



**Multidisciplinary Approaches to Cancer Symposium**

# Updates for 2023: Axillary Surgery in Breast Cancer after Neoadjuvant Therapy

Jennifer Tseng, MD

Medical Director of Breast Surgery, City of Hope Orange County

Associate Clinical Professor, Department of Surgery

# Disclosures

- Grant/Research Support from Intuitive

*This presentation and/or comments will be free of any bias toward or promotion of the above referenced companies or their product(s) and/or other business interests.*

*This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content.*

*This presentation has been peer-reviewed and no conflicts were noted.*

# Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

## **STATE LAW:**

The California legislature has passed Assembly Bill (AB) 1195, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed AB 241, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

*The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.*

## **EXEMPTION:**

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

## ***The following CLC & IB components will be addressed in this presentation:***

- *Do any individuals in different populations experience barriers to being offered breast/axillary surgery?*
- *What populations experience disparities of care in new breast and axillary surgery techniques?*

# Learning Objectives



- What are the types of axillary surgery after neoadjuvant systemic therapy (NST)?
- When can the axilla be spared after NST?
- What are ongoing questions of study in axillary management after NST?



## Alphabet Soup of Axillary Surgery: Definitions

**ARM?**

**SLNB?**

**ALND?**

**MLNB?**

**TLNB?**

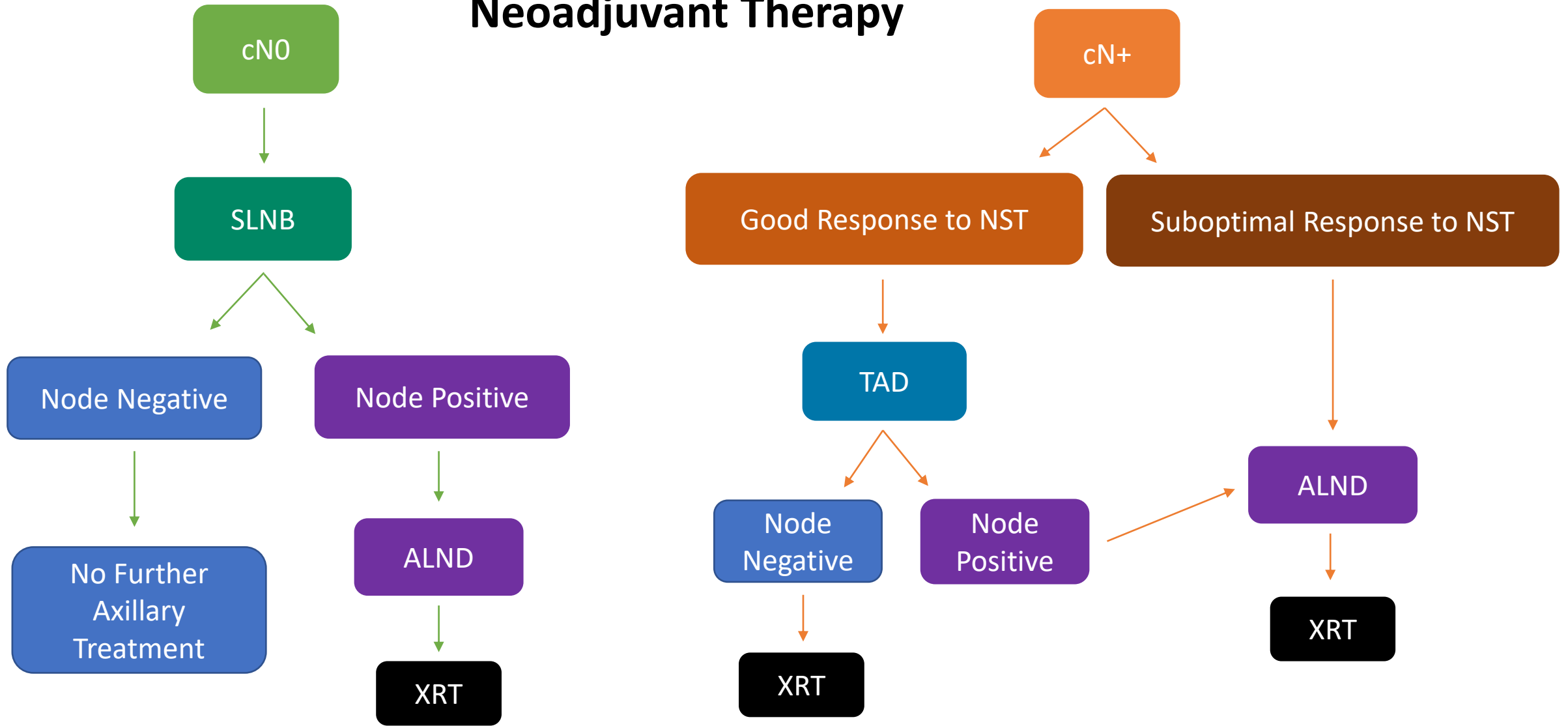
**TAD?**



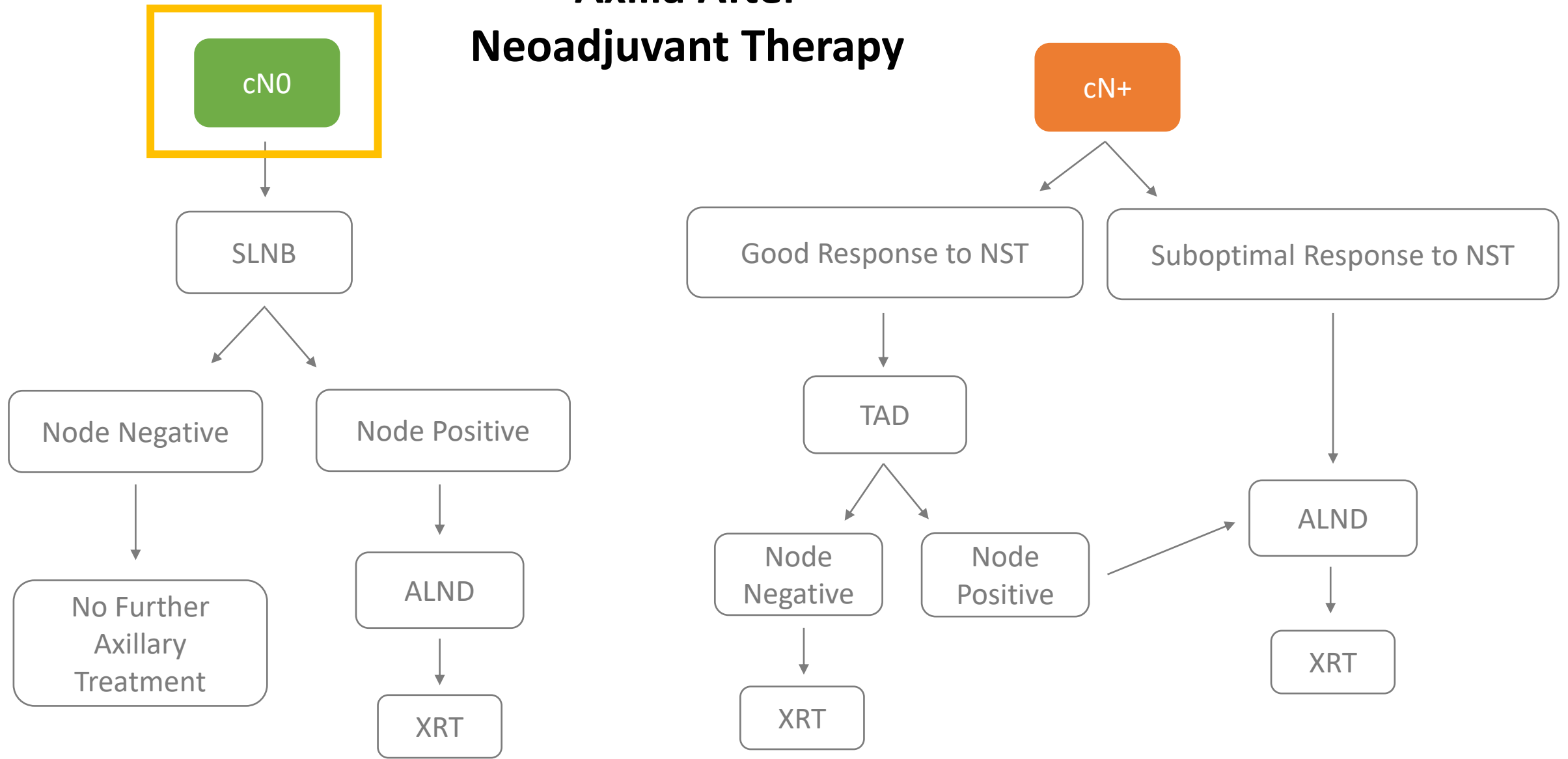
## Axillary Surgery: Definitions

Type of Axillary Surgery	Description
Sentinel Lymph Node Biopsy (SLNB)	Identification/removal of the sentinel lymph node(s) Radioactive tracer and/or blue dye
Axillary Lymph Node Dissection (ALND)	Removal of axillary lymph nodes, usually levels I/II Sometimes including level III
Targeted Lymph Node Biopsy (TLNB) or Marked Lymph Node Biopsy (MLNB)	Selective removal of metastatic lymph node Marked before neoadjuvant therapy
Targeted Axillary Dissection (TAD)	SLNB + TLNB

# Axilla After Neoadjuvant Therapy

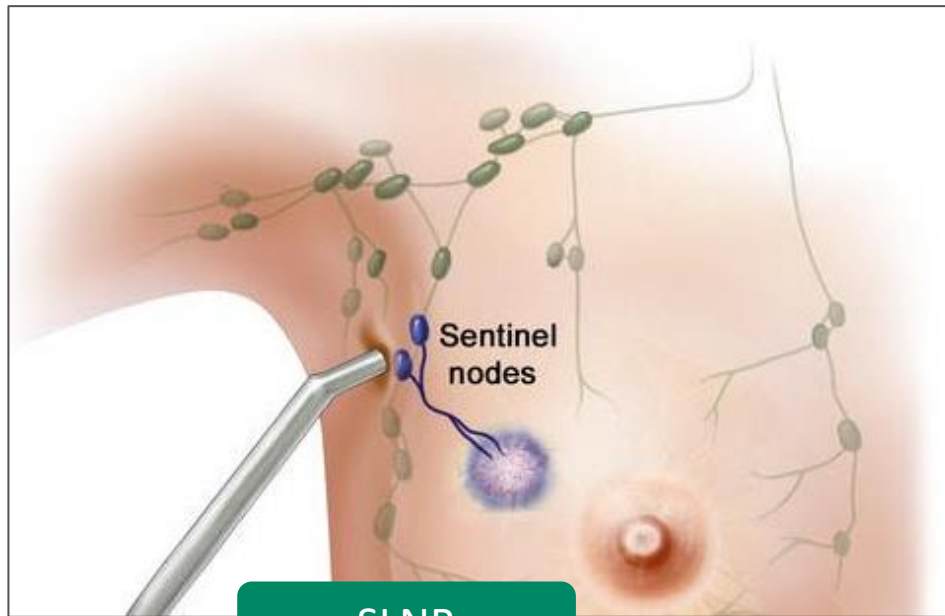


# Axilla After Neoadjuvant Therapy





## Axilla After Neoadjuvant Therapy: cN0

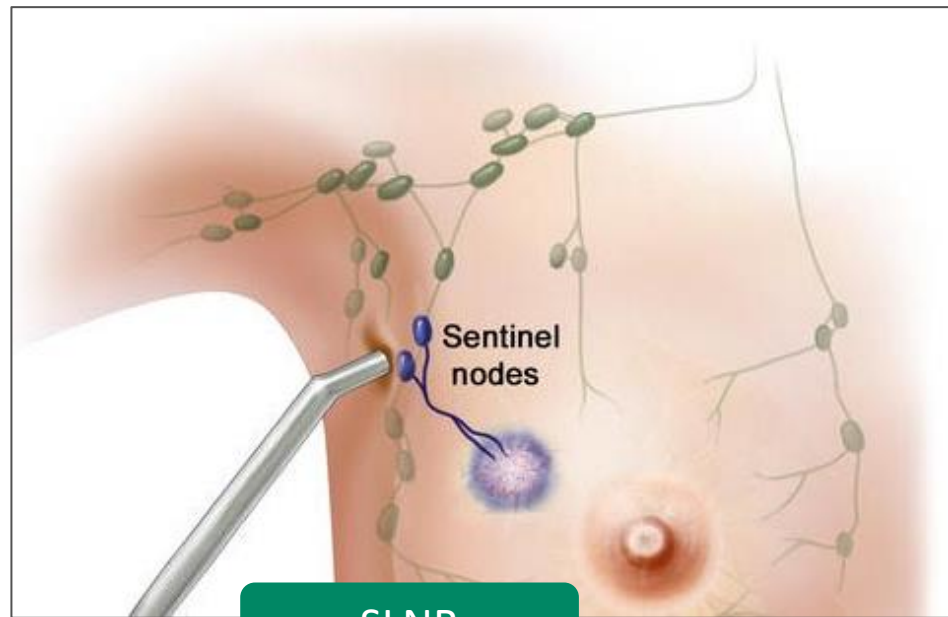


SLNB

In what % of cN0 patients are sentinel lymph nodes identified after NST?

