

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



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## Breast Cancer: Specific Situations

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- **Version 2025:**

**Ditsch / Fehm**

# Content – Specific Situations

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- **Frail, elderly patients**
  - Geriatric assessment
- **Male patients**
- **Inflammatory breast cancer (IBC, cT4d)**
- **Axillary metastases in occult breast cancer (ax. CUP)**
- **Paget's disease**
- **Malignant and Boderline Phylloides-Tumor**
- **Sarcoma, Angiosarcoma**
- **Metaplastisc breast cancer**

# Treatment for Elderly Patients

## AGO ++

- In general, treatment recommendations are the same as for the “younger patients”, taking into account different biological, physical, psychological and treatment-related factors and the geriatric assessment (GA).
- Treatment options and recommendations are based on an assessment of the patient's physical condition, vulnerability, frailty, life expectancy and individual goals, and not just on age.
- It is integrated into a collaborative decision-making process, taking into account the values and goals of the individual patient.

# Treatment for Frail Patients

(Life Expectancy < 5 yrs., Substantial Comorbidities)

	Oxford		
	LoE	GR	AGO
	<b>2b</b>	<b>C</b>	<b>++</b>
	<b>2b</b>	<b>C</b>	<b>+</b>
	<b>1a<sup>a</sup></b>	<b>A</b>	<b>+</b>
	<b>2b</b>	<b>B</b>	<b>+</b>
	<b>1a</b>	<b>A</b>	<b>+</b>
	<b>2b</b>	<b>B</b>	<b>+</b>
	<b>1b</b>	<b>A</b>	<b>+</b>
	<b>1a</b>	<b>B</b>	<b>+</b>
	<b>2b</b>	<b>B</b>	<b>+/-</b>

- **Reduced standard treatment**
- **Options extrapolated from trials in elderly:**
  - **No breast surgery to prolong life (consider endocrine therapy)**
  - **Breast surgery for local control**
  - **No axillary clearing for cN0**
  - **Endocrine therapy (HR+)**
  - **Endocrine therapy alone (without surgery/radiotherapy at first diagnosis)**
  - **No endocrine adj. therapy after BCS and radiotherapy**
  - **No radiotherapy for pT1, pN0, R0, ER / PR positive, HER2-negative, endocrine adj. therapy**
  - **No radiotherapy for pT2-3, ER /PR positive, HER2- negative, endocrine adj. therapy**

# Geriatric Assessment

Links to current frailty scales:

- **Ability to tolerate treatment varies greatly („functional reserve“)**
- **Comprehensive geriatric assessment describes a multidisciplinary evaluation of independent predictors of morbidity & mortality for older individuals (CGA)**
  - Physical, mental, and psycho-social health
  - Basic activities of daily living (dressing, bathing, meal preparation, medication management, etc.)
  - Living arrangements, social network, access to support services
- **General assessment tools:**
  - **Charlson Comorbidity Index (CCI, widely used; good predictor over a 10-year period)**
  - **12 prognostic indicators to estimate 4-year mortality risk**
  - **Short screening tests (more qualitative evaluation)**
    - **IADL (IADL = The Lawton Instrumental Activities of Daily Living Scale with 8 domains of function, that are measured)**
    - **G8 (Age plus Malnutrition Assessment, MNA)**
    - **Geriatric Prognostic Index (GPI), 3 parameters in oncological patients (food intake in the last 3 months, >3 prescribed drugs, mobility and autonomy)**
    - **Timed-up-and-go-test**
    - **Frailty Index (FI), Carolina Frailty Index (CFI)**



