

Diagnosis and Treatment of Patients with early and advanced Breast Cancer

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Loco-Regional Recurrence

Loco-Regional Recurrence

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- **Versions 2002–2023:**
**Audretsch / Bauerfeind / Blohmer/ Brunnert / Budach /
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- **Version 2024:**
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Loco-Regional Recurrence Incidence and Prognosis

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Localization	10-y. incidence (%)	5-y. Overall Survival (%)
Ipsilateral recurrence¹ (post BEO + irradiation)	10 (2–20)	65 (45–79)
Chest wall¹ (post mastectomy)	4 (2–20)	50 (24–78)
As above plus supraclavicular fossa² Axilla:	34	49 (3-y. OS)
After ALND¹	1 (0.1–8)	55 (31–77)
After SLNE⁴	1	93
Multiple localizations²	16 (8–19)	21 (18–23)

¹ Haffty et al. Int J Radiat Oncol Biol Phys 21(2):293-298, 1991;

² Reddy JP. Int J Radiat Oncol Biol Phys 80(5):1453-7, 201;

³ Karabali-Dalamaga S et al. Br Med J 2(6139):730-733,1978;

⁴ Andersson Y, et al. Br J Surg 99(2):226-31,2012

Loco-Regional Recurrence Staging

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	Oxford		
	LoE	GR	AGO
■ Tissue biopsy	3b	B	++
■ Re-assessment of ER, PR, HER2	3b	B	++
■ Complete re-staging (slice imaging*)	2b	B	++
■ „Liquid biopsy“	5	D	-

Examinations before treatment

- Tissue biopsy
- Re-assessment of ER, PR, HER2
- Complete re-staging (slice imaging*)
- „Liquid biopsy“

* Standard: CT thorax / abdomen / pelvis and bone scan, in certain cases whole body MRI or ¹⁸F FDG PET-CT may be used

Risk Factors for another Relapse*

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	Oxford		
	LoE	GR	AGO
▪ Tumor size	2a	B	
▪ Multifocality	2a	B	
▪ Localisation	2b	B	
▪ Negative progesterone receptor	3b	B	
▪ High grade	3b	C	
▪ Omitted radiotherapy at first recurrence	3b	C	
▪ Inappropriate systemic treatment at first recurrence	3b	C	
<u>Parameters of the locally recurrent tumor to define the risk for distant metastasis / survival</u>			
▪ Early (< 2-3 yrs.) vs. late recurrence	2b	B	
▪ LVSI / Grade / ER-neg / positive margins (if ≥ 2 factors positive)	3b	B	
<u>Predictive factors for treatment considerations</u>			
▪ HER2	2b	B	++
▪ ER and PR	2b	B	++

* Risk factors for local relapse see chapter “prognostic factors”

Ipsilateral Locoregional Recurrence

Surgical Treatment

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	Oxford		
	LoE	GR	AGO
▪ After mastectomy: wide exzision (aim R0)	3b	B	++
▪ After BCS:			
▪ Mastectomy (aim: R0)	3b	B	++
▪ Re-BCS with tumor-free margins (R0) +partial breast irradiation*	2b	B	+
▪ Re-BCS with tumor-free margins (R0)	2b	B	+/-
▪ rcN0:			
▪ Axillary intervention after prior AxDiss	4	C	-
▪ Re-SLNE after prior SLNE	2a	B	-
▪ in histologically confirmed axillary recurrence: Excision with clear margins	5	C	+
▪ Palliative surgery in M1-situation or R0 not achievable (e.g. pain, ulceration, psychosocial indication)	5	D	+

* After consideration of risk factors for repeated relapse (time from primary diagnosis, tumor size)



Mastectomy vs. BCS + Partial Breast Irradiation

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- **1327 pts. from 7 European countries with first local recurrence 01/1995 - 06/2017**
- **ME vs. BCS + Brachytherapy**
- **Propensity Score matched control (1:1): clinical and histopathological factors**
- **Primary endpoint: 5-y OS; secondary endpoints: e.g. 5-y-DFS, complications**
- **Median follow-up 75.4 months**
- **No differences in 5-y OS and sec. Endpoints: 5-y -OS: 88 vs. 87%**
- **cumulative incidence 2. recurrence: 2.3 vs. 2.8%**
- **5-y incidence of mastectomy after 1. recurrence 3.1%**

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Loco-regional Recurrence after R0-Resection - Systemic Treatment

Oxford

LoE GR AGO

According to pathohistological re-evaluation of the recurrent tumor (ER, PR, HER2) and in consideration of time from primary diagnosis, pre-treatment, co-morbidities and patient's preference

- | | | | |
|---|----|---|----|
| <ul style="list-style-type: none"> Endocrine therapy in endocrine responsive tumors | 2b | B | ++ |
| <ul style="list-style-type: none"> Chemotherapy (consider preoperative) in case of first HR-negative relapse | 2b | B | + |
| <ul style="list-style-type: none"> In case of HER2-positive disease, chemotherapy + HER2-targeted therapy | 5 | D | + |