- A. < 25%
- B. 25-50%
- C. > 50-95%
- D. > 95%

## Axilla After Neoadjuvant Therapy: cN0

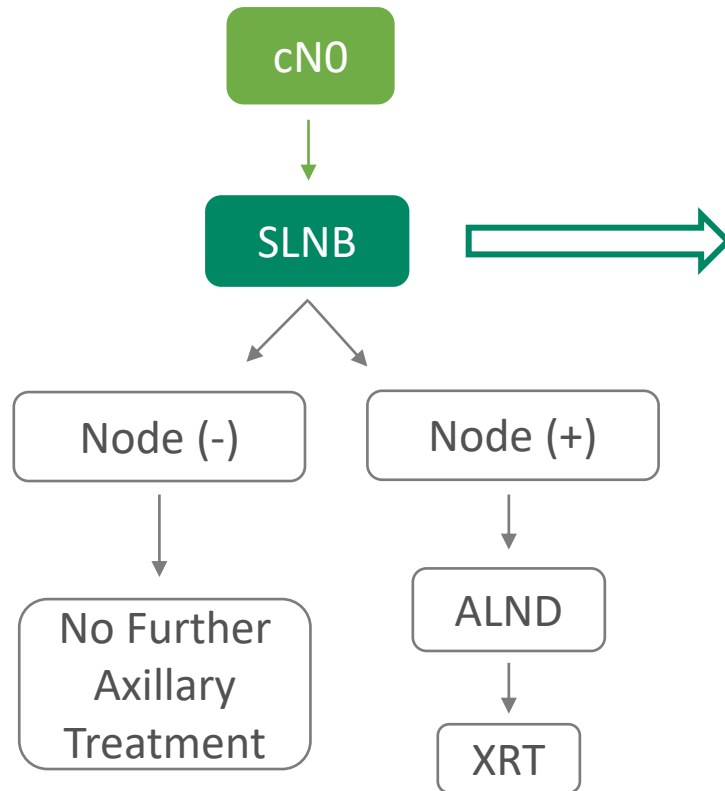


SLNB

In what % of cN0 patients are sentinel lymph nodes identified after NST?

- A. < 25%
- B. 25-50%
- C. > 50-95%
- D. > 95%**

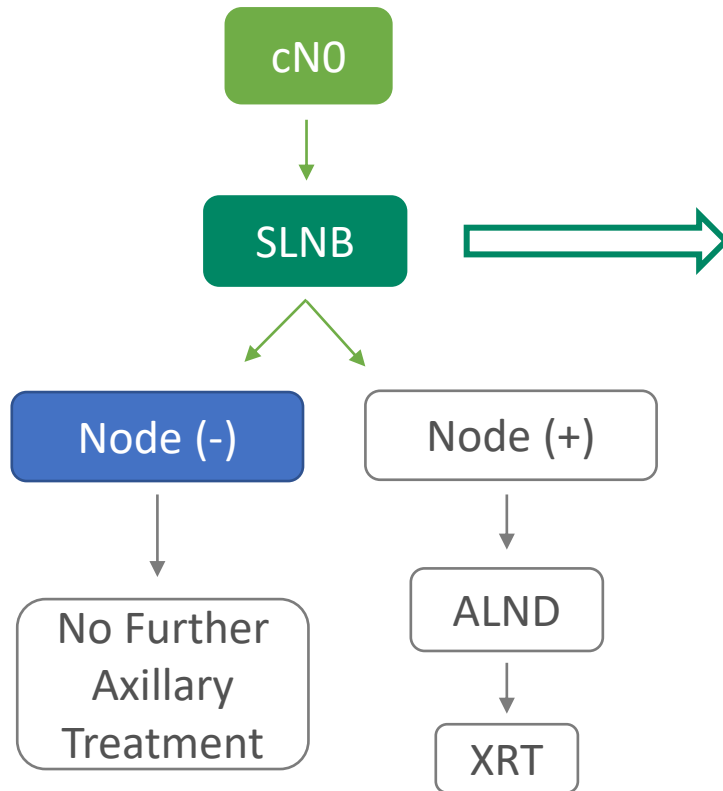
# Axilla After Neoadjuvant Therapy: cN0



cN0: Sentinel Lymph Node Biopsy (SLNB) After Neoadjuvant Chemotherapy		
Study	n	Identification Rate
NSABP B-27 <sup>1</sup>	428	84.8%
MDACC <sup>2</sup>	575	<b>97.4%</b>
GANEA2 <sup>3</sup>	589	<b>97.6%</b>

1. Mamounas et al. *J. Clin. Oncol.* 2005
2. Hunt et al. *Ann Surg* 2009
3. Classe et al. *Breast Cancer Res. Treat.* 2019

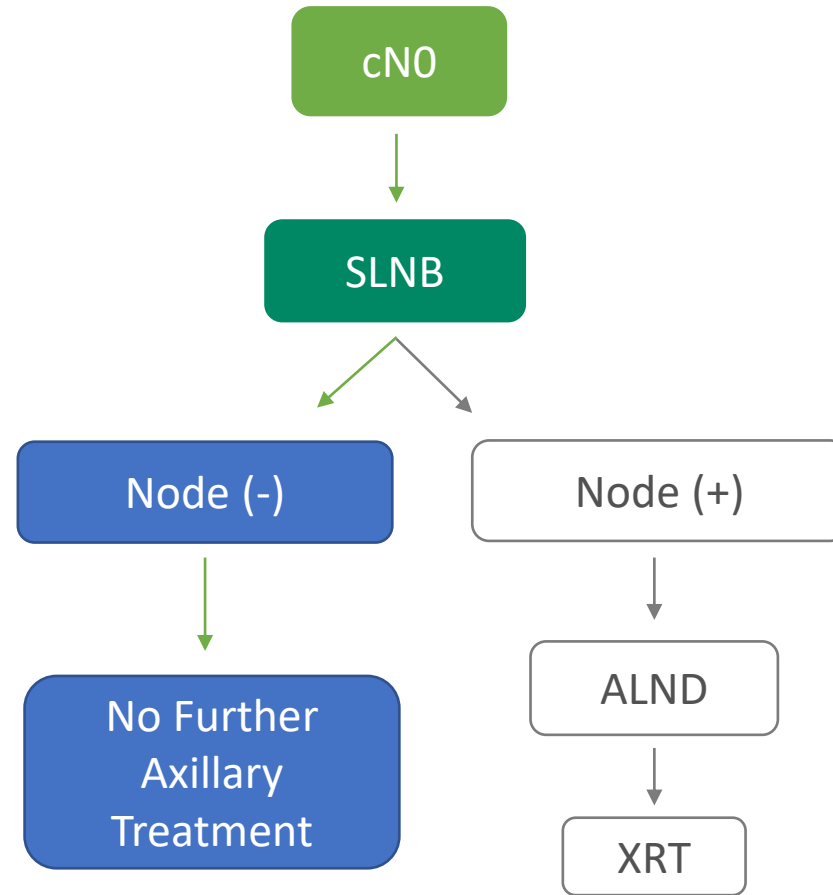
# Axilla After Neoadjuvant Therapy: cN0



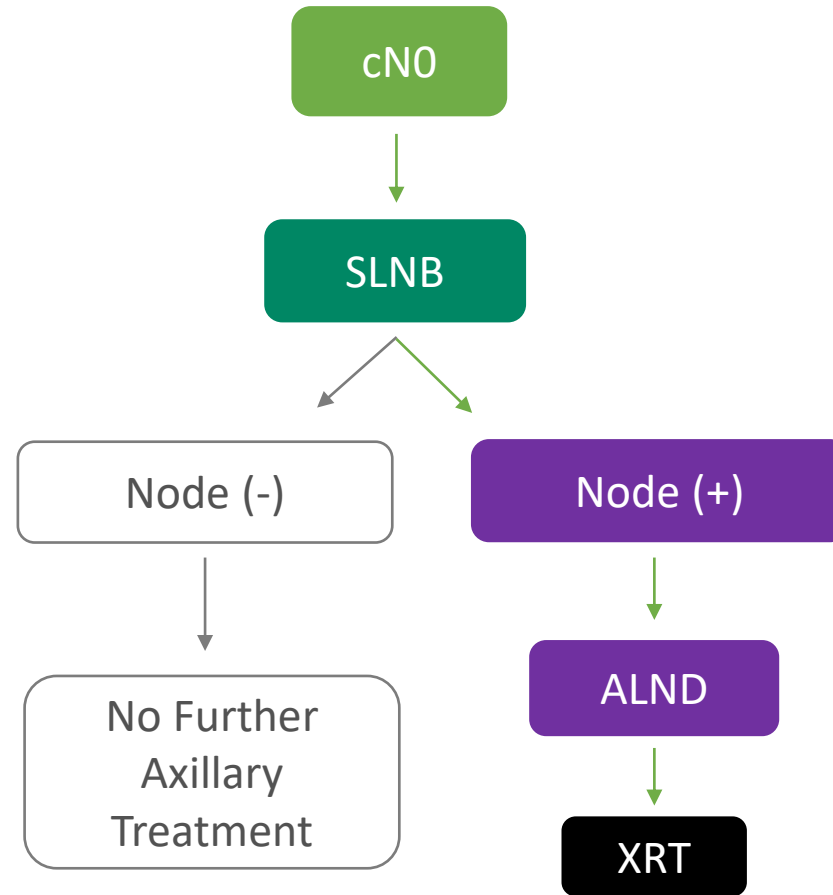
cN0: Sentinel Lymph Node Biopsy (SLNB) After Neoadjuvant Chemotherapy			
Study	n	Identification Rate	False Negative Rate
NSABP B-27 <sup>1</sup>	428	84.8%	10.7%
MDACC <sup>2</sup>	575	97.4%	<b>5.9%</b>

1. Mamounas et al. *J. Clin. Oncol.* 2005
2. Hunt et al. *Ann Surg* 2009

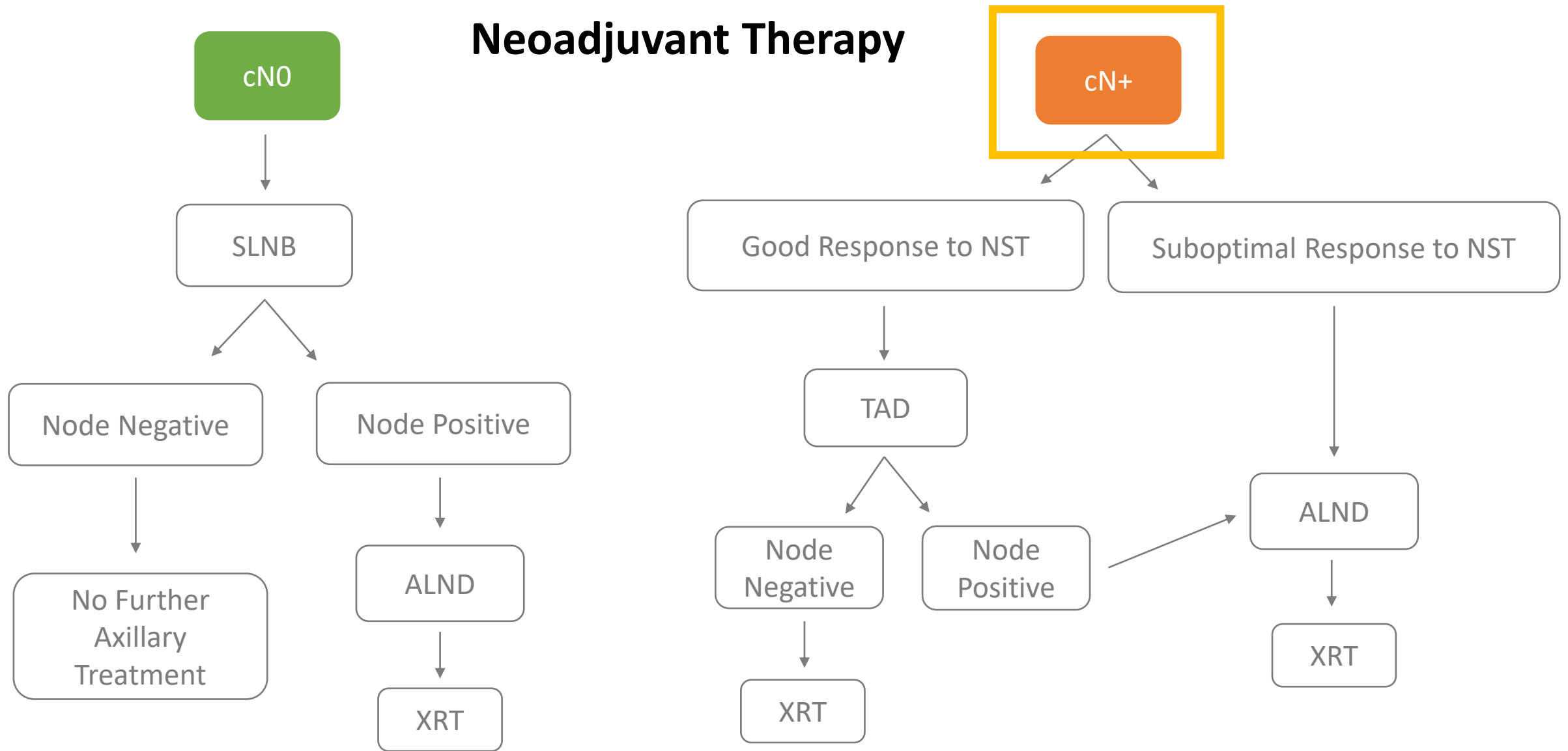
## Axilla After Neoadjuvant Therapy: cN0



