Specific Sites of Metastases
Specific Sites Of Metastases
Local Approaches to Metastatic Disease

- **Version 2002:**
  Dall / Fersis / Friedrich

- **Versions 2003–2015:**
  Bauerfeind / Bischoff / Böhme / Brunnert / Diel / Fehm / Friedrich / Friedrichs / Gerber / Hanf / Janni / Lück / Maass / Oberhoff / Rezai / Schaller / Seegenschmiedt / Solomayer / Souchon

- **Version 2016:**
  Lux / Schütz
Specific Sites of Metastases

- Liver and lung metastases
- Malignant pleural and pericardial effusions
- Ascites
- Bone marrow involvement
- Soft tissue metastases
- Any other organs

- Consider also chapter „CNS Metastases“ and „Locoregional Recurrence (Loco-Regional Recurrence Treatment Options in Non Curative Cases)“
General Aspects of Metastases Surgery or Ablation

- Histological / cytological verification
- Systemic treatment preferred
- Consider surgery only in case of good response to palliative treatment
- Metastases surgery is an option in good condition pts. with late onset oligometastases
- Surgical treatment in the case of pain, exulceration, persistence after systemic treatment, bowel obstruction, hydrocephalus occlusus, spinal cord compression
- Systemic treatment after surgery

* See chapters with systemic treatment recommendations
Local Therapy in Primary Metastatic Disease

- Local surgical treatment (R0) of primary tumor
- Axillary surgery for cN1
- Sentinel in cN0
- Local radiotherapy of primary tumor
  - Alone
  - After local surgical treatment with BCS or mastectomy and indication

Oxford / AGO

<table>
<thead>
<tr>
<th>Levels</th>
<th>LoE</th>
<th>Evidence</th>
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<tbody>
<tr>
<td>1b</td>
<td>B</td>
<td>+/-</td>
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<tr>
<td>5</td>
<td>C</td>
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<td>5</td>
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<td>3a</td>
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<td>3a</td>
<td>C</td>
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Liver Metastasis
Local Therapy

- Resection of liver metastasis (R0)
  HR positive: chemotherapy sensitive, long disease-free interval, absence of extrahepatic disease, ≤ 3 metastases
  HER2 positive: age < 50 y., metastasis < 5 cm, no further metastases

- Regional chemotherapy

- Regional radiotherapy
  [SIRT, stereotactic body radiosurgery with volumetric intensity modulated arc therapy (SRS-VMAT), radiochemoembolization, other modalities]

- Thermoablation
  (RFA, LITT, cryotherapy)
Pulmonary Metastases
Local Therapy

- Before surgery: staging and biopsy (fine-needle aspiration with CT-guidance or transbronchial needle aspiration) 3a B +
- Resection of pulmonary metastases by VATS or conventional resection
  - In case of multilocular metastatic disease 3a B -
  - In case of single metastases on one side with curative intent 3a B +/-
- Thermoablation (CT-guided RFA, LITT) 3b C +/-
- Regional radiotherapy 4 C +/-

(e.g. stereotactic body radiosurgery with volumetric intensity modulated arc therapy (SRS-VMAT))
Malignant Pleural Effusions (MPE)

Incidence:
- ~ 10% of all breast cancer patients
- ~ 50% of patients with advanced breast cancer
- ~ 30% of all MPE are caused by breast cancer

Clinical presentation:
- Extensive MPE are mostly due to malignancy
- The majority of MPE are symptomatic [dsypnea (80%), dull chest pain (30%), nonproductive cough (10%)]
- Survival is related to the presence of additional metastases, age, ECOG PS and extent of involving the pleural surface

Diagnostic procedures:
- Clinical examination
- Imaging techniques (chest X-Ray, US, CT-Scan)
- Proven malignant effusion [cytology (→ 50% false negative), histology by thoracoscopy]
Malignant Pleural Effusion (MPE)
Local Therapy

