Diagnosis and Treatment of Patients with early and advanced Breast Cancer

in der DGGG e.V.
sowie
in der DKG e.V.

Guidelines Breast
Version 2024.1E

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HEILEN

Ductal Carcinoma in Situ (DCIS)

Guidelines Breast
Version 2024.1E

Ductal Carcinoma In Situ (DCIS)

Versions 2002–2023:

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Version 2024:

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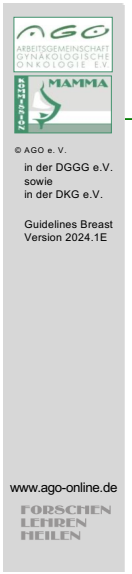


DCIS - Pretherapeutic Assessment

	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	+
Ultrasound (to rule out an accompanying invasive component)	4	C	++
For tumors with a solid part	4	C	++
MRI to determine the extension and planning of surgery	1a	B	+/-
Clinical examination	5	D	++
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	++
Interdisciplinary board presentation	5	D	++

<u>Mammographie</u>

1. Li J, Zhang H, Jiang H, Guo X et al. Diagnostic Performance of Digital Breast Tomosynthesis for Breast Suspicious Calcifications From Various Populations: A Comparison With Full-field Digital Mammography. Comput Struct Biotechnol J. 2018 Dec 20;17:82-89.
2. Adachi M, Fujioka T, Mori M et al. Detection and Diagnosis of Breast Cancer Using Artificial Intelligence Based Assessment of Maximum Intensity Projection Dynamic Contrast-Enhanced Magnetic Resonance Images. Diagnostics (Basel) 2020 May; 10(5): 330. Published online 2020 May 20. doi: 10.3390/diagnostics10050330
3. Sanmugasiva VV, Hamid MTR, Fadzli F, et al. Diagnostic accuracy of digital breast tomosynthesis in combination with 2D mammography for the characterisation of mammographic abnormalities. Sci Rep. 2020; 10: 20628. Published online 2020 Nov 26. doi: 10.1038/s41598-020-77456-6
4. Schaffter T, Buist DSM, Lee CI, et al. Evaluation of Combined Artificial Intelligence and Radiologist Assessment to Interpret Screening Mammograms. JAMA Netw Open. 2020 Mar; 3(3): e200265. Published online 2020 Mar 2. doi: 10.1001/jamanetworkopen.2020.0265

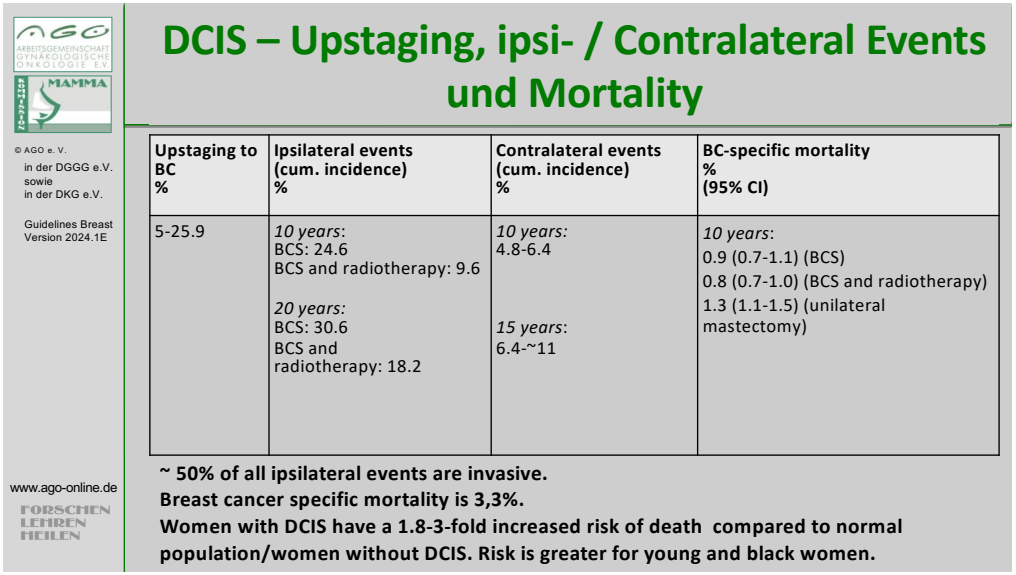
<u>Präoperatives MRT</u>

1. Vapiwala N, Hwang WT, Kushner CJ, et al. No impact of breast magnetic resonance imaging on 15-year outcomes in patients with ductal carcinoma in situ or early-stage invasive breast cancer managed with breast conservation therapy. Cancer. 2017;123(8):1324-1332.
2. Ryan R, Tawfik O, Jensen RA et al. Current Approaches to Diagnosis and Treatment of Ductal Carcinoma In Situ and Future Directions. Prog Mol Biol Transl Sci. 2017;151:33-80.
3. Preibsch H, Beckmann J, Pawlowski J et al. Accuracy of Breast Magnetic Resonance Imaging Compared to Mammography in the Preoperative Detection and Measurement of Pure Ductal Carcinoma In Situ: A Retrospective Radiol. 2018 Aug 24. pii: S1076-6332(18)30383-0.
4. So A, De La Cruz LM, Williams AD et al. impact of preoperative magnetic resonance imaging and lumpectomy cavity shavings on re-excision rate in pure ductal carcinoma in situ-A single institution's experience. J Surg Oncol. 2018 Mar;117(4):558-566.
5. Lamb LR, Oseni TO, Lehman CD et al. Pre-operative MRI in patients with ductal carcinoma in situ: Is MRI useful for identifying additional disease? Eur J Radiol. 2020 Aug;129:109130. doi: 10.1016/j.ejrad.2020.109130.
6. Lam DL, Smith J, Partridge S et al. The Impact of Preoperative Breast MRI on Surgical Management of Women with Newly Diagnosed Ductal Carcinoma In Situ. Acad Radiol. 2020 Apr;27(4):478-486. doi: 10.1016/j.acra.2019.05.013.
7. Lee J, Jung JH, Kim WW et al. Efficacy of breast MRI for surgical decision in patients with breast cancer: ductal carcinoma in situ versus invasive ductal carcinoma. BMC Cancer. 2020 Sep 29;20(1):934. doi: 10.1186/s12885-020-07443-7.
8. Canelo-Aybar C, Taype-Rondan A, Zafra-Tanaka JH, et al: Preoperative breast magnetic resonance imaging in patients with ductal carcinoma in situ: a systematic review for the European Commission Initiative on Breast Cancer (ECIBC). Eur Radiol. 2021 Aug;31(8):5880-5893. doi: 10.1007/s00330-021-07873-2.
9. Chou SHS, Romanoff J, Lehmann CD: Preoperative Breast MRI for Newly Diagnosed Ductal Carcinoma in Situ: Imaging Features and Performance in a Multicenter Setting (ECOG-ACRIN E4112 Trial). Radiology, 2021 Oct;301(1):66-77. doi: 10.1148/radiol.2021204743. Epub 2021 Aug 3.

