Lancet Oncol. 2010 Dec;11(12):1135-41.
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 Oct 3;386(10001):1341-52.
3. Rydén L 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 Apr;26:106-14
4. Mayer EL et al. Adjuvant endocrine therapy for postmenopausal women: Type and duration. Breast. 2015 Nov;24 Suppl 2:S126-8. doi: 10.1016/j.breast.2015.07.028. Epub 2015 Aug 14.


<u>Sequential therapy for first 5 years</u>
<u>Tam (2-3 yrs.) followed by AI to complete 5 years</u>
<u>AI (2-3 yrs.) followed by Tam to complete 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 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 Apr;26:106-14
3. Mayer EL el. Adjuvant endocrine therapy for postmenopausal women: Type and duration. Breast. 2015 Nov;24 Suppl 2:S126-8. doi: 10.1016/j.breast.2015.07.028. Epub 2015 Aug 14.
4. Derks MGM 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 trail. Lancet Oncol 2017;18:1211-1220

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
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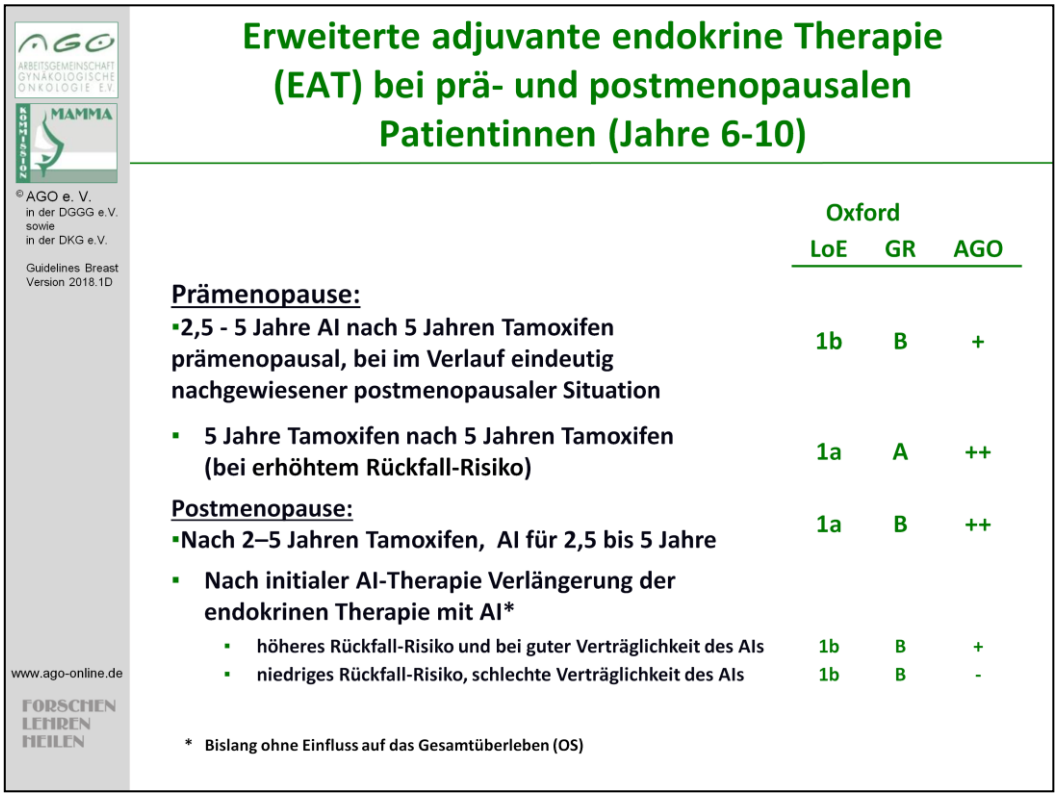
3. Rydén L et al. Aromatase inhibitors alone or sequentially combined with tamoxifen in postmenopausal early breast cancer compared with tamoxifen or placebo - Meta-analyses on efficacy and adverse events based on randomized clinical trials. Breast. 2016 Apr;26:106-14.
4. Mayer EL, Burstein HJ. Adjuvant endocrine therapy for postmenopausal women: Type and duration. Breast. 2015 Nov;24 Suppl 2:S126-8. doi: 10.1016/j.breast.2015.07.028. Epub 2015 Aug 14.

Patient care/ adherence and side effects

1. Inwa ld EC 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 Dec;141(12):2229-40.
2. Markopoulos C 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 Jun;27:27-34.
3. Kesmodel SB et al. Patient-reported Adherence to Adjuvant Aromatase Inhibitor Therapy Using the Morisky Medication Adherence Scale: An Evaluation of Predictors. Am J Clin Oncol. 2016 Jun




2.5 - 5 years AI after 5 years Tamoxifen premenopausal in patients with validated postmenopausal status in the course of therapy


1. Goss PE 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 Sep 7;97(17):1262-71.


5 years Tamoxifen after 5 years Tamoxifen (in case of increased risk of relaps)


1. Davies C 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 Mar 9;381(9869):805-16. Erratum in: Lancet. 2013 Mar 9;381(9869):804.
2. Gray RG 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.
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After 2 - 5 years Tamoxifen AI for 2.5 - 5 years


1. Goss PE 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 Sep 7;97(17):1262-71.
2. Jakesz R et al. Austrian Breast and Colorectal Cancer Study Group. Extended

adjuvant therapy with anastrozole among postmenopausal breast cancer patients: results from the randomized Austrian Breast and Colorectal Cancer Study Group Trial 6a. J Natl Cancer Inst. 2007 Dec 19;99(24):1845-53. Erratum in: J Natl Cancer Inst. 2008 Feb 6;100(3):226.
3. Mamounas EP et al. Benefit from exemestane as extended adjuvant therapy after 5 years of adjuvant tamoxifen: intention-to-treat analysis of the National Surgical Adjuvant Breast And Bowel Project B-33 trial. J Clin Oncol. 2008 Apr 20;26(12):1965-71.

