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Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Endocrine Therapy of Metastatic Breast Cancer


Endocrine Therapy of Metastatic Breast Cancer

- **Versions 2002–2018:**

**Albert / Bischoff / Dall / Fersis / Friedrich / Gerber /
Huober / Janni / Jonat / Kaufmann / Kolberg-Liedtke /
Loibl / Lück / von Minckwitz / Möbus / Müller /
Mundhenke / Nitz / Schmidt / Schneeweiß / Schütz /
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- **Version 2019:**

Lüftner / Fasching



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Endocrine Therapy in Metastatic Breast Cancer


Indication

Oxford LoE: 1a	GR: A	AGO: ++
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Endocrine-based therapy is first line treatment in patients with metastatic breast cancer and positive (or unknown) hormone receptor (HR) status.

Exception: imminent organ failure
Caveat: HR may change during the course of disease.
Histology of recurrent site should be obtained whenever possible

1. Wilcken N, Hornbuckle J, Ghersi D Chemotherapy alone versus endocrine therapy alone for metastatic breast cancer. Cochrane Database Syst Rev. 2003;(2):CD002747.
2. Gibson L, Lawrence D, Dawson C, et al. Aromatase inhibitors for treatment of advanced breast cancer in postmenopausal women. Cochrane Database Syst Rev. 2009 ;(4):CD003370. doi: 10.1002/14651858.CD003370.pub3.
3. Lee CI, Goodwin A, Wilcken N. Fulvestrant for hormone-sensitive metastatic breast cancer. Cochrane Database Syst Rev. 2017;1:CD011093. doi:10.1002/14651858.CD011093.pub2.
4. Cardoso F, et al. 3rd ESO-ESMO international consensus guidelines for Advanced Breast Cancer (ABC 3). Breast 2017;31:244-259.



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Comparison ER/PR and HER2 Metastasis vs. Primary Tumor

Meta-analysis based on 48 (mostly retrospective) analyses:

Pooled discordance proportions were


- 20% (95%CI 16-35%) for ER
- 33% (95%CI 29-38%) for PR
- 8% (95% CI 6-10%) for HER2

Pooled proportions of tumors shifting from positive to negative and negative to positive were

- 4% and 14% for ER
- 46% and 15% for PR
- 13% and 5% for HER2

1. Amir E, Miller N, et al. Prospective study evaluating the impact of tissue confirmation of metastatic disease in patients with breast cancer. J Clin Oncol 2012; 30(6):587-92.
2. Amir E, et al. Tissue confirmation of disease recurrence in breast cancer patients: pooled analysis of multi-centre, multi-disciplinary prospective studies. Cancer Treat Rev. 2012 Oct;38(6):708-14.
3. Chan A, Morey A, Brown B, et al. A retrospective study investigating the rate of HER2 discordance between primary breast carcinoma and locoregional or metastatic disease. BMC Cancer. 2012;12:555.
4. Lindström LS, Karlsson E et al. Clinically used breast cancer markers such as estrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 are unstable throughout tumor progression. J Clin Oncol ;30:2601-8, 2012.
5. Lower EE, Glass EL, Bradley DA, et al. Impact of metastatic estrogen receptor and progesterone receptor status on survival. Breast Cancer Res Treat. 2005;90(1):65-70.
6. Macfarlane R, Seal M, Speers C, et al. Molecular alterations between the primary breast cancer and the subsequent locoregional/metastatic tumor. Oncologist. 2012;17(2):172-8.
7. Niikura N, Liu J, et al. Loss of human epidermal growth factor receptor 2 (HER2) expression in metastatic sites of HER2-overexpressing primary breast tumors. J Clin Oncol;30(6):593-9, 2012.

8. Thompson AM, Jordan LB, Quinlan P, et al; Breast Recurrence in Tissues Study Group. Prospective comparison of switches in biomarker status between primary and recurrent breast cancer: the Breast Recurrence In Tissues Study (BRITS). *Breast Cancer Res.* 2010;12(6):R92
9. Sighoko D, Liu J, Hou N, et al. Discordance in hormone receptor status among primary, metastatic, and second primary breast cancers: biological difference or misclassification? *Oncologist.* 2014;19(6):592-601.
10. Curtit E, et al. Discordances in estrogen receptor status, progesterone receptor status, and HER2 status between primary breast cancer and metastasis. *Oncologist.* 2013 Jun;18(6):667-74.
11. Niikura N et al. Loss of human epidermal growth factor receptor 2 (HER2) expression in metastatic sites of HER2-overexpressing primary breast tumors. *J Clin Oncol.* 2012;30(6):593-9.