# Axilla After Neoadjuvant Therapy: cN0



# Axilla After Neoadjuvant Therapy

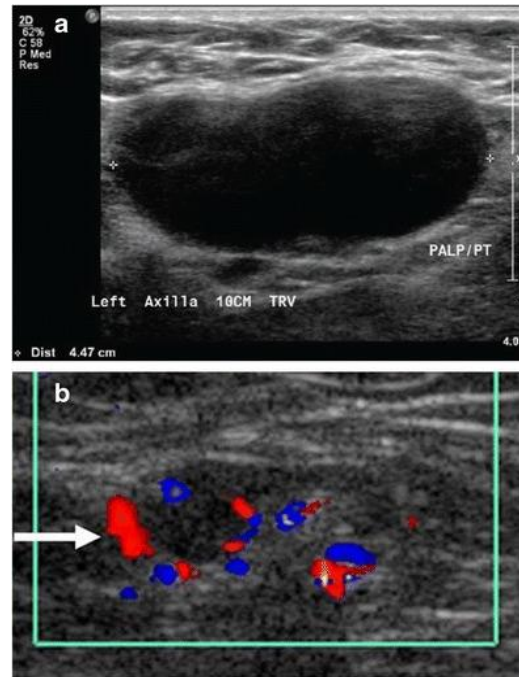


# Axilla After Neoadjuvant Therapy: cN+

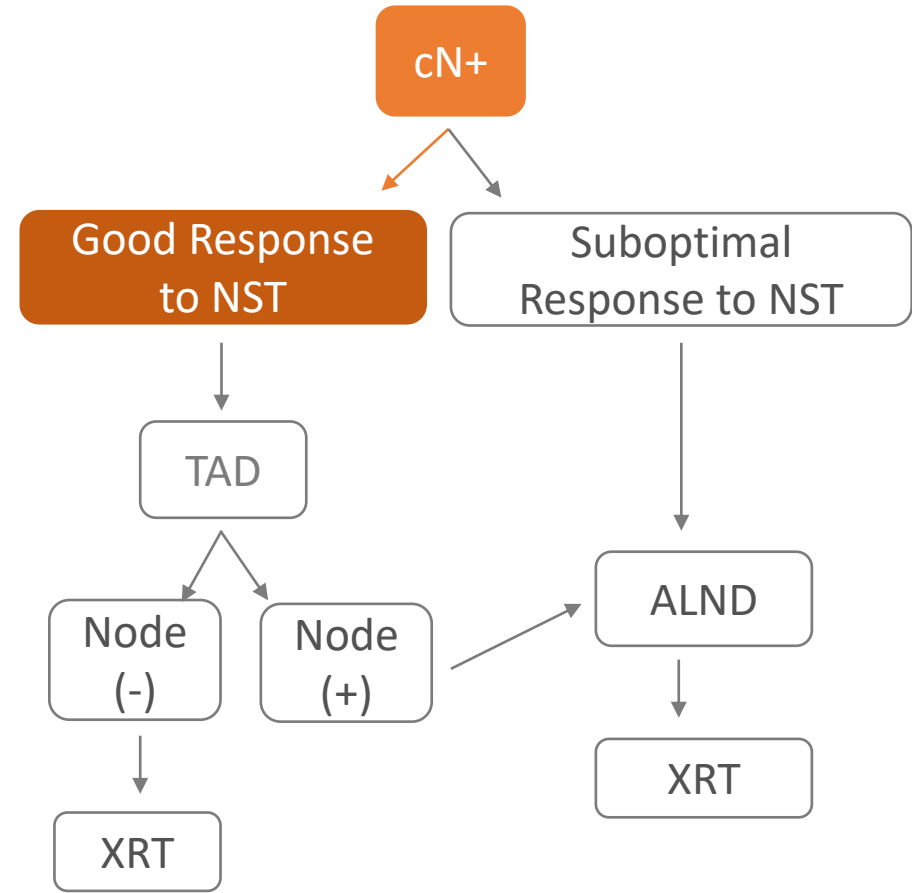
## Preoperative Assessment



Clinical Exam



Ultrasound

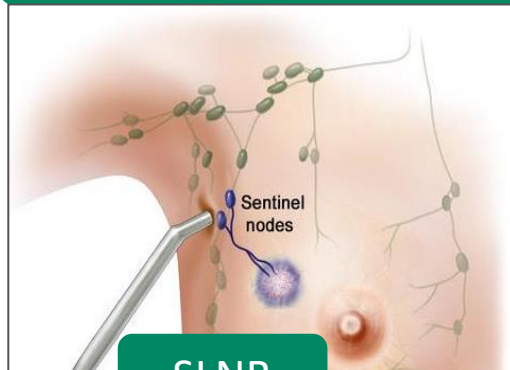




# Axilla After Neoadjuvant Therapy: cN+

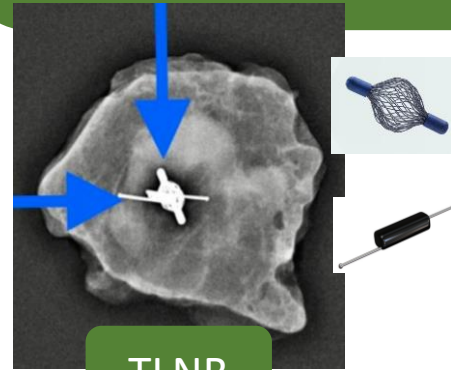
## Targeted Axillary Dissection

### Sentinel Lymph Node Biopsy

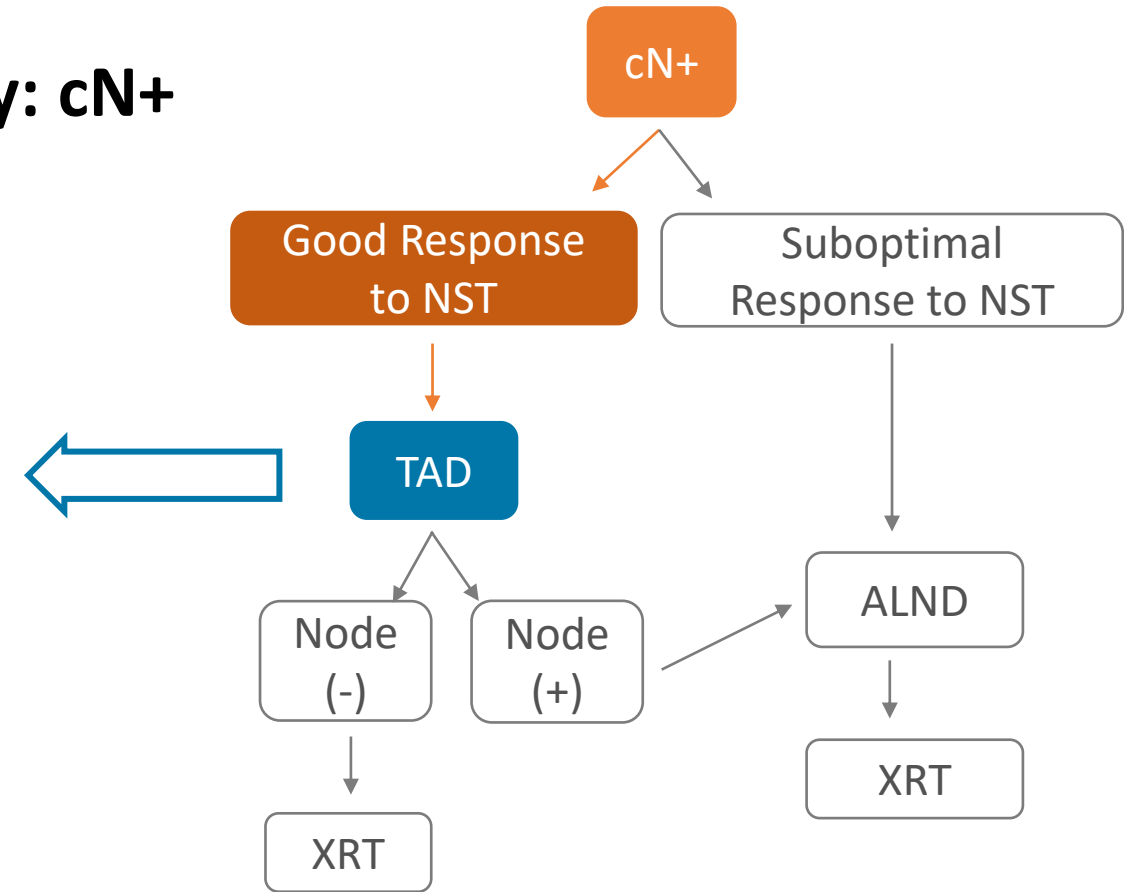


SLNB

### Targeted Lymph Node Biopsy (Retrieval of the biopsied/clipped node)

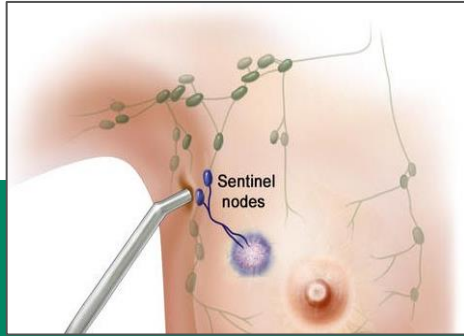


TLNB



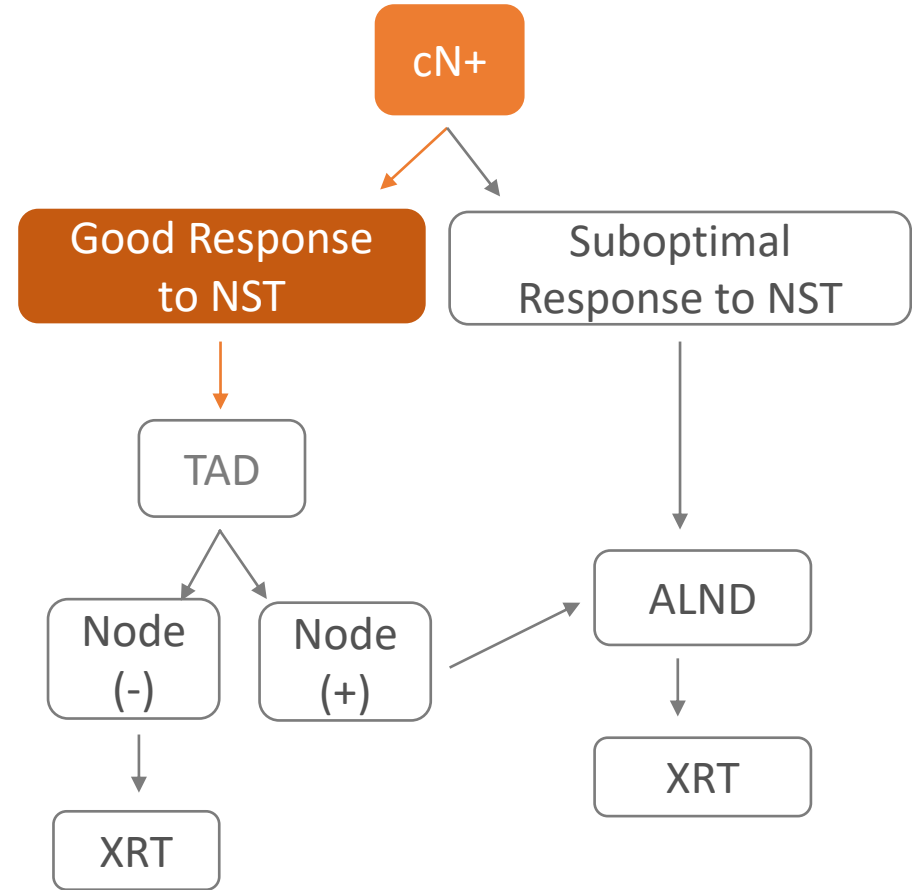
1. Cardoso et al. *Ann. Oncol.* 2019
2. Swarnkar et al. *Cancers* 2021

# Axilla After Neoadjuvant Therapy: cN+



**cN+: Sentinel Lymph Node Biopsy (SLNB)  
After Neoadjuvant Chemotherapy**

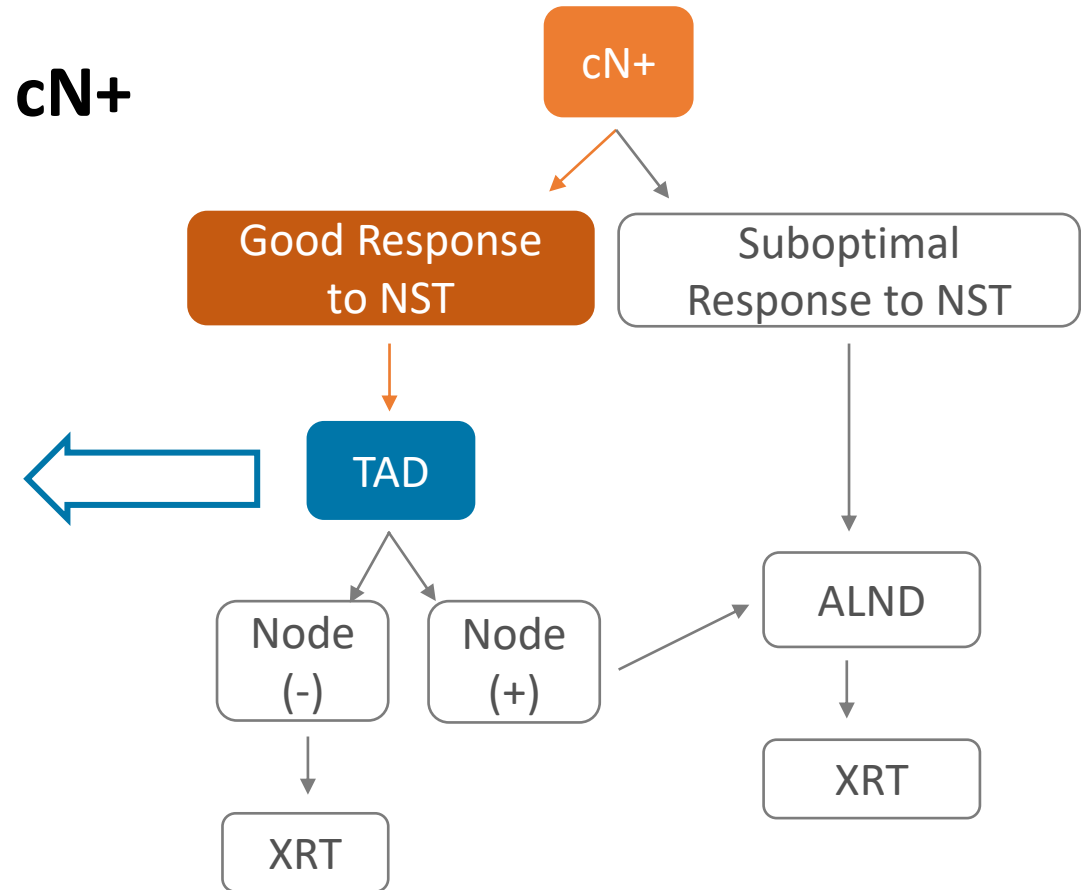
Study	n	Identification Rate	False Negative Rate
SENTINA <sup>1</sup>	592	80.1%	14.2%
ACOSOG Z1071 <sup>2</sup>	649	92.9%	12.6%
SN FNAC <sup>3</sup>	153	87.6%	8.4%
GANEA2 <sup>4</sup>	307	79.5%	11.9%



