



Sentinel lymph node biopsy following neoadjuvant chemotherapy for initially node-positive breast cancer: what have we learned?

CONFERÊNCIA BRASILEIRA DE

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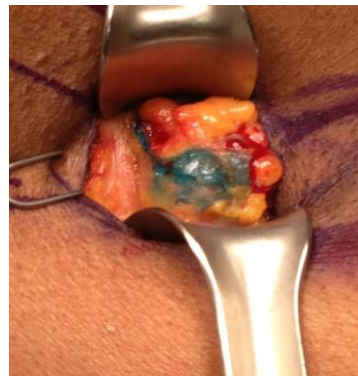
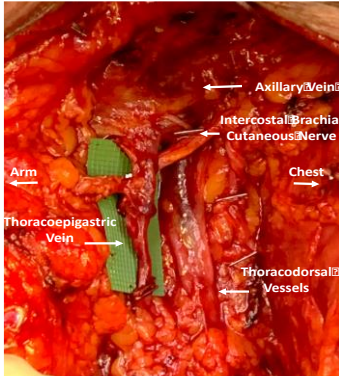
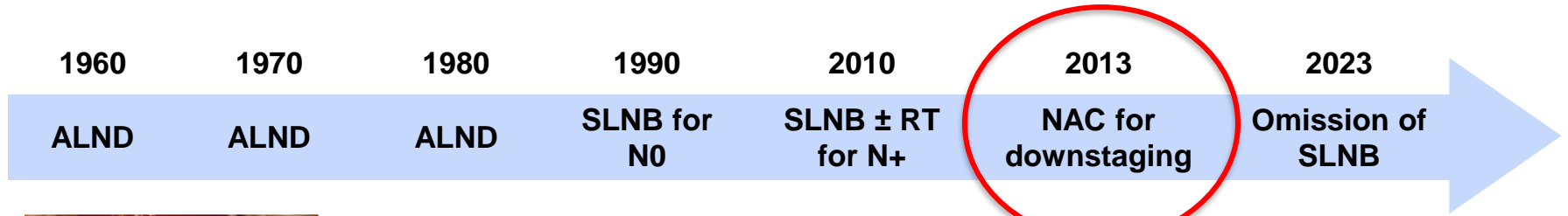
REALIZAÇÃO



Disclosures

Speaking honorarium Novartis

Evolution of Axillary Management Over Time



Shift towards less extensive axillary surgery driven by desire to reduce morbidity and an understanding that tumor biology determines prognosis and dictates treatment decisions

Axillary Management after NAC in 2024

Clinical controversies

1. Staging the axilla cN+ patients after NAC: TAD or SLNB?
2. What is the optimal SLNB technique?
3. Do patients with residual disease in SLNs after NAC need ALND?
4. Can SLNB be done in patients with LABC after NAC?

SLNB Feasibility in cN+ Patients After NAC

- 4 prospective, multi-institutional trials
- Primarily included cT1-3N1 patients
- SLNB → back-up ALND

	ACOSOG Z1071	SN FNAC	SENTINA	GANEA 2
n	689	153	592 (cN+)	307
cTN	cT0-4 N1/N2	cT0-3 N1/N2	cN0/N1/N2	pN1*
IR	92.7%	87.6%	80.1%	79.5%
FNR (Overall)	12.6%	13.3%	14.2%	11.9%

The use of dual tracer and removal of ≥ 3 SLNs resulted in FNR < 10%

Additional Methods to Decrease the FNR: Retrieving the Clipped Node

Clip can be placed in node at time of initial node biopsy, and can be targeted for retrieval at time of SLNB post-NAC

