

Diagnosis and Treatment of Patients with Early and Advanced Breast Cancer



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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

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- **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

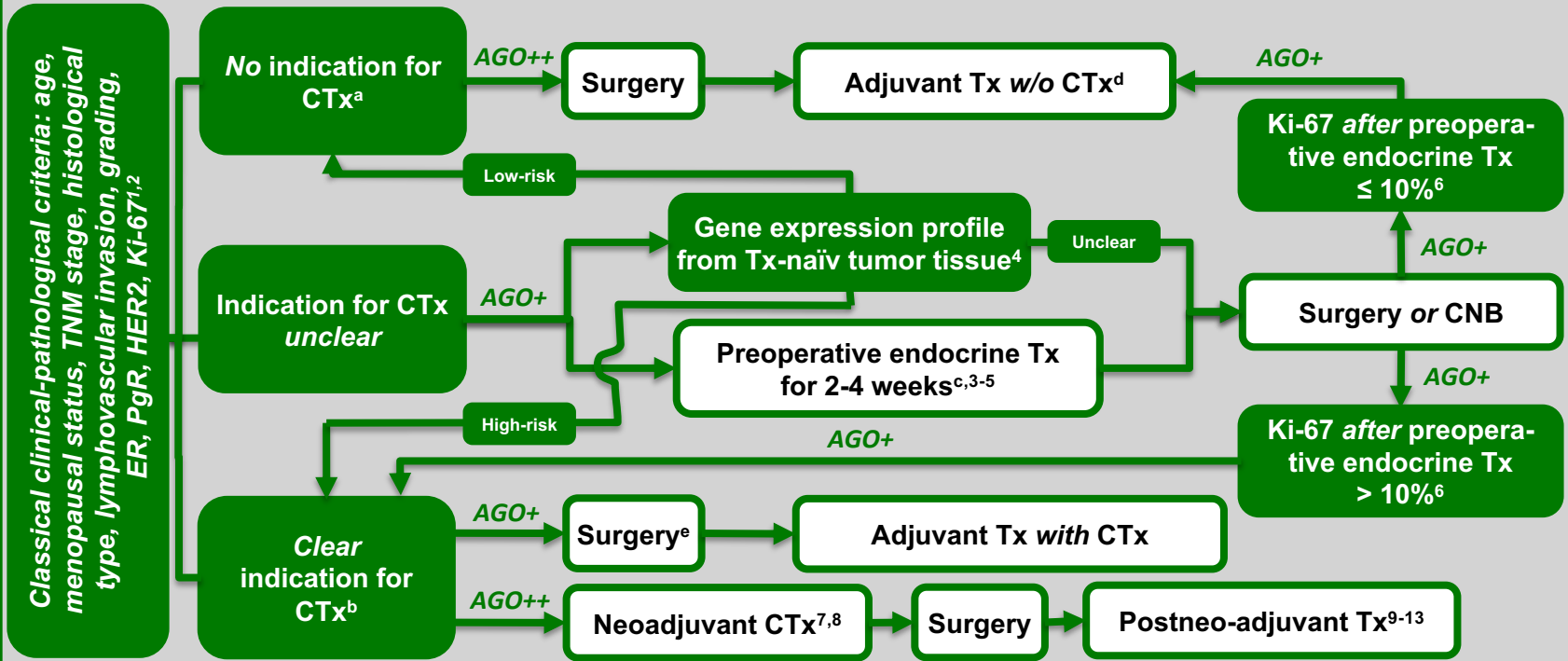
■ Metastatic breast cancer

- 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

Therapy of HR-positive, HER2-negative Early Breast Cancer: Strategies

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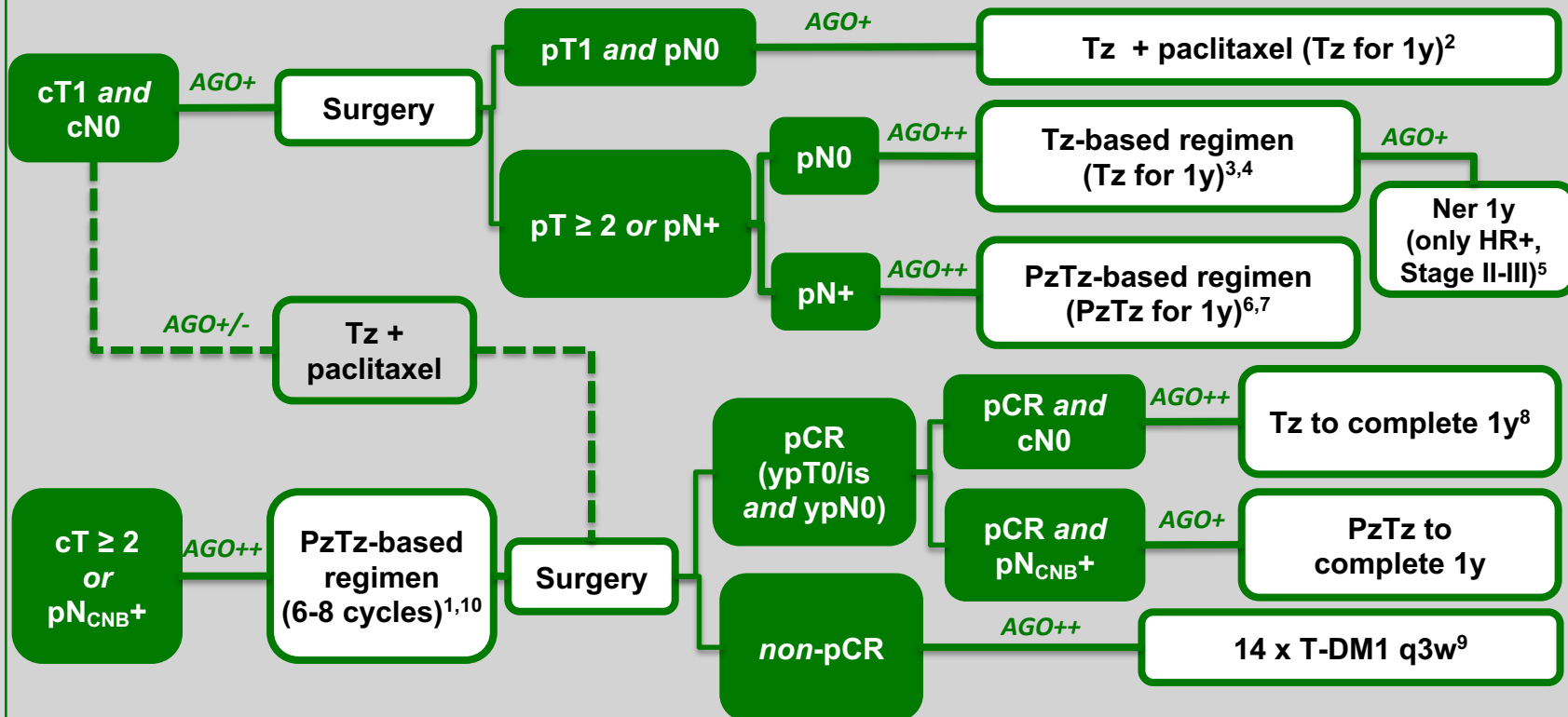
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CNB, Stanzbiopsie (core needle biopsy); CTx, chemotherapy; ER, estrogen receptor; PgR, progesterone receptor; HER2, human