1. Kuehn et al. *Lancet Oncol.* 2013
2. Boughey et al. *JAMA* 2013
3. Boileau et al. *J. Clin. Oncol.* 2015
4. Class et al. *Breast Cancer Res. Treat.* 2019

## Axilla After Neoadjuvant Therapy: cN+

False Negative Rate			
Study	n	SNLB	TAD (SLNB + TLNB)
ACOSOG Z1071 <sup>1</sup>	649	12.6%	6.8%
MDACC <sup>2</sup>	118	10.1%	<b>2.0%</b>
ILINA <sup>3</sup>	35	---	<b>4.1%</b>
RISAS <sup>4</sup>	227	---	<b>3.5%</b>
SenTA <sup>5</sup>	253	---	<b>4.3%</b>



1. Boughey et al. *JAMA* 2013
2. Caudle et al. *J. Clin. Oncol.* 2016
3. Siso et al. *Ann Surg Oncol.* 2018
4. Van Nijnatten et al. *SABCS* 2020
5. Kuemmel et al. *Ann Surg* 2020

# Axilla After Neoadjuvant Therapy: cN+



THE AMERICAN SOCIETY OF

**Breast Surgeons**

- Official Statement -

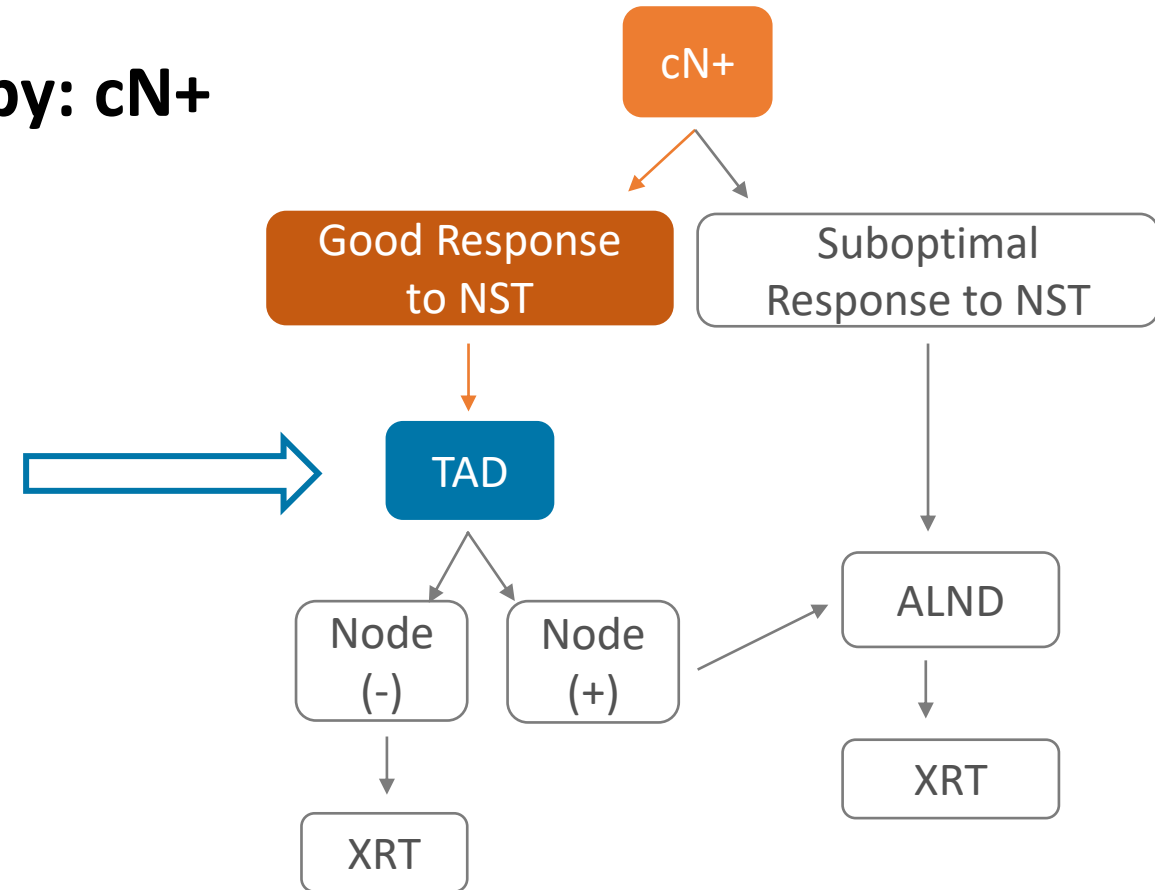
Consensus Guideline on Axillary Management for  
Patients With In-Situ and Invasive Breast Cancer:  
A Concise Overview

Early breast cancer: ESMO Clinical Practice Guidelines  
for diagnosis, treatment and follow-up<sup>†</sup>



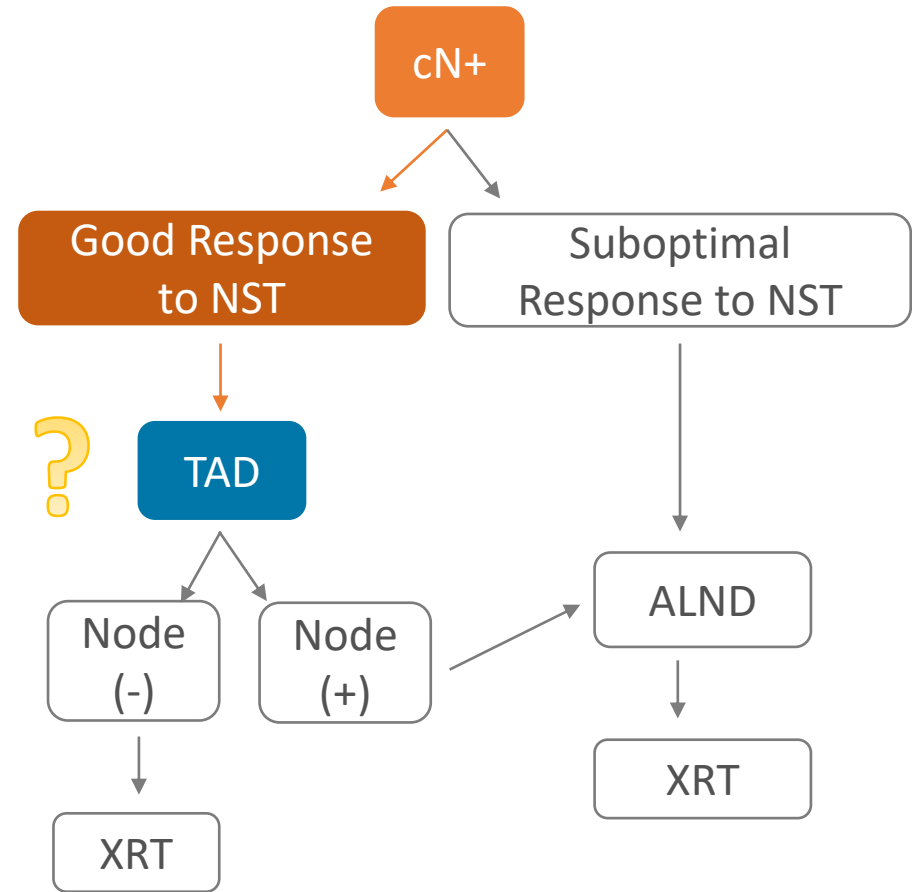
National  
Comprehensive  
Cancer  
Network®

**NCCN Guidelines Version 3.2022**  
**Invasive Breast Cancer**



## Axilla After Neoadjuvant Therapy: cN+

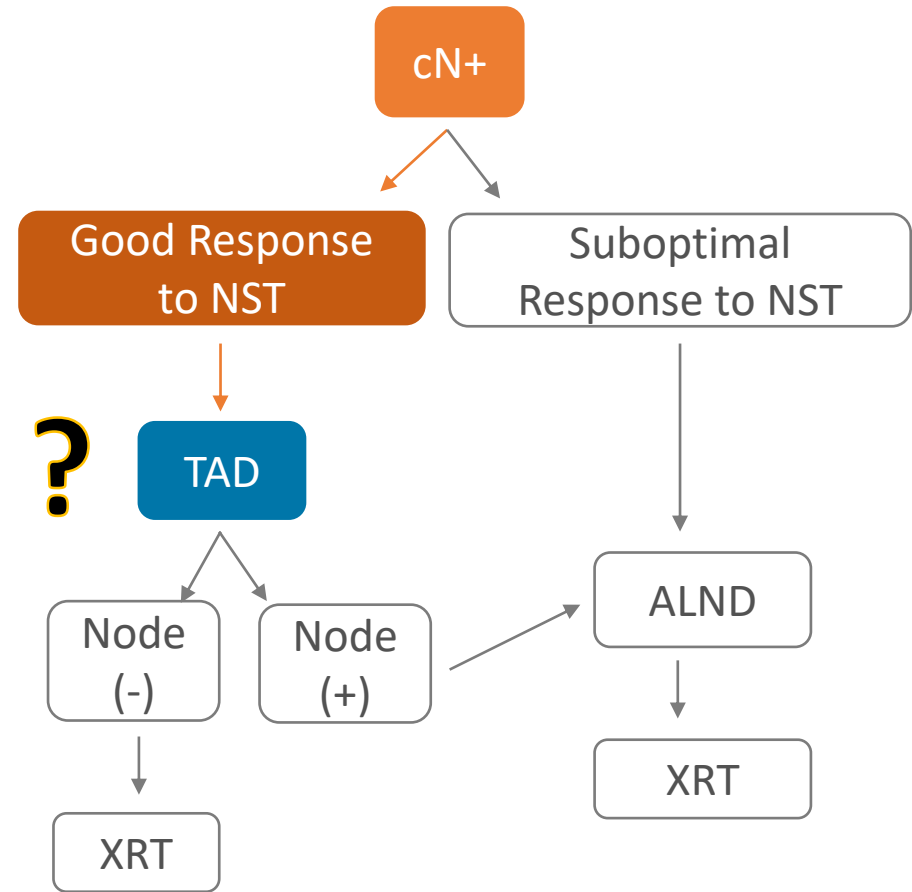
- How often is the clipped node a sentinel lymph node?
- Can just the clipped node be removed without SLNB?
- Which marking technique?
- How many nodes should be marked (removed)?



- ✓ How often is the clipped node a sentinel lymph node?

65-81%

ACOSOG Z1071  
MDACC  
University of Pittsburgh  
ILINA  
University of Istanbul  
RISAS  
SenTa



1. Boughey et al. *JAMA* 2013
2. Caudle et al. *J. Clin. Oncol.* 2016
3. Diego et al. *Ann Surg Oncol.* 2016
4. Siso et al. *Ann Surg Oncol.* 2018
5. Gurleyik et al. *Ann Surg Treat Res.* 2021
6. Van Nijnatten et al. *SABCS* 2020
7. Kuemmel et al. *Ann Surg* 2020

# Axilla After Neoadjuvant Therapy: cN+

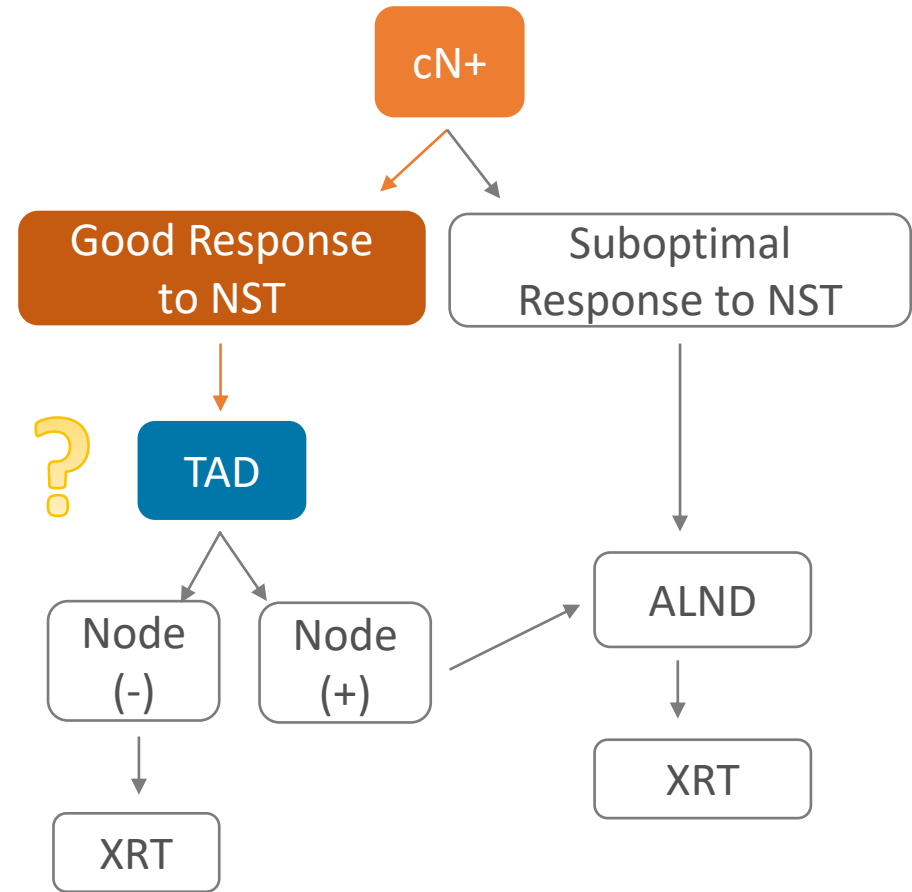
- ✓ Can just the clipped node be removed without SLNB?

