Guidelines Breast
Version 2024.1D

FORSCHEN
LEHREN
HEILEN

Läsionen mit unsicherem biologischen Potenzial (B3)

(ADH, LIN, FEA, Papillom, Radiäre Narbe/komplexe sklerosierende Läsion)

Läsionen mit unklarem biologischen Potenzial (B3)

Versionen 2005–2023:
Albert / Audretsch / Bauerfeind / Brunnert / Ditsch / Fallenberg / Fersis / Friedrich / Friedrichs / Gerber / Huober / Kolberg-Liedtke / Kreipe / Maass / Nitz / Reimer / Rody / Schmidt / Schreer / Sinn / Thomssen

Version 2024:
Friedrich / Sinn

Pubmed 2010-2023 queries

Lobular neoplasia (169 Results)

(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh]) AND ("2012/01/01"[dp] : "2023/01/01"[dp]) AND ("lobular neoplasia"[ti] OR "lobular intraepithelial neoplasia"[ti] OR "atypical lobular hyperplasia"[ti] OR "lobular carcinoma in situ"[ti] OR "LIN"[ti] OR "ALH"[ti] OR "LCIS"[ti]) AND ("english"[la] OR "german"[la])

Atypical ductal hyperplasia (101 Results)

(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh]) AND ("2012/01/01"[dp] : "2023/01/01"[dp]) AND ("atypical ductal hyperplasia"[ti] OR "atypical hyperplasia"[ti] OR "ADH"[ti]) AND ("english"[la] OR "german"[la])

Flat epithelial atypia (59 Results)

(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh])

AND ("2012/01/01"[dp] : "2023/01/01"[dp]) AND ("flat epithelial atypia"[ti] OR "columnar cell"[ti] OR "FEA"[ti]) AND ("english"[la] OR "german"[la])

Papilloma (278 Results)
(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh]) AND ("2012/01/01"[dp] : "2023/01/01"[dp]) AND ("papilloma"[ti] OR "papillary"[ti]) AND ("english"[la] OR "german"[la]) NOT virus[ti]

Radial scar (25 Results)
(Breast Diseases/CL[mh] OR Breast Diseases/DI[mh] OR Breast Diseases/EP[mh] OR Breast Diseases/GE[mh] OR Breast Diseases/MO[mh] OR Breast Diseases/PA[mh] OR Breast Diseases/RT[mh] OR Breast Diseases/SU[mh] OR Breast Diseases/TH[mh]) AND ("2012/01/01"[dp] : "2023/01/01"[dp]) AND ("radial scar"[ti] OR "complex sclerosing lesion"[ti] OR "radial sclerosing lesion"[ti]) AND ("english"[la] OR "german"[la])

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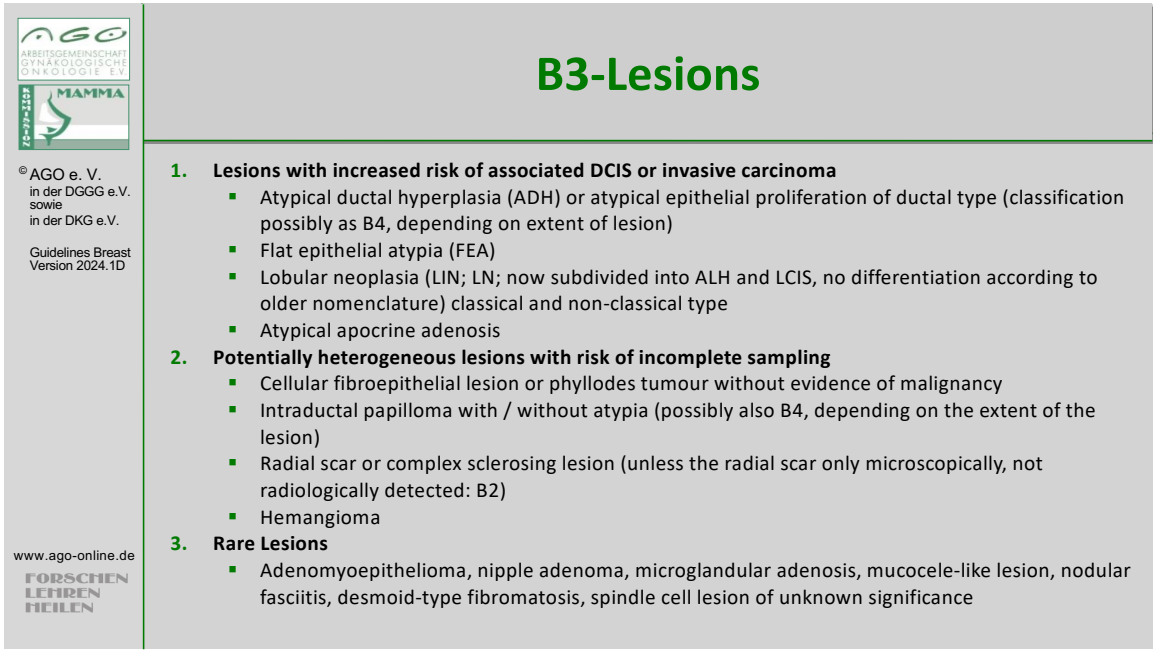