epidermal growth factor receptor 2; HR, Hormonrezeptor; Tx, therapy; w/o, without; ^ae.g. \leq T1c cN0-1 G1-2 Ki-67 \leq 5% or -if situation unclear- low-risk gene expression profile; ^be.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; ^cstandard endocrine Tx; ^dif no change of prognostic factors after surgery; ^eif not already done.

Therapy of HER2-positive Early Breast Cancer

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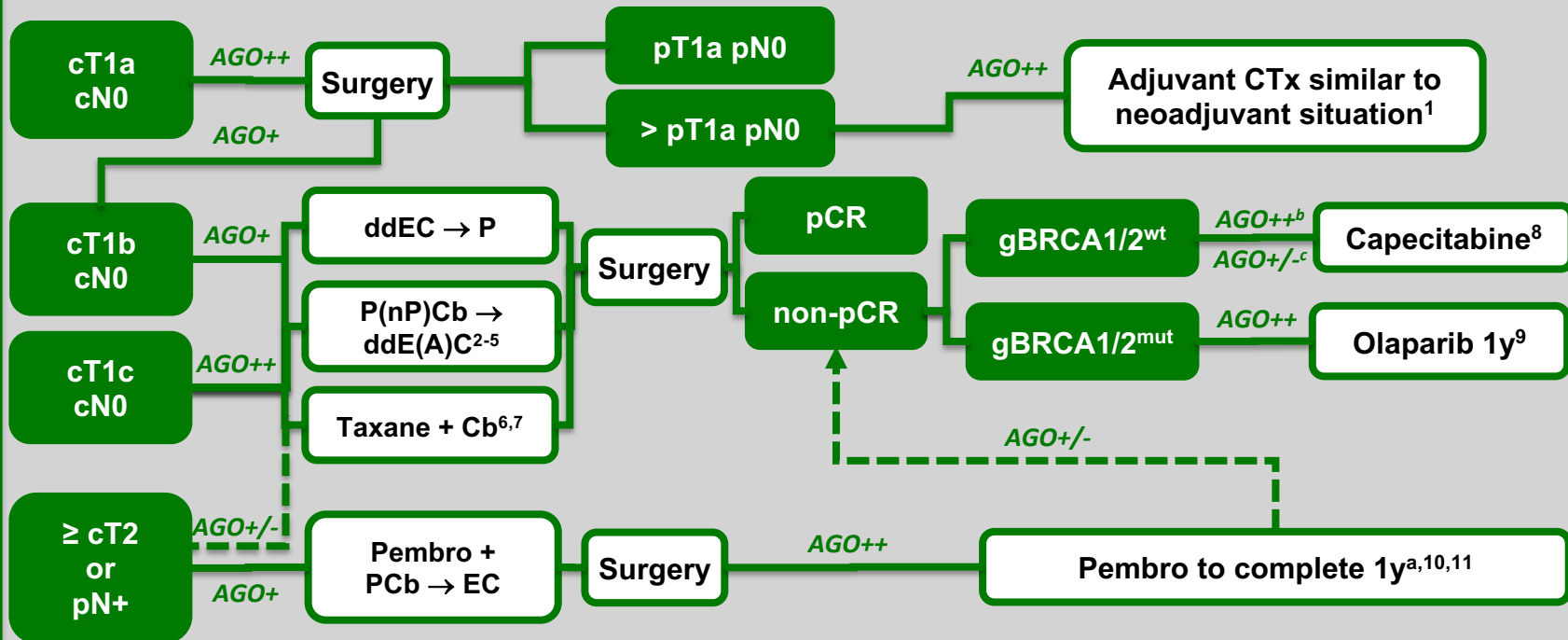
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CNB, core needle biopsy; HR, hormone receptor; Ner, Neratinib; pCR, pathological complete response; Pz, Pertuzumab; q3w, every 3 weeks; T-DM1, Trastuzumab emtansine; Tz, Trastuzumab; y, year; if HR+ adjuvant endocrine therapy

