Guidelines Breast
Version 2023.1E

FORSCHEN
LEHREN
HEILEN

Lesions of Uncertain Malignant Potential (B3)

(ADH, LIN, FEA, Papilloma, Radial Scar/Complex Sclerosing Lesion)

Lesions of Uncertain Malignant Potential (B3)

- **Versionen 2005–2022:**
  Albert / Audretsch / Bauerfeind / Brunnert / Ditsch / Fallenberg / Fersis / Friedrich / Friedrichs / Gerber / Huober / Kreipe / Maass / Nitz / Rody / Schmidt / Schreer / Sinn / Thomssen

- **Version 2023:**
  Kolberg-Liedtke / Reimer / Sinn

<u>Pubmed 2010-2022 queries</u>

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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Pathology Reporting for Minimal Invasive Biopsies

Guidelines Breast
Version 2023.1E

B-Classification*

B1 = Unsatisfactory or normal tissue only
B2 = Benign lesion
B3 = Lesion of uncertain malignant potential
B4 = Suspicion of malignancy
B5 = Malignant
- **B5a = Non-invasive**
- **B5b = Invasive**
- **B5c = In situ / invasion not assessable**
- **B5d = Non epithelial, metastatic**

* **AWMF, Deutschen Krebsgesellschaft e.V. und Deutschen Krebshilfe e.V. (Hrsg.). Interdisziplinäre S3-Leitlinie für die Diagnostik, Therapie und Nachsorge des Mammakarzinoms. Langversion 4.4, Juni 2021**

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B3-Lesions

1. **Lesions with increased risk of associated DCIS or invasive carcinoma**
   - Atypical ductal hyperplasia (ADH) or atypical epithelial proliferation of ductal type (classification possibly as B4, depending on extent of lesion)
   - Flat epithelial atypia (FEA)
   - Lobular neoplasia (LIN; LN; now subdivided into ALH and LCIS, no differentiation according to older nomenclature) classical and non-classical type
   - Atypical apocrine adenosis
2. **Potentially heterogeneous lesions with risk of incomplete sampling**
   - Cellular fibroepithelial lesion or phyllodes tumour without evidence of malignancy
   - Intraductal papilloma with / without atypia (possibly also B4, depending on the extent of the lesion)
   - Radial scar or complex sclerosing lesion (unless the radial scar only microscopically, not radiologically detected: B2)
   - Hemangioma
3. **Rare Lesions**
   - Adenomyoepithelioma, nipple adenoma, microglandular adenosis, mucocele-like lesion, nodular fasciitis, desmoid-type fibromatosis, spindle cell lesion of unknown significance

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Management after Minimally Invasive Biopsy

	Oxford		
	LoE	GR	AGO
▪ **Interdisciplinary conference: Concordant findings in pathology and imaging?**			
▪ **yes: proceed according to histologic type and dimension of lesion**	3a	C	++
▪ **no: open biopsy**	3a	C	++
Vacuum-assisted biopsy (after core biopsy)	5	D	+

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Strategy after Diagnosis of ADH in Biopsy Sypecimen

	Oxford		
	LoE	GR	AGO
ADH in core- / vacuum-assisted biopsy:			
▪ **Open excisional biopsy**	3a	C	++
▪ **Open excisional biopsy may be omitted, if all following requirements apply:**	5	C	+/-
a) No mass-lesion radiologically, and			
b) a small lesion (≤ 2 TDLU*) in vacuum biopsy, and			
c) complete removal of imaging abnormality			
ADH at margins in open biopsy specimen:			
▪ **No further surgery, if incidental finding accompanies invasive or intraductal carcinoma**	3a	C	+