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Management nach minimalinvasiver Biopsie

	Oxford LoE	Oxford GR	Oxford AGO
Interdisziplinäre Konferenz: Pathologie und Bildgebung konkordant?			
ja: Vorgehen gemäß histologischem Typ und Ausdehnung des Befundes	3a	C	++
nein: offene PE	3a	C	++
Vakuumbiopsie (nach Stanzbiopsie)	5	D	+

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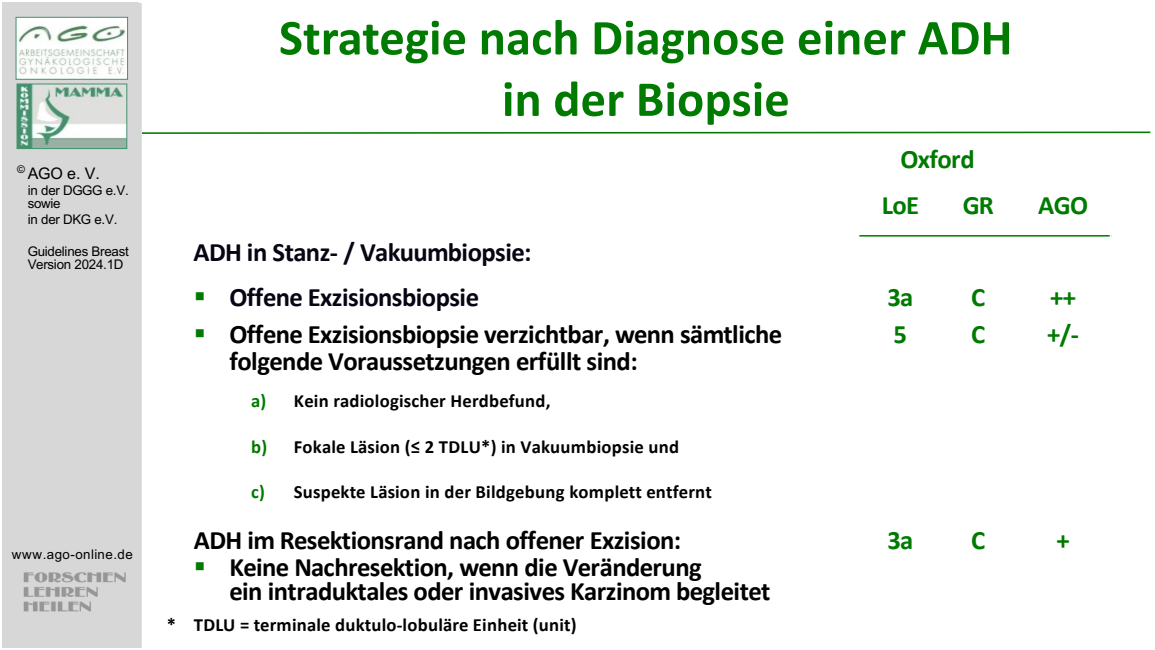

Strategie nach Diagnose einer ADH in der Biopsie

	Oxford LoE	Oxford GR	AGO
ADH in Stanz- / Vakuumbiopsie:			
▪ **Offene Exzisionsbiopsie**	**3a**	**C**	**++**
▪ **Offene Exzisionsbiopsie verzichtbar, wenn sämtliche folgende Voraussetzungen erfüllt sind:**	**5**	**C**	**+/-**
a) **Kein radiologischer Herdbefund,**			
b) **Fokale Läsion (≤ 2 TDLU*) in Vakuumbiopsie und**			
c) **Suspekte Läsion in der Bildgebung komplett entfernt**			
ADH im Resektionsrand nach offener Exzision:	**3a**	**C**	**+**
▪ **Keine Nachresektion, wenn die Veränderung ein intraduktales oder invasives Karzinom begleitet**			