Therapy of Triple-negative Early Breast Cancer

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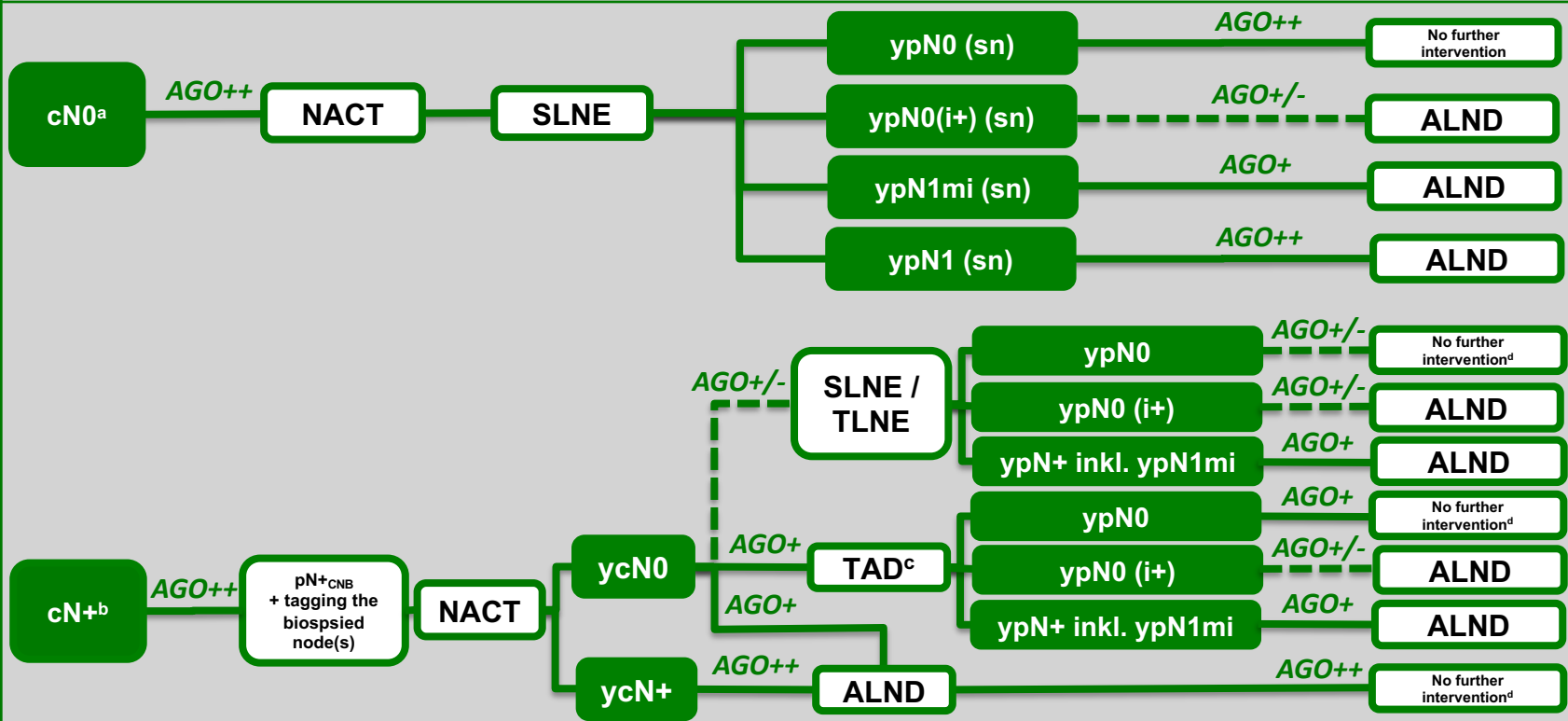


A, doxorubicin; C, cyclophosphamide; Cb, carboplatin; CTx, chemotherapy; dd, dose dense (every 2 weeks); E, epirubicin; mut, mutated; nP, nab-paclitaxel; Pembro, pembrolizumab; P, paclitaxel; wt, wild type; y, year; ^a if Pembrolizumab was started before surgery; ^b after A/T-containing chemotherapy; ^c after chemotherapy with platinum and/or pembrolizumab.