Study	n	FNR
ACOSOG Z1071		
Clip in SLN	107	6.8%

**Clipped node not an SLN up to 23% of the time,
likely related to suboptimal SLN sampling**

Targeted axillary dissection (TAD) vs SLNB: False-negative rate

TAD=SLNB + retrieval of clipped node

MD Anderson

N = 85 TAD/ALND

FNR 2%

SenTa

Prospective multicenter study

N = 77 TAD/ALND

FNR 4.3%

SLNB with retrieval of ≥ 3 SLNs

ACOSOG Z1071

N = 388 ≥ 3 SLNs retrieved

FNR = 9.1%

Meta-analysis 13 studies

N = 1921 cN+ patients

SLNB/ALND

FNR 4% (0-9%) (≥ 3 SLNs)

Targeted axillary dissection (TAD) vs SLNB: Technical Challenges

TAD=SLNB + retrieval of clipped node

1. Additional localization procedure required
2. Additional cost
3. Failure to visualize clip by sonography post-NAC (~ 20%)
4. Failure to retrieve clipped node (7-30%), resulting in unnecessary ALND

SLNB with retrieval of ≥ 3 SLNs

1. Wide variation in frequency of identifying ≥ 3 SLNs (34-93%)
2. Use of dual mapping preferred (to increase identification rate), which may increase cost

Is Dual Tracer Mapping Always Needed for SLNB in Initially N+ patients after NAC?

FNR 16-20% with single tracer vs 9-11% with dual tracer mapping
Resource constraints may limit availability of dual tracer

Fortaleza General Hospital
Feasibility of blue dye alone for SLNB after NAC

N = 100 cN+ → ycN0 SLNB blue dye alone

Identification rate 96%

Among ypN0 patients (n = 70), ≥3 SLNs detected in 78%

Median follow-up 36 months

No axillary recurrences

Nodal Recurrence Rates Are Low in cN+/ypN0 Patients Treated with SLNB Alone After NAC

Study	n	Inclusion	Median follow-up	% Nodal recurrence
European Institute of Oncology (2020)	123	cN1/N2	110 months	1.6%
Istituto Nazionale dei Tumori (2020)	81	cN1	87 months	0%
Mayo Clinic (2020)	159	cN1/N2/N3	34 months	0.9%
McGill University (2021)	58	cN1/N2	36 months	0%
NEOSENTI-TURK (2021)	211	cN1/N2/N3	36 months	0%
MSKCC (2021)	234	cN1	40 months	0.4%
OPBC-04 (2022)	1144	cN1/2/3	42 months	1%


Kahler-Ribeiro-Fontana S, Eur J Surg Oncol 2020; Martelli G, Ann Surg 2020; Piltin M, Ann Surg Oncol 2020; Wong S, Ann Surg Oncol 2021; Cabioglu N, Eur J Surg Onc 2021; Barrio AV JAMA Oncol 2021; Montagna G, JAMA Oncol *in press*

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Clipped nodes were not localized



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Nodal recurrence: TAD vs SLNB

OPBC-04 Multicenter Study

1282 T1-4 biopsy-proven N1-3 breast cancers (April 2013-December 2020)

138 Excluded

- 63** Follow-up < 1 year
- 4** Had ALND
- 1** Inflammatory breast cancer
- 1** Stage IV
- 2** Unknown adjuvant therapy
- 16** not biopsy proven N+
- 50** non-consecutive