* **TDLU = terminale duktulo-lobuläre Einheit (unit)**

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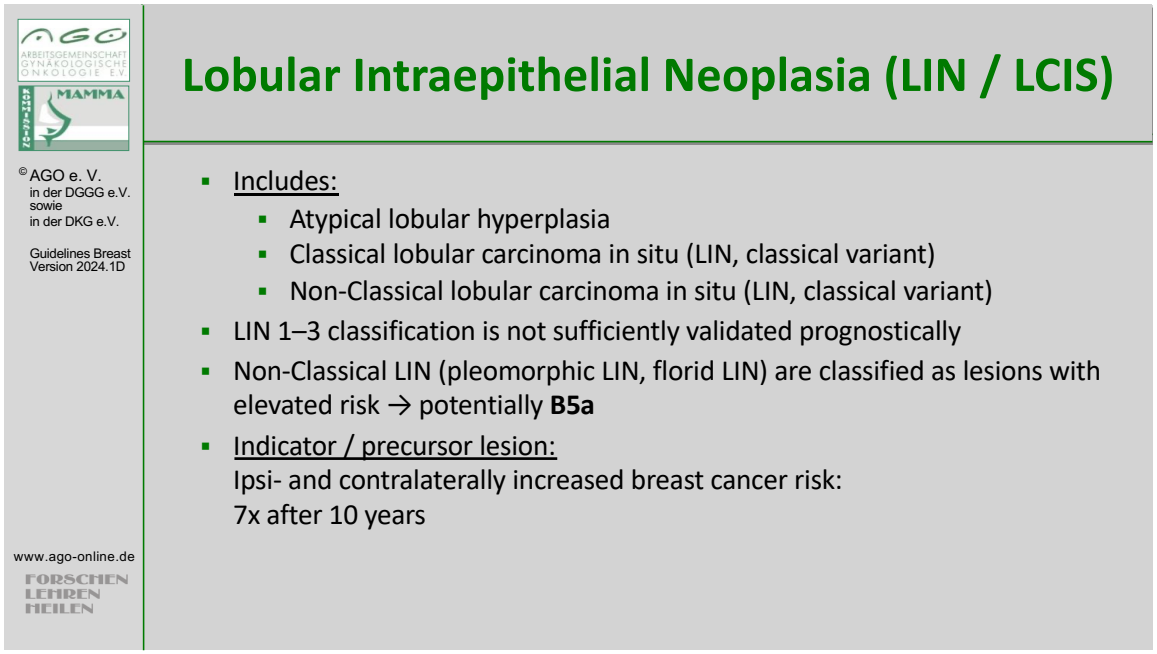

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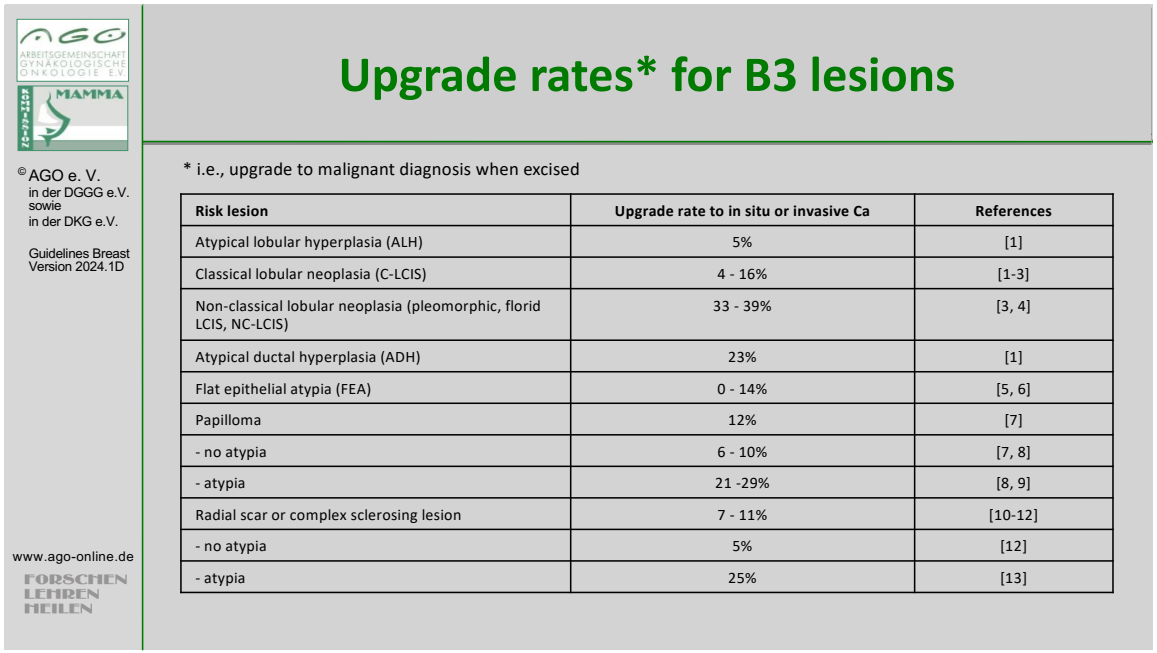

Upgrade rates* for B3 lesions

* i.e., upgrade to malignant diagnosis when excised

Risk lesion	Upgrade rate to in situ or invasive Ca	References
Atypical lobular hyperplasia (ALH)	5%	[1]
Classical lobular neoplasia (C-LCIS)	4 - 16%	[1-3]
Non-classical lobular neoplasia (pleomorphic, florid LCIS, NC-LCIS)	33 - 39%	[3, 4]
Atypical ductal hyperplasia (ADH)	23%	[1]
Flat epithelial atypia (FEA)	0 - 14%	[5, 6]
Papilloma	12%	[7]
- no atypia	6 - 10%	[7, 8]
- atypia	21 -29%	[8, 9]
Radial scar or complex sclerosing lesion	7 - 11%	[10-12]
- no atypia	5%	[12]
- atypia	25%	[13]

