

# Diagnosis and Treatment of Patients with Early and Advanced Breast Cancer



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## Algorithms of Therapeutic Strategies

### Preamble:

Therapeutic strategies 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.

# Algorithms of Therapeutic Strategies









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## Version 2021-2025:

Schneeweiss / Bauerfeind / Fehm / Müller / Thill / Thomssen / Witzel / Wöckel / Janni  
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+/-)
-  Path not recommended (grade of recommendation AGO-, only affects algorithm of axillary surgery and neoadjuvant chemotherapy)
-  Arrow points to the next therapy option
- **AGO++** AGO grade of recommendation of this path

# Content

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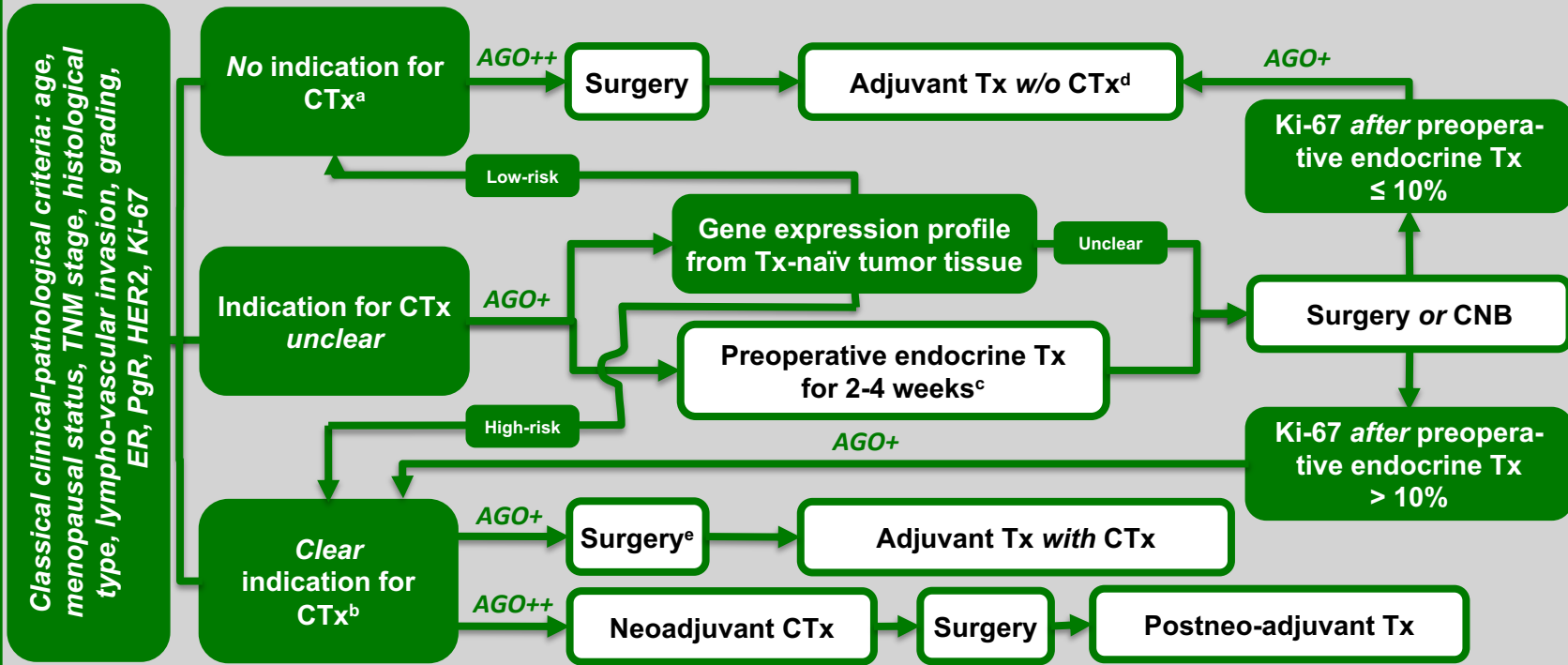
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- **Early breast cancer**
  - Therapy of HR-positive, HER2-negative early breast cancer
  - Adjuvant endocrine-based therapy in premenopausal patients
  - Adjuvant endocrine-based therapy in postmenopausal patients
  - Therapy of HER2-positive early breast cancer
  - Therapy of triple-negative early breast cancer
  - Axillary surgery and neoadjuvant chemotherapy
  
