Diagnosis and Treatment of Patients with early and advanced Breast Cancer

Guidelines Breast
Version 2023.1E

Breast Cancer
Follow-Up

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Follow-Up

- **Versions 2002–2022:**

  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 / Stickeler / Thomssen / Wöckel

- **Version 2023:**

  Friedrich / Kümmel

Breast Cancer Follow-Up Objectives

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

* 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

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Breast Cancer Follow-Up Objectives

	Oxford		
	LoE	GR	AGO
▪ Improve quality of life	2b	B	+
▪ Improve physical performance	2a	B	+
▪ 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	2b	B	+
▪ 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	3b	B	+

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Monitoring after Cardiotoxic Therapy (Anthracycliens, 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 , ≥ moderate heart defects

Breast Cancer Follow-Up Objectives

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	Oxford		
	LoE	GR	AGO
▪ **Evaluation of current adjuvant therapy**	2b	B	++
▪ **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**	5	D	++
▪ **Patient information about efficacy data for 5-10 years endocrine therapy**			
▪ **Early therapy of side effects (sports, NSAIDs, vitamin D / calcium)**			

Breast Cancer Follow-Up Objectives

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	Oxford		
	LoE	GR	AGO
▪ Psycho-social aspects of support and counseling	4	C	+
▪ Pregnancy, contraception, sexuality, quality of life, menopausal symptoms, fear of recurrence ▪ Inclusion of related persons (partner, family, friends, caregivers)			
▪ Second opinion regarding primary therapy	2c	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)	2c	C	+

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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
▪ **Treatment of type II-diabetes** (> 25% undetected DM in postmenopausal BC patients, endocrine therapy improves risk for DM)	2a	B	++
▪ **Weight/lifestyle intervention** (if BMI < 18.5 and > 30)	2a	B	+
▪ **Nightly fastening > 13 h**	2b	B	+
▪ **Reduction of dietary intake (at least 15 % calories from fat) in HR-negative BC is associated with improved overall survival**	2b	B	+
▪ **Stop smoking** (smoking causes 2-fold increase in BC-specific and 4-fold increase in not directly BC-associated mortality)	2b	B	++
▪ **Alcohol consumption reduction (below 6g/d)**	2b	B	+
▪ **Moderate sport (in patients with reduced physical activity prior to diagnosis) (at least 150 minutes/w, 2x/w)**	1b	A	++
▪ **Distress reduction**	3b	B	+

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Nightly Fasting

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

Marinac CR, Nelson SH, Breen CI et al. JAMA Oncol 2016: 2:1049-1055

Routine Follow-Up Examinations in Asymptomatic Patients

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Tests:	Oxford LoE	Oxford GR	AGO
▪ History (specific symptoms)	1a	A	++
▪ Physical examination	1a	B	++
▪ Breast self-examination	5	D	+
▪ Mammography	1a	A	++
▪ Sonography of the breast	2a	B	++
▪ Routine MRI of the breast*	3a	B	+/-
▪ Breast MRI if conventional imaging is inconclusive	3b	B	+
▪ Pelvic examination	5	D	++
▪ DXA-scan at baseline and repeat scan according to individual risk in women with premature menopause or women taking an AI	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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	Oxford		
	LoE	GR	AGO
▪ Routine biochemistry (incl. tumor markers)	1a	A	-
▪ Blood tests for monitoring of acute and late toxicities	5	D	+
▪ Ultrasound of the liver	1a	A	-
▪ Bone scan	1a	A	-
▪ Chest X-ray	1a	A	-
▪ CT of chest, abdomen, and pelvis	2a	D	-
▪ Detection of isolated / circulating tumor cells	2a	D	-
▪ PET	2b	B	-
▪ Whole body MRI	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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	Oxford		
	LoE	GR	AGO
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)

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Early Detection of Potentially Curable Events

	Oxford		
	LoE	GR	AGO
Contralateral breast cancer:			
▪ 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	+/-
Male breast cancer: analogous to BC in women**	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”

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Early Detection of Potentially Curable Events

	Oxford LoE	Oxford GR	Oxford AGO
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**	**5**	**D**	**++**
▪ **Pelvic examination and PAP smear**	**5**	**D**	**++**
▪ **Routine endometrial ultrasound / biopsy**	**1b**	**B**	**-**

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

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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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	Oxford		
	LoE	GR	AGO
▪ **Duration of follow-up**			
▪ up to 5 years	1c	A	++
▪ up to 10 years	1c	A	+
▪ **Surveillance by specialized breast nurses**	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.**

Ribelles et al. BCR 2013