

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



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Version 2022.1E

## Breast Cancer Follow-Up

# Breast Cancer Follow-Up

- **Versions 2002–2021:**

**Bauerfeind / Bischoff / Blohmer / Böhme / Costa / Diel / Friedrich / Gerber / Gluz / Hanf / Heinrich / Huober / Janni / Kaufmann / Kolberg-Liedtke / Kümmel / Lüftner / Lux / Maass / Möbus / Müller-Schimpfle / Mundhenke / Oberhoff / Rody / Scharl / Solbach / Solomayer / Thomssen / Wöckel**

- **Version 2022:**

**Blohmer / Stickeler**

# Breast Cancer Follow-Up Objectives

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	Oxford		
	LoE	GR	AGO
<b>Early detection of curable events</b>			
▪ In-breast recurrence	1a	B	++
▪ Loco-regional recurrence*	1a	B	++
<b>Early detection of contralateral cancers</b>	1a	B	++
<b>Early detection of metastasis</b>			
▪ Early detection of symptomatic metastases	3b	C	+
▪ Early detection of asymptomatic metastases	1a	A	-

## Early detection of curable events

- In-breast recurrence
- Loco-regional recurrence\*

## Early detection of contralateral cancers

## Early detection of metastasis

- Early detection of symptomatic metastases
- Early detection of asymptomatic metastases

\* loco-regional recurrence is associated with a higher risk of mortality in node-positive, PR-negative, younger patients and in patients with a short time between primary diagnosis and recurrence

# Breast Cancer Follow-Up Objectives

	Oxford		
	LoE	GR	AGO
	2b	B	+
	2a	B	+
	2b	B	+
	3b	B	+

- **Improve quality of life**
- **Improve physical performance**
- **Reduction and / or early detection of therapy-related side effects** (such as osteoporosis, cardiac failure, fatigue, neurotoxicity, lymphedema, web axillary pain syndrome (abacterial lymphangitis), sexual disorders, cognitive impairment, sterility, and secondary tumors) **and start of necessary therapies**
- **Participation in interventional programs during follow-up for breast cancer survivors in order to maximize therapy adherence, assess life-style interventions, and improve quality of life**

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# Monitoring after Cardiotoxic Therapy (Anthracyclins, anti-HER2)

## After anthracyclines / Trastuzumab:

- ECG and echocardiography:
  - 6, 12, 24 months and yearly up to 5 years after therapy.
  - After 5th year, every 5 years and if patient is symptomatic.
- If cardiovascular risk factors:
  - blood pressure at least yearly
  - lipids and HbA1c in serum yearly
- Modify risk factors if possible:
  - nicotine, body weight, bmi.
- Education about individual risk profile and lifestyle

## Risk factors:

radiotherapy of left breast, nicotine, hypertonus, diabetes mell., dyslipidaemia, adiposity, age > 60, cardiac diseases: reduced ejection fraction, post-myocardial infarction status ,  $\geq$  moderate heart defects

# Breast Cancer Follow-Up Objectives

Oxford		
LoE	GR	AGO
2b	B	++

- **Evaluation of current adjuvant therapy**
  - incl. monitoring of adherence to endocrine therapies
  - Control of menopausal status, e.g. in case of CT-induced amenorrhea (FSH/2 or bleeding history) and addition of GnRH analogs (up to 2 years after CT) if premenopausal status in women < 45 years old, or switch to aromatase inhibitors (if postmenopausal)
- **Pro-active improvement of therapy adherence**
  - Patient information about efficacy data for 5-10 years endocrine therapy
  - Early therapy of side effects (sports, NSAIDs, vitamin D / calcium)

