

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



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Guidelines Breast  
Version 2025.1E

## Treatment according to Sites of Metastases

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**FORSCHEN  
LEHREN  
HEILEN**

# Sites Of Metastases

## Specific Approaches to Metastatic Disease

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**Albert / Bauerfeind / Bischoff / Böhme / Brunnert / Dall / Diel / Fehm / Fersis / Friedrich / Friedrichs / Gerber / Hanf / Janni / Kolberg-Liedtke / Kreipe / Loibl / Lück / Lüftner / Lux / Maass / Mundhenke / Oberhoff / Park-Simon / Reimer / Rezai / Rody / Schaller / Schütz / Seegenschmiedt / Solbach / Solomayer / Souchon / Thomssen/**

### ■ Version 2025:

**Gerber / Untch**

# Sites of Metastases

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

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# General Treatment Aspects of Metastases



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- **Histological verification**
- **Cytological verification, if histology not possible**
- **Systemic therapy preferred**
- **Consider surgery of metastases in case of good response to palliative treatment, oligometastases (cave: no clear definition available)**
- **Stereotatic Radiotherapy for patients with oligometastases**
- **Local-interventional ablative procedure**
- **Local treatment in the case of pain, exulceration, persistence after systemic treatment, bowel obstruction, hydrocephalus occlusus, spinal cord compression**
- **Systemic treatment after surgery**

	Oxford		
	LoE	GR	AGO
	3	B	++
	3	B	+
	2a	B	++*
	2b	C	+/-
	2b	B	+/-
	3b	C	+/-
	5	D	+/-
	2c	B	++

\* See chapters with systemic treatment recommendations

# Different Definitions of Oligometastatic Disease (OMD)

## Societies / Organisations or inclusion criteria of prospective clinical trials (selection)

ESMO	limited or low-volume metastatic disease; up to five lesions in total, not necessarily in the same organ; all potentially amenable to receive local treatment
ESTRO/ASTRO	1-5 metastatic lesions; controlled primary tumor optional, all metastatic sites must be safely treatable
ESTRO/EORTC OligoCare project	Different clinical scenarios of OMD: synchronous vs. metachronous, repeat vs. de novo OMD, oligorecurrence vs. oligoprogression, oligopersistence vs. oligoprogression, induced vs. genuine OMD.
ABC-7	Low volume metastatic disease (up to 5 lesions and not necessarily in the same organ), potentially amenable for local treatment, aimed at achieving a complete remission status; highly dependent on the imaging method used. <b>Note:</b> OMD sites need to be solid; excludes pleural effusions, ascites, leptomeningeal disease.
SABR-COMET trial (NCT05784428)	$\leq 5$ metastatic sites; small subset for breast cancer patients (n = 18)
NRG-BR002 trial (NCT02364557)	controlled locoregional disease and $\leq 4$ metastases (standard imaging), $\leq 12$ months systemic therapy without progression
OLIGOMA trial (NCT04495309)	up to 5 clinically manifest metastases, maximum of 3 cerebral metastases known

# Local Therapy in Primary Metastatic Disease

	Oxford		
	LoE	GR	AGO
■ <b>Surgery (R0) of the primary tumor (individualized procedure in case of oligometastatic disease)</b>			
■ In case of bone metastases only	1b	B	+/-
■ In case of visceral metastases	1b	B	-
■ <b>Axillary surgery for cN1</b>	3b	B	+/-
■ <b>Sentinel biopsy if cN0</b>	5	D	-
■ <b>Radiotherapy of the primary tumor</b>			
■ Alone (without surgery)	3a	C	+/-
■ After local surgical treatment with BCS or mastectomy (according to adjuvant indication)	2c	B	+/-

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# Randomized Phase III Trials ST +/- Surgery of the Primary Tumor

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Trial	n	Therapy prior to randomization	Local Control	Improved OS Primary Endpoint	QoL
ECOG 2108 * <sup>1,2</sup> (USA/Kanada) 2001-2016	256	4-8 months systemic therapy	yes	no	ns
Tata Memorial Hospital * <sup>3</sup> (India) 2005-2012	350	chemotherapy	yes	no	-
MF07-01 * <sup>4,5,6,7</sup> (Turkey) 2008-2012	278	no systemic therapy	no 10 y LRP: LRT 1% vs 14% ST, s	10 y fu OS: LRT 19% vs. ST 5%, s (HR+, Her2-, < 55 y, solitary bone only metastasis)	ns
ABCSG-28#* <sup>8,9</sup> (Austria) 2010-2019	90	no systemic therapy	yes	no	ns
JCOG 1017 (Japan) 2011-2018	410	primary ST	Completed, results not reported so far		

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ns not significant, s: significant #trial terminated due to poor recruitment  
ST = systemic therapy, LRT= locoregional therapy, LRP = locoregional progression

# Prospective Registry Study (Bone only)

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Trial	n	Randomization	Local Control	Improved OS Primary Endpoint	QoL
BOMET MF 14-01# 2014-	505	ST vs LRT (LRT+ST vs. ST+LRT)	yes	3 y fu: improved OS in the LRT group (HR 0.40)  HR+, Her2-; Her2+ subgroups, no benefit in triple neg. patients	-