<u>After initial therapy with AI further prolongation of endocrine therapy with AI*</u>
<u>high risk and good tolerabilty of the AI</u>
<u>low risk, poor tolerabilty of the AI</u>

1. Blok EJ et al. Optimal Duration of Extended Adjuvant Endocrine Therapy for early breast cancer; results of he IDEAL trial (BOOG 2006-05). J Natl Cancer Inst 2018;110(1): djx134
2. Bychkovsky BL et al. Identifying biomarkers to select patients with early breast cancer suitable for extended adjuvant endocrine therapy. Curr Opin Oncol. 2016 Nov;28(6):461-468.
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4. Goss PE et al. Extending Aromatase-Inhibitor Adjuvant Therapy to 10 Years. N Engl J Med. 2016 Jul 21;375(3):209-19
5. Mamounas EP et al. NRG Oncology/NSABP. A randomized, double-blinded, placebo-controlled clinical trial of extended adjuvant endocrine therapy (tx) with letrozole (L) in postmenopausal women with hormone-receptor (+) breast cancer (BC) who have completed previous adjuvant tx with an aromatase inhibitor (AI): Results from NRG Oncology/NSABP B-42. 2016 San Antonio Breast Cancer Symposium, Publication Number: S1-05
6. O'Leary CG et al. Extended adjuvant endocrine therapy in hormone-receptor-positive early breast cancer. Curr Opin Oncol. 2016 Nov;28(6):455-460.
7. Sanft T et al. Prospective assessment of the decision-making impact of the Breast Cancer Index in recommending extended adjuvant endocrine therapy for patients with early-stage ER-positive breast cancer. Breast Cancer Res Treat. 2015 Dec;154(3):533-41.
8. Sestak I et al. Cross-Stratification and Differential Risk by Breast Cancer Index and Recurrence Score in Women with Hormone Receptor-Positive Lymph Node-Negative Early-Stage Breast Cancer. Clin Cancer Res. 2016 Oct 15;22(20):5043-5048
9. Tjan-Heijnen VC C et al. First results from the multicenter phase III DATA study comparing 3 versus 6 years of anastrozole after 2-3 years of tamoxifen in postmenopausal women with hormone receptor-positive early breast cancer. 2016 San Antonio Breast Cancer Symposium, Publication Number: S1-03
10. Zdenkowski N et al. Australia and New Zealand Breast Cancer Trials Group. Observation versus late reintroduction of letrozole as adjuvant endocrine therapy for hormone receptor-positive breast cancer (ANZ0501 LATER): an open-label

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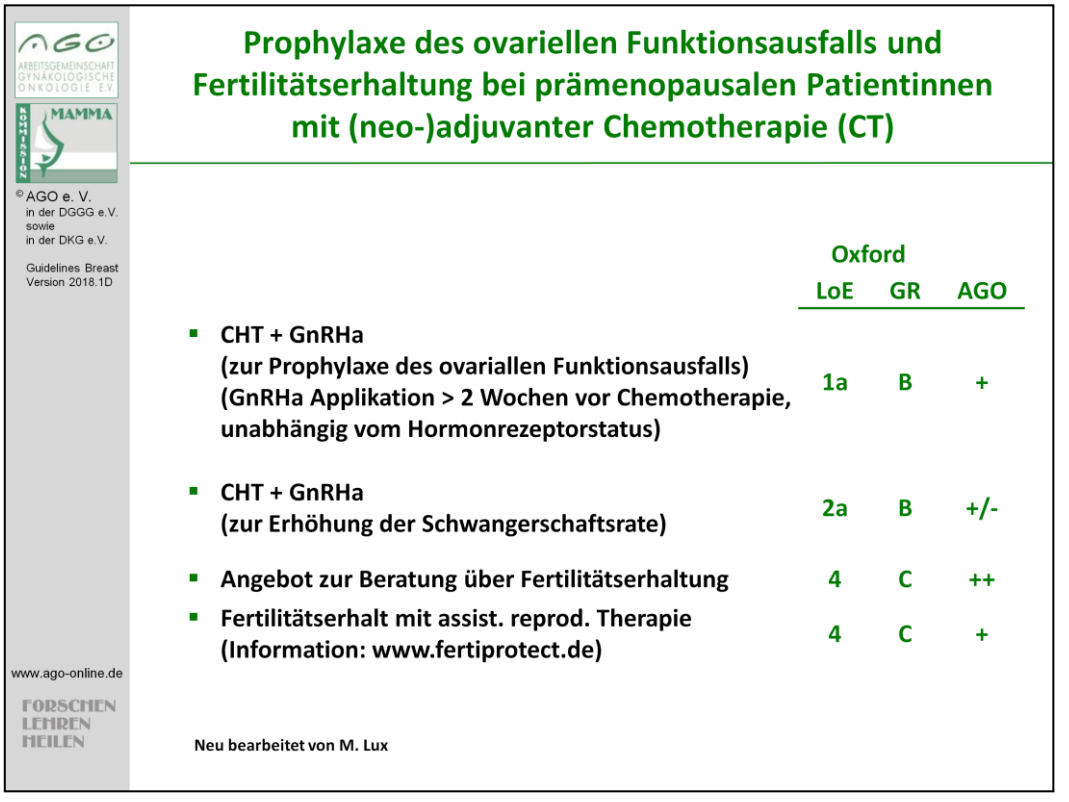
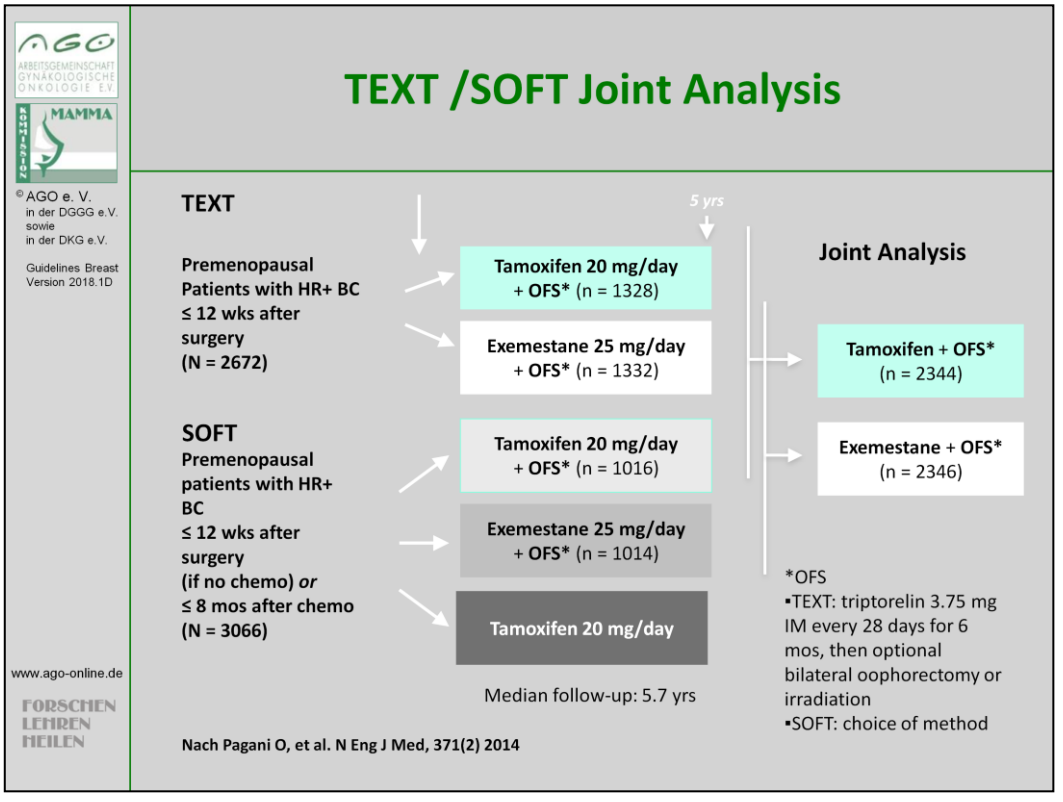


