Neoadjuvant Therapy for HR+ve/Her2 neu Negative Breast Cancer Surgery First

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NACT -Advantages, yes but a trade-off, too

Impact on surgery

Benefits:

- Downstage tumours to permit breast-conserving surgery rather than mastectomy improving cosmetic outcomes.
- De-escalate surgical treatment of the axilla
- Provide time for germline mutation test results (i.e. BRCA1/2) that may influence surgical plan.

Potential concerns:

- Cancer may progress and become inoperable (a rare event with appropriate monitoring of response.
- Reduced window of opportunity for fertility preservation .
- Increasing tumour response may not achieve a reduction in mastectomy rates, regardless of downstaging and effectiveness of therapy regimen.
- Increased locoregional recurrence rates in patients who do not undergo surgery after neoadjuvant treatment

Disease information and monitoring

Benefits

1.Provide individualised post-treatment prognostic information (e.g. pathological complete response, residual cancer burden) for management decisions.

2. Permits clinicians to monitor response to therapy at an early stage; potentially allowing time and flexibility to switch therapies if patients do not respond.

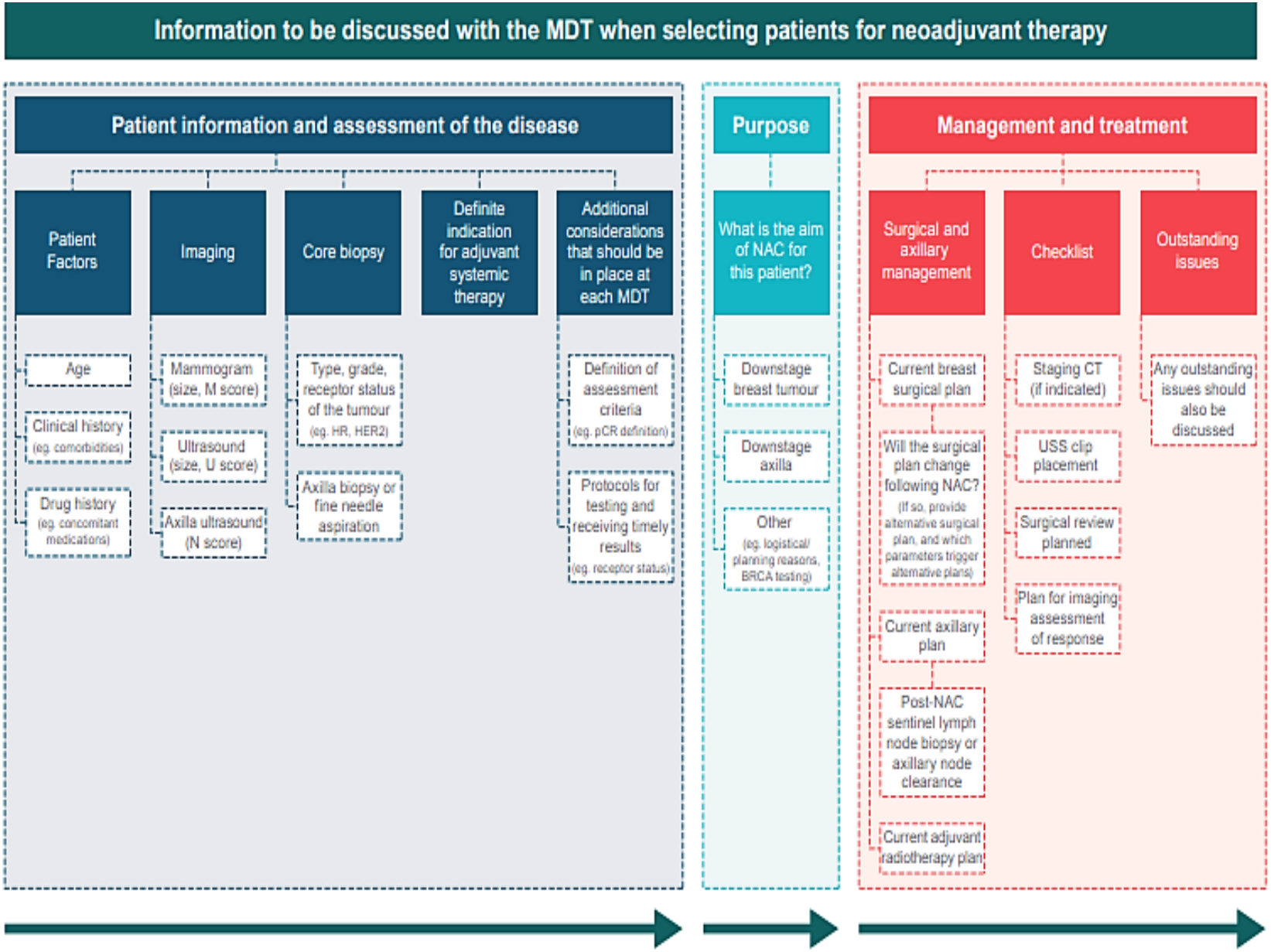
Potential Concerns

1.Potential loss of staging information.

2.Potential for over-treatment, if decision is based on incomplete information (e.g. size of lesion is overestimated because of associated ductal carcinoma in situ seen radiologically).