* Terminal ductal-lobular unit

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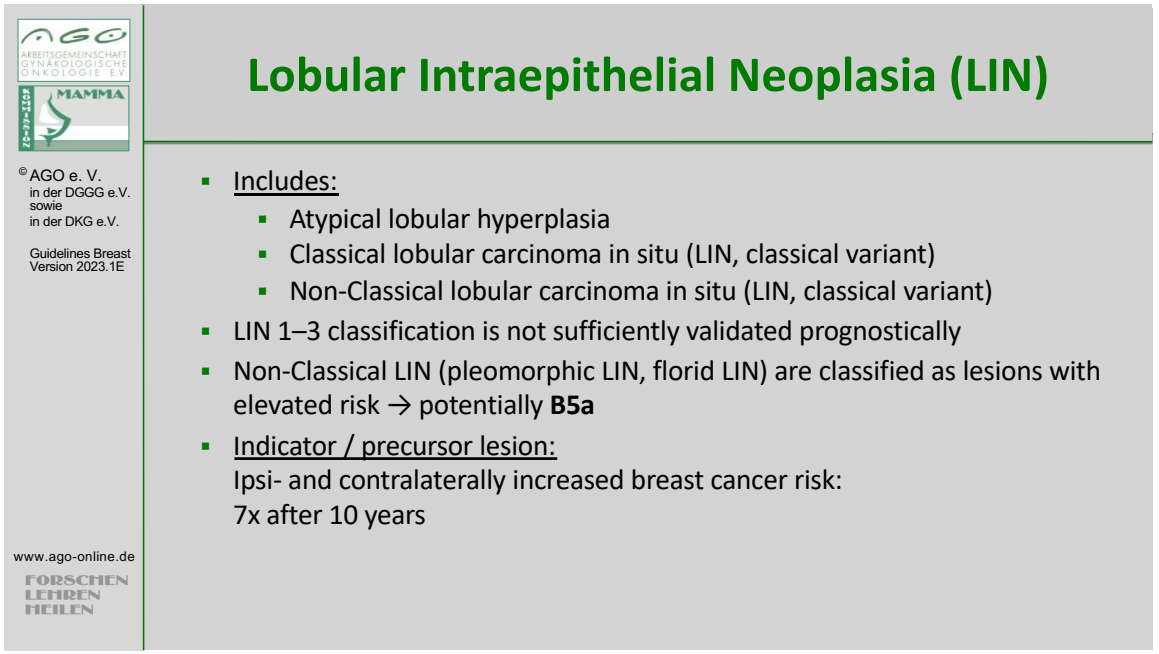

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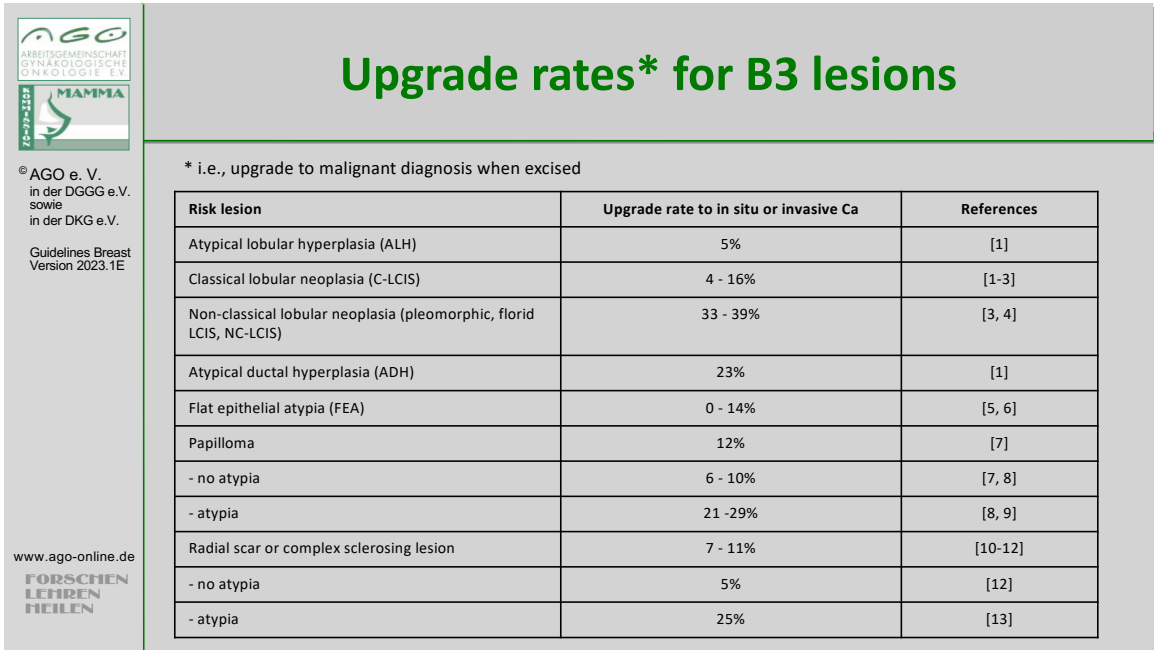

