

Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

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Guidelines Breast
Version 2009.1.0

Precursor Lesions – FEA, LN, ADH –

◀◀ START

Precursor Lesions LN, ADH

- **Version 2005:**
Audretsch / Thomssen
- **Version 2006–2008:**
**Brunnert / Fersis / Friedrich / Nitz /
Schreer**
- **Version 2009:**
Albert / Brunnert

Further
Information

References

Definitions

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Documentation of Pathology in MIB (EWGBSP)

Pathology report („B“) categories

- B1 unsatisfactory/normal tissue only
- B2 benign
- B3 benign, but of uncertain malignant potential
- B4 suspicious of malignancy
- B5 malignant
 - a) intraductal
 - b) invasive
 - c) not certain
 - d) non epithelial, metastatic

Further
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References

FEA (CCL), LN and ADH are frequent casual findings due to enhanced screening activities.

LN 3 (pleomorphic LCIS) and DCIS are classified as B5 lesions, the other lesions as B3.

Pathophysiology of Precursor Lesions

Oxford LoE / GR

➤ **Concurrent multiple benign breast lesions with or without atypia in breast biopsies are significant predictors for progression to breast cancer**

2b B

➤ **Atypical hyperplasia (ADH, LN 1) is associated with an approximately four-fold increased risk of breast cancer**

2a B

Further Information

References

Surgical Strategy after Diagnosis of ADH / ALH (LN1) in Core Biopsy

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 LoE / GR

- **ADH / ALH (LN1) in core biopsies is associated with an increased risk of other high grade lesions or even carcinoma in open biopsies** 2a C

- **(Segmental) resection of the lesion after diagnosis of ADH in stereotactic needle biopsy / VAB** 4 C ++

- **Resection of the lesion after diagnosis of ALH (LN1) by stereotactic needle biopsy / VAB** 4 C +
 - **Exception: low grade lobular intraepithelial neoplasia (LN 1), if no mammographically suspicious lesion**

Further Information

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Pathophysiology of LN 2–3 (LCIS)

Oxford
LoE / GR

- **Similar to DCIS, LN 2–3 (LCIS) may be a precursor lesion** 2c C
- **Localisation of IBC in the same quadrant as LN 2–3 (LCIS)** 2c C
- **LN 2–3 (LCIS) is frequently diagnosed in patients aged between 40 to 55 years** 2c C
- **LN 2–3 (LCIS) is most frequently HR pos., HER-2 neg., E-Cadherin neg.** 2c C

Further Information

References

Surgical Strategy after Diagnosis of Lobular Neoplasia (LN 1–3)

| | Oxford / AGO LoE / GR | | |
|--|----------------------------------|----------|-----------|
| | | | |
| <p>➤ LN in needle biopsy (core needle / VAB) → Open biopsy Exception: Low grade lobular intraepithelial neoplasia (LN 1), if no mammographically suspicious lesion</p> | 4 | C | + |
| <p>➤ LN in open biopsy → No further therapy (independent of the resection margins) Exception: High grade lobular neoplasia (LN 3), pleomorphic LCIS and mixed carcinoma in situ → complete resection or therapy as for DCIS</p> | 4 | C | + |
| <p>➤ LN at margins of BCT specimen for IBC → no further resection (Exception: Pleomorphic LCIS (LN 3))</p> | 3b | B | ++ |
| | 5 | D | + |

Presence of LCIS in Patients with Breast Cancer Stage 0–II with BCT

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| Author | Years | Stage | Control # | LCIS # | Median follow-up (years) | % Local recurrence | | P value |
|-------------------------------|------------|-------|-----------|--------|--------------------------|--------------------|--------|---------|
| | | | | | | LCIS+ | LCIS– | |
| Sasson et al. ¹¹ | 79–95 | I, II | 1208 | 65 | 6.3 | 29 | 6/10y | 0.0003 |
| Moran et al. ¹⁰ | prior 1992 | 0–II | 1045 | 51 | 10.6 | 23 | 17/10y | NS |
| Abner et al. ⁷ | 68–86 | I–II | 1062 | 137 | 13.4 | 13 | 12/8y | NS |
| Jolly et al. ⁹ | 80–96 | I–II | 551 | 56 | 8.7 | 14 | 7/10y | 0.04 |
| Ben-David et al. ⁸ | 89–03 | 0–II | 121 | 66 | 3.9 | 0 | 0.9/5y | NS |
| Current study | 74–07 | 0–II | 2607 | 290 | 5.2 | 6 | 6/10y | NS |

LCIS, lobular carcinoma in situ; NS, not significant.

