Guidelines Breast
Version 2018.1

Endocrine Therapy of Metastatic Breast Cancer

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Endocrine Therapy of Metastatic Breast Cancer

- **Versions 2002–2017:**

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

- **Version 2018:**

  Loibl / Lück

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Endocrine Therapy in Metastatic Breast Cancer

Indication

Oxford LoE: 1a	GR: A	AGO: ++

Endocrine-based therapy is first line treatment in patients with metastatic breast cancer and positive (or unknown) hormone receptor (HR) status.

Exception: acute life-threatening disease

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

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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

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**
- **All premenopausal patients should receive OFS and be treated according to postmenopausal patients**

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

	Oxford		
	LoE	GR	AGO
▪ GnRH-A + Fulvestrant + Palbociclib	2b	B	++
▪ GnRH-A + AI + Palbociclib*	5	D	++
▪ GnRH-A + AI/Tamoxifen + Ribociclib	1b[a]	B	++
▪ GnRH-A + Fulvestrant + Abemaciclib	2b	B	+
▪ GnRH-A + Tamoxifen (vs. OFS or Tam)	1a	A	++
▪ Ovarial function suppression (OFS)	2b	B	+
▪ Tamoxifen	2b	B	+
▪ GnRH-A + AI (first + second line)	2b	B	+
▪ GnRH-A + Fulvestrant	1b	B	+
▪ Aromatase inhibitors without OFS	3	D	--

* Extrapolated from data of postmenopausal patients (with AI)

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Endocrine 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.

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

	Oxford		
	LoE	GR	AGO
▪ Letrozol* + Palbociclib	1b	B	++
▪ Fulvestrant + Palbociclib	1b	B	++
▪ Letrozol* + Ribociclib	1b	B	++
▪ Letrozol /Anastrozol+ Abemaciclib	1b	B	+
▪ Fulvestrant + Abemaciclib	1b	B	+
▪ Abemaciclib Monotherapie	3	C	+/-
▪ Exemestan + Everolimus	1b	A	+
▪ Tamoxifen + Everolimus	2b	B	+
▪ Letrozol + Everolimus	2b	B	+/-
▪ Fulvestrant + Everolimus	2b[a]	B	+
▪ CDK4/6i beyond progression	5	D	-

* Data can be extrapolated on other AIs

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

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	Oxford		
	LoE	GR	AGO
▪ Maintenance bevacizumab plus endocrine therapy after remission with chemotherapy and bevacizumab	1b	B	+/-
▪ Bevacizumab plus endocrine treatment as first line therapy for advanced disease	1b	B	+/-

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

	Oxford		
	LoE	GR	AGO
▪ **Olaparib**	1b	B	+
▪ **TNBC**	2b	B	+
▪ **ER+**	2b	C	+/-

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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

Concomitant or Sequential Endocrine-Cytostatic Treatment

	Oxford LoE	Oxford GR	AGO
▪ **Concomitant endocrine-cytotoxic treatment** ▪ May increase response rate and progression free interval but not overall survival ▪ May increase toxicity	1b	A	-
▪ **Endocrine Maintenance therapy after chemotherapy +/- anti-HER2 therapy induced response +/- anti HER2 therapy** ▪ Increases progression free interval	2b	B	+