Upgrade rates* for B3 lesions

* 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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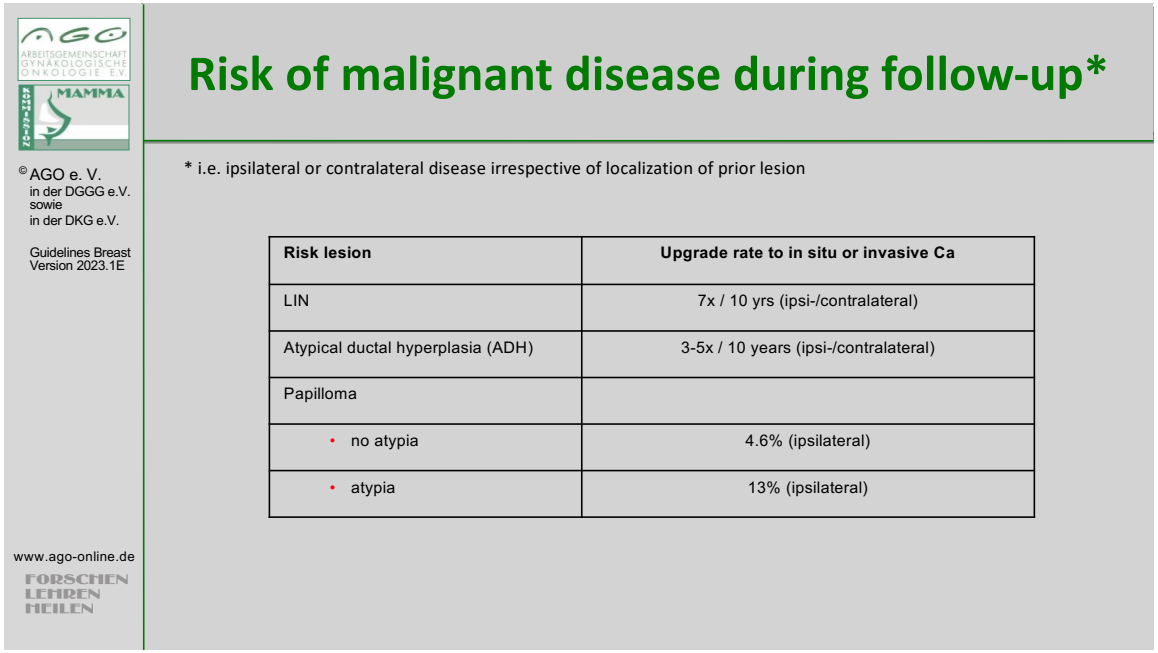

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Papillome

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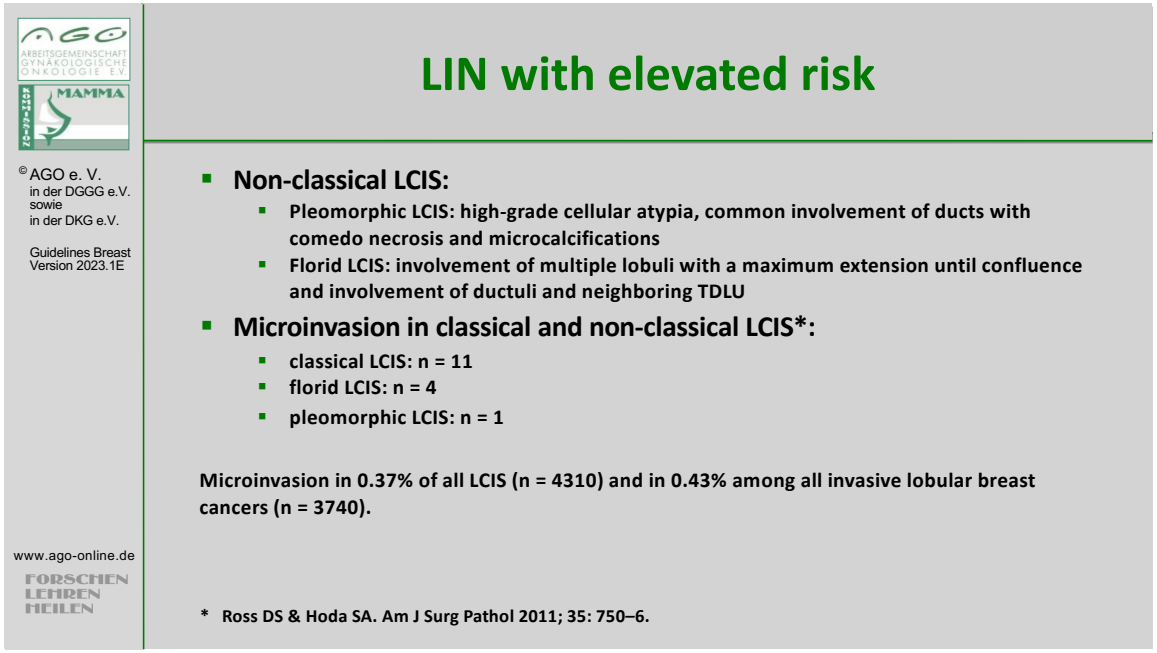