Ciocca RM, Li T, Freedman GM, Morrow M. Presence of lobular carcinoma in situ does not increase local recurrence in patients treated with breast-conserving therapy. *Ann of Surg Oncol* 2008;15:2263-2271

Further
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Therapeutic Options for LN

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| | Oxford / AGO LoE / GR | | |
|---|--------------------------|----------|-----------|
| ➤ Regular breast imaging | 3a | C | + |
| ➤ Tamoxifen 20 mg for 5 years | 2a | C | +* |
| ➤ Bilateral prophylactic mastectomy | 3a | D | - |
| ➤ Radiotherapy | 5 | D | -- |
| ➤ Patients with LN should be informed about risk | 3a | C | ++ |

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References

* Study participation recommended

Medical Prevention after Precursor Lesions

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Reduction of invasive breast cancer by Tamoxifen or Raloxifen

- After ER/PgR positive DCIS
- After LCIS (LN2–3)
- After ADH

1a A +*

2a C +

2a C +

2a C +

Aromatase inhibitors

5 D +/-*

Further
Information

References

* Study participation recommended

Medical Prevention for Women at Increased Risk

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- | | | | |
|---|----|---|-------|
| ➤ Tamoxifen for women > 35 years - reduction of invasive BrCa and DCIS | 1a | A | +* |
| ➤ Raloxifen for postmenopausal women - reduction of invasive BrCa only | 1b | A | +* |
| ➤ Aromatase inhibitors for postmenopausal women | 5 | D | +/-** |

Chemopreventive regimes should only be offered after individual and comprehensive counseling; the net benefit strongly depends on risk status, age and pre-existing risk factors for side effects

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Outcome of Medical Prevention

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NSABP-P1 Study , update 2005

| | Placebo Rate / 1000 WE | Tamoxifen Rate / 1000 WE | RR | 95% CI |
|--------------------------------------|------------------------------|-----------------------------|------|-----------|
| All women | 6.29 | 3.59 | 0.57 | 0.46-0.70 |
| w/o LCIS | 5.93 | 3.41 | 0.58 | 0.46-0.72 |
| W LCIS | 11.70 | 6.27 | 0.54 | 0.27-1.02 |
| w/o AH | 5.87 | 3.69 | 0.63 | 0.50-0.78 |
| w AH | 10.42 | 2.55 | 0.25 | 0.10-0.52 |
| 5 y risk <2% | 4.77 | 3.18 | 0.67 | 0.43-1.01 |
| 5 y risk > 5% | 11.98 | 5.15 | 0.43 | 0.28-0.64 |
| One 1 st ° relatives | 6.47 | 3.48 | 0.54 | 0.34-0.83 |
| >= three 1 st ° relatives | 11.24 | 5.48 | 0.49 | 0.16-1.34 |
| Fractures | 2.88 | 1.97 | 0.91 | 0.51-0.92 |
| Endometrial Ca | 0.68 | 2.24 | 3.28 | 1.87-6.03 |

Should only be offered to women at high risk, e.g.

- with LCIS (LN 2–3)
- with AH
- with a strong family history

NSABP-P2 Study, STAR trial 2006

| | Tamoxifen Rate / 1000 WE | Raloxifen Rate / 1000 WE | RR | 95% CI |
|-----------------------------------|--------------------------------|-----------------------------|------|-----------|
| All women | 4.30 | 4.41 | 1.02 | 0.82-1.28 |
| W/O LCIS | 3.76 | 3.89 | 1.03 | 0.81-1.33 |
| W LCIS | 9.83 | 9.61 | 0.98 | 0.58-1.63 |
| W/O AH | 4.06 | 4.03 | 0.99 | 0.76-1.28 |
| W AH | 5.21 | 5.81 | 1.12 | 0.72-1.74 |
| 5 y risk <3% | 2.03 | 2.83 | 1.40 | 0.87-2.28 |
| 5 y risk > 5% | 6.77 | 7.35 | 1.09 | 0.78-1.52 |
| One 1 st ° relatives | 4.99 | 5.18 | 1.04 | 0.69-1.55 |
| >=two 1 st ° relatives | 5.16 | 5.00 | 0.97 | 0.60-1.56 |
| Endometrial CA | 2.00 | 1.25 | 0.62 | 0.35-1.08 |
| Thromboembolisms | 3.71 | 2.61 | 0.70 | 0.54-0.91 |

Should not be offered to women

- with a moderate risk over the age of 50
- with an increased risk for thromboembolic events

Further
Information

References