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Endocrine Therapy

General Considerations

- **Within all lines of treatment, treatment options should take previous endocrine therapies, age and comorbidities into consideration as well as respective approval status.**
- **Premenopausal patients treated with GnRH analogues or after ovariectomy can be treated like postmenopausal patients.**

1. Partridge AH, et al. Chemotherapy and targeted therapy for women with human epidermal growth factor receptor 2-negative (or unknown) advanced breast cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. 2014;32(29):3307-29.
2. Rugo HS, et al. Endocrine Therapy for Hormone Receptor-Positive Metastatic Breast Cancer: American Society of Clinical Oncology Guideline. J Clin Oncol 2016;34(25):3069-103.

 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2019.1</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	Endocrine Therapy in Premenopausal Patients with HER2-Negative Metastatic Breast Cancer		
	Oxford		
<ul style="list-style-type: none"> ■ GnRH-A + Fulvestrant + Palbociclib ■ GnRH-A + AI + Palbociclib* ■ GnRH-A + AI + Ribociclib ■ GnRH-A + Fulvestrant + Abemaciclib ■ GnRH-A + Tamoxifen (vs. OFS or Tam) ■ Ovarial function suppression (OFS) ■ Tamoxifen ■ GnRH-A + AI (first + second line) ■ GnRH-A + Fulvestrant ■ Aromatase inhibitors without OFS 	LoE	GR	AGO
	2b	B	++
	5	D	++
	1b ^a	B	++
	2b	B	++
	1a	A	++
	2b	B	+
	2b	B	+
	2b	B	+
	1b	B	+
	3	D	--
* Extrapolated from data of postmenopausal patients (with AI)			

GnRHa plus fulvestrant plus palbociclib

1. Turner N et al. Palbociclib in Hormone-Receptor–Positive Advanced Breast Cancer. N Engl J Med 2015; 373:209-219
2. Loibl S, et al. Palbociclib Combined with Fulvestrant in Premenopausal Women with Advanced Breast Cancer and Prior Progression on Endocrine Therapy: PALOMA-3 Results. Oncologist. 2017;22(9):1028-1038.

GnRHa plus AI/Tamoxifen plus ribociclib

Tripathy D et al. First-line ribociclib vs placebo with goserelin and tamoxifen or a non-steroidal aromatase inhibitor in premenopausal women with hormone receptor-positive, HER2-negative advanced breast cancer: Results from the randomized phase III MONALEESA-7 trial. SABCS 2017, GS-2

GnRHa plus tamoxifen (vs. OFS or tam)

1. Klijn JG, Blamey RW, Boccardo F, et al. Combined tamoxifen and luteinizing hormone-releasing hormone (LHRH) agonist versus LHRH agonist alone in premenopausal advanced breast cancer: a meta-analysis of four randomized trials. J Clin Oncol.

2001;19(2):343-53.

2. Rugo HS, et al. Endocrine Therapy for Hormone Receptor-Positive Metastatic Breast Cancer: American Society of Clinical Oncology Guideline. J Clin Oncol. 2016 ;34(25):3069-103.

Ovarian function suppression (OFS), tamoxifen

1. Taylor CW, Green S, Dalton WS, et al: Multicenter randomized clinical trial of goserelin versus surgical ovariectomy in premenopausal patients with receptor-positive metastatic breast cancer: an intergroup study. J Clin Oncol 1998;16:994-999.
2. Osborne CK: Tamoxifen in the treatment of breast cancer. N Engl J Med 1998;339
3. Crump M, Sawka CA, DeBoer G, et al: An individual patient-based meta-analysis of tamoxifen versus ovarian ablation as first line endocrine therapy for premenopausal women with metastatic breast cancer. Breast Cancer Res Treat 1997;44:201-210.


GnRHa plus AI (first or second line)

1. Forward DP, Cheung KL, Jackson L, et al. Clinical and endocrine data for goserelin plus anastrozole as second-line endocrine therapy for premenopausal advanced breast cancer. Br J Cancer. 2004 ;90(3):590-4.
2. Park IH, Ro J, Lee KS, et al. Phase II parallel group study showing comparable efficacy between premenopausal metastatic breast cancer patients treated with letrozole plus goserelin and postmenopausal patients treated with letrozole alone as first-line hormone therapy. J Clin Oncol. 2010;28(16):2705-11.
3. Carlson RW, et al. Phase II trial of anastrozole plus goserelin in the treatment of hormone receptor-positive, metastatic carcinoma of the breast in premenopausal women. J Clin Oncol. 2010;28(25):3917-21.

