Current surgical management of Breast Cancer
The Search for the optimal loco-regional Treatment
Aim: Optimal loco-regional treatment decreased rates of morbidity.
- without compromising outcome –

• Disease burden and biology determine patients’ risk of recurrence, which guides the selection loco-regional treatment and of appropriate adjuvant systemic therapies.

• Big surgery cannot overcome bad biology!
## Current surgical management of breast cancer

### Management of the Breast
- Breast Conserving Therapy (BCT)
- Mastectomy (MX)

### Axillary Staging and Management
- Sentinel Lymph Node Biopsy (SLB)
- Axillary Lymph Node Dissection (ALND)

### Upfront surgery / Neoadjuvant Chemo Therapy (NACT)

### Risk reducing surgery
- Prophylactic contralateral Mastectomy (PCM)
- Prophylactic bilateral mastectomy (PBM)

### Surgery in stage IV disease (primary / distant disease)

### Surgical management of recurrent disease

### Oncoplastic surgical procedures
Invasive Breast Cancer
Clinical exam (exclude inoperability)
Diagnostic imaging work-up (Mammography, Ultrasound, MRI)
Core biopsy  breast / axillary nodes (biological profile)
STAGING for distant disease

Locally advanced ?
Yes

No

Downstaging breast / axillary disease ?
Yes

No

Candidate for BCT ?

Stage IV : systemic treatments. Surgery of the primary for palliative indications only (Bleeding / ulceration/ pain)

Downstaging Breast / axillary disease
(allow more limited surgery / avoid ALND)

Inoperability
- inflammatory carcinoma
- fixation of the tumor to the bony chest wall (ribs, sternum)
- Extensive skin involvement with ulceration or satellite skin nodules
- fixed/matted axillary lymphadenopathy
- involvement of neurovascular structures of the axilla,
- lymphedema of the ipsilateral arm.
Upfront surgery

Candidate For BCT?

MASTECTOMY

Candidate for SLNB?

NO

Mastectomy + SLNB

Positive SLN?

NO

+/- PMRT

Positive SLN?

YES

Z0011 (only BCT)

AMAROS 18% MX

BCT

Candidate for SLNB?

NO

Lumpectomy + ALND

Positive SLN?

NO

0,1 or 2 SLN +

XRT

YES

Mastectomy + ALND

Lumpectomy + ALND

->2 SLN


Current surgical management of breast cancer

KEY POINTS:

• Breast-conserving therapy (BCT) and mastectomy are well-established local therapies for early-stage (I+II) invasive breast cancer and have equivalent survival and recurrence outcomes with multimodal therapy. (RCT, up to 20 yrs FU)

• Rates of local recurrence differ significantly among breast cancer subtypes, regardless of whether patients are treated with mastectomy or BCT. (↑ TNBC / HR + HER2 - ↓)

EVIDENCE

Management of the Breast: Breast Conserving Therapy (BCT)

- BCT involves excision of the tumor followed by adjuvant whole-breast irradiation (WBI). (radioguided surgery for non palpable lesions)

- **Negative margins** (‘no ink on margin’)*

- Good / acceptable cosmetic outcome

Contraindications
- Diffuse malignant-appearing microcalcifications
- Radiotherapy contraindicated (prior RT breast field, active scleroderma)

- Young age, aggressive tumor subtype (HER2-positive and triple negative), and lobular histology are **not** contraindications to BCT
- Despite this higher risk, a BRCA mutation is **not an absolute** contraindication to BCT


**Management of the Breast: Mastectomy (MX)**

- Total mastectomy (simple mastectomy)
- Skin-sparing mastectomy
- Nipple areolar–sparing mastectomy (NSM)

*Intraoperative retro-areolar biopsy*
NACT

RATIONAL AND FACTS
SELECTION CRITERIA FOR BEST CANDIDATES
INITIAL WORK-UP
RESPONSE MONITORING / ADJUSTMENT
SURGERY AFTER NACT: BREAST + AXILLARY MANAGEMENT
Primary surgery resulted in high LRR and poor OAS

In the 80’ NACT was used for LABC/ IBC (T4a-d)
- demonstrated improved DFS and OAS and
- major reduction of tumour burden.