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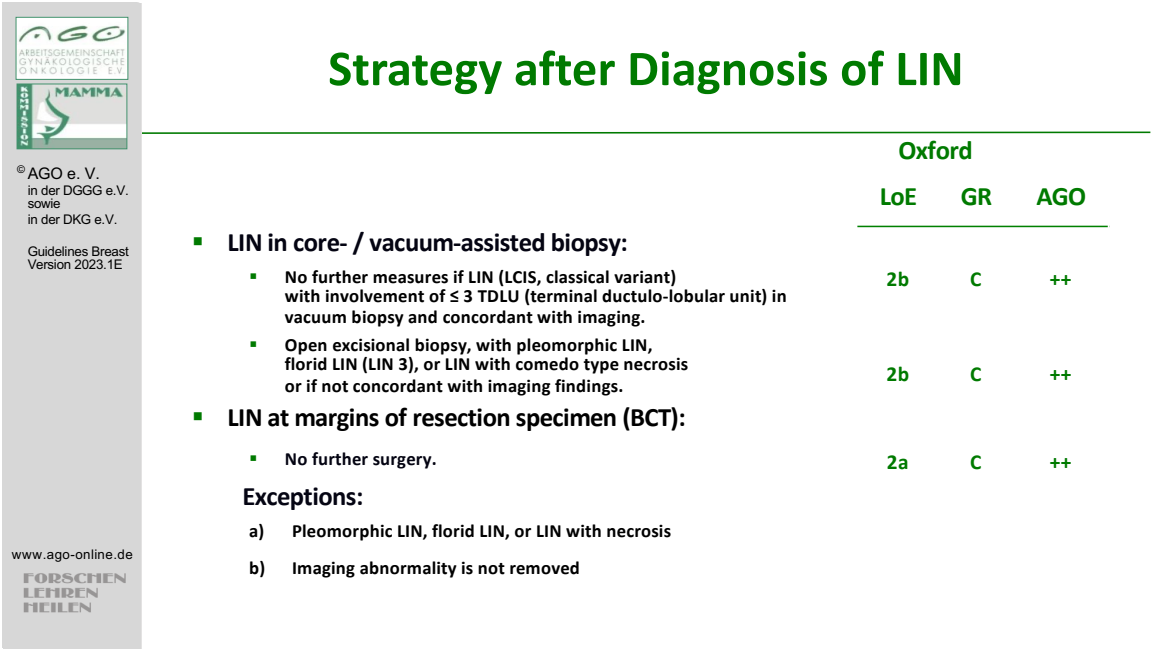

LIN in core- / vacuum-assisted biopsy (LoE 2b)

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<u>LIN accompanying intraductal or invasive carcinoma in patients with BCT (LoE 2a</u>)