# Liver Metastases

## Local Therapy

Oxford

LoE GR AGO

	LoE	GR	AGO
<ul style="list-style-type: none"> <li>▪ <b>Resection of liver metastases (R0)</b> <ul style="list-style-type: none"> <li>• HR-positive: chemotherapy-sensitive, long disease-free interval, absence of extrahepatic disease, <math>\leq 3</math> metastases</li> <li>• HER2-positive: age &lt; 50 y, metastases &lt; 5 cm, no further metastases</li> </ul> </li> </ul>	3a	B	+/-
<ul style="list-style-type: none"> <li>▪ <b>Interventional regional chemotherapy (TACE)*</b></li> </ul>	3b	C	+/-
<ul style="list-style-type: none"> <li>▪ <b>Interventional regional radiotherapy (SIRT/TARE)*</b></li> </ul>	3a	B	+/-
<ul style="list-style-type: none"> <li>▪ <b>Stereotactic Radiotherapy with VMAT (SRS-VMAT), other modalities*</b></li> </ul>	2a	B	+/-
<ul style="list-style-type: none"> <li>▪ <b>Regional ablative procedures (RFA, MWA)</b> <ul style="list-style-type: none"> <li>▪ IRE, LITT, HIFU</li> <li>▪ Cryoablation</li> </ul> </li> </ul>	3b 5 3b	C D C	+/- - -

\* interdisciplinary decision

# Pulmonary Metastases

## Local Therapy

Oxford

LoE GR AGO

- |   | LoE | GR | AGO |
|---|-----|----|-----|
| <ul style="list-style-type: none"> <li>Before any local therapy: staging and biopsy, histology for exclusion of second tumor</li> </ul>   | 3a  | B  | +   |
| <ul style="list-style-type: none"> <li>Resection of pulmonary metastases by VATS or conventional resection                             <ul style="list-style-type: none"> <li>In case of multi-locular metastatic disease</li> <li>In case of single / few unilateral metastasis</li> </ul> </li> </ul> | 3a  | B  | -   |
| <ul style="list-style-type: none"> <li>In case of single / few unilateral metastasis</li> </ul>   | 3a  | B  | +/- |
| <ul style="list-style-type: none"> <li>Thermoablation (CT-guided RFA, LITT)</li> </ul>  | 3b  | C  | +/- |
| <ul style="list-style-type: none"> <li>Regional radiotherapy<br/>(stereotactic radiotherapy with volumetric intensity modulated arc therapy (SRS-VMAT))</li> </ul>  | 2a  | B  | +/- |

\* VATS = video-assisted thoracic surgery

# Malignant Pleural Effusion (MPE)

## Local Therapy



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	Oxford		
	LoE	GR	AGO
■ If short life expectancy, less invasive procedures should be considered	4	C	++
■ VATS and Talcum-pleurodesis*	1b	B	++
■ Continuous pleural drainage	2a	B	++
■ Chemical pleurodesis*			
■ Talcum powder	1a	B	+
■ Intrathoracic chemotherapy	2b	C	+/-
■ Povidone-iodine (20 ml of 10% solution)	1b	B	+
■ Serial thoracentesis	4	C	+/-

\* Adequate pain-relief

VATS: video-assisted thoracoscopic surgery

# Malignant Ascites

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### Ascites:

- Puncture, drainage in symptomatic patients
- Continuous drainage of ascites
- Systemic therapy
- Local chemotherapy

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

# Malignant Pericardial Effusion

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### Symptomatic pericardial effusion:

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

### Oxford

LoE	GR	AGO
3b	B	++
4	C	++
4	C	+
4	C	+/-

# Bone Marrow Infiltration Associated with Pancytopenia

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

■ **Weekly chemotherapy with\*:**

- Epirubicin, Doxorubicin, Paclitaxel
- Capecitabine

■ **HER2-positive:**

- anti-HER2-treatment

■ **Hormone receptor-positive:**

- Endocrine-based therapy

\* Consider pre-treatment

# Soft Tissue / Skin Metastasis

## Local Therapy

### Oxford

LoE	GR	AGO
-----	----	-----

4	C	+/-
---	---	-----

- **Surgery of limited locoregional metastasis (e.g. skin, muscle, nodal) with complete resection (R0) after exclusion of further metastases**

- **Radiotherapy for\*:**

- **Soft tissue metastases** 3b C +/-
- **Paresis, spinal cord compression** 2b C ++
- **Plexus infiltration** 3b C ++
- **Additional regional hyperthermia with radiotherapy\*\*** 4 C +/-

- **Electrochemotherapy** 4 C +/-

\* Exception: acute indication for surgery

\*\* In centers listed on the DKG website

<https://www.krebsgesellschaft.de/deutsche-krebsgesellschaft-wtrl/deutsche-krebsgesellschaft/ueber-uns/organisation/sektion-bearbeitungsgemeinschaften/iah.html>

# Oligo-Metastases

## Contralateral Axillary Metastasis

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**“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%)