



*Ospedaletto di Pescantina, 21 marzo 2014*

# **La biopsia del linfonodo sentinella prima o dopo la chemioterapia neoadiuvante Quale impatto sulla pratica clinica**

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# Axillary Staging

- SLN surgery recommended for patients with early stage clinically node negative breast cancer
- Questions in neoadjuvant chemotherapy:
  - ✓ How to clinically stage patients prior to neoadjuvant chemo?
  - ✓ When and how to surgically stage the regional nodes?
    - ✓ SLN prior to chemo or after?
    - ✓ Clinically node negative
    - ✓ Clinically node positive

# Pathologic Complete Response

## 3 definitions:

- No residual disease in breast or axilla - ypT0/N0
- No residual invasive disease in breast or axilla - ypT0/N0 or ypTis/N0
- No residual invasive disease in breast - ypT0 or ypTis

## Meta-analysis

- pCR definition which included nodal pCR was associated with improved event-free survival and overall survival compared to ypT0/is

# How to clinically stage patients prior to neoadjuvant chemo?



# How to clinically stage axilla in patients prior to neoadjuvant chemotherapy?



- Clinical and ultrasound N stage (N vs N1)
- From cytology (FNA) or histology (core needle biopsy) of lymph node
  - Positive – cN1
  - Negative – cN0

**When and how  
to surgically stage the regional nodes  
in clinically node negative (cN0) patients**

## PRIOR TO CHEMOTHERAPY

### Advantages

- Classical TNM staging - guides adjuvant therapy, especially post-mastectomy radiotherapy
- Accurate - False negative rate known
- Chemotherapy does not interfere with axillary staging

### Disadvantages

- Two operations
- If SLN is positive and perform ALND – will delay onset of systemic therapy
- More patients node positive - more ALNDs - increased morbidity
- Loose ability to assess axillary response to chemotherapy, which is known to correlate with survival

## AFTER CHEMOTHERAPY

### Advantages

- One operation
- Less node positive patients - less ALND - lower morbidity
- Able to assess response in axilla
- Prognostic information

### Disadvantages

- Effect of chemotherapy on lymphatics unknown
- Unclear which patients should receive nodal radiation

# SLN FN Rates

## NSABP Studies

### Prior to therapy (NSABP B-32)

SLN identified 97.2%

False negative 9.8%

### After chemotherapy (NSABP B-27)

SLN identified 85%

- with blue dye 78%
- with isotope + blue dye 89%

False negative 10.7%

- with blue dye 14%
- with isotope + blue dye 8.4%



# Meta-analysis of SLN after Neoadjuvant Chemotherapy

21 published studies  
(1273 patients)

- Accuracy rate .....94%
- Sensitivity .....88%
- NPV .....90%
- Identification rate...90%

False negative rate 12%

24 published studies trials  
(1799 patients)

- Node positive ... 37%
- SLN ID rate ..... 89.6%

False negative rate 8,4%

**Similar to without neoadjuvant chemo**

# Conclusion re axillary staging for cN0 disease

- SLN after chemotherapy is as accurate as prior to chemotherapy
- SLN after chemotherapy allows informed decisions regarding further local regional therapy and systemic treatment based on the most powerful discriminator of outcome: **Response**

**When and how  
to surgically stage the regional nodes  
in clinically node positive (cN1) patients**

# Z1071 - ALLIANCE

**T0-4, N1-2, M0 invasive breast cancer**  
(pretreatment axillary ultrasound with FNA or core biopsy  
documenting axillary metastases)

↓  
**REGISTER\***

↓  
**Neoadjuvant chemotherapy**

↓  
**REGISTER\***

↓  
**SLN and ALND**



### Primary aim

To determine the false-negative rate (FNR) for SLN surgery following chemotherapy in women initially presenting with biopsy-proven cN1 breast cancer

### Primary endpoint

Determine if the FNR is  $< 10\%$  among women with cN1 disease who had at least 2 SLNs excised

- 10% FNR selected based on previous studies
- FNR of SLN in early breast cancer without NAC

NSABP B-32.....9.8%

- FNR of SLN after NAC

NSABP B-27.....10.7%

Meta-analysis of 21 studies .....12%

## Summary

- SLN correctly identified nodal status ..... 91.2%
- Complete pathologic nodal response rate... 40.0%
- FNR in cN1 pts with 2+ SLNs examined .... 12.6%
- FNR significantly lower with:
  - use of dual tracer ..... 10.8%
  - more than 2 SLNs examined ..... 9.1%