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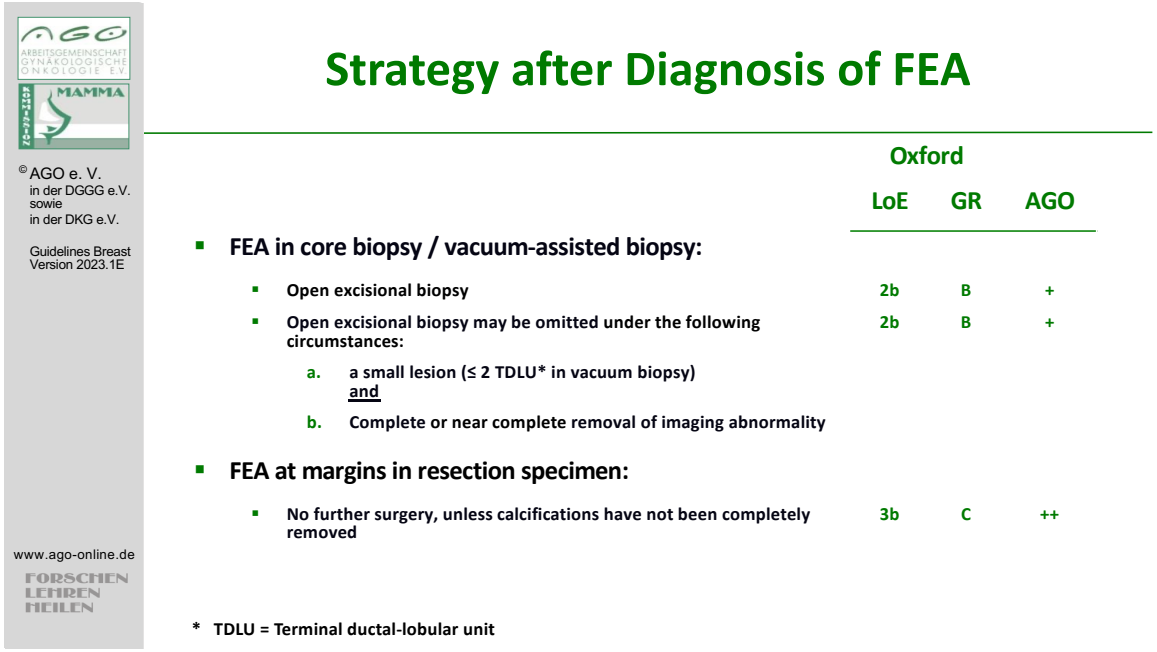

Strategy after Diagnosis of FEA

	Oxford LoE	Oxford GR	Oxford AGO
FEA in core biopsy / vacuum-assisted biopsy:			
Open excisional biopsy	2b	B	+
Open excisional biopsy may be omitted under the following circumstances:	2b	B	+
a. a small lesion (≤ 2 TDLU* in vacuum biopsy) and			
b. Complete or near complete removal of imaging abnormality			
FEA at margins in resection specimen:			
No further surgery, unless calcifications have not been completely removed	3b	C	++

* TDLU = Terminal ductal-lobular unit

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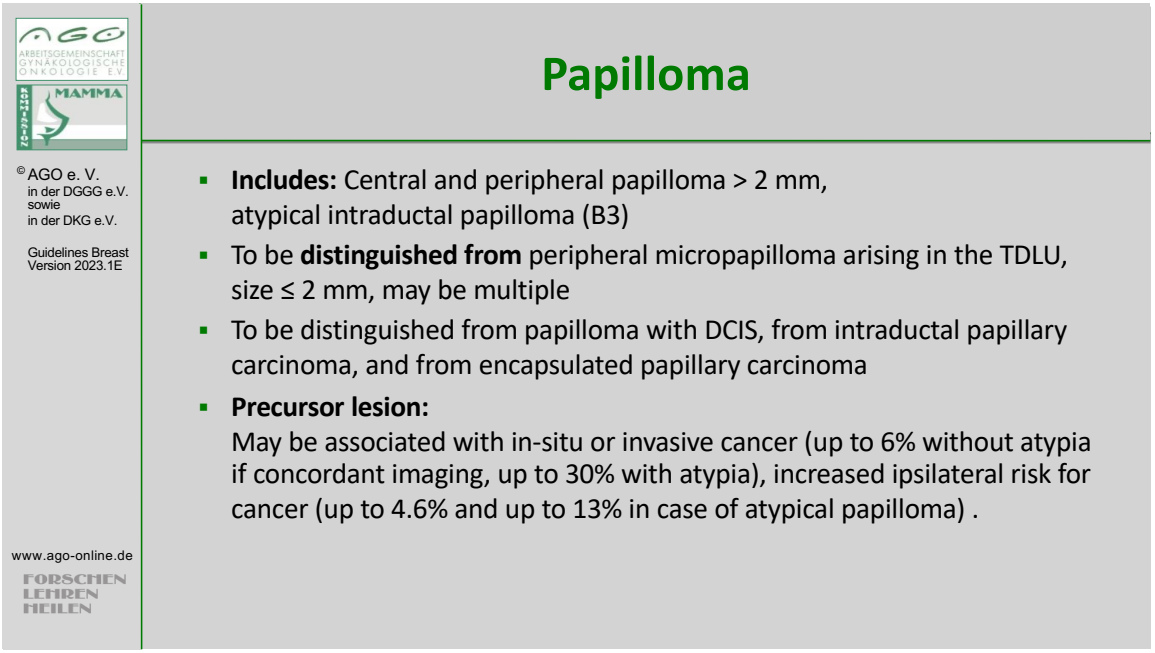