Axillary Surgery and Neoadjuvant Chemotherapy (NACT)

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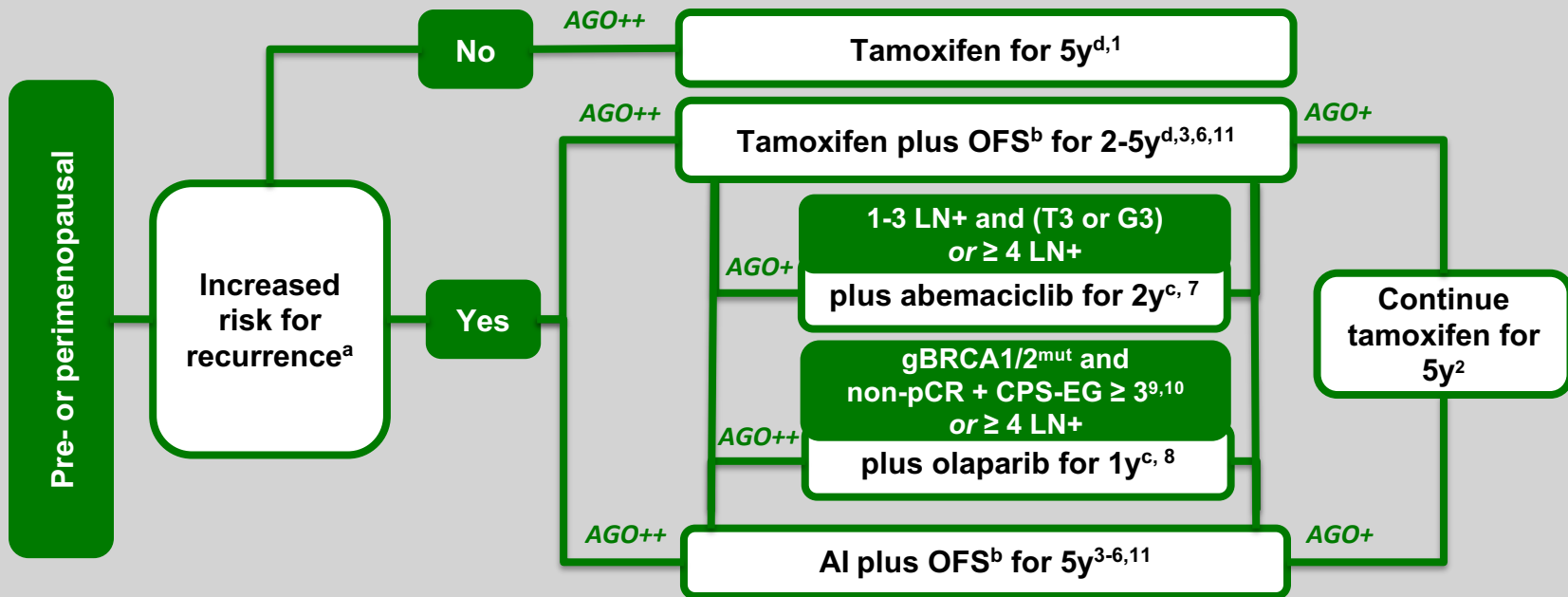


ALND, axillary lymph node dissection; CNB, core needle biopsy; NACT, neoadjuvant chemotherapy; sn, sentinel node; SLNE, sentinel lymph node excision; TAD, targeted axillary dissection (SLNE + TLNE); TLNE, targeted lymph node excision; ^a participation in EUBREAST-01 study recommended; ^b participation in AXSANA study recommended; ^c TAD in case of 1-3 suspicious lymph nodes before NACT: +, in case of ≥ 4 suspicious lymph nodes before NACT: +/-; ^d for radiotherapy procedures see recommendations for radiotherapy.

