SABCS Review
Localized Therapy: Updates from a Surgery Perspective

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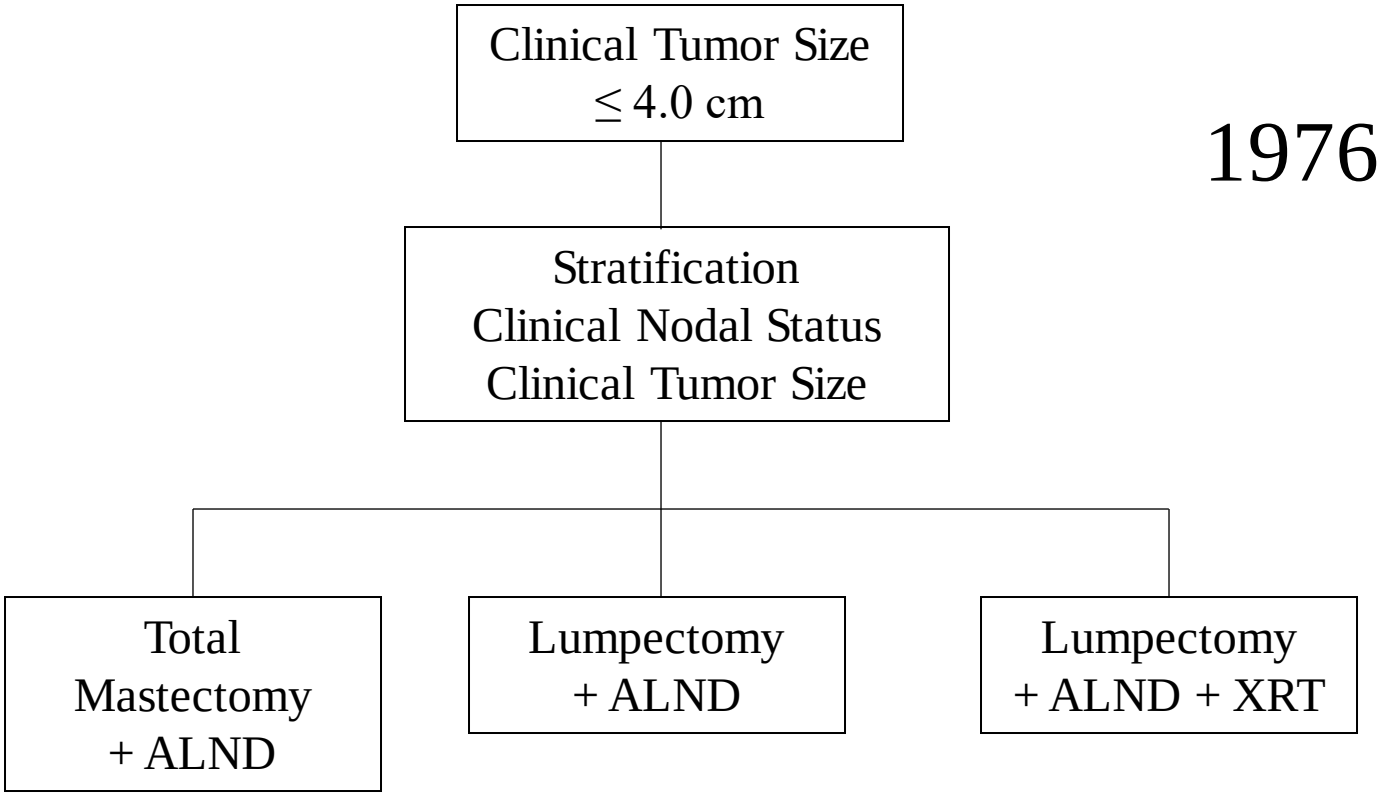
Disclosures

- Sponsored research agreement with prior institution, from Myriad Laboratories Inc. (Closed)

- Permissions have been obtained from Drs. Boughey and Montagna to present their slides from SABCS