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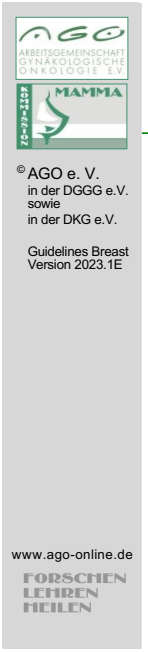

Strategy after Diagnosis of Papilloma

	Oxford LoE	Oxford GR	Oxford AGO
▪ **Papilloma without atypia in core needle or vacuum biopsy:**			
→ **no further therapy, if biopsy sufficiently representative (100mm3) and concordant with imaging**	2b	C	+
▪ **Multiple papillomas (>2 mm)**			
→ **open biopsy**	3a	C	++
▪ **Papilloma with atypia in core needle or vacuum biopsies:**			
→ **open biopsy**	3a	C	++
▪ **Papilloma at resection margin:**			
→ **no published data available**			

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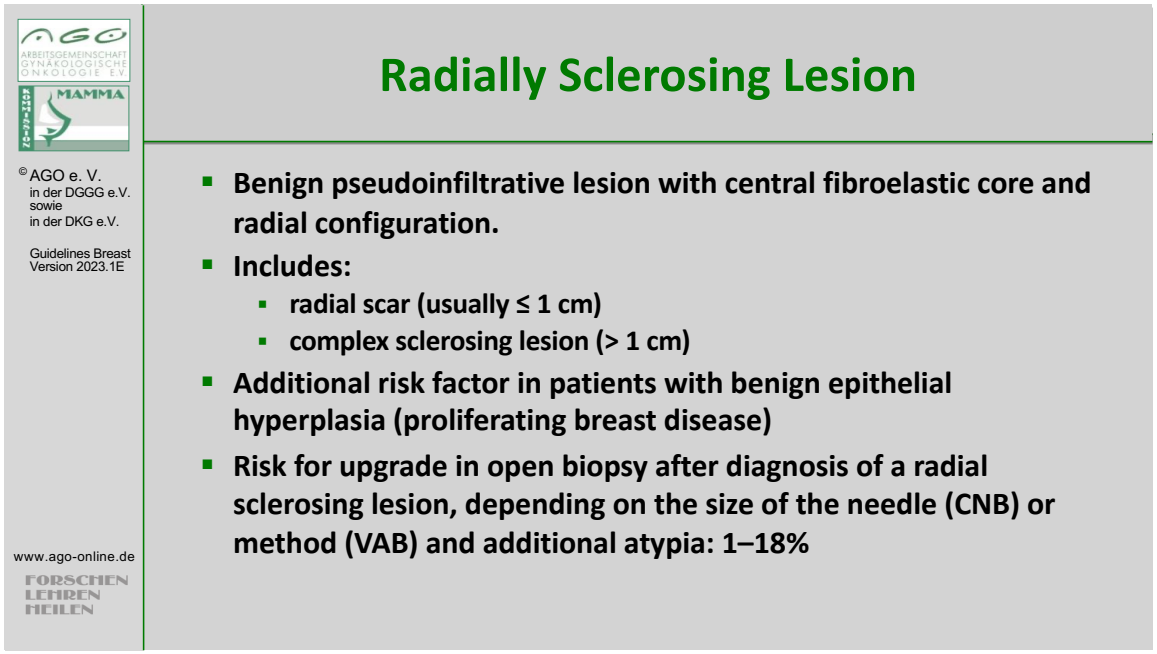

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Strategy after Diagnosis of Radial Scar, Complex Sclerosing Lesion (CSL)

