

Diagnosis and Treatment of Patients with early and advanced Breast Cancer

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Breast Cancer: Specific Situations

Breast Cancer: Specific Situations

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- **Versions 2005–2022:**

**Dall / Ditsch / Fehm / Fersis / Friedrich / Gerber / Gluz / Göhring /
Harbeck / Huober / Janni / Kolberg-Liedtke / Loibl / Lück / Lux / Maass /
Mundhenke / Müller / Oberhoff / Rody / Scharl / Schneeweiss / Schütz /
Sinn / Solomayer / Stickeler / Thomssen**

- **Version 2023**

Mundhenke / Schmidt

Breast Cancer: Specific Situations

- **Young patients**
- **Pregnancy- and breast-feeding-associated BC**
- **Elderly patients**
- **Male patients**
- **Inflammatory BC**
- **Occult Breast Cancer (Cancer of unknown primary – axillary CUP)**
- **Paget's disease**
- **Malignant and Borderline Phyllodes Tumor**
- **Angiosarcoma**
- **Breast Implant-Associated Anaplastic Large-Cell Lymphoma (BIA-ALCL)**
- **Metaplastic breast cancer**

Breast Cancer in Young Women ≤ 40 Years

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	Oxford		
	LoE	GR	AGO
▪ Aggressive biological behavior with worse prognosis	2a	B	
▪ Local therapy independent of young age	2b	B	+
▪ Guidelines adapted (neo-)adjuvant systemic treatment (see respective chapters)	1b	A	++
▪ ET interruption (max. 2 years after at least 18 months of previous therapy) in case of desire to have children without short-term survival disadvantage	2b	B	+
▪ GnRHa as ovarian protection (see chapter gynecological problems)	1a	B	+
▪ Genetic and fertility counseling	2b	B	++
▪ Contraception counseling	2b	B	++

Breast Cancer During Pregnancy* or Breast Feeding – Diagnostics and Surgery

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	Oxford		
	LoE	GR	AGO
■ Breast imaging and biopsy like as in non-pregnant patients (no general indication for MRI)	4	C	++
■ Staging if indicated (bone scan after delivery)	5	D	+
■ Full body MRI (without contrast agent)	4	C	+/-
■ Surgery like in non-pregnant patients	4	C	++
■ Sentinel node excision (technetium only)	2b	B	+
■ SLNE during 1 st trimester	5	D	+/-
■ Sensitivity and specificity not established (during lactation); breast feeding should be avoided for 24 hrs	4	C	++
■ Blue dye (not tested in pregnant animals or humans)	4	C	--

* Participation in register study recommended

Breast Cancer During Pregnancy

- (Neo-)adjuvant Therapy -

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- Radiation therapy during pregnancy
- (Neo-)adjuvant chemotherapy only after first trimester (indication as in non-pregnant)
 - Anthracyclines: AC, EC
 - Taxanes
 - Platinum salts (carboplatin, cisplatin)
 - MTX (e.g. CMF)
- Endocrine treatment
- HER2-targeted treatment
- Checkpoint inhibitors
- Bisphosphonates, denosumab

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

Treatment (Chemotherapy, surgical procedure and radiotherapy) of patients with breast cancer during pregnancy should be as similar as possible to standard treatment of young, not pregnant patients with breast cancer.

Breast Cancer During Pregnancy*

– Delivery and Breast-Feeding –

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- Delivery should be postponed until sufficient fetal maturation (avoid iatrogenic prematurity)
- Termination of pregnancy does not improve maternal outcome
- Delivery mode like in healthy women; avoid delivery during chemotherapy-induced leucocyte nadir
- If further systemic therapy is needed after delivery, breast feeding may be contra-indicated depending on drug toxicities

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

Breast Cancer and Pregnancy*

– Family Planning –

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- After breast cancer diagnosis, reproductive techniques can be used to induce pregnancy
- Success rates for getting pregnant and for delivering a child lower in breast cancer patients compared to non-cancer patients
- Breast cancer patients of reproductive age should be offered fertility counseling before starting any kind of treatment
- Breast cancer patients should not be advised against getting pregnant independent of their tumor's hormone receptor status and *gBRCA* status

Oxford		
LoE	GR	AGO
3b	D	
3b	D	
5	D	++
3a	D	

* Participation in register study recommended

Breast Cancer During Pregnancy and Lactation*

- Outcome -

**Oxford
LoE**

- **BC during pregnancy**
 - Prognosis is not worse if adequately treated
- **BC during lactation and within the first year after pregnancy**
 - Prognosis worse than in BCP and if unrelated to pregnancy
- **Pregnancy / lactation after BC**
 - Outcome not compromised