Likely Not

## Marking Axillary Lymph Nodes With Radioactive Iodine Seeds for Axillary Staging After Neoadjuvant Systemic Treatment in Breast Cancer Patients

### The MARI Procedure

Donker, Mila MD<sup>\*</sup>; Straver, Marieke E. MD, PhD<sup>\*</sup>; Wesseling, Jelle MD, PhD<sup>†</sup>; Loo, Claudette E. MD<sup>‡</sup>; Schot, Margaret<sup>§</sup>; Drukker, Caroline A. MD<sup>\*</sup>; van Tinteren, Harm PhD<sup>¶</sup>; Sonke, Gabe S. MD, PhD<sup>§</sup>; Rutgers, Emiel J. Th. MD, PhD<sup>\*</sup>; Vrancken Peeters, Marie-Jeanne T. F. D. MD, PhD<sup>\*</sup>



# Axilla After Neoadjuvant Therapy: cN+

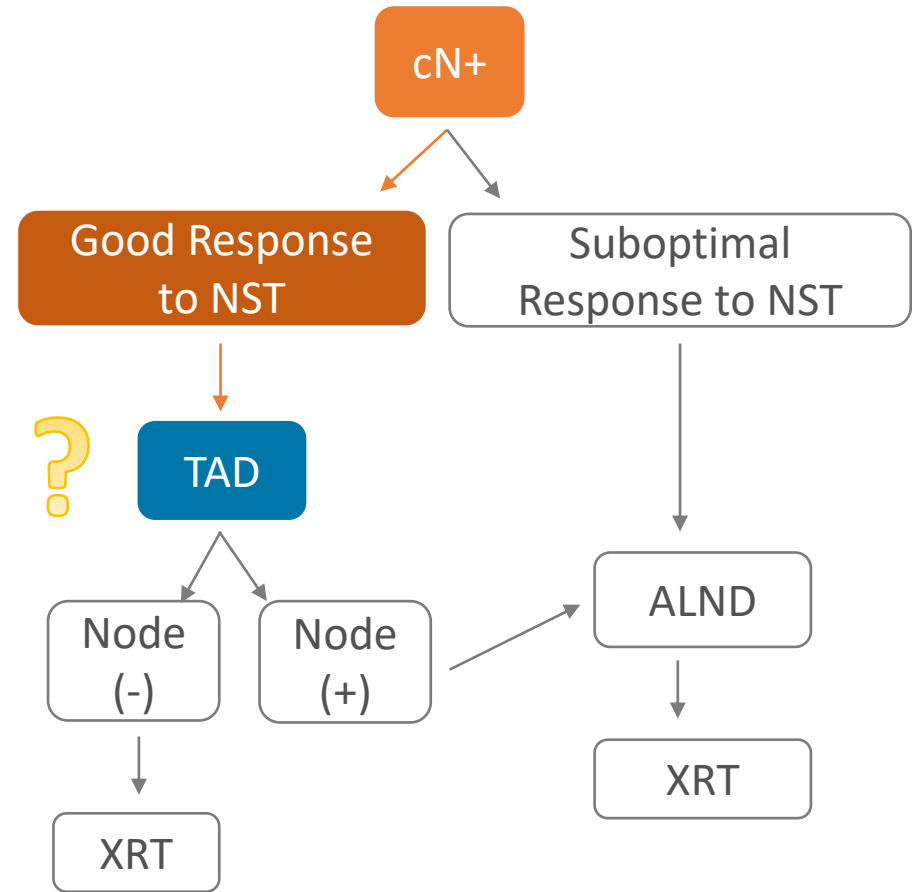
✓ Which marking technique?



Clip  
Vision  
O-Twist  
Hydromark  
Radar  
Reflector  
RFID  
Iodine I-125  
RRL  
Intraoperative US

Magseed  
Carbon Suspension  
Savi Scout  
Envisio  
Ink injection  
Skin marking  
Radioactive Seed  
Tattoo  
Wireless  
Etc.

**PENDING**





# Axilla After Neoadjuvant Therapy: cN+

✓ How many nodes should be marked (removed)?

- Balance of FNR with increased morbidity
- Unclear long-term results

**The Oncologist**  
Clinical Trial Results

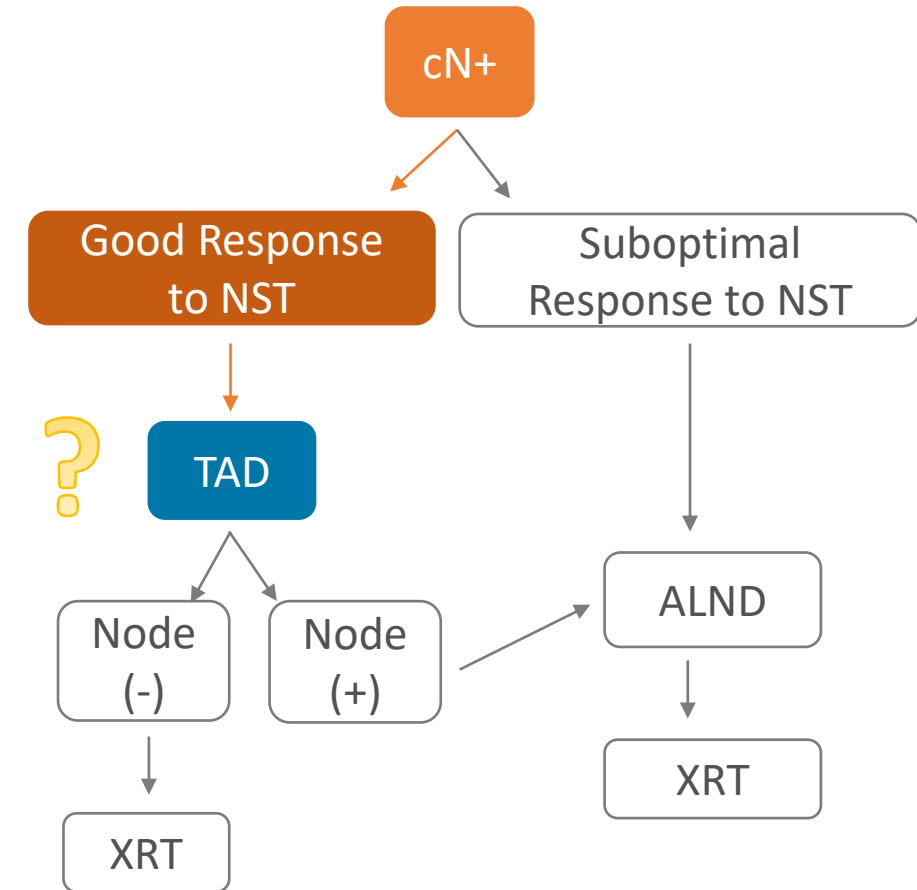
**Would Removal of All Ultrasound Abnormal Metastatic Lymph Nodes Without Sentinel Lymph Node Biopsy Be Accurate in Patients with Breast Cancer with Neoadjuvant Chemotherapy?**

GEOK HOON LIM,<sup>a,c</sup> MIHIR GUDI,<sup>b</sup> SZE YIUN TEO,<sup>c</sup> RUEY PYNG NG,<sup>d</sup> ZHIYAN YAN,<sup>a</sup> YIEN SIEN LEE,<sup>c</sup> JOHN C. ALLEN JR.,<sup>f</sup> LESTER CHEE HAO LEONG<sup>e</sup>

<sup>a</sup>Breast Department, <sup>b</sup>Departments of Pathology and Laboratory Medicine and <sup>c</sup>Diagnostic & Interventional Imaging, and <sup>d</sup>Division of Nursing, KK Women's and Children's Hospital, Singapore; <sup>e</sup>Duke-NUS Medical School, Singapore; <sup>f</sup>Centre for Quantitative Medicine, Duke-NUS Medical School, Singapore; <sup>g</sup>Department of Diagnostic Radiology, Singapore General Hospital, Singapore

Axillary Lymph Node Tattooing and Targeted Axillary Dissection in Breast Cancer Patients Who Presented as cN+ Before Neoadjuvant Chemotherapy and Became cN0 After Treatment

Ioannis Natsiopoulos,<sup>1</sup> Stavros Intzes,<sup>1</sup> Triantafyllos Liappis,<sup>1</sup>  
Konstantinos Zarampoukas,<sup>1</sup> Thomas Zarampoukas,<sup>2</sup> Vasiliki Zacharopoulou,<sup>3</sup>  
Konstantinos Papazisis<sup>4</sup>



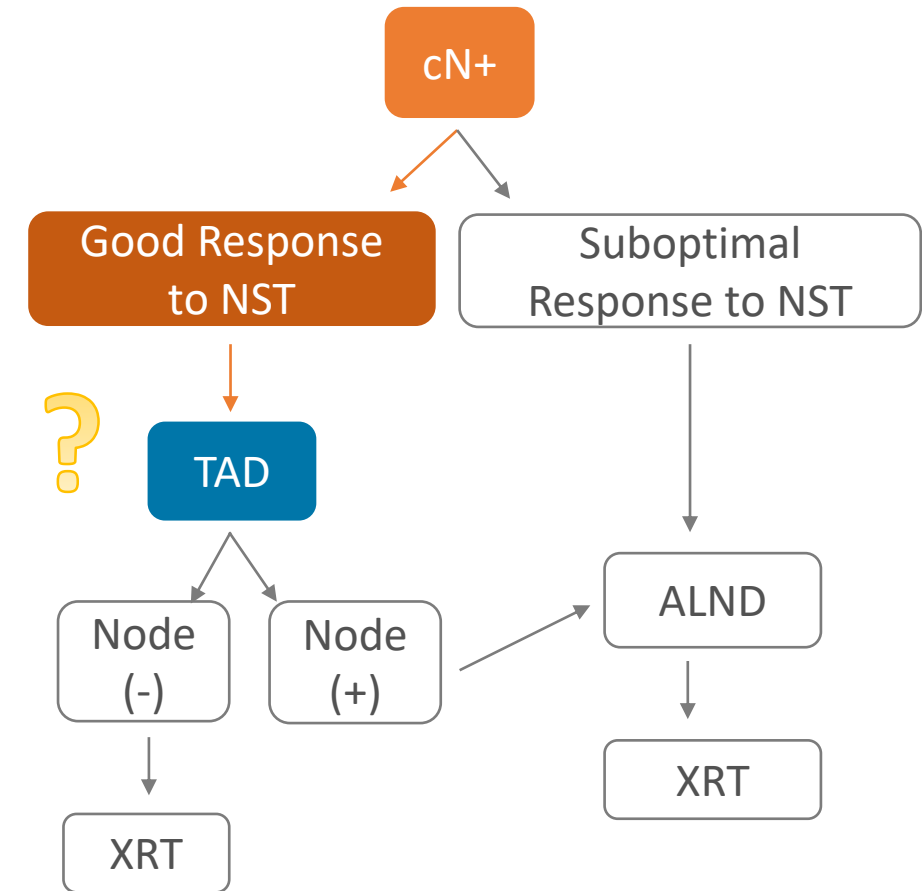
Lim et al. *Oncologist*. 2020  
Natsiopoulos et al. *Breast Cancer* 2019

# Axilla After Neoadjuvant Therapy: cN+

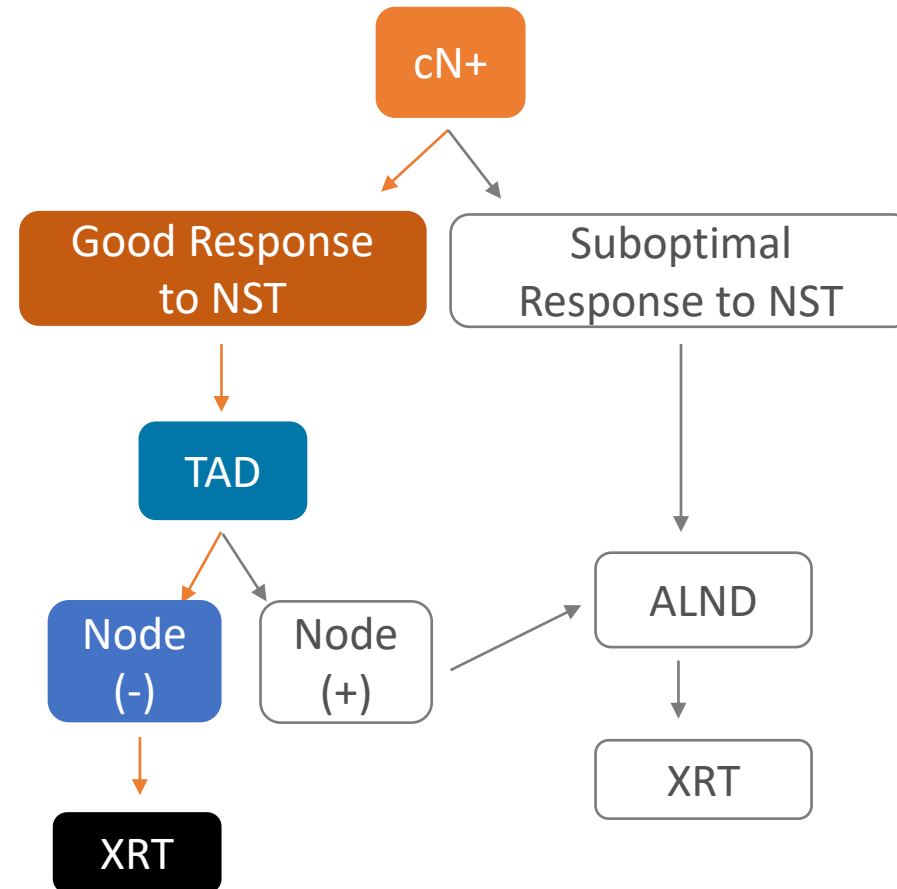
**PENDING**

## Surgical Management of the Axilla in Clinically Node-Positive Breast Cancer Patients Converting to Clinical Node Negativity through Neoadjuvant Chemotherapy: Current Status, Knowledge Gaps, and Rationale for the EUBREAST-03 AXSANA Study

Maggie Banys-Paluchowski <sup>1,2,\*</sup>, Maria Luisa Gasparri <sup>3,4</sup>, Jana de Boniface <sup>5,6</sup>, Oreste Gentilini <sup>7</sup>, Elmar Stickeler <sup>8</sup>, Steffi Hartmann <sup>9</sup>, Marc Thill <sup>10</sup>, Isabel T. Rubio <sup>11</sup>, Rosa Di Micco <sup>7</sup>, Eduard-Alexandru Bonci <sup>12,13</sup>, Laura Niinikoski <sup>14</sup>, Michalis Kontos <sup>15</sup>, Guldeniz Karadeniz Cakmak <sup>16</sup>, Michael Hauptmann <sup>17</sup>, Florentia Peintinger <sup>18</sup>, David Pinto <sup>19</sup>, Zoltan Matrai <sup>20</sup>, Dawid Murawa <sup>21</sup>, Geeta Kadayaprath <sup>22</sup>, Lukas Dostalek <sup>23</sup>, Helidon Nina <sup>24</sup>, Petr Krivorotko <sup>25</sup>, Jean-Marc Classe <sup>26</sup>, Ellen Schlichting <sup>27</sup>, Matilda Appelgren <sup>5</sup>, Peter Paluchowski <sup>28</sup>, Christine Solbach <sup>29</sup>, Jens-Uwe Blohmer <sup>30</sup>, Thorsten Kühn <sup>31</sup> and the AXSANA Study Group ‡

