Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

Endocrine Therapy of Metastatic Breast Cancer
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
# Endocrine Therapy in Metastatic Breast Cancer

## Indication

<table>
<thead>
<tr>
<th>Oxford LoE: 1a</th>
<th>GR: A</th>
<th>AGO: ++</th>
</tr>
</thead>
</table>

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**

---


### 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

---


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

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

* Extrapolated from data of postmenopausal patients (with AI)

GnRHa plus fulvestrant plus palbociclib


GnRHa plus AI/Tamoxifen plus ribociclib

1. Tripathy D et al. First-line ribociclib vs placebo with goserelin and tamoxifen or a non-steroidal aromatase inhibitor in premenopausal women with hormone receptor-positive, HER2-negative advanced breast cancer: Results from the randomized phase III MONALEESA-7 trial. SABCS 2017, GS-2

GnRHa plus tamoxifen (vs. OFS or tam)

Ovarian function suppression (OFS), tamoxifen


GnRHa plus AI (first or second line)


GnRHa plus fulvestrant


Fulvestrant 500 mg (vs. anastrozole)


Fulvestrant 500 mg >> 250 mg


Aromatase inhibitors (3rd generation)*


2. Thürlimann B, et al: Anastrozole (Arimidex) versus tamoxifen as first-line therapy in postmenopausal women with advanced breast cancer: results of the double-blind cross-over SAKK trial 21/95 – a substudy of the TARGET (Tamoxifen or Arimidex Randomized Group Efficacy and Tolerability) trial. Breast Cancer Res
Aromatase inhibitors (3rd generation) (>non-AI)
1. Bonneterre, J, et al. Anastrozole is superior to tamoxifen as first-line therapy in hormone receptor positive advanced breast carcinoma Cancer 2001 92
Letrozole and palbociclib (vs. letrozole alone)

Fulvestrant 500 mg plus Palbociclib (vs. Fulvestrant alone)

Letrozol plus Ribociclib

Fulvestrant plus Abemaciclib
Non-steroidal AI plus Abemaciclib

Exemestane and everolimus (vs. exemestane alone)

Tamoxifen and everolimus

Fulvestrant and everolimus
1. Kornblum NS, et al. PrECOG 0102: A randomized, double-blind, phase II trial of fulvestrant plus everolimus or placebo in post-menopausal women with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) resistant to aromatase inhibitor (AI) therapy. SABCS 2016,#S1-02

Letrozole and everolimus

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

- Bevacizumab plus endocrine treatment as first line therapy for advanced disease
  
  Oxford LoE GR AGO
  1b B +/-

Maintenance of bevacizumab plus endocrine therapy


Bevacizumab plus endocrine treatment as first line


Olaprib

Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

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

**Anastrozole and trastuzumab**


**Letrozole and trastuzumab**


Letrozole and lapatinib

Fulvestrant and lapatinib

AI and trastuzumab/pertuzumab
1. Arpino G, et al. 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

- **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

<table>
<thead>
<tr>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1b</td>
<td>A</td>
<td>-</td>
</tr>
<tr>
<td>2b</td>
<td>B</td>
<td>+</td>
</tr>
</tbody>
</table>

Concomitant endocrine-cytotoxic treatment


Maintenance endocrine therapy after chemotherapy induced response