<u>Sonographie</u>

1. Watanabe T, Yamaguchi T, Tsunoda H, et al. Ultrasound image classification of ductal carcinoma in situ (DCIS) of the breast: Analysis of 705 DCIS lesions. Ultrasond Med Biol. 2017;43:918–25.
2. Bragg A, Candelaria R, et al: Imaging of Noncalcified Ductal Carcinoma In SituJ Clin Imaging Sci. 2021 Jun 16;11:34. doi: 10.25259/JCIS_48_2021

3. Grimm L, Rahbar H, Abdelmalak M et al.: Ductal Carcinoma in Situ: State-of-the-Art Review. Radiology . 2021 Dec 21;211839.
4. Rauch GM, Kuerer HM, et al:Clinicopathologic, mammographic, and sonographic features in 1,187 patients with pure ductal carcinoma in situ of the breast by estrogen receptor status. Breast Cancer Res Treat. 2013 Jun; 139(3):639-47.



DCIS – Upstaging, ipsi- / Contralateral Events und Mortality

Upstaging to BC %	Ipsilateral events (cum. incidence) %	Contralateral events (cum. incidence) %	BC-specific mortality % (95% CI)
5-25.9	*10 years*: BCS: 24.6 BCS and radiotherapy: 9.6 *20 years:* BCS: 30.6 BCS and radiotherapy: 18.2	*10 years:* 4.8-6.4 *15 years*: 6.4-~11	*10 years*: 0.9 (0.7-1.1) (BCS) 0.8 (0.7-1.0) (BCS and radiotherapy) 1.3 (1.1-1.5) (unilateral mastectomy)

~ 50% of all ipsilateral events are invasive.
Breast cancer specific mortality is 3,3%.
Women with DCIS have a 1.8-3-fold increased risk of death compared to normal population/women without DCIS. Risk is greater for young and black women.

Upstaging

1. Brennan ME, Turner RM, Ciatto S, et al. Ductal carcinoma in situ at coreneedle biopsy: meta-analysis of underestimation and predictors of invasive breast cancer. Radiology 2011;260(1):119–128.
2. Oseni TO, Smith BL, Lehman CD, et al:Do Eligibility Criteria for Ductal Carcinoma In Situ (DCIS) Active Surveillance Trials Identify Patients at Low Risk for Upgrade to Invasive Carcinoma? Ann Surg Oncol. 2020 Oct;27(11):4459-4465. doi: 10.1245/s10434-020-08576-6..

Ipsilateral

1. Narod SA, Iqbal J, Giannakeas V, et al. Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ. JAMA Oncol. 2015 Oct;1(7):888-96
2. Giannakeas V, Sopik V, Narod SA. et al. Association of a Diagnosis of Ductal Carcinoma In Situ With Death From Breast Cancer. JAMA Netw Open. 2020 Sep 1;3(9):e2017124. doi: 10.1001/jamanetworkopen.2020.17124
3. Mannu GS, Wang Z, Broggio J, et al: Invasive breast cancer and breast cancer mortality after ductal carcinoma in situ in women attending for breast screening in England, 1988-2014: population based observational cohort

study. BMJ. 2020 May 27;369:m1570.

4. van Seijen M , Lips EH , Fu L: Long-term risk of subsequent ipsilateral lesions after surgery with or without radiotherapy for ductal carcinoma in situ of the breast. British Journal of Cancer (2021) 125:1443–1449; https://doi.org/10.1038/s41416-021-01496-6

Kontralateral

1. Wärnberg F, Garmo H, Emdin St: Effect of Radiotherapy After Breast-Conserving Surgery for Ductal Carcinoma in Situ: 20 Years Follow-Up in the Randomized SweDCIS Trial. JCO, 32: 32, 2014

2. Elshof LE, Schaapveld M, Schmidt MK: Subsequent risk of ipsilateral and contralateral invasive breast cancer after treatment for ductal carcinoma in situ: incidence and the effect of radiotherapy in a population-based cohort of 10,090 women. Breast Cancer Res Treat. 2016; 159(3): 553–563.

3. Miller ME , Muhsen, Zabor EC, et al: Risk of Contralateral Breast Cancer in Women with Ductal Carcinoma In Situ Associated with Synchronous Ipsilateral Lobular Carcinoma In Situ. Ann Surg Oncol. 2019 Dec;26(13):4317-4325. doi: 10.1245/s10434-019-07796-9.

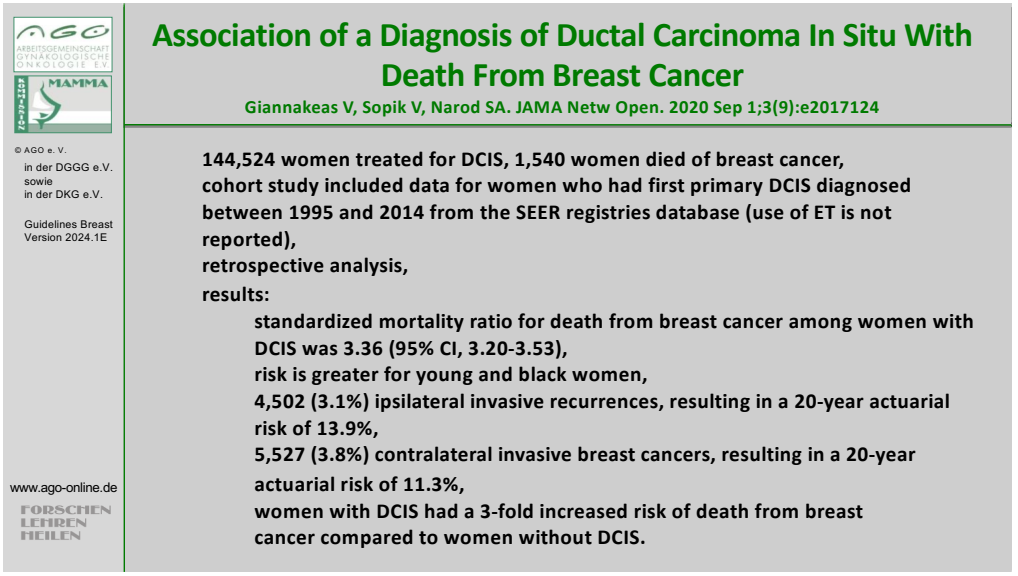
4. Giardiella D, Kramer I, Maartje J, et al: Contralateral breast cancer risk in pts with ductal carcinoma in situ and invasive breast cancer. Npj Breast Cancer 6:60, 2020

5. Hovis K, Mercaldo S, Kim G: Contralateral breast cancer after curative-intent treatment for ductal carcinoma in situ: Rate and associated clinicopathological and imaging risk factors. Clin Imaging. 2021 Nov 20;82:179-192. doi: 10.1016/j.clinimag.2021.11.018.