Breast Surgery Updates

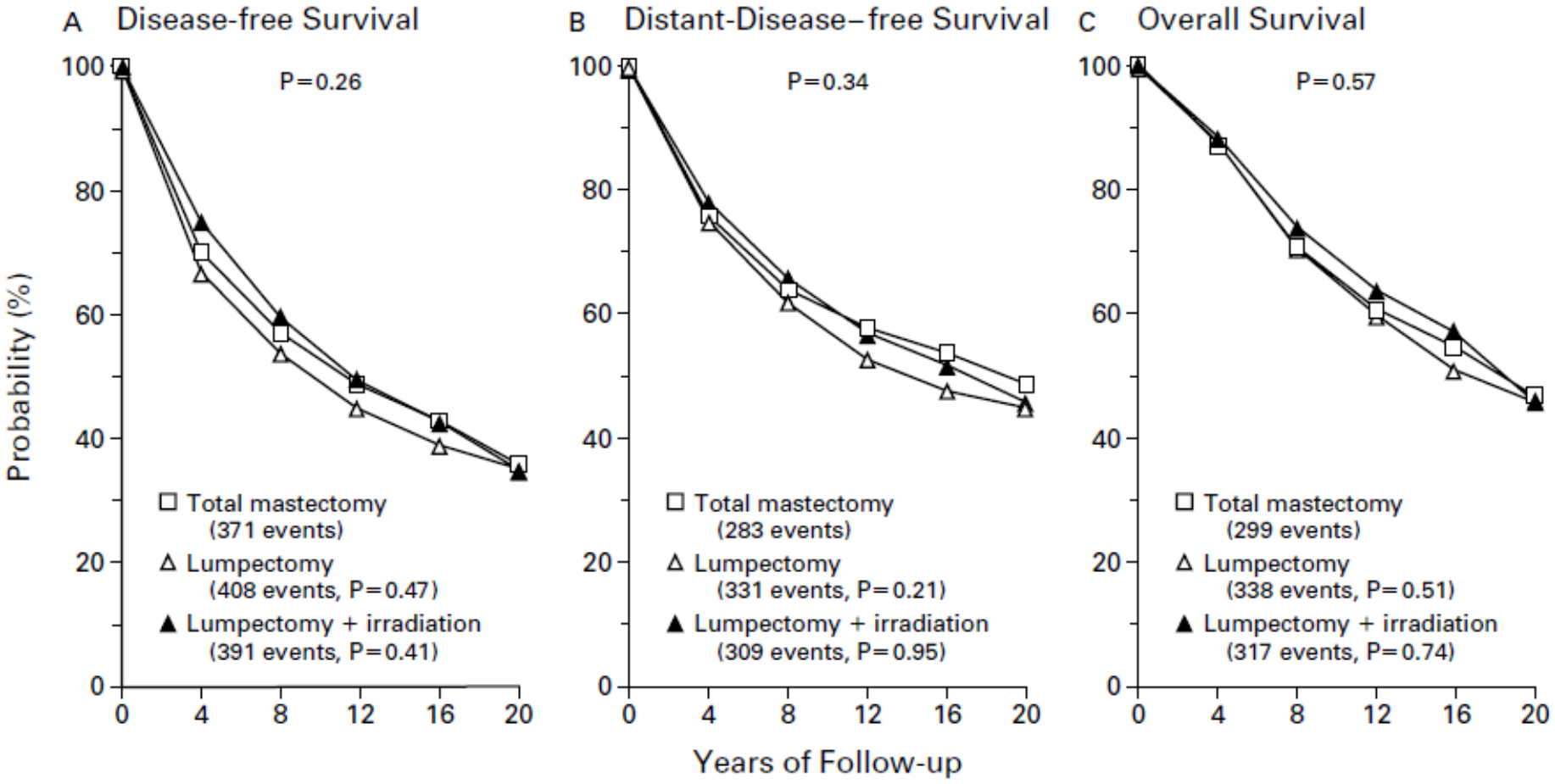
Breast conservation: NSABP B-06



1976-1984

- All patients with histologically positive axillary lymph nodes received melphalan + 5-FU
- Total mastectomy performed in event of ipsilateral breast tumor recurrence