3a

3a

3a

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Geriatric Assessment

- **No specific algorithm is available**
- **Ability to tolerate treatment varies greatly („functional reserve“)**
- **Comprehensive geriatric assessment (CGA) describes a multidisciplinary evaluation of independent predictors of morbidity and mortality for older individuals**
 - 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
- **Assessment tools:**
 - Charlson Comorbidity Index (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
 - Geriatric Prognostic Index (GPI), 3 parameters in oncological patients (psychological distress or acute disease, >3 prescribed drugs, neuropsychological problems)

Treatment for Fit Elderly Patients

(Life Expectancy > 5 yrs. and Acceptable Comorbidities)

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- **Clinical geriatric assessment**
- **Treatment according to guidelines**
 - Surgery similar to „younger“ age
 - Endocrine treatment (endocrine responsive)
 - Chemotherapy (standard regimens)
 - < 70 years
 - > 70 years (especially N+, ER / PR-)
 - Radiotherapy
 - Omit radiotherapy after BCS if low-risk, and if endocrine treatment is administered
 - Anti-HER2-therapy

Oxford		
LoE	GR	AGO
2b	B	++
2a	C	++
2b	B	++
1a	A	++
1a	A	+
2a	C	++*
1a	A	+
1b	B	+
2b	C	+

* Study participation recommended

Treatment for Frail Patients

(Life Expectancy < 5 yrs., Substantial Comorbidities)

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- **Reduced standard treatment**
- **Options extrapolated from trials in elderly:**
 - No breast surgery (consider endocrine options)
 - No axillary clearing (≥ 60 y, cN0, HR-pos)
 - No radiotherapy (Tumor size < 3 cm, pN0, HR-pos)
 - Hypofractionated radiotherapy
 - No chemotherapy if > 70 yrs. and negative risk-benefit analysis

Oxford		
LoE	GR	AGO
2b	C	++
2b	C	+
2b	B	+
1b	B	++
2b	B	+
2b	C	+

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

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■ Diagnostic work-up as in women

- Ultrasound
- Mammography

■ Standard-surgery: Mastectomy

- BCT is an option (tumor / breast relation)
- Sentinel-node excision (SLNE)

■ Radiotherapy as in women (consider tumor / breast relation!)

■ Genetic counseling if one additional relative affected (breast / ovarian cancer)

■ Screening for 2nd malignancies according to guidelines

Oxford		
LoE	GR	AGO
4	C	+
2b	B	++
3b	C	+
4	C	++**
4	C	++**
2b	B	+
4	C	+
2b	B	++
GCP		++

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* 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 (e.g. OncotypeDx)**

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
 - GnRHa and AI
 - Aromatase inhibitors without GnRHa
 - Fulvestrant (metastatic BC)
 - CDK4/6i (in combination)
- **Palliative chemotherapy as in women**

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

Inflammatory Breast Cancer (IBC, cT4d)

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

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

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- **Incidence: < 1% of metastatic axillary disease**
- **In > 95% occult breast cancer, < 5% other primary**
- **Immunhistology**
 - 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 (Axillary CUP) Imaging Diagnostics

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- **Breast imaging incl. Breast-MRI**
- **Exclude contralateral cancer**
- **Exclude non-breast malignancy, especially in case of TNBC** (e.g. skin, female genital tract, lung, thyroid gland, stomach)
- **Staging** (CT thorax / abdomen, pelvis, in certain circumstances also thyroid sonography, HNT-exam)
- **PET / PET-CT**

Oxford		
LoE	GR	AGO
3	B	++
3	B	++
5	D	++
3	B	++
3b	B	+

Axillary Metastasis in Occult Breast Cancer (ex. CUP)

Pathology, Molecular Pathology

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	LoE	GR	AGO
■ ER, PR, HER2, GATA3 (in some cases Ck5/6, Ck7, Ck20, SOX-10, PAX-8, TTF1, and others)	5	D	++
■ Exclusion of other primary malignancies in case of triple-negative phenotype or unusual histology, e.g. lung, female genital tract, HNT tumors, neuroendocrine ca.	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 (Axillary CUP): Therapy