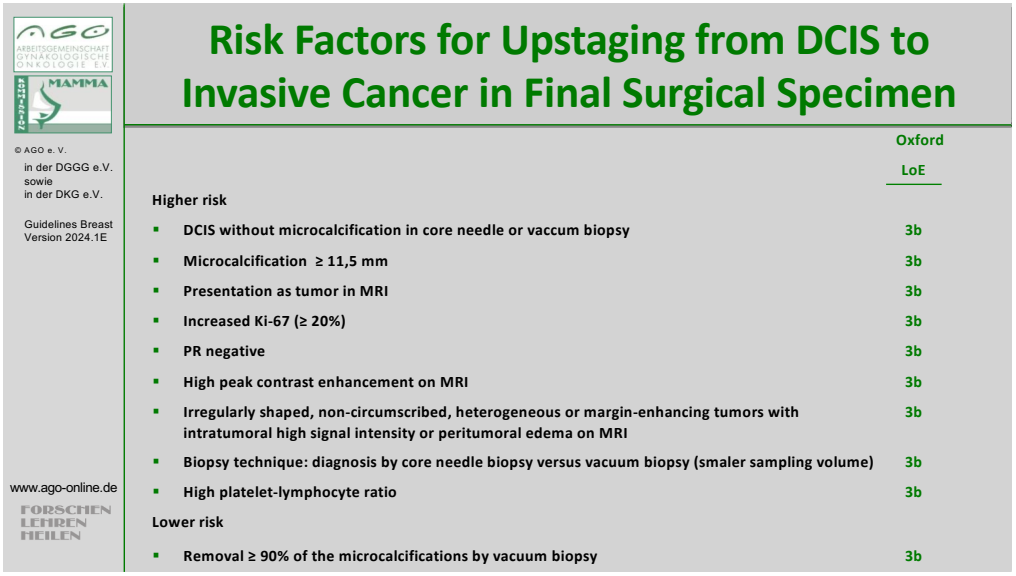
Überleben

1. Narod SA, Iqbal J, Giannakeas V, et al. Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ. JAMA Oncol. 2015 Oct;1(7):888-96

2. Giannakeas V, Sopik V, Narod SA. et al. Association of a Diagnosis of Ductal Carcinoma In Situ With Death From Breast Cancer. JAMA Netw Open. 2020 Sep 1;3(9):e2017124. doi: 10.1001/jamanetworkopen.2020.17124



1. Giannakeas V, Sopik V, Narod SA. et al. Association of a Diagnosis of Ductal Carcinoma In Situ With Death From Breast Cancer. JAMA Netw Open. 2020 Sep 1;3(9):e2017124. doi: 10.1001/jamanetworkopen.2020.17124.



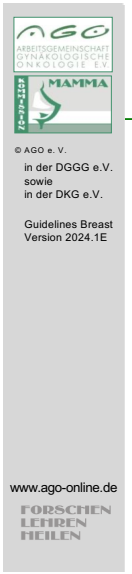
1. Cheung YC, Chen SC, Ueng SH, et al. Ductal Carcinoma In Situ Underestimation of Microcalcifications Only by Stereotactic Vacuum-Assisted Breast Biopsy: A New Predictor of Specimens without Microcalcifications. J Clin Med. 2020 Sep; 9(9): 2999. Published online 2020 Sep 17. doi: 10.3390/jcm9092999
2. Visser LL, Elshof LE, Van de Vijver K, et al. Discordant Marker Expression Between Invasive Breast Carcinoma and Corresponding Synchronous and Preceding DCIS. Am J Surg Pathol 2019;43(11):1574–1582.
3. Yoon GY, Choi WJ, Cha JH, et al. The role of MRI and clinicopathologic features in predicting the invasive component of biopsy-confirmed ductal carcinoma in situ. BMC Med Imaging. 2020; 20: 95. Published online 2020 Aug 12. doi: 10.1186/s12880-020-00494-z
4. Takada K, Kashiwagi S, Asano Y, et al. Factors predictive of invasive ductal carcinoma in cases preoperatively diagnosed as ductal carcinoma in situ. BMC Cancer. 2020; 20: 513. Published online 2020 Jun 3. doi: 10.1186/s12885-020-07001-1

Good Clinical Practice (GCP)

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 weighted against risk reduction.

1. Kirsty E. Stuart, Nehmat Houssami, Richard Taylor, et al. Long-term outcomes of ductal carcinoma in situ of the breast: a systematic review, meta-analysis and meta-regression analysis. BMC Cancer (2015) 15:890.
2. Katrina B. Mitchell and Henry Kuerer. Ductal Carcinoma In Situ: Treatment Update and Current Trends. Curr Oncol Rep (2015) 17: 48
3. Elizabeth M. Ward, Carol E. DeSantis, Chun Chieh Lin,et al. Cancer Statistics: Breast Cancer In Situ. CA Cancer J Clin 2015;65:481–495.
4. Benjamin D. Smith. When Is Good Enough Really Good Enough? Defining the Role of Radiation in Low-Risk Ductal Carcinoma In Situ. J Clin Oncol 2015; 33(7): 686 – 692.
5. Laura Esserman, Christina Yau. Rethinking the Standard for Ductal Carcinoma In Situ Treatment. JAMA Oncology Published online August 20, 2015.
6. Steven A. Narod, Javaid Iqbal, Vasily Giannakeas, et al. Breast Cancer Mortality After a Diagnosis of Ductal Carcinoma In Situ. JAMA Oncol. doi:10.1001/jamaoncol.2015.2510 Published online August 20, 2015.
7. Hamilton SN, Nichol A, Wai E et al. Local Relapse After Breast-Conserving Therapy Versus Mastectomy for Extensive Pure Ductal Carcinoma In Situ ≥4 cm. Int J Radiat Oncol Biol Phys. 2018 Sep 22. pii: S0360-3016(18)33801-X
8. Gradishar WJ, Anderson BO, Balassanian R et al. Breast Cancer, Version 4.2017, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2018 Mar;16(3):310-320.



Surgical Treatment for Histologically Proven DCIS I

	Oxford		
	LoE	GR	AGO
Excisional biopsy (wire guided)	2b	B	++
Localization with wire-free procedure	3b	C	+/-
Bracketing wire localization in large lesions	3a	C	+
Specimen radiography	2b	B	++
Intraoperative ultrasound (pre-op visible lesion)	3a	C	+/-
Immediate re-excision in case of incomplete resection (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

Exzision (drahtmarkiert)

1. Houssami N, Ambrogetti D, Marinovich L et al. Accuracy of a preoperative model for predicting invasive breast cancer in women with ductal carcinoma in situ on vacuum assisted core needle biopsy. Ann Surg Oncol 2011;18(5):1364-71
2. Ryan R, Tawfik O, Jensen RA, et al. Current Approaches to Diagnosis and Treatment of Ductal Carcinoma In Situ and Future Directions. Prog Mol Biol Transl Sci. 2017;151:33-80.
3. Janssen NNY, van la Parra RFD, Loo CE et al. Breast conserving surgery for extensive DCIS using multiple radioactive seeds. Eur J Surg Oncol. 2018 Jan;44(1):67-73.
4. Hong YK, McMasters KM, Egger ME, et al. Ductal carcinoma in situ current trends, controversies, and review of literature. Am J Surg. 2018 Nov;216(5):998-1003
5. Kuerer HM, Smith BD, Chavez-MacGregor M, et al. DCIS Margins and Breast Conservation: MD Anderson Cancer Center Multidisciplinary Practice Guidelines and Outcomes. J Cancer. 2017;8(14):2653-2662.
6. DVerstehenden DPA, Keizer LGG, Schlooz-Vries MS, et al: Performance characteristics of specimen radiography for margin assessment for ductal carcinoma in situ: a systematic review. Breast Cancer Res Treat 2017:166:669–679.
7. Pieszko K, Wichtowski M, Cieciorowski M, et al. Evaluation of the nonradioactive inducible magnetic seed system Magseed for preoperative localization of nonpalpable breast lesions – initial clinical experience Contemp Oncol (Pozn) 2020; 24(1): 51–54. Published online 2020 Mar 13. doi: 10.5114/wo.2020.93677

8. Colombe Agahozo M, Berghuis SAM, van den Broek E, et al. Radioactive Seed Versus Wire-Guided Localization for Ductal Carcinoma in Situ of the Breast: Comparable Resection Margins. Ann Surg Oncol. 2020; 27(13): 5296–5302. Published online 2020 Jun 23. doi: 10.1245/s10434-020-08744-8

Intraoperative Sonographie (darstellbarer Befund)

1. Ahmed M, Douek M. Intra-operative ultrasound versus wire-guided localization in the surgical management of non-palpable breast cancers: systematic review and meta-analysis. Breast Cancer Res Treat. 2013; 140(3): 435-446.

Sofortige Nachresektion bei knappen Resektionsrändern (Präparateradiographie)

1. Thill M, Dittmer C, Baumann K, et al. MarginProbe®--final results of the German post-market study in breast conserving surgery of ductal carcinoma in situ. Breast. 2014 Feb;23(1):94-6. doi: 10.1016/j.breast.2013.11.002. Epub 2013 Dec 2.
2. Kuerer HM, Smith BD, Chavez-MacGregor M, et al. DCIS Margins and Breast Conservation: MD Anderson Cancer Center Multidisciplinary Practice Guidelines and Outcomes. J Cancer. 2017;8(14):2653-2662.

Intraoperative Schnellschnittdiagnostik

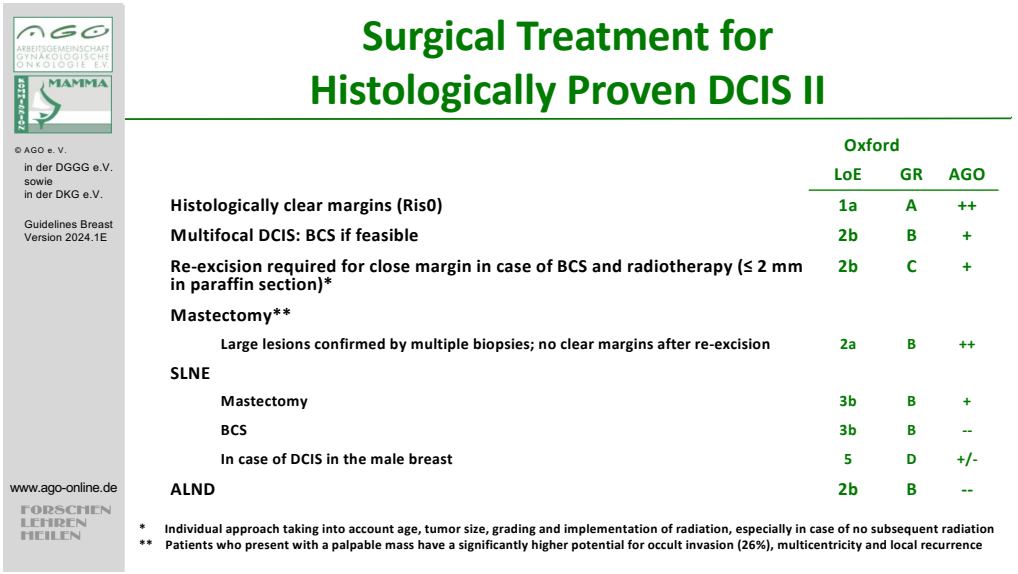
1. Kuerer HM, Smith BD, Chavez-MacGregor M et al. DCIS Margins and Breast Conservation: MD Anderson Cancer Center Multidisciplinary Practice Guidelines and Outcomes. J Cancer. 2017;8(14):2653-2662.
2. Laws A, Brar MS, Bouchard-Fortier A, et al. surgery for ductal carcinoma in situ. J Surg Oncol. 2018 Dec;118(7):1205-1211.
3. Morrow M, Van Zee KJ, Solin LJ, Houssami N et al: Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery with Whole-Breast Irradiation in Ductal Carcinoma In Situ. Ann Surg Oncol. 2016 Nov;23(12):3801-3810.

Statement: Non-palpable lesions or lesions

1. Morrow M, Strom E, Bassett L et al. Standard for the management of ductal carcinoma in situ of the breast (DCIS). CA Cancer J Clin 2002; 52: 256-276.

Tumorboard

1. Farante G, Toesca A, Magnoni F, et al: Advances and controversies in management of breast ductal carcinoma in situ (DCIS). PMID: 34772587, DOI: 10.1016/j.ejso.2021.10.030



Surgical Treatment for Histologically Proven DCIS II

	Oxford LoE	GR	AGO
Histologically clear margins (Ris0)	1a	A	++
Multifocal DCIS: BCS if feasible	2b	B	+
Re-excision required for close margin in case of BCS and radiotherapy (≤ 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	--

* Individual approach taking into account age, tumor size, grading and implementation of radiation, especially in case of no subsequent radiation
** Patients who present with a palpable mass have a significantly higher potential for occult invasion (26%), multicentricity and local recurrence

Histologisch freie Resektionsränder (pR0)

1. Badruddoja M. Ductal carcinoma in situ of the breast: a surgical perspective. Int J Surg Oncol. 2012;2012:761364. doi: 10.1155/2012/761364. Epub 2012 Sep 4.
2. Hassani A, Griffith C, Harvey J. Size does matter: High volume breast surgeons accept smaller excision margins for wide local excision--a national survey of the surgical management of wide local excision margins in UK breast cancer patients. Breast. 2013 Oct;22(5):718-22.
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4. Salvatorelli L, Puzzo L, Vecchio GM, et al. Ductal Carcinoma In Situ of the Breast: An Update with Emphasis on Radiological and Morphological Features as Predictive Prognostic Factors. Cancers (Basel) 2020 Mar; 12(3): 609. Published online 2020 Mar 6. doi: 10.3390/cancers12030609
5. Livingston-Rosanoff D, Trentham-Dietz A, Hampton JM, et al: Does margin width impact breast cancer recurrence rates in women with breast conserving surgery for ductal carcinoma in situ? Breast Cancer Res Treat. 2021 Sep;189(2):463-470. doi: 10.1007/s10549-021-06278-5.

Multifokalität: BET falls möglich (inkl. RT)

1. Meijnen P, Bartelink H. Multifocal ductal carcinoma in situ of the breast: A contraindication for breast-conserving treatment? J Clin Oncol 2007;25:5548–5549
2. Rakovitch E, Pignol JP, Hanna W, et al. Significance of multifocality in ductal carcinoma in situ: outcomes of women treated with breast-conserving therapy. J Clin Oncol 2007;25:5591–5596

Nachresektion bei knappem Resektionsrand (< 2 mm im Paraffinschnitt)

1. Dunne, C., J. P. Burke, et al. (2009). "Effect of margin status on local recurrence after breast conservation and radiation therapy for ductal carcinoma in situ." J Clin Oncol 27(10): 1615-1620.
2. Van Cleef A, Altintas S, Huizing M et al. Current view on ductal carcinoma in situ and importance of the margin thresholds: A review. Facts Views Vis Obgyn. 2014;6(4):210-8.
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4. Morrow M. De-escalating and escalating surgery in the management of early breast cancer. Breast. 2017 Aug;34 Suppl 1:S1-S4.

Mastektomie* (große Läsionen; keine sicheren Ränder im Nachresektat)

1. Carlson, G. W., A. Page, et al. (2007). "Local recurrence of ductal carcinoma in situ after skin-sparing mastectomy." J Am Coll Surg 204(5): 1074-1078; discussion 1078-1080.
2. Rudloff U, E Brogi et al. (2010): “The Influence of Margin Width and Volume of Disease Near Margin on Benefit of Radiation Therapy for Women With DCIS Treated With Breast-Conserving Therapy” Ann Surg (251) 583 – 591
3. Polyak K. Molecular markers for the diagnosis and management of ductal carcinoma in situ. J Natl Cancer Inst Monogr 2010; 41: 210-213
4. Houssami N, Ambrogetti D, Marinovich L et al. Accuracy of a preoperative model for predicting invasive breast cancer in women with ductal carcinoma in situ on vacuum assisted core needle biopsy. Ann Surg Oncol 2011;18(5):1364-71

SLNE* /Axilladissektion

1. Killelea BK, Long JB, Dang W, et al. Associations Between Sentinel Lymph Node Biopsy and Complications for Patients

with Ductal Carcinoma In Situ. Ann Surg Oncol. 2018 Jun;25(6):1521-1529.
2. Hong YK, McMasters KM, Egger ME, et al. Ductal carcinoma in situ current trends, controversies, and review of literature. Am J Surg. 2018 Nov;216(5):998-1003
3. Karakatsanis A, Hersi AF, Pistiolis L: Effect of preoperative injection of superparamagnetic iron oxide particles on rates of sentinel lymph node dissection in women undergoing surgery for ductal carcinoma in situ (SentiNot study). Br J Surg. 2019 May;106(6):720-728. doi: 10.1002/bjs.11110. Epub 2019 Mar 6.
4. Price A, Schnabel F, Chun J et al. Sentinel lymph node positivity in patients undergoing mastectomies for ductal carcinoma in situ (DCIS). Breast J. 2020 May;26(5):931-936. doi: 10.1111/tbj.13737.
5. Pyfer BJ, Jonczyk M, Jean J et al. Analysis of Surgical Trends for Axillary Lymph Node Management in Patients with Ductal Carcinoma In Situ Using the NSQIP Database: Are We Following National Guidelines? Ann Surg Oncol. 2020 Sep;27(9):3448-3455. doi: 10.1245/s10434-020-08374-0

DCIS beim Mann

1. Chern J, Liao L, Baraldi R, et al. Case report: ductal carcinoma in situ in the male breast. Case Rep Radiol. 2012;2012:532527. doi: 10.1155/2012/532527. Epub 2012 Sep 26.

BET

1. Meijnen P, Oldenburg HS, Loo CE, et al. Risk of invasion and axillary lymph node metastasis in ductal carcinoma in situ diagnosed by core-needle biopsy. Br J Surg 2007;94:952-6
2. Miyake T, Shimazu K, Ohashi H, et al. Indication for sentinel lymph node biopsy for breast cancer when core biopsy shows ductal carcinoma in situ. The American Journal of Surgery 2011; 202: 59-65 :394095. doi: 10.5402/2012/394095. Epub 2012 May 14.
3. De Lorenzi F, Di Bella J, Maisonneuve P et al. Oncoplastic breast surgery for the management of ductal carcinoma in situ (DCIS): is it oncologically safe? A retrospective cohort analysis. Eur J Surg Oncol. 2018 Jul;44(7):957-962

Prognostic Factors for an Ipsilateral Recurrence after DCIS I

	LoE
Resection margins	1a
Age	1a
Size	1a
Grade	1a
Comedo necrosis	1a
Method of diagnosis	1a
Focality	1a
HER2-overexpression	1a
ER / PR (positive vs. negative)	1a

See also chapter “Prognostic Faktors“

1. Visser LL, Elshof LE, Schaapveld M et al. Clinicopathological Risk Factors for an Invasive Breast Cancer recurrence after Ductal Carcinoma In Situ-A Nested Case-Control Study. Clin Cancer Res. 2018 Aug 1;24(15):3593-3601.
2. Rakovitch E, Gray R, Baehner FL et al. Refined estimates of local recurrence risks by DCIS score adjusting for clinicopathological features: a combined analysis of ECOG-ACRIN E5194 and Ontario DCIS cohort studies. Breast Cancer Res Treat. 2018 Jun;169(2):359-369
3. Cutuli B: Ductal carcinoma in situ in 2019: Diagnosis, treatment, prognosis. Presse Med. 2019 Oct;48(10):1112-1122
4. Badve SS, Gökmen-Polar: Ductal carcinoma in situ of breast: update 2019. Pathology. 2019 Oct;51(6):563-569.
5. Van Bockstal MR, Agahozo MC, Koppert LB: A retrospective alternative for active surveillance trials for ductal carcinoma in situ of the breast. Int J Cancer. 2020 Mar 1;146(5):1189-1197
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10.1007/s10549-020-05816-x

Diagnostische Methode

1. Park HS, Park S, Cho J, et al. Risk predictors of underestimation and the need for sentinel node biopsy in patients diagnosed with ductal carcinoma in situ by preoperative needle biopsy. J Surg Oncol. 2013 Mar;107(4):388-92. doi: 10.1002/jso.23273. Epub 2012 Sep 24.
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1. Meijnen P, Bartelink H. Multifocal ductal carcinoma in situ of the breast: A contraindication for breast-conserving treatment? J Clin Oncol 2007;25:5548–5549
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(mod.) Van Nuys Prognose Index und MSKCC Nomogramm

1. Lagios MD, Page DL, Silverstein MJ. Prospective study of wide excision alone for ductal carcinoma in situ of the breast. J Clin Oncol 2006;24:3809-11
2. Rudloff U, Jacks LM, Goldberg JL, et al. Nomogram for predicting the risk of local recuurence after breast conserving surgery for ductal carcinoma in situ. J Clin Oncol 2010; 28(23): 3762-9
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a European single-center experience and external validation of the Memorial Sloan-Kettering Cancer Center DCIS nomogram. Cancer J 2014; 20(1): 1-7.

5. Lei RY, Carter DL, Antell AG, et al. A Comparison of Predicted Ipsilateral Tumor Recurrence Risks in Patients With Ductal Carcinoma in Situ of the Breast After Breast-Conserving Surgery by Breast Radiation Oncologists, the Van Nuys Prognostic Index, the Memorial Sloan Kettering Cancer Center DCIS Nomogram, and the 12-Gene DCIS Score Assay. Adv Radiat Oncol 2020;6(2):100607.
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Palpables DCIS
Palpabel + COX-2+p16+Ki-67+
Palpabel + ER-, HER2, +Ki-67+
HER2-Überexpression
ER/PgR (positiv vs. negativ)
DCIS-Score

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DCIS mit Mikroinvasion – Behandlung analog zum invasiven Karzinom

1. Eng-Wong J, JP Costantino et al. The Impact of Systemic Therapy Following Ductal Carcinoma In Situ. J Natl Cancer Inst Monogr 2010; 41: 200 – 203
2. Ryan R, Tawfik O, Jensen RA, Anant S. Current Approaches to Diagnosis and Treatment of Ductal Carcinoma In Situ and Future Directions. Prog Mol Biol Transl Sci. 2017;151:33-80.

Intrinsische Subgruppen (Luminal A,B, HER+, triple negativ)

1. Noh JM, Lee J, Choi DH, et al. HER-2 overexpression is not associated with increased ipsilateral breast tumor recurrence in DCIS treated with breast-conserving surgery followed by radiotherapy. Breast. 2013 Oct;22(5):894-7.
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Familiäre Karzinombelastung, Menopausenstatus, BMI und Brustdichte

1. Alaeikhanehshir S, Engelhardt EG, van Duijnhoven FH, et al. The impact of patient characteristics and lifestyle factors on

the risk of an ipsilateral event after a primary DCIS: A systematic review. Breast. 2020 Apr; 50: 95–103. Published online 2020 Feb 19. doi: 10.1016/j.breast.2020.02.006

Kontralaterales Mammakarzinom

1. Giardiello D, Kramer I, Hooning MJ, et al. Contralateral breast cancer risk in patients with ductal carcinoma in situ and invasive breast cancer. NPJ Breast Cancer. 2020; 6: 60. Published online 2020 Nov 3. doi: 10.1038/s41523-020-00202-8

Molecular Subtyping

1. Nofech-Mozes S, Hanna W, Rakovitch E. Molecular Evaluation of Breast Ductal Carcinoma in Situ with Oncotype DX DCIS. Am J Pathol. 2018 Dec 31. pii: S0002-9440(18)30581-9
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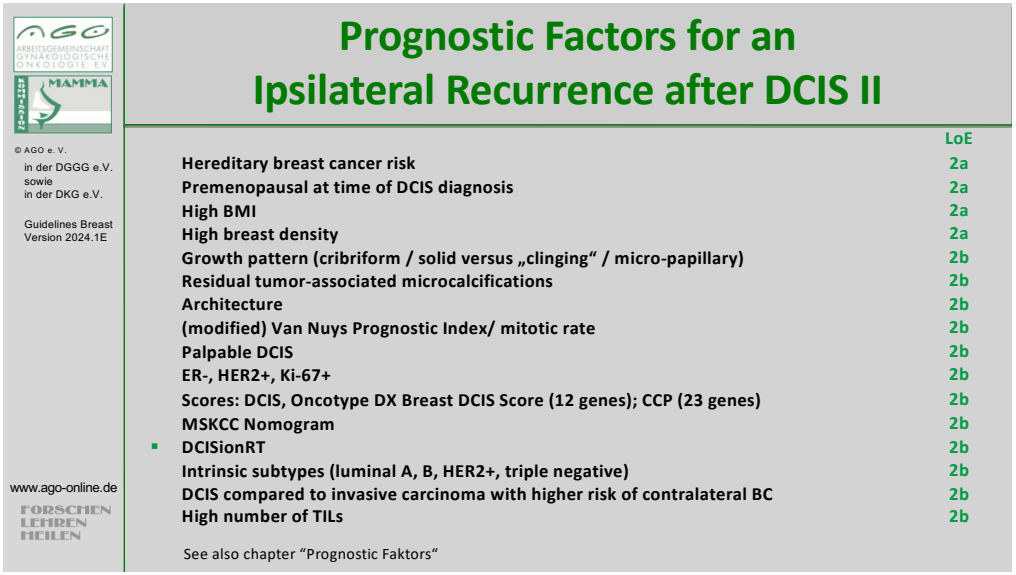

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DCISionRT:

1. Weinmann S, Leo MC, Francisco M, et al. Validation of a Ductal Carcinoma *In Situ* Biomarker Profile for Risk of Recurrence after Breast-Conserving Surgery with and without Radiotherapy. Clin Cancer Res. 2020 Aug 1;26(15):4054-4063.
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Molecular Profile

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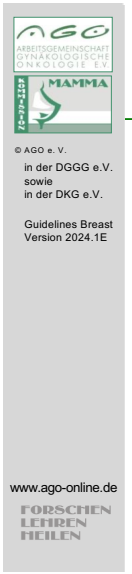

DCIS – Radiotherapy Statements

Radiotherapy has no impact on survival	**LoE 1a**
Radiotherapy reduces the risk of ipsilateral (invasive and non invasive) recurrences by 50 %	**LoE 1a**
The number needed to treat (for ipsilateral breast recurrence) is 9 (over all risk groups).	

1. Bagenal J, Roche N, Ross G, Kirby A, Dodwell D: Should patients with ductal carcinoma in situ be treated with adjuvant whole breast radiotherapy after breast conservation surgery? BMJ. 2018 May 17;361:k1410. doi: 10.1136/bmj.k1410. Review.
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4. Weinmann S, Leo MC, Francisco M et al. Validation of a Ductal Carcinoma In Situ Biomarker Profile for Risk of Recurrence after Breast-Conserving Surgery with and without Radiotherapy. Clin Cancer Res. 2020 Aug 1;26(15):4054-4063. doi: 10.1158/1078-0432.CCR-19-1152. DCISionRT test, the DS was prognostic for the risk of later breast events for women diagnosed with DCIS, following BCS.
5. Yang L, Lu D, Lai Y et al. Prognostic Score-Based Stratification Analysis Reveals Universal Benefits of Radiotherapy on Lowering the Risk of Ipsilateral Breast Event for Ductal Carcinoma In Situ Patients with Different Risk Levels. Ann Surg Oncol. 2020 Aug 13. doi: 10.1245/s10434-020-09003-6.
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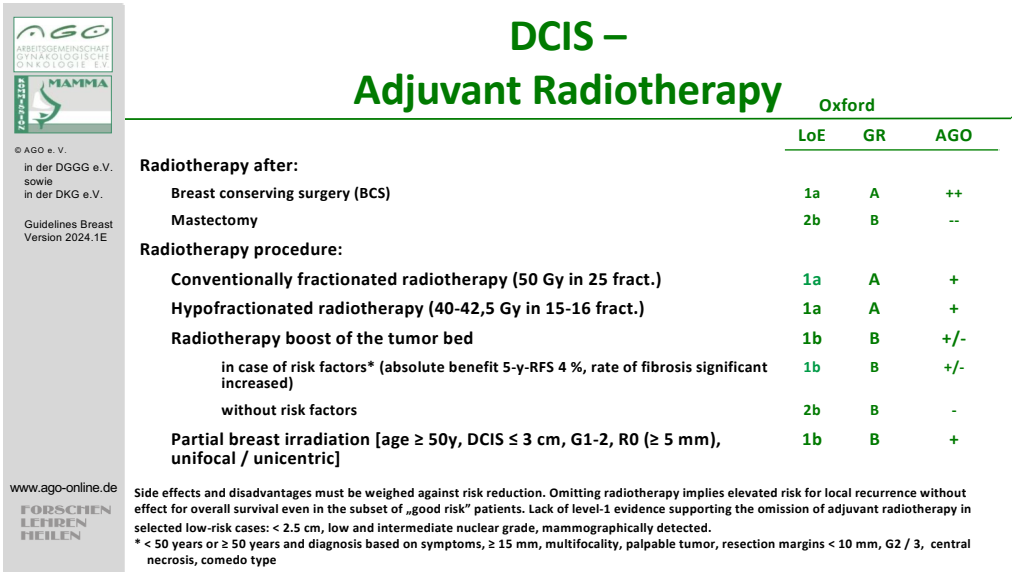
Excision for Good-Risk Ductal Carcinoma In Situ: Long-Term Report From NRG Oncology/RTOG 9804.J Clin Oncol. 2021 Nov 10;39(32):3574-3582. doi: 10.1200/JCO.21.01083.



DCIS – Adjuvant Radiotherapy

	Oxford LoE	GR	AGO
Radiotherapy after:			
Breast conserving surgery (BCS)	1a	A	++
Mastectomy	2b	B	--
Radiotherapy procedure:			
Conventionally fractionated radiotherapy (50 Gy in 25 fract.)	1a	A	+
Hypofractionated radiotherapy (40-42,5 Gy in 15-16 fract.)	1a	A	+
Radiotherapy boost of the tumor bed	1b	B	+/-
in case of risk factors* (absolute benefit 5-y-RFS 4 %, rate of fibrosis significant increased)	1b	B	+/-
without risk factors	2b	B	-
Partial breast irradiation [age ≥ 50y, DCIS ≤ 3 cm, G1-2, R0 (≥ 5 mm), unifocal / unicentric]	1b	B	+

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.
* < 50 years or ≥ 50 years and diagnosis based on symptoms, ≥ 15 mm, multifocality, palpable tumor, resection margins < 10 mm, G2 / 3, central necrosis, comedo type

Radiotherapie nach: Brusterhaltender Operation (BEO) (gesamte Brust, WBI)

1. EBCTCG Correa C et al. Overview of the randomized trials of radiotherapy in ductal carcinoma in situ of the breast. J Natl Cancer Inst Monogr. 2010 (41); 162 – 77
2. Abram Recht. Are the Randomized Trials of Radiation Therapy for Ductal Carcinoma in Situ Still Relevant? J Clin Oncol 2014; 32(22): 3588
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Boost

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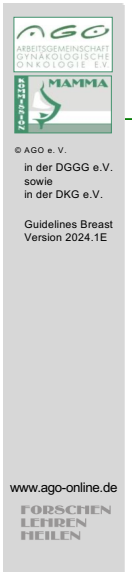

DCIS – Adjuvant Systemic Treatment

Adjuvant endocrine treatment has no impact on survival (RR 1.11; 95% CI 0.89-1.39)	**LoE 1a**
Endocrine treatment may have a small effect on ipsilateral invasive (HR 0.79; 95% CI 0.62-1.01) and DCIS (HR 0.75; 95% CI 0.61-0.92) recurrences	**LoE 1a**
Endocrine treatment for DCIS has an effect on contralateral invasive (RR 0.57; 95% CI 0.39-0.83) and non-invasive (RR 0.50; 95% CI 0.28-0.87) cancer	**LoE 1a**
The number needed to treat for any ipsilateral breast event is 15	**LoE 1a**
The number needed to treat to prevent invasive breast cancer is 29 for anastrozole vs. 59 for tamoxifen*	**LoE 1b**

*** within 12 years; according to IBIS II-trial**

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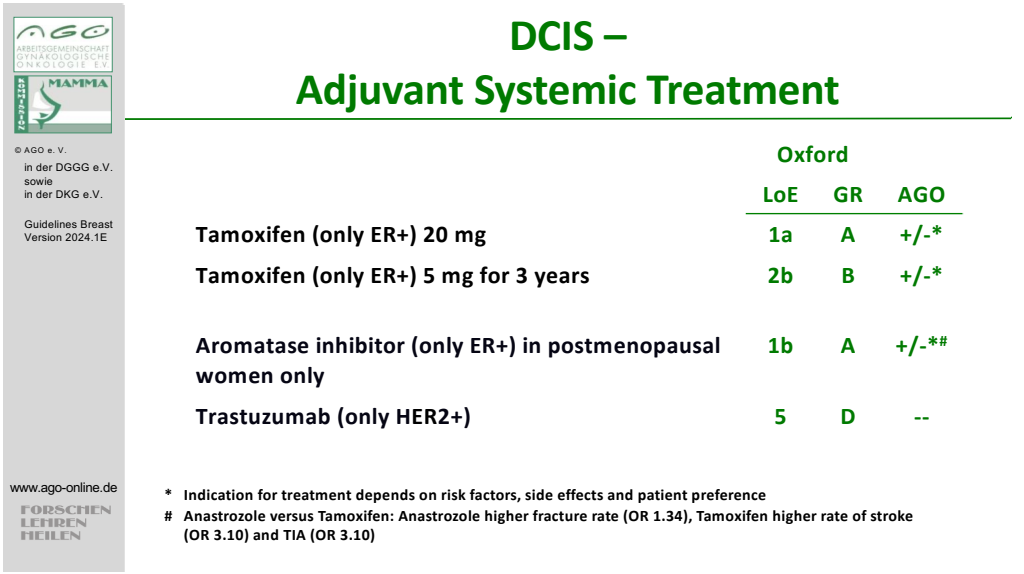

DCIS – Adjuvant Systemic Treatment

	Oxford		
	LoE	GR	AGO
Tamoxifen (only ER+) 20 mg	1a	A	+/-*
Tamoxifen (only ER+) 5 mg for 3 years	2b	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

\# Anastrozole versus Tamoxifen: Anastrozole higher fracture rate (OR 1.34), Tamoxifen higher rate of stroke (OR 3.10) and TIA (OR 3.10)

Tamoxifen (nur ER+, nur BET)

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AI (wenn postmenopausal)

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AI vs. Tamoxifen

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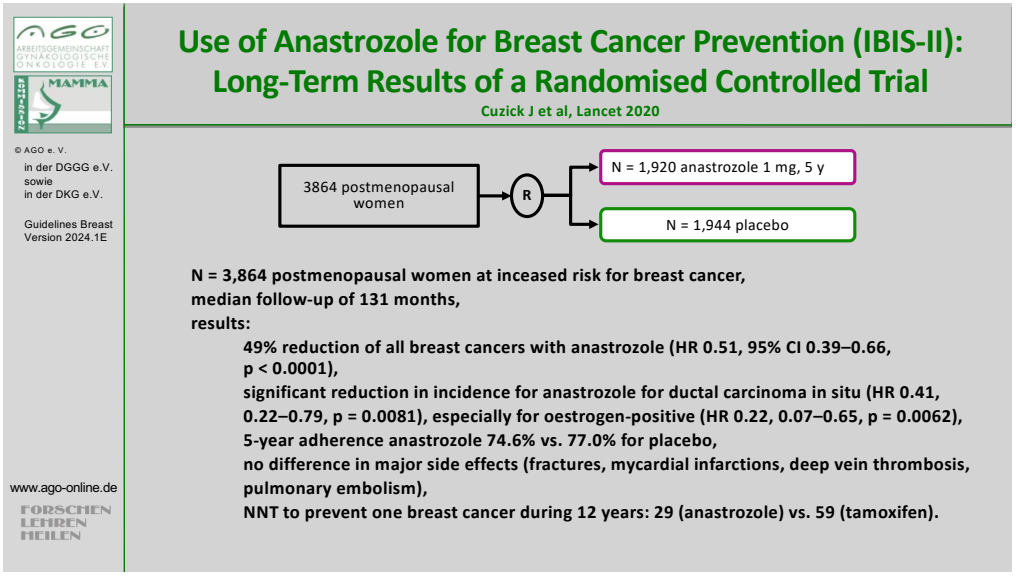

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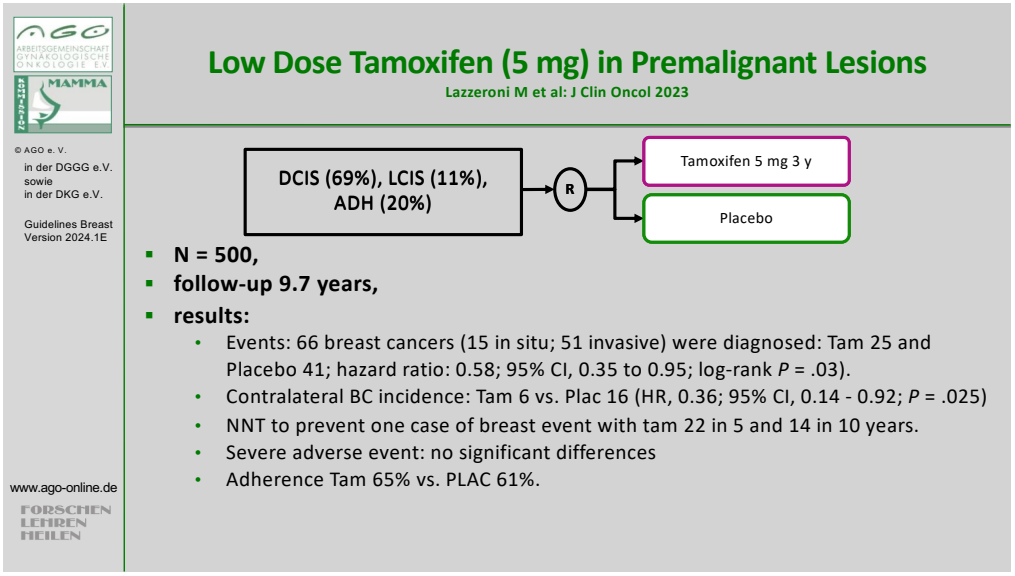

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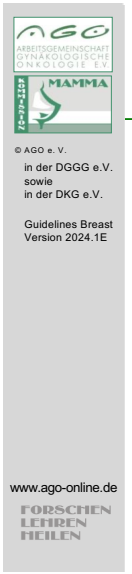

Therapy of Local DCIS Recurrence after Tumorectomy

	Oxford		
	LoE	GR	AGO
After Radiation:			
Simple mastectomy	3a	C	+
+ SLNE	5	D	+
Secondary breast conserving surgery	4	C	+/-
Without radiation after first tumorectomy			
Treatment like primary disease	3	C	++

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Nach Radiatio

Einfache Mastektomie

+ SN B

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Sekundäre Tumorektomie führt zu Rezidiven in bis zu 30 % der Fälle (NSABP B17)

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