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

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

- **Versionen 2003–2016:**
  Bauerfeind / Bischoff / Böhme / Brunnert / Diel / Fehm / Friedrich / Friedrichs / Gerber / Hanf / Janni / Lück / Lux / Maass / Oberhoff / Rezai / Schaller / Schütz / Seegenschmiedt / Solomayer / Souchon

- **Version 2017:**
  Thomssen / Bischoff
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
Surgery or Ablation of Metastases

- Histological / cytological verification
- Systemic treatment preferred
- Consider surgery only in case of good response to palliative treatment
- Metastases surgery is an option for pts in good conditions with late onset oligometastases
- Local 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

Oxford / AGO LoE / GR

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Local Therapy in Primary Metastatic Disease

- Surgery (R0) of the primary tumor
  - In case of bone metastases only
  - In case of visceral metastases

- Axillary surgery for cN1

- Sentinel if cN0

- Radiotherapy of the primary tumor
  - Alone (without surgery)
  - After local surgical treatment with BCS or mastectomy (acc. adjuvant indication)

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LoE / GR

- 2b\textsuperscript{a} B  
- 2b\textsuperscript{a} B
- 5 D
- 5 D
- 3a C
- 3a C
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 any surgery: staging and biopsy (CT-guided FNA / CNB or transbronchial FNA)
- Resection of pulmonary metastases by VATS or conventional resection
  - In case of multilocular metastatic disease
  - In case of single / few unilateral metastases with curative intent
- Thermoablation (CT-guided RFA, LITT)
- Regional radiotherapy
  (e.g. stereotactic body radiosurgery with volumetric intensity modulated arc therapy (SRS-VMAT))

Oxford / AGO
LoE / GR

3a B +
3a B -
3a B +/-
3b C +/-
4 C +/-

*VATS = video-assisted thoracic surgery
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 [dyspnea (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
- VATS and Talcum-pleurodesis*
- Chemical pleurodesis*
  - Talcum powder
  - Bleomycin, Doxycycline, Mitoxantrone
  - Povidone-iodine (20 ml of 10% solution)
- Continuous pleural drainage
- Systemic treatment after pleurodesis
- Local antibody therapy (i.e. Catumaxomab)
- Serial thoracocentesis

* Adequate pain-relief
VATS: video-assisted thoracoscopic surgery

Oxford / AGO LoE / GR

4  C  ++

1b  B  ++

1a  B  +

2b  C  +/-

1b  B  +

2a  B  ++

3b  C  +/-

3b  C  -

4  C  +/-
Malignant Ascites
Local Therapy

Ascites:

- Puncture, drainage in symptomatic patients 4 D ++
- Systemic therapy 3b D ++
- Local chemotherapy 3b D +/-
- Local antibody therapy (i.e. Catumaxomab) 3b D +/-
Symptomatic pericardial effusion:

- Drainage, fenestration  
  - Oxford / AGO LoE / GR: 3b B ++

- Combination with optimized systemic therapy  
  - Oxford / AGO LoE / GR: 4 C ++

- VATS (video-assisted thoracic surgery)  
  - Oxford / AGO LoE / GR: 4 C +

- Ultrasound guided puncture and instillation of cytotoxic compounds  
  - Oxford / AGO LoE / GR: 4 C +/-
    - Bleomycin, cisplatinum, mitomycin C, mitoxantrone etc.
    - Bevacizumab
Bone Marrow Infiltration
Associated with Pancytopenia

- Weekly chemotherapy with*:
  - Epirubicin, Doxorubicin, Paclitaxel
  - Capecitabine
- HER2 pos.:
  - add anti-HER2 -treatment

* Consider pre-treatment
### Soft Tissue Metastasis

#### Local Therapy

1. **Surgery of locoregional limited metastases** (skin, muscular, nodal) with complete resection (R0) after exclusion of further metastases

   - **Grade:** 4, **Evidence:** C, **Recommendation:** +

2. **Radiotherapy (after surgery or, if immediate surgery is not indicated):**

   - **Soft tissue metastases**
     - **Grade:** 3b, **Evidence:** C, **Recommendation:** +
   - **Paresis, spinal cord compression**
     - **Grade:** 2b, **Evidence:** C, **Recommendation:** ++
   - **Plexus infiltration**
     - **Grade:** 3b, **Evidence:** C, **Recommendation:** ++
Specific Sites of Metastases (2/13)

No further information

References

Sources for this chapter of the AGO-Guideline

Pubmed 1.1.2016 bis 31.1.2017


Specific Sites Of Metastases (3/13)

No further information

No references
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 (1b B +/-)

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
14. Soran A et al. A randomized controlled trial evaluating resection of the primary tumor in women presenting with de novo stage IV breast cancer; Turkish study (MF07-01). J Clin Oncol 34, 2016 (suppl; abstr 1005)

**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 +)
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 +/-)**


Statement: 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:*

2016 Vote result of the AGO recommendation (complete slide without further changes): yes = 19/ no = 1

With regard to quality of life, in several cohorts a rather good effects of patient-controlled pleural drainage using an indwelling catheter was demonstrated. A small and well designed trial has demonstrated substantially higher efficacy and improved 30-days activity in patients with pleural drainage compared to patients with pleurodesis. The ABC3-recommendations considered continous pleural drainage for at least equivalent to pleurodesis.

**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: Continuous pleural drainage (2a B +)

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

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

Malignant Ascites - Local Therapy (10/13)

Further information:

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 consist 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 payed 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:*