# Conclusions

- SLN surgery is a useful tool for detection of residual nodal disease in women with node positive disease receiving NAC
- Surgical technique important to minimize FNR
  - Use of dual tracer
  - Resection of minimum of 2 SLNs
- Potential further refinement with:
  - Clip placement in LNs at diagnosis
  - Pathologic review of SLNs for treatment effect
- Use of SLN surgery in these patients will enable reduction in extent of axillary surgery

# The SN FNAC study

**Sentinel Node biopsy Following NeoAdjuvant Chemotherapy in biopsy proven node positive breast cancer: The SN FNAC study**

- ✓ SLNs with metastases of any size (ypN0(i+) ypN1mi and ypN1) were classified positive
- ✓ March 2009 – December 2012
- ✓ 153 patients enrolled



# The SN FNAC study

- SLN identified in 127 patients (87.6%)
- 83 node positive patients
- **FNR 9.6%** (8/83)
- On central path review – FNR only 8.4% (7/83)
- Of the 7 FN cases 4 had a single SLN resected
- FNR in 2+ SLNs removed = 4.9%
- If define ypN0(i+) as node negative, then FNR 13.3% (11/83)

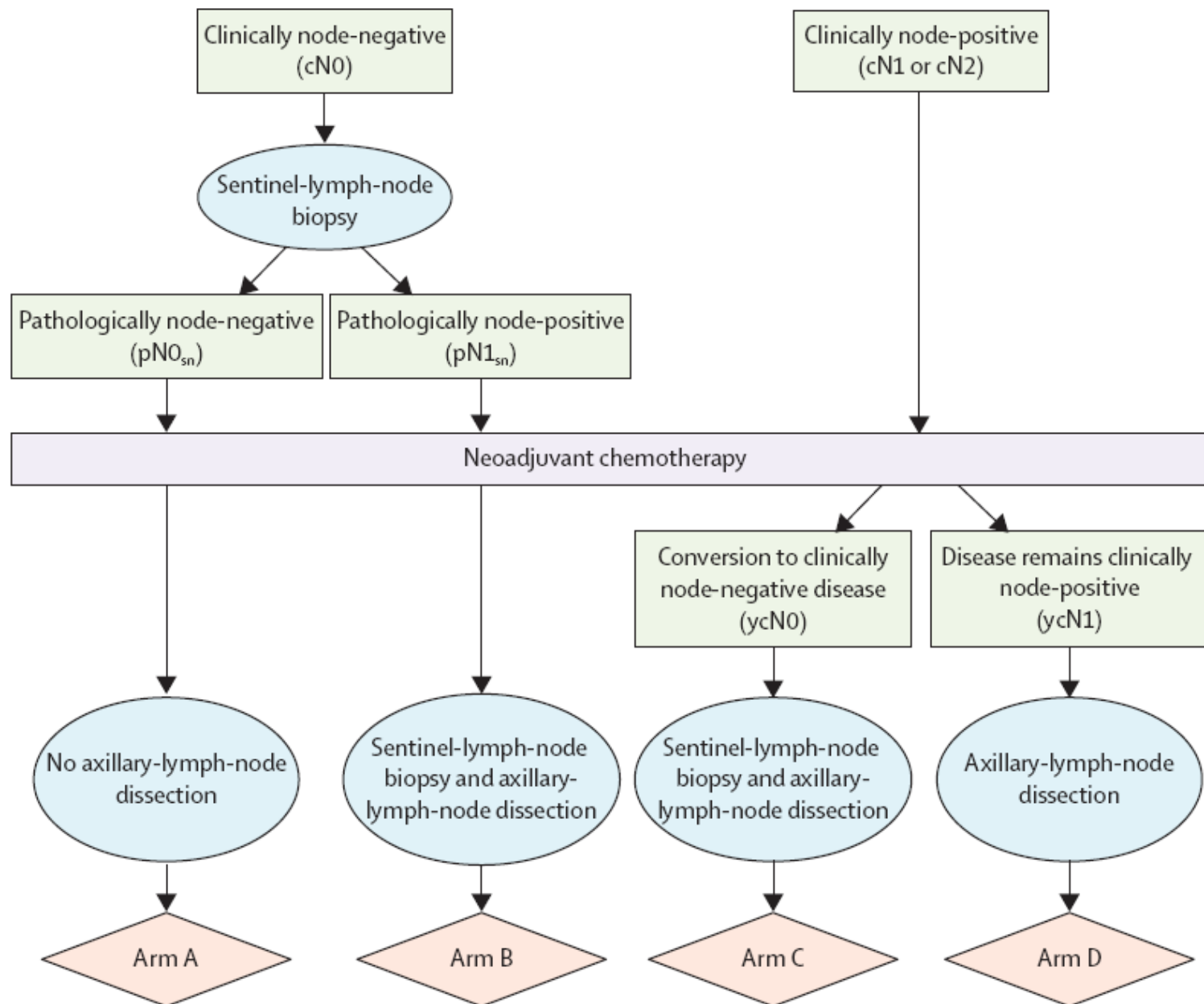
# The SN FNAC study

## Presenters Conclusion of SN FAC study

- FNR (<10%) of SLN biopsy after NAC in biopsy proven node positive breast cancer is **acceptable** and similar to patients with clinically negative nodes in the absence of NAC
- The technical success rate of SLN biopsy (87.6%) is slightly inferior to 90%. In the presence of a technical failure, ALND is warranted
- Following NAC, SLNs with metastases of any size should be considered as positive
- The accuracy of SLN is increased when more than one node is removed

# SENTINA trial

Kuehn, Lancet 2013



# Conclusions from the studies

- Approximately 40% of node positive patients convert to node negative with NAC (up to 70% in Her2+)
- SLN surgery in this setting has a FNR of 8.4%-14.2%
- Varies by definition of positive SLN, mapping technique and number of SLNs resected
- Single SLN has a high FNR in this setting in all studies
- Dual mapping agent had lower FNR in all studies
- No data per specific biological subtypes



# Conclusions from the studies cN+

Clinical Trial	Patients Enrolled	Patients With SLN Identified	FNR Reported in Primary Paper	FNR When 2+ SLNs Resected
ACOSOG Z1071	756	637	12.6%	9.1%
SN FNAC	153	127	9.6%	4.9%