Adjuvant Endocrine-based Therapy in Premenopausal Patients

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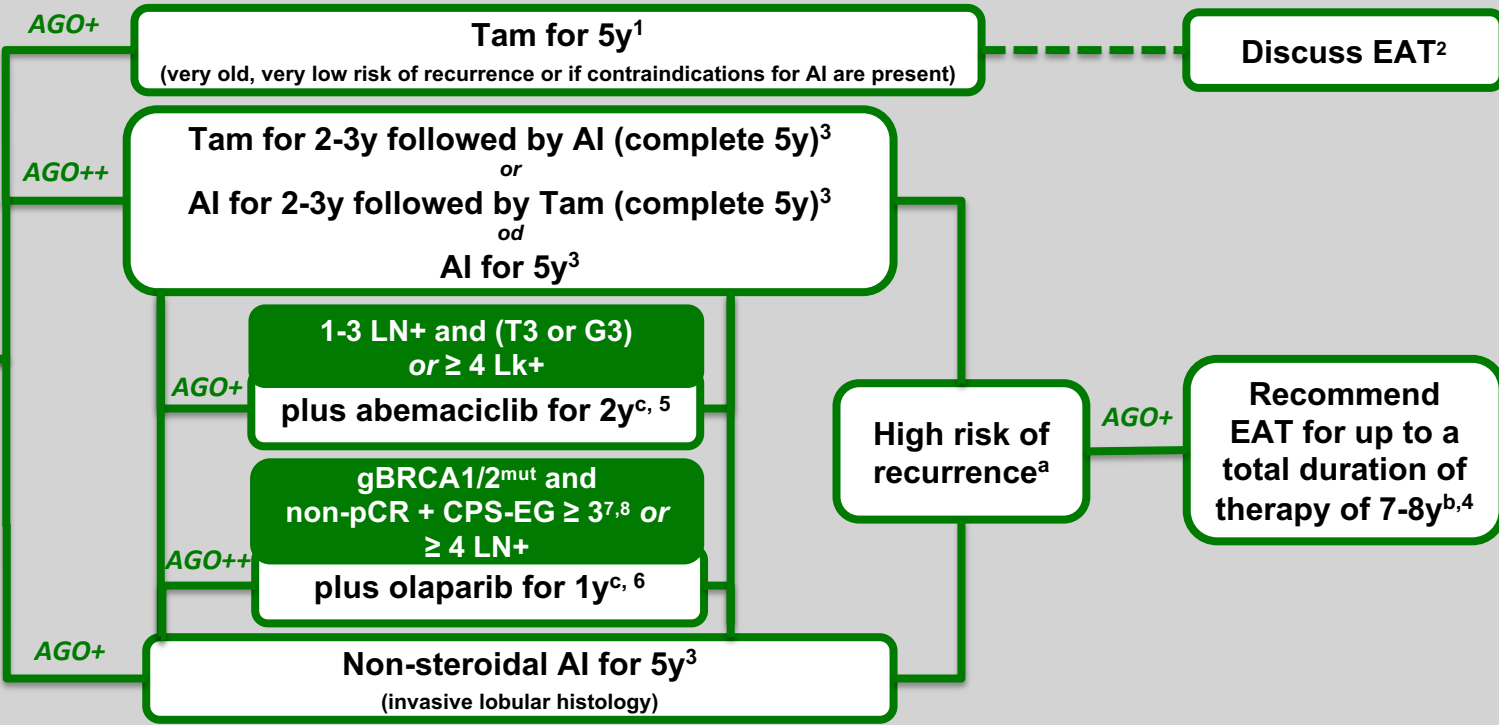
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AI, aromatase inhibitor; CPS-EG, clinical pathological stage + estrogen receptor status and grade score; gBRCA1/2^{mut}, germ line BRCA1/2 mutation; LN, lymph node; OFS, ovarian function suppression; pCR, pathologic complete response; y, years; ^aAdministration of chemotherapy was a surrogate marker for higher risk of recurrence in clinical trials; ^bOFS also in case of remaining or recurring ovarian function within 24 months after chemotherapy induced amenorrhea; ^conly HER2-negative; ^dIn 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

Postmenopausal before the start of adjuvant therapy



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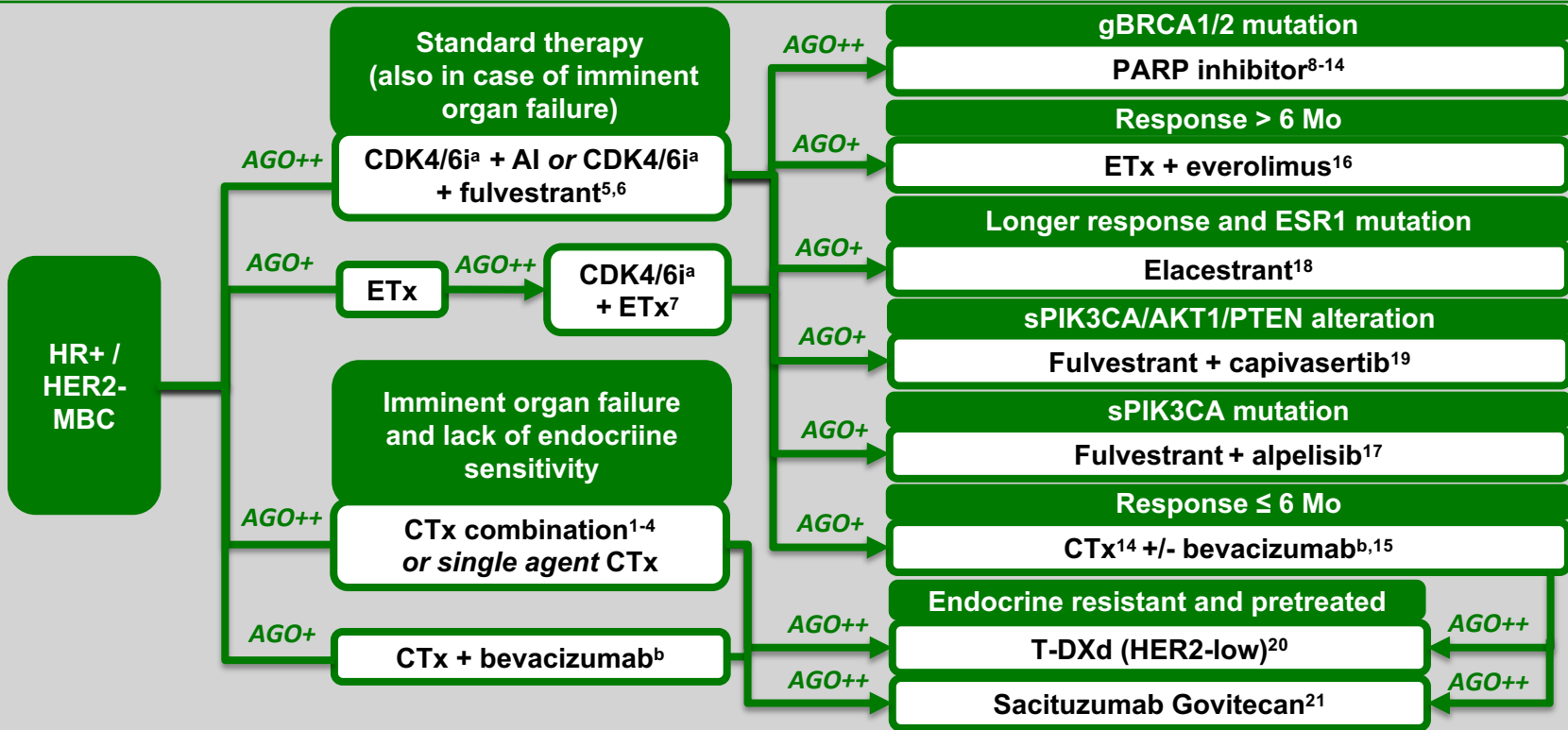
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AI, aromatase inhibitor; CPS-EG, clinical pathological stage + estrogen receptor status and grade score; EAT, extended adjuvant therapy; gBRCA1/2^{mut}, germ line BRCA1/2 mutation; LN, lymph node; Tam, tamoxifen; y, years; ^a decision criteria may 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, high CTS5-Score; ^b up to date no impact on overall survival; ^c only HER2 negative.