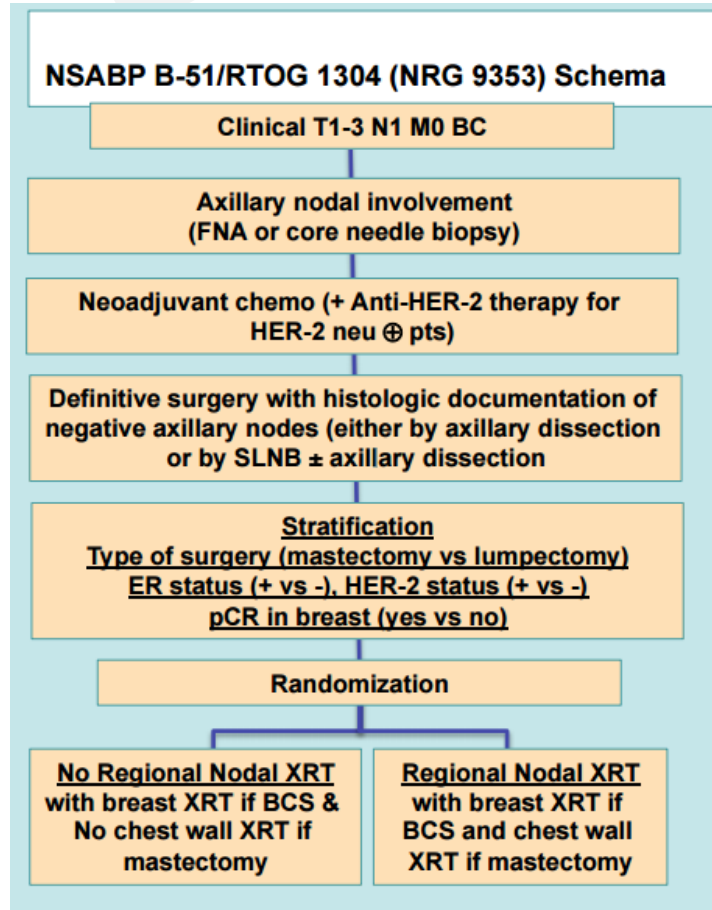


# Axilla After Neoadjuvant Therapy: cN+

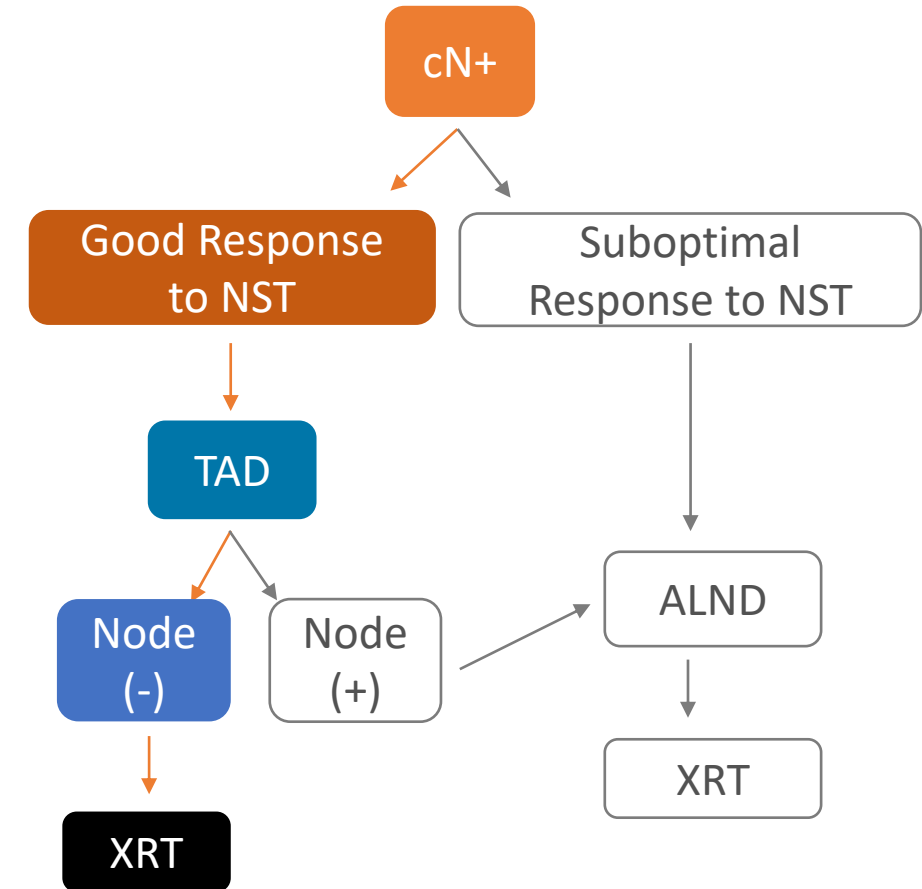


# Axilla After Neoadjuvant Therapy: cN+

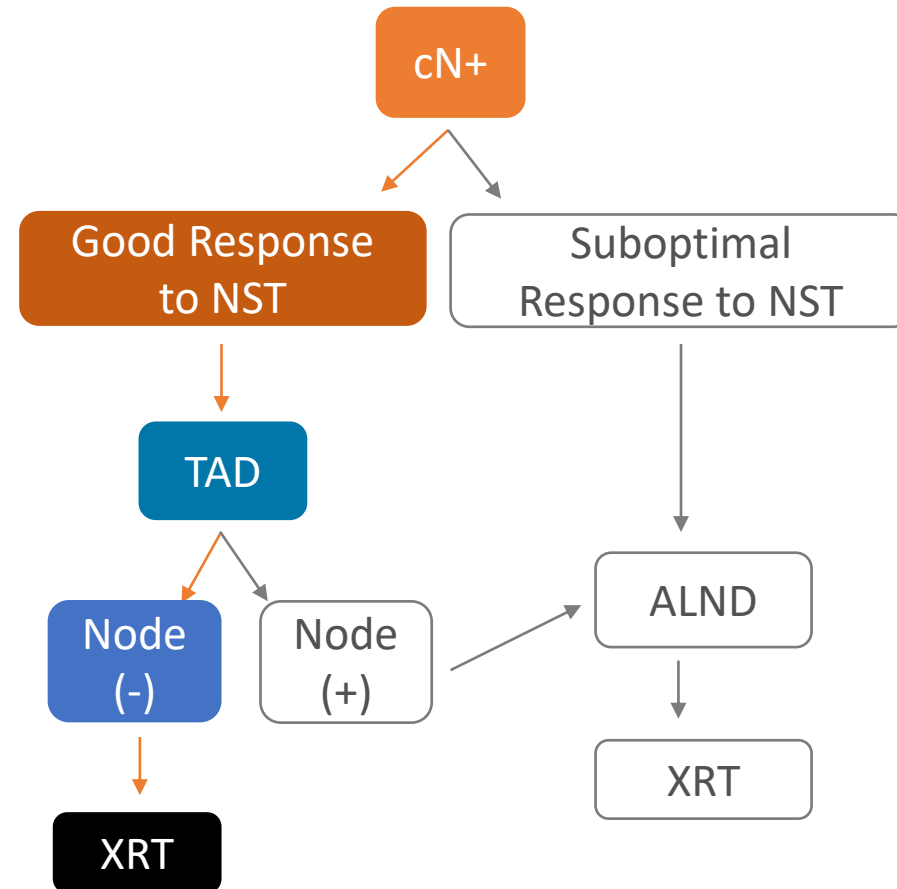
**PENDING**



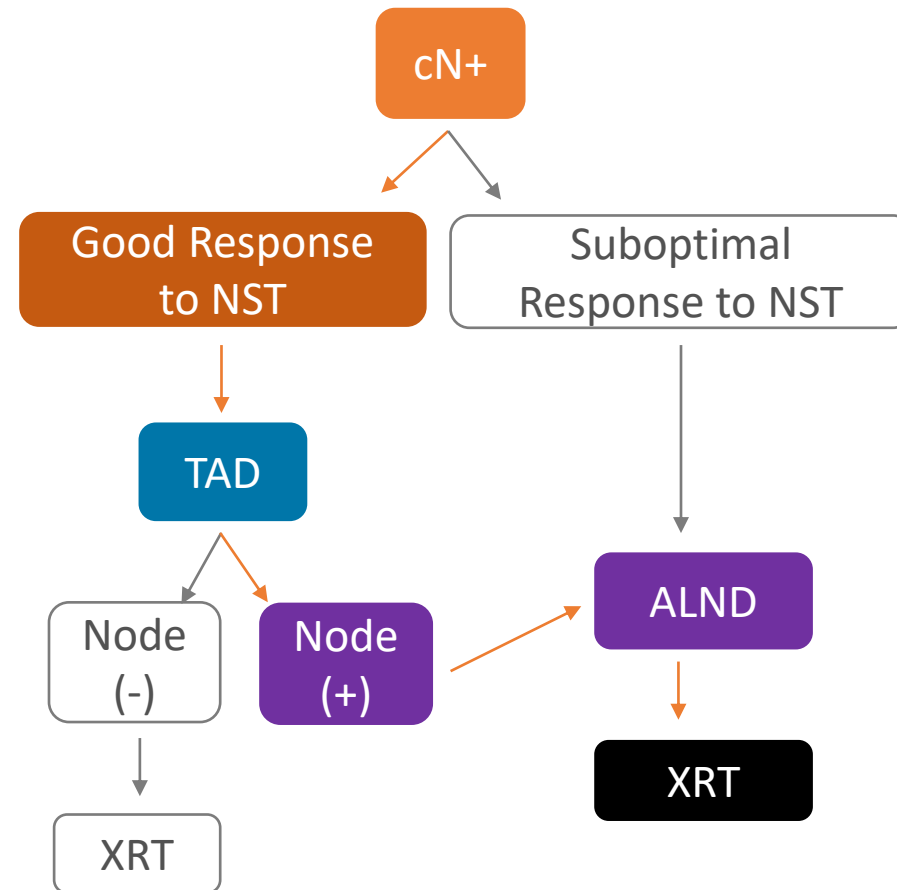
cN+ → ypN0  
Regional nodal XRT vs. no XRT