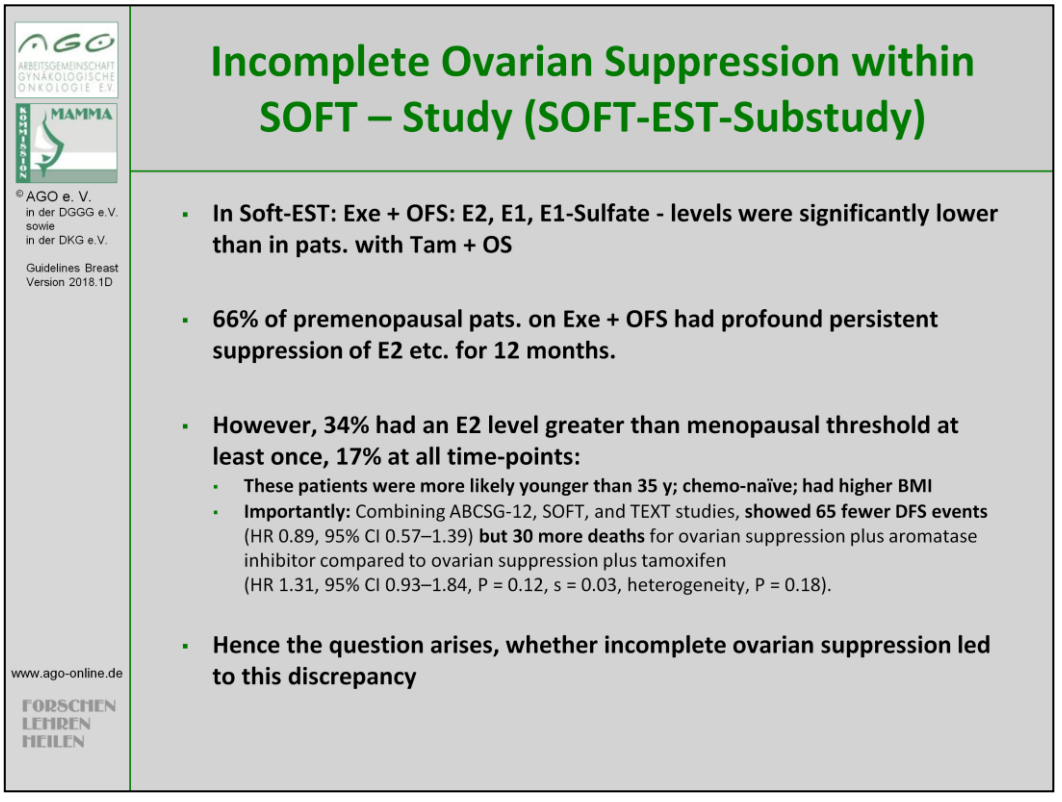


1. Munholz RR, Pereira AA, Sasse AD et al., Gonadotropin-releasing hormone agonists for ovarian preservation in premenopuasal women undergoing chemotherapy for early-stage breast cancer. JAMA Oncol 2016;2(1): 65-73
2. Shandley LM, Spencer JB, Fothergill A et al., Impact of tamoxifen on fertility in breast cancer survivors. Fertil Steril 2017;107(1):243-252

