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Diagnostik und Therapie früher und fortgeschrittener Mammakarzinome

Duktales Carcinoma in situ (DCIS)



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Duktales Carcinoma in situ (DCIS)

- **Versionen 2002–2021:**

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

- **Version 2022:**

Ditsch / Kühn

DCIS - Prätherapeutische Abklärung			
	Oxford		
	LoE	GR	AGO
■ Mammographie	1b	B	++
■ Vergrößerungsaufnahmen von Mikroverkalkungen	4	C	++
■ Steigerung der Detektionsrate von G1 / G2 DCIS durch digitale Mammographie (versus konventionell)	2b	B	+
■ Sonographie (zum Ausschluss eines begleitenden inv. Anteils)	4	C	++
■ Bei Tumoren mit solidem Anteil	4	C	++
■ MRT zur Festlegung der Ausdehnung und OP-Planung	1a	B	+/-
■ Klinische Untersuchung	5	D	++
■ Stereotaktische Stanzbiopsie / Vakuumbiopsie (VAB)	2b	B	++
■ Präparateradiographie	2b	B	++
■ Setzen eines Markierungsclips in der Biopsieregion, wenn die Läsion komplett entfernt wurde	5	D	++
■ Interdisziplinäre Tumorboard-Präsentation	5	D	++

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Mammographie

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

Präoperatives MRT

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.

Sonographie

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. *Ultrason Med Biol*. 2017;43:918–25.
2. Bragg A, Candelaria R, et al: Imaging of Noncalcified Ductal Carcinoma In Situ *J 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			
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	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%
BC-specific mortality % (95% CI) 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



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Association of a Diagnosis of Ductal Carcinoma In Situ With Death From Breast Cancer

Giannakeas V, Sopik V, Narod SA. JAMA Netw Open. 2020 Sep 1;3(9):e2017124

- **144,524 women treated for DCIS, 1,540 women died of breast cancer,**
- **cohort study included data for women who had first primary DCIS diagnosed between 1995 and 2014 from the SEER registries database (use of ET is not reported),**
- **retrospective analysis,**
- **results:**
 - **standardized mortality ratio for death from breast cancer among women with DCIS was 3.36 (95% CI, 3.20-3.53),**
 - **risk is greater for young and black women,**
 - **4,502 (3.1%) ipsilateral invasive recurrences, resulting in a 20-year actuarial risk of 13.9%,**
 - **5,527 (3.8%) contralateral invasive breast cancers, resulting in a 20-year actuarial risk of 11.3%,**
 - **women with DCIS had a 3-fold increased risk of death from breast cancer compared to women without DCIS.**

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.


Risk Factors for Upstaging from DCIS to Invasive Cancer in Final Surgical Specimen	
	Oxford
	LoE
Higher risk	
▪ DCIS without microcalcification in core needle or vacuum biopsy	3b
▪ Microcalcification $\geq 11,5$ mm	3b
▪ Presentation as tumor in MRI	3b
▪ Increased Ki-67 ($\geq 20\%$)	3b
▪ PR negative	3b
▪ High peak contrast enhancement on MRI	3b
▪ Irregularly shaped, non-circumscribed, heterogeneous or margin-enhancing tumors with intratumoral high signal intensity or peritumoral edema on MRI	3b
▪ Biopsy technique: diagnosis by core needle biopsy versus vacuum biopsy (smaller sampling volume)	3b
▪ High platelet-lymphocyte ratio	3b
Lower risk	
▪ Removal $\geq 90\%$ of the microcalcifications by vacuum biopsy	3b

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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



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Gute klinische Praxis (GKP)

Exzision (BEO oder Mastektomie) ist die therapeutische Basis für die Behandlung des DCIS.

Die adjuvante Therapie (Strahlentherapie, endokrine Therapie) muss mit der Patientin auf der Basis einer Risiko-Nutzen-Bewertung individuell erörtert werden.

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.

Operative Maßnahmen zur Therapie des histologisch gesicherten DCIS I			
	Oxford		
	LoE	GR	AGO
▪ Exzision (drahtmarkiert)	2b	B	++
▪ Markierung mit drahtfreien Verfahren	3b	C	+/-
▪ Flankierende Drahtmarkierung bei großen Läsionen	3a	C	+
▪ Präparatradiographie bei Drahtmarkierung	2b	B	++
▪ Intraoperative Sonographie (präop. darstellbarer Befund)	3a	C	+/-
▪ Sofortige Nachresektion bei unvollständiger Resektion (Präparateradiographie)	1c	B	++
▪ Intraoperative Schnellschnittdiagnostik (Einzelfall für Schnittränder)	3a	D	+/-
▪ Interdisziplinäre Tumorboard-Präsentation	2b	C	++
Offene Biopsien suspekter Läsionen (mammographische Mikrokalzifikationen, suspekter US, MRI etc.) ohne präoperative Stanzbiopsie sollten vermieden werden.			