1144 consecutive cases included

666 SLNB

100% dual tracer mapping
Median f/u 4.2 years

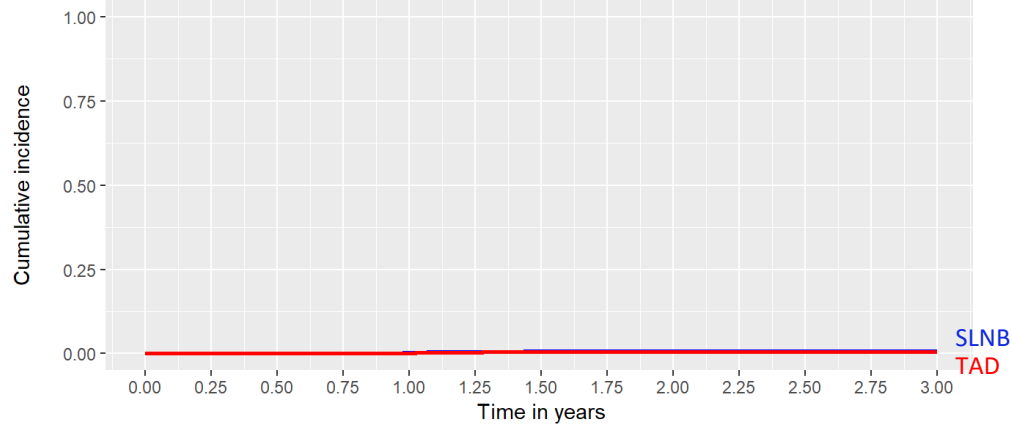
478 TAD

Clipped node retrieved 99%
Median f/u 2.7 years

Nodal recurrence: TAD vs SLNB

OPBC-04 Multicenter Study

**3-year rate of any axillary recurrence TAD vs SLNB
(0.5% vs 0.8%, p = 0.55)**



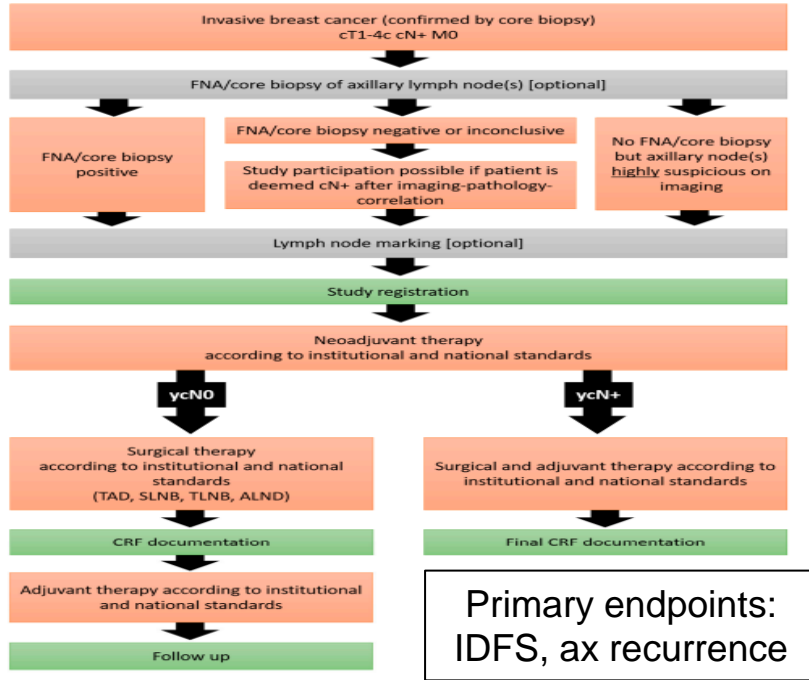
TAD — No — Yes

Number at risk

Strata	0.00	0.25	0.50	0.75	1.00	1.25	1.50	1.75	2.00	2.25	2.50	2.75	3.00
SLNB	666	664	660	653	641	615	600	572	540	511	481	448	420
TAD	478	477	471	462	439	401	366	336	308	271	250	230	213