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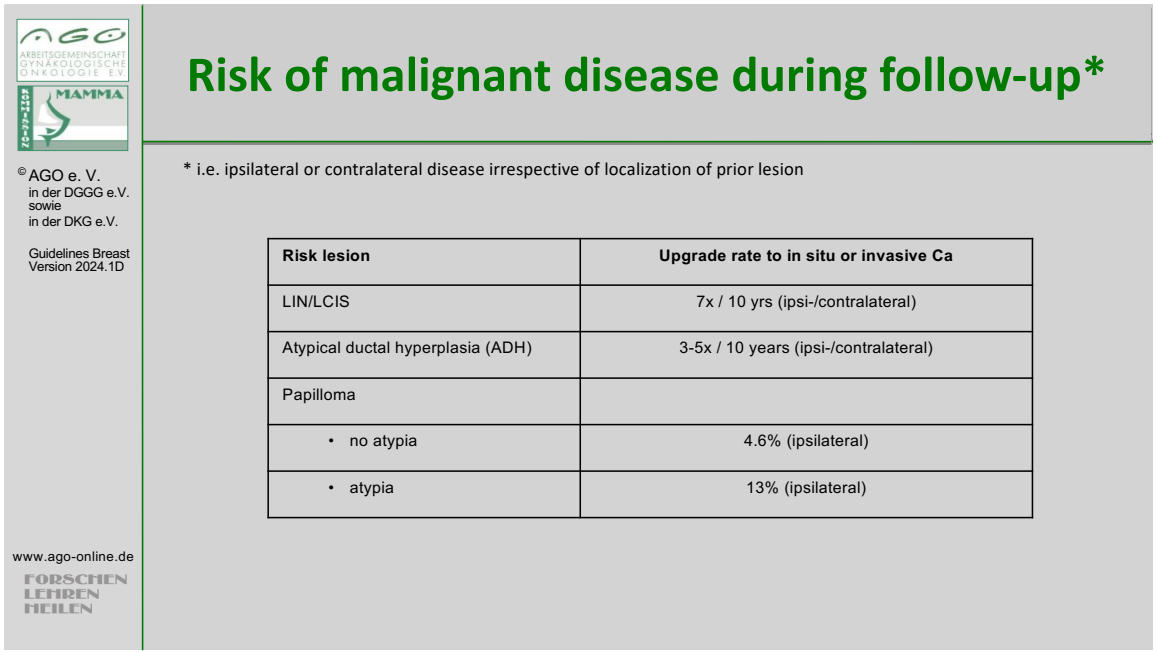

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Papillome

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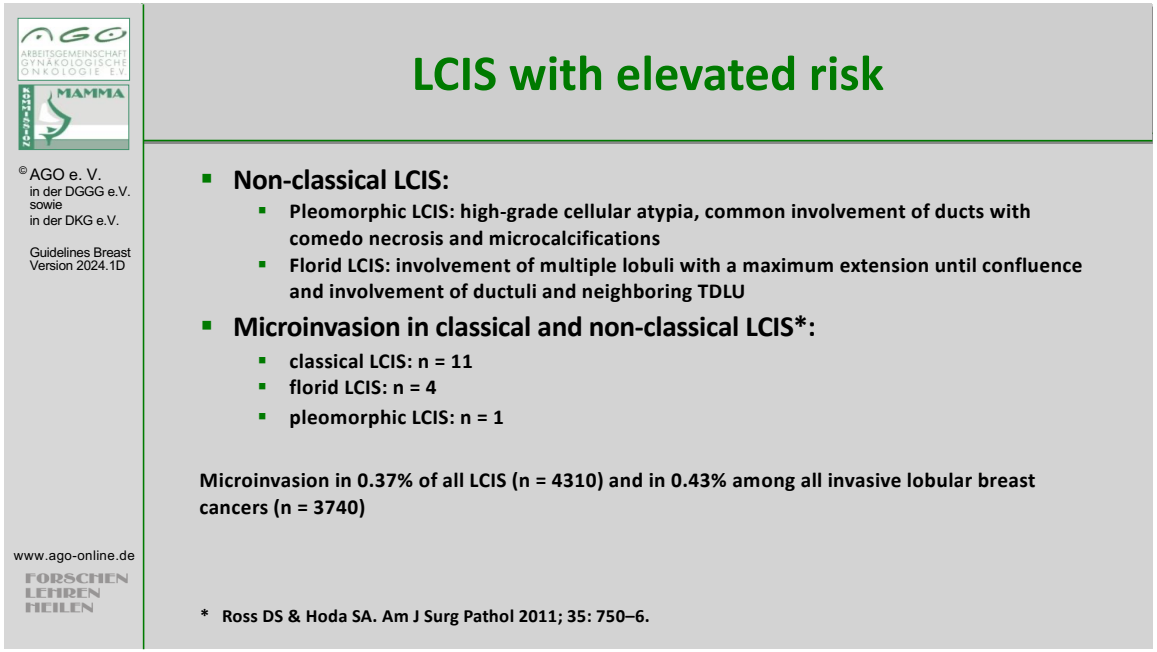

