"NEOADJUVANT SYSTEMIC TREATMENT (NST) IN BREAST CANCER (BC)"

A BRIEF UPDATE

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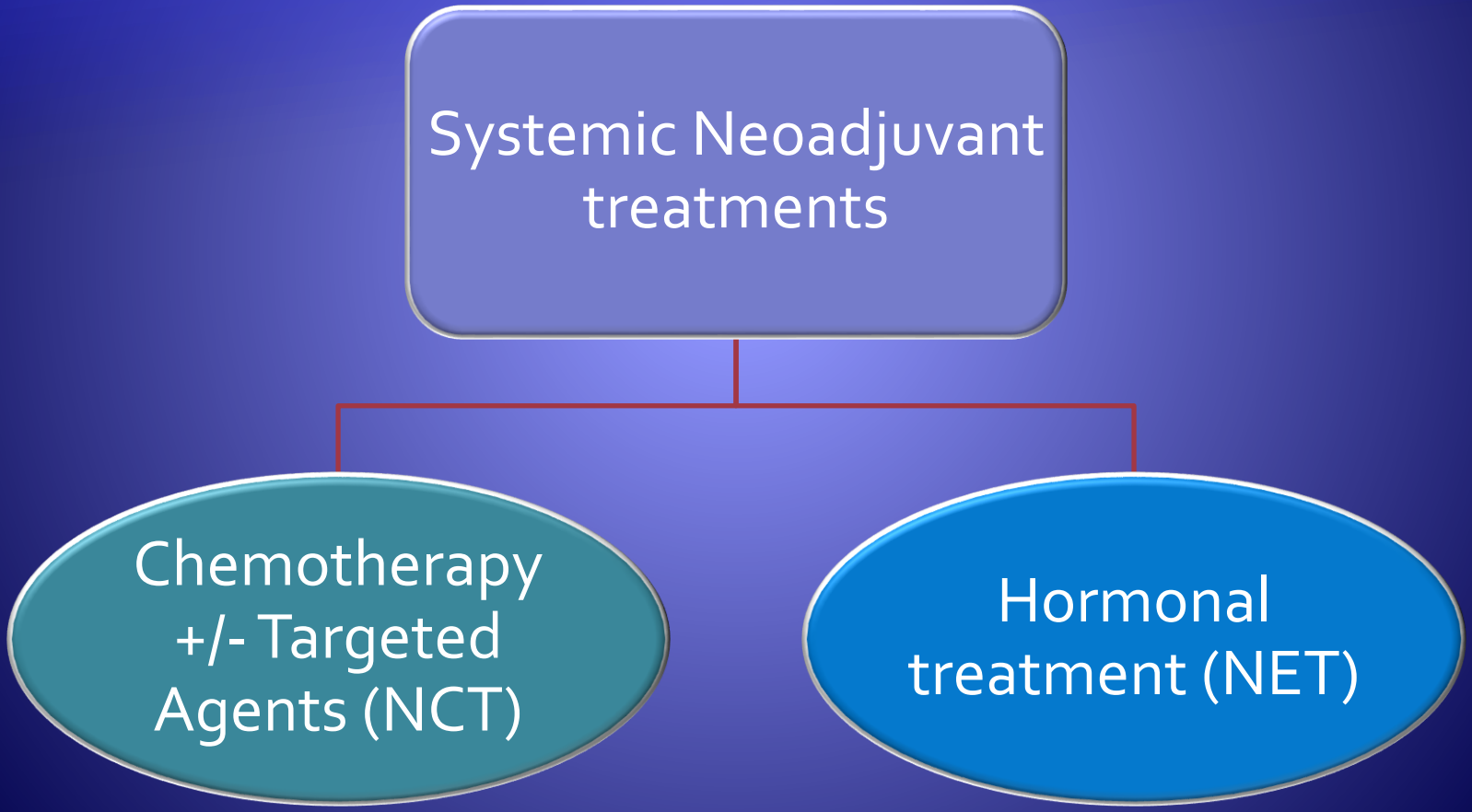
Topics to be discussed

- Benefits of neoadjuvant systemic treatment (NST).
- Pathological complete response (pCR): definition and significance.
- Available NST options (Chemo, targeted, and hormonal).
- Monitoring the response to NST.
- Multimodality approach in locally advanced breast cancer (LABC).

