

Diagnosis and Treatment of Patients with early and advanced Breast Cancer



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Loco-Regional Recurrence

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LEHREN
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Loco-regional Recurrence

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- **Versions 2002–2021:**
**Audretsch / Bauerfeind / Blohmer/ Brunnert / Budach /
Costa / Dall / Ditsch/ Fehm / Fersis / Friedrich / Harbeck /
Gerber / Göhring / Hanf / Kühn/ Lisboa / Lux / Maass /
Mundhenke / Rezai / Simon / Solbach / Solomayer /
Souchon / Thomssen / Wenz / Wöckel**
- **Version 2022:**
Gluz / Heil

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, 2011;

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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Examinations before treatment

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

Oxford		
LoE	GR	AGO

3b	B	++
3b	B	++
2b	B	++
5	D	-

* Standard: CT thorax / abdomen 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	
▪ Omitted chemotherapy 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

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 AxDis	4	C	-
▪ Re-SLNE after prior SLNE	2a	B	-
▪ rfnN+: (Re-)Axillary dissection (R0)	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)

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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

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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

	Oxford		
	LoE	GR	AGO
■ Endocrine therapy in endocrine responsive tumors	2b	B	++
■ Chemotherapy (consider preoperative) in particular in case of first HR-negative relapse	2b	B	+
■ In case of HER2-positive disease, chemotherapy + HER2-targeted therapy	5	D	+

Locoregional Recurrence Chemotherapy

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■ CALOR Trial update

- **n = 163 (2003–2010), median follow-up of 4.9 years, all R0 resection**
- **5-y DFS: 69% (95% CI 56–79) with chemotherapy vs. 57% (44–67) without chemotherapy (hazard ratio 0.59 [95% CI 0.35–0.99]; p = 0.046): 24 (28%) patients vs. 34 (44%).**
- **Adjuvant chemotherapy was significantly more effective in ER negative disease ($p_{\text{interaction}} = 0.046$).**
- **Multivariate analysis: predictors of survival**
- **chemotherapy for primary cancer (HR 3.55, p = 0.03)**
- **interval from primary surgery (HR 0.87, p = 0.05)**

Loco-regional Recurrence Chemotherapy

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■ 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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Oxford		
LoE	GR	AGO

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	++

Ipsilateral Recurrence after BCT Radiotherapy

	Oxford		
	LoE	GR	AGO
<ul style="list-style-type: none"> Whole breast irradiation (in case of no prior adjuvant radiotherapy) 	3b	C	++
<ul style="list-style-type: none"> Repeated (2.)-breast irradiation (Partial breast irradiation, brachytherapy/ external beam RT, in case of prior adjuvant radiotherapy) 	2b	B	+
<u>After mastectomy</u>			
<ul style="list-style-type: none"> Radiation of chest wall +/- regional lymph nodes (in case of no prior adjuvant radiotherapy) 	2b	B	+
<ul style="list-style-type: none"> Radiation dose escalation (+ 10 %) 	3b	C	-
<ul style="list-style-type: none"> Repeated (2.) irradiation <ul style="list-style-type: none"> in case of R0 resection (according to risk factors, preferentially with hyperthermia) in case of R1/R2 resection (e.g. as brachytherapy) with hyperthermia 	1b	B	+/-
	1b	B	+

After Re-BCS

- Whole breast irradiation (in case of no prior adjuvant radiotherapy)
- Repeated (2.)-breast irradiation (Partial breast irradiation, brachytherapy/ external beam RT, in case of prior adjuvant radiotherapy)

After mastectomy

- Radiation of chest wall +/- regional lymph nodes (in case of no prior adjuvant radiotherapy)
- Radiation dose escalation (+ 10 %)
- Repeated (2.) irradiation
 - in case of R0 resection (according to risk factors, preferentially with hyperthermia)
 - in case of R1/R2 resection (e.g. as brachytherapy) with hyperthermia

Loco-Regional Recurrence

Treatment Options in Non-Curative Cases

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	Oxford		
	LoE	GR	AGO
■ Concomitant radio-chemotherapy	3b	C	+
■ Hyperthermia (in centers listed on DKG website)			
■ In combination with radiotherapy	1b	B	+
■ In combination with chemotherapy	4	C	+/-
■ Intra-arterial chemotherapy	4	C	+/-
■ Photodynamic therapy	4	C	+/-
■ Electrochemotherapy	3b	C	+/-