- **Metastatic breast cancer**
  - HR-positive, HER2-negative metastatic breast cancer
  - HER2-positive metastatic breast cancer
  - Triple-negative metastatic breast cancer

# Therapy of HR-positive, HER2-negative Early Breast Cancer

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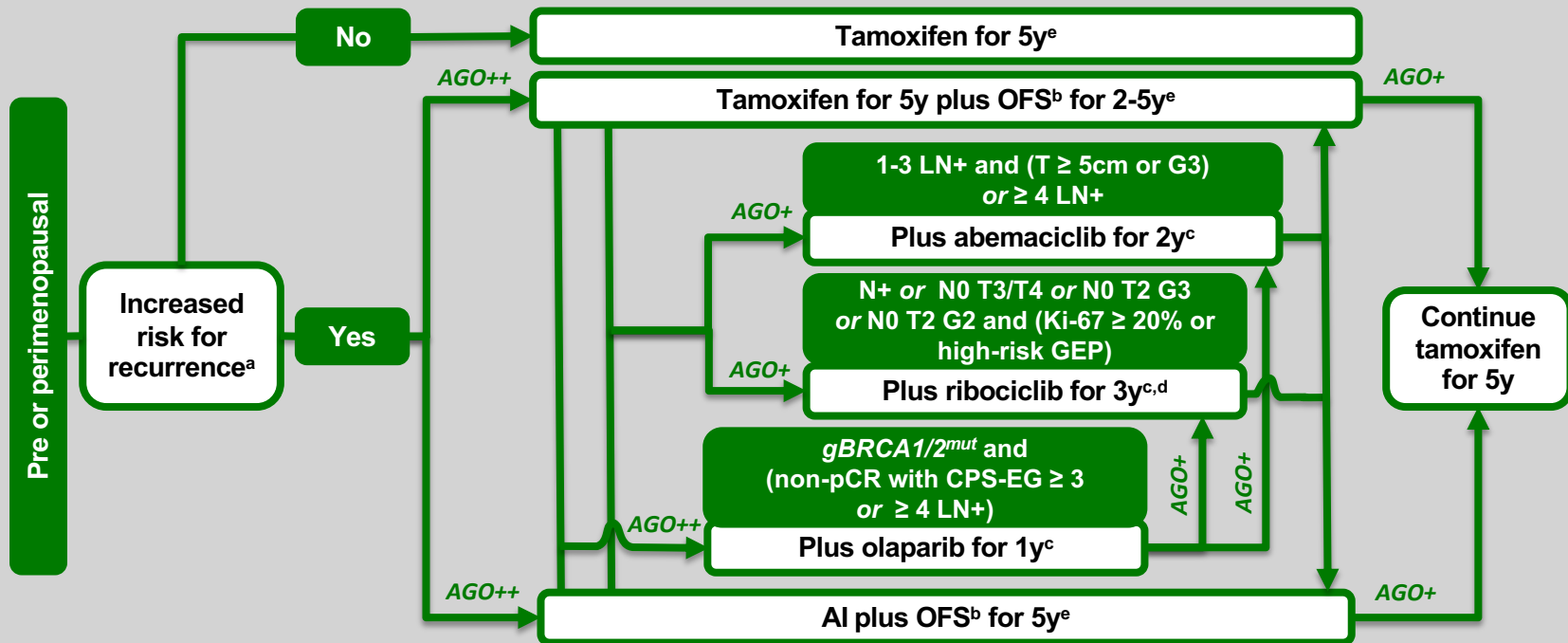
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CNB, core needle biopsy; CTx, chemotherapy; ER, estrogen receptor; PgR, progesterone receptor; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; Tx, therapy; w/o, without; <sup>a</sup>e.g.  $\leq$  cT1c cN0-1 G1-2 Ki-67  $\leq$  5% or -if situation unclear- low-risk gene expression profile; <sup>b</sup>e.g. inoperable tumor or  $\geq$  4 clinically involved axillary nodes or G3 and Ki-67  $\geq$  35% or -if situation unclear- high-risk gene expression profile; <sup>c</sup>standard endocrine Tx; <sup>d</sup>if no change of prognostic factors after surgery; <sup>e</sup>if not done already.

