

Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

© AGO e. V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2017.1

Specific Sites of Metastases

Specific Sites Of Metastases

Local Approaches to Metastatic Disease



© AGO e. V.
in der DGGO e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2017.1

➤ **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

Further
Information

References

**FORSCHEN
LEHREN
HEILEN**

www.ago-online.de

Specific Sites of Metastases

© AGO e. V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2017.1

- **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)“**

Further
Information

References

www.ago-online.de

General Aspects

Surgery or Ablation of Metastases

Oxford / AGO
LoE / GR

➤	Histological / cytological verification	3	B	+
➤	Systemic treatment preferred	2a	B	++*
➤	Consider surgery only in case of good response to palliative treatment	2b	C	+
➤	Metastases surgery is an option for pts in good conditions with late onset oligometastases	3a	B	+
➤	Local treatment in the case of pain, exulceration, persistence after systemic treatment, bowel obstruction, hydrocephalus occlusus, spinal cord compression	5	D	+/-
➤	Systemic treatment after surgery	5	D	++

* See chapters with systemic treatment recommendations

Local Therapy in Primary Metastatic Disease

Oxford / AGO
LoE / GR

© AGO e. V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2017.1

- | | | | |
|---|--|-------------------------|------------|
| ➤ | Surgery (R0) of the primary tumor | | |
| ➤ | In case of bone metastases only | 2b^a B | +/- |
| ➤ | In case of visceral metastases | 2b^a B | - |
| ➤ | Axillary surgery for cN1 | 5 D | +/- |
| ➤ | Sentinel if cN0 | 5 D | - |
| ➤ | Radiotherapy of the primary tumor | | |
| ➤ | Alone (without surgery) | 3a C | +/- |
| ➤ | After local surgical treatment with BCS or mastectomy (acc. adjuvant indication) | 3a C | + |

www.ago-online.de

Further
Information

References

Liver Metastasis

Local Therapy

Oxford / AGO
LoE / GR

➤ **Resection of liver metastasis (R0)**

3a B +/-

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**

3b C +/-

➤ **Regional radiotherapy**

4 C +/-

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

➤ **Thermoablation**

3b C +/-

(RFA, LITT, cryotherapy)

Pulmonary Metastases

Local Therapy

Oxford / AGO

LoE / GR

➤ Before any surgery: staging and biopsy (CT-guided FNA / CNB or transbronchial FNA)	3a	B	+
➤ Resection of pulmonary metastases by VATS or conventional resection			
➤ In case of multilocular metastatic disease	3a	B	-
➤ In case of single / few unilateral metastases 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))			

*VATS = video-assisted thoracic surgery

Malignant Pleural Effusions (MPE)

Incidence:

- ~ 10 % of all breast cancer patients
- ~ 50 % of pat. 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

Oxford / AGO
LoE / GR

- | | | | |
|---|----|---|-----|
| ➤ 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 | + |
| ➤ Continous 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

Oxford / AGO
LoE / GR

Ascites:

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

Further
Information

References

Malignant Pericardial Effusion

Local Therapy

Oxford / AGO
LoE / GR

Symptomatic pericardial effusion:

- | | | | |
|--|----|---|-----|
| ➤ Drainage, fenestration | 3b | B | ++ |
| ➤ Combination with optimized systemic therapy | 4 | C | ++ |
| ➤ VATS (video-assisted thoracic surgery) | 4 | C | + |
| ➤ Ultrasoung guided puncture and instillation of cytotoxic compounds | | | |
| ➤ Bleomycin, cisplatinum, mitomycin C, mitoxantrone etc. | 4 | C | +/- |
| ➤ Bevacizumab | 4 | C | +/- |

Bone Marrow Infiltration Associated with Pancytopenia

Oxford / AGO
LoE / GR

➤ **Weekly chemotherapy with*:**

➤ Epirubicin, Doxorubicin, Paclitaxel

4 D ++

➤ Capecitabine

4 D ++

➤ **HER2 pos.:**
add anti-HER2 -treatment

5 D ++

Further
Information

References

* Consider pre-treatment

Soft Tissue Metastasis

Local Therapy

Oxford / AGO
LoE / GR

- | | | | |
|--|-----------|----------|-----------|
| ➤ Surgery of locoregional limited metastases (skin, muscular, nodal) with complete resection (R0) after exclusion of further metastases | 4 | C | + |
| ➤ Radiotherapy (after surgery or, if immediate surgery is not indicated): | | | |
| ➤ Soft tissue metastases | 3b | C | + |
| ➤ Paresis, spinal cord compression | 2b | C | ++ |
| ➤ Plexus infiltration | 3b | C | ++ |

© AGO e. V.
in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2017.1

www.ago-online.de

Further
Information

References

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

1. ABC 2: Cardoso F, Costa A, Norton L, Senkus E, Aapro M, André F, Barrios CH, Bergh J, Biganzoli L, Blackwell KL, Cardoso MJ, Cufer T, El Saghir N, Fallowfield L, Fenech D, Francis P, Gelmon K, Giordano SH, Gligorov J, Goldhirsch A, Harbeck N, Houssami N, Hudis C, Kaufman B, Krop I, Kyriakides S, Lin UN, Mayer M, Merjaver SD, Nordström EB, Pagani O, Partridge A, Penault-Llorca F, Piccart MJ, Rugo H, Sledge G, Thomssen C, Van't Veer L, Vorobiof D, Vrieling C, West N, Xu B, Winer E. ESO-ESMO 2nd international consensus guidelines for advanced breast cancer (ABC2). *Ann Oncol.* 2014 Oct;25(10):1871-88.
2. ABC 3: Cardoso F, Costa A, Senkus E, Aapro M, André F, Barrios CH, Bergh J, Bhattacharyya G, Biganzoli L, Cardoso MJ, Carey L, Corneliussen-James D, Curigliano G, Dieras V, El Saghir N, Eniu A, Fallowfield L, Fenech D, Francis P, Gelmon K, Gennari A, Harbeck N, Hudis C, Kaufman B, Krop I, Mayer M, Meijer H, Mertz S, Ohno S, Pagani O, Papadopoulos E, Peccatori F, Pernault-Llorca F, Piccart MJ, Pierga JY, Rugo H, Shockney L, Sledge G, Swain S, Thomssen C, Tutt A, Vorobiof D, Xu B, Norton L, Winer E. 3rd ESO-ESMO international consensus guidelines for Advanced Breast Cancer (ABC 3). *Breast.* 2017 Feb;31:244-259.

Specific Sites Of Metastases (3/13)

No further information

No references

General Aspects of Metastases Surgery or Ablation (4/13)

No further information

References:

1. Khan SA, Stewart AK, Morrow M. Does aggressive local therapy improve survival in metastatic breast cancer? *Surgery* 2002; 132:620.
2. Rapiti E, Verkooijen HM, Vlastos G, et al. Complete excision of primary breast tumor improves survival of patients with metastatic breast cancer at diagnosis. *J Clin Oncol* 2006; 24:2743.
3. Babiera GV, Rao R, Feng L, et al. Effect of primary tumor extirpation in breast cancer patients who present with stage IV disease and an intact primary tumor. *Ann Surg Oncol* 2006; 13:776.
4. Gnerlich J, Jeffe DB, Deshpande AD, et al. Surgical removal of the primary tumor increases overall survival in patients with metastatic breast cancer: analysis of the 1988-2003 SEER data. *Ann Surg Oncol* 2007; 14:2187.
5. Fields RC, Jeffe DB, Trinkaus K, et al. Surgical resection of the primary tumor is associated with increased long-term survival in patients with stage IV breast cancer after controlling for site of metastasis. *Ann Surg Oncol* 2007; 14:3345.
6. Blanchard DK, Shetty PB, Hilsenbeck SG, Elledge RM. Association of surgery with improved survival in stage IV breast cancer patients. *Ann Surg* 2008; 247:732.
7. Hazard HW, Gorla SR, Scholtens D, et al. Surgical resection of the primary tumor, chest wall control, and survival in women with metastatic breast cancer. *Cancer* 2008; 113:2011.
8. Ruiterkamp J, Ernst MF, van de Poll-Franse LV, et al. Surgical resection of the primary tumour is associated with improved survival in patients with distant metastatic breast cancer at diagnosis. *Eur J Surg Oncol* 2009; 35:1146.
9. Cady B, Nathan NR, Michaelson JS, et al. Matched pair analyses of stage IV breast cancer with or without resection of primary breast site. *Ann Surg Oncol* 2008; 15:3384.
10. Botteri E et al: Biopsy of liver metastasis for women with breast cancer: Impact on survival. *Breast*. 2011 Dec 31. [Epub ahead of print]

11. Bhullar JS et al: Receptor changes in metachronous breast tumors-our experience of 10 years. *Am J Surg*. 2011 Dec 27. [Epub ahead of print]
12. Bu-Ali H et al: Receptor characteristics of the second tumor in synchronous versus metachronous breast cancer. *Am Surg*. 2008 Aug;74(8):702-5
13. Ruiterkamp J et al: The role of surgery in metastatic breast cancer. *Eur J Cancer*. 2011 Sep;47 Suppl 3:S6-22.
14. Noguchi M et al: Local therapy and survival in breast cancer with distant metastases. *J Surg Oncol*. 2012 Jan;105(1):104-10.
15. Samiee S, Berardi P, Bouganim N, Vandermeer L, Arnaout A, Dent S, Mirsky D, Chasen M, Caudrelier JM, Clemons M Excision of the primary tumour in patients with metastatic breast cancer: a clinical dilemma. *Curr Oncol*. 2012 Aug;19(4):e270-9. doi: 10.3747/co.19.974.
16. Badwe R, et al: Surgical removal of primary tumor and axillary lymph nodes in women with metastatic breast cancer at first presentation: A randomized controlled trial. *SABCS [S2-02]*, 2013
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
18. Janssen S, Rades D. Primary Breast Cancer with Synchronous Metastatic Disease - Indications for Local Radiotherapy to the Breast and Chest Wall. *Anticancer Res*. 2015 Nov;35(11):5807-12. Review.
19. Badwe R, Hawaldar R, Nair N, Kaushik R, Parmar V, Siddique S, Budrukkar A, Mitra I, Gupta S. Locoregional treatment versus no treatment of the primary tumour in metastatic breast cancer: an open-label randomised controlled trial. *Lancet Oncol*. 2015 Oct;16(13):1380-8. doi: 10.1016/S1470-2045(15)00135-7. Epub 2015 Sep 9.

Local Therapy in Primary Metastatic Disease (5/13)

Further information and references:

Statements:

Local surgical treatment (R0) of primary tumor (1b B +/-)

1. Perez CB et al: Local therapy for the primary breast tumor in women with metastatic disease. Clin Adv Hematol Oncol. 2011 Feb;9(2):112-9.
2. Rapiti E et al: Complete excision of primary breast tumor improves survival of patients with metastatic breast cancer at diagnosis. J Clin Oncol 24:2743-2749, 2006
3. Khan SA et al: Does aggressive local therapy improve survival in metastatic breast cancer? Surgery 132:620-627, 2002
4. Holmes FA et al: Combined-modality approach for patients with isolated recurrences of breast cancer (IV-NED): The MD Anderson experience. Breast Disease 7:7-20, 1994
5. Vlastos G et al: Long-term survival after an aggressive surgical approach in patients with breast cancer hepatic metastases. Ann Surg Oncol 11:869-874, 2004
6. Rashaan ZM et al: Surgery in metastatic breast cancer: Patients with a favorable profile seem to have the most benefit from surgery. Eur J Surg Oncol. 2012 Jan;38(1):52-6. Epub 2011 Oct 26.
7. Dominici L et al: Surgery of the primary tumor does not improve survival in stage IV breast cancer. Breast Cancer Res Treat. 2011 Sep;129(2):459-65.
8. Badwe R, et al: Surgical removal of primary tumor and axillary lymph nodes in women with metastatic breast cancer at first presentation: A randomized controlled trial. SABCS [S2-02], 2013
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
10. Khodari W et al. Impact of loco-regional treatment on metastatic breast cancer outcome: a review. Crit Rev Oncol Hematol. 2013;87(1):69-79.
11. Suryanarayana Deo SV et al. Role of Loco-regional Surgery in metastatic breast cancer. J Cancer Res Ther. 2013;9(2):181-6.

12. Cameron D. Removing the primary tumour in metastatic breast cancer. *Lancet Oncol.* 2015 Oct;16(13):1284-5. doi: 10.1016/S1470-2045(15)00221-1. Epub 2015 Sep 9.
13. Criscitiello C, Giuliano M, Curigliano G, De Laurentiis M, Arpino G, Carlomagno N, De Placido S, Golshan M, Santangelo M. Surgery of the primary tumor in de novo metastatic breast cancer: To do or not to do? *Eur J Surg Oncol.* 2015 Oct;41(10):1288-92. doi: 10.1016/j.ejso.2015.07.013. Epub 2015 Jul 29. Review.
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

1. Furka A, et al: Treatment of liver metastases from breast cancer. Hepatogastroenterology. 2008 Jul-Aug;55(85):1416-8.
2. Caralt M, et al: Hepatic resection for liver metastases as part of the "oncosurgical" treatment of metastatic breast cancer. Ann Surg Oncol. 2008 Oct;15(10):2804-10.
3. Lubrano J, et al: Liver resection for breast cancer metastasis: does it improve survival? Surg Today. 2008;38(4):293-9.
4. J Thelen A, Benckert C, Jonas S, Lopez-Hänninen E, Sehouli J, Neumann U, Rudolph B, Neuhaus P. Liver resection for metastases from breast cancer. Surg Oncol. 2008 Jan 1;97(1):25-9.
5. Ly BH et al: Loco-regional treatment in metastatic breast cancer patients: Is there a survival benefit? Breast Cancer Res Treat. 2010 Feb;119(3):537-45.
6. Howlader M, et al: Resection of liver metastases from breast cancer: towards a management guideline. Int J Surg. 2011;9(4):285-91.
7. Chua TC, et al: Hepatic resection for metastatic breast cancer: a systematic review. Eur J Cancer. 2011 Oct;47(15):2282-90.
8. Bergenfeldt M, et al: Liver resection and local ablation of breast cancer liver metastases--a systematic review. Eur J Surg Oncol. 2011 Jul;37(7):549-57.
9. van Walsum GA, de Ridder JA, Verhoef C, Bosscha K, van Gulik TM, Hesselink EJ, Ruers TJ, van den Tol MP, Nagtegaal ID, Brouwers M, van Hillegersberg R, Porte RJ, Rijken AM, Strobbe LJ, de Wilt JH; Dutch Liver

- Surgeons Group Resection of liver metastases in patients with breast cancer: survival and prognostic factors. *Eur J Surg Oncol.* 2012 Oct;38(10):910-7. doi: 10.1016/j.ejso.2012.04.015. Epub 2012 Jun 7.
10. Abbott DE, Brouquet A, Mittendorf EA, Andreou A, Meric-Bernstam F, Valero V, Green MC, Kuerer HM, Curley SA, Abdalla EK, Hunt KK, Vauthey JN Resection of liver metastases from breast cancer: estrogen receptor status and response to chemotherapy before metastasectomy define outcome. *Surgery.* 2012 May;151(5):710-6. doi: 10.1016/j.surg.2011.12.017. Epub 2012 Jan 29.
 11. Fitzgerald TL, Brinkley J, Banks S, Vohra N, Englert ZP, Zervos EE. The benefits of liver resection for non-colorectal, non-neuroendocrine liver metastases: a systematic review. *Langenbecks Arch Surg.* 2014 Dec;399(8):989-1000. doi: 10.1007/s00423-014-1241-3. Epub 2014 Aug 23.
 12. Sadot E, Lee SY, Sofocleous CT, Solomon SB, Gönen M, Peter Kingham T, Allen PJ, DeMatteo RP, Jarnagin WR, Hudis CA, D'Angelica MI. Hepatic Resection or Ablation for Isolated Breast Cancer Liver Metastasis: A Case-control Study with Comparison to Medically Treated Patients. *Ann Surg.* 2015 Oct 1. [Epub ahead of print]
 13. Bacalbaşa N, Balescu I, Dima S, Popescu I. Long-term Survivors After Liver Resection for Breast Cancer Liver Metastases. *Anticancer Res.* 2015 Dec;35(12):6913-7.
 14. Vertriest C, Berardi G, Tomassini F, Vanden Broucke R, Depypere H, Cocquyt V, Denys H, Van Belle S, Troisi RI. Resection of single metachronous liver metastases from breast cancer stage I-II yield excellent overall and disease-free survival. Single center experience and review of the literature. *Dig Surg.* 2015;32(1):52-9. doi: 10.1159/000375132. Epub 2015 Feb 11.
 15. Dittmar Y, Altendorf-Hofmann A, Schüle S, Ardelt M, Dirsch O, Runnebaum IB, Settmacher U. Liver resection in selected patients with metastatic breast cancer: a single-centre analysis and review of literature. *J Cancer Res Clin Oncol.* 2013 Aug;139(8):1317-25. doi: 10.1007/s00432-013-1440-2. Epub 2013 May 4.

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

1. Vogl TJ et al. Transarterial chemoembolization (TACE) with mitomycin C and gemcitabine for liver metastases in breast cancer. *Eur Radiol.* 2010;20(1):173
2. Martin RC et al. Optimal outcomes for liver-dominant metastatic breast cancer with transarterialchemoembolization with drug-eluting beads loaded with doxorubicin. *Breast Cancer Res Treat.* 2012;132(2):753-63.

3. Petrelli F, Borgonovo K, Lonati V, Elia S, Barni S. Regression of liver metastases after treatment with intraperitoneal catumaxomab for malignant ascites due to breast cancer. *Target Oncol.* 2012 Nov 30
4. Eichler K et al. Transarterial chemoembolisation (TACE) with gemcitabine: phase II study in patients with liver metastases of breast cancer. *Eur J Radiol.* 2013;82(12):e816-22
5. Ang C et al. Hepatic arterial infusion and systemic chemotherapy for breast cancer liver metastases. *Breast J.* 2013;19(1):96-9.
6. Camacho LH, Kurzrock R, Cheung A, Barber DF, Gupta S, Madoff DC, Wallace MJ, Kim EE, Curley SA, Hortobagyi GN, Mavligit G. Pilot study of regional, hepatic intra-arterial paclitaxel in patients with breast carcinoma metastatic to the liver. *Cancer.* 2007 Jun 1;109(11):2190-6.
7. Vogl TJ, Zangos S, Scholtz JE, Schmitt F, Paetzold S, Trojan J, Orsi F, Lotz G, Ferrucci P. Chemosaturation with percutaneous hepatic perfusions of melphalan for hepatic metastases: experience from two European centers. *Rofo.* 2014 Oct;186(10):937-44. doi: 10.1055/s-0034-1366081. Epub 2014 Apr 11.

Statement: Regional radiotherapy (4 C +/-)

1. Hoffmann RT, et al: Radiofrequency ablation after selective internal radiation therapy with Yttrium90 microspheres in metastatic liver disease-Is it feasible? *Eur J Radiol.* 2010 Apr;74(1):199-205
2. Sofocleous CT et al: Radiofrequency ablation in the management of liver metastases from breast cancer. *AJR Am J Roentgenol.* 2007 Oct;189(4):883-9
3. Vogl TJ, Farshid P, Naguib NN, Zangos S. Thermal ablation therapies in patients with breast cancer liver metastases: A review. *Eur Radiol.* 2012 Oct 13. [Epub ahead of print]
4. Akhlaghpour S, Aziz-Ahari A, Amoui M, Tolooee S, Poorbeigi H, Sheybani S. Short-term effectiveness of radiochemoembolization for selected hepatic metastases with a combination protocol. *World J Gastroenterol.* 2012 Oct 7;18(37):5249-59.
5. Macchia G, Deodato F, Cilla S, Torre G, Corrado G, Legge F, Gambacorta MA, Tagliaferri L, Mignogna S, Scambia G, Valentini V, Morganti AG, Ferrandina G. Volumetric intensity modulated arc therapy for stereotactic body radiosurgery in oligometastatic breast and gynecological cancers: feasibility and clinical results. *Oncol Rep.* 2014 Nov;32(5):2237-43. doi: 10.3892/or.2014.3412. Epub 2014 Aug 18.

Statement: Thermoablation (3b C +/-)

1. Dwivedi DN, Pal S, Pande GK. Management of liver metastases: cut, cryo, coagulate or chemotherapy. Trop Gastroenterol. 2001 Apr-Jun;22(2):57-64. Review
2. Seifert JK, et al. Cryotherapy for liver tumors: current status, perspectives, clinical results, and review of literature. Technol Cancer Res Treat. 2004 Apr;3(2):151-63.
3. Vogl TJ, et al. MR-guided laser-induced thermotherapy (LITT) of liver tumours: experimental and clinical data. Int J Hyperthermia. 2004 Nov;20(7):713-24
4. Keil S, et al. Radiofrequency Ablation of Liver Metastases-Software-Assisted Evaluation of the Ablation Zone in MDCT: Tumor-Free Follow-Up Versus Local Recurrent Disease. Cardiovasc Intervent Radiol. 2009 Aug 18.
5. Vogl TJ, et al. Magnetic resonance-guided laser-induced interstitial thermotherapy of breast cancer liver metastases and other noncolorectal cancer liver metastases: an analysis of prognostic factors for long-term survival and progression-free survival. Invest Radiol. 2013;48(6):406-12.

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 +/-)

1. Tanaka F, et al: Surgery for pulmonary nodules in breast cancer patients. Ann Thorac Surg. 2005 May;79(5):1711-4; discussion 1714-5.
2. Rena O, et al: The role of surgery in the management of solitary pulmonary nodule in breast cancer patients. Eur J Surg Oncol. 2007 Jun;33(5):546-50.
3. Welter S, et al: Pulmonary metastases of breast cancer. When is resection indicated? Eur J Cardiothorac Surg. 2008 Dec;34(6):1228-34.
4. Erhunmwunsee L, D'Amico TA Surgical management of pulmonary metastases. Ann Thorac Surg. 2009 Dec;88(6):2052-60
5. Chen F, et al: Clinical features of surgical resection for pulmonary metastasis from breast cancer. Eur J Surg Oncol. 2009 Apr;35(4):393-7.
6. García-Yuste M, Pulmonary metastasectomy in breast cancer. J Thorac Oncol. 2010 Jun;5(6 Suppl 2):S170-1.
7. Nichols FC Pulmonary metastasectomy Thorac Surg Clin. 2012 Feb;22(1):91-9, REVIEW
8. Omar M. Rashid and Kazuaki Takabe The evolution of the role of surgery in the management of breast cancer lung metastasis. J Thorac Dis. 2012 August; 4(4): 420–424. REVIEW
9. Kycler W, Laski P: Surgical approach to pulmonary metastases from breast cancer. Breast J. 2012 Jan;18(1):52-7.

10. Meimarakis G et al. Prolonged overall survival after pulmonary metastasectomy in patients with breast cancer. *Ann Thorac Surg.* 2013;95(4):1170-80.
11. Fan J, Chen D, Du H, Shen C, Che G. Prognostic factors for resection of isolated pulmonary metastases in breast cancer patients: a systematic review and meta-analysis. *J Thorac Dis.* 2015 Aug;7(8):1441-51. doi: 10.3978/j.issn.2072-1439.2015.08.10.
12. Lumachi F, Mazza F, Del Conte A, Lo Re G, Ermani M, Chiara GB, Basso SM. *Anticancer Res.* 2015 Jun;35(6):3563-6. Erratum in: *Anticancer Res.* 2015 Jul;35(7):4371. Short-term Survival of Patients with Lung Metastases from Colorectal and Non-colorectal Cancer Who Underwent Pulmonary Metastasectomy.

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

1. Vogl TJ, et al: Microwave ablation therapy: clinical utility in treatment of pulmonary metastases. *Radiology.* 2011 Nov;261(2):643-51.
2. Ewert R, Opitz C. Pulmonary function testing before ablative methods] *Radiologe.* 2004 Jul;44(7):708-10. 4.
3. Diederich S, Hosten N: Percutaneous ablation of pulmonary tumours: state-of-the-art 2004 *Radiologe.* 2004 Jul;44(7):658-62.

Statement: Regional radiotherapy (4 C +/-)

1. Louie J, et al.: Radio frequency ablation of lung metastasis using sonographic guidance. *J Ultrasound Med.* 2004 Sep;23(9):1241-4.
2. Macchia G, Deodato F, Cilla S, Torre G, Corrado G, Legge F, Gambacorta MA, Tagliaferri L, Mignogna S, Scambia G, Valentini V, Morganti AG, Ferrandina G. Volumetric intensity modulated arc therapy for stereotactic body radiosurgery in oligometastatic breast and gynecological cancers: feasibility and clinical results. *Oncol Rep.* 2014 Nov;32(5):2237-43. doi: 10.3892/or.2014.3412. Epub 2014 Aug 18

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,
2. Bielsa S et al: Tumor type influences the effectiveness of pleurodesis in malignant effusions. Lung. 2011 Apr;189(2):151-5.
3. Ried M, Hofmann HS.: The treatment of pleural carcinosis with malignant pleural effusion. Dtsch Arztebl Int. 2013 May;110(18):313-8.
4. Zamboni MM, da Silva CT Jr, Baretta R, Cunha ET, Cardoso GP. Important prognostic factors for survival in patients with malignant pleural effusion. BMC Pulm Med. 2015 Mar 28;15:29. doi: 10.1186/s12890-015-0025-z.
5. Li Z, Pantanowitz L, Khalbuss WE, Arya P, Monaco SE. Challenges in diagnosing metastatic breast carcinoma in fluid cytology. Diagn Cytopathol. 2014 Nov;42(11):1006-8. doi: 10.1002/dc.23067. Epub 2014 Mar 8.
6. Guerrini GP, Lo Faso F, Vagliasindi A, Lembo R, Solaini L, Soliani P, Taviani M, Porrello C. The Role of Minimally Invasive Surgery in the Treatment of Lung Metastases. J Invest Surg. 2016 Oct 3:1-6.
7. Meyer C, Bartsch D, Mirow N, Kirschbaum A. Video-Assisted Laser Resection of Lung Metastases-Feasibility of a New Surgical Technique. Thorac Cardiovasc Surg. 2017 Jan 22.

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 ++)

1. Zamboni MM, da Silva CT Jr, Baretta R, Cunha ET, Cardoso GP. Important prognostic factors for survival in patients with malignant pleural effusion. BMC Pulm Med. 2015 Mar 28;15:29. doi: 10.1186/s12890-015-0025-z.

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 +/-)

1. Hirata T et al: Efficacy of pleurodesis for malignant pleural effusions in breast cancer patients. Eur Respir J. 2011 Dec;38(6):1425-30
2. Mohsen TA et al: Local iodine pleurodesis versus thoracoscopic talc insufflation in recurrent malignant pleural effusion: a prospective randomized control trial. Eur J Cardiothorac Surg. 2011 Aug;40(2):282-6.

3. Shaw P, Agarwal R. Pleurodesis for malignant pleural effusions. Cochrane Database of Systematic Reviews 2004,
4. Lombardi G, et al: Diagnosis and Treatment of Malignant Pleural Effusion: A Systematic Literature Review and New Approaches. *Am J Clin Oncol*. 2010 Aug;33(4):420-3.
5. Olden AM, Holloway R. Treatment of Malignant Pleural Effusion: PleuRx((R)) Catheter or Talc Pleurodesis? A Cost-Effectiveness Analysis. *J Palliat Med*. 2010 Jan;13(1):59-65.
6. Bazerbashi S, et al: Ambulatory Intercostal Drainage for the Management of Malignant Pleural Effusion: A Single Center Experience. *Ann Surg Oncol*. 2009 Dec;16(12):3482-7
7. Ried M, Hofmann HS.: The treatment of pleural carcinosis with malignant pleural effusion. *Dtsch Arztebl Int*. 2013 May;110(18):313-8.
8. Korsic M, Badovinac S, Cucevic B, Janevski Z. Talc pleurodesis improves survival of patients with malignant pleural effusions: case-control study. *Wien Klin Wochenschr*. 2015 Dec;127(23-24):963-9. doi: 10.1007/s00508-015-0716-8. Epub 2015 Apr 10.
9. Ibrahim IM, Dokhan AL, El-Sessy AA, Eltaweel MF. Povidone-iodine pleurodesis versus talc pleurodesis in preventing recurrence of malignant pleural effusion. *J Cardiothorac Surg*. 2015 May 1;10:64. doi: 10.1186/s13019-015-0270-5.

Statement: Continous pleural drainage (2a B +)

1. Cases E, et al: Use of indwelling pleural catheter in the outpatient management of recurrent malignant pleural effusion *Arch Bronconeumol*. 2009 Dec;45(12):591-6.
2. Demmy TL, Gu L, Burkhalter JE, Toloza EM, D'Amico TA, Sutherland S, Wang X, Archer L, Veit LJ, Kohman L; Cancer and Leukemia Group B. Optimal management of malignant pleural effusions (results of CALGB 30102). *J Natl Compr Canc Netw*. 2012 Aug;10(8):975-82.
3. Davies HE et al., Effect of an indwelling pleural catheter vs chest tube and talc pleurodesis for relieving dyspnea in patients with malignant pleural effusion: the TIME2 randomized controlled trial. *JAMA*. 2012 Jun 13;307(22):2383-9. doi: 10.1001/jama.2012.5535.
4. Warren WH, Kalimi R, Khodadadian LM, Kim AW. Management of malignant pleural effusions using the Pleur(x) catheter. *Ann Thorac Surg*. 2008 Mar;85(3):1049-55.
5. Hak CC, Sivakumar P, Ahmed L. Safety of indwelling pleural catheter use in patients undergoing chemotherapy: a five-year retrospective evaluation. *BMC Pulm Med*. 2016 Mar 11;16:41.

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

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

1. Sebastian M, Kiewe P, Schuette W, Brust D, Peschel C, Schneller F, Rühle KH, Nilius G, Ewert R, Lodziewski S, Passlick B, Siene W, Wiewrodt R, Jäger M, Lindhofer H, Friccius-Quecke H, Schmittel A. Treatment of malignant pleural effusion with the trifunctional antibody catumaxomab (Removab) (anti-EpCAM x Anti-CD3): results of a phase 1/2 study. J Immunother. 2009 Feb-Mar;32(2):195-202

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:

1. Saâda E, et al: Pathogenesis and management of refractory malignant ascites. Bull Cancer. 2011 Jun;98(6):679-87.
2. Barni S, et al: A novel perspective for an orphan problem: old and new drugs for the medical management of malignant ascites.Crit Rev Oncol Hematol. 2011 Aug;79(2):144-53.
3. Petrelli F, Borgonovo K, Lonati V, Elia S, Barni S. Regression of liver metastases after treatment with intraperitoneal catumaxomab for malignant ascites due to breast cancer. Target Oncol. 2013 Dec;8(4):291-4.
4. Kurbacher CM, Horn O, Kurbacher JA, Herz S, Kurbacher AT, Hildenbrand R, Bollmann R. Outpatient Intraperitoneal Catumaxomab Therapy for Malignant Ascites Related to Advanced Gynecologic Neoplasms. Oncologist. 2015 Nov;20(11):1333-41.

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:

1. Cozzi S, et al: Management of neoplastic pericardial effusions. *Tumori*. 2010 Nov-Dec;96(6):926-9.
2. Kim SH, et al: Clinical characteristics of malignant pericardial effusion associated with recurrence and survival. *Cancer Res Treat*. 2010 Dec;42(4):210-6.
3. Kawase T, et al: Intense accumulation of Tc-99m MDP in pericardial metastasis from breast cancer. *Clin Nucl Med*. 2009 Mar;34(3):173-4.
4. Kil UH, et al: Prognosis of large, symptomatic pericardial effusion treated by echo-guided percutaneous pericardiocentesis. *Clin Cardiol*. 2008 Nov;31(11):531-7.
5. Dequanter D et al: Severe pericardial effusion in patients with concurrent malignancy: a retrospective analysis of prognostic factors influencing survival. *Ann Surg Oncol*. 2008 Nov;15(11):3268-71.
6. Toth I et al: Mediastinoscope-controlled parasternal fenestration of the pericardium: definitive surgical palliation of malignant pericardial effusion. *J Cardiothorac Surg*. 2012 Jun 19;7:56.
7. Saltzman AJ, Paz YE, et al, Comparison of Surgical Pericardial Drainage With Percutaneous Catheter Drainage for Pericardial Effusion, *J Invasive Cardiol*. 2012 November ; 24(11): 590–593.
8. Danielle El Haddad, MD,* Cezar Iliescu, MD, et al, Outcomes of Cancer Patients Undergoing Percutaneous Pericardiocentesis for Pericardial Effusion, 2015, *J American Coll Cardiol*, 66, NO. 10, 1119-1125

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 capecitabine) 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:

1. Kopp HG, et al: Symptomatic bone marrow involvement in breast cancer-clinical presentation, treatment, and prognosis: a single institution review of 22 cases. *Anticancer Res.* 2011 Nov;31(11):4025-30.
2. Freyer G, et al: Palliative hormone therapy, low-dose chemotherapy, and bisphosphonate in breast cancer patients with bone marrow involvement and pancytopenia: report of a pilot experience. *Eur J Intern Med.* 2000 Dec 20;11(6):329-333.
3. Ardavanis A, et al: Low-dose capecitabine in breast cancer patients with symptomatic bone marrow infiltration: a case study. *Anticancer Res.* 2008 Jan-Feb;28(1B):539-41.
4. Krockenberger M, et al: Prolonged clinical benefit from platinum-based chemotherapy in a patient with metastatic triple negative breast cancer. *Eur J Gynaecol Oncol.* 2009;30(4):449-51. 2.
5. Pahouja G, Wesolowski R, et al, Stabilization of bone marrow infiltration by metastatic breast cancer with continuous doxorubicin, *Cancer Treat Commun.* 2015 ; 3: 28–32.

6. Artac M, Koral L, Toy H, Guler T, Boruban MC, Altundag K. Complete response and long-term remission to anti-HER2 combined therapy in a patient with breast cancer presented with bone marrow metastases. *J Oncol Pharm Pract.* 2014 Apr;20(2):141-5.
7. Pahouja G, Wesolowski R, Reinbolt R, Tozbikian G, Berger M, Mangini N, Lustberg MB.: Stabilization of bone marrow infiltration by metastatic breast cancer with continuous doxorubicin. *Cancer Treat Commun.* 2015;3:28-32.

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:

1. Wilson B, et al: Resolution of extensive leptomeningeal metastasis and clinical spinal cord compression from breast cancer using weekly docetaxel chemotherapy. *Breast Cancer Res Treat.* 2012 Jan;131(1):343-6. Epub 2011 Oct 26.
2. Tancioni F et al: Surgery followed by radiotherapy for the treatment of metastatic epidural spinal cord compression from breast cancer. *Spine (Phila Pa 1976).* 2011 Sep 15;36(20):E1352-9.
3. Tancioni F, et al: Multimodal approach to the management of metastatic epidural spinal cord compression (MESCC) due to solid tumors. *Int J Radiat Oncol Biol Phys.* 2010 Dec 1;78(5):1467-73. Epub 2010 Mar 16.
4. Rades, D et al.; Outcome after radiotherapy alone for metastatic spinal cord compression in patients with oligometastases. *J. Clin. Oncol.*,2007,25;50-6.
5. Gerszten PC, Monaco EA 3rd: Complete percutaneous treatment of vertebral body tumors causing spinal canal compromise using a transpedicular cavitation, cement augmentation, and radiosurgical technique. *Neurosurg Focus.* 2009 Dec;27(6):E9.
6. Souchon R, et al: DEGRO practice guidelines for palliative radiotherapy of metastatic breast cancer: bone metastases and metastatic spinal cord compression (MSCC). *Strahlenther Onkol.* 2009 Jul;185(7):417-24.
7. Abed R,et al: Soft-tissue metastases: their presentation and origin. *J Bone Joint Surg Br.* 2009 Aug;91(8):1083-5.
8. Kong JH, et al: Patterns of skin and soft tissue metastases from breast cancer according to subtypes: relationship between EGFR overexpression and skin manifestations. *Oncology.* 2011;81(1):55-62. Epub 2011 Sep 16.

9. Berlière M, Duhoux FP, Taburiaux L, Lacroix V, Galant C, Leconte I, Fellah L, Lecouvet F, Bouziane D, Piette P, Lengele B. The place of extensive surgery in locoregional recurrence and limited metastatic disease of breast cancer: preliminary results. *Biomed Res Int.* 2015;2015:782654. doi: 10.1155/2015/782654. Epub 2015 Mar 18.