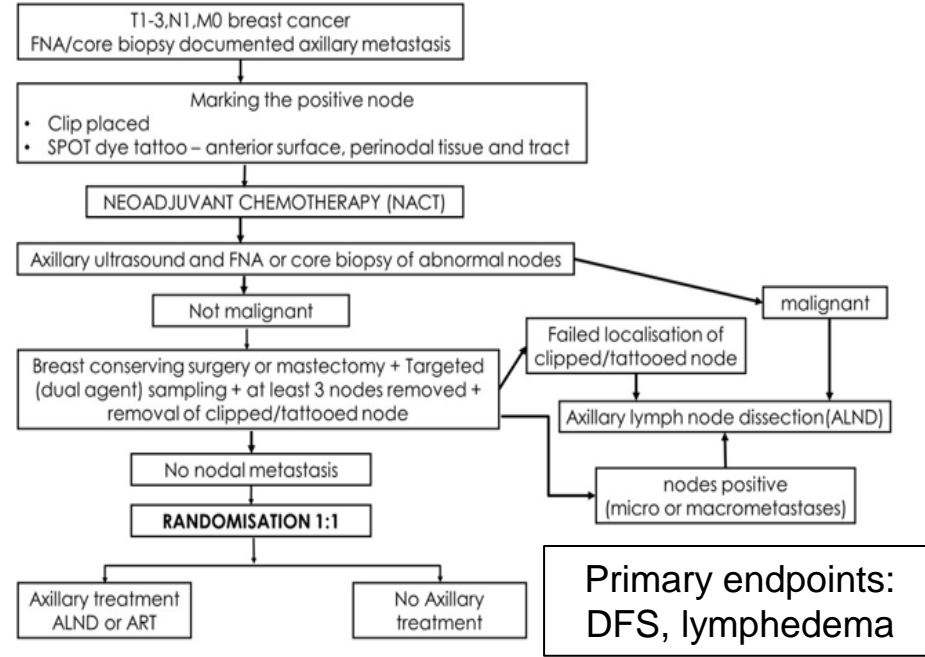
Ongoing Prospective Clinical Trials

AXSANA PI: Thorsten Kuhn



<https://clinicaltrials.gov/ct2/NCT04373655>

ATNEC PI: Amit Goyal



<https://clinicaltrials.gov/ct2/NCT04109079>

Nodal pCR Varies by Receptor Subtype

Systematic Review and Meta-analysis

33 studies

n = 57,531 cN+ patients

Receptor Status	Nodal pCR (%)
HR+/HER2-	18%
HR+/HER2+	45%
HR-/HER2+	60%
Triple Negative	48%

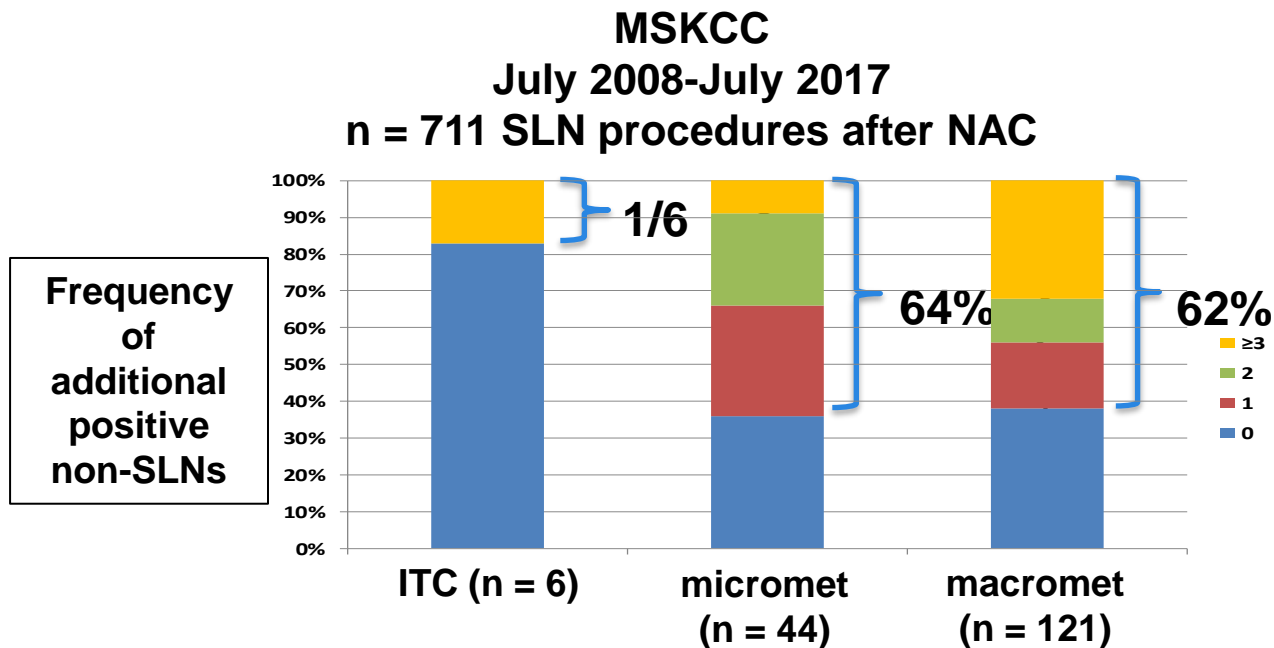
**In patients with residual disease in the SLN after NAC,
what is the most appropriate axillary treatment?**