- If expected life time is short, less invasive procedures should be considered
  - 4 C ++
- VATS and Talcum-pleurodesis*
  - 1b B ++
- Chemical pleurodesis*
  - Talcum powder
    - 1a B +
  - Bleomycin, Doxycycline, Mitoxantrone
    - 2b C +/-
  - Povidone-iodine (20 ml of 10% solution)
    - 1b B +
- Continuous pleural drainage
  - 2a B +
- Systemic treatment after pleurodesis
  - 3b C +/-
- Local antibody therapy (i.e. Catumaxomab)
  - 3b C -
- Serial thoracocentesis
  - 4 C +/-

* Adequate pain-relief
VATS: video-assisted thoracoscopic surgery
## Malignant Ascites

### Local Therapy

<table>
<thead>
<tr>
<th>Ascites:</th>
<th>Oxford / AGO LoE / GR</th>
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<tbody>
<tr>
<td>Puncture, drainage in symptomatic patients</td>
<td>4 D ++</td>
</tr>
<tr>
<td>Systemic therapy</td>
<td>3b D ++</td>
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<tr>
<td>Local chemotherapy</td>
<td>3b D +/-</td>
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<tr>
<td>Local antibody therapy (i.e. Catumaxomab)</td>
<td>3b D +/-</td>
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</tbody>
</table>
Malignant Pericardial Effusion
Local Therapy

Symptomatic pericardial effusion:

- Drainage, fenestration: 3b B ++
- VATS (video-assisted thorac. surgery): 4 D +
- US-guided puncture + instillation of mitoxantrone, cisplatin: 4 D +/-
Bone Marrow Involvement
Associated with Pancytopenia

- Weekly chemotherapy with*:
  - Epirubicin, Doxorubicin, Paclitaxel
  - Capecitabine

- HER2 pos.: add anti-HER2 treatment

* Consider pre-treatment

Oxford / AGO LoE / GR

4 D ++

4 D ++

5 D ++
Soft Tissue Metastasis
Local Therapy

Surgery in locoregional limited metastatic disease (skin, muscular, nodal) in case of complete resection (R0) and no further metastases after staging

Radiotherapy (if no immediate surgery is indicated or even after surgery):

- Paresis, spinal cord compression  
  2b C ++
- Plexus infiltration  
  3b C ++
- Soft tissue metastasis  
  3b C +
Specific Sites of Metastases (2/13)

No further information

No references
No further information

No references
General Aspects of Metastases Surgery or Ablation (4/13)

No further information

References:

17. Soran A et al. Early follow up of a randomized trial evaluating resection of the primary breast tumor in women presenting with de novo stage IV breast cancer; Turkish study (protocol MF07-01) SABCS [S2-03], 2013
Local Therapy in Primary Metastatic Disease (5/13)

Further information and references:

Statements:
Local surgical treatment (R0) of primary tumor (1bB +/-)

Statement: Axillary surgery for cN1 (5 C +/-)

Statement: Sentinel in cN0 (5 C -)

Statements:
Local radiotherapy of primary tumour
Alone  (3a C +/-)
After local surgical treatment with BCS or mastectomy and indication (3a C +)

9. Soran A et al. Early follow up of a randomized trial evaluating resection of the primary breast tumor in women presenting with de novo stage IV breast cancer; Turkish study (protocol MF07-01) SABCS [S2-03], 2013
Liver Metastasis - Local Therapy (6/13)

Further information and references:

Vote result of the AGO recommendation (complete slide without further changes): yes = 23/ no = 2

Statements:
Resection of liver metastasis (R0) (3a B+/-)
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


**Statement: Regional chemotherapy (3b C +/-)**


Statement: Regional radiotherapy (4 C +/-)


Thermoablation (3b C +/-)


Pulmonary Metastases Local Therapy (7/13)

Further information and references:

Vote result of the AGO recommendation (complete slide without further changes): yes = 20/ no = 1

Statements:
Before surgery: staging and biopsy (fine-needle aspiration with CT-guidance or transbronchial needle aspiration) (3a B +)

Resection of pulmonary metastases by VATS or conventional resection
In case of multilocular metastatic disease (3a B -)
In case of single metastases on one side with curative intent (3a B +/-)