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

Operative Maßnahmen zur Therapie des histologisch gesicherten DCIS II			
	Oxford		
	LoE	GR	AGO
▪ Histologisch freie Resektionsränder (pRi0)	1a	A	++
▪ Multifokalität: BEO falls möglich (inkl. RT)	2b	B	+
▪ Nachresektion bei knappem Resektionsrand im Rahmen der BET (< 2 mm im Paraffinschnitt)*	2b	C	+
▪ Mastektomie** (große Läsionen; keine sicheren Ränder im Nachresektat)	2a	B	++
▪ SLNE			
▪ Mastektomie	3b	B	+
▪ BET	3b	B	--
▪ DCIS beim Mann	5	D	+/-
▪ Axilladisektion	2b	B	--

* individuelles Vorgehen mit Berücksichtigung Alter, Tumorgröße, Grading und Durchführung einer Bestrahlung, besonders wenn nicht nachbestrahlt wird.

** Patientinnen mit einem tastbaren Tumor haben signifikant höhere Wahrscheinlichkeiten für eine okkulte Invasion (26 %), Multizentrität und ein Lokalrezidiv.

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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.
3. Morrow M., 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 J CO 2016 34;33 :4040-4046
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.
3. 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.
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* /Axilladisektion

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
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Prognostische Faktoren für das Auftreten eines ipsilateralen Rezidivs nach DCIS I		
		LoE
■ Resektionsränder		1a
■ Alter		1a
■ Größe		1a
■ Grading		1a
■ Komedonekrose		1a
■ Diagnostische Methode		1a
■ Fokalität		1a
■ HER2-Überexpression		1a
■ ER / PR (positiv vs. negativ)		1a

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.
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7. Giannakeas V, Sopik V, Narod SA. Association of a Diagnosis of Ductal Carcinoma In Situ With Death From Breast Cancer. JAMA Netw Open. 2020 Sep; 3(9): e2017124. Published online 2020 Sep 16. doi: 10.1001/jamanetworkopen.2020.17124
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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.
2. Schulz S, Sinn P, Golatta M, et al. Prediction of underestimated invasiveness in patients with ductal carcinoma in situ of the breast on percutaneous biopsy as rationale for recommending concurrent sentinel lymph node biopsy. Breast. 2013 Aug;22(4):537-42.
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Fokalität

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

(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 recurrence after breast conserving surgery for ductal carcinoma in situ. J Clin Oncol 2010; 28(23): 3762-9
3. Van Zee KJ, Patil S. Validation of a nomogram for predicting risk of local recurrence for ductal carcinoma in situ. J Clin Oncol 2012; 30(25): 3143-4.
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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.

6. Grimm LJ, Rahbar H, Abdelmalak M, et al: Ductal Carcinoma in Situ: State-of-the-Art Review. *Radiology*. 2021 Dec 21;211839. doi: 10.1148/radiol.211839. Online ahead of print.
7. Wärnberg F, Karlsson P, Holmberg E, et al: Prognostic Risk Assessment and Prediction of Radiotherapy Benefit for Women with Ductal Carcinoma In Situ (DCIS) of the Breast, in a Randomized Clinical Trial (SweDCIS). *Cancers* 2021, 13,6103

Palpables DCIS

Palpabel + COX-2+p16+Ki-67+

Palpabel + ER-, HER2, +Ki-67+

HER2-Überexpression

ER/PgR (positiv vs. negativ)