Rates of Non-SLN Positivity in Patients with + SLNs After NAC

Study	n	Non-SLN positivity
Jeruss	104	71%
Galimberti	396	71.5%
Moo	171	61%

Rates of Non-SLN positivity high after NAC across all studies

Volume of Disease in SLN Is Not a Predictor of Likelihood of Non-SLN Disease After NAC



Management of axilla in patients with ITCs after NAC to be discussed by Dr. Millen

Limited Data on Nodal Recurrence in Patients with Residual Disease in SLN Treated with SLNB Alone

Study	n	Inclusion	Median follow-up	% Nodal recurrence
European Institute of Oncology	9	cN1/N2	110 months	22%
Istituto Nazionale dei Tumori	18	cN1	87 months	0%
Mayo Clinic	19	cN1/N2/N3	34 months	0%
NEOSENTI-TURK	73	cN1/N2/N3	36 months	1.4%

Outside of a clinical trial, patients with residual disease in SLNs post-NAC should be treated with ALND

Increase in Use of SLNB Alone in Patients with Residual Disease After NAC: Real World Data

NCDB

2012-2015
n = 30,173 cT0-4 N1/2 NAC

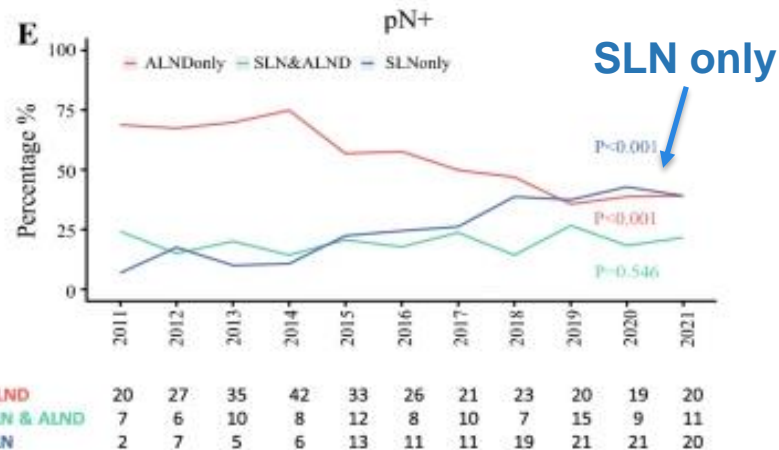
TABLE 2 Pathologic ypN stage and lymph node results

	All patients (n = 30,173) n (%)	SNB (n = 5157) n (%)
<i>Pathologic ypN stage</i>		
0	11,566 (38.3)	3429 (66.5)
1	11,215 (37.2)	1563 (30.3)
2	5325 (17.6)	142 (2.8)
3	2066 (6.8)	23 (0.4)
Nodes examined: n (IQR)	11 (5–18)	3 (2–6)
Nodes positive: n (IQR)	2 (1–5)	1 (0–2)