HR-positive/HER2-negative Metastatic Breast Cancer: Strategies

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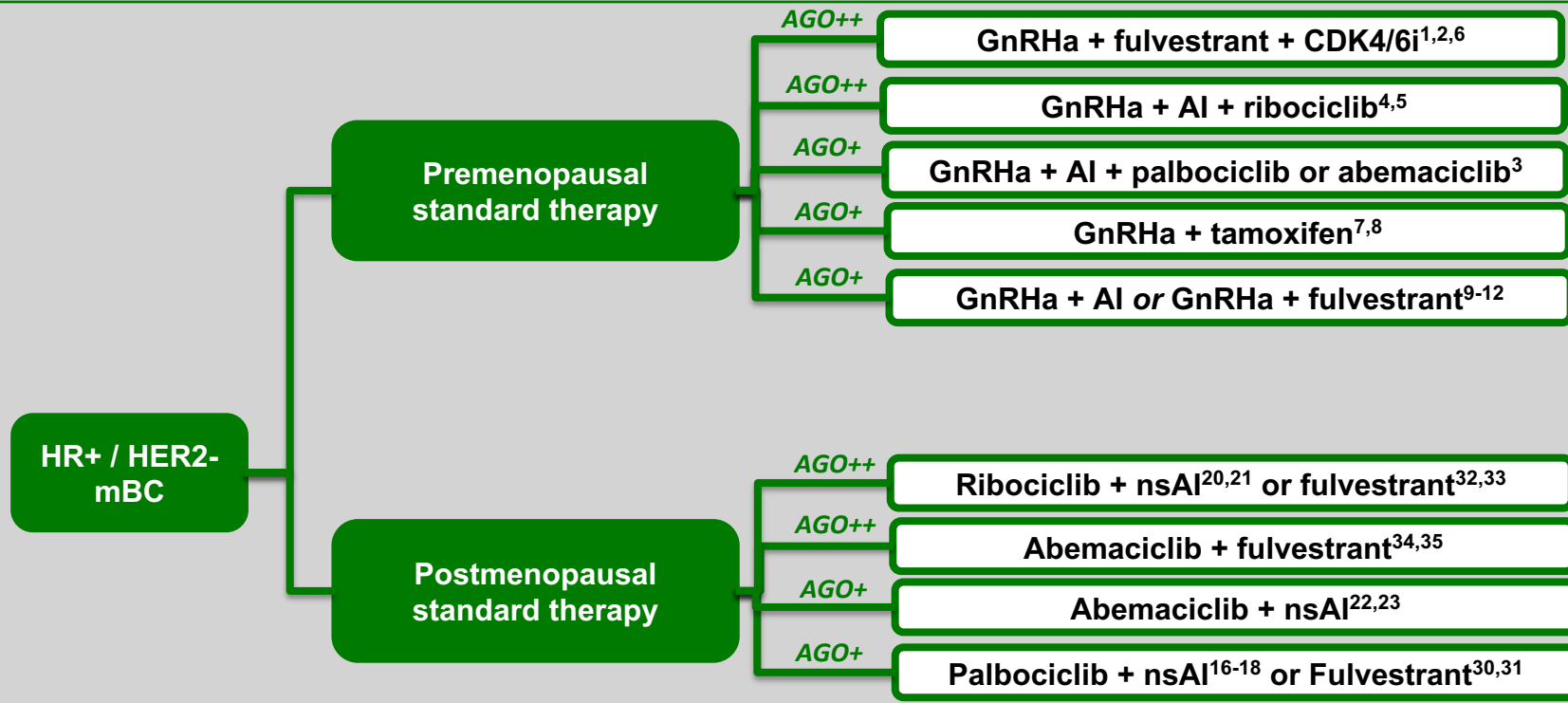