# Adjuvant Endocrine-based Therapy in Premenopausal Patients

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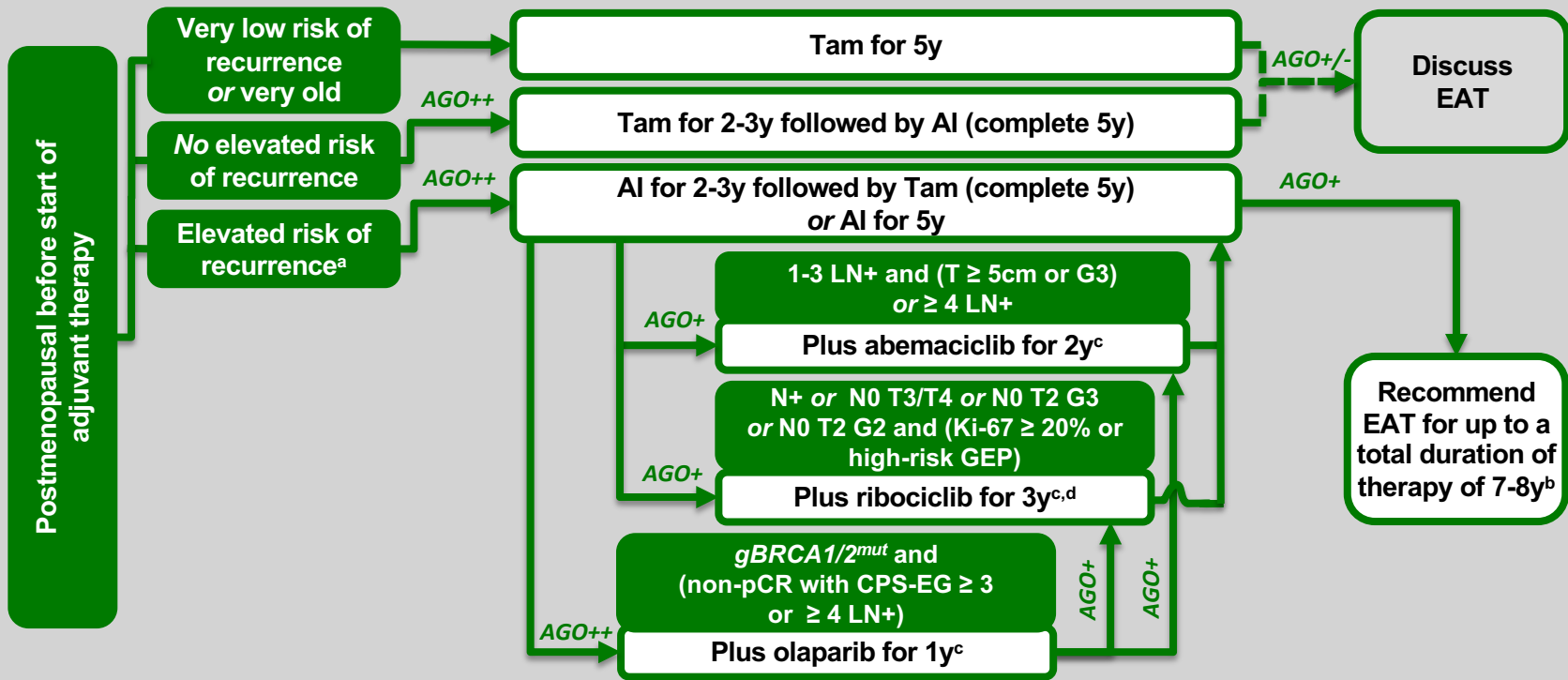
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AI, aromatase inhibitor; CPS-EG, clinical pathological stage + estrogen receptor status and grade score; *gBRCA1/2<sup>mut</sup>*, germline *BRCA1/2* mutation; GEP, gene expression profile; LN, lymph node; non-pCR, no pathological complete response; OFS, ovarian function suppression; y, years; <sup>a</sup>administration of chemotherapy was a surrogate marker for higher risk of recurrence in clinical trials; <sup>b</sup>OFS in case of remaining or recurring ovarian function within 24 months after chemotherapy induced amenorrhea; <sup>c</sup>only HER2-negative; <sup>d</sup>only combined with AI + OFS; <sup>e</sup>in case patients wish to become pregnant interruption of adjuvant endocrine therapy after 18 months for a maximum of 2 years is possible without short-term survival disadvantage with a median F/U of only 3.5 years (AGO+).