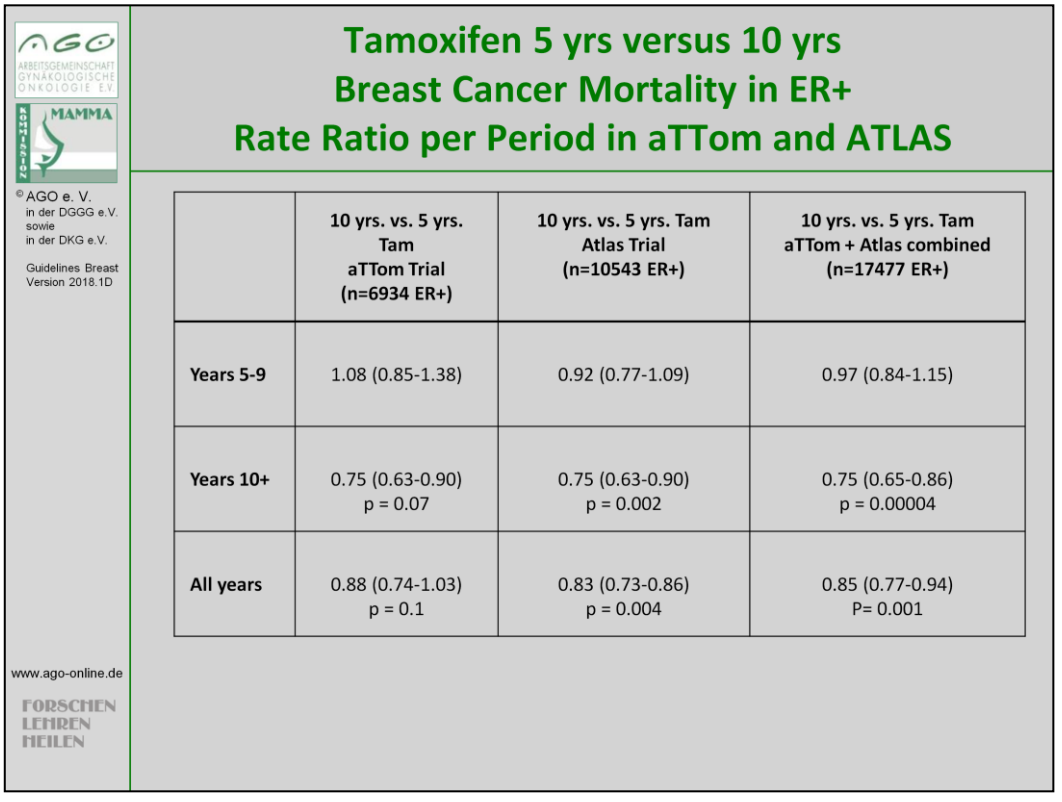




1. Pagani O et al. TEXT and SOFT Investigators; International Breast Cancer Study Group. Adjuvant exemestane with ovarian suppression in premenopausal breast cancer. N Engl J Med. 2014 Jul 10;371(2):107-18.
2. Francis PA et al. The SOFT Investigators and the International Breast Cancer Study Group. Adjuvant Ovarian Suppression in Premenopausal Breast Cancer. N Engl J Med. 2015 Jan 29;372(5): 436-46.



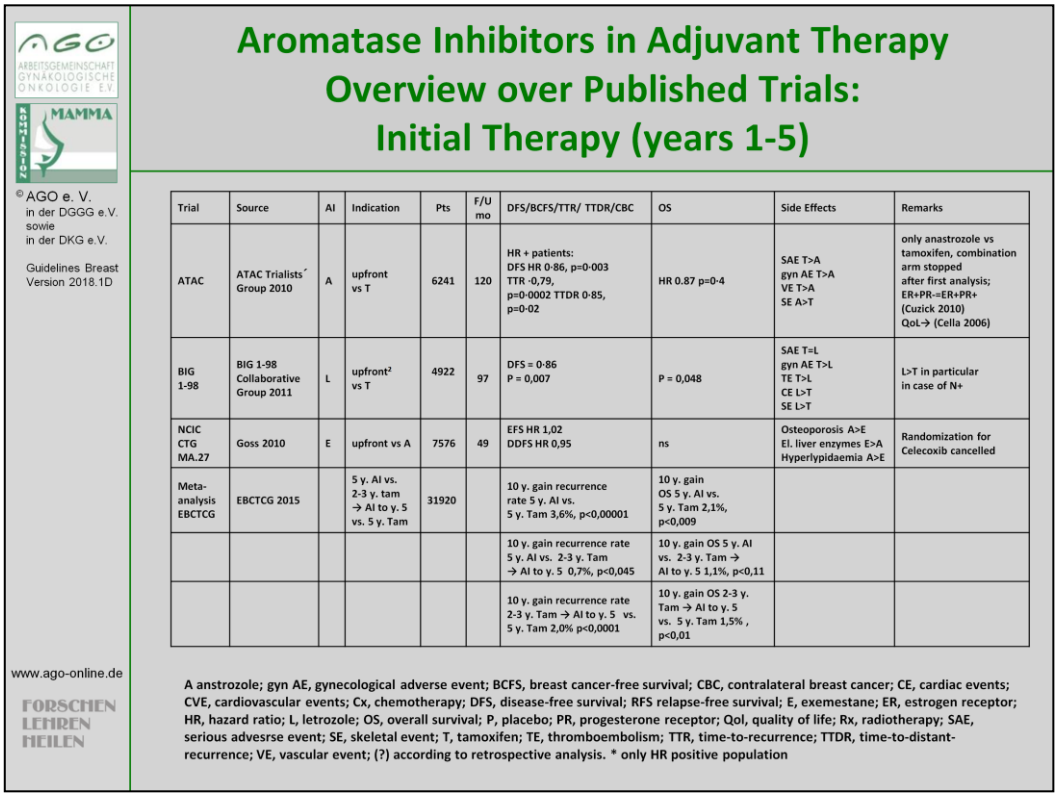

1. Chlebowski RT, Pan K, Col NF. Ovarian suppression in combination endocrine adjuvant therapy in premenopausal women with early breast cancer. Breast Cancer Res Treat. 2017 Jan;161(2):185-190. doi: 10.1007/s10549-016-4024-4. Review.




## Tamoxifen 5 yrs versus 10 yrs Breast Cancer Mortality in ER+ Rate Ratio per Period in aTTom and ATLAS

| | 10 yrs. vs. 5 yrs. Tam aTTom Trial (n=6934 ER+) | 10 yrs. vs. 5 yrs. Tam Atlas Trial (n=10543 ER+) | 10 yrs. vs. 5 yrs. Tam aTTom + Atlas combined (n=17477 ER+) |
|---|---|---|---|
| **Years 5-9** | 1.08 (0.85-1.38) | 0.92 (0.77-1.09) | 0.97 (0.84-1.15) |
| **Years 10+** | 0.75 (0.63-0.90) p = 0.07 | 0.75 (0.63-0.90) p = 0.002 | 0.75 (0.65-0.86) p = 0.00004 |
| **All years** | 0.88 (0.74-1.03) p = 0.1 | 0.83 (0.73-0.86) p = 0.004 | 0.85 (0.77-0.94) P= 0.001 |


1. Gray RG et al., et al. aTTom: Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years in 6953 women with earyl breast cancer J Clin Oncol 31, 2013 (suppl; abstract 5)
2. Davies C, 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: 805–16.



