



Diagnosis and Treatment of Patients with early and advanced Breast Cancer

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Ductal Carcinoma in Situ (DCIS)

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FORSCHEN
LEHREN
HEILEN

Duktales Carcinoma in situ (DCIS)

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- **Versions 2002–2019:**

**Audretsch / Bauerfeind / Blohmer / Brunnert / Budach / Costa / Fersis /
Friedrich / Gerber / Hanf / Junkermann / Kühn / Lux / Maass / Möbus /
Mundhenke / Nitz / Oberhoff / Scharl / Schütz / Solomayer / Souchon / Thill
/ Thomssen / Wenz**

- **Version 2020:**

Friedrich / Gerber

Pretherapeutic Assessment of Suspicious Lesions (BIRADS 4-5)

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	Oxford		
	LoE	GR	AGO
■ Mammography	1b	B	++
■ Magnification view of microcalcifications	4	C	++
■ Increased detection rate of G1/G2 DCIS by full-field digital mammography (versus screen-film)	2b	B	+
■ Stereotactic core needle / vacuum biopsy (VAB)	2b	B	++
■ Specimen radiography	2b	B	++
■ Marker (clip) left at biopsy site for localization if lesion is completely removed	5	D	++
■ Assessment of extension			
■ MRI	1b	B	+/-
■ Clinical examination	5	D	++
■ FNA / ductal lavage	5	D	-
■ Interdisciplinary board presentation	5	D	++

Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ

Narod A. et al.: JAMA Oncol. 2015 Oct; 1(7): 888-96

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- **108,196 patients from the SEER data base**
- **Retrospective analysis**
- **Breast cancer specific mortality 3.3 %**
- **Increased in young women (< 35 years) and black ethnicity**
- **The risk of death increases after ipsilateral invasive recurrence HR 18 (95%CI, 14,0–23,6)**
- **Prevention of invasive recurrence by radiotherapy does not diminish mortality at 10 years**

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Treatment	Cases, No	10-Year BCS Mortality (95%CI), %	Univariate HR (95% CI)	P Value	Multivariate ³ HR (95%)	P Value
Lumpectomy						
Without radiotherapy	19762	0.9 (0.7 - 1.1)	1 [Reference]		1 [Reference]	
With radiotherapy	42250	0.8 (0.7 – 1.0)	0.86 (0.67 – 1.10)	0.22	0.81 (0.63 – 1.04)	0.10
all	63319	0.8 (0.7 – 1.0)	1 [Reference]		1 [Reference]	
Unilateral mastectomy	19515	1.3 (1.1 – 1.5)	1.45 (1.18 – 1.79)	< 0.001	1.20 (0.96 – 1.50)	0.11

³ Adjusted for year of diagnosis, age of diagnosis, ethnicity, income, ER-status, tumor size and grade

General Therapeutic Principles

Surgical excision (BCS or mastectomy) is the standard treatment for DCIS.

Adjuvant treatment (radiotherapy, endocrine treatment) must be discussed with the patient individually. Adverse effects should be weighed against risk reduction.

Surgical Treatment for Histologically Proven DCIS I

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	Oxford		
	LoE	GR	AGO
■ Excisional biopsy (wire guided)	2b	B	++
■ Bracketing wire localization in large lesions	3a	C	+
■ Specimen radiography	2b	B	++
■ Intraoperative ultrasound (visible lesion)	3a	C	+/-
■ Immediate re-excision for close margins (specimen radiography)	1c	B	++
■ Intraoperative frozen section (in individual cases for margin assessment)	3a	D	+/-
■ Interdisciplinary board presentation	2b	C	++

Open biopsy in suspicious lesions (mammographic microcalcifications, suspicious US, MRI etc.) without preoperative needle biopsy should be avoided

Surgical Treatment for Histologically Proven DCIS II

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	Oxford		
	LoE	GR	AGO
■ Histologically clear margins (R0)	1a	A	++
■ Multifocal DCIS: BCS if feasible	2b	B	+
■ Re-excision required for close margin (≤ 2 mm in paraffin section)*	2b	C	+
■ Mastectomy**			
■ Large lesions confirmed by multiple biopsies; no clear margins after re-excision	2a	B	++
■ SLNE			
■ Mastectomy	3b	B	+
■ BCS	3b	B	-
■ In case of DCIS in the male breast	5	D	+/-
■ ALND	2b	B	--

* Especially if postoperative radiation therapy is not performed

** Patients who present with a palpable mass have a significantly higher potential for occult invasion (26%), multicentricity and local recurrence.