5	D	++
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# Breast Cancer Follow-Up Objectives

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	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li>■ <b>Psycho-social aspects of support and counseling</b> <ul style="list-style-type: none"> <li>■ Pregnancy, contraception, sexuality, quality of life, menopausal symptoms, fear of recurrence</li> <li>■ Inclusion of related persons (partner, family, friends, caregivers)</li> </ul> </li> </ul>	<b>4</b>	<b>C</b>	<b>+</b>
<ul style="list-style-type: none"> <li>■ <b>Second opinion regarding primary therapy</b></li> </ul>	<b>2c</b>	<b>B</b>	<b>++</b>
<ul style="list-style-type: none"> <li>■ <b>General counseling (e.g. changes in family history of breast, ovarian, prostate, pancreas carcinoma with new indication for genetic counseling, HRT, prophylactic surgery, breast reconstruction)</b></li> </ul>	<b>2c</b>	<b>C</b>	<b>+</b>

# Breast Cancer Follow-Up

## Recommended Interventions

### Interventions regarding lifestyle risks and comorbidity in order to reduce an unfavorable impact on disease outcome

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> <li> <b>Treatment of type II-diabetes</b>            (&gt; 25% undetected DM in postmenopausal BC patients, endocrine therapy improves risk for DM)         </li> </ul>	2a	B	++
<ul style="list-style-type: none"> <li> <b>Weight/lifestyle intervention</b> (if BMI &lt; 18.5 and &gt; 30)         </li> </ul>	2a	B	+
<ul style="list-style-type: none"> <li> <b>Nightly fastening &gt; 13 h</b> </li> </ul>	2b	B	+
<ul style="list-style-type: none"> <li> <b>Reduction of dietary intake (at least 15 % calories from fat) in HR-negative BC is associated with improved overall survival</b> </li> </ul>	2b	B	+
<ul style="list-style-type: none"> <li> <b>Stop smoking</b> (smoking causes 2-fold increase in BC-specific and 4-fold increase in not directly BC-associated mortality)         </li> </ul>	2b	B	++
<ul style="list-style-type: none"> <li> <b>Alcohol consumption reduction (below 6g/d)</b> </li> </ul>	2b	B	+
<ul style="list-style-type: none"> <li> <b>Moderate sport (in patients with reduced physical activity prior to diagnosis) (at least 150 minutes/w, 2x/w)</b> </li> </ul>	1b	A	++
<ul style="list-style-type: none"> <li> <b>Distress reduction</b> </li> </ul>	3b	B	+

# Nightly Fasting

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## **Prolonged nightly fasting improves prognosis in breast cancer patients**

retrospective cohort study:

2413 BC-pat. (no diabetes), nightly fasting more or less than 13 hrs

**Fasting < 13 hrs: HR 1.36, 36% increase of risk for recurrence**  
**HR 1.21, n.s. increase of risk for mortality**

**every 2-hrs-prolonged fasting was correlated with a 20% increase of sleeping duration**

# Routine Follow-Up Examinations in Asymptomatic Patients

Oxford

## Tests:

- **History (specific symptoms)**
- **Physical examination**
- **Breast self-examination**
- **Mammography**
- **Sonography of the breast**
- **Routine MRI of the breast\***
- **Breast MRI if conventional imaging is inconclusive**
- **Pelvic examination**
- **DXA-scan at baseline and repeat scan according to individual risk in women with premature menopause or women taking an AI**

LoE	GR	AGO
1a	A	++
1a	B	++
5	D	+
1a	A	++
2a	B	++
3a	B	+/-
3b	B	+
5	D	++
5	D	+

\* Consider in case of increased risk (age < 50 y, HR-neg., diagnostic assessability C/D in mammography + ultrasound)

# Routine Follow-Up Examinations in Asymptomatic Patients

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- **Routine biochemistry (incl. tumor markers)**
- **Blood tests for monitoring of acute and late toxicities**
- **Ultrasound of the liver**
- **Bone scan**
- **Chest X-ray**
- **CT of chest, abdomen, and pelvis**
- **Detection of isolated / circulating tumor cells**
- **PET**
- **Whole body MRI**

	Oxford		
	LoE	GR	AGO
	1a	A	-
	5	D	+
	1a	A	-
	1a	A	-
	1a	A	-
	2a	D	-
	2a	D	-
	2b	B	-
	2b	B	-

