Therapy Algorithms

_Preamble:_
Therapy options shown in the algorithms are based on the current AGO recommendations, but cannot represent all evidence-based treatment options, since prior therapies, performance status, comorbidities, patient preference, special tumor biology etc. must be taken into account for the actual treatment choice. Normally only recommendations with the recommendation grades AGO+ and AGO++ are taken into account.

In individual cases, other evidence-based treatment options (not listed here) may also be appropriate and justified. After failure of effective standard treatments discussion in a molecular tumor board should be considered.

Regardless of approval status, the algorithms only take into account drugs that were available in Germany at the time the algorithm was last updated.
Therapy Algorithms

- **Version 2021-2023:**
  Schneeweiss / Bauerfeind / Fehm / Müller / Thill / Thomssen / Witzel / Wöckel / Janni

- **Version 2024:**
  Schneeweiss/ Müller with the Breast Committee of the AGO

**Format legend:**
- Definitions, features, parameters
- Therapy with grade of recommendation AGO+ or AGO++
- Therapy with grade of recommendation AGO+/-(case by case decision)
- Recommended path with grade of recommendation AGO+ oder AGO++
- Crossing without transition
- Path of case by case decision (grade of recommendation AGO+/−)
- Arrow points to the next therapy option
- AGO++
  AGO grade of recommendation of this path
Content

- Early breast cancer
  - Therapy of HR-positive, HER2-negative early breast cancer: strategies
  - Therapy of HER2-positive early breast cancer
  - Therapy of early triple-negative breast cancer
  - Axillary surgery and neoadjuvant chemotherapy (NACT)
  - Adjuvant endocrine therapy in premenopausal patients
  - Adjuvant endocrine therapy in postmenopausal patients

- Metastatic breast cancer
  - HR-positive / HER2-negative metastatic breast cancer: strategies
  - HR-positive / HER2-negative metastatic breast cancer: endocrine-based first line treatment
  - HER2-positive metastatic breast cancer: 1st-3rd-line
  - Triple-negative metastatic breast cancer


7. Loibl S, et al. VP6-2022: Adjuvant pertuzumab and trastuzumab in patients with early HER-2 positive breast cancer in APHINITY:
8.4 years' follow-up. Ann Oncol. DOI: https://doi.org/10.1016/j.annonc.2022.06.009


9. Loibl S, et al. Phase III study of adjuvant ado-trastuzumab emtansine vs. Trastuzumab for residual invasive HER2-positive early breast cancer after neoadjuvant chemotherapy and HER2-targeted therapy: KATHERINE final IDFS and updated OS analysis. SABCS 2023 (GS03-12)


3. Loibl S, Sikov W, Huober J, et al. Event-free survival (EFS), overall survival (OS), and safety of adding veliparib (V) plus carboplatin (Cb) or carboplatin alone to neoadjuvant chemotherapy in triple-negative breast cancer (TNBC) after ≥4 years of follow-up: BrighTNess, a randomized phase III trial. Annals of Oncology (2021) 32 (suppl_5): S407-S446.


7. Gluz O, Nitz U, Liedtke C, et al. Comparison of Neoadjuvant Nab-Paclitaxel+Carboplatin vs Nab-Paclitaxel+Gemcitabine in Triple-


1. Giuliano AE, Ballman KV, McCall L et al. Effect of axillary dissection vs no axillary dissection on 10-year overall survival among women with invasive breast cancer and sentinel node metastasis: The acosog z0011 (alliance) randomized clinical trial. JAMA 2017, 318, 918-926

2. Reimer TS, Nekljudova V, Loibl, S et al. Restricted axillary staging in clinically and sonographically node-negative early invasive breast cancer (c/i t1-2) in the context of breast conserving therapy: First results following commencement of the intergroup-sentinel-mamma (insensa) trial. Geburtsh Frauenheilk 2017, 77, 149-157


11. Partridge A, et al on behalf of the POSITIVE Consortium: Pregnancy Outcome and Safety of Interrupting Therapy for women with endocrine responsIIVE breast cancer: Initial Results from the POSITIVE Trial (IBCSG 48-14 / BIG 8-13 / Alliance A221405). SABCS 2022 (GS04-09)


4. 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


Chemotherapy mBC


CDK4/6i meta-analysis


CDK4/6i 2nd-line

7. Sonke G, van Ommen A, Wortelboer N et al. Primary outcome analysis of the phase 3 SONIA trial (BOOG 2017-03) on selecting the optimal position of cyclin-dependent kinases 4 and 6 (CDK4/6) inhibitors for patients with hormone receptor-positive (HR+), HER2-negative (HER2-) advanced breast cancer (ABC). J Clin Oncol. 2023;41, 17S. LBA1000

Olaparib


Talazoparib


Chemotherapy 2nd line


ET+ Ev/Alp

16. Kornblum NS, et al. PrECOG 0102: A randomized, double-blind, phase II trial of fulvestrant plus everolimus or placebo in postmenopausal women with hormone receptor (HR)-positive, HER2-negative metastatic breast cancer (MBC) resistant to aromatase inhibitor (AI) therapy. SABCS 2016,#S1-02


Elacestrant

**Fulvestrant + Capivasertib**

**Trastuzumab Deruxtecan**

**Sacituzumab Govitecan**
GnRHa plus fulvestrant plus palbociclib

GnRHa plus AI plus palbociclib

GnRHa plus AI/Tamoxifen plus ribociclib
4. Tripathy D et al. First-line ribociclib vs placebo with goserelin and tamoxifen or a non-steroidal aromatase inhibitor in premenopausal women with hormone receptor-positive, HER2-negative advanced breast cancer: Results from the randomized phase III MONALEESA-7 trial. SABCS 2017, GS-26

**GnRH plus Fulvestrant + Abemaciclib**


**GnRHa plus tamoxifen (vs. OFS or tam)**


**GnRHa plus AI (first or second line)**


**GnRHa plus fulvestrant**

Letrozole and palbociclib (vs. letrozole alone)


Letrozol plus Ribociclib


Non-steroidal AI plus Abemaciclib


**Fulvestrant 500 mg plus Palbociclib (vs. Fulvestrant alone)**


**Fulvestrant plus Ribociclib**


**Fulvestrant plus Abemaciclib**


18. Cortés J, Kim SB, Chung, WP, et al., Trastuzumab Deruxtecan (T-DXd) vs Trastuzumab Emtansine (T-DM1) in Patients with HER2+ Metastatic Breast Cancer: Results of the Ranomized Phase 3 Study DESTINY-Breast03. ESMO, 2021; Presidential symposium 1, Abstract No. LBA1


15. Zielinski C, Láng I, Inbar M, et al TURANDOT investigators. Bevacizumab plus paclitaxel versus bevacizumab plus capecitabine as first line treatment for HER2-negative metastatic breast cancer (TURANDOT): primary endpoint results of a randomised, open-label,