# Adjuvant Endocrine-based Therapy in Postmenopausal Patients

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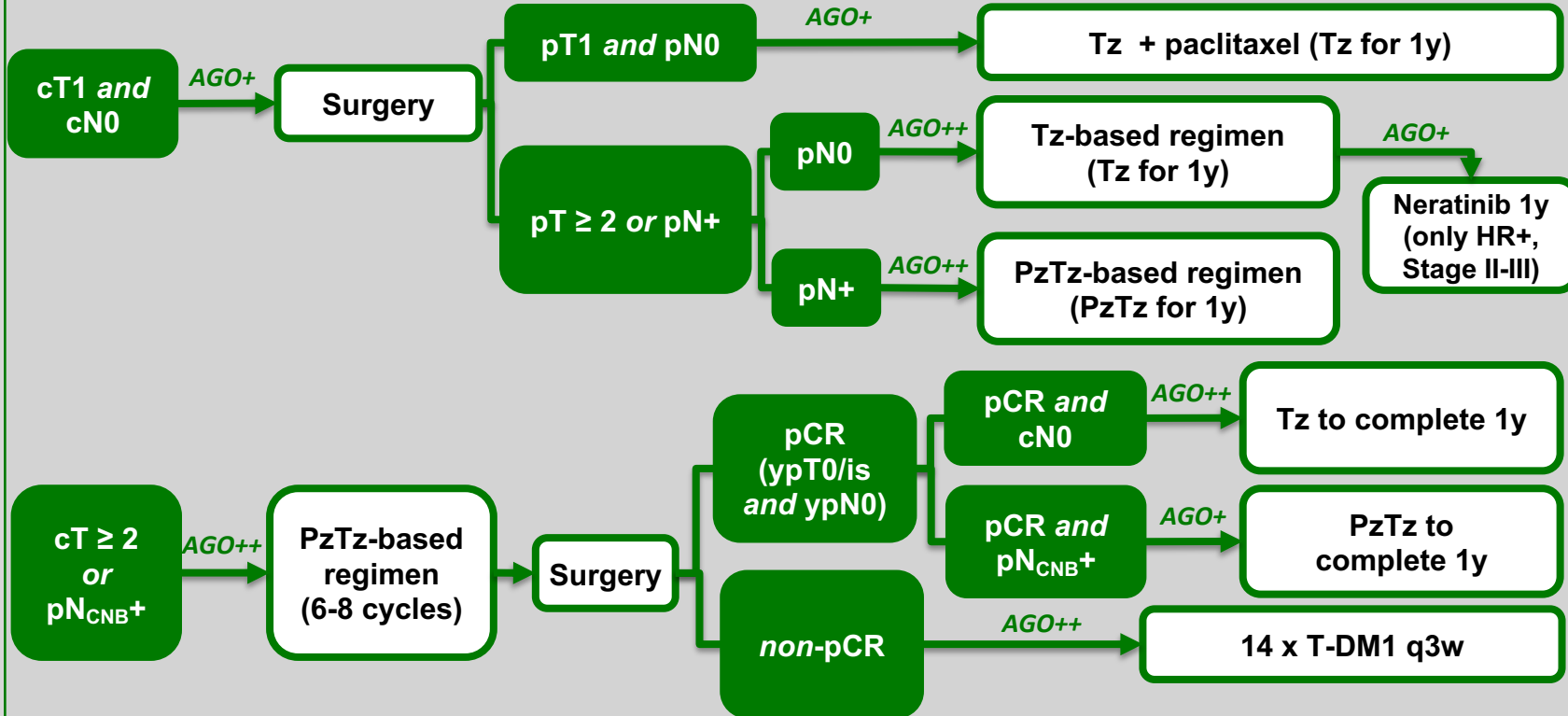


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AI, aromatase inhibitor; CPS-EG, clinical pathological stage + estrogen receptor status and grade score; EAT, extended adjuvant therapy; *gBRCA1/2<sup>mut</sup>*, germline *BRCA1/2* mutation; GEP, gene expression profile; LN, lymph node; non-pCR, no pathological complete response; Tam, tamoxifen; y, years; <sup>a</sup>decision criteria may include: condition after neo(adjuvant) chemotherapy (indicating high risk), positive lymph node status, T2/T3 tumors, elevated risk of recurrence based on immuno-histochemical criteria or based on multi-gene expression assays, regarding EAT high CTS5-Score; <sup>b</sup>up to date no impact on overall survival; <sup>c</sup>only HER2 negative; <sup>d</sup>only combined with AI.