Breast conservation: NSABP B-06

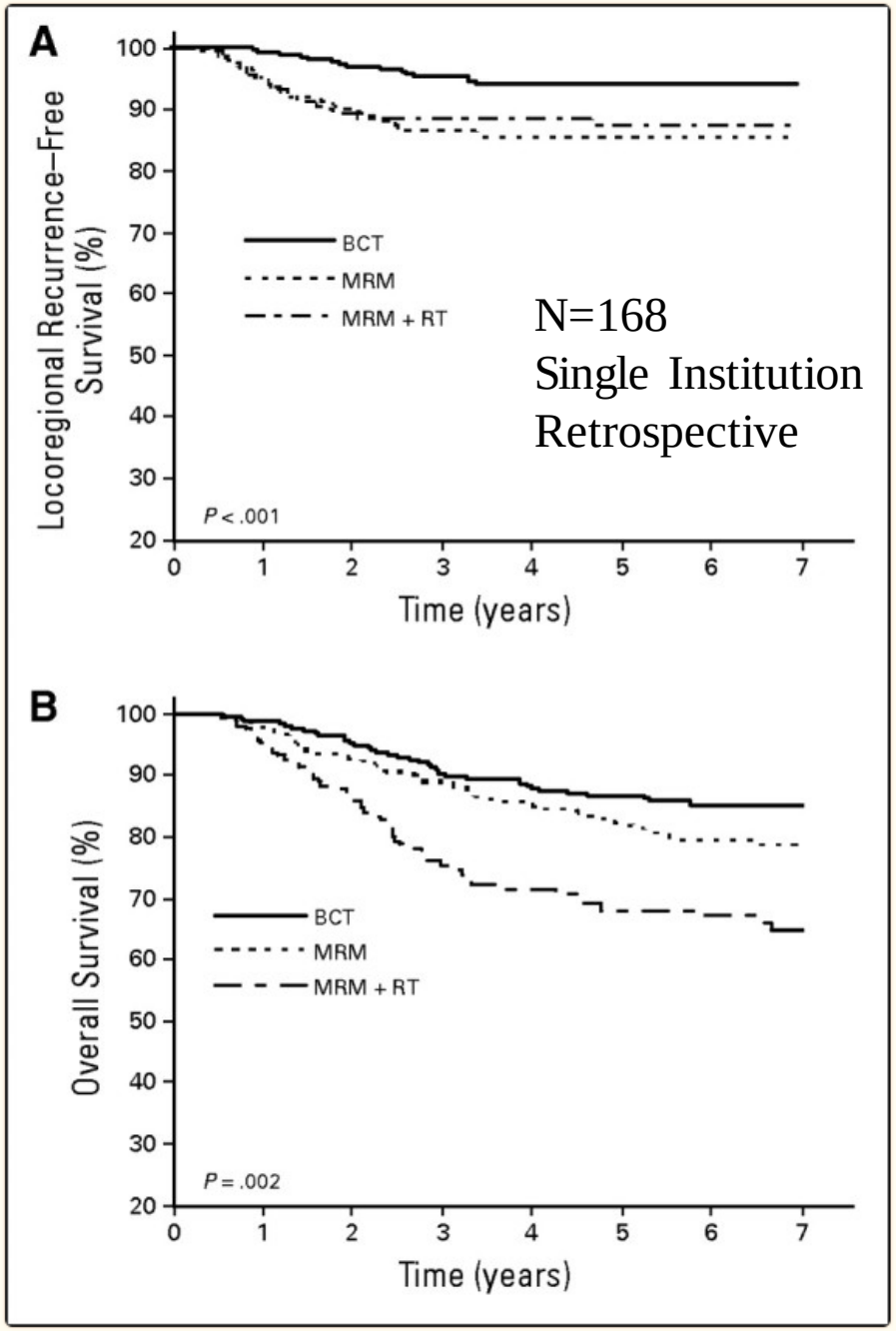


Fisher B. N Engl J Med 2002

Breast conservation

- Superior to mastectomy?