# Male Breast Cancer\*: Diagnostic Work-Up and Loco-Regional Therapy

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	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>■ <b>Diagnostic work-up as in women</b> <ul style="list-style-type: none"> <li>■ Ultrasound</li> <li>■ Mammography</li> </ul> </li> <li>■ <b>Standard-surgery: Mastectomy</b> <ul style="list-style-type: none"> <li>■ BCS is an option (tumor / breast relation)</li> <li>■ Sentinel-node excision (SLNE)</li> <li>■ In occult breast cancer</li> </ul> </li> <li>■ <b>Radiotherapy as in women (consider tumor / breast relation!)</b></li> <li>■ <b>Genetic counseling (see genetics chapter)</b></li> <li>■ <b>Screening for 2<sup>nd</sup> malignancies according to guidelines</b></li> </ul>	4	C	+
	2b	B	++
	3b	C	+
	4	C	++**
	4	C	++**
	2a	B	+
	2b	B	+
	2a	C	+
	2b	B	++
	GCP		++

\* Treatment in certified breast cancer centers recommended; \*\* Participation in register study recommended

# Male Breast Cancer: Prognostic Factors

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- **Nodal status**
- **Age**
- **Tumor size**
- **ER / PR Expression**
- **Ki-67 Expression**
- **Grade**
- **Genomic signatures**

Oxford		
LoE	GR	AGO
2b	A	++
2b	B	+
2b	A	++
2b	A	++
2b	C	+/-
2b	C	+/-
2b	B	+

# Male Breast Cancer: Systemic Therapy

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- **(Neo-)adjuvant chemotherapy as in women**
- **HER2-targeted therapy (if HER2-positive)**
- **Endocrine therapy**
  - Tamoxifen
  - GnRH $\alpha$  and AI
  - Aromatase inhibitors without GnRH $\alpha$
  - Fulvestrant (metastatic BC)
  - CDK4/6i (in combination)
- **Palliative chemotherapy as in women**

Oxford		
LoE	GR	AGO
<b>2a</b>	<b>B</b>	<b>++</b>
<b>5</b>	<b>D</b>	<b>++</b>
<b>4</b>	<b>D</b>	<b>++</b>
<b>2b</b>	<b>B</b>	<b>++</b>
<b>4</b>	<b>C</b>	<b>+</b>
<b>2b</b>	<b>B</b>	<b>-</b>
<b>4</b>	<b>C</b>	<b>+/-</b>
<b>2b</b>	<b>B</b>	<b>+</b>
<b>4</b>	<b>C</b>	<b>++</b>

# Inflammatory Breast Cancer (IBC, cT4d)

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	LoE	GR	AGO
▪ <b>Invasive BC and clinical signs of inflammation (e.g. <math>\geq 1/3</math> of the breast affected) determine stage cT4d</b>			++
▪ <b>Staging (including adequate breast imaging)</b>	2c	B	++
▪ <b>Skin punch biopsy (at least 2; detection rate &lt; 75%)</b>	2c	B	+
▪ <b>Treatment according to guidelines (neoadjuvant or adjuvant – as in non-IBC)</b>	2b	B	++
▪ <b>Neoadjuvant chemotherapy</b>	2b	B	++
▪ <b>Mastectomy after chemotherapy</b>	2c	B	+
▪ <b>Breast conserving therapy in case of pCR (individual)</b>	2b	C	+/-
▪ <b>Delayed breast reconstruction</b>	3b	C	+
▪ <b>Sentinel excision only</b>	3b	C	-
▪ <b>Radiotherapy of the chest wall including regional lymph nodes independent of therapy response</b>	2c	B	++

# Axillary Metastasis in Occult Breast Cancer (ax. CUP) Diagnostic Imaging

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	Oxford		
	LoE	GR	AGO
▪ <b>Breast imaging incl. Breast-MRI</b>	<b>3</b>	<b>B</b>	<b>++</b>
▪ <b>Exclude contralateral cancer</b>	<b>3</b>	<b>B</b>	<b>++</b>
▪ <b>Staging</b> (CT thorax / abdomen, pelvis, bone scan)	<b>3</b>	<b>B</b>	<b>++</b>
<b>If histological diagnosis is not certain</b>			
▪ <b>Exclude non-breast malignancy, especially in case of TNBC</b> (e.g. NEC, female genital tract, lung, thyroid gland, stomach, skin, ENT)	<b>5</b>	<b>D</b>	<b>++</b>
▪ <b>PET / PET-CT</b>	<b>3b</b>	<b>B</b>	<b>+</b>