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	Oxford		
	LoE	GR	AGO
■ Axillary dissection			
■ Targeted axillary dissection after NACT (in case of clinical complete remission)	3a	C	++
	3b	C	+/-
■ Mastectomy if breast MRI is negative	3a	C	--
■ (Neo-)adjuvant systemic therapy according to breast cancer guidelines (AGO)	5	D	++
■ Breast irradiation if breast MRI is negative	2c	B	+
■ Irradiation of regional lymph nodes according to breast cancer guidelines (AGO)	3b	B	+

Paget's Disease of the Breast

- **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

Paget's Disease of the Breast Diagnosis

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- **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	++

Paget's Disease of the Breast - Therapy

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Oxford		
LoE	GR	AGO
<hr/>		
5	D	++
1c	B	++
1c	B	++
4	D	++
2b	B	--

- **Paget's disease with underlying disease (invasive breast cancer, DCIS)**
 - Therapy according to standard of underlying disease
 - Surgery must achieve R0
- **Isolated Paget's disease of the NAC:**
 - Surgery must achieve R0
 - Surgical resection only, no adjuvant radiotherapy
 - Sentinel-node excision (SLNE)

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

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

Borderline and Malignant Phyllodes Tumor

Diagnosis

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- **Mammography, sonography**
- **Diagnosis on core biopsy, grade determination on resection specimen**
- **Breast MRI**
- **Staging only malignant PT (CT thorax, skeletal system)**

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

Borderline and Malignant Phyllodes Tumor Surgery

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- **Borderline / malignant phyllodes tumor: Complete resection with adequate margins, min. > 1 mm**
- **SLNE / Axillary dissection**
- **Treatment of local recurrence**
 - **R0 resection or simple mastectomy**

Oxford		
LoE	GR	AGO
2b	B	++
4	C	--
4	C	++

Borderline and Malignant Phyllodes Tumor

Adjuvant Therapy

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- **Adjuvant radiotherapy (younger age, increased tumor volume > 5 cm, close resection margin)**

- Local control
- Effect on disease-free survival

- **Systemic adjuvant therapy (chemo, endocrine)**

- **Adjuvant Treatment of local recurrence**

- Radiotherapy, chemotherapy after R1 resection

- **Distant metastasis (very rare)**

- Treatment like soft tissue sarcomas

Oxford

LoE GR AGO

2b	B	+
2b	B	-
4	C	-
4	C	+/-
4	C	++

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*

Diagnosis

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- Mammography, sonography to determine extent of disease
- Preoperative MRI to determine the extent of disease
- Diagnosis by core biopsy
- Diagnosis by FNB
- Staging (CT thorax & abd.; angiosarcoma: MRI brain)
- Prognostic factors: size, grade, margins

Oxford		
LoE	GR	AGO
3a	C	--
3a	C	++
3a	C	++
3a	C	--
4	D	++
3a	C	++

* Therapy in specialized centers recommended

Primary Angiosarcoma of the Breast*

Therapy

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- **Surgery with wide clear margins, mostly as mastectomy**
 - Breast-conserving therapy
- **SLNE or axillary dissection if cN0**
- **Adjuvant chemotherapy (anthracycline / taxane-based)**
- **Adjuvant radiotherapy if high risk (size > 5 cm, R1)**

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LoE	GR	AGO
2b	C	++
3a	C	-
3a	C	--
4	C	+/-
4	C	+/-

Secondary Angiosarcoma of the Breast Therapy

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- **Tumor resection (BCT / mastectomy)**
Radical surgery ist not associated with better outcome
- **(Neo-)adjuvant chemotherapy**
- **Adjuvant radiotherapy if high risk
(size > 5 cm, R1)**
- **Regional hyperthermia (to improve local control)
plus chemotherapy and / or radiotherapy**

Oxford		
LoE	GR	AGO
3a	C	+
3a	C	+/-
2b	B	+/-
2b	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%**

Angiosarcoma of the Breast

Treatment of Local Recurrence and Metastases

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Treatment of Local Recurrence:

- R0 resection
- Adjuvant radiotherapy for high-risk patients (tumor size > 5 cm, R1)

Distant Metastases / Unresectable Tumors:

- Treatment like as for soft tissue sarcomas (according to S3 guideline)
- Paclitaxel weekly / liposomal doxorubicin (as in angiosarcoma)
- Antiangiogenic treatment (e.g. in angiosarcoma)

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

Breast Implant Associated Anaplastic Large Cell Lymphoma (BIA-ALCL)