BCT	1		
MRM	3.44	2.04 to 5.80	< .001
MRM + RT	0.72	0.36 to 1.43	.34



Abdulkarim J Clin Oncol 2011

Overall survival following breast conserving surgery and adjuvant radiotherapy compared with mastectomy for early stage breast cancer: A systematic review and meta-analysis

KK Rajan[1,2], K Fairhurst[1,4], B Birkbeck[1], R Wilson[1], J Savovic[1], C Holcombe[3] and S Potter[1,4]

1) Bristol Medical School, University of Bristol, Bristol, UK 2) University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, UK 3) Liverpool University Hospitals NHS Trust, Liverpool, UK 4) North Bristol NHS Trust, Bristol, UK

University of BRISTOL

Results

- **Thirty-seven studies** reported overall survival in **1,321,291 patients** (729,789 undergoing BCS+RT and 591,502 undergoing mastectomy). The pooled hazard ratio was **0.73 (95% confidence interval (CI) 0.65– 0.81, p<0.001, I^2 97.6%)** demonstrating improved overall survival for patients undergoing BCS+RT compared with those receiving mastectomy.
- **Nine studies** with **triple negative breast cancer** results showed a hazard ratio of 0.76 (95% CI 0.67 – 0.87, p<0.001, I^2 29.3%).
- **Nineteen studies** comparing BCT+RT to **mastectomy without radiotherapy** showed hazard ratio of 0.69 (95% CI 0.64 – 0.74, p<0.001, I^2 71.8%).
- **Ten studies** including patients **less than 50 year old** showed a hazard ratio of 0.88 (95% CI 0.77 – 1.01, p=0.073, I^2 52.4%).

Pathologic complete response and breast-conserving surgery are associated with improved prognosis in patients with early-stage triple-negative breast cancer treated with neoadjuvant chemotherapy

David Krug[1], Valentina Vladimirova[2], Michael Untch[3], Thorsten Kühn[4], Andreas Schneeweiss[5], Carsten Denkert[6], Beyhan Ataseven[7], Christine Solbach[8], Bernd Gerber[9], Hans Tesch[10], Michael Golatta[11], Sabine Seiler[2], Jörg Heil[11], Valentina Nekljudova[2], Sibylle Loibl[2]

PD15-06

[1]Department of Radiation Oncology, University Hospital Schleswig-Holstein, Kiel, Germany, [2]German Breast Group, Neu-Isenburg, Germany, [3]Helios Klinikum Berlin-Buch, Germany, [4]Department of Gynecology, Klinikum Esslingen, Esslingen, Germany, [5]Nationales Centrum für Tumorerkrankungen, Universitätsklinikum und Deutsches Krebsforschungszentrum, Heidelberg, Germany, [6]Institut für Pathologie UKGM-Universitätsklinikum Marburg, Germany, [7]Kliniken-Essen-Mitte, Germany, [8]Universität Klinikum Frankfurt, Frankfurt am Main, Germany,