SENTINA	797	474	14.2%	9.6%

**We can move to SNL biopsy after surgery**

# **Incorporating these recent trial results into clinical practice**

# Incorporating these recent trial results into clinical practice

**Oncologist: discuss trial results with multidisciplinary  
team at your institution**

- **Radiology / Surgery**

consider placement of clip in lymph nodes at time of  
percutaneous lymph node biopsy

- **Pathology**

assessment of response to therapy effect in lymph  
nodes

# **Incorporating these recent trial results into clinical practice cN0 at presentation**

Staging of the regional lymph nodes with sentinel lymph node biopsy after neoadjuvant chemotherapy has been shown to have a similar false-negative rate to the use of sentinel lymph node surgery without any prior systemic therapy



# **Incorporating these recent trial results into clinical practice cN1**

## **Which patients to consider**


- Good clinical and radiological response of disease in breast and lymph nodes
- Surgeon experience in SLN after chemotherapy

**If not: go to ALND, avoiding SLNB**

# Incorporating these recent trial results into clinical practice

## At surgery

- Use dual tracer
- Resect all sentinel lymph nodes (palpable, blue, radioactive) at time of surgery
- Frozen section of SLNs
- Pathologist have to comment on presence of treatment effect in the SLNs
- If 0 SLNs or only 1 SLN convert to ALND
- If node positive proceed to ALND

The image is a composite of a photograph and a graph. The background is a photograph of a calm lake at sunset, with a warm orange and yellow sky. In the distance, there are mountains and a small building with a chimney. In the foreground, a wooden pier extends into the water, where a man, a woman, and two children are sitting and fishing. Overlaid on the left side of the image is a white line graph. The graph has a vertical y-axis with five tick marks and a horizontal x-axis with five tick marks. A white line starts at the top of the y-axis and trends downwards to the right, with several small, irregular steps or fluctuations along its path, ending near the bottom right of the graph area.

**... il nostro lavoro deve servire  
a guadagnare vita  
e qualità di vita  
affinchè i nostri pazienti  
possano godersi  
momenti come questi...**

*Courtesy of Alain Herrera*