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- **Aproximately 10.000.000 implant carrier**
- **Rare disease, 3% of T-cell Non-Hodgkin Lymphomas, 0.04-0.5% of all malignant breast diseases**
- **1:3.000 – 30.000 in women with textured implants (caveat: underreporting!)**
- **Estimated incidence 0.6-1.2/100.000 women with implants (median age: 54 y)**
- **Mainly associated with textured implants (1:300 women)**
- **Interval to diagnosis: 8 years (median)**
- **Clinical symptoms**
 - Erythema, swelling and seroma. (60%)
 - Solid tumor (17%)
 - Seroma and solid tumor (20%)
 - Axillary lymphadenopathia (20%)
- **Histology: CD30+ / ALK-T-Cell Lymphoma**
- **Compulsory registration as SAE (§3 MPSV to BfArM)**
(<https://www.bfarm.de/SharedDocs/Formulare/DE/Medizinprodukte/BIA-ALCL-Meldung.html>)

BIA-ALCL– Diagnosis

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- **Breast US (assessment of new seromas > 1 year after implant insert, solid lesion (sensitivity: 84%, specificity: 75%))**
- **Mamma-MRT in confirmed cases**
- **Staging (Imaging, e.g. CT, PET-CT)**
- **Cytology of late seromas**
 - - > 50 ml
 - - Complete assessment
 - - flow-cytology (T-cell clone)
 - - BIA-ALCL specific cytologic diagnostic (e.g. CD 30+)
- **Core needle biopsy in solid lesions**
- **Lymphoma assessment of resected tissue and histologic staging**
- **Documentation of the implant and enter in registry**

Oxford

LoE	GR	AGO
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3a	D	++
----	---	----

3a	D	++
----	---	----

3a	D	++
----	---	----

3a	D	++
----	---	----

3a	D	++
----	---	----

5	D	++
---	---	----

BIA-ALCL – Therapy

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■ Implant resection and complete capsulectomy including tumorectomy	3a	C	++
■ Contralateral implant resection including capsulectomy in case of bilateral implants (2-4% BIA-ALCL bilateral)	4	D	+/-
■ Resection of suspicious lymph nodes, no routine use of Sentinel-Node-Biopsy, no axillarx dissection	4	D	++
■ Systemic therapy in cases of extra capsular extension	4	D	+
■ Radiotherapy in unresectable tumors	5	D	+/-
■ Case discussion in an interdisciplinary tumor board in the presence of a specialist for lymphomas	5	D	++

TNM Staging of BIA-ALCL (proposed)

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	TNM-Kategorie	Definition
Tumor extent (cT/pT)	T1	Confined to seroma or a layer on luminal side of capsule
	T2	Early capsule infiltration
	T3	Cell aggregates or sheets infiltrating the capsule
	T4	Lymphoma infiltrates beyond the capsule
Regional lymph nodes (cN/pN)	N0	No lymph node involvement
	N1	One regional lymph node positive
	N2	Multiple regional lymph nodes positive
Metastasis (cM/pM)	M0	No distant spread
	M1	Spread to other organs or distant sites