GBG GERMAN BREAST GROUP

AGO-B BREAST STUDY GROUP

Fig. 1a Disease-free survival according to pCR-status

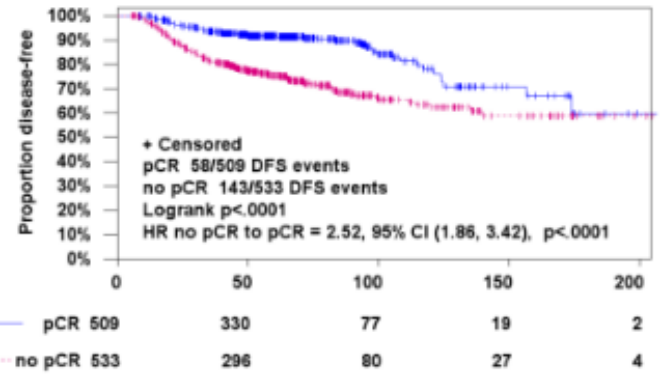


Fig. 1b Overall survival according to pCR-status

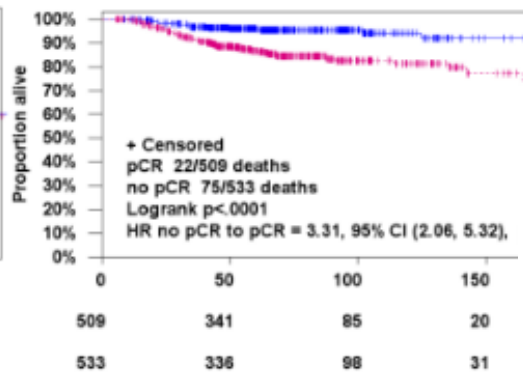


Table 4: Disease-free survival + overall survival

		Multivariate Cox-regression analysis - DFS		Multivariate Cox-regression analysis - OS	
Parameter	**Category**	**Hazard ratio (95%CI)**	**P-value**	**Hazard ratio (95%CI)**	**P-value**
Surgery type	BCS mastectomy	0.51 (0.36-0.72)	<0.001	0.43 (0.27-0.68)	<0.001
Age	≤50 >50	1.03 (0.77-1.37)	0.855	1.01 (0.67-1.53)	0.948
cT	cT1 cT2	0.71 (0.50-1.01)	0.058	0.76 (0.46-1.28)	0.306
pCR (landmark)	no pCR pCR	2.43 (1.78-3.31)	<0.001	3.15 (1.94-5.10)	<0.001

Fig. 2a Disease-free survival according to surgery

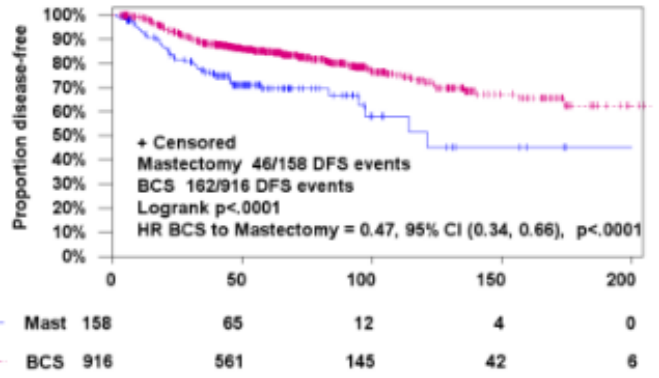
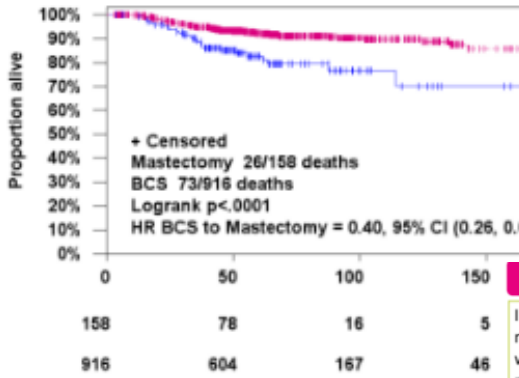


Fig. 2b Overall survival according to surgery



Conclusions

In this retrospective analysis from the GBG meta-database, treatment response, e.g. pCR, was the main determinant of locoregional recurrence in patients with early stage TNBC treated with NACT, while type of surgery had no impact. BCT was associated with improved DFS and OS compared to mastectomy, which may reflect favorable patient selection.

Interpretation

- BCT is not superior, but certainly equal in contemporary practice
- Radiation improves survival for TNBC

Breast conservation for multiple ipsilateral tumors

San Antonio Breast Cancer Symposium®, December 6-10, 2022

Impact of Breast Conservation Therapy on Local Recurrence in Patients with Multiple Ipsilateral Breast Cancer – Results from ACOSOG Z11102 (Alliance)

Judy C. Boughey, Kari M. Rosenkranz, Karla V. Ballman, Linda McCall, Bruce G. Haffty, Laurie W. Cuttino, Charlotte D. Kubicky, H. Carisa Le-Petross, Armando E. Giuliano, Kimberly J. Van Zee, Kelly K. Hunt, Olwen M. Hahn, Lisa A. Carey, Ann H. Partridge

Background - MIBC

- Increased diagnosis of multiple ipsilateral breast cancer (MIBC)
  - Improved imaging, increased use of breast MRI
- Historical, retrospective studies showing high rates of local regional recurrence with BCT

Primary Author of Study	Surgical Years	Number of Patients (n)	Median Follow-up (Months)	Number of Recurrences	Outcome
Leopold	1968-1981	10	64	4	NA
Kurtz	1975-1983	61	71	15	NA
Wilson	Prior to 12/1988	13	71	3	6-year LRR: 25%