# Aromatase Inhibitors in Adjuvant Therapy
## Overview over Published Trials:
## Initial Therapy (years 1-5)

| Trial | Source | AI | Indication | Pts | F/U mo | DFS/BCFS/TTR/ TTDR/CBC | OS | Side Effects | Remarks |
|---|---|---|---|---|---|---|---|---|---|
| ATAC | ATAC Trialists´ Group 2010 | A | upfront vs T | 6241 | 120 | HR + patients: DFS HR 0·86, p=0·003 TTR -0,79, p=0·0002 TTDR 0·85, p=0·02 | HR 0.87 p=0·4 | SAE T>A<br>gyn AE T>A<br>VE T>A<br>SE A>T | only anastrozole vs tamoxifen, combination arm stopped after first analysis; ER+PR-=ER+PR+ (Cuzick 2010) QoL→ (Cella 2006) |
| BIG 1-98 | BIG 1-98 Collaborative Group 2011 | L | upfront² vs T | 4922 | 97 | DFS = 0·86 P = 0,007 | P = 0,048 | SAE T=L<br>gyn AE T>L<br>TE T>L<br>CE L>T<br>SE L>T | L>T in particular in case of N+ |
| NCIC CTG MA.27 | Goss 2010 | E | upfront vs A | 7576 | 49 | EFS HR 1,02 DDFS HR 0,95 | ns | Osteoporosis A>E<br>El. liver enzymes E>A<br>Hyperlypidaemia A>E | Randomization for Celecoxib cancelled |
| Meta-analysis EBCTCG | EBCTCG 2015 | | 5 y. AI vs. 2-3 y. tam → AI to y. 5 vs. 5 y. Tam | 31920 | | 10 y. gain recurrence rate 5 y. AI vs. 5 y. Tam 3,6%, p<0,00001 | 10 y. gain OS 5 y. AI vs. 5 y. Tam 2,1%, p<0,009 | | |
| | | | | | | 10 y. gain recurrence rate 5 y. AI vs. 2-3 y. Tam → AI to y. 5 0,7%, p<0,045 | 10 y. gain OS 5 y. AI vs. 2-3 y. Tam → AI to y. 5 1,1%, p<0,11 | | |
| | | | | | | 10 y. gain recurrence rate 2-3 y. Tam → AI to y. 5 vs. 5 y. Tam 2,0% p<0,0001 | 10 y. gain OS 2-3 y. Tam → AI to y. 5 vs. 5 y. Tam 1,5% , p<0,01 | | |

A anstrozole; gyn AE, gynecological adverse event; BCFS, breast cancer-free survival; CBC, contralateral breast cancer; CE, cardiac events; CVE, cardiovascular events; Cx, chemotherapy; DFS, disease-free survival; RFS relapse-free survival; E, exemestane; ER, estrogen receptor; HR, hazard ratio; L, letrozole; OS, overall survival; P, placebo; PR, progesterone receptor; Qol, quality of life; Rx, radiotherapy; SAE, serious advesrse event; SE, skeletal event; T, tamoxifen; TE, thromboembolism; TTR, time-to-recurrence; TTDR, time-to-distant-recurrence; VE, vascular event; (?) according to retrospective analysis. * only HR positive population



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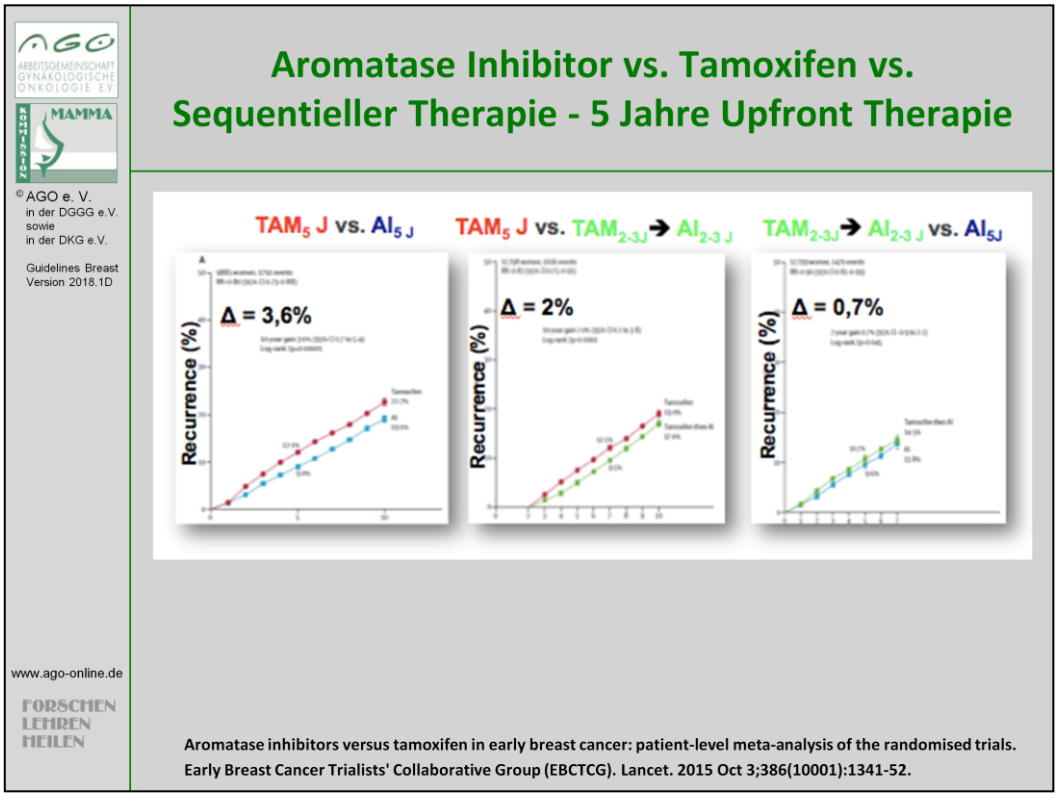


