Endocrine and “Targeted” Therapy in Metastatic Breast Cancer
Endocrine Therapy of Metastatic Breast Cancer

- **Version 2002:**
  Gerber / Friedrichs

- **Versionen 2003–2016:**
  Albert / Bischoff / Dall / Fersis / Friedrich / Gerber / Huober / Janni / Jonat / Kaufmann / Liedtke / Loibl / Lück / von Minckwitz / Möbus / Müller / Mundhenke / Nitz / Schneeweß / Schütz / Stickeler

- **Version 2017:**
  Schmidt / Thill
Endocrine Therapy in Metastatic Breast Cancer

Indication

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

Endocrine-based therapy represents the first choice for metastatic breast cancer with positive (or unknown) hormone receptor (HR) status.

- Exception: acute life-threatening disease
- Caveat: HR might change during the course of disease. Histology of recurrent site should be obtained whenever possible
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
Within all lines of treatment, treatment options should take previous endocrine therapies, age and comorbidities into consideration as well as respective approval status.
# Endocrine Therapy in Premenopausal Patients with HER2-Negative Metastatic Breast Cancer

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Oxford / AGO LoE / GR</th>
</tr>
</thead>
<tbody>
<tr>
<td>GnRHa + Fulvestrant + Palbociclib</td>
<td>2b B ++</td>
</tr>
<tr>
<td>GnRHa + AI + Palbociclib</td>
<td>5 D +</td>
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<tr>
<td>GnRHa + tamoxifen (vs. OFS or Tam)</td>
<td>1a A ++</td>
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<tr>
<td>Ovarian function suppression (OFS)</td>
<td>2b B +</td>
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<tr>
<td>Tamoxifen</td>
<td>2b B +</td>
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<tr>
<td>GnRHa + AI (first or second line)</td>
<td>2b B +</td>
</tr>
<tr>
<td>GnRHa + Fulvestrant</td>
<td>1b B +</td>
</tr>
<tr>
<td>Aromatase inhibitors without OFS</td>
<td>3 D - -</td>
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</tbody>
</table>

- **GnRHa**: GnRH antagonists
- **AI**: aromatase inhibitors
- **OFS**: ovarian function suppression
Endocrine Therapy in Postmenopausal Patients with HER2-Negative Metastatic Breast Cancer

*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 preferred in first line.

- Letrozole + Palbociclib
- Fulvestrant 500 mg + Palbociclib
- Fulvestrant 500 mg
- Aromatase inhibitors (3rd generation)*
- Tamoxifen
- Exemestane + Everolimus
- Tamoxifen + Everolimus
- Letrozole + Everolimus
- Fulvestrant + Everolimus
- Fulvestrant 250 mg + Anastrozole
- Repeat prior treatments

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

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

Oxford / AGO
LoE / GR

1b B +/-
HER2 Positive and HR-Positive Metastatic Breast Cancer
Endocrine Therapy in Postmenopausal HER2-Positive Metastatic Breast Cancer Patients

- 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

- Concomitant endocrine-cytotoxic treatment
  - May increase response rate and progression free interval but not overall survival
  - May increase toxicity
- Maintenance endocrine therapy after chemotherapy induced response
  - Increases progression free interval

Oxford / AGO LoE / GR

1b A -
2b B +
Endocrine and “Targeted” Therapy in Metastatic Breast Cancer (2/11)

No further information

No references
Endocrine and “Targeted” Therapy in Metastatic Breast Cancer (3/11)

No further information

References:

Comparison ER/PR and HER2 Metastasis vs. Primary Tumor (4/11)

No further information

References:

No further information

References:


**Endocrine Therapy in Premenopausal Patients with HER2-Negative Metastatic Breast Cancer (6/11)**

No further information

**References:**

GnRHa plus fulvestrant plus palbociclib


GnRHa plus tamoxifen (vs. OFS or tam)

Ovarian function suppression (OFS), tamoxifen


GnRHa plus AI (first or second line)


GnRHa plus fulvestrant

Endocrine Therapy in Postmenopausal Patients with HER2-Negative Metastatic Breast Cancer (7/11)

No further information

References:

Letrozole and palbociclib (vs. letrozole alone)


Fulvestrant 500 mg plus Palbociclib (vs. Fulvestrant alone)

**Fulvestrant 500 mg (vs. anastrozole)**


**Fulvestrant 500 mg >> 250 mg**


**Aromatase inhibitors (3rd generation)**


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

1. Bonneterre, J, Buzdar, A, Nabholtz, JA, Robertson, JFR, Thuerlimann, B, von Euler, M. Anastrozole is superior to tamoxifen as first-line therapy in hormone receptor positive advanced breast carcinoma. Cancer 2001 92

Exemestane and everolimus (vs. exemestane alone)

Tamoxifen and everolimus


Fulvestrant and everolimus


Letrozole and everolimus

Endocrine Therapy in Postmenopausal HER2-Negative Metastatic Breast Cancer Patients in Combination with Bevacizumab (8/11)

No further information

References

Maintenance of bevacizumab plus endocrine therapy


Bevacizumab plus endocrine treatment as first line


Endocrine Therapy in Postmenopausal HER2-Positive Metastatic Breast Cancer Patients (10/11)

No further information

References

Anastrozole and trastuzumab


Letrozole and trastuzumab


Letrozole and lapatinib


Fulvestrant and lapatinib

AI and trastuzumab/pertuzumab

1. Arpino G, Ferrero J-M, de la Haba-Rodriguez J, Easton V, Schuhmacher C, Restuccia E, Rimawi M. Primary analysis of PERTAIN: 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
Concomitant or Sequential Endocrine-Cytostatic Treatment (11/11)

No further information

References:

Concomitant endocrine-cytotoxic treatment


Maintenance endocrine therapy after chemotherapy induced response