

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

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Version 2009.1.0

## Endocrine Therapy of Metastatic Breast Cancer

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- **Version 2002:**  
**Gerber / Friedrichs**
- **Version 2003–2008:**  
**Fersis / Friedrich / Gerber / Huober / Janni  
/ Kaufmann / Nitz / Schneeweiß**
- **Version 2009:**  
**Lück / Jonat**

Further  
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# Endocrine Therapy in Metastatic Breast Cancer

## Indication

**Oxford LoE: 1a**

**GR: A**

**AGO: ++**

**Endocrine therapy represents the first choice for metastatic breast cancer with positive (unknown) hormone receptor status.**

- **Exception: acute life threatening disease**
- **Cave: HR might change during the course of the disease. Histology of recurrent site should be obtained, when possible**

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# Comparison HR and HER-2 Metastasis vs. Primary Tumor

- **29 pts. with evaluable histopathological result in primary tumor and metastasis**
- **40% differ with respect to HR-Status**
- **8% differ with respect to HER-2 expression**
- **Biopsy of metastasis lead to change of treatment strategy in 20% of all pts. (6/29,  $p=0.002$ )**

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# Endocrine Therapy in Premenopausal Patients with HER-2 Negative Metastatic Breast Cancer

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	Oxford / AGO LoE / GR		
➤ <b>GnRHa + tamoxifen (vs. OFS or Tam)</b>	<b>1a</b>	<b>A</b>	<b>++</b>
➤ <b>Ovarian function suppression (OFS)</b>	<b>2b</b>	<b>B</b>	<b>+</b>
➤ <b>Tamoxifen</b>	<b>2b</b>	<b>B</b>	<b>+</b>
➤ <b>GnRHa + AI after GnRHa + Tam</b>	<b>2b</b>	<b>B</b>	<b>+</b>
➤ <b>Aromatase inhibitors without OFS</b>	<b>3</b>	<b>D</b>	<b>--</b>

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# Endocrine Therapy in HER-2 Negative Metastatic Breast Cancer

## Drugs for postmenopausal patients

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➤ <b>Aromatase inhibitors</b> (3rd gen) ( <b>&gt; Non-AI*</b> )	<b>1a</b>	<b>a</b>	<b>++</b>
➤ <b>Tamoxifen (vs no therapy)</b>	<b>1a</b>	<b>a</b>	<b>++</b>
➤ <b>Fulvestrant (= AI)</b>	<b>2b</b>	<b>b</b>	<b>+</b>
➤ <b>Toremifen (= tamoxifen)</b>	<b>1a</b>	<b>a</b>	<b>+/-</b>
➤ <b>MPA/MA (&lt; aromatase inhibitors)</b>	<b>1a</b>	<b>a</b>	<b>+/-</b>

\*There is no evidence for superiority of a single aromatase inhibitor.

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# Cochrane Meta-Analysis 2007 AI vs. Non-AI in MBC

- **Totally, 25 trials were analyzed**
- **Subject: AI (any) vs. non-AI-treatment in MBC pts.**
- **9,416 patients**
- **Significant overall survival benefit (HR 0.88, (95% CI 0.80 to 0.96))**
- **HR similar for all three AIs**

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# Cochrane Meta-Analysis 2007 AI vs. Non-AI in MBC

- **Data for PFS not significant (HR 0.92, 95% CI 0.75 - 1.13); significant heterogeneity**
- **Significantly higher rate of CB (HR 0.78, 95% CI 0.63 to 0.96)**
- **Significantly higher objective response rate (HR 0.77, 95% CI 0.62 to 0.96)**

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# Endocrine Therapy in HER-2 Negative Metastatic Breast Cancer

## Drugs for postmenopausal patients pretreated by adjuvant tamoxifen or nothing

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➤ <b>Aromatase inhibitors</b> (3rd gen) (> non-AI*)	1a A ++
➤ <b>Tamoxifen (vs no therapy)</b>	1a A ++
➤ <b>Fulvestrant (= AI)</b>	2b B +
➤ <b>Toremifen (= tamoxifen)</b>	1a A +/-
➤ <b>MPA/MA (&lt; AI)</b>	1a A +/-

\*There is no evidence for superiority of a single aromatase inhibitor.