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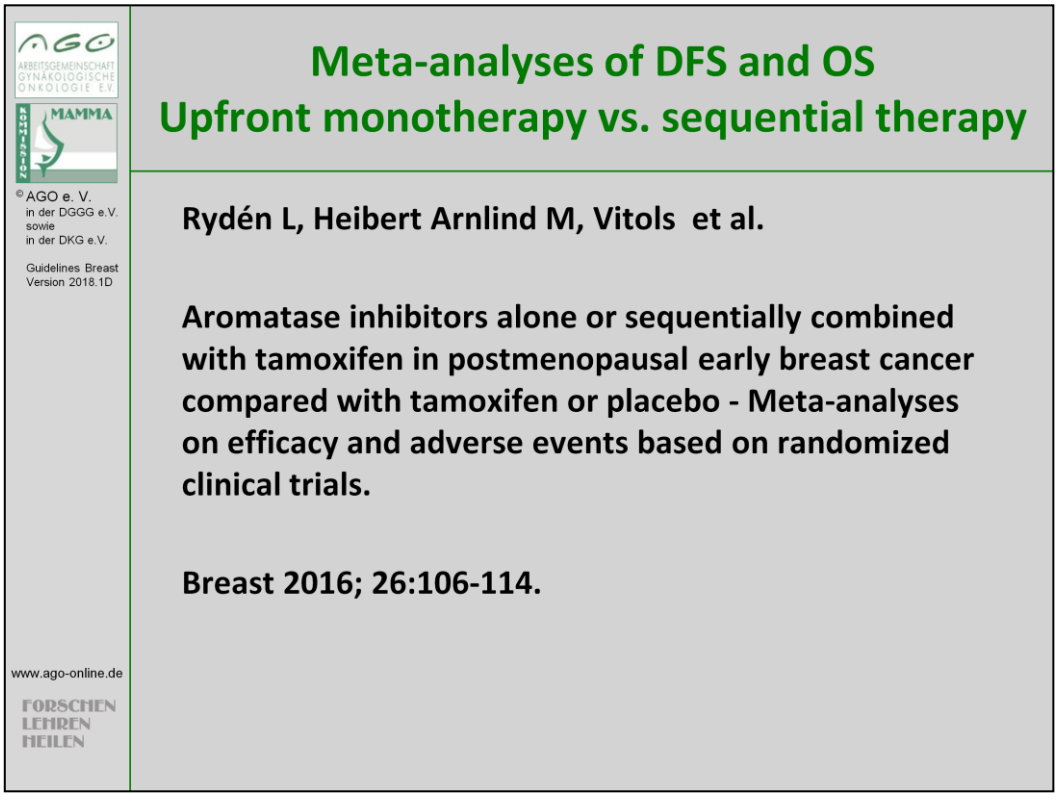


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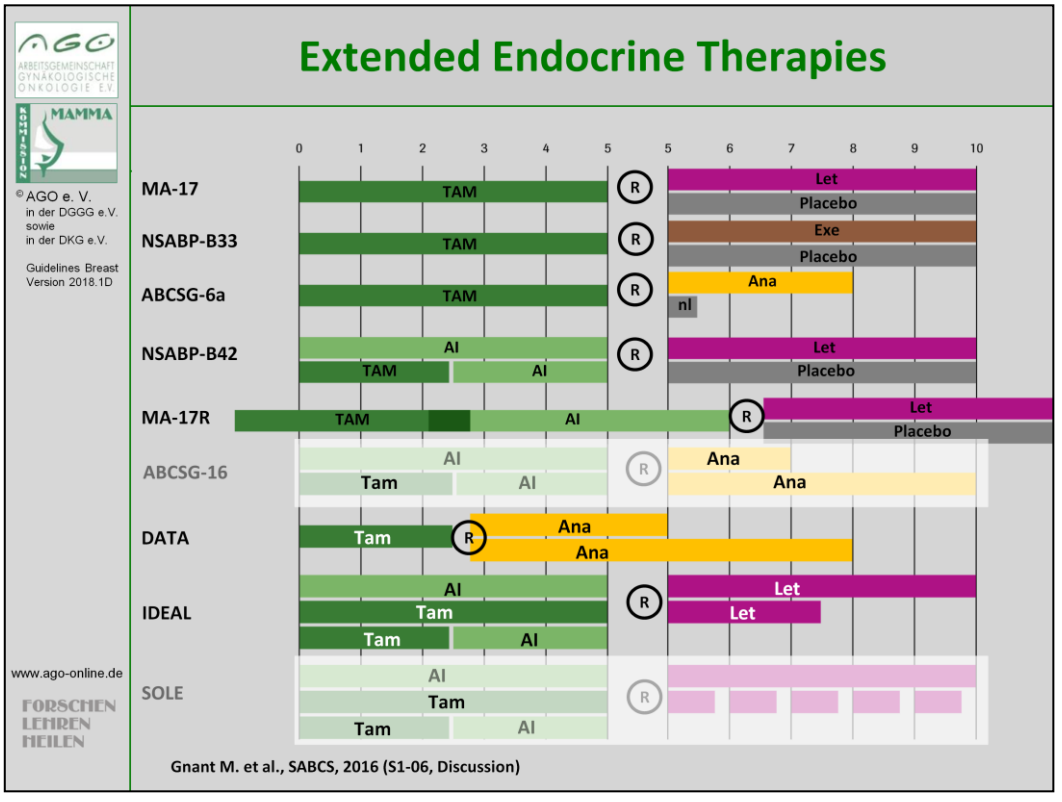
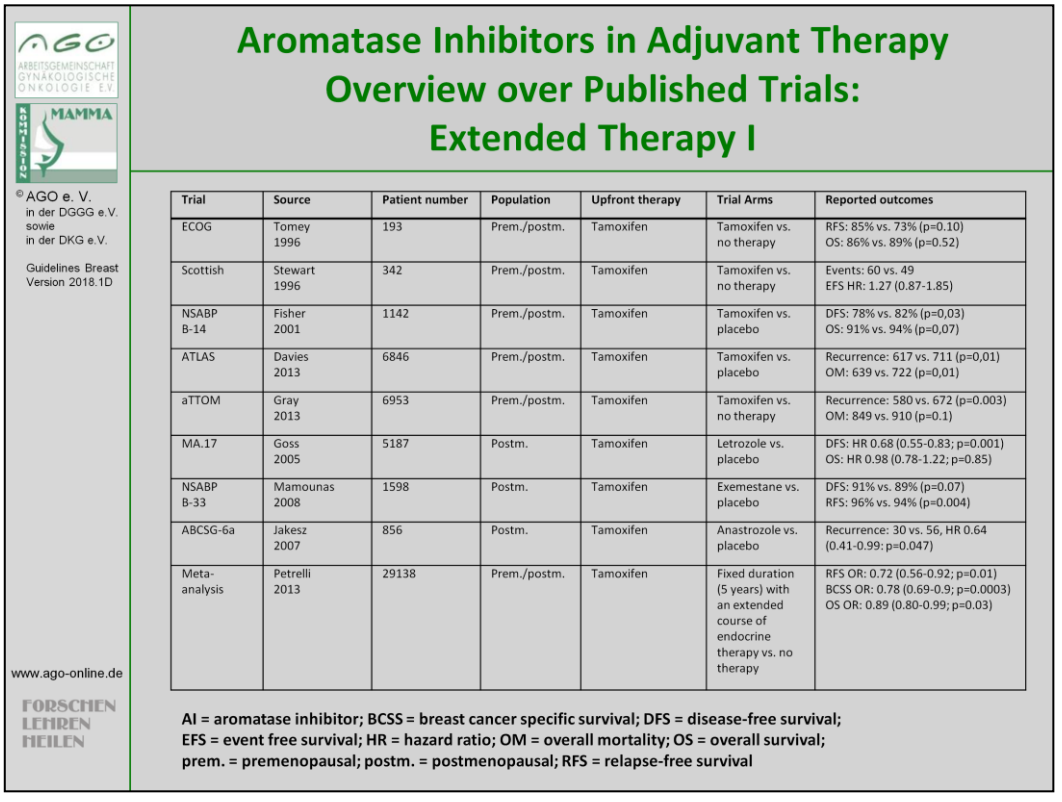