3.Potential for under-treatment if therapy is stopped or changed mid-course.

4.Limited evidence base to guide adjuvant radiotherapy decisions or management of patients with residual disease.


Information to be discussed with the MDT when selecting patients for neoadjuvant therapy
Patient information and assessment of the disease
Patient Factors
Age
Clinical history (eg. comorbidities)
Drug history (eg. concomitant medications)
Imaging
Mammogram (size, M score)
Ultrasound (size, U score)
Axilla ultrasound (N score)
Core biopsy
Type, grade, receptor status of the tumour (eg. HR, HER2)
Axilla biopsy or fine needle aspiration
Definite indication for adjuvant systemic therapy
Additional considerations that should be in place at each MDT
Definition of assessment criteria (eg. pCR definition)
Protocols for testing and receiving timely results (eg. receptor status)
Purpose
What is the aim of NAC for this patient?
Downstage breast tumour
Downstage axilla
Other (eg. logistical/ planning reasons, BRCA testing)
Management and treatment
Surgical and axillary management
Current breast surgical plan
Will the surgical plan change following NAC? (If so, provide alternative surgical plan, and which parameters trigger alternative plans)
Current axillary plan
Post-NAC sentinel lymph node biopsy or axillary node clearance
Current adjuvant radiotherapy plan
Checklist
Staging CT (if indicated)
USS clip placement
Surgical review planned
Plan for imaging assessment of response
Outstanding issues
Any outstanding issues should also be discussed

Does "ONE-SIZE- FITS- ALL" approach right?

- Does NACT is suitable in every subset ?
- If NACT has its own advantages, then why not use it
- Does NACT really changes surgical management in every case.

Factors favouring NAC in patients with operable breast cancer include

- High tumour volume-to-breast ratio.
- Lymph node-positive disease;
- Biological features of primary cancer
  - High grade,
  - Hormone receptor-negative,
  - HER2-positive,
  - TNBC
  - Younger age.

Factors associated with surgical management

- following neoadjuvant therapy
- type of planned surgery at diagnosis,
- tumor multicentricity,
- ER status,
- tumor size at baseline
- presence of residual tumor on breast palpation
- Strikingly, the radiological response to treatment appeared to have played no role in the surgical decision T

Does NACT really changes surgical management in every case

- National Surgical Adjuvant Breast and Bowel Project (NSABP18) compared the use of neoadjuvant (AC) with the same regimen administering postoperatively.
- complete clinical response rate (cCR) and pathological complete response rate (pCR) were 36% and 13%, respectively.
- In primarily operable breast cancer, NAC can down- stage tumor and lead to small increase of breast conserving rate (60% vs 67%, p = 0.002).
- Although substantial response was found with neoadjuvant approach, there was no statistically significant difference in terms of DFS and OS at a 9-year follow up .

- EORTC compared the efficacy of FEC preoperatively and postoperatively .
- Like NSABP-B18 trial, the OS, PFS and relapse rate were similar between both groups
- Local recurrence, was more frequent with neoadjuvant chemotherapy than with adjuvant chemotherapy, with 15-year rates of local recurrence of 21.4% versus 15.9%, respectively (P=.0001).

- NSABP-B27 the usage of taxane in low-risk patients or ER-positive patients may provide minimal benefit outrage of the risk of adverse effect
- overall survival (OS) was affected only if pCR in the breast and axillary nodes was achieved
- pCR is between 15% and 20% in hormone receptor positive breast cancer

Early Breast Cancer Trialists Collaborative Group (EBCTCG)

- The benefit of NAC as an approach to convert inoperable breast cancer to an operable tumor
- Downstaging to increase breast conserving rate.
- No difference in survival in patients with operable breast cancer whether chemotherapy is given before or after surgery.
- To explore the prediction of long term relapse free survival - are less obvious in hormone receptor positive breast cancers

BIOLOGY DOES MATTERS

- Histological subtype is also important.
- Invasive lobular cancers (ILCs) represent 10-15% of breast cancers and are typically hormone receptor-positive and histological grade 2.
- NAC is less beneficial in this group: fewer patients are downstaged to permit successful BCS,
- Re-excision rates after BCS are higher and the likelihood of pCR is significantly lower than invasive cancers of no special type (NST).

- Lower response rates have also been reported in
  - mucinous,
  - metaplastic and
  - apocrine carcinomas

WHAT WE LEARNT

- When discussing neoadjuvant treatment, MDT/Tumor board discussion is must.
- Provisional histological grade , hormone receptor status and HER2 results should be available
- Radiological results and complete staging work up should be available at the MDT meeting .
- The decision to use chemotherapy in addition to hormonal therapy in the treatment of (ER) –positive N0 breast cancer should be based on not only baseline risk (prognostic information) but also prediction of degree of benefit from chemotherapy

- There should be consensus on the role of BCS in patients responding to neoadjuvant therapy.

- Modern breast cancer surgery should orientate its strategy focusing mainly on post-treatment outcomes rather than the baseline tumor characteristics.

- Optimizing chemotherapy regimen should be considered individually based on reliable prognostic factor, patient’s status and their preference after discussing of the risk and benefit of the treatment.

THANK YOU