Statement: Pleomorphic lobular carcinoma in situ (PLCIS)

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Statement: Florid lobular carcinoma in situ (FLCIS)

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Statement: Lobular carcinoma in situ with microinvasion

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Strategie nach Diagnose einer LIN / eines LCIS

	Oxford LoE	Oxford GR	Oxford AGO
LIN / LCIS in Stanz- / Vakuumbiopsie			
Keine weitere Abklärung bei isoliertem oder inzidentellem Befund einer LIN (klassisches LCIS) mit Befall von ≤ 3 TDLU (terminale duktulolobuläre Einheit) in Vakuumbiopsie und Konkordanz mit der Bildgebung.	2b	C	++
Offene Exzisionsbiopsie bei pleomorpher LIN, florider LIN (LIN3), LIN mit Komedotypnekrosen, oder wenn Befund nach Korrelation mit der Bildgebung diskordant ist.	2b	C	++
LIN / LCIS am Resektionsrand von BET			
Keine Nachresektion.	2a	C	++

Ausnahmen

a) Pleomorphe, floride oder LIN / LCIS mit Nekrosen

b) Bildgebende Veränderung wurde nicht entfernt

LIN in core- / vacuum-assisted biopsy (LoE 2b)

1. Kunjummen, J., Rodriguez, K., Newell, M. S., Hanley, K. & Cohen, M. A. Management of Lobular Neoplasia Found on Core Needle Biopsy Performed for Calcifications Using Precise Radiologic-Pathologic Correlation. *Am J Roentgenol* **216**, 1476–1485 (2021).
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<u>LIN accompanying intraductal or invasive carcinoma in patients with BCT (LoE 2a</u>)
1. Ciocca R: Presence of lobular carcinoma in situ does not increase recurrence in patients treated with breast-conserving therapy. Ann Surg Oncol 2008; 15:2263-2271

Strategie nach Diagnose einer FEA

	Oxford LoE	Oxford GR	Oxford AGO
FEA in Stanz- / Vakuumbiopsie:			
Offene Exzisionsbiopsie	2b	B	+
Auf offene Biopsie kann verzichtet werden unter folgenden Voraussetzungen:	2b	B	+
a. Kleinherdiger Befund (≤ 2 TDLU* in Vakuumbiopsie) und			
b. Entfernung oder weitgehend vollständige Entfernung der auffälligen Läsion in der Bildgebung (≥ 90 %)			
FEA im Resektionsrand nach Exzisionsbiopsie:			
Keine Nachresektion, außer bei verbliebenem mammographischem Korrelat	3b	C	++

* TDLU = terminale duktulolobuläre Einheit

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11. Liu, C. *et al.* Pure flat epithelial atypia identified on core needle biopsy does not require excision. *Eur J Surg Oncol* **46**, 235–239 (2020).
12. Srour, M. K. *et al.* Flat epithelial atypia on core needle biopsy does not always mandate excisional biopsy. *Breast J* **26**, 679–684 (2020).
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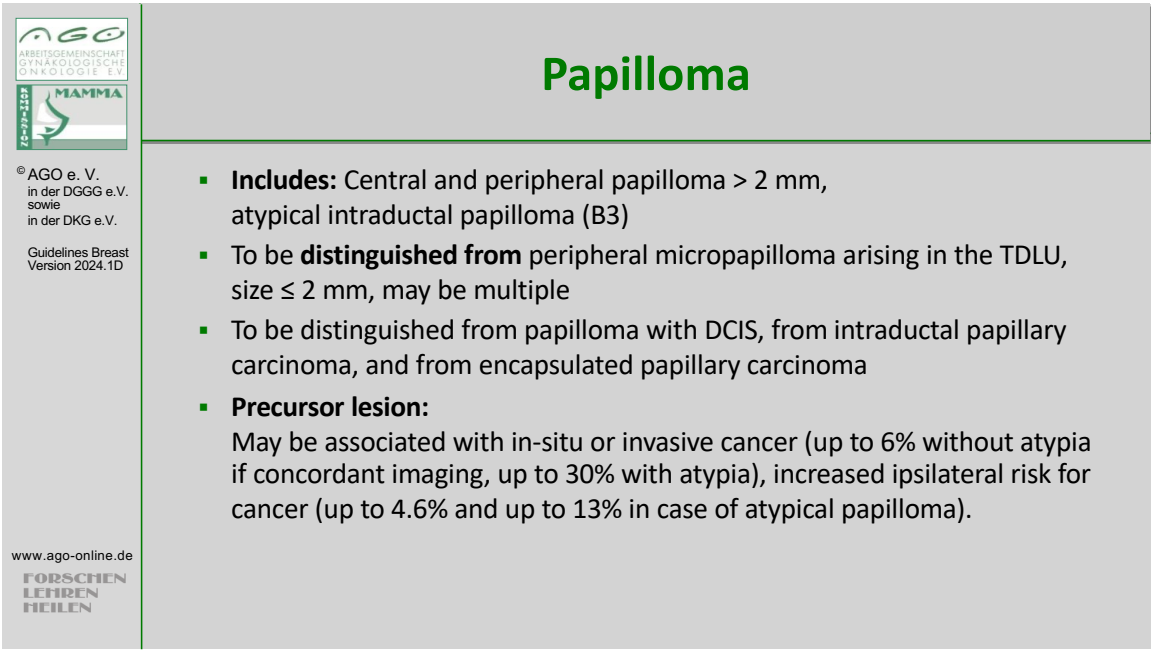