Types of NST


Systemic Neoadjuvant treatments
Chemotherapy +/- Targeted Agents (NCT)
Hormonal treatment (NET)

Benefits of NST

- Significant improvement of both DFS & OS; same like the one seen by the adjuvant treatment.
- Permits in vivo chemosensitivity testing.
- Allows tumor down-staging; so it can:
  - Convert initially inoperable breast cancers to operable ones.
  - Convert patients with BC requiring mastectomy to be candidates for a breast conservative surgery (BCS).
  - Potentially improve the cosmetic outcome in those patients initially are candidates to BCS *(unproven)*.
- Achieving ***pCR*** at the time of surgery correlates with significant improvement in DFS.

Benefits of NST …. Continued

Response Rates with NST

- Tumor response rates for NCT:
  - cOR rate: 80 - 90%
  - cCR rate: 20 - 50%
  - pCR rate: 15 - 40%

- Tumor OR to NET is variable, but may reach up to 70% in selected cases.

Benefits of NST …. Continued

pCR

- **Definition:** a CR based on histopathological assessment revealing absence of both invasive and non-invasive disease in both breast and axilla.

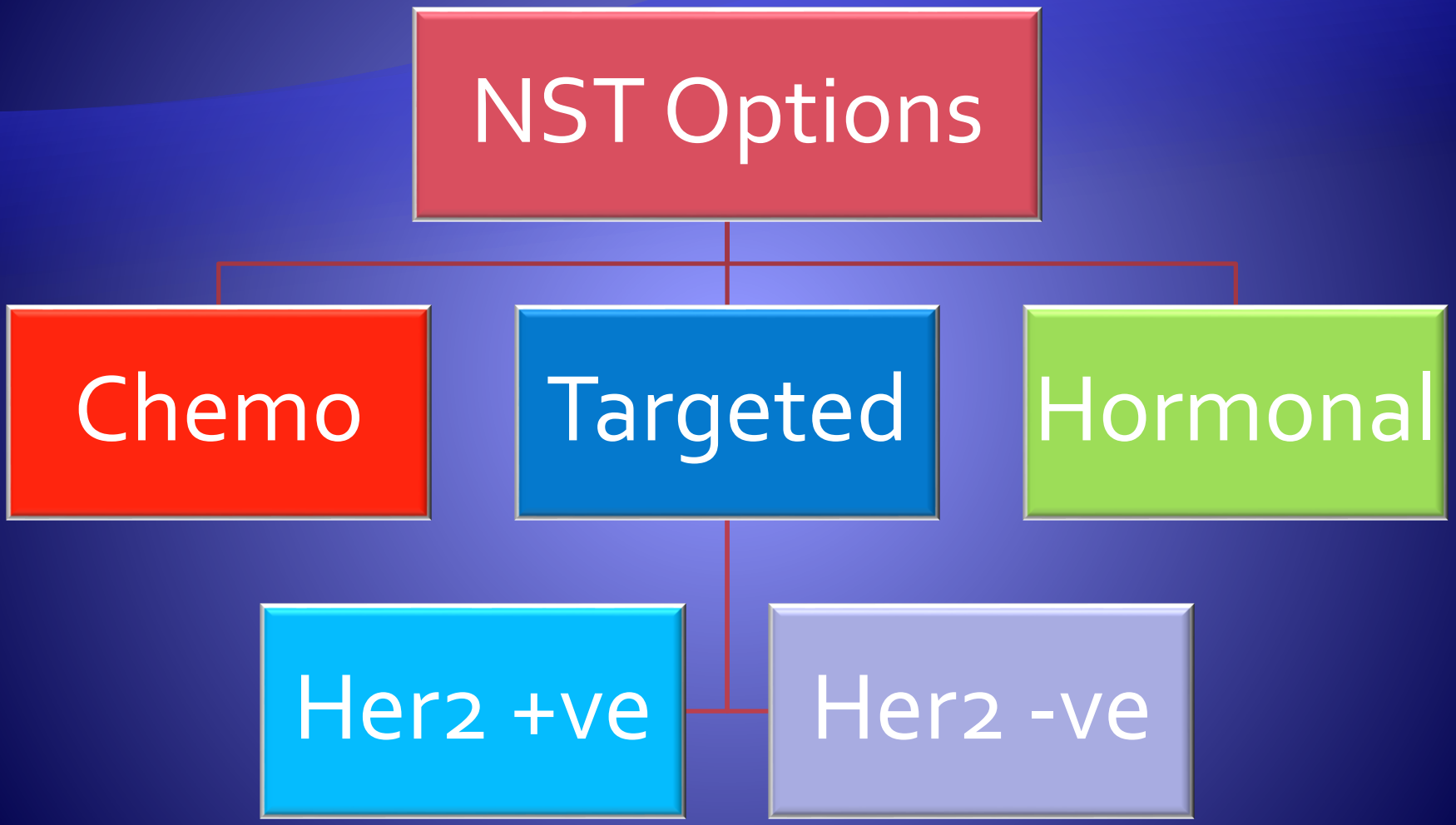
- **Significance:** ***pCR*** is considered to be the gold standard for predicting long-term outcome in BC patients after NST. ***pCR*** is a primary end-point in all NST trials in BC. However, evaluation by intrinsic subtype showed that the long-term survival benefit associated with ***pCR*** for TNBC and Her2-amplified subgroups, in contrast, in luminal A&B subgroups, ***pCR*** did not have prognostic impact. ***pCR*** after NET is less frequent and can not be considered as a surrogate of long-term benefit , instead, other markers can be used e.g. proliferation indices (Ki-67).