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# Endocrine Therapy in Postmenopausal HER-2 Negative Metastatic Breast Cancer Patients after Adjuvant Tamoxifen



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<b>1<sup>st</sup> line: aromatase inhibitors (3rd gen)*</b>	<b>1a A ++</b>
<b>AI and celecoxib</b>	<b>2b B -</b>
<b>2<sup>nd</sup> line: fulvestrant</b>	<b>2b B +</b>
<b>tamoxifen</b>	<b>3b C +</b>
<b>aromatase inhibitor**</b>	<b>2b B +</b>
<b>Further lines: MPA/MA</b>	<b>4 D +</b>
<b>repeating of previous treatments</b>	<b>5 D +</b>

To date, there is no evidence for superiority of a single aromatase inhibitor.

\*\* steroidal or non-steroidal depending on previous AI

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<b>1<sup>st</sup> line: tamoxifen</b>	<b>2b</b>	<b>B</b>	<b>++</b>
steroidal after non-steroidal AI			
non-steroidal after steroidal AI	<b>2b</b>	<b>B</b>	<b>+</b>
<b>2<sup>nd</sup> line: fulvestrant</b>	<b>2b</b>	<b>B</b>	<b>+</b>
tamoxifen (if previously not given)	<b>5</b>	<b>D</b>	<b>+</b>
<b>Further lines:</b>			
MPA/MA	<b>4</b>	<b>C</b>	<b>+</b>
repeating of previous treatments	<b>5</b>	<b>D</b>	<b>+/-</b>

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# Endocrine Therapy in Postmenopausal HER-2 negative Metastatic Breast Cancer Patients after Adjuvant AI



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## 1<sup>st</sup> line:

- tamoxifen

2b B ++

## 2<sup>nd</sup> line (alternatives):

- fulvestrant

2b B +

- steroidal after non-steroidal AI

2b B +

- non-steroidal after steroidal AI

2b B +

- tamoxifen (if previously not given)

5 D +

## Further lines:

- MPA/MA

4 C +

- repeating of previous treatments

5 D +/-

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# Endocrine Therapy in Postmenopausal HER-2 Neg. Metastatic Breast Cancer Pts. after Switch Adjuvant Tamoxifen → AI

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## If short treatment free intervall:

- |                        |   |   |     |
|------------------------|---|---|-----|
| ➤ fulvestrant          | 4 | D | +   |
| ➤ aromatase inhibitor* | 4 | D | +   |
| ➤ tamoxifen            | 4 | D | +/- |

## If treatment free intervall > 1 year:

- |                        |   |   |     |
|------------------------|---|---|-----|
| ➤ tamoxifen            | 4 | D | +   |
| ➤ aromatase inhibitor* | 4 | D | +   |
| ➤ fulvestrant          | 4 | D | +/- |

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\* Steroidal or non-steroidal depending on previous AI

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## HER-2 Positive and HR-Positive Metastatic Breast Cancer

START

# Lapatinib + Letrozole vs. Letrozole

## Postmenopausal HR+ Metastatic Breast Cancer: First Analysis of EGF30008

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	HER 2+ Patientinnen N= 219		ITT N= 1286	
	LET	LET + Lap	LET	LET + Lap
PFS	3,0 Monate	8,2 Monate	10,9 Monate	11,9 Monate
	Hazard Ratio = 0,71 [95%CI 0,53, 0,96], p=0,019		Hazard Ratio = 0,86 [95% CI: 0,76 - 0,98], p=0,026)	
ORR	14,8%	37,9%		
	Odds Ratio = 0,4 [0,2 - 0,9], p=0,021			
Clinical Benefit Rate	28,7%	48,7%		
	OR=0,4 [0,2 - 0,8], p=0,003)			
OS	HR=0,77 [95% CI:0,52 - 1,14], p=0,185			

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# Endocrine Therapy in Postmenopausal HER-2 Positive Metastatic Breast Cancer Patients

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**Anastrozole and trastuzumab**

**2b<sup>a</sup> B +/-**

**Letrozole and lapatinib**

**2b<sup>a</sup> B +/-**

**Consider chemotherapy + anti-HER-2-therapy!**

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# Concomitant or Sequential Endocrine-Cytostatic Treatment

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## ➤ Concomitant endocrine-cytotoxic treatment

1b A - -

- Increases response rates without prolongation of progression free interval or overall survival
- Increases toxicity

## ➤ Maintenance endocrine therapy after chemotherapy induced response

3 C ++

- Increases progression free interval and overall survival

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