

# Diagnosis and Treatment of Patients with early and advanced Breast Cancer



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Guidelines Breast  
Version 2019.1

## Endocrine Therapy of Metastatic Breast Cancer

# Endocrine Therapy of Metastatic Breast Cancer

- **Versions 2002–2018:**

**Albert / Bischoff / Dall / Fersis / Friedrich / Gerber /  
Hober / Janni / Jonat / Kaufmann / Kolberg-Liedtke /  
Loibl / Lück / von Minckwitz / Möbus / Müller /  
Mundhenke / Nitz / Schmidt / Schneeweiß / Schütz /  
Stickeler / Thill**

- **Version 2019:**

**Lüftner / Fasching**

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## Indication

<b>Oxford LoE: 1a</b>	<b>GR: A</b>	<b>AGO: ++</b>
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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**

# Comparison ER/PR and HER2 Metastasis vs. Primary Tumor

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**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

# 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.**

# Endocrine Therapy in Premenopausal Patients with HER2-Negative Metastatic Breast Cancer

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- 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

	Oxford		
	LoE	GR	AGO
	2b	B	++
	5	D	++
	1b <sup>a</sup>	B	++
	2b	B	++
	1a	A	++
	2b	B	+
	2b	B	+
	2b	B	+
	1b	B	+
	3	D	--

\* Extrapolated from data of postmenopausal patients (with AI)

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



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- Fulvestrant 500 mg
- Aromataseinhibitor (3rd generation)\*
- Tamoxifen
- Fulvestrant 250 mg + Anastrozol
- Repeat prior treatments

Oxford		
LoE	GR	AGO
1b	B	++
1a	A	++
1a	A	+
1b	B	+/-
5	D	+/-

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FORSCHEN  
LEHREN  
HEILEN

\* 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.

# Endokrine Based Treatment Option for Postmenopausal Patients with HER2-Negative Metastatic Breast Cancer

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	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>■ <b>CDK4/6-Inhibitor (Abemaciclib, Palbociclib, Ribociclib)</b> <ul style="list-style-type: none"> <li>■ + nicht-steroidaler AI</li> <li>■ + Fulvestrant</li> </ul> </li> </ul>	1b	B	++
	1b	B	++
■ <b>Abemaciclib Monotherapie</b>	3	C	+/-
■ <b>Everolimus</b> <ul style="list-style-type: none"> <li>■ + Exemestan</li> <li>■ + Tamoxifen</li> <li>■ + Letrozol</li> <li>■ + Fulvestrant</li> </ul>	1b	A	+
	2b	B	+
	2b	B	+/-
	2b <sup>a</sup>	B	+
■ <b>CDK4/6i beyond progression</b>	5	D	-



# Endocrine Therapy in Postmenopausal HER2-Negative Metastatic Breast Cancer Patients in Combination with Bevacizumab



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- **Maintenance bevacizumab plus endocrine therapy after remission with chemotherapy and bevacizumab**
- **Bevacizumab plus endocrine treatment as first line therapy for advanced disease**

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

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

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- **Olaparib**
  - TNBC
  - ER+

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

- **Talazoparib**

Oxford		
LoE	GR	AGO
1b	B	+/-

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## HER2 Positive and HR-Positive Metastatic Breast Cancer

# Endocrine Therapy in Postmenopausal HER2-Positive Metastatic Breast Cancer Patients



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- Anastrozole plus trastuzumab
- Letrozole plus trastuzumab
- Letrozole plus lapatinib
- Fulvestrant plus lapatinib
- Aromatase inhibitors plus Trastuzumab / Pertuzumab\*

Oxford		
LoE	GR	AGO
1b	B	+/-
2b	B	+/-
1b	B	+/-
1b	B	+/-
2b <sup>a</sup>	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

# Concomitant or Sequential Endocrine-Cytostatic Treatment

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- **Concomitant endocrine-cytotoxic treatment**
  - 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**
  - Increases progression free interval

Oxford		
LoE	GR	AGO
1b	A	-
2b	B	+