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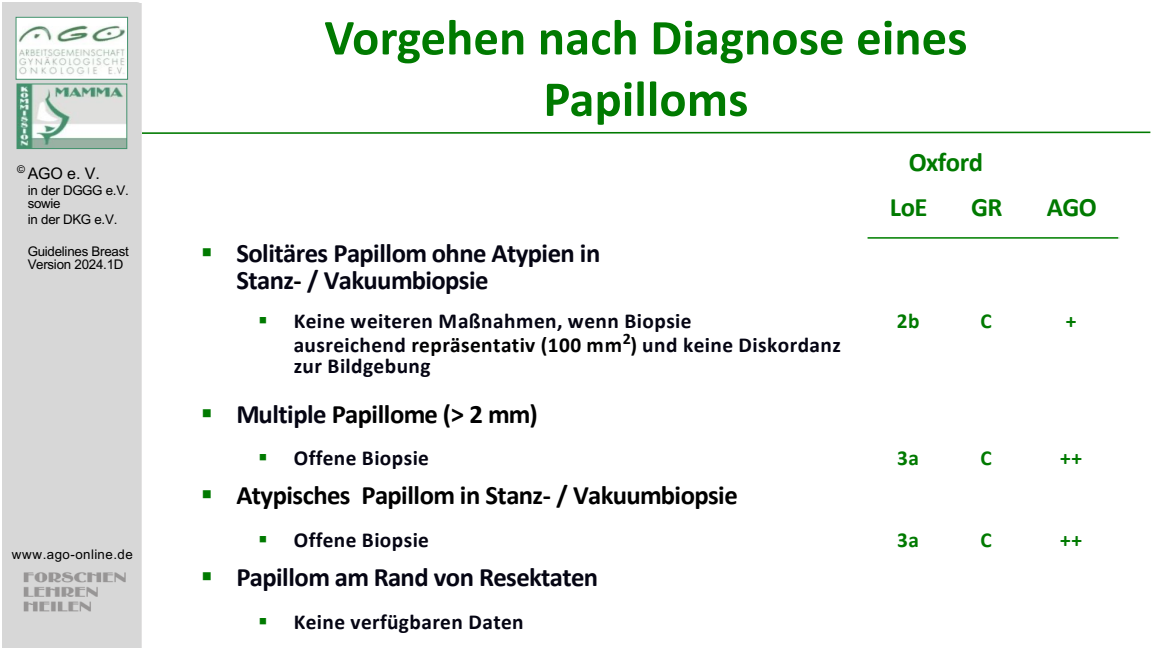

Vorgehen nach Diagnose eines Papilloms

	Oxford LoE	Oxford GR	Oxford AGO
Solitäres Papillom ohne Atypien in Stanz- / Vakuumbiopsie			
Keine weiteren Maßnahmen, wenn Biopsie ausreichend repräsentativ (100 mm^2) und keine Diskordanz zur Bildgebung	2b	C	+
Multiple Papillome (> 2 mm)			
Offene Biopsie	3a	C	++
Atypisches Papillom in Stanz- / Vakuumbiopsie			
Offene Biopsie	3a	C	++
Papillom am Rand von Resektaten			
Keine verfügbaren Daten			