# Therapy of HER2-positive Early Breast Cancer

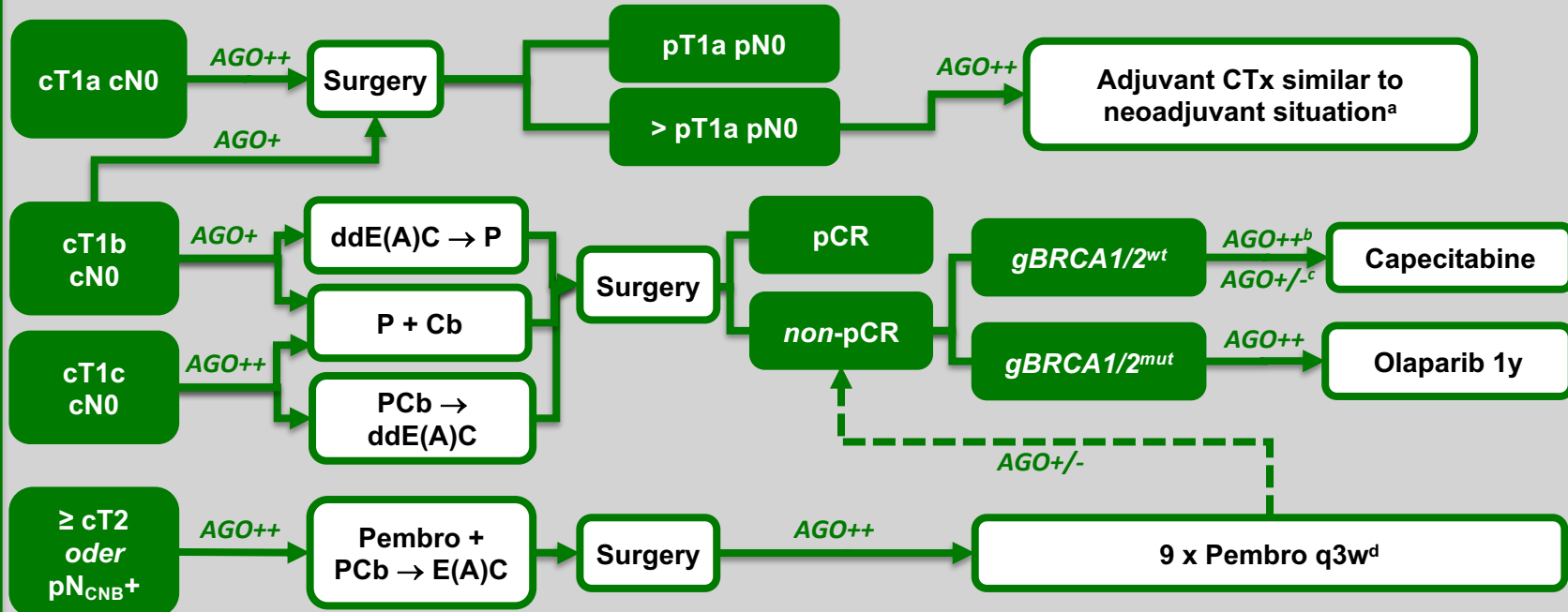
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CNB, core needle biopsy; HR, hormone receptor; pCR, pathological complete response; Pz, Pertuzumab; q3w, every 3 weeks; T-DM1, Trastuzumab emtansine; Tz, Trastuzumab; y, year; if HR+ additional adjuvant endocrine therapy.