**Downstaging:** Allow more limited surgery

**Prognostic information (cPR)**

**Breast:** Decreases rates of mastectomies

- Reduced volume of resection in patients candidates for BCT

**Axillary nodes:** Potential for decreasing the extent of axillary surgery using SLNB

**Decreasing morbidity of surgery without jeopardizing outcomes**
Addition of NACT to the treatment regimen failed to demonstrate an improvement in OAS compared with adjuvant therapy.

No survival advantage or disadvantage

Addition of NACT to the treatment regimen failed to demonstrate an improvement in OAS compared with adjuvant therapy.


Both anatomical and biological factors are useful in selecting best candidates for NACT.

Generally, any patients considered for adjuvant chemotherapy

Patients less than optimal for BCT (tumour/breast ratio)
NACT : SELECTION CRITERIA FOR BEST CANDIDATES

Effectiveness of NACT varies by molecular subtypes:

NACT is most likely to result in tumour downstaging in:

- unicentric
- high-grade
- ER-negative and/or HER2-positive /TNBC

Degree of pathologic response correlets with both DFS and OA.

pCR powerful prognostic factor


NACT: OAS by Response (TNBC vs non-TNBC)

Clinical examination
Imaging: mammography, ultrasound
*MRI 9% additional + 3% contral.
Staging
(Pre-treatment photo documentation of extent of skin involvement)
* Has not been demonstrated to improve outcome (mortality / RR)

Core needle biopsy:

histological type, G, ER, PgR, HER, Ki-67

(define type/ schedule of pre-treatment)

Ultrasound of axillary nodes:

US + FNA: Specificity 97-100%
US: Sensitivity 49-87%

All suspicious lesion
- Clip in case of complete clinical/radiological response

u/c N-: SNL
suspicious: FNA/CNB
Clip biopsied nodes (NCCN 2016 GL)
- "Targeted Axillary Dissection" TAD
NACT: RESPONSE MONITORING / ADJUSTMENT OF THERAPY

SURGICAL CHALLENGES

• Need a standard method for monitoring response
• Need accurate imaging tools for quantifying response
• Take into consideration the differences in response by subtype
**NACT: RESPONSE MONITORING / ADJUSTMENT OF THERAPY**

Modality comparison for residual tumor size compared to pathologic tumor size

<table>
<thead>
<tr>
<th>Modality</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBE</td>
<td>49–50</td>
<td>49–50</td>
<td>54</td>
</tr>
<tr>
<td>Mammography</td>
<td>79–81</td>
<td>79–81</td>
<td>32</td>
</tr>
<tr>
<td>Ultrasonography</td>
<td>89–90</td>
<td>30–33</td>
<td>60</td>
</tr>
<tr>
<td>MRI</td>
<td>86–92</td>
<td>60–86</td>
<td>90</td>
</tr>
</tbody>
</table>

*CBE* clinical breast examination, *MRI* magnetic resonance imaging,

Need for improved diagnostic tools to more accurately quantify disease response! (Dynamic contrast enhanced MRI, MRI spectroscopy, PET etc.)

Meta-analysis: 14 prospective randomized trials of neoadjuvant versus adjuvant chemotherapy in a total of 5,500 patients with breast cancer demonstrated that **NACT was associated with an absolute decrease in the mastectomy rate of 16.6%**


Paradoxically, although rates of pCR to NACT have increased markedly with the use of newer therapeutic agents and targeted therapies, **rates of BCS have not risen.**

**Possible explanations:**
- Evaluation of the extent of residual disease?
- Volume to be resected (former / new tumour bed)?
- Residual ductal carcinoma *in situ* (DCIS)?
- Patients upfront candidates for BCS
- Patient preference for mastectomy?
- Surgeon (advice/decision making process?)

Abbreviations: BCS, breast-conserving surgery; pCR, pathological complete response; NSABP, National Surgical Adjuvant Breast and Bowel Project; NACT, neoadjuvant chemotherapy; CHER-LOB, Breast cancer: Chemotherapy and HER2 Expression (2002-2007) - Long-Term Outcomes; NeoALTO, Neoadjuvant and Adjuvant Paclitaxel Trial; FEC, 5-fluorouracil, epirubicin, and cyclophosphamide;
Surgery is necessary for every patient (microscopic residual disease in complete clinical/radiological response) (Define extent of residual disease)

Experienced and dedicated breast surgeon, radiologist, pathologist. Multidisciplinary approach is key!