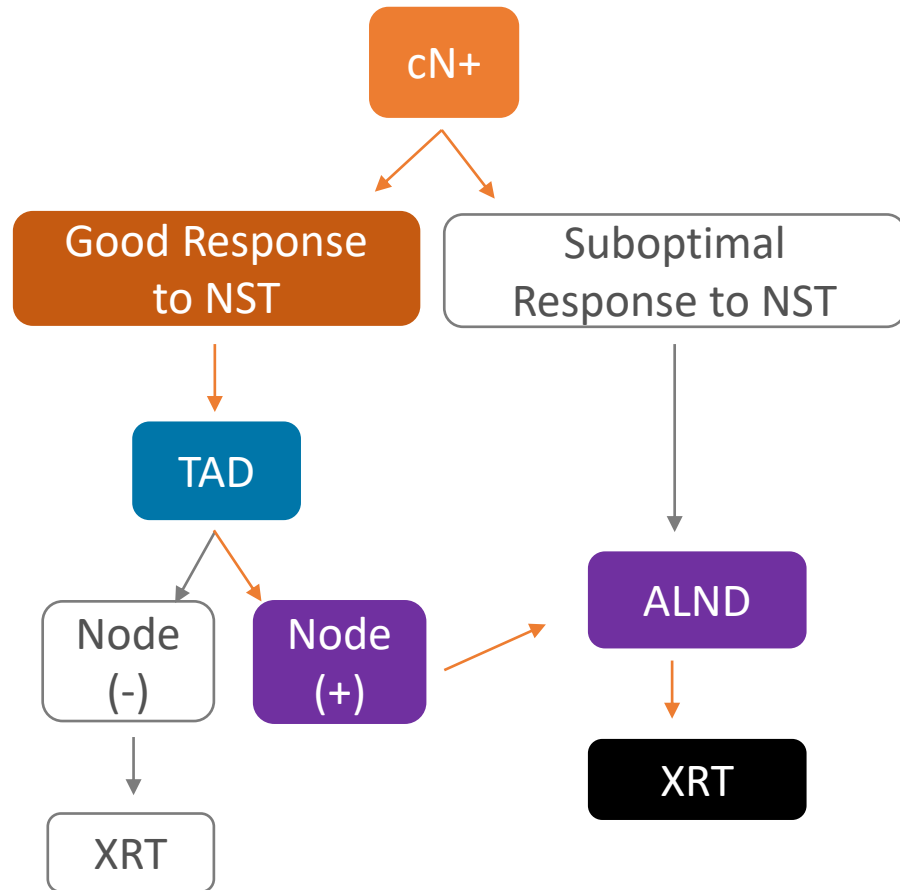
# Axilla After Neoadjuvant Therapy: cN+



# Axilla After Neoadjuvant Therapy: cN+

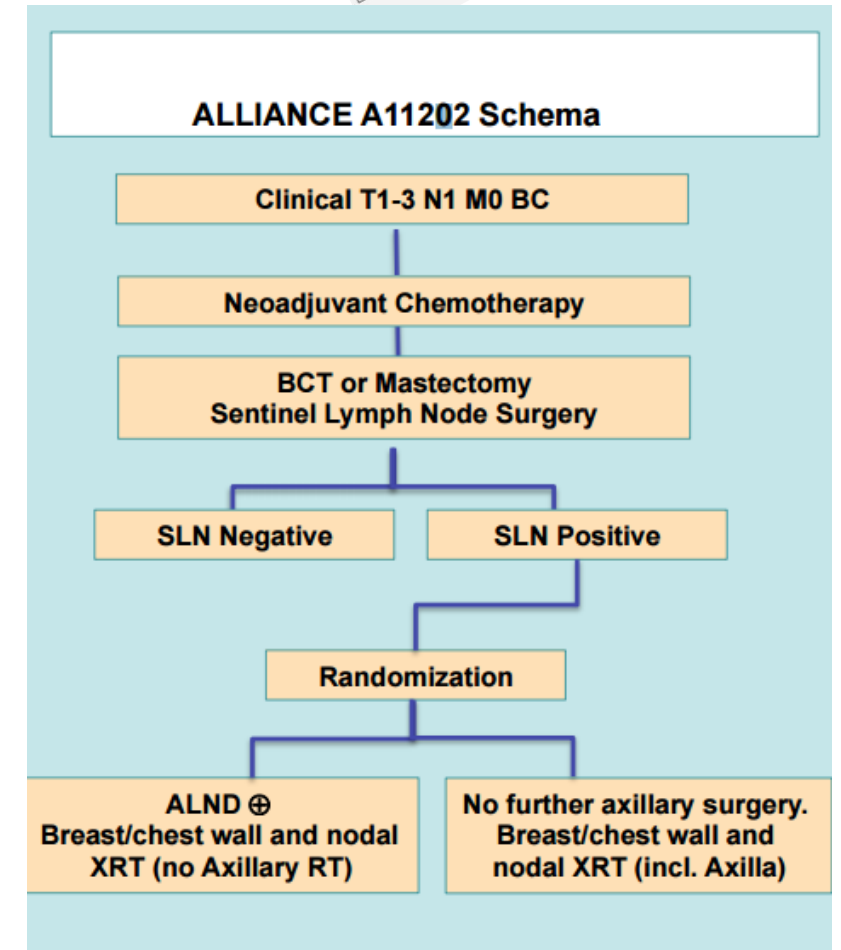


# Axilla After Neoadjuvant Therapy: cN+

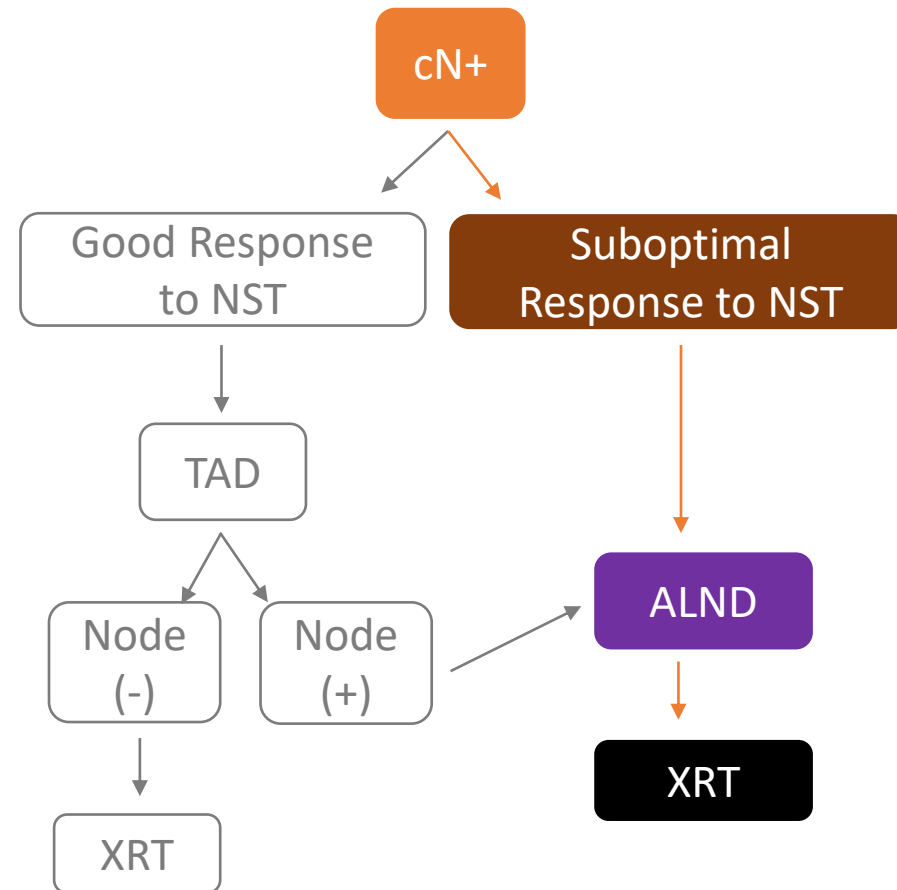


Path nodal micromets  
ALND vs. no ALND

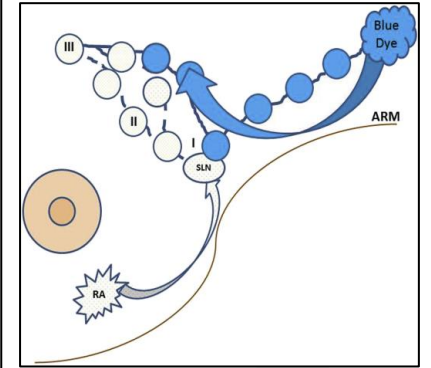
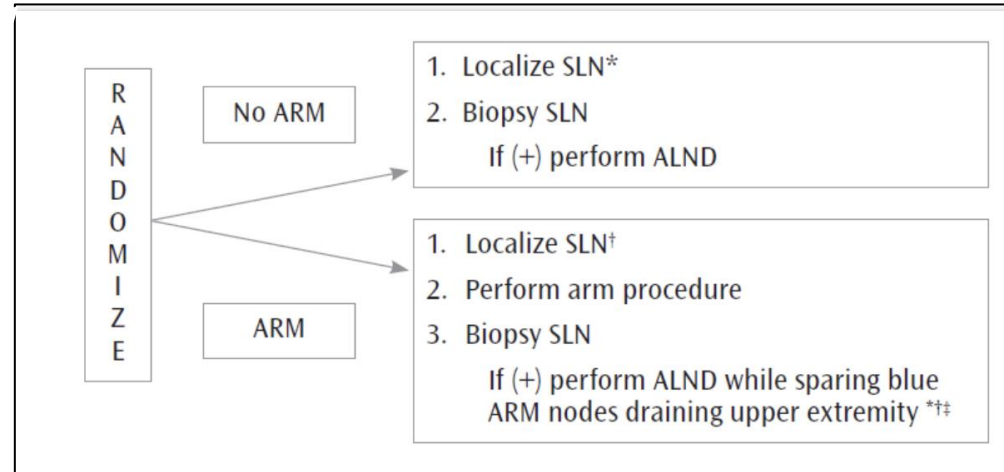
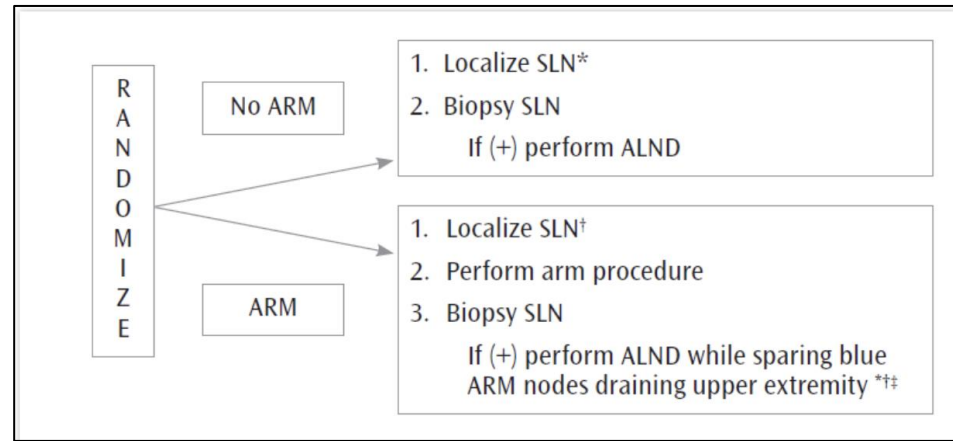
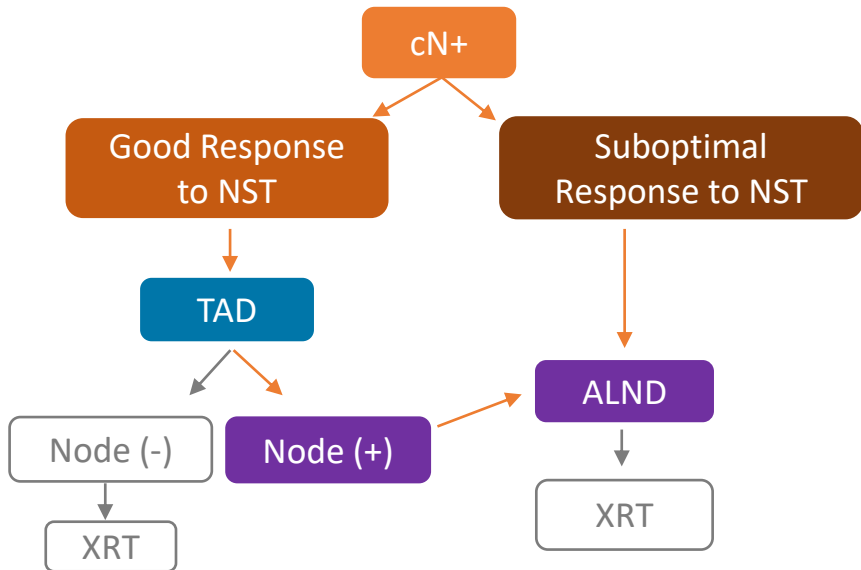
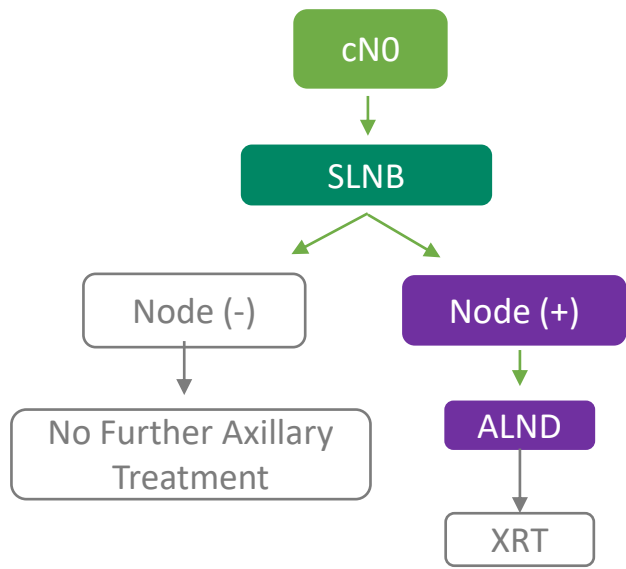
**PENDING**



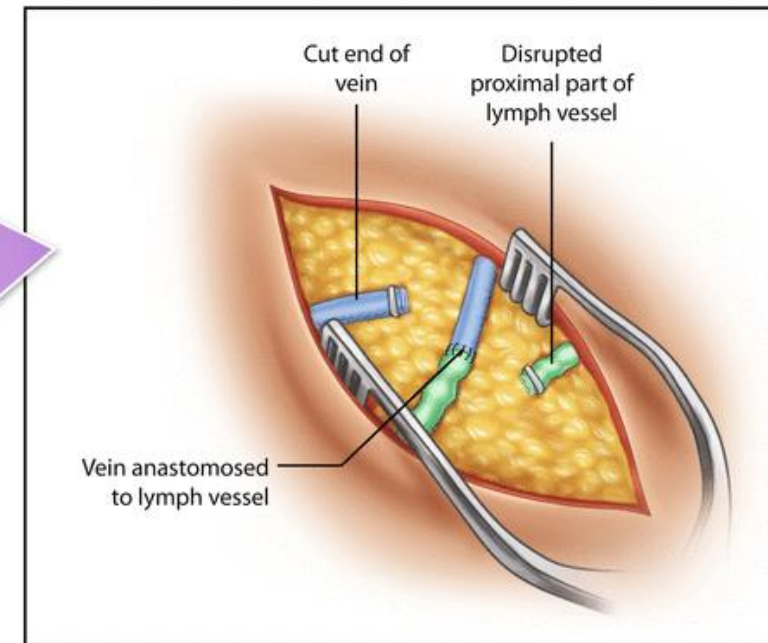
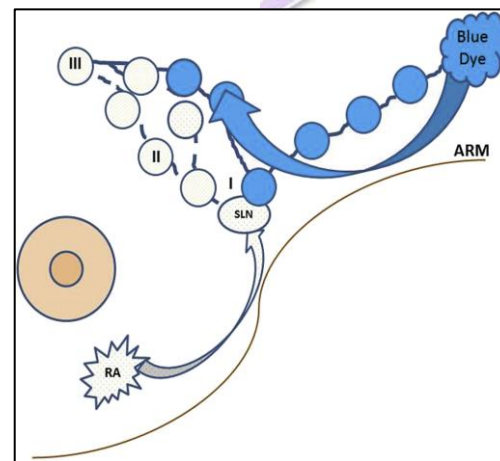
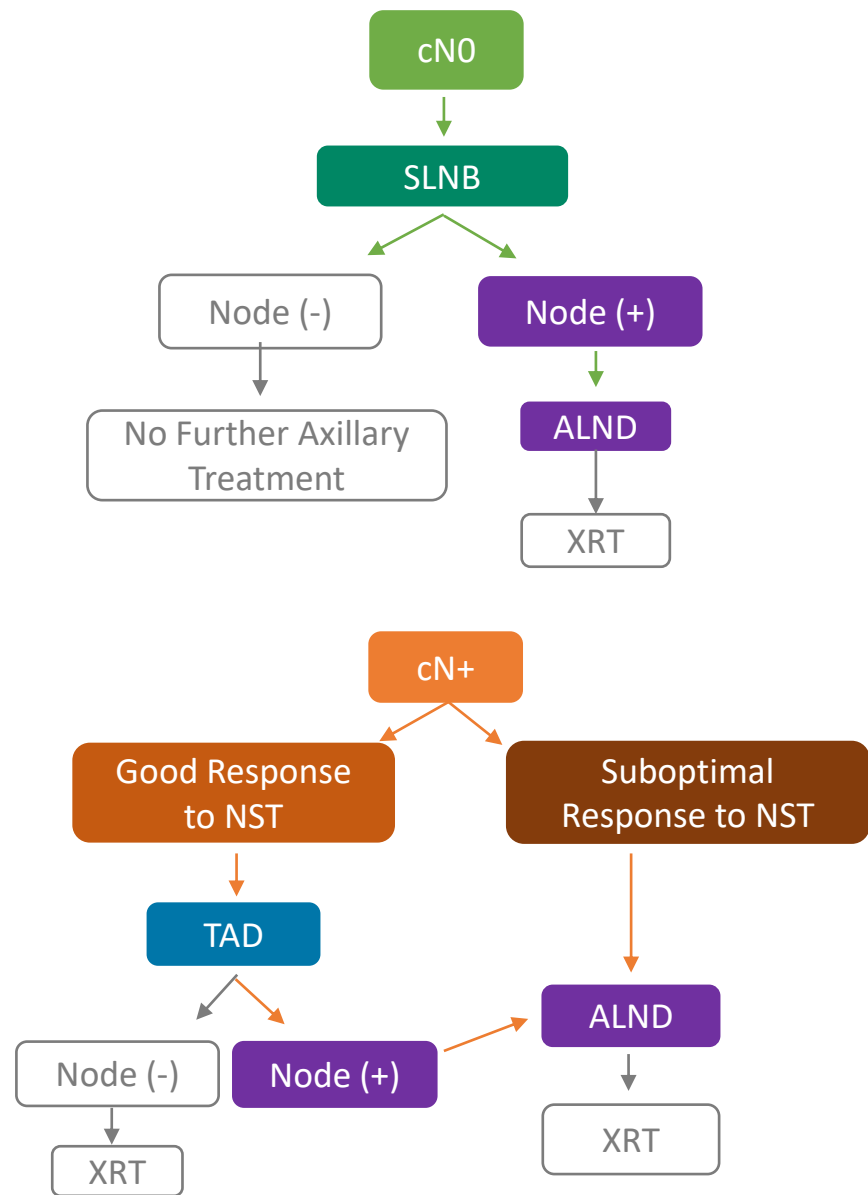
# Axilla After Neoadjuvant Therapy: cN+