# Therapy of Triple-negative Early Breast Cancer

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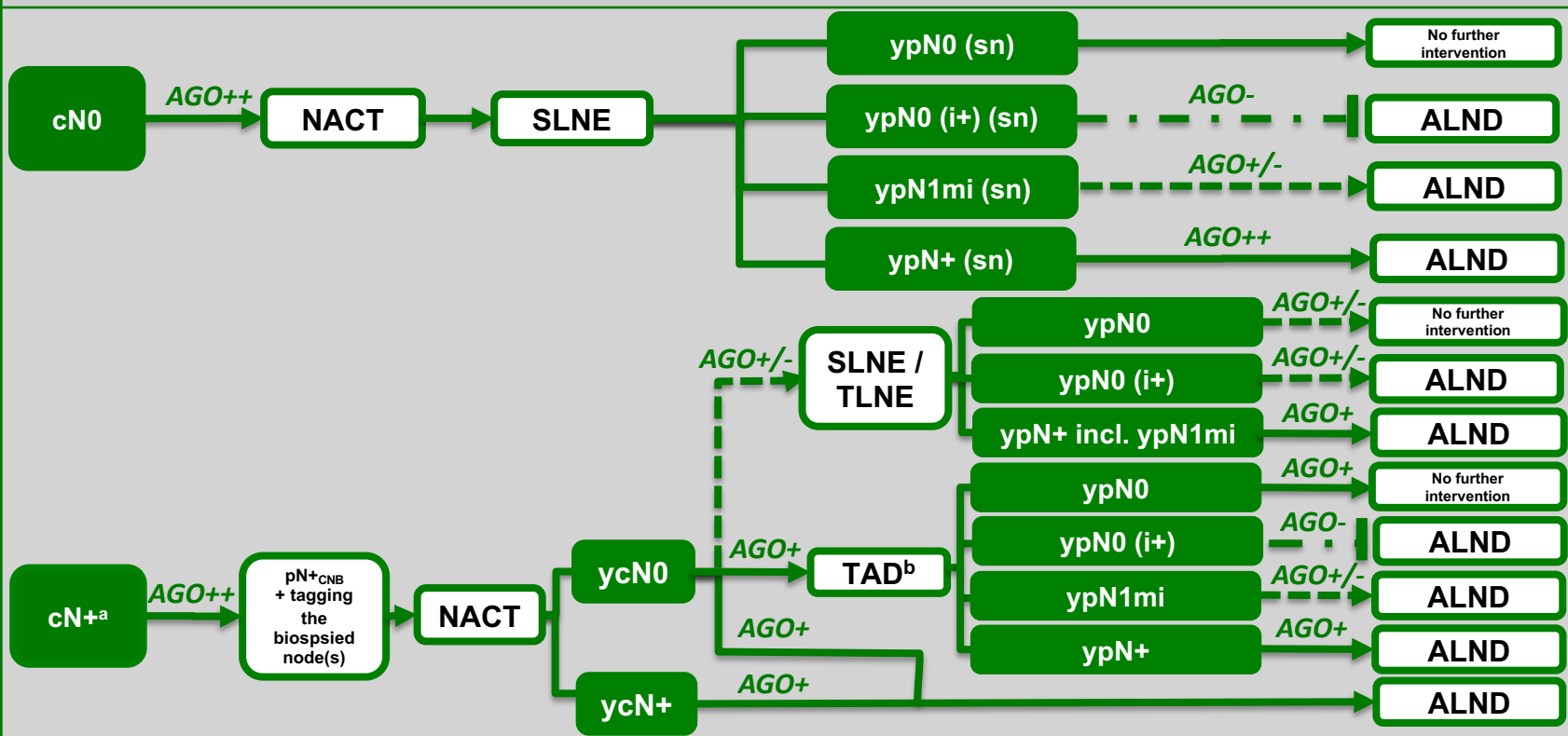


A, doxorubicin; C, cyclophosphamide; Cb, carboplatin; CNB, core needle biopsy; CTx, chemotherapy; dd, dose dense (every 2 weeks); E, epirubicin; *gBRCA1/2<sup>mut</sup>*, germline *BRCA1/2* mutated; *gBRCA1/2<sup>wt</sup>*, germline *BRCA1/2* wild type; pCR, pathological complete response; Pembro, pembrolizumab; P, paclitaxel; y, year; <sup>a</sup>if no change of prognostic factors after surgery; <sup>b</sup>after A/T-containing chemotherapy; <sup>c</sup>after chemotherapy with platinum and/or pembrolizumab; <sup>d</sup>if Pembrolizumab was started before surgery.