Benefits of NST …pCR… Continued

Q: How to predict the likelihood of achieving ***pCR*** after NST?

A: By either:

- **Clinicopathologic characteristics:** with higher likelihood of achieving ***pCR*** when: patient's age <40 years, tumor: size <2 cm, ductal, G3, with high *ki-67* and basal or Her2-overexpressed intrinsic subtypes. One drawback of using this method is that it can not predict likelihood with certainty as the positive predictive value is 30 – 50%.
- **Nomograms:** using them is encouraged as the their predictive strength is as good as or even better than that of gene signature.


NST Options
Chemo
Targeted
Hormonal
Her2 +ve
Her2 -ve

NST Options … Continued

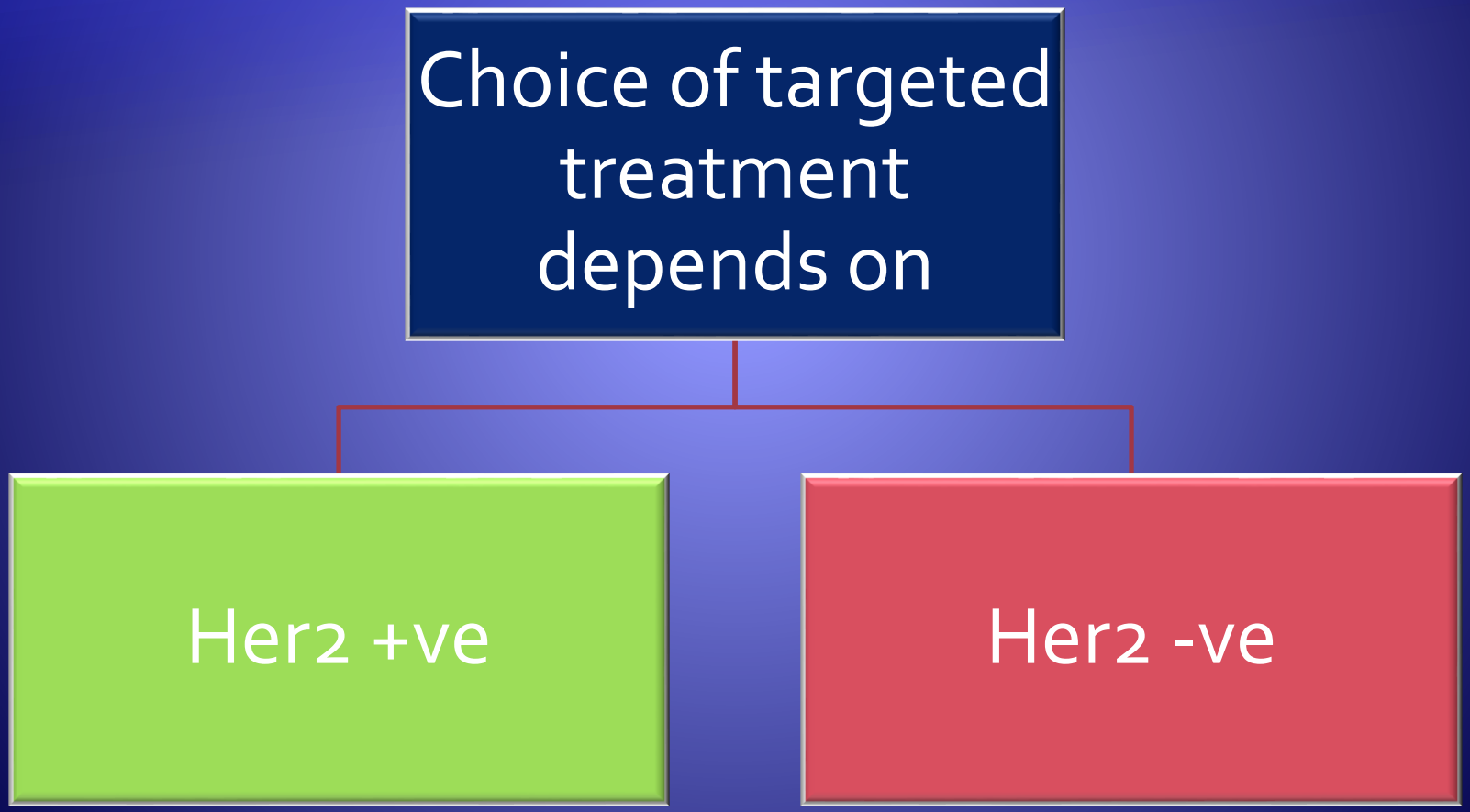
Neoadj. Chemotherapy (NCT)