If possible BCT (optimal selection criteria still matter of debate: Volume, Margins)
Loco-regional therapy decision is based on:
• extend of the disease pre- and after treatment

Success of BCT depends on:
• careful patients selection
• achievement of negative margins (invasive + DCIS)
• removal of any suspicious clinical or radiological finding
• generous sample of “normal” breast tissue
• specimen radiography useful to assess margins
• Malignant appearing microcalcifications should be completely excised!


• IT IS NOT NECESSARY TO REMOVE THE ENTIRE VOLUME OF TISSUE INITIALLY OCCUPIED BY THE TUMOUR

RT is mandatory after BCT
APPROACH TO BCT AFTER NACT

LRR after Neoadjuvant therapy

- LRR not different in patients downstaged to BCT
- No differences in LRR after NAC by surgery type

<table>
<thead>
<tr>
<th>Surgery</th>
<th>10-yr incidence of LRR</th>
<th>Local</th>
<th>Regional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mastectomy</td>
<td>12.3 %</td>
<td>8.9 %</td>
<td>3.4 %</td>
</tr>
<tr>
<td>BCT</td>
<td>10.3 %</td>
<td>8.1 %</td>
<td>2.2 %</td>
</tr>
</tbody>
</table>

Factors associated with LRR: N2 / N3, LVI, multifocal pattern after NACT, residual disease >2 cm after NACT

RE-EXCISION

In the setting of downstaging for BCT after NACT, if “viable tumour is present throughout the specimen even if it does not extent to the margins a further re-excision should be considered”


MASTECTOMY

Persistent positive margins

multicentric lesions

widespread DCIS or microcalcifications

planned contralateral mastectomy
Scattered microscopic foci of residual viable tumour, has been shown to predict an increased risk of local recurrence.

- Specimen radiography might be useful.
- Resection and detailed pathology review are often the only way to determine suitability for BCT.

Axillary Staging and Management

Clinically Positive Axilla
- Primary Surgery
- Neoadjuvant Therapy
  - Possible SLN biopsy
  - ALND

Clinically Negative Axilla
- Primary Surgery
- Neoadjuvant Therapy
  - SLN biopsy
  - ypN+ ALND
Axillary Staging and Management

Clinically negative axilla  negative sentinel Lymph node (s)

STANDARD OF CARE

- high level of accuracy/identification rate (IR) 88-95%
- low false negative rate (FNR) 7-10%
- regional recurrence rate < 1%
- ALND is not required
- No difference in terms of DDFS and OAS

(Low I evidence)

Krag et al Lancet Onc 2010 ;
Mansel RE et al. JNCI 2006)
Axillary Staging and Management

Clinically negative axilla  positive sentinel Lymph node(s)

- **Clinically Positive Axilla**
  - Primary Surgery
  - Neoadjuvant Therapy
- **Clinically Negative Axilla**
  - Primary Surgery
  - Neoadjuvant Therapy

- **ALND**
- **Possible SLN biopsy**
- **SLN biopsy**
  - ypN+ ALND
- **≥ 3 SLN + ALND**
- **BCT**
  - 1-2 SLN +
    - ACOSOG Z0011
    - AMAROS
    - OTOASOR
    - IBCSG 23-01
    - AATRM
- **MASTECTOMY**
  - 1-2 SLN +
    - AMAROS
    - IBCSG 23-01

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# Axillary Staging and Management

## Clinical Trials, cT1-2N0 with 1-2+ SLN

<table>
<thead>
<tr>
<th>Trials</th>
<th>Randomization</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>observation vs ALND</td>
</tr>
<tr>
<td></td>
<td>AxRT vs ALND</td>
</tr>
<tr>
<td>ACOSOG Z0011 (n=856)</td>
<td>macro or micromets</td>
</tr>
<tr>
<td>IBCSG 23-01 (n=933)</td>
<td>micromets</td>
</tr>
<tr>
<td>AATRM (n=233)</td>
<td>micromets</td>
</tr>
<tr>
<td>AMAROS (n=1425)</td>
<td>macro or micromets</td>
</tr>
<tr>
<td>OTOASAR (n=474)</td>
<td>macro or micromets</td>
</tr>
</tbody>
</table>