Loco-Regional Recurrence Chemotherapy

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- **CALOR Trial update (CHT vs. no CHT)**
 - **n = 163 (2003 - 2010), median follow-up of 9 years, all R0 resection**
 - **Time interval until recurrence: 3.6 years (ER neg)
6.8 years (ER pos)**
 - **CHT is effective in ER neg disease (primary tumor and recurrence)**
 - **CHT is not effective in ER pos disease (primary tumor and recurrence)**
 - **The results were independent from the site of recurrence, previous chemotherapy and time interval from primary surgery**

Loco-Regional Recurrence Chemotherapy

■ CALOR Trial update

	ER-positive			ER-negative		
Endpoint	CT	No-CT	HR (95% CI)	CT	No-CT	HR (95% CI)
10-yr DFS	50%	59%	1.07 (0.57 – 2.00)	70%	34%	0.29 (0.13 – 0.67)
	Interaction P-Value =0.013					
10-yr OS	76%	66%	0.70 (0.32 – 1.55)	73%	53%	0.48 (0.19 – 1.20)
	Interaction P-value =0.53					
10-yr BCFI	58%	62%	0.94 (0.47 – 0.85)	70%	34%	0.29 (0.13 – 0.67)
	Interaction P-value = 0.034					

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Locoregional Recurrence in Case of R1-Resection / Inoperability – Systemic Treatment

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According to pathohistological re-evaluation of the recurrent tumor (ER, PR, HER2)

- | | | | |
|---|----|---|----|
| <ul style="list-style-type: none"> Endocrine based therapy in endocrine responsive tumors corresponding to metastatic disease | 2b | B | ++ |
| <ul style="list-style-type: none"> Chemotherapy and targeted therapy (pre- or postoperative) corresponding to metastatic disease | 2b | B | ++ |

Resectable ipsilateral Breast Tumor Recurrence after BCS – Radiotherapy

	Oxford		
	LoE	GR	AGO
<u>After Re-BCS</u>			
▪ Whole breast irradiation (in case of no prior adjuvant radiotherapy)	3b	C	++
▪ Repeated (2.)-breast irradiation (Partial breast irradiation, brachytherapy/ external beam RT, in case of prior adjuvant radiotherapy) *	2b	B	+
<u>After mastectomy</u>			
▪ Radiation of chest wall +/- regional lymph nodes (in case of no prior adjuvant radiotherapy, according to risk factors)	2b	B	+
▪ Radiation dose escalation	3b	C	-
▪ Repeated (2.) irradiation			
▪ in case of R0 resection (according to risk factors)	3b	B	+/-
▪ in case of R1-resection (e.g. as brachytherapy)	3b	B	+
▪ Additional regional hyperthermia (especially for R1-resections)	2a	B	+/-

* Preoperative consultation with Radiation Oncology to determine if re-irradiation is possible.

** In Sites listed on the DKG Website

<https://www.krebsgesellschaft.de/deutsche-krebsgesellschaft-wtr1/deutsche-krebsgesellschaft/ueber-uns/organisation/sektion-b-arbeitsgemeinschaften/iah.html>

Resectable Thoracic Wall Recurrence after Mastectomy and Axillary Recurrence – Radiotherapy



Oxford

LoE GR AGO

Thoracic wall recurrence after mastectomy

<ul style="list-style-type: none"> ▪ No prior radiotherapy <ul style="list-style-type: none"> ▪ Curative situation: Radiotherapy to the thoracic wall +/- regional nodal irradiation ▪ Re-irradiation of the thoracic wall <ul style="list-style-type: none"> ▪ R0-resection ▪ R1-resection (e.g. brachytherapy) ▪ Additional regional hyperthermia (especially for R1-resections)* 	2b	B	+
	3b	B	+/-
	3b	B	+/-
	3b	B	+
	2a	B	+

Axillary recurrence

<ul style="list-style-type: none"> ▪ Radiotherapy to the axilla (R0-resection) <ul style="list-style-type: none"> ▪ No prior radiotherapy to the axilla ▪ Prior radiotherapy to the axilla 	3b	C	+
	5	D	+/-

* In Sites listed on the DKG Website

<https://www.krebsgesellschaft.de/deutsche-krebsgesellschaft-wtrl/deutsche-krebsgesellschaft/ueber-uns/organisation/sektion-b-arbeitsgemeinschaften/iah.html>

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Unresectable Loco-Regional Recurrence (cM0)

Locoregional Treatment



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<ul style="list-style-type: none"> ■ Radiotherapy with curative intent (If no prior RT given) <ul style="list-style-type: none"> ■ Additional systemic treatment to increase the efficacy of RT 	2b	B	++
<ul style="list-style-type: none"> ■ Repeat Irradiation (if prior RT given) <ul style="list-style-type: none"> ■ Additional regional hyperthermia* 	3b	C	+
<ul style="list-style-type: none"> ■ Intra-arterial chemotherapy 	3b	B	+
<ul style="list-style-type: none"> ■ Electrochemotherapy 	2a	B	+
	4	C	+/-
	3b	C	+/-

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<https://www.krebsgesellschaft.de/deutsche-krebsgesellschaft-wtrl/deutsche-krebsgesellschaft/ueber-uns/organisation/sektion-b-arbeitsgemeinschaften/iah.html>