**Statement: Thermoablation (CT-guided RFA, LITT) (3b C +/-)**


**Statement: Regional radiotherapy (4 C +/-)**


Malignant Pleural Effusion (8/13)

No further information

References:

1. Shaw P, Agarwal R. Pleurodesis for malignant pleural effusions. Cochrane Database of Systematic Reviews 2004,
   Apr;189(2):151-5.
   May;110(18):313-8.
4. Zamboni MM, da Silva CT Jr, Baretta R, Cunha ET, Cardoso GP. Important prognostic factors for survival in
5. Li Z, Pantanowitz L, Khalbuss WE, Arya P, Monaco SE. Challenges in diagnosing metastatic breast carcinoma in
Malignant Pleural Effusion - Local Therapy (9/13)

Further information and references:

Vote result of the AGO recommendation (complete slide without further changes): yes = 19/ no = 1

Statement: If expected survival is short, less invasive procedures should be considered (4 C ++)


Statements:
- VATS and Talcum-pleurodesis (1b B ++)
- Chemical pleurodesis
- Talcum powder (1a B +)
- Bleomycin, Doxycycline, Mitoxantrone (2b C +/-)
- Povidone-iodine (20 ml of 10% solution) (1b B +)
- Serial thoracocentesis (4 C +/-)


**Statement:** Continous pleural drainage (2a B +)


**Statement:** Systemic treatment after pleurodesis (3b C +/-)

**Statement:** Local antibody therapy (i.e. Catumaxomab) (3b C -)

Malignant ascites are the cancer-associated accumulation of fluids in the peritoneal cavity. The cancers most commonly associated to ascites are ovarian (37%), pancreato-biliary (21%), gastric (18%), oesophageal (4%), colorectal (4%), and breast (3%). After histological confirmation and re-evaluation of receptors the most effective treatment consists in adequate systemic treatment. Management of malignant ascites takes place in the context of palliative care and aims at improving the quality of life of these patients. Patients with symptomatic ascites should undergo drainage. Local antibody therapy with catumaxomab remains an option in individual cases. It has to be paid attention to the side effects.

References:

Malignant Pericardial Effusion - Local Therapy (11/13)

Further information:

Malignant pericardial effusion and cardiac tamponade remains a rarity, which are known complications of many advanced malignancies such as breast cancer, lung cancer, lymphomas and leukemias. In general overall survival is low, due to other metastatic localizations. The standard treatment of malignant effusion and cardiac tamponade has not yet been defined. Physicians should consider the status and the prognosis of each case.

In symptomatic patients drainage and fenestration are the treatment options of choice. VATS is an alternative treatment option. In individual cases US-guided puncture with instillation of mitoxantrone is possible.

References:

Bone Marrow Involvement Associated with Pancytopenia (12/13)

Further information:

The choice between supportive care or specific anticancer treatment for poor performance status (PS) breast cancer patients with multimetastatic disease and pancytopenia due to bone marrow involvement (BMI) often remains a clinical dilemma. If hormonal treatment options have been exhausted, concomitant weekly low-dose chemotherapy (anthracycline, paclitaxel or cabecitabine) and either bisphosphonates or RANK-Ligands antibodies are indicated. Low-dose chemotherapy with epirubicin or paclitaxel as well as treatment with anti-HER2-therapy is the therapy of choice for patients with bone marrow involvement and pancytopenia. Otherwise it has been reported that even in patients with severe BMI-associated cytopenia, aggressive combination treatment regimens were effective, since most patients show improved marrow function after chemotherapy and long-lasting survival is possible.

References:

Soft Tissue Metastasis - Local Therapy (13/13)

Further information:

Local radiotherapy is the most important treatment for patients with paresis or spinal cord compression, who cannot be operated or have failed to systemic treatment. Even after surgery a concomitant radiotherapy and a systemic treatment is indicated. Plexus infiltration and other inoperable soft tissue metastasis should be treated by radiotherapy.

References: