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# Diagnosis and Treatment of Patients with early and advanced Breast Cancer

## Specific Sites of Metastases



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## Specific Sites Of Metastases


### Local Approaches to Metastatic Disease

- **Versions 2002–2018:**  
 Bauerfeind / Bischoff / Böhme / Brunnert / Dall /  
 Diel / Fehm / Fersis / Friedrich / Friedrichs / Gerber /  
 Hanf / Janni / Kreipe / Lück / Lux / Maass / Oberhoff  
 / Rezai / Schaller / Schütz / Seegenschmiedt /  
 Solomayer / Souchon / Thommssen / Bischoff
  
- **Version 2019:**  
 Albert / Kolberg-Liedtke

Pubmed 1.1.2014 bis 01.01.2019

Cochrane database

1. ABC 2: Cardoso F, Costa A, Norton L et al. 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 et al. 3rd ESO-ESMO international consensus guidelines for Advanced Breast Cancer (ABC 3). Breast. 2017 Feb;31:244-259.



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## 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)“

1. Ruiterkamp J et al: The role of surgery in metastatic breast cancer. Eur J Cancer. 2011 Sep;47 Suppl 3:S6-22.
2. Noguchi M et al: Local therapy and survival in breast cancer with distant metastases. J Surg Oncol. 2012 Jan;105(1):104-10.
3. 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.
4. 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
5. 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
6. 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.
7. Badwe R, Hawaldar R, Nair N et al. 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.

## General Treatment Aspects of Metastases

	Oxford		
	LoE	GR	AGO
■ <b>Histological / cytological verification</b>	3	B	+
■ <b>Systemic treatment preferred</b>	2a	B	++*
■ <b>Consider surgery only in case of good response to palliative treatment</b>	2b	C	+
■ <b>Radiation for patients in good physical condition with late onset of oligometastases</b>	3a	B	+
■ <b>Local treatment in the case of pain, exulceration, persistence after systemic treatment, bowel obstruction, hydrocephalus occlusus, spinal cord compression</b>	5	D	+/-
■ <b>Systemic treatment after surgery</b>	5	D	++

\* See chapters with systemic treatment recommendations

### Local surgical

1. 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
2. Cameron D. Removing the primary tumour in metastatic breast cancer. Lancet Oncol. 2015 Oct;16(13):1284-5.
3. 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.
4. 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)
5. Warschkow R, Güller U, Tarantino I et al. Improved Survival After Primary Tumor Surgery in Metastatic Breast Cancer: A Propensity-adjusted, Population-based SEER Trend Analysis. Ann Surg. 2016 Jun;263(6):1188-98.
6. Yoo TK, Chae BJ, Kim SJ et al. Identifying long-term survivors among metastatic breast cancer patients undergoing primary tumor surgery. Breast Cancer Res Treat. 2017 Aug;165(1):109-118
7. [Barinoff J](#), [Schmidt M](#), [Schneeweiss A](#), [Schoenegg W](#), [Thill M](#), [Keitel S](#), [Lattrich CR](#), [Hinke A](#), [Kutscheidt A](#), [Jackisch C](#). Primary metastatic breast cancer in the era of targeted therapy - Prognostic impact and the role of breast tumour surgery. [Eur J Cancer](#). 2017 Sep;83:116-124.

8. Poggio F, Lambertini M, de Azambuja E. Controversies in Oncology: Surgery of the primary tumour in patients presenting with de novo metastatic breast cancer: to do or not to do? ESMO Open 2018;3:e000324. doi:10.1136/esmoopen-2018-000324

#### Oligometastasierung

#### Radical radiotherapy

1. [Scorsetti M](#), [Franceschini D](#), De Rose F, [Comito T](#), [Villa E](#), [Iftode C](#), [Navarria P](#), [D'Agostino GR](#), [Masci G](#), [Torrise R](#), [Testori A](#), [Tinteri C](#), Santoro A. Stereotactic body radiation therapy: A promising chance for oligometastatic breast cancer. [Breast](#). 2016 Apr;26:11-7.
2. [Trovo M](#), [Furlan C](#), [Polesel J](#), [Fiorica F](#), [Arcangeli S](#), [Giai-Levra N](#), [Alongi F](#), [Del Conte A](#), [Militello L](#), [Muraro E](#), [Martorelli D](#), [Spazzapan S](#), [Berretta M](#) Radical radiation therapy for oligometastatic breast cancer: Results of a prospective phase II trial. [Radiother Oncol](#). 2018 Jan;126(1):177-180.


Local Therapy in Primary Metastatic Disease			
	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>■ <b>Surgery (R0) of the primary tumor</b> <ul style="list-style-type: none"> <li>■ In case of bone metastases only</li> <li>■ In case of visceral metastases</li> </ul> </li> <li>■ <b>Axillary surgery for cN1</b></li> <li>■ <b>Sentinel if cN0</b></li> <li>■ <b>Radiotherapy of the primary tumor</b> <ul style="list-style-type: none"> <li>■ Alone (without surgery)</li> <li>■ After local surgical treatment with BCS or mastectomy (acc. adjuvant indication)</li> </ul> </li> </ul>	2b <sup>a</sup>	B	+/-
	2b <sup>a</sup>	B	-
	5	D	+/-
	5	D	-
	3a	C	+/-
	3a	C	+

## Operation (R0) des Primärtumors

1. [Badwe R](#), [Hawaldar R](#), [Nair N](#) et al. Locoregional treatment versus no treatment of the primary tumour in metastatic breast cancer: an open-label randomised controlled trial. *Lancet* 2015 Oct;16(13):1380-8.
2. Headon H, Wazir U, Kasem A et al. Surgical treatment of the primary tumour improves the overall survival in patients with metastatic breast cancer: A systematic review and meta-analysis. *Molecular and Clinical Oncol.* 2016;4;863-867
3. [Xiao W](#), [Zou Y](#), [Zheng S](#) et al. Primary tumor resection in stage IV breast cancer: A systematic review and meta-analysis. [Eur J Surg Oncol.](#) 2018 Oct;44(10):1504-1512.
4. [Tosello G](#), [Torloni MR](#), [Mota BS](#) et al. Breast surgery for metastatic breast cancer. [Cochrane Database Syst Rev.](#) 2018 Mar 15;3:CD011276. doi: 10.1002/14651

## Radiotherapy

1. 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.

Liver Metastases Local Therapy			
	Oxford		
	LoE	GR	AGO
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<ul style="list-style-type: none"> <li> <b>Resection of liver metastases (R0)</b>            HR positive: chemotherapy sensitive, long disease-free interval, absence of extrahepatic disease, ≤ 3 metastases            HER2 positive: age &lt; 50 y., metastasis &lt; 5 cm, no further metastasis         </li> </ul>	3a	B	+/-
<ul style="list-style-type: none"> <li> <b>Regional chemotherapy</b> </li> </ul>	3b	C	+/-
<ul style="list-style-type: none"> <li> <b>Regional radiotherapy</b>            [SIRT, stereotactic body radiosurgery with volumetric intensity modulated arc therapy (SRS-VMAT), radiochemo-embolization, other modalities]         </li> </ul>	3b	C	+/-
<ul style="list-style-type: none"> <li> <b>Thermoablation</b>            (RFA, LITT, cryotherapy)         </li> </ul>	3b	C	+/-

### 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

- van Dam PJ, van der Stok EP, Teuwen LA et al. International consensus guidelines for scoring the histopathological growth patterns of liver metastasis. Br J Cancer. 2017 Nov 7;117(10):1427-1441.

### Local surgery

- van Walsum GA, de Ridder JA, Verhoef C et al. 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.
- Abbott DE, Brouquet A, Mittendorf EA et al. 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..



3. Sadot E, Lee SY, Sofocleous CT et al. 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]
4. Bacalbaşa N, Balescu I, Dima S et al. Long-term Survivors After Liver Resection for Breast Cancer Liver Metastases. *Anticancer Res.* 2015 Dec;35(12):6913-7.
5. Vertriest C, Berardi G, Tomassini F et al. 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.
6. Golse N, Adam R. Liver Metastases From Breast Cancer: What Role for Surgery? Indications and Results. *Clin Breast Cancer.* 2017 Jul;17(4):256-265
7. Yoo TG, Cranshaw I, Broom R et al. Systematic review of early and long-term outcome of liver resection for metastatic breast cancer: Is there a survival benefit? *Breast.* 2017 Apr;32:162-172
8. Labgaa I, Slankamenac K, Schadde E et al. Liver resection for metastases not of colorectal, neuroendocrine, sarcomatous, or ovarian (NCNSO) origin: A multicentric study. *Am J Surg.* 2018 Jan;215(1):125-130.

#### Statement: Regional chemotherapy

1. Martin RC et al. Optimal outcomes for liver-dominant metastatic breast cancer with transarterial chemoembolization with drug-eluting beads loaded with doxorubicin. *Breast Cancer Res Treat.* 2012;132(2):753-63.
2. Petrelli F, Borgonovo K, Lonati V et al. Regression of liver metastases after treatment with intraperitoneal catumaxomab for malignant ascites due to breast cancer. *Target Oncol.* 2012 Nov 30
3. 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
4. Ang C et al. Hepatic arterial infusion and systemic chemotherapy for breast cancer liver metastases. *Breast J.* 2013;19(1):96-9.
5. Camacho LH, Kurzrock R, Cheung A et al. 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.
6. Vogl TJ, Zangos S, Scholtz JE et al. 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


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. Vogl TJ, Farshid P, Naguib NN et al. Thermal ablation therapies in patients with breast cancer liver metastases: A review. Eur Radiol. 2012 Oct 13. [Epub ahead of print]
3. Akhlaghpour S, Aziz-Ahari A, Amoui M et al. Short-term effectiveness of radiochemoembolization for selected hepatic metastases with a combination protocol. World J Gastroenterol. 2012 Oct 7;18(37):5249-59.
4. Macchia G, Deodato F, Cilla S et al. 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.
5. Bale R, Richter M, Dünser M et al. Stereotactic Radiofrequency Ablation for Breast Cancer Liver Metastases. J Vasc Interv Radiol. 2017 Dec 19. pii: S1051-0443(17)30911-9
6. [Trovo M](#), [Furlan C](#), [Polesel J](#) et al. Radical radiation therapy for oligometastatic breast cancer: Results of a prospective phase II trial. [Radiother Oncol](#). 2018 Jan;126(1):177-180.

#### Statement: Thermoablation

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.
6. Xiao YB, Zhang B, Wi YL. Radiofrequency ablation versus hepatic resection for breast cancer liver metastasis: a systematic review and meta-analysis J Zhejiang Univ-Sci B (Biomed & Biotechnol) 2018 19(11):829-843

 <p>© AGO e. V. in der DGGG e.V. sowie in der DKG e.V.</p> <p>Guidelines Breast Version 2019.1</p> <p>www.ago-online.de</p> <p>FORSCHEN LEHREN HEILEN</p>	Pulmonary Metastases Local Therapy		
	Oxford		
	LoE	GR	AGO
■ 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 metastasis with curative intent	3a	B	+/-
■ Thermoablation (CT-guided RFA, LITT)	3b	C	+/-
■ Regional radiotherapy (e.g. stereotactic body radiosurgery with volumetric intensity modulated arc therapy (SRS-VMAT))	3a	B	+/-
* VATS = video-assisted thoracic surgery			

Before surgery: staging and biopsy (fine-needle aspiration with CT-guidance or transbronchial needle aspiration)

Resection of pulmonary metastases by VATS or conventional resection

In case of multilocular metastatic disease

In case of single metastases on one side with curative intent

1. García-Yuste M, Pulmonary metastasectomy in breast cancer. J Thorac Oncol. 2010 Jun;5(6 Suppl 2):S170-1.
2. Nichols FC Pulmonary metastasectomy Thorac Surg Clin. 2012 Feb;22(1):91-9, REVIEW
3. 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
4. Kycler W, Laski P: Surgical approach to pulmonary metastases from breast cancer. Breast J. 2012 Jan;18(1):52-7.
5. Meimarakis G et al. Prolonged overall survival after pulmonary metastasectomy in patients with breast cancer. Ann Thorac Surg. 2013;95(4):1170-80.
6. Fan J, Chen D, Du H et al. 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.
7. Lumachi F, Mazza F, Del Conte A et al. 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.


8. Patrini D, Panagiotopoulos N, Lawrence D et al. Surgical management of lung metastases. Br J Hosp Med (Lond). 2017 Apr 2;78(4):192-198.
9. [Meng D](#), Fu L, Wang L et al. Video-assisted thoracoscopic surgery versus open thoracotomy in pulmonary metastasectomy: a meta-analysis of observational studies. [Interact Cardiovasc Thorac Surg](#). 2016 Feb;22(2):200-6.

Statement: Thermoablation (CT-guided RFA, LITT)

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

1. Macchia G, Deodato F, Cilla S et al. 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
2. Ricco A, Davis J, Rate W et al. Lung metastases treated with stereotactic body radiotherapy: the RSSearch® patient Registry's experience. Radiation Oncology (2017) 12: oi: 10.1186/s13014-017-0773-4



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## 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 [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]

1. Bielsa S et al: Tumor type influences the effectiveness of pleurodesis in malignant effusions. Lung. 2011 Apr;189(2):151-5.
2. Ried M, Hofmann HS.: The treatment of pleural carcinosis with malignant pleural effusion. Dtsch Arztebl Int. 2013 May;110(18):313-8.
3. Zamboni MM, da Silva CT Jr, Baretta R et al. Important prognostic factors for survival in patients with malignant pleural effusion. BMC Pulm Med. 2015 Mar 28;15:29..
4. Li Z, Pantanowitz L, Khalbuss WE et al. 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.
5. Guerrini GP, Lo Faso F, Vagliasindi A et al. The Role of Minimally Invasive Surgery in the Treatment of Lung Metastases. J Invest Surg. 2016 Oct 3:1-6.
6. Meyer C, Bartsch D, Mirow N et al. Video-Assisted Laser Resection of Lung Metastases-Feasibility of a New Surgical Technique. Thorac Cardiovasc Surg. 2017 Jan 22.

Malignant Pleural Effusion (MPE) Local Therapy			
	Oxford		
	LoE	GR	AGO
▪ 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			

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

1. Zamboni MM, da Silva CT Jr, Baretta R et al. 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.

VATS and Talcum-pleurodesis

Chemical pleurodesis

Talcum powder

Bleomycin, Doxycycline, Mitoxantrone

Povidone-iodine (20 ml of 10% solution)

Serial thoracocentesis

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. 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.

4. 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.
5. Ried M, Hofmann HS.: The treatment of pleural carcinosis with malignant pleural effusion. Dtsch Arztebl Int. 2013 May;110(18):313-8.
6. Korsic M, Badovinac S, Cucevic B et al. Talc pleurodesis improves survival of patients with malignant pleural effusions: case-control study. Wien Klin Wochenschr. 2015 Dec;127(23-24):963-9.
7. Ibrahim IM, Dokhan AL, El-Sessy AA et al. 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: Continuous pleural drainage

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 et al. 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 et al. 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

#### Statement: Local antibody therapy (i.e. Catumaxomab)

1. Sebastian M, Kiewe P, Schuette W et al. 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



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## Malignant Ascites Local Therapy

Oxford


LoE	GR	AGO
4	D	++
3b	D	++
3b	D	+/-
3b	D	+/-

**Ascites:**

- Puncture, drainage in symptomatic patients
- Systemic therapy
- Local chemotherapy
- Local antibody therapy (i.e. Catumaxomab)

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.





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## Malignant Pericardial Effusion


### Local Therapy

**Symptomatic pericardial effusion:**

- Drainage, fenestration
- Combination with optimized systemic therapy
- VATS (video-assisted thoracic surgery)
- Ultrasound guided puncture and instillation of cytotoxic compounds
  - Bleomycin, cisplatin, mitomycin C, mitoxantrone etc.
  - Bevacizumab

	Oxford		
	LoE	GR	AGO
	<b>3b</b>	<b>B</b>	<b>++</b>
	<b>4</b>	<b>C</b>	<b>++</b>
	<b>4</b>	<b>C</b>	<b>+</b>
	<b>4</b>	<b>C</b>	<b>+/-</b>
	<b>4</b>	<b>C</b>	<b>+/-</b>

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## Bone Marrow Infiltration Associated with Pancytopenia


Oxford

LoE	GR	AGO
4	D	++
4	D	++
5	D	++

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

\* Consider pre-treatment

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## Soft Tissue Metastasis Local Therapy

Oxford		
LoE	GR	AGO
4	C	+
3b	C	+
2b	C	++
3b	C	++

- **Surgery of locoregional limited metastasis (skin, muscular, nodal) with complete resection (R0) after exclusion of further metastasis**
- **Radiotherapy (after surgery or, if immediate surgery is not indicated):**
  - Soft tissue metastasis
  - Paresis, spinal cord compression
  - Plexus infiltration

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