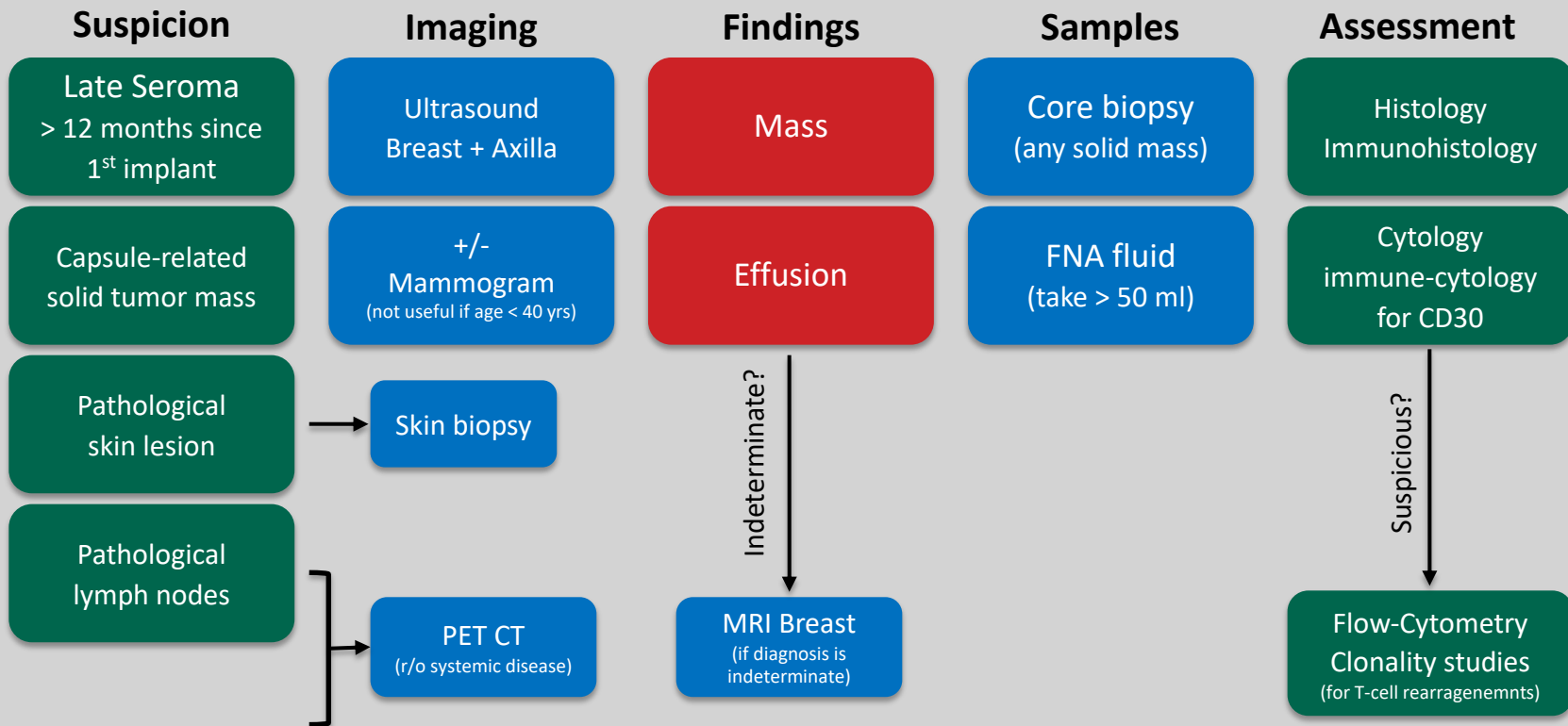
Stage	Definition
IA	T1 N0 M0
TB	T2 N0 M0
TC	T3 N0 M0
IIA	T4 N0 M0
IIB	T1-3 N1 M0
III	T4 N1-2 M0
IV	T any N any M1

Diagnostic Pathways and Assessment

Adapted from the NCCN and UK guidelines

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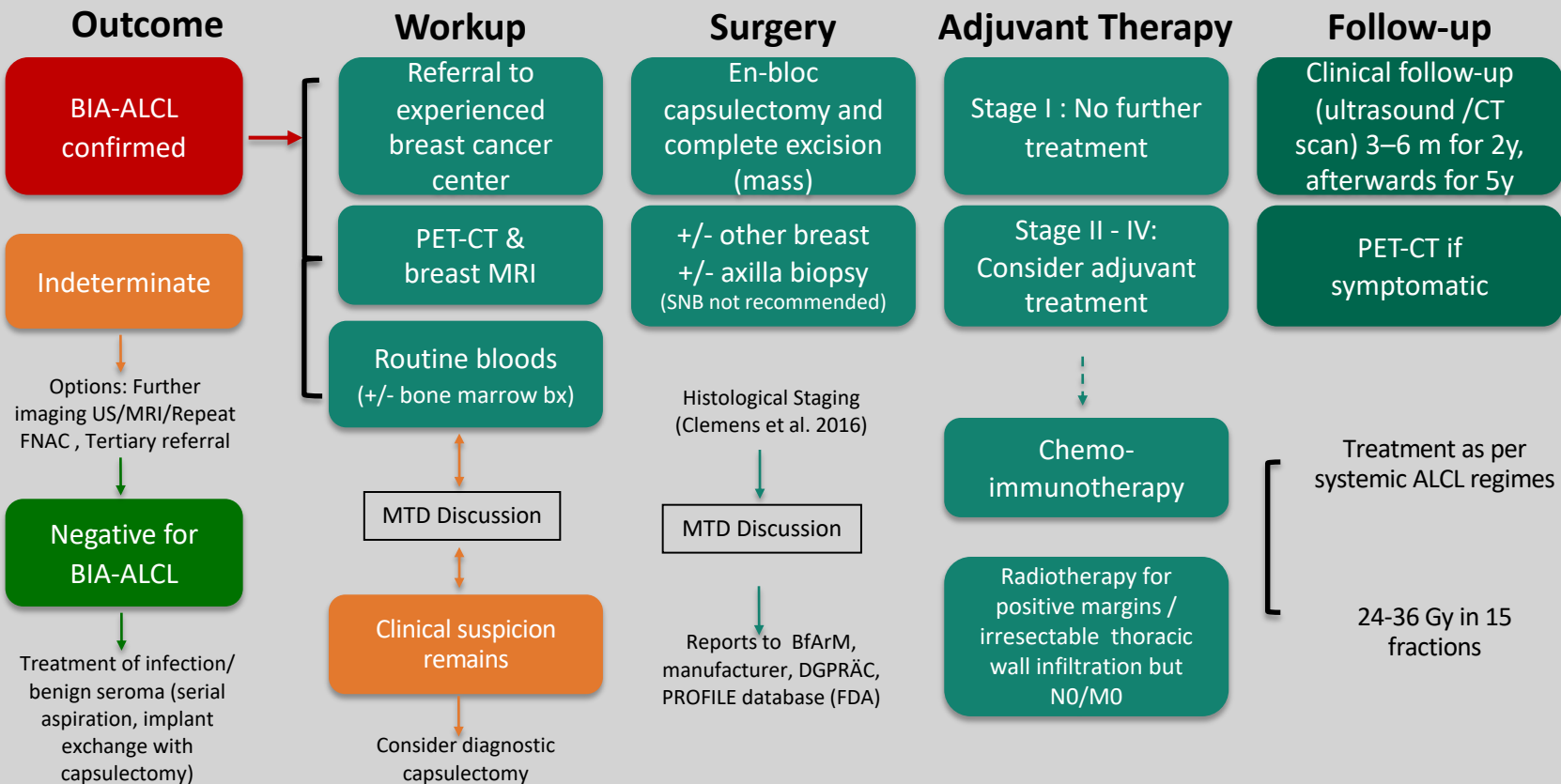


