Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Sites of Metastases
Sites of Metastases

- Liver and lung metastases
- Malignant pleural and pericardial effusions
- Ascites
- Bone marrow involvement
- Soft tissue metastases
- Contralateral axillary metastasis

See also chapters „CNS Metastases“ and „Locoregional Recurrence“ (Loco-Regional Recurrence Treatment Options in Non Curative Cases)” and „Osteo-oncology“
General Treatment Aspects of Metastases

- **Histological verification**
  - Oxford: LoE 3, GR B, AGO ++

- **Cytological verification, if histology not possible**
  - Oxford: LoE 3, GR B, AGO +

- **Systemic therapy preferred**
  - Oxford: LoE 2a, GR B, AGO ++*

- **Consider surgery of metastases in case of good response to palliative treatment, oligometastases** (cave: no clear definition available)
  - Oxford: LoE 2b, GR C, AGO +/-

- **Stereotactic Radiotherapy for patients with oligometastases**
  - Oxford: LoE 2b, GR B, AGO +/-

- **Local-interventional ablative procedure**
  - Oxford: LoE 3b, GR C, AGO +/-

- **Local treatment in the case of pain, exulceration, persistence after systemic treatment, bowel obstruction, hydrocephalus occlusus, spinal cord compression**
  - Oxford: LoE 5, GR D, AGO +/-

- **Systemic treatment after surgery**
  - Oxford: LoE 2c, GR B, AGO ++

* See chapters with systemic treatment recommendations

**Wording**

Stereotactic Therapy can be referred to as:

- SBRT
- Stereotactic Body Radiation Therapy
- SABR
- Stereotactic Ablative Radiotherapy
- IGRT
- Image Guided Radiation Therapy

**Histology**


**Local surgery**


8. Khan SA Plenary Session ASCO 2020 Late Breaking Abstract 2


Radiotherapy in oligometastatic breast cancer
Overviews

Combined surgery of the primary side and metastasis
### Different Definitions of Oligometastatic Disease (OMD)

<table>
<thead>
<tr>
<th>Societies / Organisations or inclusion criteria of prospective clinical trials (selection)</th>
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</thead>
<tbody>
<tr>
<td><strong>ESMO</strong></td>
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<tr>
<td><strong>ESTRO/ASTRO</strong></td>
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<tr>
<td><strong>ESTRO/EORTC OligoCare project</strong></td>
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<tr>
<td><strong>ABC-7</strong></td>
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<tr>
<td><strong>SABR-COMET trial</strong>&lt;sup&gt;1&lt;/sup&gt; (NCT03784428)</td>
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<tr>
<td><strong>NRG-BR002 trial</strong>&lt;sup&gt;2&lt;/sup&gt; (NCT02364557)</td>
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<tr>
<td><strong>OLIGOMA trial</strong>&lt;sup&gt;3&lt;/sup&gt; (NCT04495309)</td>
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</tbody>
</table>

4. **ABC-7 consensus:** Cardoso F et al., Breast 2024 (in preparation)
Local Therapy in Primary Metastatic Disease

- **Surgery (R0) of the primary tumor (individualized procedure in case of oligometastatic disease)**
  - In case of bone metastases only
  - In case of visceral metastases
  - Axillary surgery for cN1
  - Sentinel biopsy if cN0
  - Radiotherapy of the primary tumor
    - Alone (without surgery)
    - After local surgical treatment with BCS or mastectomy (according to adjuvant indication)

**Oxford LoE GR AGO**

- In case of bone metastases only 1b B +/-
- In case of visceral metastases 1b B -
- Axillary surgery for cN1 3b B +/-
- Sentinel biopsy if cN0 5 D -
- Radiotherapy of the primary tumor
  - Alone (without surgery) 3a C +/-
  - After local surgical treatment with BCS or mastectomy (according to adjuvant indication) 2c B +/-

**Surgery of the primary tumor (R0)**
5. Khan SA Plenary Session ASCO 2020 Late Breaking Abstract 2
8. Kahn SA. Educational Session SABCS 2021, Thursday 9th Dec; Session: Local Therapy of the Primary and Beyond in Patients with Advanced Disease, Presentation: Local therapy of the primary tumor in de novo Stage IV breast cancer.

Axillary surgery

Primary metastatic breast cancer - Locoregional therapy (local RT vs. surgery + RT vs. surgery)
1. Khan SA Plenary Session ASCO 2020 Late Breaking Abstract 2
2. Kahn SA. Educational Session SABCS 2021, Thursday 9th Dec; Session: Local Therapy of the Primary and Beyond in Patients with Advanced Disease, Presentation: Local therapy of the primary tumor in de novo Stage IV breast cancer.
### Liver Metastases
#### Local Therapy

<table>
<thead>
<tr>
<th>Method</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resection of liver metastases (R0)</td>
<td>3a</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>- HR-positive: chemotherapy-sensitive, long disease-free interval,</td>
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<tr>
<td>absence of extrahepatic disease, ≤ 3 metastases</td>
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<tr>
<td>- HER2-positive: age &lt; 50 y, metastases &lt; 5 cm, no further metastases</td>
<td></td>
<td></td>
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<tr>
<td>Interventional regional chemotherapy (TACE)*</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>Interventional regional radiotherapy (SIRT/TARE)*</td>
<td>3a</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Stereotactic Radiotherapy with VMAT (SRS-VMAT), other modalities*</td>
<td>2a</td>
<td>B</td>
<td>+/-</td>
</tr>
<tr>
<td>Regional ablative procedures (RFA, MWA)</td>
<td>3b</td>
<td>C</td>
<td>+/-</td>
</tr>
<tr>
<td>- IRE, LITT, HIFU</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>- Cryoablation</td>
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</tbody>
</table>