1. Jee, Y. *et al.* Intraductal Papilloma on Breast Biopsy: Upstaging Rate and Implications for Practice Guidelines. *Am Surg***88**, 1467–1470 (2022).
2. Corbin, H. *et al.* Upgrade rates of intraductal papilloma with and without atypia diagnosed on core needle biopsy and clinicopathologic predictors. *Hum Pathol* **128**, 90–100 (2022).
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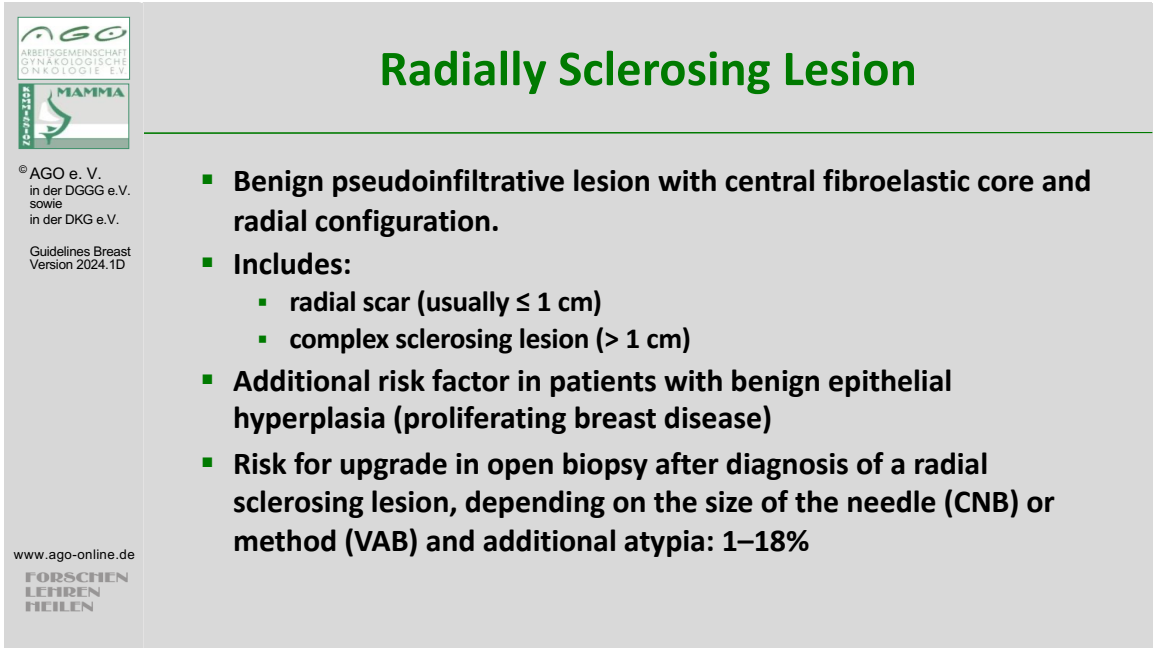

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16. Trombadori, C. M. L. *et al.* Radial Scar: a management dilemma. *La Radiologia Medica* **126**, 774–785 (2021).
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Vorgehen bei radiärer Narbe, komplexer sklerosierender Läsion (CSL)

	Oxford		
	LoE	GR	AGO
▪ **Radiäre Narbe / CSL in Stanz- oder Vakuumbiopsie:**			
▪ **Offene Biopsie**	3a	C	+
▪ **ohne Atypien**	3a	C	+
▪ **mit Atypien**	3a	C	++
▪ **Verzicht auf offene Biopsie, wenn Läsion klein (≤ 5 mm) oder in der Vakuumbiopsie bereits (weitgehend) vollständig enthalten**	5	C	+
▪ **Radiäre Narbe / CSL im Resektionsrand nach offener Exzision:**			
▪ **Keine Nachresektion**	3b	C	++

1. Donaldson, A. R., Sieck, L., Booth, C. N. & Calhoun, B. C. Radial scars diagnosed on breast core biopsy: Frequency of atypia and carcinoma on excision and implications for management. *Breast (Edinburgh, Scotland)* **30**, 201–207 (2016).
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Brustkrebs-Früherkennung: Follow-up nach B3-Läsionen für Frauen im Alter zwischen 50 und 69 Jahren

	Oxford		
	LoE	GR	AGO
▪ **FEA, Papillom ohne Atypien, Radiäre sklerosierende Läsion**			
▪ **Screening-Mammographie**	5	C	++
▪ **LIN / LCIS**			
▪ **Kurative Mammographie (12 Monate)**	3a	C	++
▪ **ADH**			
▪ **Kurative Mammographie (12 Monate)**	3a	C	++
▪ **Frauen mit LIN und ADH sind über ihr persönlich erhöhtes Brustkrebsrisiko zu informieren**	3a	C	++

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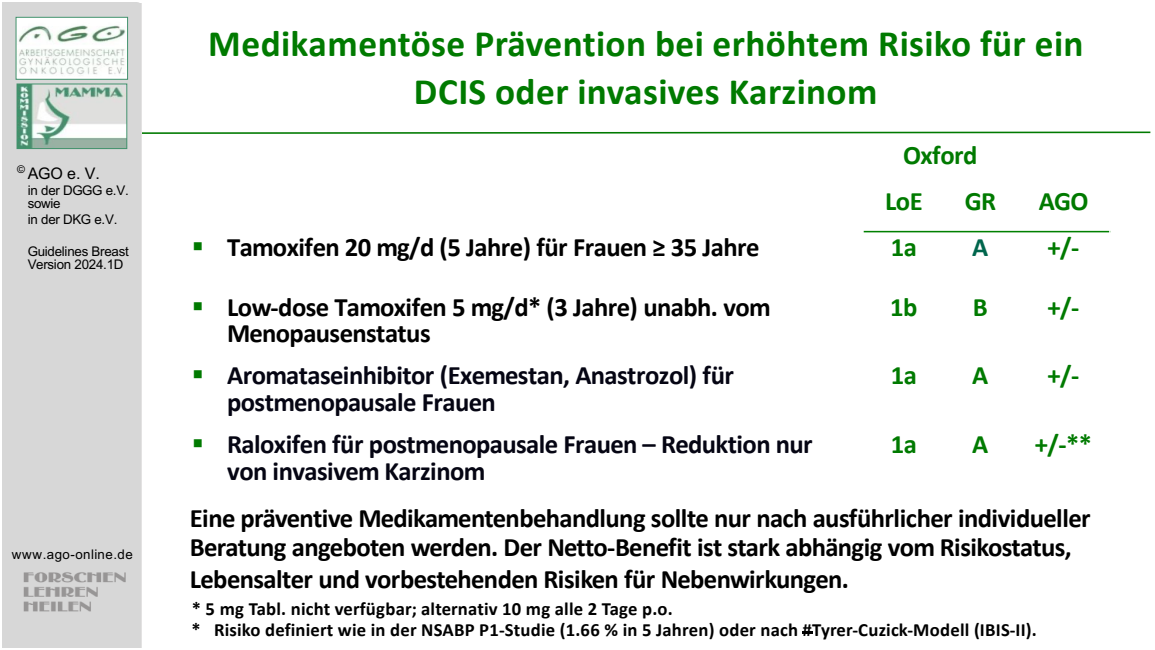