BIA-ALCL Treatment Pathways

Adapted from the NCCN and UK guidelines

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BIA-ALCL – EUSOMA-Recommendation

- **Despite an increase of BIA-ALCL in association with texture implants the use of textured implants is still permitted!**

„For the moment, textured implants can safely continue to be used with patient's fully informed consent, and that women that have these type of implants already in place don't need to remove or substitute them, which would undoubtedly cause harm to many tens of thousands of women, to prevent an exceptionally rare, largely curable and currently poorly understood disease.“

Metaplastisches Mammakarzinom

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Definition: Metaplastische Transformation der glandulären Tumorzellen

- Bei epithelialer Differenzierung: Plattenepithelkarzinom, Spindelzellkarzinom
- Bei heterologer (mesenchymaler) Differenzierung: chondroides, ossäres oder rhabdoides metaplastisches Mammakarzinom

Klinisch-pathologische Charakteristika:

- < 1 % der Malignome der Mamma
- Gleiche Altersgruppe wie NST-Karzinome
- Umschrieben, tastbar
- Schnell wachsend, schlechtes Ansprechen auf Chemotherapie
- > 90 % triple-negativ

Aggressivität:

- Hoch maligne bei heterologer (mesenchymaler), plattenepithelialer oder high-grade spindelzelliger Differenzierung
- Unsicheres malignes Potential (low-grade) bei adenosquamöser oder Fibromatose-ähnliche Differenzierung

Frequent mutations:

- TP53, EGFR, PIK3CA, PTEN

Metaplastic breast carcinoma*

- high-grade -

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	Oxford		
	LoE	GR	AGO
■ Operative therapy surgery and axillary staging according to standard	4	C	++
■ Adjuvant chemotherapy (rather chemoresistant)	4	C	+/-
■ Neoadjuvant chemotherapy (rather chemoresistant)	4	C	-
■ Adjuvant endocrine therapy if HR-positive	4	C	+
■ Adjuvant radiotherapy according to standard	4	C	++

* Reference pathology recommended

Metaplastic Breast Carcinoma with Uncertain Malignant Potential (Fibromatous and Adenosquamous Ca.)*

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	Oxford		
	LoE	GR	AGO
■ Operative therapy and axillary staging according to standard	4	C	++
■ Adjuvant chemotherapy	4	C	-
■ Neoadjuvant chemotherapy	4	C	--
■ Adjuvant endocrine therapy (not applicable, since triple-negative tumors)	4	C	-
■ Adjuvant radiotherapy according to standard	4	C	+

* Reference pathology recommended