AI, aromatase inhibitor; CDK4/6i, CDK4/6 inhibitor; CTx, chemotherapy; ETx, endocrine therapy; gBRCA1/2 mutation, germ line BRCA1/2 mutation; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; MBC, metastatic breast cancer; mo, months; sPIK3CA mutation, somatic PIK3CA mutation; sPIK3CA/AKT1/PTEN alteration, somatic PIK3CA/AKT1/PTEN alteration; T-DXd, trastuzumab deruxtecan; ^a if premenopausal add ovarian function suppression; ^b bevacizumab + paclitaxel or + capecitabine.

HR-positive / HER2-negative Metastatic Breast Cancer: Endocrine-based First Line Treatment

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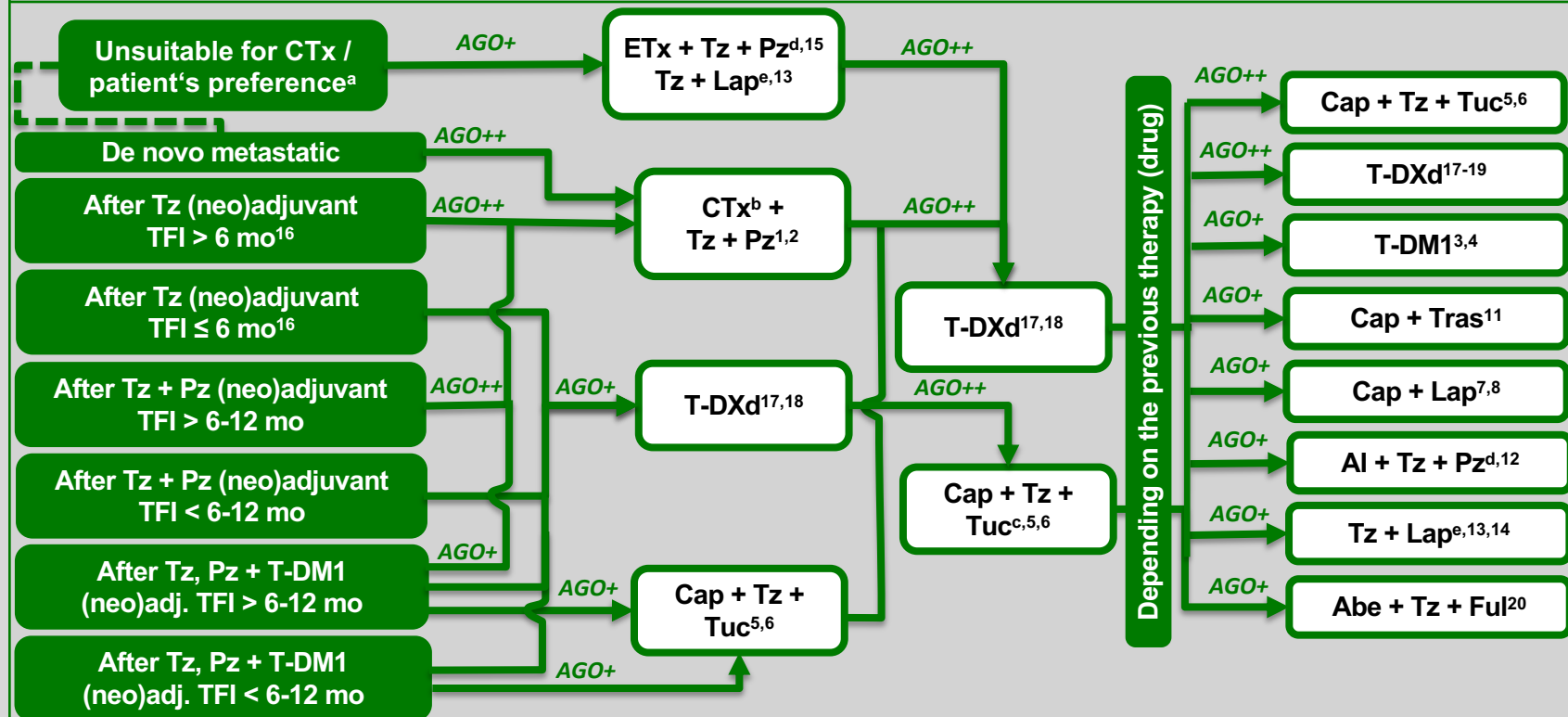
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AI, aromatase inhibitor; CDK4/6i, CDK4/6 inhibitor; GnRHa, GnRH agonist; HR, hormone receptor; ns, non-steroidal; mBC, metastatic breast cancer; mo, months; TFI, treatment-free interval.