Prognostic Factors for an Ipsilateral Recurrence

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	Oxford LoE
▪ Resection margins	1a
▪ Age	1a
▪ Size	1a
▪ Grade	1a
▪ Comedo necrosis	1a
▪ Method of diagnosis	1a
▪ Focality	1a
▪ HER2-overexpression	1a
▪ ER/PgR (positive vs. negative)	1a
▪ Residual tumor-associated microcalcifications	2b
▪ Architecture	2b
▪ (modified) Van Nuys Prognostic Index	2b
▪ Palpable DCIS	2b
▪ Palpable and ER-, HER2+, Ki-67+	2b
▪ DCIS-Score (9 Gene recurrence score)	2b
▪ MSKCC Nomogram	2b
▪ Intrinsic subtypes (luminal A, B, HER2+, triple negative)	2b

DCIS Radiotherapy Statements

- Radiotherapy has no impact on survival **LOE 1a**
- Radiotherapy reduces the risk of ipsilateral (invasive and non invasive) recurrences by 50 % **LOE 1a**
- Avoidance of invasive recurrence is probably not associated with survival benefit **LOE 2b**
- The absolute (individual) benefit of radiotherapy depends on the individual risk of local recurrence
- The number needed to treat (for ipsilateral breast recurrence) is 9 (over all risk groups)

Adjuvant Radiotherapy

Oxford		
LoE	GR	AGO

Radiotherapy after:

- Breast conserving surgery (BCS)
- Mastectomy

1a A ++

2b B --

Modality:

- Partial breast radiotherapy (PBI) (DCIS < 3 cm)
- Hypofractionated radiotherapy regimens
- Radiotherapy boost on the tumor bed
 - Women younger than 45-50 years
- Intraoperative Radiotherapy

2a B +/-

2b D +/-*

2b D --

2b C +/-

2b C -

Side effects and disadvantages must be weighed against risk reduction. Omitting radiotherapy implies elevated risk for local recurrence without effect for overall survival even in the subset of „good risk“ patients. **Lack** of level-1 evidence supporting the omission of adjuvant radiotherapy in selected low-risk cases: < 2.5 cm, low and intermediate nuclear grade, mammographically detected

* Analysis in ongoing trials

DCIS –

Adjuvant Systemic Treatment

- **Adjuvant endocrine treatment has no impact on survival** **LOE 1a**
- **Endocrine treatment may have a small effect on ipsilateral invasive and DCIS recurrences** **LOE 1a**
- **Endocrine treatment for DCIS has an effect on contralateral invasive and non-invasive cancer** **LOE 1a**
- **The number needed to treat for any ipsilateral breast event is 15** **LOE 1a**

DCIS –

Adjuvant Systemic Treatment

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	Oxford		
	LoE	GR	AGO
■ Tamoxifen (only ER+) 20mg	1a	A	+/-*
■ Tamoxifen (only ER+) 5mg (long-term data missing)	2b ^a	B	+/-*
■ Aromatase inhibitor (only ER+) in postmenopausal women only	1b	A	+/-*
■ Trastuzumab (only HER2+)	5	D	--

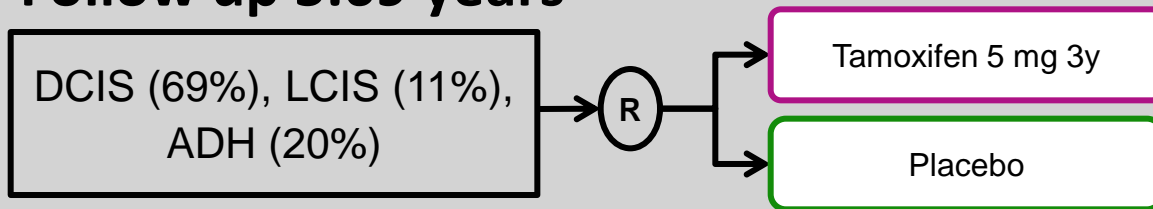
* Indication for treatment depends on risk factors, side effects and patient preference

Low dose Tamoxifen (5mg) in premalignant lesions

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- **N = 500**
- **Follow up 5.69 years**



- **EFS: TAM 5.5% (14/253) vs. PLAC 11.3% (28/247)**
- **Severe adverse Event with same incidence (Endometrial cancer TAM 1 vs. PLAC 0, thrombo-embolic event TAM 1 vs. PLAC 1)**
- **Adherence TAM 65% vs. PLAC 61%**

Lazzeroni M et al: Breast 2019

Therapy of Local DCIS Recurrence after Tumorectomy

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After Radiation:

- **Simple Mastectomy
+ SLNE**
- **Secondary breast conserving surgery**

Without radiation after first tumorectomy

- **Treatment like primary disease**

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

Prognosis seems to be better for invasive recurrences than for primary invasive breast cancer. About 50% of recurrences are invasive.