# Axillary Surgery and Neoadjuvant Chemotherapy

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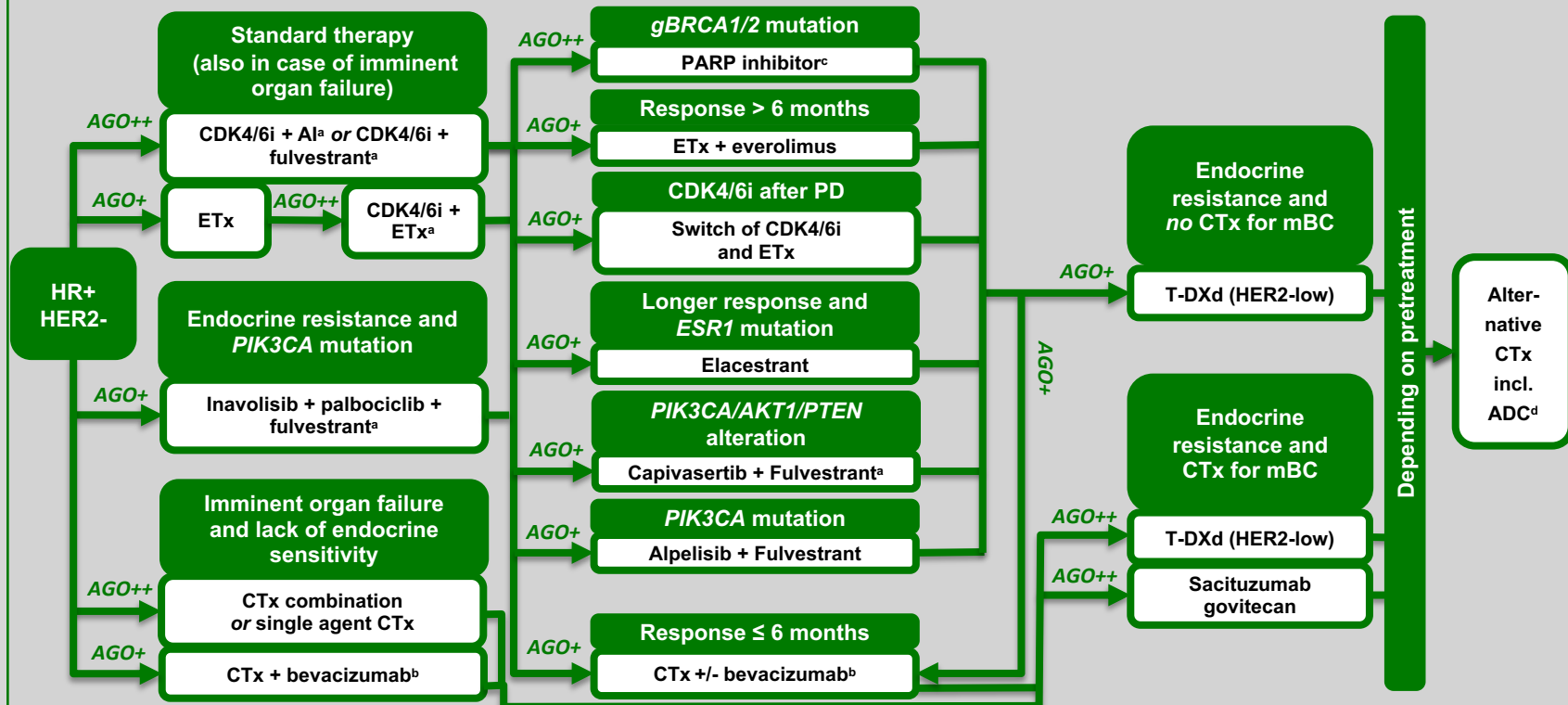


ALND, axillary lymph node dissection; CNB, core needle biopsy; incl., including; NACT, neoadjuvant chemotherapy; sn, sentinel node; SLNE, sentinel lymph node excision; TAD, targeted axillary dissection (SLNE + TLNE); TLNE, targeted lymph node excision; <sup>a</sup>participation in AXSANA study recommended; <sup>b</sup>TAD in case of 1-3 suspicious lymph nodes before NACT AGO+, in case of ≥ 4 suspicious lymph nodes before NACT AGO +/-.

