

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

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Guidelines Breast  
Version 2009.1.0

START

## Neoadjuvant (Primary) Systemic Therapy

# Neoadjuvant Systemic Therapy

- **Version 2002:**  
**Costa**
- **Version 2003 – 2008:**  
**Dall / Fersis / Göhring / Heinrich /  
Jackisch / Kaufmann / Nitz /  
Schneeweiss / Solomayer / Untch**
- **Version 2009:**  
**von Minckwitz / Untch**

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# Neoadjuvant Systemic Chemotherapy Clinical Benefit



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- |  |    |   |     |
|--|----|---|-----|
| ➤ Survival is similar after neoadjuvant (preoperative, primary) and adjuvant systemic therapy                              | 1a | A |     |
| ➤ Pathological complete response (no invasive residuals in breast and axilla) is associated with high survival probability | 1b | A |     |
| ➤ May achieve operability in primary inoperable tumors   | 1b | A | ++  |
| ➤ Improved options for breast conserving surgery   | 1b | A | ++  |
| ➤ Allows individualization of therapy according to mid-course treatment effect   | 1b | B | ++* |

\* Study participation recommended

# Neoadjuvant Systemic Chemotherapy Indications

- **Inflammatory breast cancer**
- **Inoperable breast cancer**
- **Large operable breast cancer primarily requiring mastectomy and adjuvant chemotherapy with the goal of breast conservation**
- **If similar postoperative adjuvant chemotherapy is indicated**

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**2b B ++**

**1c A ++**

**1b B +**

**1b A + \***

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# Neoadjuvant Systemic Chemotherapy Response Prediction



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## Factors predicting a high chance for a pathological complete response:

➤ <b>Age &lt; 35 yrs</b>	<b>1a<sup>a</sup></b>	<b>A</b>	<b>++</b>
➤ <b>cT1 / cT2 tumor</b>	<b>1a<sup>a</sup></b>	<b>A</b>	<b>++</b>
➤ <b>Negative nodal status</b>	<b>1a<sup>a</sup></b>	<b>A</b>	<b>++</b>
➤ <b>Grade 3 tumor</b>	<b>1a<sup>a</sup></b>	<b>A</b>	<b>++</b>
➤ <b>Negative ER and PgR status</b>	<b>1a<sup>a</sup></b>	<b>A</b>	<b>++</b>
➤ <b>Positive HER2 status</b>	<b>1a<sup>a</sup></b>	<b>A</b>	<b>++</b>
➤ <b>Non-lobular tumor type</b>	<b>1a<sup>a</sup></b>	<b>A</b>	<b>+/-</b>
➤ <b>Prediction algorithm/score</b>	<b>2b</b>	<b>B</b>	<b>+/-</b>

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# Neoadjuvant Systemic Chemotherapy

## Recommended regimens and schedules

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➤ <b>Planned neoadjuvant treatment should last at least 18 weeks</b>	<b>1a<sup>a</sup></b>	<b>A</b>	<b>++</b>
➤ <b>AC or EC → D q3w or P q1w</b>	<b>2b</b>	<b>A</b>	<b>+</b>
➤ <b>DAC</b>	<b>2b</b>	<b>B</b>	<b>+</b>
➤ <b>AP → CMF</b>	<b>2b</b>	<b>B</b>	<b>+</b>
➤ <b>P weekly → FAC</b>	<b>2b</b>	<b>B</b>	<b>+/-</b>
➤ <b>Dose-Dense E → P</b>	<b>2b</b>	<b>B</b>	<b>+</b>

**AGO-recommendation reflects treatment efficacy in the adjuvant setting.**

**D = Docetaxel; P = Paclitaxel**

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# Neoadjuvant Systemic Chemotherapy in HER-2 Positive Tumors

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- **Chemotherapy concomitantly with trastuzumab**
- **Chemotherapy concomitantly with lapatinib (+/- trastuzumab)**

**1b A ++**

**2b<sup>a</sup> C -\***

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# Neoadjuvant Systemic Therapy Procedures in Case of Early Response

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## In case of early response

- **Continue and complete all chemotherapy before surgery**

**1b A ++**

**Patients with partial mid-course response may achieve a higher pCR rate with of longer treatment duration (at least 18 weeks)**

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# Neoadjuvant Systemic Therapy Procedures in Case of No Early Response

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## In case of stable disease:

- |   |           |          |           |
|---|-----------|----------|-----------|
| ➤ <b>Completion of NST, followed by surgery</b>               | <b>2b</b> | <b>C</b> | <b>++</b> |
| ➤ <b>Continuation of NST with non cross-resistant regimen</b> | <b>2b</b> | <b>B</b> | <b>+</b>  |
| ➤ <b>AC or EC x 4 → D x 4 or Pw x 12</b>                      | <b>2b</b> | <b>B</b> | <b>+</b>  |
| ➤ <b>DAC x 2 → NX x 4</b>                                     | <b>2b</b> | <b>B</b> | <b>+</b>  |

## In case of progressive disease:

- |  |          |          |            |
|--|----------|----------|------------|
| ➤ <b>Stop of NST and immediate surgery or radiotherapy</b>                 | <b>4</b> | <b>D</b> | <b>++*</b> |
| ➤ <b>Additional adjuvant chemotherapy with non cross-resistant regimen</b> | <b>4</b> | <b>D</b> | <b>+/-</b> |

\* Study participation recommended

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# Neoadjuvant Systemic Therapy Surgical Procedures

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- **Precise documentation of tumor location before, during and at the end of NST** 5 D ++
- **Adequate surgery after NST** 2b C ++
- **Microscopically clear margins** 5 D ++
- **Excision within new margins** 3b C +
- **Sentinel node biopsy  
(see chapter “Breast Cancer Surgery”)**

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# Neoadjuvant Systemic Therapy

## Indications for Breast Conserving Surgery

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- **In case of clinical complete response**
  - **Inflammatory breast cancer** 3 C -\*
  - **cT4a-c breast cancer** 3 C +/-\*
  - **Multicentric disease** 3 C +/-\*
- **Extensive microcalcifications** 5 D - -
- **Radiotherapy not feasible** 5 D - -

\* Study participation recommended

# Neoadjuvant Systemic Therapy

## Timing of Surgery and Radiotherapy

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### Surgery

4 C ++

- **After leucocyte nadir  
(2 to 4 weeks after last course of  
chemotherapy)**

### Radiotherapy after mastectomy

2b B ++

- **2–3 weeks after surgery**
- **Indications according to stage of  
disease before NST (cN+, cT3/4a-d)**

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# Neoadjuvant Systemic Therapy

## Postneoadjuvant Systemic Treatment

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- **Start of endocrine treatment in endocrine responsive disease** 1a A ++
- **Complete trastuzumab treatment for up to 1 year in HER2-positive disease** 2b B ++
- **In case of insufficient response**
  - **Further chemotherapy** 3 C -
  - **Experimental treatments** 5 D +\*

Further Information

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\* Study participation recommended

# Neoadjuvant Endocrine Therapy

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➤ **Postmenopausal patients with endocrine responsive breast cancers who are inoperable and can / will not receive chemotherapy**

5 D +

➤ **Aromatase inhibitors (for > 3 months) (instead of tamoxifen)**

1b B +/-

➤ **Increased rate of breast conserving surgery**

➤ **Concurrent chemo-endocrine therapy**

1b A - -

**Optimal duration of neoadjuvant endocrine therapy is unknown**

**No long term results for neoadjuvant endocrine therapy (vs. adjuvant endocrine therapy)**

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