# Axillary Metastasis in Occult Breast Cancer (Cancer of Unknown Primary – AxCUP)

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- **Incidence: < 1% of metastatic axillary disease**
- **In > 95% occult breast cancer, < 5% other primary**
- **Immunohistology**
  - ER-positive: 55%
  - HER2 3+: 35%
  - Triple-negative: 38%
- **Nodal status:**
  - 1 - 3 Ln-Met. in 48%
  - > 3 Ln-Met in 52%
- **Outcome similar or better compared to breast cancer with similar tumor biology and tumor stage**

# Axillary Metastasis in Occult Breast Cancer (ax. CUP)

## Pathology, Molecular Pathology

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	Oxford		
	LoE	GR	AGO
■ Immunohistochemistry (ER, PR, HER2, Ki-67, GATA)	5	D	++
■ Immunohistochemistry (e.g. Ck5/6, Ck7, Ck20, SOX-10, PAX-8, TTF1, Synaptophysin etc.) to exclude other primary malignancies in case of TNBC phenotype or unusual histology, e.g. NEC, female genital tract, lung, ENT tumors, thyroid, stomach, skin	5	D	++
■ Gene expression profiling for determination or primary site (e.g. CUPprint, Pathwork, TOT, CancerType)	2c	B	+/-
■ NGS, epigenetics for determination of primary site (Panel-Sequencing, e.g. EPICup)	2c	B	+/-
■ Prognostic gene expression tests	5	D	--

# Axillary Metastasis in Occult Breast Cancer (ax. CUP): Therapy

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- **Axillary dissection**
  - Targeted axillary dissection after NACT (in case of clinical complete remission)
- Irradiation of regional lymph nodes according to breast cancer guidelines (AGO)
- Breast irradiation if breast MRI is negative (acc. BCT)
- Mastectomy if breast MRI is negative
- (Neo-)adjuvant systemic therapy according to breast cancer guidelines (AGO)

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

# „BCT“ in patients with axillary met's and occult primary (AxCUP, OBC)



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**Kim H, Park W, Kim SS et al. Prognosis of patients with axillary lymph node metastases from occult breast cancer analysis of multicenter data. Radiat Oncol J. 2021 Jun;39(2):107-112.**

Retrospective analysis, n = 53 with AxCUP and OBC (adenocarcinoma); exclusion of a primary by extensive imaging. Eleven pts received blind upper quadrantectomy, 42 no breast surgery; 46 pts received whole breast irradiation (WBI), 7 did not; median F/U 85 months .

Result: 2 in-breast recurrences, 1 RLN rec., 1 combined in-breast and RLN, no distant metastases.

**5 year DFS with WBI: 97.8% without WBI 83,3% (p = 0.01 univariate;** in multivariate analysis nor biology nor extent of the disease nor therapy had a significant impact).

Discussion: ..in patients confirmed to have no lesion in the breast by contemporary imaging studies, it is necessary to include the ipsilateral breast in the radiation field in females with OBC presenting as AxCUP.

**Tsai C, Zhao B, Chan T, Blair SL. Treatment for occult breast cancer: A propensity score analysis of the National Cancer Database. Am J Surg. 2020 Jul;220(1):153-160.**

Given the equipoise in overall survival among the treatment options, we conclude that after axillary clearance, **breast preservation and radiation therapy alone may be sufficient** in the treatment of patients with occult breast cancer.