Nearly 1/3 patients treated with SLNB alone were ypN+

I SPY-2

2011-2021
N = 525 ypN+ after NAC

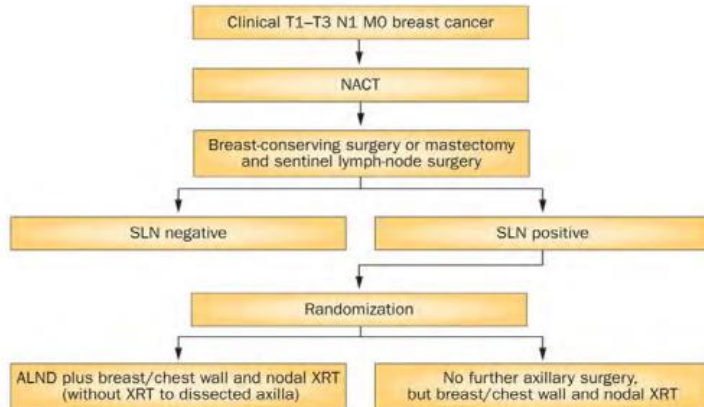


SLN-only ↑ 6.9% to 39.2% (p < 0.0001)

Ongoing Randomized Clinical Trials



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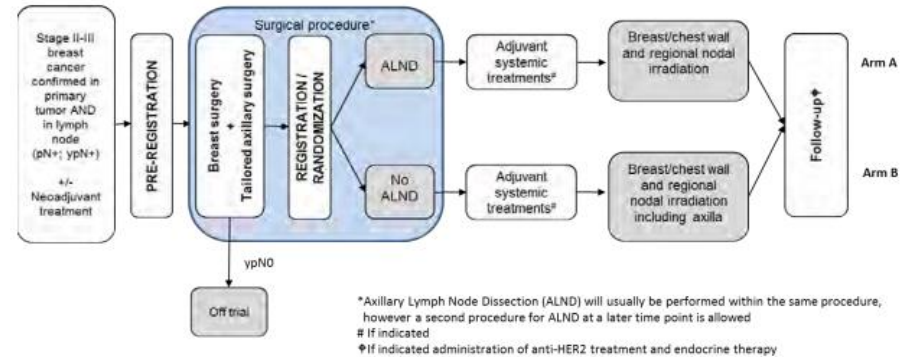


PI: Judy Boughey

<https://www.clinicaltrials.gov/ct2/show/NCT01901094>



TAXIS



PI: Walter P. Weber

<https://clinicaltrials.gov/ct2/show/NCT03513614>

Ongoing Clinical Trials for Micromets in SLN

Accrual began June 2019
Planned accrual N = 850

NEONOD2



cT1-3N+ breast cancer

NAC

ycN0 (lumpectomy or mastectomy)

SLNB

ypN1mic (experimental)
No ALND or nodal RT

ypN0/ypN0i+ (standard)
No ALND or nodal RT

PI: Corrado Tinterri

SLNB for Locally Advanced Breast Cancer: Limited Data

Studies of SLNB in IBC

	N	IR	FNR
Stearns	8	75%	25%
Hidar	20	80%	18%
DeSnyder	16	25%	NR
Karanlik	25	68%	20%