Many surgeons recommend mastectomy

Z11102 - Prospective single arm phase II trial to evaluate breast conservation in women with two or three lesions in the breast

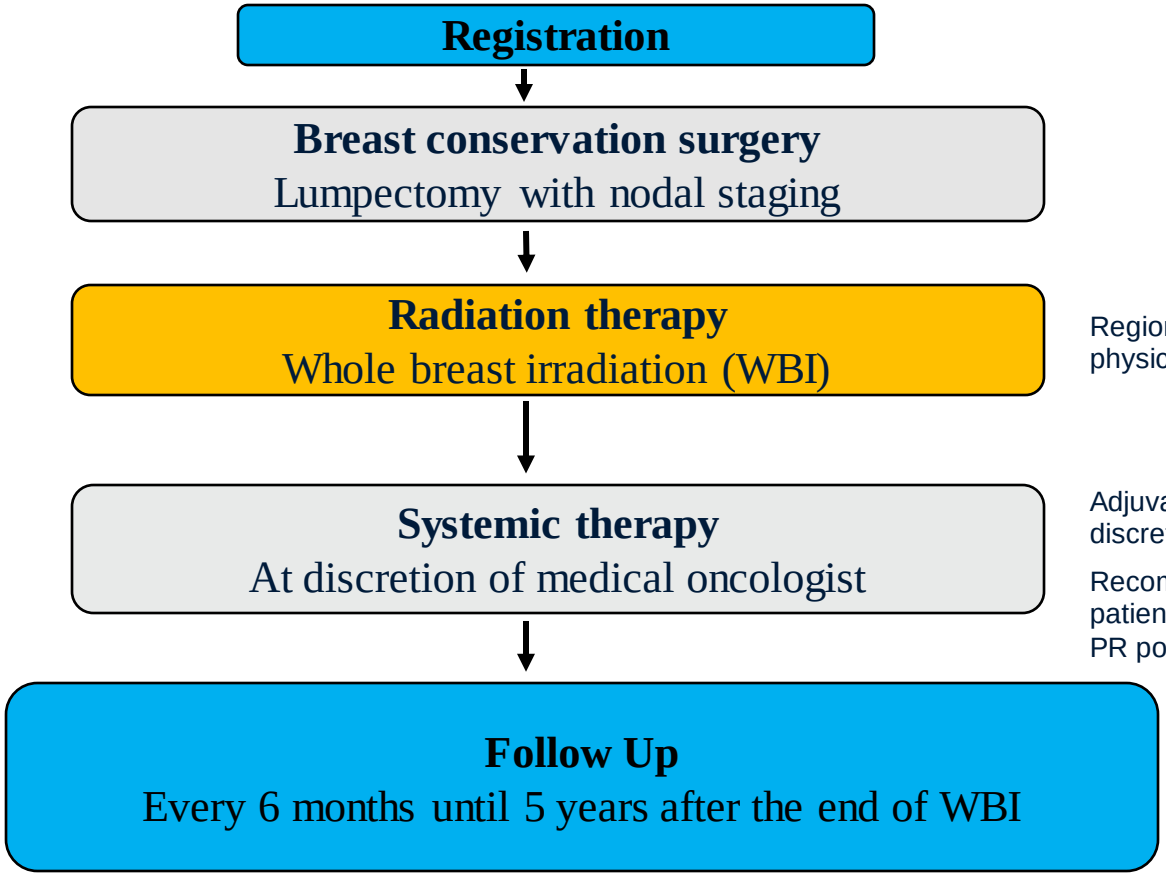
Inclusion Criteria

- Women age ≥40
- 2 or 3 foci of breast cancer
- At least one foci of invasive disease
- ≥ 2 cm normal tissue between lesions
- No more than 2 quadrants with disease
- cN0 or cN1 disease

Exclusion Criteria

- Focus of disease >5cm on imaging
- Bilateral breast cancer
- Prior ipsilateral breast cancer
- Known BRCA 1/2 mutations
- Neoadjuvant therapy
- Men

San Antonio Breast Cancer Symposium®, December 6-10, 2022



Z11102 Secondary Objectives

- Rate of conversion to mastectomy
  - 7.1% (14 patients converted due to positive margins)
  - 67.6% achieved margin-negative excision in a single operation
- Cosmetic outcome
  - PRO - good or excellent in 70.6% at 2 years
- Adherence to protocol directed radiation
  - Increasing radiation boost volume associated with acute dermatitis, but not associated with worse overall cosmesis