Medikamentöse Prävention bei erhöhtem Risiko für ein DCIS oder invasives Karzinom

	Oxford LoE	Oxford GR	AGO
▪ Tamoxifen 20 mg/d (5 Jahre) für Frauen ≥ 35 Jahre	1a	A	+/-
▪ Low-dose Tamoxifen 5 mg/d* (3 Jahre) unabh. vom Menopausenstatus	1b	B	+/-
▪ Aromataseinhibitor (Exemestan, Anastrozol) für postmenopausale Frauen	1a	A	+/-
▪ Raloxifen für postmenopausale Frauen – Reduktion nur von invasivem Karzinom	1a	A	+/-**

Eine präventive Medikamentenbehandlung sollte nur nach ausführlicher individueller Beratung angeboten werden. Der Netto-Benefit ist stark abhängig vom Risikostatus, Lebensalter und vorbestehenden Risiken für Nebenwirkungen.

*** 5 mg Tabl. nicht verfügbar; alternativ 10 mg alle 2 Tage p.o.**
*** Risiko definiert wie in der NSABP P1-Studie (1.66 % in 5 Jahren) oder nach #Tyrer-Cuzick-Modell (IBIS-II).**

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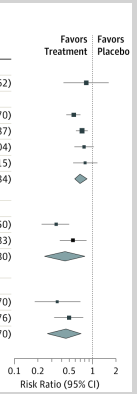
Medical endocrine Prevention

Risk Reduction of Invasive Breast Cancer: Meta-analysis of Primary Prevention Trials

Source	Trial	Mean, y: Intended Treatment Duration	Mean, y: Total Follow-up	No. With Invasive Breast Cancer/Total Participants (%): Treatment	No. With Invasive Breast Cancer/Total Participants (%): Placebo	Rate per 1000 Women-Years: Treatment	Rate per 1000 Women-Years: Placebo	Risk Ratio (95% CI)
Tamoxifen, low dose								
DeCensi et al,[41] 2013	HOT	5	6.2	18/938 (1.9)	22/946 (2.3)	3.13	3.78	0.83 (0.42-1.62)
Tamoxifen								
Fisher et al,[82] 2005	NSABP-1	5	6.1	145/6681 (2.2)	250/6707 (3.7)	3.59	6.29	0.57 (0.46-0.70)
Cuzick et al,[74] 2015	IBIS-I	5	16.0	214/3579 (6.0)	289/3575 (8.1)	3.86	5.29	0.73 (0.61-0.87)
Powles et al,[83] 2007	Marsden	5	13.2	82/1238 (6.6)	104/1233 (8.4)	4.80	6.10	0.78 (0.58-1.04)
Veronesi et al,[84] 2007	Italian	4[a]	11.2	53/2700 (2.0)	66/2708 (2.4)	1.77	2.21	0.80 (0.56-1.15)
Combined								0.69 (0.59-0.84)
I^2 = 38.7%; Q = 4.9 for heterogeneity; P = .18								
Raloxifene								
Martino et al,[45] 2004	MORE/CORE	4 or 8[b]	5.4[b]	40/5129 (0.8)	58/2576 (2.3)	1.40	4.20	0.34 (0.22-0.50)
Barrett-Connor et al,[48] 2006	RUTH	5.1[a]	5.6	40/5044 (0.8)	70/5057 (1.4)	1.43	2.49	0.56 (0.38-0.83)
Combined								0.44 (0.24-0.80)
I^2 = 66.4%; Q = 3.0 for heterogeneity; P = .08								
Aromatase inhibitor								
Goss et al,[44] 2011	MAP.3	5[c]	2.9	11/2285 (0.5)	32/2275 (1.4)	1.66	4.85	0.35 (0.18-0.70)
Cuzick et al,[4] 2014	IBIS-II	5	5	32/1920 (1.7)	64/1944 (3.3)	3.29	6.62	0.50 (0.32-0.76)
Combined								0.45 (0.26-0.70)
I^2 = 0.0%; Q = 0.8 for heterogeneity; P = .39								



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