

# Diagnosis and Treatment of Patients with Primary and Metastatic Breast Cancer

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

Guidelines Breast  
Version 2009.1.0

## Prognostic and Predictive Factors



# Prognostic and Predictive Factors

- **Version 2002:**  
**Thomssen / Harbeck**
- **Version 2003–2008:**  
**Costa / Gerber / Göhring / Schaller /  
Schmutzler / Simon / Solomayer /  
Thomssen**
- **Version 2009:**  
**Friedrichs / Harbeck**

Further  
Information

References

# Definition

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

Guidelines Breast  
Version 2009.1.0

**A Prognostic Factor is any parameter available at the time of surgery that correlates with disease-free or overall survival in the absence of systemic adjuvant therapy and, as a result, is able to correlate with the natural history of the disease.**

**A Predictive Factor is any parameter associated with response to a given therapy.**

Further  
Information

References

# Quality Criteria

- **Biological hypothesis**
- **Simple and reliable determination method, quality assurance (QA) of the test**
- **Prospectively planned statistical evaluation (primary objective)**
- **Validation of the clinical significance according to „Oxford Level of Evidence (LoE)“ criteria and „Grades of Recommendation“**
- **Clinical relevance for treatment decisions**

Further  
Information

References

# Prognostic Factors I

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

Guidelines Breast  
Version 2009.1.0

## Factor

## Oxford / AGO LoE / GR

|   |    |   |    |
|---|----|---|----|
| ➤ Tumor size  | 1a | A | ++ |
| ➤ Nodal status  | 1a | A | ++ |
| ➤ Metastases  | 1a | B | ++ |
| ➤ Histological tumor type (colloid, mucinous, tubular etc.)     | 2b | B | ++ |
| ➤ Grade<br>(Elston-Ellis)                                       | 2a | B | ++ |
| ➤ Age   | 2a | B | ++ |
| ➤ Peritumoral lymphatic vessel<br>and vascular invasion (L1 V1) | 2b | B | +  |

Further  
Information

References

# Prognostic Factors II

## Oxford / AGO LoE / GR

### Factor

- ER / PgR
- uPA / PAI-1 (ELISA)
- Triple-negative / basal cell-like tumor
- HER-2 (IHC, FISH)
- Tumor cell detection in bone marrow
- Proliferation markers
  - Thymidine-labeling index
  - S-phase fraction
  - Ploidy
  - Ki-67
- Currently available gene, methylation or protein profiles
- Computer guided decision tools ([www.adjuvantonline.com](http://www.adjuvantonline.com))

|       |   |     |
|-------|---|-----|
| 2a    | B | ++  |
| 1a    | A | +   |
| 2b    | B | +   |
| 2b    | B | +/- |
| 1a    | B | +/- |
| 2b    | B | +/- |
| 1b    | B | +/- |
| 2b    | B | +/- |
| 2b    | B | +/- |
| 2b    | B | +/- |
| 2b(-) | D | -*# |
| 2b(-) | D | +   |

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

Guidelines Breast  
Version 2009.1.0

Further  
Information

References

# Predictive Factors – Adjuvant Therapy

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

Guidelines Breast  
Version 2009.1.0

| Treatment                | Factor                    | Oxford / AGO    |    |      |
|--------------------------|---------------------------|-----------------|----|------|
|                          |                           | LoE             | GR |      |
| Endocrine therapy        | ER/PgR Status             | 1a              | A  | ++   |
|                          | HER-2                     | 2b              | D  | -    |
|                          | Oncotype DX™              | 2b              | B  | +/-* |
| Tamoxifen therapy        | Cyp2D6 polymorphism       | 2b              | B  | +/-* |
| Ovarian ablation         | menopausal status         | 1c              | A  | ++   |
| Aromatase inhib.         | menopausal status         | 1c              | A  | ++   |
| Chemotherapy             | HER-2                     | 2b              | D  | -    |
|                          | ER/PgR status             | 2a              | B  | +/-  |
|                          | uPA/PAI-1                 | 2a              | C  | +/-  |
|                          | Oncotype DX™              | 2b              | B  | +/-* |
| HER-2 directed therapies | HER-2                     | 2b              | D  | ++   |
| Anthracyclines           | Topoisomerase II $\alpha$ | 2b <sup>a</sup> | B  | -    |

Further  
Information

References

# Prognostic Factors in Node-Negative Breast Cancer

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

Guidelines Breast  
Version 2009.1.0

## Factor

Oxford / AGO  
LoE / GR

|                                      |    |   |      |
|--------------------------------------|----|---|------|
| ➤ Grade                              | 2b | B | ++   |
| ➤ Tumor size                         | 2b | B | +    |
| ➤ Age                                | 2b | B | +    |
| ➤ uPA / PAI-1 (ELISA)                | 1a | A | +    |
| ➤ Proliferation<br>(SPF, TLI, Ki-67) | 2b | C | +/-  |
| ➤ Oncotype DX™                       | 2b | B | +/-* |
| ➤ Mammaprint™                        | 2b | B | +/-* |

Further  
Information

References

# Predictive Factors

## Metastatic Breast Cancer

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

Guidelines Breast  
Version 2009.1.0

| Therapy                            | Factor                        | Oxford / AGO<br>LoE / GR |
|------------------------------------|-------------------------------|--------------------------|
| Endocrine therapy                  | ER/PgR Status                 | 1a A ++                  |
|                                    | HER-2                         | 3a C +/-                 |
| 2 <sup>nd</sup> line endocrine th. | response 1 <sup>st</sup> line | 2b B +                   |
| GnRHa                              | menop. status                 | 1c A ++                  |
| Aromatase inhibitors               | menop. status                 | 1c A ++                  |
| Taxanes                            | HER-2                         | 2b C -                   |
| Anthracyclines                     | HER-2                         | 3b C +/-                 |
| Chemotherapy                       | circ. tumor cells*            | 1b B +/-                 |
| HER-2 directed therapies           | HER-2                         | 1b A ++                  |
|                                    | HER-2 shed antigen            | 2b C +/-                 |

Further  
Information

References

# Therapy Monitoring

## Metastatic Breast Cancer

**AGO**

---

- **Imaging (lead lesion)** +
- **Tumor markers (any if elevated at time of metastasis) CA15-3 or CEA or CA-27.29** +
- **HER-2 shed antigen (ECD)** +
- **Circulating tumor cells\*** +/-
- **PET** -

Further  
Information

References