## Axillary Staging and Management

### Clinical Trials, cT1-2N0 with 1-2+ SLN

<table>
<thead>
<tr>
<th></th>
<th>Z0011 N=856</th>
<th>AMAROS N=1425</th>
<th>OTOASOR N=474*</th>
<th>IBCSG 23-01 N=933</th>
<th>AATRM N=233</th>
</tr>
</thead>
<tbody>
<tr>
<td>Additional positive nodes ALND</td>
<td>27.3%</td>
<td>32.8%</td>
<td>38.5%</td>
<td>13%</td>
<td>13%</td>
</tr>
<tr>
<td>Axillary recurrence: ALND</td>
<td>0.5%</td>
<td>0.4%</td>
<td>2%</td>
<td>0.2%</td>
<td>1.0%</td>
</tr>
<tr>
<td>Axillary recurrence: other tx</td>
<td>1.1%</td>
<td>1.2%</td>
<td>1.7%</td>
<td>1%</td>
<td>1.7%</td>
</tr>
<tr>
<td>Median follow-up</td>
<td>9.25yrs</td>
<td>6.1yrs</td>
<td>8yrs (mean)</td>
<td>5yrs</td>
<td>5.1yrs</td>
</tr>
<tr>
<td>Breast Conservation</td>
<td>100%</td>
<td>83%</td>
<td>84%</td>
<td>91%</td>
<td>88%</td>
</tr>
</tbody>
</table>

No difference in axillary recurrence rates between ALND and "other" treatment (observation or AxRT)

NO difference in DFS or OS between ALND or observation in Z011, IBCSG, AATRM between ALND or nodal RT in AMAROS or OTOASOR
Clinical Trials Axillary Management Z0011
Breast Conservation

<table>
<thead>
<tr>
<th></th>
<th># patients</th>
<th>% spared ALND</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ngui et al</td>
<td>119</td>
<td>22%</td>
</tr>
<tr>
<td>Verhuevel et al</td>
<td>916</td>
<td>61%</td>
</tr>
<tr>
<td>Delpech et al</td>
<td>125</td>
<td>70%</td>
</tr>
<tr>
<td>Yi et al</td>
<td>488</td>
<td>75%</td>
</tr>
<tr>
<td>Morrow et al</td>
<td>793</td>
<td>84%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Study</th>
<th>Inclusion Criteria</th>
<th>Randomization</th>
<th>Arms</th>
</tr>
</thead>
<tbody>
<tr>
<td>POSNOC ¹</td>
<td>uni- or multifocal cT₁-₂ N₀</td>
<td>1:1</td>
<td>1. AD or RT</td>
</tr>
<tr>
<td></td>
<td>1-2 macrometastatic SNs</td>
<td></td>
<td>2. No further local treatment</td>
</tr>
<tr>
<td></td>
<td>BCS or mastectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SINODAR ONE²</td>
<td>40–75 year old women</td>
<td>1:1</td>
<td>1. AD</td>
</tr>
<tr>
<td></td>
<td>unifocal cT₁-2 N₀</td>
<td></td>
<td>2. No further axillary surgery</td>
</tr>
<tr>
<td></td>
<td>1–2 macrometastatic SNs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>BCS or mastectomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SENOMAC ³</td>
<td>uni- or multifocal cT₁-₃ N₀</td>
<td>1:1</td>
<td>1. AD</td>
</tr>
<tr>
<td></td>
<td>1-2 macrometastatic SNs</td>
<td></td>
<td>2. No further axillary surgery</td>
</tr>
<tr>
<td></td>
<td>BCS or mastectomy</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

• **NACT downstages the axilla in about 20-40%**
  
  (varies by subtype; > 50% in HER+ disease with CHT + Anti Her+ therapy)

• **Potential to consider SLNB after NACT to avoid ALND**
TIMING: post NACT!

(disadvantage pre: - two surgical procedures
- does not take advantage of the potential downstaging
- commits all patients with +SN pre NACT to ALND
- uncertain prognostic value of negative nodes if the SN was the only positive node and was removed.)

