Adjuvante endokrine Therapie bei prä- und postmenopausalen Patientinnen
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- **Versionen 2002–2018:**
  Bauerfeind / Dall / Diel / Fersis / Friedrichs / Gerber / Göring / Hanf / Harbeck / Huober / Jackisch / Lisboa / Lück / Lux / Maass / von Minckwitz / Möbus / Müller / Oberhoff / Schaller / Scharl / Schneeweiss / Schütz / Solomeyer / Stickeler / Thomssen / Untch

- **Version 2019:**
  Fehm / Gerber
Endocrine responsiveness:


In case of ER negative / PR positive (>10% cells): consider immunohistochemical re-evaluation:

1. Viale G, Regan MM, Maiorano E et al. Prognostic and predictive value of centrally reviewed expression of estrogen and progesterone receptors in a randomized trial comparing letrozole and tamoxifen adjuvant therapy for postmenopausal early


8. Regan MM, Walley BA, Francis PA et al. Concurrent and sequential initiation of ovarian function suppression with chemotherapy.
Generelle Prinzipien der adjuvanten endokrinen Therapie AGO ++

- Die adjuvante endokrine Therapie wird in die initiale Therapie (Jahre 0–5) und die erweiterte adjuvante Therapie (EAT, Jahre 6–15) eingeteilt.
- Standard Therapiedauer der adjuvanten Therapie: 5 Jahre
- Erweiterte Therapiedauer nach individueller Nutzen-Risiko-Abwägung.
- Der Wechsel auf eine andere endokrine Therapie (Tam oder Al) ist besser als die Therapie zu stoppen.
- Beginn mit Al bei postmenopausalen Patientinnen insbesondere bei lobulären Karzinomen und erhöhtem Rückfall-Risiko.
- Es existiert kein ausreichend validierter Biomarker für einen frühen versus einen späten Rückfall.

### Tamoxifen 5–10 yrs:


### GnRH as monotherapy:

1. Cuzick J, Ambroisine L, Davidson N et al: Use of luteinising-hormone-releasing hormone agonists as adjuvant treatment in...

In patients with ovarian function (within 8 mon.) after adjuvant chemotherapy:

OFS 5 years + Tam 5 years
OFS 5 years + AI 5 years
in patients < 35 y.

8. Kim HA, Ahn SH, Nam SJ et al. The role of the addition of ovarian suppression to tamoxifen in young women with hormone-sensitive breast cancer who remain premenopausal or regain menstruation after chemotherapy (ASTRA): study protocol for a

Adjuvante endokrine Therapie bei postmenopausalen Patientinnen (Jahre 0-5)

<table>
<thead>
<tr>
<th>Oxford</th>
<th>LoE</th>
<th>GR</th>
<th>AGO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aromatasehemmer für die ersten 5 Jahre</td>
<td>1a</td>
<td>A</td>
<td>++</td>
</tr>
<tr>
<td><strong>Nicht-steroidaler AI bei lobulärem Karzinom</strong></td>
<td>2b</td>
<td>B</td>
<td>+</td>
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<tr>
<td><strong>Hohes Rezidivrisiko</strong></td>
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<tr>
<td>Sequentielle Therapie für die ersten 5 Jahre*</td>
<td></td>
<td></td>
<td>++</td>
</tr>
<tr>
<td>Tam (2–3 Jahre) gefolgt von Al bis zur Gesamtdauer von 5 Jahren</td>
<td>1a</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>AI (2–3 Jahre) gefolgt von Tamoxifen bis zur Gesamtdauer von 5 Jahren</td>
<td>1b</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Tamoxifen 20 mg/d für die ersten 5 Jahre**</td>
<td>1a</td>
<td>A</td>
<td>+</td>
</tr>
</tbody>
</table>

* Die endokrane adjuvante Therapie postmenopausaler Patientinnen sollte in den ersten 5 Jahren für 2–3 Jahre einen Aromatasehemmer enthalten

** Eine Monotherapie mit Tamoxifen kann bei Patientinnen im Senium, bei niedrigem Risiko oder bei Kontraindikation für Aromatasehemmer eingesetzt werden

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AI for first 5 years:


- Especially in case of lobular cancer

3. Strasser-Weippl K et al. Outcomes in women with invasive ductal or invasive lobular early stage breast cancer treated with anastrozole or exemestane in CCTG (NCIC CTG) MA.27. Eur J Cancer 2018;90:19-25. doi: 10.1016/j.ejca.2017.11.014

- High risk of recurrence:

Sequential therapy for first 5 years:
Tam (2-3 yrs.) followed by AI to complete 5 years
AI (2-3 yrs.) followed by Tam to complete 5 years


Tamoxifen 20 mg/d for first 5 yrs:

Patient care/ adherence and side effects


5 Years Tamoxifen after 5 Years Tamoxifen:


2–5 years AI after 5 years Tamoxifen in initially premenopausal patients with validated postmenopausal status in the course of therapy:


5 years Tamoxifen after 5 years Tamoxifen:

2–5 years AI after 5 years Tamoxifen


7. Gray R (EBCTCG ) et al. Extended aromatase inhibitor treatment following 5 or more years of endocrine therapy: a metaanalysis of 22192 women in 11 randomised trials. SABCS 2018;GS3-03


After initial AI containing therapy (upfront or switch) further prolongation of endocrine therapy with AI 2-5 years*:
high risk and good tolerabilty of the AI
low risk, poor tolerabilty of the AI
6. Gray R (EBCTCG ) et al. Extended aromatase inhibitor treatment following 5 or more years of endocrine therapy: a metaanalysis of 22192 women in 11 randomised trials. SABCS 2018;GS3-03

**Interruption of endocrine treatment up to 3 months during EAT:**

1. Gray R (EBCTCG) et al. Extended aromatase inhibitor treatment following 5 or more years of endocrine therapy: a metaanalysis of 22192 women in 11 randomised trials. SABCS 2018;GS3-03


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**Gonadotropin-Releasing Hormone Agonists During Chemotherapy for Preservation of Ovarian Function and Fertility in Premenopausal Patients With Early Breast Cancer: A Systematic Review and Meta-Analysis of Individual Patient-Level Data**

N = 837 patients from 5 trial, median follow-up time 5.0 years (IQR, 3.0–6.3 years)

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>GnRH</th>
<th>HR (95%-CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>POI&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>30.9%</td>
<td>14.1%</td>
<td>0.38; 0.26 to 0.57</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pregnancy&lt;sup&gt;3&lt;/sup&gt;</td>
<td>5.5%</td>
<td>10.3%</td>
<td>1.83; 1.06 to 3.15;</td>
<td>0.03</td>
</tr>
</tbody>
</table>

<sup>1</sup>premature ovarian insufficiency, <sup>2</sup>different definitions and time points were used<br><sup>3</sup>in most trials POI and not pregnancy was defined as the primary endpoint

No significant differences in disease-free survival and overall survival were observed between groups.

_Lambertini M et al. J Clin Oncol 2018_
Adjuvante endokrine Therapie
Prä- und Postmenopause im Überblick

Tamoxifen
Exemestan, Tam + GnRH
Letrozol (MA.17)

Tamoxifen
Tamoxifen
Tamoxifen
AI
Tamoxifen / AI
AI
Tamoxifen
AI
AI
TAM
AI
Letrozol (MA.17)
Letrozol (MA.17R)

PRÄMENOPAUSE
POSTMENOPAUSE

Adjuvant Jahr 0-5
EAT Jahr 6-10
Carry over effect > 10