1. Gnant M. et al., SABCS, 2016 (S1-06, Discussion)




## Aromatase Inhibitors in Adjuvant Therapy Overview over Published Trials: Extended Therapy I

| Trial | Source | Patient number | Population | Upfront therapy | Trial Arms | Reported outcomes |
|---|---|---|---|---|---|---|
| ECOG | Tomey 1996 | 193 | Prem./postm. | Tamoxifen | Tamoxifen vs. no therapy | RFS: 85% vs. 73% (p=0.10)<br>OS: 86% vs. 89% (p=0.52) |
| Scottish | Stewart 1996 | 342 | Prem./postm. | Tamoxifen | Tamoxifen vs. no therapy | Events: 60 vs. 49<br>EFS HR: 1.27 (0.87-1.85) |
| NSABP B-14 | Fisher 2001 | 1142 | Prem./postm. | Tamoxifen | Tamoxifen vs. placebo | DFS: 78% vs. 82% (p=0,03)<br>OS: 91% vs. 94% (p=0,07) |
| ATLAS | Davies 2013 | 6846 | Prem./postm. | Tamoxifen | Tamoxifen vs. placebo | Recurrence: 617 vs. 711 (p=0,01)<br>OM: 639 vs. 722 (p=0,01) |
| aTTOM | Gray 2013 | 6953 | Prem./postm. | Tamoxifen | Tamoxifen vs. no therapy | Recurrence: 580 vs. 672 (p=0.003)<br>OM: 849 vs. 910 (p=0.1) |
| MA.17 | Goss 2005 | 5187 | Postm. | Tamoxifen | Letrozole vs. placebo | DFS: HR 0.68 (0.55-0.83; p=0.001)<br>OS: HR 0.98 (0.78-1.22; p=0.85) |
| NSABP B-33 | Mamounas 2008 | 1598 | Postm. | Tamoxifen | Exemestane vs. placebo | DFS: 91% vs. 89% (p=0.07)<br>RFS: 96% vs. 94% (p=0.004) |
| ABCSG-6a | Jakesz 2007 | 856 | Postm. | Tamoxifen | Anastrozole vs. placebo | Recurrence: 30 vs. 56, HR 0.64 (0.41-0.99: p=0.047) |
| Meta-analysis | Petrelli 2013 | 29138 | Prem./postm. | Tamoxifen | Fixed duration (5 years) with an extended course of endocrine therapy vs. no therapy | RFS OR: 0.72 (0.56-0.92; p=0.01)<br>BCSS OR: 0.78 (0.69-0.9; p=0.0003)<br>OS OR: 0.89 (0.80-0.99; p=0.03) |

**AI = aromatase inhibitor; BCSS = breast cancer specific survival; DFS = disease-free survival; EFS = event free survival; HR = hazard ratio; OM = overall mortality; OS = overall survival; prem. = premenopausal; postm. = postmenopausal; RFS = relapse-free survival**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# Aromatase Inhibitors in Adjuvant Therapy
# Overview over Published Trials:
# Extended Therapy II