* interdisciplinary decision

CA = cryoablation  
HIFU = high-intensity focused ultrasound  
IRE = irreversible electroporation  
LITT = laser-induced interstitial thermotherapy  
MWA = microwave ablation  
RFA = radiofrequency ablation  
SIRT = selective internal radiotherapy = TARE  
SRS = stereotactic radiosurgery with volumetric modulated arc therapy (VMAT)  
TACE = transarteriel chemoembolization  
TARE = transarteriel radioembolization

**Statements:**

Resection of liver metastasis (R0)  
HR positive: chemotherapy sensible, long disease-free interval, absence of extrahepatic disease, ≤ 3 metastases

Her2 positive: age < 50 y., metastasis < 5 cm, no further metastases
Diagnostics

Overview

Local surgery
Statement: Regional chemotherapy

Statement: Regional radiotherapy
7. Ridouani F, Soliman MM, England RW et al. Relationship of radiation dose to efficacy of radioembolization of liver metastasis from


Statement: Thermoablation


Overview


Resection of pulmonary metastases by VATS or conventional resection


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**Pulmonary Metastases**

**Local Therapy**

- Before any local therapy: staging and biopsy, histology for exclusion of second tumor
  - Oxford LoE B AGO

- Resection of pulmonary metastases by VATS or conventional resection
  - In case of multi-locular metastatic disease
    - Oxford LoE B AGO
  - In case of single / few unilateral metastasis
    - Oxford LoE B AGO

- Thermoablation (CT-guided RFA, LITT)
  - Oxford LoE C AGO

- Regional radiotherapy
  - (stereotactic radiotherapy with volumetric intensity modulated arc therapy (SRS-VMAT))
    - Oxford LoE B AGO

* VATS = video-assisted thoracic surgery
**Statement: Thermoablation (CT-guided RFA, LITT)**


**Statement: Regional Radiotherapy**

If expected survival is short, less invasive procedures should be considered


VATS and Talcum-pleurodesis

Chemical pleurodesis

Talcum powder

Bleomycin, Doxycycline, Mitoxantrone

Povidone-iodine (20 ml of 10% solution)

Serial thoracocentesis


Statement: Continuous pleural drainage

Statement: Intrathoracic chemotherapy
# Malignant Ascites

## Local Therapy

<table>
<thead>
<tr>
<th>Ascites:</th>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
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</thead>
<tbody>
<tr>
<td>Puncture, drainage in symptomatic patients</td>
<td>4</td>
<td>D</td>
<td>++</td>
</tr>
<tr>
<td>Continuous drainage of ascites</td>
<td>3b</td>
<td>D</td>
<td>+</td>
</tr>
<tr>
<td>Systemic therapy</td>
<td>3b</td>
<td>D</td>
<td>++</td>
</tr>
<tr>
<td>Local chemotherapy</td>
<td>3b</td>
<td>D</td>
<td>-</td>
</tr>
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**Bone Marrow Infiltration Associated with Pancytopenia**

<table>
<thead>
<tr>
<th>Weekly chemotherapy with*</th>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epirubicin, Doxorubicin, Paclitaxel</td>
<td>4</td>
<td>D</td>
<td>++</td>
</tr>
<tr>
<td>Capecitabine</td>
<td>4</td>
<td>D</td>
<td>++</td>
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<tr>
<td>HER2-positive:</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>anti-HER2-treatment</td>
<td>5</td>
<td>D</td>
<td>++</td>
</tr>
<tr>
<td>Hormone receptor-positive:</td>
<td></td>
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<tr>
<td>Endocrine-based therapy</td>
<td>3b</td>
<td>C</td>
<td>+</td>
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</table>

* Consider pre-treatment
## Soft Tissue Metastasis

### Local Therapy

<table>
<thead>
<tr>
<th>Oxford LoE</th>
<th>GR</th>
<th>AGO</th>
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<tbody>
<tr>
<td>4</td>
<td>C</td>
<td>+/-</td>
</tr>
</tbody>
</table>

- **Surgery of limited locoregional metastasis** (e.g. skin, muscular, nodal) with complete resection (R0) after exclusion of further metastases
- **Radiotherapy in***:
  - Soft tissue metastases 3b C +/-
  - Paresis, spinal cord compression 2b C ++
  - Plexus infiltration 3b C ++

* Exception: acute indication for surgery

Oligo-Metastases
Contralateral Axillary Metastasis

“Contralateral axillary nodal metastasis (in the absence of contralateral primary) as initial diagnosis of recurrent disease is considered stage 4 metastatic breast cancer. However, after prior local therapy to ipsilateral axilla for early breast cancer, subsequent metachronous contralateral axillary nodal metastasis, either alone or concurrent with an in-breast ipsilateral recurrence, could be considered and treated as a regional metastasis (due to altered lymphatic drainage), and has the potential for long survival or cure with a multidisciplinary approach”

ABC-7 (2023): LoE: Expert opinion/NA (85%)

4. SABCS 2021 Educational Session Local Therapy of the Primary and Beyond in Patients with Advanced Disease
5. ABC-7 consensus: Cardoso F et al., Breast 2024 (in preparation)