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# Paget's Disease of the Breast Diagnosis

## „Mammary Paget Disease is a Sentinel Sign“

- **Histological verification by skin biopsy\***
- **Mammography, sonography**
- **MRI of the breast if other imaging negative**
- **Immunohistochemistry (ER, PR, HER2, CK7) to detect benign and HER2-negative cases**

Oxford		
LoE	GR	AGO
		++
4	D	++
4	C	+
5	D	++

\* including all skin strata (e.g. by punch biopsy or wedge excision)

# Paget's Disease of the Breast

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- **Definition: Paget's disease of the breast is characterized by an intraepidermal tumor manifestation originating in intraductal or invasive breast cancer.**
- **Clinical presentation: skin eczema of the nipple, areola and surrounding skin; thickening, pigmentation and scaly skin**

Feature	Frequency
Presentation	Paget's disease with invasive Ca. (37-58%) Paget's disease mit DCIS (30-63%) Isolated Paget's disease (4-7%) Isolated Paget's disease with invasion (rare)
IHC	HER2-positive (83-97%) ER-positive (10-14%) AR-positive (71-88%)
Prognosis and tumor biology	Better in isolated Paget's disease Worse if in combination with invasive breast cancer or DCIS compared to isolated Paget's disease



# Borderline and Malignant Phyllodes Tumor Diagnosis

- **Mammography, sonography**
- **Diagnosis on core biopsy, grade determination on resection specimen**
- **Breast MRI**
- **Staging only malignant PT (CT thorax / abdomen, bone scan)**

Oxford		
LoE	GR	AGO
3	C	++
3	C	++
3	C	+/-
5	D	++

# Borderline and Malignant Phyllodes Tumor

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- **Name derived from greek term of “Phyllon” (leaf) due to its lobulated histological aspect**
- **Differential diagnosis may be problematic on core biopsy**
- **Resection margin is independent prognostic parameter**
- **Comparable rates of recurrence in association with BCT or mastectomy**
- **In-Breast recurrence relatively frequently seen (10 - 30%)**
- **Distant metastasis relatively rare (< 10%) and almost exclusively seen in malignant phyllodes tumor.**
- **Adverse pathological criteria: marked stromal cellularity and overgrowth, increased nuclear atypia, presence of large necrohemorrhagic areas, and high mitotic activity associated with increased risk of distant recurrence**

# Phyllodes Tumor

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- Frequency 0.3 – 1% of all primary breast tumors

parameter	frequencies
<b>Grading (3-STEP histological grading system)</b>	<b>Benign (75%) Borderline (16%) Malignant (9%)</b>
<b>Median age at time of diagnosis</b>	<b>Benign PT: 39 y Borderline PT: 45 y Malignant PT: 47 y</b>
<b>Local recurrence</b>	<b>Benign PT: 4 – 17% Borderline PT: 14 – 25% Malignant PT: 23 – 30%</b>
<b>Metastasis</b>	<b>Benign PT: &lt; 1% Borderline: PT: 1.6% Malignant PT: 16-22%</b>

**10 y OS: 86–90% (range: 57–100%) depending on subtype and unfavorable histological criteria**

# Borderline and Malignant Phyllodes Tumor Surgery



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- **Fibroepithelial lesions with rapid growth or size > 3 cm should be excised (independently from the any CNB result)**
- **If the result of the CNB is unclear or suspicious for PT, excision with clear margins should be performed**
- **SLNE / Axillary dissection (if clinically unsuspecting)**
- **Treatment of local recurrence**
  - **R0 resection or simple mastectomy**

Oxford		
LoE	GR	AGO
5	D	++
5	D	++
4	C	--
4	C	++

# Phyllodes Tumors of the Breast: Canadian National Consensus Document Using Modified Delphi Methodology

**Canadian Phyllodes Tumor Consensus Panel** (23 panelists): Example of one out of 109 statements on diagnosis and therapy of phyllodes tumors that were discussed (73 with consensus).

