Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Guidelines Breast
Version 2020.1

Endocrine and targeted Therapy of Metastatic Breast Cancer

Endocrine Therapy of Metastatic Breast Cancer

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- **Versions 2002–2019:**
  Albert / Bischoff / Dall / Fasching / Fersis / Friedrich / Gerber / Huober / Janni / Jonat / Kaufmann / Kolberg-Liedtke / Loibl / Lüftner / Lück / von Minckwitz / Möbus / Müller / Mundhenke / Nitz / Schmidt / Schneeweiß / Schütz / Stickeler / Thill

- **Version 2020:**
  Thill / Untch

Endocrine Therapy in Metastatic Breast Cancer

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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: imminent organ failure

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 (N=5.521)

Meta-analysis based on 39 (mostly retrospective) analyses, exclusively comparing primary tumor and metastasis (no lymph nodes):

Pooled discordance proportions were:

- 19,3% (95% CI 1⁄4 15.8% to 23.4%) for ER
- 30,9% (95% CI1⁄4 26.6% to 35.6%) for PR
- 10,3% (95% CI 1⁄4 7.8% to 13.6%) for HER2

Pooled proportions of tumors shifting from positive to negative

- 22.5% (95% CI = 16.4% to 30.0%) for ER
- 49.4% (95% CI = 40.5% to 58.2%) for PR
- 21.3% (95% CI = 14.3% to 30.5%)) for HER2

Pooled proportions of tumors shifting from negative to positive

- 21.5% (95% CI = 18.1% to 25.5%) for ER
- 15.9% (95% CI = 11.3% to 22.0%) for PR
- 9.5% (95% CI = 7.4% to 12.1%) for HER2

Endocrine Therapy
General Considerations

- **Within all lines of treatment, treatment options should consider prior endocrine therapies, age and comorbidities as well as the respective approval status.**
- **Premenopausal patients treated with GnRH analogues or after ovarectomy can be treated like postmenopausal patients.**

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

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	Oxford		
	LoE	GR	AGO
▪ GnRH-A + Fulvestrant + Palbociclib	2b	B	++
▪ GnRH-A + AI + Palbociclib*	3b[a]	C	++
▪ GnRH-A + AI + Ribociclib	1b	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)

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

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	Oxford		
	LoE	GR	AGO
▪ Fulvestrant 500 mg	1b	B	+
▪ Aromatase inhibitor*	1a	A	+
▪ Tamoxifen	1a	A	+
▪ Fulvestrant 250 mg + Anastrozole	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 used in first line.

Endocrine-Based Treatment Options for Postmenopausal Patients with HER2-Negative Metastatic Breast Cancer

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	Oxford		
	LoE	GR	AGO
▪ CDK4/6-Inhibitor (Abemaciclib, Palbociclib, Ribociclib)			
▪ + non-steroidal AI	1b	B	++
▪ + Fulvestrant	1b	B	++
▪ Abemaciclib Monotherapie	3	C	+/-
▪ Alpelisib + Fulvestrant (PIK3CA mutated)	1b	B	+
▪ Everolimus			
▪ + Exemestane	1b	A	+
▪ + Tamoxifen	2b	B	+
▪ + Letrozole	2b	B	+/-
▪ + Fulvestrant	2b[a]	B	+
▪ CDK4/6i beyond progression	5	D	-
▪ CDK4/6i switch based on toxicity	5	D	+/-

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

	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, Metastatic Breast Cancer

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	Oxford		
	LoE	GR	AGO
▪ Olaparib	1b	A	++

	Oxford		
	LoE	GR	AGO
▪ Talazoparib	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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	Oxford		
	LoE	GR	AGO
▪ Anastrozole plus trastuzumab	1b	B	+/-
▪ Letrozole plus trastuzumab	2b	B	+/-
▪ Letrozole plus lapatinib	1b	B	+/-
▪ Fulvestrant plus lapatinib	1b	B	+/-
▪ Abemaciclib plus fulvestrant plus trastuzumab (after T-DM1)	2b[a]	B	+/-
▪ Aromatase inhibitors plus trastuzumab / pertuzumab*	2b	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**

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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	+