GnRHa plus fulvestrant

1. Bartsch R, Bago-Horvath Z, et al. Ovarian function suppression and fulvestrant as endocrine therapy in premenopausal women with metastatic breast cancer. European Journal of Cancer 48: 1932–1938, 2012.
2. Turner M et al. Palbociclib in Hormone-Receptor–Positive Advanced Breast Cancer. N Engl J Med 2015; 373:209-219

3. Loibl S, et al. Palbociclib Combined with Fulvestrant in Premenopausal Women with Advanced Breast Cancer and Prior Progression on Endocrine Therapy: PALOMA-3 Results. *Oncologist*. 2017;22(9):1028-1038.



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Endocrine Mono-Therapy in Postmenopausal Patients with HER2-Negative Metastatic Breast Cancer

	Oxford		
	LoE	GR	AGO
▪ Fulvestrant 500 mg	1b	B	++
▪ Aromataseinhibitor (3rd generation)*	1a	A	++
▪ Tamoxifen	1a	A	+
▪ Fulvestrant 250 mg + Anastrozol	1b	B	+/-
▪ Repeat prior treatments	5	D	+/-

* There is no evidence for superiority of a single aromatase inhibitor. As everolimus plus exemestane is indicated after AI treatment, a non-steroidal AI should be utilized as first line.

Fulvestrant 500 mg (vs. anastrozole)

1. Ellis MJ, et al. Fulvestrant 500 mg Versus Anastrozole 1 mg for the First-Line Treatment of Advanced Breast Cancer: Overall Survival Analysis From the Phase II FIRST Study. J Clin Oncol. 2015;33(32):3781-7
2. Robertson JF, et al. Fulvestrant 500 mg versus anastrozole 1 mg for hormone receptor-positive advanced breast cancer (FALCON): an international, randomised, double-blind, phase 3 trial. Lancet. 2016 ;388(10063):2997-3005.

Fulvestrant 500 mg >> 250 mg

1. Di Leo A, et al. Final overall survival: fulvestrant 500 mg vs 250 mg in the randomized CONFIRM trial. J Natl Cancer Inst. 2014;106(1):djt337.

Aromatase inhibitors (3rd generation)*

1. Bonnetterre J, et al: Anastrozole versus Tamoxifen as First-Line Therapy for Advanced Breast Cancer in 668 Postmenopausal Women: Results of the Tamoxifen or Arimidex Randomized Group Efficacy and tolerability Study. J Clin Oncol 2000;18:3748-3757

2. Thürlimann B, et al: Anastrozole (Arimidex) versus tamoxifen as first-line therapy in postmenopausal women with advanced breast cancer: results of the double-blind cross-over SAKK trial 21/95 – a substudy of the TARGET (Tamoxifen or Arimidex Randomized Group Efficacy and Tolerability) trial. Breast Cancer Res Treat 2004;85:247-254

Aromatase inhibitors (3rd generation) (>non-AI)

1. Bonnetterre, J, et al. Anastrozole is superior to tamoxifen as first-line therapy in hormone receptor positive advanced breast carcinoma Cancer 2001 92
2. Mouridsen, H, et al, Phase III study of letrozole versus tamoxifen as first-line therapy of advanced breast cancer in postmenopausal women: analysis of survival and update of efficacy from the International Letrozole Breast Cancer Group Journal of Clinical Oncology. J Clin Oncol. 2003;21(11):2101-9.
3. Paridaens R, et al; European Organization for the Research and Treatment of Cancer (EORTC)- Investigational Drug Branch for Breast Cancer (IDBBC). Mature results of a randomized phase II multicenter study of exemestane versus tamoxifen as first-line hormone therapy for postmenopausal women with metastatic breast cancer. Ann Oncol. 2003 Sep;14(9):1391-8.
4. Gibson L, Lawrence D, Dawson C, et al. Aromatase inhibitors for treatment of advanced breast cancer in postmenopausal women. Cochrane Database Syst Rev. 2009;(4):CD003370.
5. Xu HB, Liu YJ, Li L. Aromatase inhibitor versus tamoxifen in postmenopausal woman with advanced breast cancer: a literature-based meta-analysis. Clin Breast Cancer. 2011;11(4):246-51.
6. Rugo HS, et al. Endocrine Therapy for Hormone Receptor-Positive Metastatic Breast Cancer: American Society of Clinical Oncology Guideline. J Clin Oncol. 2016 ;34(25):3069-103.
7. Sini V, et al. Endocrine therapy in post-menopausal women with metastatic breast cancer: From literature and guidelines to clinical practice. Crit Rev Oncol Hematol. 2016;100:57-68.