DCIS-Score

1. Solin LJ, Gray R, Baehner FL, et al. A multigene expression assay to predict local recurrence risk for ductal carcinoma in situ of the breast. *J Natl Cancer Inst*. 2013 May 15;105(10):701-10.
2. Sarah Patricia Cate, Alyssa Gillego, Manjeet Chadha, et al. Does the Oncotype DCIS score impact treatment decisions? *J Clin Oncol* 31, 2013 (suppl 26; abstr 91)
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4. Wood WC, Alvarado M, Buchholz DJ, et al. The current clinical value of the DCIS Score. *Oncology (Williston Park)*. 2014 May;28 Suppl 2:C2, 1-8, C3.
5. O'Keefe TJ, Blair SL, Hosseini A et al. HER2-Overexpressing Ductal Carcinoma In Situ Associated with Increased Risk of Ipsilateral Invasive Recurrence, Receptor Discordance with Recurrence. *Cancer Prev Res (Phila)*. 2020 Sep;13(9):761-772. doi: 10.1158/1940-6207.CAPR-20-0024.
6. Lazzeroni M, DeCensi A, Guerrieri-Gonzaga A et al. Prognostic and predictive value of cell cycle progression (CCP) score in ductal carcinoma in situ of the breast. *Mod Pathol*. 2020 Jun;33(6):1065-1077. doi: 10.1038/s41379-020-0452-0.
7. Hwang KT, Suh YJ, PARK CH, et al: Hormone Receptor Subtype in Ductal Carcinoma in Situ: Prognostic and Predictive Roles of the Progesterone Receptor. *The Oncologist* 2021;26:e1939–e1950

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.
2. Solin LJ.: Management of Ductal Carcinoma In Situ (DCIS) of the Breast: Present Approaches and Future Directions. Curr Oncol Rep. 2019 Mar 5;21(4):33. doi: 10.1007/s11912-019-0777-3.
3. Visser LL, Groen EJ, van Leeuwen FE, et al.: Predictors of an Invasive Breast Cancer Recurrence after DCIS: A Systematic Review and Meta-analyses. Cancer Epidemiol Biomarkers Prev. 2019 May;28(5):835-845. doi: 10.1158/1055-9965.EPI-18-0976. Epub 2019 Apr 25.
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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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Prognostische Faktoren für das Auftreten eines ipsilateralen Rezidivs nach DCIS II

	LoE
▪ Wachstumsmuster (kribriform / solide versus „clinging“ / mikropapillär)	2b
▪ Residuelle Tumor-assoziierte Mikrokalzifikationen	2b
▪ Architektur	2b
▪ (mod.) Van Nuys Prognose Index / Mitoserate	2b
▪ Palpables DCIS	2b
▪ ER-, HER2+, Ki-67+	2b
▪ Scores: Oncotype DX Breast DCIS Score (12 Gene), CCP (23 Gene)	2b
▪ MSKCC Nomogram	2b
▪ DCISionRT	2b
▪ Intrinsische Subgruppen (Luminal A,B, HER+, triple negativ)	2b
▪ Familiäre Mammakarzinombelastung	2a
▪ Prämenopause bei DCIS Erkrankung	2a
▪ Hoher BMI	2a
▪ Hohe Brustdichte	2a
▪ DCIS im Vergleich zum invasiven Karzinom mit höherem Risiko für kontralaterales MaCa	2b

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.
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FORSCHEN
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HEILEN

DCIS Strahlentherapie Statements

- **Strahlentherapie reduziert das ipsilaterale Lokalrezidivrisiko (invasiv und nicht-invasiv) um 50 %.** LoE 1a
- **Strahlentherapie hat keinen Einfluss auf das Gesamtüberleben.** LoE 1a
- **The number needed to treat (für jedes Auftreten eines In-Brust-Rezidivs) ist 9 (über alle Risikogruppen).**

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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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. doi: 10.1136/bmj.m1570.
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.
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10.1200/JCO.21.01083.

DCIS adjuvante Strahlentherapie			
	Oxford		
	LoE	GR	AGO
Radiotherapie nach:			
▪ Brusterhaltender Operation (BEO) ; (gesamte Brust, WBI)	1a	A	++
▪ Mastektomie	2b	B	--
Durchführung der Radiotherapie:			
▪ Konventionell fraktionierte Radiotherapie (50 Gy in 25 Frakt.)	1a	A	+
▪ Hypofraktionierte Radiotherapie (40-42,5 Gy in 15-16 Frakt.)	1a	A	+
▪ Boost-RT des Tumorbettes	1b	B	+/-
▪ Bei Risikofaktoren* (absoluter Vorteil 5-J-RFS 4 %, Fibroserate signifikant erhöht)	1b ^a	B	+/-
▪ Ohne Risikofaktoren	2b	B	-
▪ Teilbrustbestrahlung [Alter ≥ 50 Jahre, DCIS ≤ 3 cm, G1-2, R0 (≥ 5 mm), unifokal / unizentrisch]	1b	B	+
<p>NW und Nachteile der Radiotherapie müssen gegenüber der erreichbaren Risikoreduktion abgewogen werden. Ein Verzicht auf eine Strahlentherapie nach BEO bedeutet ein erhöhtes lokales Rezidivrisiko ohne Einfluss auf das Überleben. Dieses gilt auch für Patientinnen mit günstigen prognostischen Faktoren (low-risk-Subgruppe; Level I-Evidenz): < 2,5 cm, low and intermediate nuclear grade, mammographisch entdeckt.</p> <p>* < 50 J. oder ≥ 50 J. und Diagnose durch Symptomatik, ≥ 15 mm, Multifokalität, tastbarer Tumor, Resektionsränder < 10 mm, G2/3, zentrale Nekrose, Komedo-Typ</p>			