# HR-positive, HER2-negative Metastatic Breast Cancer

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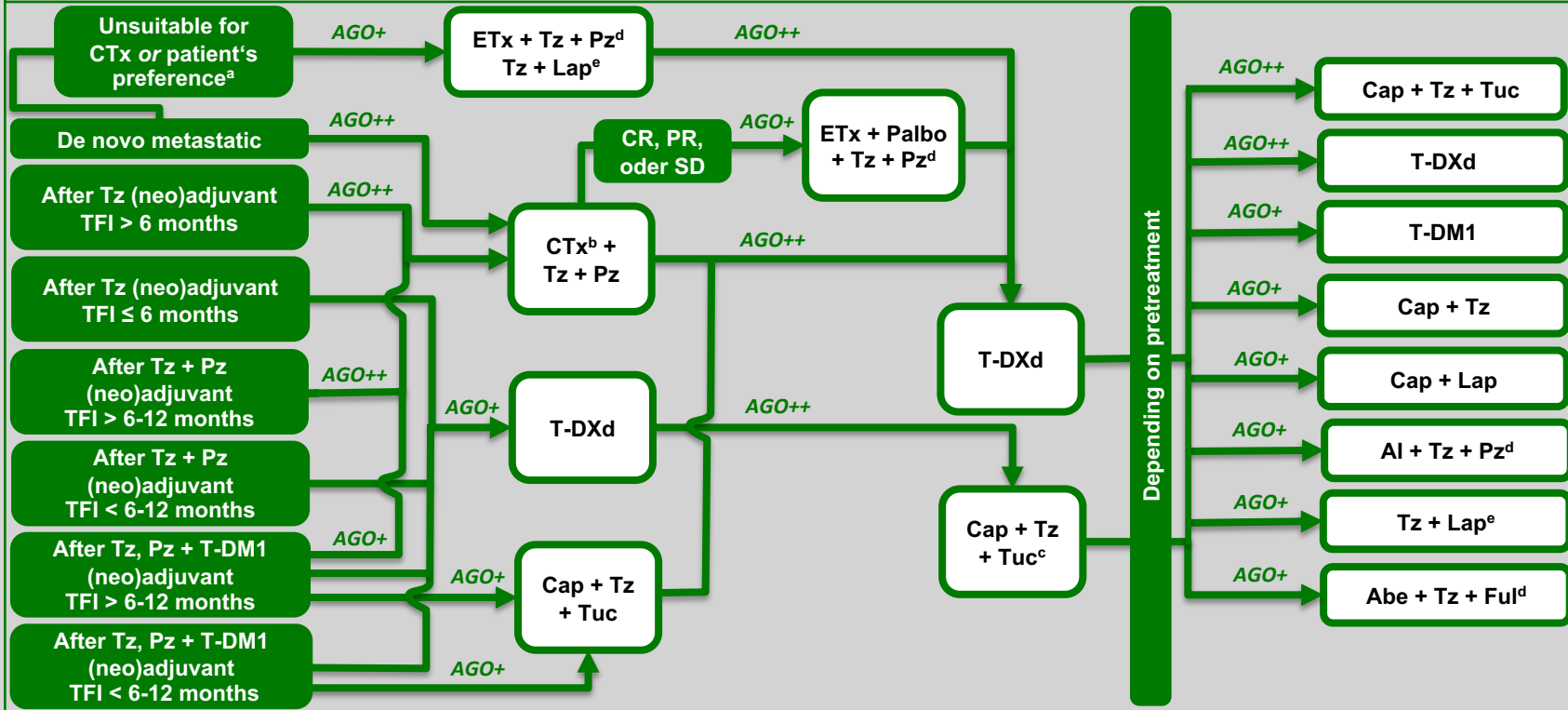


ADC, antibody drug conjugate; AI, aromatase inhibitor; CDK4/6i, CDK4/6 inhibitor; CTx, chemotherapy; ETx, endocrine therapy; gBRCA1/2 mutation, germline BRCA1/2 mutation; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; incl., including; mBC, metastatic breast cancer; PD, progressive disease; T-DXd, trastuzumab deruxtecan; <sup>a</sup>if premenopausal add ovarian function suppression; <sup>b</sup>bevacizumab + paclitaxel or bevacizumab + capecitabine; <sup>c</sup>olaparib also in case of germline PALB2 mutation or somatic BRCA1/2 mutation (AGO+); <sup>d</sup>use of not previously used compounds or regimen.

# HER2-positive Metastatic Breast Cancer

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Abe, Abemaciclib; AI, aromatase inhibitor; Cap, capecitabine; CR, complete response; CTx, chemotherapy; ETx, endocrine therapy; Ful, Fulvestrant; HR, hormone receptor; Lap, lapatinib; Palbo, palbociclib; PR, partial response; Pz, pertuzumab; SD, stable disease; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TFI, treatment-free interval; Tuc, tucatinib; Tz, trastuzumab; <sup>a</sup>no overall survival benefit, consider induction chemotherapy; <sup>b</sup>docetaxel (AGO++), paclitaxel (AGO++) or nab-paclitaxel (AGO+); <sup>c</sup>only after T-DM1; <sup>d</sup>only if HR positive; <sup>e</sup>only if HR negative.