Endokrine Based Treatment Option for Postmenopausal Patients with HER2-Negative Metastatic Breast Cancer			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> CDK4/6-Inhibitor (Abemaciclib, Palbociclib, Ribociclib) <ul style="list-style-type: none"> + nicht-steroidaler AI + Fulvestrant Abemaciclib Monotherapie Everolimus <ul style="list-style-type: none"> + Exemestan + Tamoxifen + Letrozol + Fulvestrant CDK4/6i beyond progression 	1b 1b 3 1b 2b 2b 2b ^a 5	B B C A B B B D	++ ++ +/- + + +/- + -

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Letrozole and palbociclib (vs. letrozole alone)

1. Finn RS, et al. Palbociclib and Letrozole in Advanced Breast Cancer. N Engl J Med. 2016;375(20):1925-1936.
2. Finn RS, et al. The cyclin-dependent kinase 4/6 inhibitor palbociclib in combination with letrozole versus letrozole alone as first-line treatment of oestrogen receptor-positive, HER2-negative, advanced breast cancer (PALOMA-1/TRIO-18): a randomised phase 2 study. Lancet Oncol 2015;16(1):25-35.

Fulvestrant 500 mg plus Palbociclib (vs. Fulvestrant alone)

1. Turner NC, Ro J, André F, et al; PALOMA3 Study Group. Palbociclib in Hormone-Receptor-Positive Advanced Breast Cancer. N Engl J Med. 2015 Jul 16;373(3):209-19.
2. Turner NC et al. Overall Survival with Palbociclib and Fulvestrant in Advanced Breast Cancer N Engl J Med 2018; 379:1926-1936 DOI: 10.1056/NEJMoa1810527

Letrozol plus Ribociclib

1. Hortobagyi GN, et al. Ribociclib as First-Line Therapy for HR-Positive, Advanced Breast Cancer. N Engl J Med. 2016;375(18):1738-1748.

Fulvestrant plus Abemaciclib

1. Sledge GW Jr, et al. MONARCH 2: Abemaciclib in Combination With Fulvestrant in Women With HR+/HER2- Advanced Breast Cancer Who Had Progressed While Receiving Endocrine Therapy. J Clin Oncol. 2017;35(25):2875-2884.

Non-steroidal AI plus Abemaciclib

1. Goetz MP, et al. MONARCH 3: Abemaciclib As Initial Therapy for Advanced Breast Cancer. J Clin Oncol. 2017 ;35(32):3638-3646.

Exemestane and everolimus (vs. exemestane alone)

1. Baselga J, Campone M et al. Everolimus in postmenopausal hormone-receptor-positive advanced breast cancer. N Engl J Med.;366(6):520-9. 2012
2. Jerusalem G, et al. Safety of everolimus plus exemestane in patients with hormone-receptor-positive, HER2-negative locally advanced or metastatic breast cancer progressing on prior non-steroidal aromatase inhibitors: primary results of a phase IIIb, open-label, single-arm, expanded-access multicenter trial (BALLET). Ann Oncol. 2016;27(9):1719-25

Tamoxifen and everolimus

1. Bachelot T, et al. Randomized Phase II Trial of Everolimus in Combination With Tamoxifen in Patients With Hormone Receptor-Positive, Human Epidermal Growth Factor Receptor 2-Negative Metastatic Breast Cancer With Prior Exposure to Aromatase Inhibitors: A GINECO Study. J Clin Oncol 2012; 30: 2718-2724.

Fulvestrant and everolimus

1. Kornblum NS, et al. PrECOG 0102: A randomized, double-blind, phase II trial of fulvestrant plus everolimus or placebo in post-


menopausal women with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) resistant to aromatase inhibitor (AI) therapy. SABCS 2016, #S1-02

Letrozole and everolimus

1. Gradishar WJ, et al. BOLERO-4: Multicenter, open-label, phase II study of everolimus plus letrozole as first-line therapy in ER+, HER2-metastatic breast cancer. J Clin Oncol 31, 2013 (suppl; abstr TPS661)

Abemaciclib Monotherapie

1. Dickler MN, et al. MONARCH 1, A Phase II Study of Abemaciclib, a CDK4 and CDK6 Inhibitor, as a Single Agent, in Patients with Refractory HR⁺/HER2⁻ Metastatic Breast Cancer. Clin Cancer Res. 2017;23(17):5218-5224.