*The following statements are referring to MALIGNANT phyllodes (diagnosed on biopsy)*

- If the diagnosis of malignant PT is known preoperatively, malignant PT should under-go wide excision (clinical 1 cm), with the goal of negative microscopic margins 87%
- In patients with negative margins who undergo wide excision (clinical 1cm) – if the microscopic margin is:
    - < 2 mm: reexcision of margin can be offered 82%
    - 2–10 mm: no re-excision should be offered 65%
    - > 10 mm: no reexcision should be offered 100%
  - Patients with tumor on ink after breast conservation, should be offered reexcision (this includes “shelled out” and positive margins) 96%



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# Borderline and Malignant Phyllodes Tumor - Margins -



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- **Intended lesion-free surgical margins are\***

- in borderline PT:  $\geq 2$  mm
- in malignant PT:  $\geq 10$  mm

- **Intended pathologically lesion-free margins are\***

- in borderline PT: negative (no ink on the tumor)
- in malignant PT:  $\geq 2$  mm

- **Re-resection recommended**

- in borderline PT: if margin\* positive (ink on tumor)
- in malignant PT: if margin  $< 2$  mm

## Oxford

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

2b	B	++
----	---	----

2b	B	++
----	---	----

2b	B	++
----	---	----

\* Margins related to breast tissue only (but not to skin or to the thoracic wall)

# Borderline and Malignant Phyllodes Tumor - Adjuvant Radiotherapy -

Adjuvant radiotherapy of the breast and the thoracic wall is aimed at local control.

- **BCS, R0-resection**

- Borderline PT: no
- Malignant PT: yes (independently from the size of the lesion)

- **Mastectomy, R0-resection**

- Borderline PT: no
- Malignant PT: < 5 cm: no
- Malignant PT: ≥ 5 cm: with aggressive pathology or growth

- **Mastectomy, R1-resection**

- Borderline PT: no
- Maligner PT: ja (independently from the size of the lesion)

Oxford

LoE GR AGO

2b B +

2b B +

2b B +

# Borderline and Malignant Phyllodes Tumor

## Systemic Adjuvant Therapy



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- **Systemic adjuvant therapy (chemo, endocrine)**
  - Adjuvant endocrine therapy (irrespect. of ER/PR)
  - Adjuvant chemotherapy
  - Primary systemic therapy, if complete resection (R0) presumably cannot be achieved (Adriamycin/Ifosfamid)
- **Adjuvant Treatment of local recurrence**
  - Radiotherapy, chemotherapy after R1 resection
- **Distant metastasis (very rare)**
  - Multidisciplinary case discussion („Sarcoma board“)
  - Treatment like soft tissue sarcomas
  - Surgical resection of metastatic lesions

	Oxford		
	LoE	GR	AGO
■ Adjuvant endocrine therapy (irrespect. of ER/PR)	4	C	-
■ Adjuvant chemotherapy	4	C	-
■ Primary systemic therapy, if complete resection (R0) presumably cannot be achieved (Adriamycin/Ifosfamid)	4	C	+
■ Radiotherapy, chemotherapy after R1 resection	4	C	+/-
■ Multidisciplinary case discussion („Sarcoma board“)	5	D	++
■ Treatment like soft tissue sarcomas	4	C	++
■ Surgical resection of metastatic lesions	4	C	+

# Primary Angiosarcoma of the Breast\*

## Diagnosis



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	LoE	GR	AGO
■ Mammography, sonography to determine extent of disease	3a	C	-
■ Preoperative MRI to determine the extent of disease	3a	C	++
■ Diagnosis by core biopsy	3a	C	++
■ Diagnosis by FNB	3a	C	--
■ Staging (CT thorax & abd.; angiosarcoma: MRI brain)	4	D	++
■ Prognostic factors: size, grade, margins	3a	C	++

\* Therapy in specialized centers recommended

# Sarcomas of the Breast

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- **Not infrequently associated with familial syndromes (Li-Fraumeni, familial adenomatous polyposis, neurofibromatosis type 1)**
- **Primary sarcomas: angiosarcoma, undifferentiated sarcoma, leiomyosarcoma, liposarcoma, osteosarcoma**
- **Secondary malignancies of the breast:**
  - Radiotherapy-Associated Angiosarcoma
  - Breast Implant Associated Large-Cell Anaplastic Lymphoma (BI-ALCL)
- **Rare: intramammary sarcoma metastases**
- **Staging: TNM (UICC) or AJCC scheme of the soft tissue sarcoma analogous to sarcoma of the breast**
- **Grading: Analogous to the FNCLCC system for sarcoma or according to Rosen (1988) for angiosarcomas**