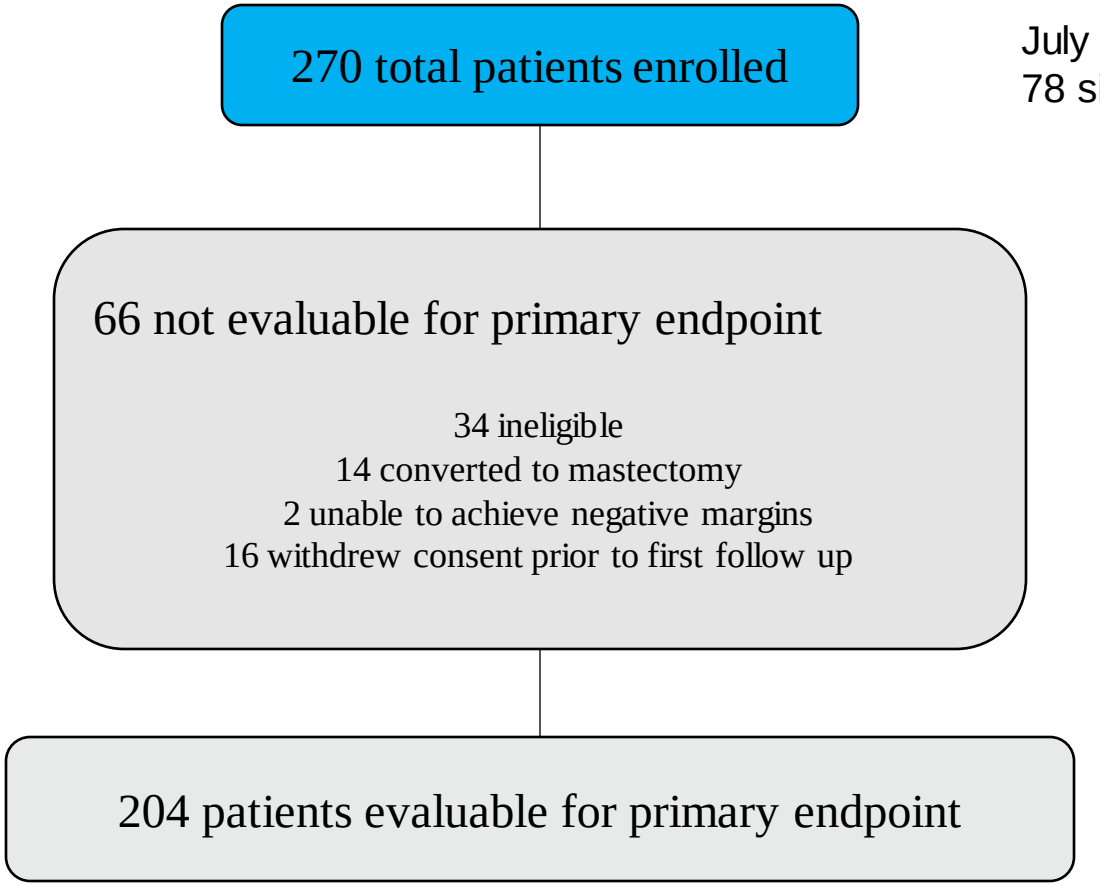
Rosenkranz et al. Ann Surg Oncol. 2018 Oct;25(10):2858-2866
Rosenkranz et al. Ann Surg Oncol. 2020 Nov;27(12):4650-4661
Cuttino et al. Int J Radiat Oncol Biol Phys. 2022 Mar 1;112(3):636-642

Z11102 Primary Objective

To assess the local recurrence (LR) rate with breast conservation in patients with multiple ipsilateral breast cancer (MIBC)