Endocrine Therapy in Postmenopausal HER2-Negative Metastatic Breast Cancer Patients in Combination with Bevacizumab			
	Oxford		
	LoE	GR	AGO
<div> <div>  <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V. Guidelines Breast Version 2019.1</p> <p>www.ago-online.de FORSCHEN LEHREN HEILEN</p> </div> <div> <ul style="list-style-type: none"> ■ Maintenance bevacizumab plus endocrine therapy after remission with chemotherapy and bevacizumab ■ Bevacizumab plus endocrine treatment as first line therapy for advanced disease </div> </div>	1b	B	+/-
	1b	B	+/-

Maintenance of bevacizumab plus endocrine therapy

1. Tredan O, et al. A phase III trial of exemestane plus bevacizumab maintenance therapy in patients with metastatic breast cancer after first-line taxane and bevacizumab: a GINECO group study. Ann Oncol 2016; 27(6):1020–1029.

Bevacizumab plus endocrine treatment as first line

1. Martín M, Loibl S, et al. Bevacizumab plus endocrine treatment as first line therapy for advanced disease Phase III trial evaluating the addition of bevacizumab to endocrine therapy as first-line treatment for advanced breast cancer: the letrozole/fulvestrant and avastin (LEA) study. J Clin Oncol. 2015 ;33(9):1045-52.
2. Dickler MN, et al. Phase III Trial Evaluating Letrozole As First-Line Endocrine Therapy With or Without Bevacizumab for the Treatment of Postmenopausal Women With Hormone Receptor-Positive Advanced-Stage Breast Cancer: CALGB 40503 (Alliance). J Clin Oncol. 2016;34(22):2602-9.



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PARP Inhibitors in Patients with HER2-negative, gBRCA Mutant, Metastatic Breast Cancer

- **Olaparib**
 - TNBC
 - ER+

- **Talazoparib**

Oxford		
LoE	GR	AGO
1b	B	+
2b	B	+
2b	C	+/-


Oxford		
LoE	GR	AGO
1b	B	+/-

Olaparib

1. Robson M, et al. Olaparib for Metastatic Breast Cancer in Patients with a Germline BRCA Mutation. N Engl J Med. 2017;377(6):523-533.
2. Litton J. et al. Talazoparib in Patients with Advanced Breast Cancer and a Germline BRCA Mutation. N Engl J Med 2018; 379:753-763
DOI: 10.1056/NEJMoa1802905

Diagnosis and Treatment of Patients with early and advanced Breast Cancer

HER2 Positive and HR-Positive Metastatic Breast Cancer



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Endocrine Therapy in Postmenopausal HER2-Positive Metastatic Breast Cancer Patients

	Oxford		
	LoE	GR	AGO
■ Anastrozole plus trastuzumab	1b	B	+/-
■ Letrozole plus trastuzumab	2b	B	+/-
■ Letrozole plus lapatinib	1b	B	+/-
■ Fulvestrant plus lapatinib	1b	B	+/-
■ Aromatase inhibitors plus Trastuzumab / Pertuzumab*	2b ^a	B	+/-

**Poor efficacy of endocrine therapy alone.
Consider induction chemotherapy + anti-HER2-therapy (followed by endocrine + anti-HER2-therapy as maintenance therapy)!**

* Study participation recommended

Anastrozole and trastuzumab

1. Kaufman B, et al. Trastuzumab plus anastrozole versus anastrozole alone for the treatment of postmenopausal women with human epidermal growth factor receptor 2-positive, hormone receptor-positive metastatic breast cancer: results from the randomized phase III TAnDEM study. J Clin Oncol. 2009 Nov 20;27(33):5529-37.
2. Giordano SH, et al. American Society of Clinical Oncology. Systemic therapy for patients with advanced human epidermal growth factor receptor 2-positive breast cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jul 1;32(19):2078-99.
3. Riemsma R, et al. Systematic review of lapatinib in combination with letrozole compared with other first-line treatments for hormone receptor positive (HR+) and HER2+ advanced or metastatic breast cancer (MBC). Curr Med Res Opin. 2012 Aug;28(8):1263-79.