# Primary Angiosarcoma of the Breast

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- **Most common primary sarcoma of the breast**
- **Young age (median: 24–46 years)**
- **Indistinct tumor borders**
- **Large tumor (median: 5–7 cm)**
- **Uncharacteristic findings on mammography and sonography**
- **High local recurrence risk, even after mastectomy**
- **More unfavorable prognosis than other primary sarcoma of the breast**
- **Metastasize early, often to the lung and liver**

# Primary Angiosarcoma of the Breast\*

## Therapy

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	Oxford		
	LoE	GR	AGO
■ <b>Surgery with wide clear margins, mostly as mastectomy</b>	<b>2b</b>	<b>C</b>	<b>++</b>
■ <b>Breast-conserving surgery (wide excision)</b>	<b>3a</b>	<b>C</b>	<b>+/-</b>
■ <b>SLNE or axillary dissection if cN0</b>	<b>3a</b>	<b>C</b>	<b>--</b>
■ <b>Adjuvant chemotherapy (anthracycline / taxane-based)</b>	<b>4</b>	<b>C</b>	<b>+/-</b>
■ <b>Adjuvant radiotherapy if high risk (size &gt; 5 cm, R1)</b>	<b>4</b>	<b>C</b>	<b>+/-</b>
■ <b>Presentation in a sarcoma board</b>	<b>5</b>	<b>D</b>	<b>++</b>

\* Therapy in specialized centres recommended

# Secondary Angiosarcoma of the Breast Therapy

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<ul style="list-style-type: none"> <li> <b>Tumor resection (BCT / mastectomy)</b>  <b>Radical surgery ist not associated with better outcome</b> </li> </ul>	<b>3a</b>	<b>C</b>	<b>+</b>
<ul style="list-style-type: none"> <li> <b>(Neo-)adjuvant chemotherapy</b> <ul style="list-style-type: none"> <li>Consider „trimodality treatment“ in case of locally advanced angiosarcoma (neoadjuvant taxanes =&gt; neoadjuvant radiochemotherapy =&gt; surgical resektion)</li> </ul> </li> </ul>	<b>3a</b>	<b>C</b>	<b>+/-</b>
<ul style="list-style-type: none"> <li> <b>Adjuvant radiotherapy if high risk (size &gt; 5 cm, R1)</b> </li> </ul>	<b>2b</b>	<b>B</b>	<b>+/-</b>
<ul style="list-style-type: none"> <li> <b>Regional hyperthermia (to improve local control) plus chemotherapy and / or radiotherapy</b> </li> </ul>	<b>2b</b>	<b>B</b>	<b>+/-</b>

# Secondary (Radiotherapy-associated) Angiosarcoma of the Breast

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- **Cumulative incidence of radiotherapy-associated sarcoma: 3.2 per 1,000 after 15 years**
- **Clinical presentation**
  - > 5 years after BCT or mastectomy with irradiation
  - usually intracutaneously or subcutaneously in the irradiation area with livid discoloration
  - multiple foci
  - most often in advanced stages (II - III)
  - metastasis mostly pulmonary
  - lymph node metastasis possible
- **Prognosis is more unfavorable than in non-radiotherapy-associated sarcoma**
- **Survival: after 5 yrs. up to 50.5%, after 10 yrs. up to 25.2%**

# Trimodality Therapy Improves Disease Control in Radiation-Associated Angiosarcoma of the Breast (RAASB)

38 patients (median age 69 years) with RAASB; median F/U 5,6 y

- **Trimodality therapy** consisted of
  - (i) taxane induction therapy, followed by
  - (ii) concurrent taxane and irradiation therapy, followed by
  - (iii) surgical resection with wide margins.