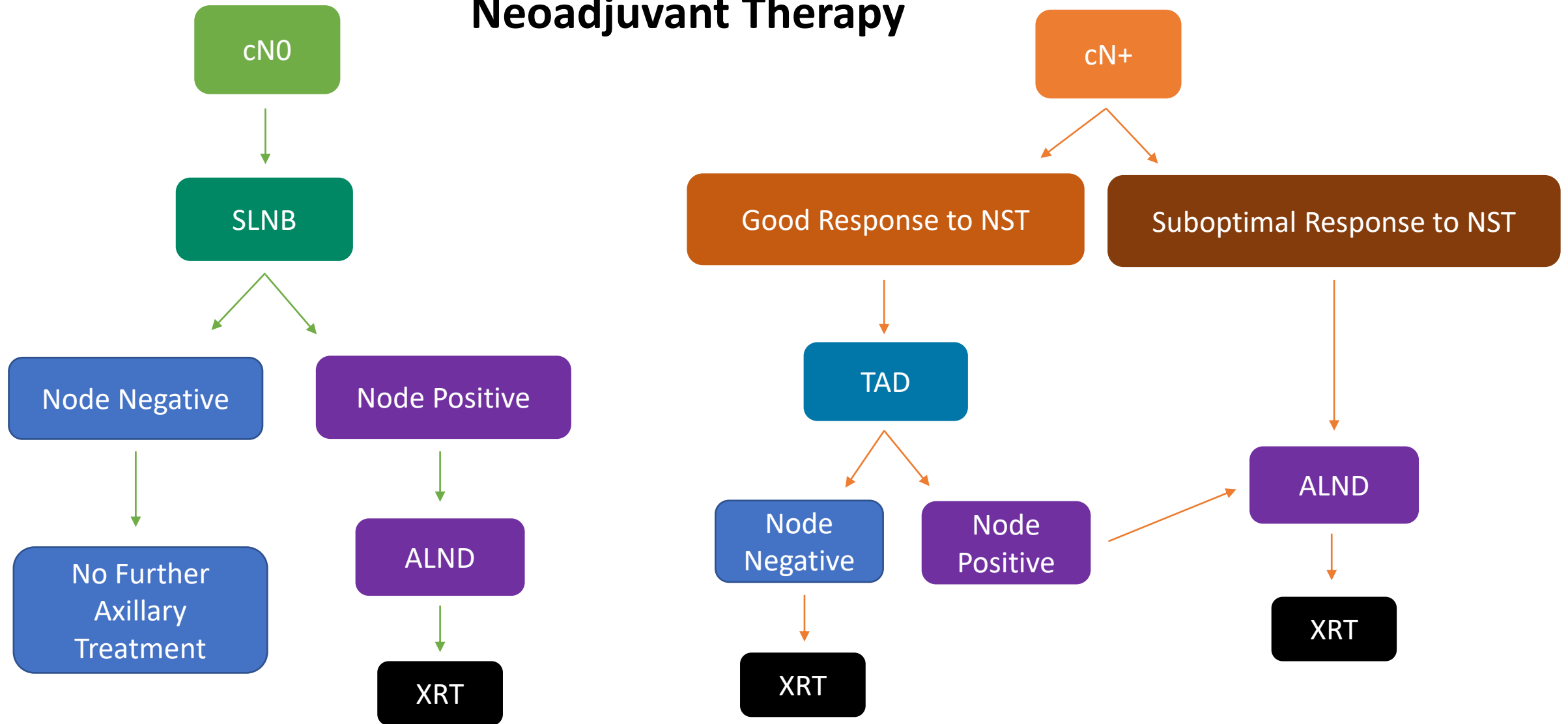




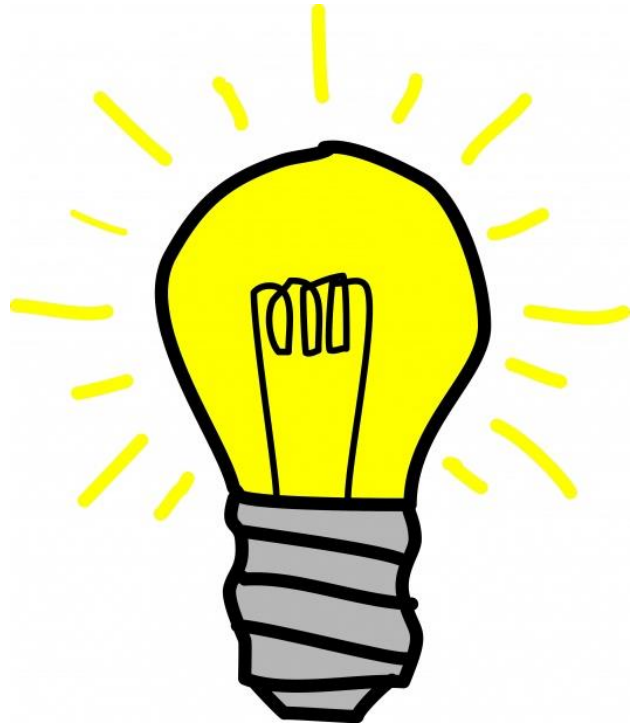
**PENDING**



# Axilla After Neoadjuvant Therapy



## Take Home Points



- ✓ Consider TAD for axillary sampling for initially cN+ patients with good response to NST
- ✓ Consider ALND with ypN+ after NST
- ✓ ALND can be deferred with ypN0 after NST

# References

- Banys-Paluchowski M, Gasparri ML, de Boniface J, et al; The Axsana Study Group. Surgical Management of the Axilla in Clinically Node-Positive Breast Cancer Patients Converting to Clinical Node Negativity through Neoadjuvant Chemotherapy: Current Status, Knowledge Gaps, and Rationale for the EUBREAST-03 AXSANA Study. *Cancers (Basel)*. 2021 Mar 29;13(7):1565. PMID: 33805367; PMCID: PMC8037995.
- Boileau JF, Poirier B, Basik M, et al. Sentinel node biopsy after neoadjuvant chemotherapy in biopsy-proven node-positive breast cancer: the SN FNAC study. *J Clin Oncol*. 2015 Jan 20;33(3):258-64. PMID: 25452445.
- Boughey JC, Suman VJ, Mittendorf EA, et al; Alliance for Clinical Trials in Oncology. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive breast cancer: the ACOSOG Z1071 (Alliance) clinical trial. *JAMA*. 2013 Oct 9;310(14):1455-61. PMID: 24101169; PMCID: PMC4075763.
- Breast Cancer. National Comprehensive Cancer Network. [https://www.nccn.org/professionals/physician\\_gls/pdf/breast.pdf](https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf).
- Caudle AS, Yang WT, Krishnamurthy S, et al. Improved Axillary Evaluation Following Neoadjuvant Therapy for Patients With Node-Positive Breast Cancer Using Selective Evaluation of Clipped Nodes: Implementation of Targeted Axillary Dissection. *J Clin Oncol*. 2016 Apr 1;34(10):1072-8. PMID: 26811528; PMCID: PMC4933133.
- Classe JM, Loaec C, Gimbergues P, et al. Sentinel lymph node biopsy without axillary lymphadenectomy after neoadjuvant chemotherapy is accurate and safe for selected patients: the GANEA 2 study. *Breast Cancer Res Treat*. 2019 Jan;173(2):343-352. PMID: 30343457.
- Consensus Guideline on Axillary Management for Patients With In-Situ and Invasive Breast Cancer: A Concise Overview. The American Society of Breast Surgeons. <https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-the-Management-of-the-Axilla-Concise-Overview.pdf>.
- Cardoso F, Kyriakides S, Ohno S, et al.; ESMO Guidelines Committee. Early breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol*. 2019 Oct 1;30(10):1674. PMID: 31236598.
- Diego EJ, McAuliffe PF, Soran A, et al. Axillary Staging After Neoadjuvant Chemotherapy for Breast Cancer: A Pilot Study Combining Sentinel Lymph Node Biopsy with Radioactive Seed Localization of Pre-treatment Positive Axillary Lymph Nodes. *Ann Surg Oncol*. 2016 May;23(5):1549-53. PMID: 26727919.
- Donker M, Straver ME, Wesseling J, et al. Marking axillary lymph nodes with radioactive iodine seeds for axillary staging after neoadjuvant systemic treatment in breast cancer patients: the MARI procedure. *Ann Surg*. 2015 Feb;261(2):378-82. PMID: 24743607.
- Gurleyik G, Aksu SA, Aker F, Tekyol KK, Tanrikulu E, Gurleyik E. Targeted axillary biopsy and sentinel lymph node biopsy for axillary restaging after neoadjuvant chemotherapy. *Ann Surg Treat Res*. 2021 Jun;100(6):305-312. PMID: 34136426; PMCID: PMC8176200.
- Hunt KK, Yi M, Mittendorf EA, Guerrero C, et al. Sentinel lymph node surgery after neoadjuvant chemotherapy is accurate and reduces the need for axillary dissection in breast cancer patients. *Ann Surg*. 2009 Oct;250(4):558-66. PMID: 19730235.
- Kuehn T, Bauerfeind I, Fehm T, et al. Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study. *Lancet Oncol*. 2013 Jun;14(7):609-18. PMID: 23683750.
- Kuemmel S, Heil J, Rueland A, et al. A Prospective, Multicenter Registry Study to Evaluate the Clinical Feasibility of Targeted Axillary Dissection (TAD) in Node-Positive Breast Cancer Patients. *Ann Surg*. 2020 Nov 4. PMID: 33156057.
- Lim GH, Gudi M, Teo SY, et al. Would Removal of All Ultrasound Abnormal Metastatic Lymph Nodes Without Sentinel Lymph Node Biopsy Be Accurate in Patients with Breast Cancer with Neoadjuvant Chemotherapy? *Oncologist*. 2020 Nov;25(11):e1621-e1627. PMID: 32537791; PMCID: PMC7648324.
- Mamounas EP, Brown A, Anderson S, et al. Sentinel node biopsy after neoadjuvant chemotherapy in breast cancer: results from National Surgical Adjuvant Breast and Bowel Project Protocol B-27. *J Clin Oncol*. 2005 Apr 20;23(12):2694-702. PMID: 15837984.
- Natsiopoulos I, Intzes S, Liappis T, et al. Axillary Lymph Node Tattooing and Targeted Axillary Dissection in Breast Cancer Patients Who Presented as cN+ Before Neoadjuvant Chemotherapy and Became cN0 After Treatment. *Clin Breast Cancer*. 2019 Jun;19(3):208-215. PMID: 30922804.
- Ochoa D, Korourian S, Boneti C, Adkins L, Badgwell B, Klimberg VS. Axillary reverse mapping: five-year experience. *Surgery*. 2014 Nov;156(5):1261-8. PMID: 25444319; PMCID: PMC4354953.
- Simons JM, van Nijnatten TJA, Smidt ML et al. San Antonio Breast Cancer Symposium 2020. <https://www.abstractsonline.com/pp8/#!/9223/presentation/2793%20>
- Siso C, de Torres J, Esgueva-Colmenarejo A, et al. Intraoperative Ultrasound-Guided Excision of Axillary Clip in Patients with Node-Positive Breast Cancer Treated with Neoadjuvant Therapy (ILINA Trial) : A New Tool to Guide the Excision of the Clipped Node After Neoadjuvant Treatment. *Ann Surg Oncol*. 2018 Mar;25(3):784-791. PMID: 29197044.
- Swarnkar PK, Tayeh S, Michell MJ, Mokbel K. The Evolving Role of Marked Lymph Node Biopsy (MLNB) and Targeted Axillary Dissection (TAD) after Neoadjuvant Chemotherapy (NACT) for Node-Positive Breast Cancer: Systematic Review and Pooled Analysis. *Cancers (Basel)*. 2021 Mar 26;13(7):1539. PMID: 33810544; PMCID: PMC8037051.