Letrozole and trastuzumab

1. Huober J, et al. Higher efficacy of letrozole in combination with trastuzumab compared to letrozole monotherapy as first-line treatment in patients with HER2-positive, hormone-receptor-positive metastatic breast cancer - results of the eLECTRA trial.

Breast. 2012 ;21(1):27-33.

2. Giordano SH, et al. American Society of Clinical Oncology. Systemic therapy for patients with advanced human epidermal growth factor receptor 2-positive breast cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jul 1;32(19):2078-99.
3. Riemsma R, et al. Systematic review of lapatinib in combination with letrozole compared with other first-line treatments for hormone receptor positive(HR+) and HER2+ advanced or metastatic breast cancer(MBC). Curr Med Res Opin. 2012 Aug;28(8):1263-79.

Letrozole and lapatinib


1. Johnston S, Pippin J Jr, Pivot X, et al. Lapatinib combined with letrozole versus letrozole and placebo as first-line therapy for postmenopausal hormone receptor-positive metastatic breast cancer. J Clin Oncol. 2009 Nov 20;27(33):5538-46.
2. Riemsma R, Forbes CA, Amonkar MM, et al. Systematic review of lapatinib in combination with letrozole compared with other first-line treatments for hormone receptor positive(HR+) and HER2+ advanced or metastatic breast cancer(MBC). Curr Med Res Opin. 2012 Aug;28(8):1263-79.
3. Grassadonia A, Caporale M, Tinari N, et al. Effect of targeted agents on the endocrine response of breast cancer in the neoadjuvant setting: a systematic review. J Cancer. 2015 May 12;6(6):575-82.
4. Giordano SH, Temin S, Kirshner JJ, et al; American Society of Clinical Oncology. Systemic therapy for patients with advanced human epidermal growth factor receptor 2-positive breast cancer: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2014 Jul 1;32(19):2078-99.

Fulvestrant and lapatinib

1. Burstein HJ, Cirincione CT, Barry WT et al: Endocrine Therapy With or Without Inhibition of Epidermal Growth Factor Receptor and Human Epidermal Growth Factor Receptor 2: A Randomized, Double-Blind, Placebo-Controlled Phase III Trial of Fulvestrant With or Without Lapatinib for Postmenopausal Women With Hormone Receptor-Positive Advanced Breast Cancer-CALGB 40302 (Alliance). J Clin Oncol 32:3959-3966 (2014)

AI and trastuzumab/pertuzumab

1. Arpino G, et al. A randomized, two-arm, open-label, multicenter phase II trial assessing the efficacy and safety of pertuzumab given in combination with trastuzumab plus an aromatase inhibitor in first-line patients with HER2-positive and hormone receptor-positive metastatic or locally advanced breast cancer. SABCS 2016, #S3-04



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Concomitant or Sequential Endocrine-Cytostatic Treatment

	Oxford LoE	GR	AGO
<ul style="list-style-type: none"> ■ Concomitant endocrine-cytotoxic treatment <ul style="list-style-type: none"> ■ May increase response rate and progression free interval but not overall survival ■ May increase toxicity ■ Endocrine Maintenance therapy after chemotherapy +/- anti-HER2 therapy induced response +/- anti HER2 therapy <ul style="list-style-type: none"> ■ Increases progression free interval 	1b	A	-
	2b	B	+

Concomitant endocrine-cytotoxic treatment

1. Sledge GW, Hu P, Falkson G, et al. Comparison of chemotherapy with chemohormonal therapy as first-line therapy for metastatic, hormone-sensitive breast cancer: An eastern cooperative oncology group study. J Clin Oncol 18, 262-266, 2000.
2. Partridge AH, Burstein HJ, Winer EP. Side effects of chemotherapy and combined chemohormonal therapy in women with early-stage breast cancer. J Natl Cancer Inst Monogr. 2001;(30):135-42.
3. Boccardo F1, Amoroso D, Rubagotti A, et al. Endocrine therapy of breast cancer. The experience of the Italian Cooperative Group for Chemohormonal Therapy of Early Breast Cancer (GROCTA). Ann N Y Acad Sci. 1993 Nov 30;698:318-29.

Maintenance endocrine therapy after chemotherapy induced response

1. Sutherland S, Miles D, Makris A. Use of maintenance endocrine therapy after chemotherapy in metastatic breast cancer. Eur J Cancer. 2016 Dec;69:216-222.
2. Rossi S, Schinzari G, Basso M, et al. Maintenance hormonal and chemotherapy treatment in metastatic breast cancer: a systematic review. Future Oncol. 2016 May;12(10):1299-307