

Diagnosis and Treatment of Patients with early and advanced Breast Cancer



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Sites of Metastases

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FORSCHEN
LEHREN
HEILEN

Sites Of Metastases

Specific Approaches to Metastatic Disease

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- **Versionen 2002–2021:**

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

- **Version 2022:**

Kolberg-Liedtke / Solbach

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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Distribution of Breast Cancer Metastases

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Risk of breast cancer metastases

- is approx. 20%
- is dependent on molecular breast cancer subtype (i.e., lower in luminal A and higher in HER2-enriched and basal-like breast cancer)
- is decreasing due to more efficacious therapeutic regimens
- about 6% of new breast cancer diagnosis are stage IV and have an estimated 5-y OS rate of 27%

Pattern of breast cancer metastases

- Bone metastases are most common metastases (30-40%), followed by lung (20%) pleura (8%) and liver metastases (isolated liver metastases approx. 5%). Other locations are rare
- Breast cancer is the most common origin of cutaneous metastases and is considered to be the most prevalent primary tumor of all metastases to the orbit
- Metastatic pattern strongly depends on breast cancer molecular biology and efficacy of (targeted) therapy (i.e., compared with luminal A tumors, luminal/HER2 and HER2-enriched tumors are associated with a significantly higher rate of brain, liver, and lung metastases, while Basal-like tumors show a higher rate of brain, lung, and distant nodal metastases but a significantly lower rate of liver and bone metastases)
- Pattern of breast cancer metastases is one of several factors determining disease prognosis

General Treatment Aspects of Metastases



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- **Histological / cytological verification**
- **Systemic therapy preferred**
- **Consider surgery of metastases only in case of good response to palliative treatment, oligometastases**
- **Stereotatic Radiotherapy for patients with oligometastases**
- **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	+
2a	B	++*
2b	C	+
2a	B	+
5	D	+/-
2c	B	++

* See chapters with systemic treatment recommendations

Local Therapy in Primary Metastatic Disease

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

- **Surgery (R0) of the primary tumor (individualized procedure in case of oligometastatic disease)**
 - In case of bone metastases only
 - In case of visceral metastases
- **Axillary surgery for cN1**
- **Sentinel biopsy if cN0**
- **Radiotherapy of the primary tumor**
 - Alone (without surgery)
 - After local surgical treatment with BCS or mastectomy (according to adjuvant indication)

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

Trial	n	Therapy prior to randomization	Local Control	Improved OS Primary Endpoint	QoL
ECOG 2108 * ^{1,2} (USA/Kanada) 2001-2016	256	4-8 months systemic therapy	yes	no	ns
Tata Memorial Hospital * ³ (India) 2005-2012	350	chemotherapy	yes	no	-
MF07-01 * ^{4,5,6,7} (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
ABC SG-28#* ^{8,9} (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
3a	B	+/-
3b	C	+/-
3b	C	+/-
2a	B	+/-
3b	C	+/-
5	D	-
3b	C	-

- **Resection of liver metastases (R0)**
 - **HR-positive: chemotherapy-sensitive, long disease-free interval, absence of extrahepatic disease, ≤ 3 metastases**
 - **HER2-positive: age < 50 y, metastases < 5 cm, no further metastases**
- **Interventional regional chemotherapy (TACE)***
- **Interventional regional radiotherapy (SIRT/TARE)***
- **Stereotactic Radiotherapy with VMAT (SRS-VMAT), other modalities***
- **Regional ablative procedures (RFA, MWA)**
 - **IRE, LITT, HIFU**
 - **Cryoablation**

* interdisciplinary decision

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Pulmonary Metastases

Local Therapy

	Oxford		
	LoE	GR	AGO
■ Before any local therapy: staging and biopsy (CT-guided FNA / CNB or transbronchial FNA, EBUS, VATS)	3a	B	+
■ Resection of pulmonary metastases by VATS or conventional resection			
■ In case of multi-locular 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 (stereotactic radiotherapy with volumetric intensity modulated arc therapy (SRS-VMAT))	2a	B	+/-

- Before any local therapy: staging and biopsy (CT-guided FNA / CNB or transbronchial FNA, EBUS, VATS)
- Resection of pulmonary metastases by VATS or conventional resection
 - In case of multi-locular metastatic disease
 - In case of single / few unilateral metastasis with curative intent
- Thermoablation (CT-guided RFA, LITT)
- Regional radiotherapy
(stereotactic radiotherapy with volumetric intensity modulated arc therapy (SRS-VMAT))

* 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	+
■ Bleomycin, Doxycycline, Mitoxantrone	2b	C	+/-
■ Povidone-iodine (20 ml of 10% solution)	1b	B	+
■ Systemic treatment after pleurodesis	3b	C	+/-
■ Serial thoracocentesis	4	C	+/-

* Adequate pain-relief

VATS: video-assisted thoracoscopic surgery

Malignant Ascites

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Ascites:

- Puncture, drainage in symptomatic patients
- Continous 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

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

- **Weekly chemotherapy with*:**

- Epirubicin, Doxorubicin, Paclitaxel

- Capecitabine

- **HER2-positive:**

- Add anti-HER2-treatment

- **Hormone receptor-positive:**

- Endocrine-based therapy

* Consider pre-treatment

Soft Tissue Metastasis

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

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

Oligo-Metastases

Contralateral Axillary Metastasis

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“OLIGO-METASTATIC DISEASE in CONTRALATERAL AXILLA 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”

ABC6 2021: LoE: Expert opinion/NA (85%)