- Routine practice is to use anthracyclines and taxanes, as in the adjuvant setting, concurrently or sequentially for 4 to 6 months. **Examples** of available regimens: FAC or FEC → weekly paclitaxel or every 3 weeks docetaxel, TAC, and AC. Recently, an emerging evidence suggests using dose-dense (dd) regimens may improve ***pCR*** rate.
- The use of Carboplatin with standard chemo (weekly paclitaxel and doxorubicin) in both TNBC and Her2 +ve disease, has led to a nearly 10% more improvement in ***pCR*** rate compared to the same chemo regimen without carboplatin.

- All chemo should be provided pre-operatively rather than splitting it into pre & post-operative. However, performing part of the chemo post-operatively is still acceptable *(but not preferred).*

NST Options … Continued

Neoadj. Targeted Treatment (NTT)



NST Options …NTT … Continued

Her2 +ve Disease

- **Trastuzumab:** should be started with the Taxane part of the NCT as this strategy proved to increase the probability of achieving a ***pCR*** . *Trastuzumab* must not be given concurrently with anthracyclines. *Trastuzumab* can be given alone in patients whom can not tolerate Chemo.

- **Trastuzumab** with **Pertuzumab** added to NCT (docetaxel): has led an increase in ***pCR*** rate and DFS compared to Trastuzumab and docetaxel alone.

NST Options …NTT … Continued

Her2 -ve Disease

- **Bevacizumab:** the use of this VEGFR inhibitor together with chemotherapy has significantly improved pCR rate compared to chemotherapy alone (20 vs 15% respectively). **ICC** on breast cancer stated that *Bevacizumab* is promising in the NST setting specially in TNBC and BRCA mutation +ve disease. However, still *Bevacizumab*, in the in this setting, can only be provided within the context of clinical trials.

- **mTOR inhibitors:** according to the ICC, it's promising but still investigational.