SLNB in other cT4, N2/N3

cT4

n = 33 in Z1071
FNR not reported separately

cN2

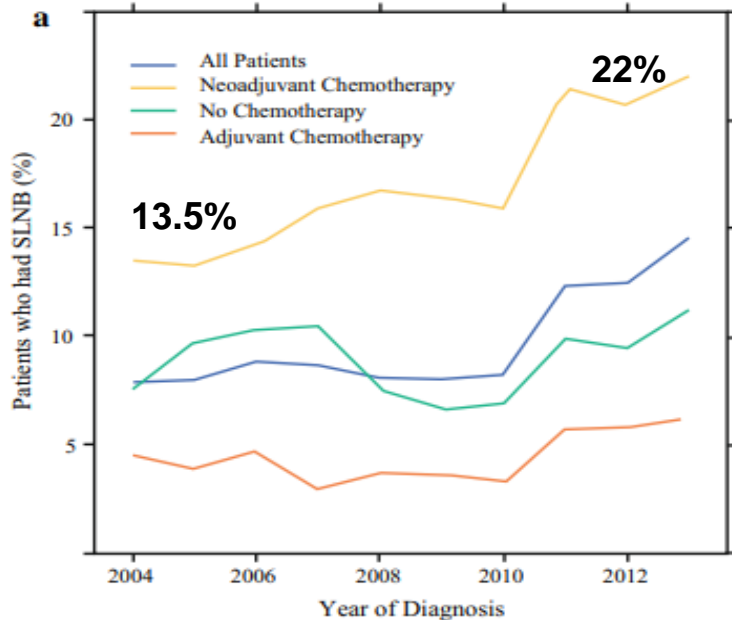
n = 38 in Z1071 and SN FNAC
FNR 0%, but limited numbers

cN3

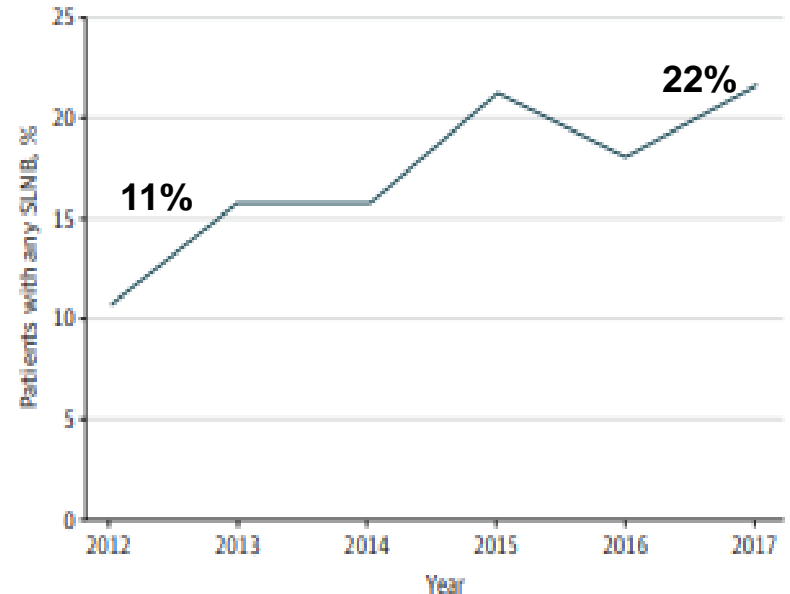
No studies evaluating SLNB feasibility

Increasing Use of SLNB in Locally Advanced Breast Cancer: Real World Data

SLNB in cN2/3 disease
NCDB n = 22,156



SLNB in IBC
NCDB n = 1,096



Tumor Biology Predicts Response to NAC in Locally Advanced Breast Cancer

MSKCC (2006-2016) cT4 and/or cN2/N3 n = 310 biopsy-proven N+		
Nodal pCR		
Receptor Subtype	n	%
All	310	38
HR+HER2-	132	17
HR-HER2-	70	41
HER2+	108	63

MDACC (2002-2018) Inflammatory Breast Cancer n = 66 biopsy-proven N+		
Nodal pCR		
Receptor Subtype	n	%
All	66	36
HR+HER2-	17	6
HR-HER2-	21	24
HER2+	28	66

Given high nodal pCR rates, SLNB would be appropriate if IR high and if SLNB accurately predicts status of axilla