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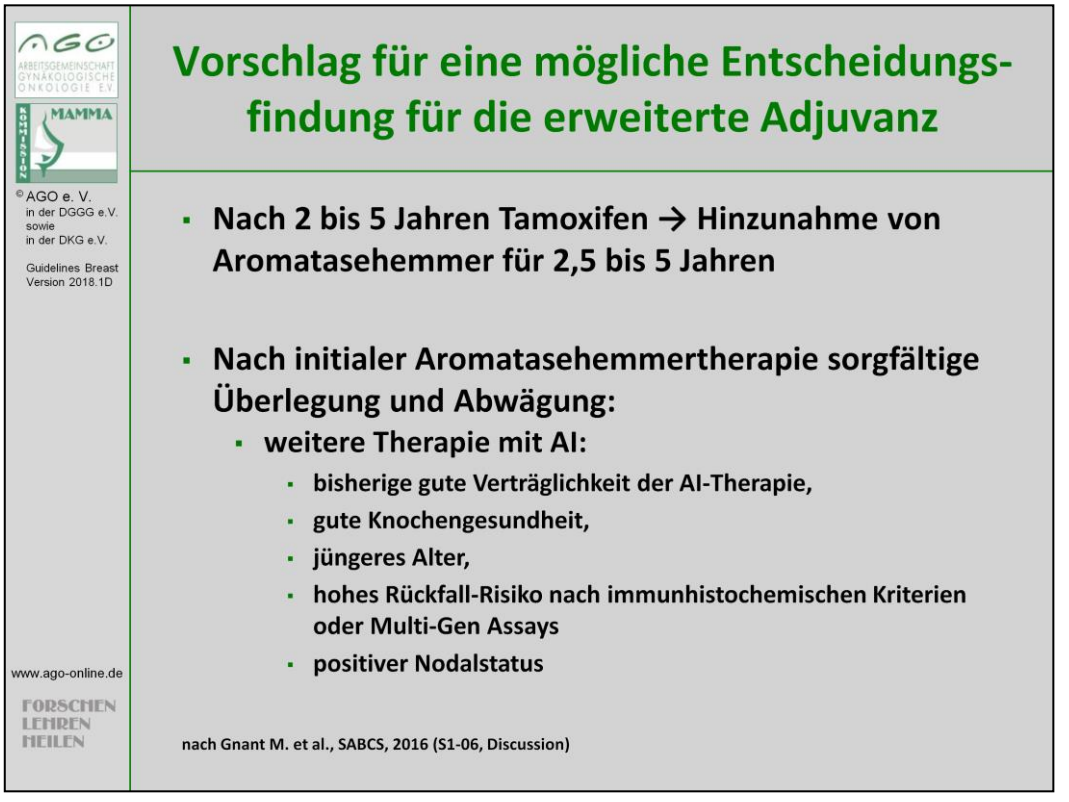
| Trial | Source | Patient number | Population | Upfront therapy | Trial Arms | Reported outcomes |
|---|---|---|---|---|---|---|
| LATER | Zdenkowski 2016 | 360 | Postm. | ≥ 4 years of endocrine therapy (11.7% AI, 50.3% Tam, 38.0% other) | 5 y. letrozole vs. observation | Breast cancer recurrence difference: 8.4% (3.8%-13.0%), p=0.0004 |
| MA17R | Goss 2016 | 1918 | Postm. | 5 years of any other AI with or without prior tamoxifen | Letrozole vs. placebo | DFS: 95% vs. 91% (HR for disease recurrence or occurrence of contralateral breast cancer: 0.66; p=0.01)<br>OS: 93% vs. 94% (HR: 0.97; p=0.83) |
| IDEAL | Blok 2016 | 1824 | Postm. | 5 years of tamoxifen, AI or tamoxifen → AI | Letrozole 2.5 vs. 5 years | DFS HR: 0.88 (0.64-1.21; p=0.43)<br>5-year DFS: 88.4 vs. 87.9%<br>OS HR: 1.09 (0.70-1.70) |
| DATA | Tjan-Heijnen 2016 | 1912 | Postm. | Tamoxifen 2-3 years | Anastrozole 6 vs. 3 years | DFS HR: 0.79 (0.62-1.02; p=0.07)<br>5-year DFS: 83.1 vs. 79.4<br>OS HR: 0.91 (0.65-1.29) |
| NSABP B-42 | Mamounas 2016 | 3923 | Postm. | AI or tamoxifen → AI 5 years | Letrozole vs. placebo | DFS HR: 0.85 (0.73-0.999; p=0.048*)<br>* did not reach statistical significance level of 0.0418 |

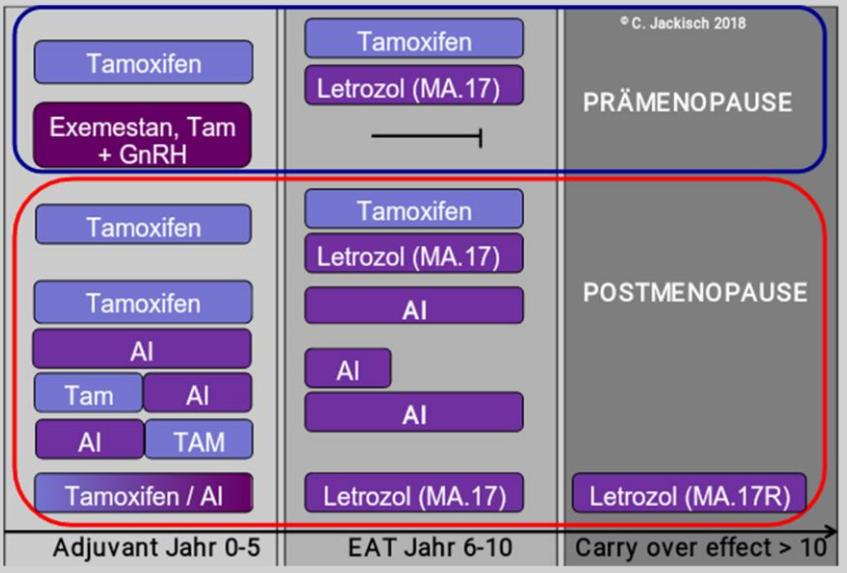


**AI = aromatase inhibitor; BCSS = breast cancer specific survival; DFS = disease-free survival; EFS = event free survival; HR = hazard ratio; OM = overall mortality; OS = overall survival; prem. = premenopausal; postm. = postmenopausal; RFS = relapse-free survival**




1. Gnant M. et al., SABCS, 2016 (S1-06, Discussion)

# Adjuvante endokrinen Therapie
# Prä- und Postmenopause im Überblick



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