NST Options … Continued

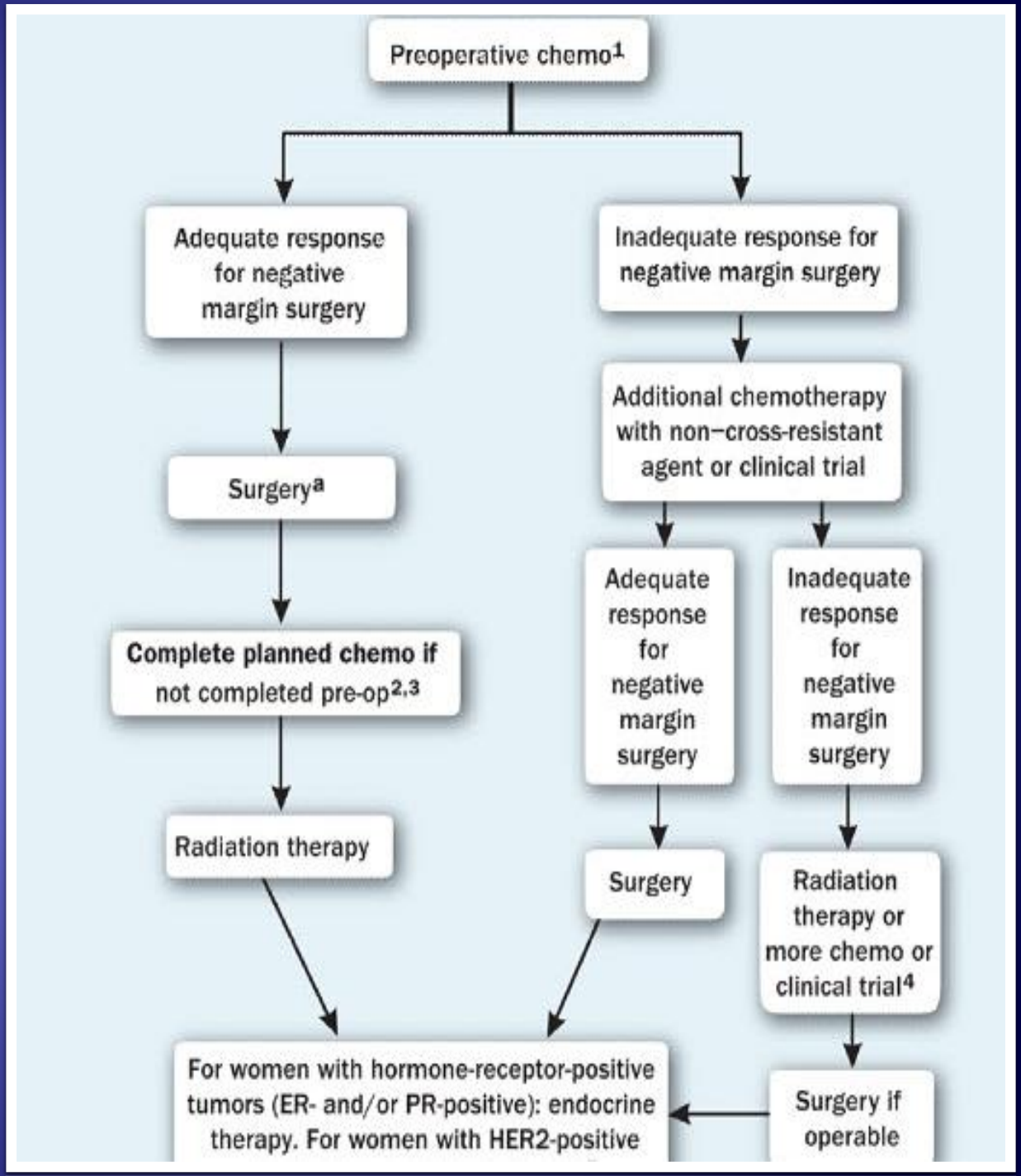
Hormonal Treatment

- **Indication:** candidates of ET in the neoadjuvant setting of BC are those postmenopausal patients with highly endocrine responsive disease.
- **Duration of treatment:** 4 to 8 months, or until maximal response is obtained.
- **Agent to be used:** Aromatase inhibitors (Ais) are used rather than SERM. No difference between the 3 available AIs was seen.

Monitoring Response to NST

- **Performing baseline assessment:**
  - Physical examination of the breast and all nodal areas.
  - Bilateral sono-mammography.
  - Tumor core biopsies (minimum 2 – 3) should be taken for the determination of type and grade of the tumor , as well as ER/PR and Her2 assessment. Placement of surgical clips at that time is highly recommended for tumor bed localization.
- **Monitoring during treatment:**
  - Clinical assessment before each NST cycle.
  - By imaging studies: Nature and frequency is controversial, but generally, it imaging studies should be repeated after NST to assess response and plan for surgery

Multimodality approach to locally advanced breast cancer



THANK YOU

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