	Oxford		
	LoE	GR	AGO
▪ **Radial scar / CSL in core- / vacuum-assisted biopsy:**			
▪ **Open excisional biopsy**	3a	C	+
▪ **Without atypia**	3a	C	+
▪ **With atypia**	3a	C	++
→ **Omission of open excisional biopsy if small (< 5mm) lesion or (near) complete removal of imaging abnormality**	5	C	+
▪ **Radial scar / CSL at margins in resection specimen:**			
→ **No further surgery**	3b	C	++

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Breast Cancer Early Detection: Follow-up Imaging for Women Age 50–69 Years with B3-Lesions

	Oxford		
	LoE	GR	AGO
▪ **FEA, non-atypical papilloma, radial sclerosing lesion**			
▪ **Screening mammography**	5	C	++
▪ **LIN**			
▪ **Mammography (12 months)**	3a	C	++
▪ **ADH**			
▪ **Mammography (12 months)**	3a	C	++
▪ **Women with LIN and ADH should be informed about their elevated risk of breast cancer**	3a	C	++

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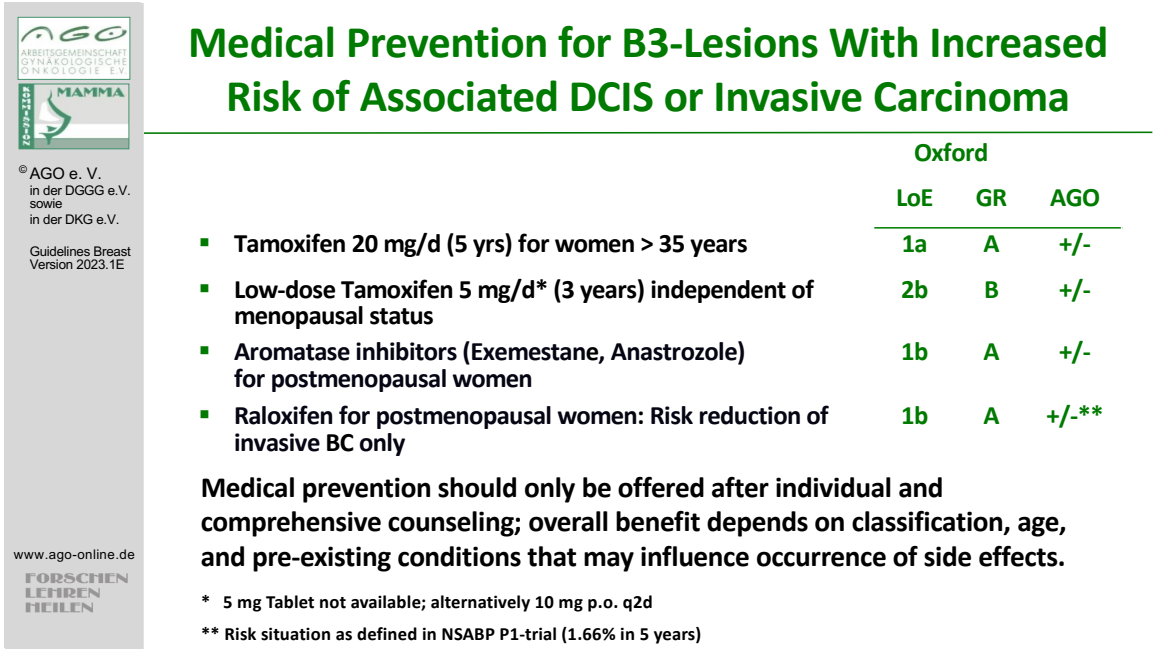

Medical Prevention for B3-Lesions With Increased Risk of Associated DCIS or Invasive Carcinoma

	Oxford		
	LoE	GR	AGO
▪ Tamoxifen 20 mg/d (5 yrs) for women > 35 years	1a	A	+/-
▪ Low-dose Tamoxifen 5 mg/d* (3 years) independent of menopausal status	2b	B	+/-
▪ Aromatase inhibitors (Exemestane, Anastrozole) for postmenopausal women	1b	A	+/-
▪ Raloxifen for postmenopausal women: Risk reduction of invasive BC only	1b	A	+/-**

Medical prevention should only be offered after individual and comprehensive counseling; overall benefit depends on classification, age, and pre-existing conditions that may influence occurrence of side effects.

* 5 mg Tablet not available; alternatively 10 mg p.o. q2d

** Risk situation as defined in NSABP P1-trial (1.66% in 5 years)

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