Results:

- n = 16 trimodal therapy: pCR 12/16.  
**Loc.rec.: 0/16; dist.met.: 1/16; death 1/16**  
Wound break / sec. wound-healing: 100%
- n = 22 monotherapy/dual therapy:  
**Loc.rec.: 10/22; dist.met.: 8/22; death 7/22**  
Wound break / sec. wound-healing: 48% (p < 0.001)
- **RFS; 93.8% vs. 42.9%; P = 0.004; HR, 7.6 (95% CI: 1.3-44.2)**

# Angiosarcoma of the Breast

## Treatment of Local Recurrence and Metastases

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	Oxford		
	LoE	GR	AGO
<b><u>Treatment of Local Recurrence:</u></b>			
▪ R0 resection	4	C	++
▪ Adjuvant radiotherapy for high-risk patients (tumor size > 5 cm, R1)	4	C	+/-
<b><u>Distant Metastases / Unresectable Tumors:</u></b>			
▪ Treatment like as for soft tissue sarcomas (according to S3 guideline)	4	C	++
▪ Paclitaxel weekly / liposomal doxorubicin (as in angiosarcoma)	2b	B	+
▪ Antiangiogenic treatment (e.g. in angiosarcoma)	4	C	+/-
<b><u>If clinically resistant to therapy</u></b>			
▪ Molecular diagnostics (Multidisciplinary molecular board)	5	D	+

# Metaplastic Breast Carcinoma

## - High-Grade -

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### Consider reference pathology and subtyping.

- **Surgical therapy and axillary staging as in case of NST**
- **Neoadjuvant chemotherapy (frequently chemoresistant)\***
  - **If initially inoperable**
  - **ER pos.**
  - **TNBC, if ICPI (Pembrolizumab) indicated**
  - **HER2 pos. (incl. Anti-HER2-therapy)**
- **Adjuvant chemotherapy (frequently chemoresistant)**
  - **Consider platin/taxane combination in case of mesenchymal differentiation (e.g. spindle cell)**
- **Adjuvant endocrine therapy if HR-positive**
- **Adjuvant radiotherapy according therapy of NST**

Oxford		
LoE	GR	AGO
4	C	++
5	D	+
4	C	--
4	C	+
4	C	+
4	C	-
4	C	+
4	C	+
4	C	++

\* Note: control of local response in short intervals

# Metaplastic Breast Carcinoma – Low Grade With Uncertain Malignant Potential (Fibromatous and Adenosquamous Ca.)\*

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	Oxford		
	LoE	GR	AGO
▪ Surgical therapy and axillary staging as in case of NST	4	C	++
▪ Adjuvant chemotherapy (frequently chemoresistant)	4	C	-
▪ Neoadjuvant chemotherapy (frequently chemoresistant)	4	C	--
▪ Adjuvant endocrine therapy (not applicable, since triple-negative tumors)	4	C	-
▪ Adjuvant radiotherapy according therapy of NST	4	C	+

\* Reference pathology recommended

# Metaplastic Breast Cancer

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## Definition: Metaplastic transformation of epithelial tumor cells

- Epithelial differentiation: squamous cell carcinoma, spindle-cell carcinoma
- Heterologous (mesenchymal) differentiation: chondroid, osseous or otherwise metaplastic breast cancer

## Clinical and pathological characteristics:

- < 1 % of malignant breast neoplasms
- Similar age group as NST breast cancer
- Localized, mostly palpable
- Rapidly growing, poor response to chemotherapy
- > 90 % triple-negative

## Subtypes:

- Highly aggressive with squamous cell or high-grade spindle-cell differentiation
- Less aggressive (low-grade) with mesenchymal, low grade adenosquamous or fibromatosis-like differentiation

## Frequent mutations:

- *TP53*, *EGFR*, *PIK3CA*, *PTEN*
- Possible association to *gBRCA1*-mutation/HRD-positivity