HER2-positive Metastatic Breast Cancer: 1st-3rd-line

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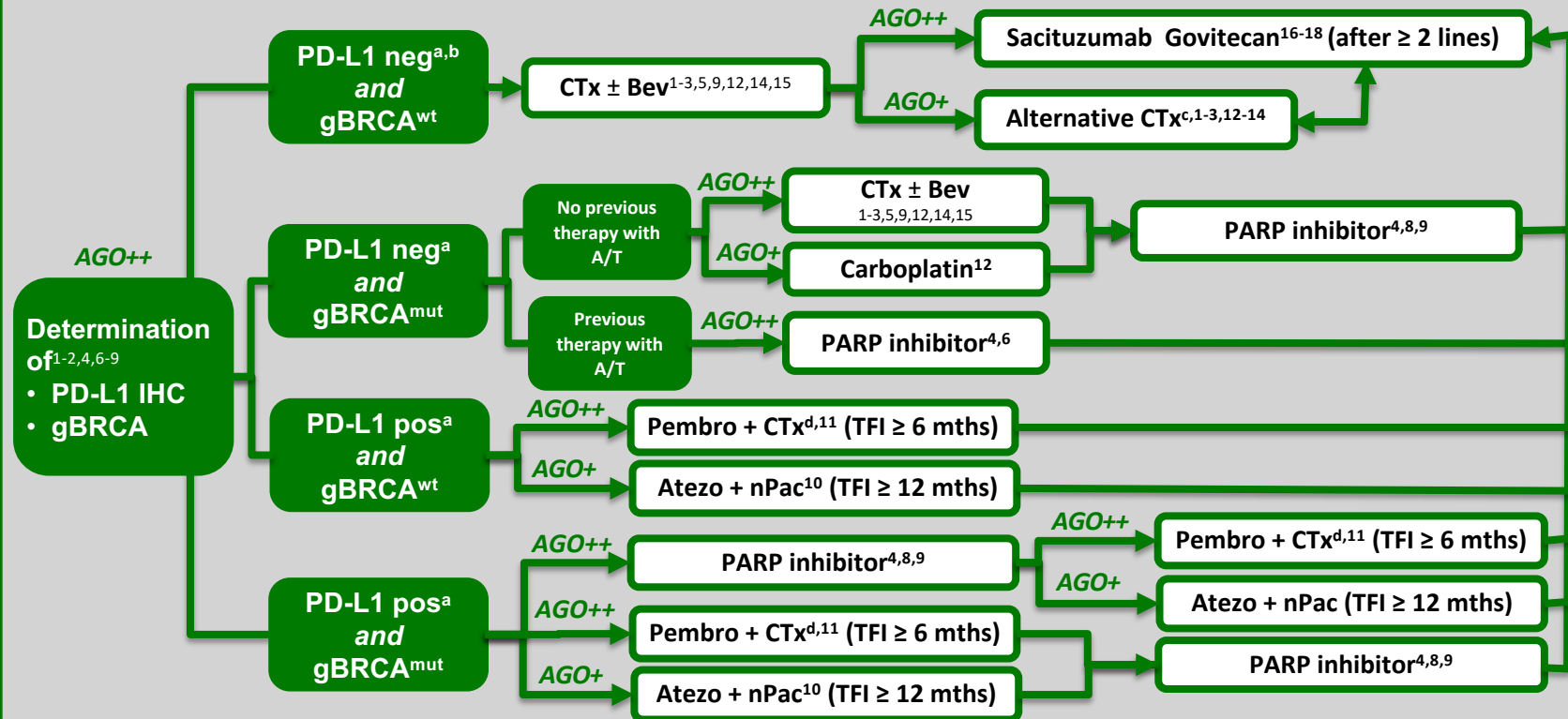


Abe, Abemaciclib; AI, aromatase inhibitor; Cap, capecitabine; CTx, chemotherapy; ETx, endocrine therapy; Ful, Fulvestrant; HR, hormone receptor; Lap, lapatinib; mo, months; Ner, neratinib; Pz, pertuzumab; T-DM1, trastuzumab emtansine; T-DXd, trastuzumab deruxtecan; TFI, treatment-free interval; Tuc, tucatinib; Tz, trastuzumab; ^a no overall survival benefit, consider induction chemotherapy; ^b docetaxel (++) , paclitaxel (++) or nab-paclitaxel (+); ^c only after T-DM1; ^d only if HR pos; ^e only if HR neg.

Triple-negative Metastatic Breast Cancer

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A, anthracycline; Atezo, atezolizumab; Bev, bevacizumab; CTx, chemotherapy; gBRCA, germ line BRCA status; IHC, immunohistochemistry; mths, months; mut, mutated; neg, negative; ; nPac, nab-paclitaxel; Pembro, pembrolizumab; PD-L1, programmed cell death ligand 1; pos, positive; T, taxane; TFI, treatment-free interval; wt, wild type; ^aPembro: CPS < 10 (neg) oder CPS ≥ 10 (pos), Atezo: IC < 1% (neg), IC ≥ 1% (pos); ^bPD-L1 pos with a TFI < 6-12 Mo; ^cuse of not previously used compounds or regimen; ^dnPac, Pac or Carboplatin+Gemcitabin.