FEASIBILITY (IR )
ACCURACY (FNR)
SAFETY (LRR)
# AXILLA: SLNB and NACT

Rates of Nodal Positivity Among Women Undergoing Axillary Staging Prior to Systemic Therapy vs Following Neoadjuvant Chemotherapy

<table>
<thead>
<tr>
<th>Source</th>
<th>Upfront Surgery %</th>
<th>NAC %</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP B-18,² 1997</td>
<td>48</td>
<td>33</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>NSABP B-27,¹ 2003</td>
<td>49</td>
<td>40</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Hunt et al,¹³ 2009</td>
<td>T1: 19</td>
<td>13</td>
<td>.04</td>
</tr>
<tr>
<td></td>
<td>T2: 37</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T3: 51</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: NAC, neoadjuvant chemotherapy; NSABP, National Surgical Adjuvant Breast and Bowel Project.
Axillary Staging and Management

Clinically negative axilla and NACT

- Clinically Positive Axilla
  - Primary Surgery
  - Neoadjuvant Therapy
    - ALND
    - Possible SLN biopsy

- Clinically Negative Axilla
  - Primary Surgery
  - Neoadjuvant Therapy
    - SLN biopsy
      - ypN- GANE trial 2
      - ypN+ ALND
Axillary Staging and Management
 Clinically negative axilla and NACT: axillary recurrence rates with SLNB only after NACT N-

GANE A 2 trial

Prospective Multi-institutional French Cohort

Events
418 Patients SLN alone without ALND
Median Follow-up = 36 months

<table>
<thead>
<tr>
<th>Relapse</th>
<th>N=10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metastasis</td>
<td>3</td>
</tr>
<tr>
<td>Breast relapse</td>
<td>3 homo L</td>
</tr>
<tr>
<td></td>
<td>3 contra L</td>
</tr>
<tr>
<td>Axillary relapse</td>
<td>1 (0.2%)</td>
</tr>
</tbody>
</table>

3 years survival

<table>
<thead>
<tr>
<th>N=418 (SLN alone)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall survival</td>
</tr>
<tr>
<td>Disease free survival</td>
</tr>
</tbody>
</table>
SLNB after NACT

Intraoperative frozen section examination of SLN

ALND:

for failed mapping

for any positive SLN including micrometastasis /ITC

RT decisions made with combination of pre-treatment factors and final pathohistological status of nodes and breast
Axillary Staging and Management

Clinically positive axilla and NACT

- Clinically Positive Axilla
  - Primary Surgery
  - Neoadjuvant Therapy
    - ALND
    - Possible SLN biopsy

- Clinically Negative Axilla
  - Primary Surgery
  - Neoadjuvant Therapy
    - SLN biopsy
    - ypN+ ALND

SENTINA
ACOSOG Z1071
SN FNAC

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Axillary Staging and Management

Clinically/ biopsy proven positive axilla converted to cN- after NACT

<table>
<thead>
<tr>
<th>Study</th>
<th>Population cN1-2</th>
<th>Biopsy mandatory</th>
<th>cN0 after NACT</th>
<th>IR</th>
<th>FNR</th>
</tr>
</thead>
<tbody>
<tr>
<td>SENTINA</td>
<td>592</td>
<td>no</td>
<td>100 us</td>
<td>80</td>
<td>14</td>
</tr>
<tr>
<td>ACOSOG Z1071</td>
<td>689</td>
<td>yes</td>
<td>93</td>
<td>93</td>
<td>13</td>
</tr>
<tr>
<td>SN FNAC</td>
<td>153</td>
<td>yes</td>
<td>88</td>
<td>88</td>
<td>13</td>
</tr>
</tbody>
</table>

Kuehn T. GBG: SENTINA. Lancet Oncol 2013 May;14:609-18
Boughhey JC. ACOSOG; Z1071. JAMA 2013 Oct;310(14):1455-61
# Axillary Staging and Management

Clinically/biopsy proven positive axilla converted to cN- after NACT

Results from the prospective trials in SLN after NAT in clinically positive patients.

<table>
<thead>
<tr>
<th></th>
<th>ACOSOG 0171</th>
<th>SN FNAC</th>
<th>SENTINA</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (N)</td>
<td>756</td>
<td>153</td>
<td>592</td>
<td>1501</td>
</tr>
<tr>
<td>FNR ≥ 2 SLNS</td>
<td>12.6%</td>
<td>4.9%</td>
<td>9.6%</td>
<td>10.8%</td>
</tr>
<tr>
<td>FNR dual tracer</td>
<td>10.8%</td>
<td>5.2%</td>
<td>8.6%</td>
<td>9.5%</td>
</tr>
<tr>
<td>FNR inclusion of N0(i+)</td>
<td>8.7%</td>
<td>8.4%</td>
<td>N/A</td>
<td>8.6%</td>
</tr>
<tr>
<td>FNR clip nodes</td>
<td>7.4%</td>
<td>N/A</td>
<td>N/A</td>
<td>7.4%</td>
</tr>
</tbody>
</table>

FNR — False negative rate.

N0(i+) — Isolated tumor cells in the sentinel node.
Minimize FNR:

- Remove at least 3 SLN
- dual tracer
- Intraoperative frozen section of all nodes removed + ICH

- TAD + SLN, RISAS study (Netherlands MARI and SLN)

- Perform ALND:
  - Failed mapping
  - Less than 3 SLN (non retrieval of a clipped node)
  - Any positive SLN (including micromets and ITCs)*

*No relationship between size of SLN mets and likelihood of additional nodal disease.
Concern that residual disease resistant to therapy
Axillary recurrence rates with SLNB after NACT N-/N+

Patients scheduled for neoadjuvant treatment
- Initially cN0
  - cN0 post-neoadjuvant (n=249)
  - SN- (n=157) SN+ (n=92)
    - Axillary recurrences 1 (0.6%) 0
    - Ipsilateral breast recurrences 10 (6.4%) 5 (5.4%)
    - Distant metastases 12 (7.6%) 18 (19.5%)
  - cN1/2 post-neoadjuvant (n=147)
- Initially cN1/2
  - cN0 post-neoadjuvant

Contraindication to SLNB at presentation
- T4 = 15
- cN2/N3 = 25
- n = 40

Pre-Neoadjuvant
- Downstaging to SLNB possible
  - n = 155

Downstaging to SLNB possible
- Converted to clinically node negative: SLNB eligible
  - n = 132

Post-Neoadjuvant
- Converted to persistently node positive: SLNB ineligible
  - n = 23

Positive SLNs = 54
Failed matching = 3
<3 negative SLNs removed = 9
Intraoperative clinical decision = 4
n = 70

ALND
n = 40
ALND
n = 65
SLNB alone, with ≥3 SLNs retrieved
n = 62
ALND
n = 23

Median FU 60 months


TAKE HOME

- Breast-conserving therapy and mastectomy are well-established local therapies for early-stage (I+II) invasive breast cancer and have equivalent survival and recurrence outcomes with multimodal therapy. (RCT, up to 20 yrs FU)

- Rates of local recurrence differ significantly among breast cancer subtypes, regardless of whether patients are treated with mastectomy or BCT. (TNBC / HR + HER2 - )
TAKE HOME

• Neoadjuvant chemotherapy (NACT) is increasingly used to downstage disease in the breast and axilla, allowing breast conservation and avoiding axillary lymph node dissection, and is most likely to be successful in a unicentric, high-grade, ER-negative and/or HER2-positive/TNBC.

• NACT does not prolong survival compared with adjuvant chemotherapy, but reduces the need for mastectomy and axillary lymph-node dissection, and thus surgical morbidity, without increasing the risk of locoregional recurrence.

• Increasing rates of pCR have not translated into increasing rates of BCT (likely multifactorial).

• Evaluating the extent of residual disease remains a problem.

• Tumour resection, following NACT, does not need to remove the entire volume of breast tissue initially occupied by the tumour.

• Persistent finding of scattered, viable tumour in resection specimens should prompt consideration of re-resection.
Four RCTs (AMAROS, ACOSOG Z0011, IBCSG 23- 01 and AATRM 48/13/2000) have shown evidence that SLNB either alone or followed by nodal irradiation is effective for the management of the clinically negative axilla and low axillary tumour burden in early breast cancer to avoid axillary lymph node dissection (ALND).

Sentinel lymph-node biopsy (SLNB) after NACT accurately stages the axilla and is associated with a low rate of nodal recurrence in patients presenting with clinically negative axillary lymph nodes.

In patients who convert to clinically node-negative disease, SLNB after NACT has a false-negative rate of <10% only when ≥3 sentinel nodes are identified; nodal recurrence rates after SLNB alone in this population are (still) unknown.