# Background for Toxicity Management

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Tamoxifen:	Cholesterol, Triglycerides, Bilirubin, ALAT, ASAT, gamma-GT, Glucose
Aromatase inhibitors:	Cholesterol, Triglycerides, Bilirubin, ALAT, ASAT, gamma-GT
Anthracyclines:	pro-BNP, possibly Troponin
Trastuzumab:	pro-BNP, possibly Troponin
Checkpoint inhibitors:	Bilirubin, ALAT, ASAT, gamma-GT, Creatinine, TSH, fT3/T4, Myoglobin

# Early Detection of Potentially Curable Events

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## Locoregional recurrence (chest wall, in-breast):

- |  |    |   |     |
|--|----|---|-----|
| ▪ Incidence 7–20% (depending on time of F/U) |    |   |     |
| ▪ Breast self-examination                    | 5  | D | +   |
| ▪ Physical examination, mammography & US     | 1a | A | ++  |
| ▪ Magnetic resonance imaging (MRI)*          | 3a | B | +/- |

\* Consider in case of increased risk (age < 50 y, HR-neg., diagnostic assessability C/D in mammography + ultrasound)

# Early Detection of Potentially Curable Events

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	LoE	GR	AGO
<b>Contralateral breast cancer:</b>			
▪ Relative risk: 2.5–5			
▪ Incidence: 0.5–1.0 %/year			
▪ Breast self-examination	5	D	+
▪ Physical examination, mammography & US	1a	A	++
▪ Routine breast MRI*	3b	B	+/-
<b>Male breast cancer: analogous to BC in women**</b>	5	D	+

\* Consider in case of increased risk: age < 50 y, HR-neg., diagnostic assessability C/D in mammography + ultrasound.

\*\* See chapter “Breast Cancer Specific Situations”

# Early Detection of Potentially Curable Events

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## Unrelated site carcinoma:

- MDS (RR 10.9), AML (RR 2.6–5.3), Colon RR 3.0; endometrium RR 1.6; ovary RR 1.5; lymphoma RR
- Screening for secondary malignancies according to current guidelines
- Pelvic examination and PAP smear
- Routine endometrial ultrasound / biopsy

	Oxford		
	LoE	GR	AGO
	5	D	++
	5	D	++
	1b	B	-

# Follow-Up Care for invasive / non-invasive Breast Cancer

## Recommendations for asymptomatic pts.

(mod. according to ASCO-ACS recommendations 2016, NCCN 2021, ESMO 2019 and S3-guidelines 2017)

Clinical follow-up		Follow-up*				Screening/ Follow-up	
Years after primary therapy		1	2	3	4	5	> 5
History, physical examination, counseling		every 3 months DCIS every 6 months			every 6 months		inv.: every 12 months
Self-examination		monthly					
Imaging modalities and biochemistry		indicated only if complaints, clinical findings, or suspicion of recurrence Monitoring of side effects of therapy					
Mammo-graphy and additional sonography	BCT**	both sides: every 12 months					
	Mastectomy	contralateral every 12 months					
Echocardiography		6,12,24 months and yearly up to 5 years after completion of cardiotoxic therapy, after 5th year, every 5 years and if patient is symptomatic.					

\* Continued follow-up visits if still on adjuvant treatment

\*\* In pts after breast-conserving therapy (BCT): First mammography 1 year after initial mammography or at least 6 months after completion of radiotherapy

# Breast Cancer Follow-up

## Duration and Breast Nurses

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- **Duration of follow-up**
  - up to 5 years
  - up to 10 years
  
- **Surveillance by specialized breast nurses**

Oxford		
LoE	GR	AGO
1c	A	++
1c	A	+
2b	B	+/-*

\* Studies recommended

# Luminal-like, HER2-positive and Triple-negative Breast Cancer Patients

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- **Intrinsic typing of breast cancer leads to subgroups with different course of disease. Thus, postoperative surveillance should be adapted to specific time-dependent hazards of recurrence.**
- **ER-positive patients have stable risk over many years requiring long term surveillance.**
- **However, patients with HER2-positive disease and TNBC have more risk in the early phase of follow-up and should therefore receive more intense surveillance in the first years of follow-up.**