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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4. Beryl McCormick, Kathryn Winter, Clifford Hudis, et al. RTOG 9804: A Prospective Randomized Trial for Good-Risk Ductal Carcinoma In Situ Comparing Radiotherapy With Observation. J Clin Oncol 2015; 33(7): 709
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	<h2 style="text-align: center;">DCIS – adjuvante Systemtherapie</h2>	
<p>© AGO e. V. in der DGGG e. V. sowie in der DKG e. V.</p>	<ul style="list-style-type: none"> ■ Adjuvante endokrine Therapie hat keinen Einfluss auf das Gesamtüberleben. 	<p>LoE 1a</p>
<p>Guidelines Breast Version 2022.1D</p>	<ul style="list-style-type: none"> ■ Endokrine Therapie kann einen geringen Effekt auf die ipsilateralen invasiven und DCIS-Rezidive haben. 	<p>LoE 1a</p>
<p>www.ago-online.de FORSCHEN LEHREN HEILEN</p>	<ul style="list-style-type: none"> ■ Endokrine Therapie hat einen Effekt auf die kontralateralen invasiven und in-situ Karzinome. 	<p>LoE 1a</p>
	<ul style="list-style-type: none"> ■ The number needed to treat (für jedes In-Brust-Rezidiv) ist 15. 	<p>LoE 1a</p>
	<ul style="list-style-type: none"> ■ The number needed to treat zur Prävention eines invasiven Mammakarzinoms ist 29 für Anastrozol vs. 59 für Tamoxifen.* 	<p>LoE 1b</p>
	<p>* innerhalb von 12 Jahren; entsprechend der IBIS II-Studie</p>	

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	<h2 style="text-align: center;">DCIS – adjuvante Systemtherapie</h2>		
© AGO e. V. in der DGGG e.V. sowie in der DKG e.V. Guidelines Breast Version 2022.1D www.ago-online.de FORSCHEN LEHREN HEILEN			
	Oxford		
	LoE	GR	AGO
	1a	A	+/-*
	2b ^a	B	+/-*
■ Aromataseinhibitor (nur ER+) bei postmeno- pausalen Patientinnen	1b	A	+/-**
	5	D	--
■ Trastuzumab (nur HER2+)			
* Indikation zur Therapie ist von Risikofaktoren, Nebenwirkungen und Patientinnenpräferenz abhängig # Anastrozol versus Tamoxifen: Anastrozol mehr Frakturen (OR 1,34), Tamoxifen mehr Schlaganfälle (OR 3,10) und TIA (OR 3,10)			

Tamoxifen (nur ER+, nur BET)