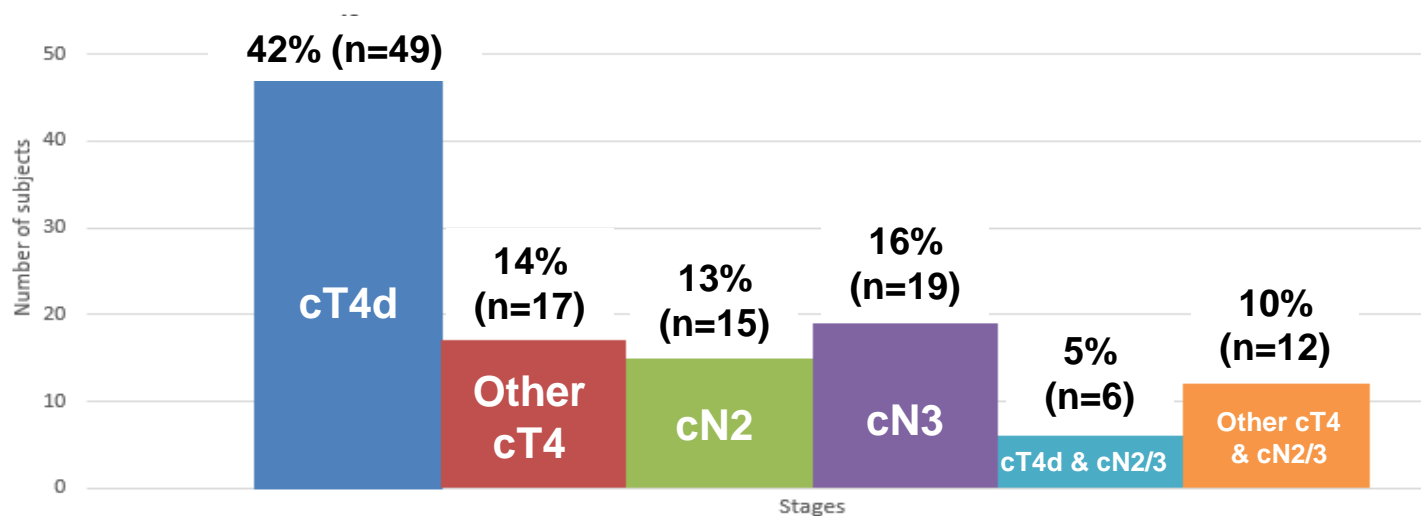
SLNB After NAC in Patients Presenting with Locally Advanced Breast Cancer: A Prospective Study

- **Eligibility:**
 - Female breast cancer patients
 - cT4 and/or cN2/N3 treated with NAC
 - Clinically node negative after NAC
- **Design:**
 - Single-arm prospective trial, multi-institutional (MSKCC and MCI)
 - Eligible patients undergo SLNB with dual-tracer mapping, followed by completion axillary dissection
 - Attempt to retrieve ≥ 3 SLNs
- **Primary Objective:**
 - Prospectively determine false-negative rate of SLNB after NAC in locally advanced breast cancer patients

SLNB After NAC in Patients Presenting with Locally Advanced Breast Cancer: A Prospective Study

Accrual began August 2017
Target accrual n = 150

cT4 and/or cN2/N3
n = 118



n = 118 completed surgery; Nodal pCR 44%

What Have We Learned?

- Avoidance of ALND in cN+ patients who achieve nodal pCR after NAC is oncologically safe with low rates of nodal recurrence with either TAD or SLNB

BASED ON RETROSPECTIVE DATA TAD = SLNB

- While dual tracer mapping is preferred in cN+ patients after NAC, in resource constrained settings SLNB with single tracer is feasible, although longer follow-up is needed regarding oncologic safety

What Have We Learned?

- In patients with residual disease in the nodes after NAC (excluding ITCs), ALND remains the standard of care due to the higher residual nodal burden and limited data on nodal recurrence in patients treated without ALND
- In patients with locally advanced breast cancer, ALND is indicated after NAC irrespective of response to treatment; ongoing studies are evaluating the feasibility of SLNB in this cohort

Thank You