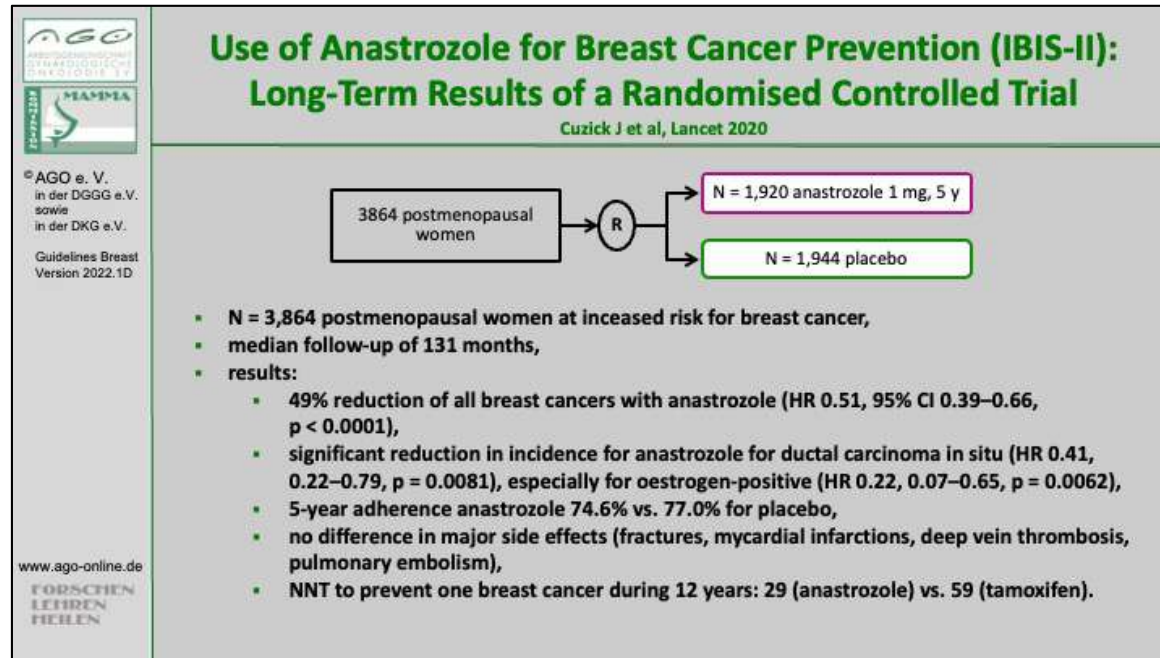
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AI (wenn postmenopausal)

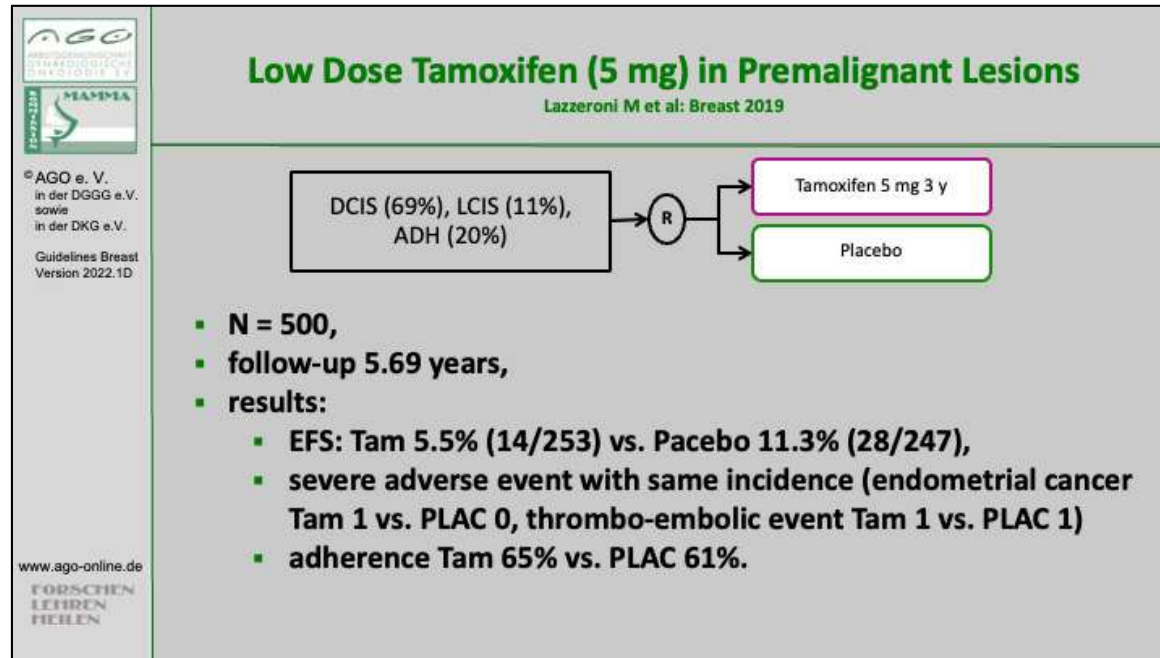
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Behandlung des Lokalrezidivs des DCIS nach Tumorektomie			
	Oxford		
	LoE	GR	AGO
Nach vorangegangener Bestrahlung:			
▪ Einfache Mastektomie	3a	C	+
+ SLNE	5	D	+
▪ Sekundäre brusterhaltende Operation	4	C	+/-
Ohne vorangegangene Bestrahlung:			
▪ Therapieindikation wie bei primärer Erkrankung	3	C	++

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Nach Radiatio

Einfache Mastektomie

+ SN B

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