Acceptable 5-year LR rate for BCT was defined as less than 8%

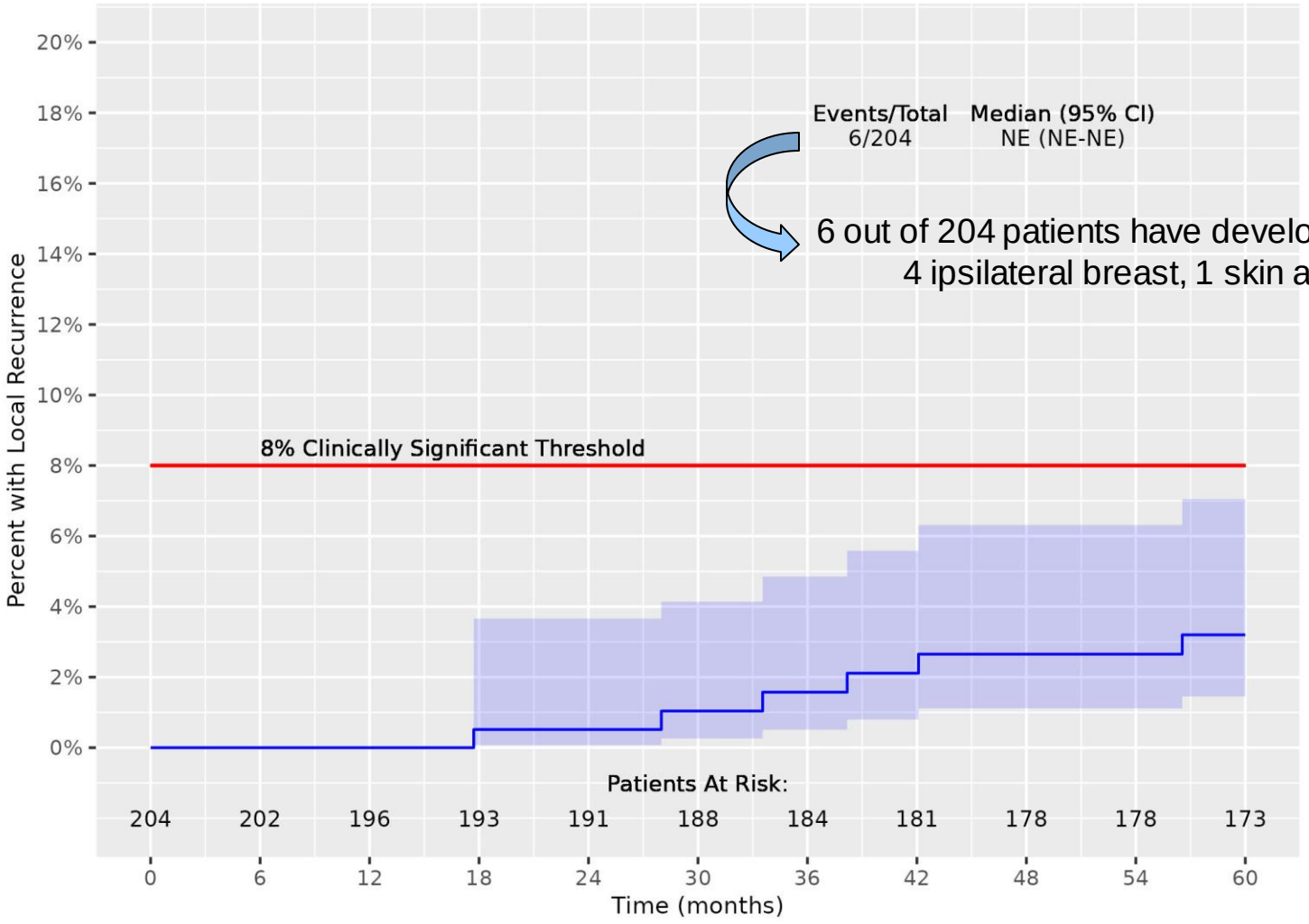
San Antonio Breast Cancer Symposium®, December 6-10, 2022



July 2012 - August 2016
78 sites enrolled patients

Amended in 2015 to:

- Allow enrollment of patients without MRI
- Allow post-surgical enrollment of patients with BCS for MIBC


Events/Total
6/204
Median (95% CI)
NE (NE-NE)
6 out of 204 patients have developed LR
4 ipsilateral breast, 1 skin and 1 chest wall
8% Clinically Significant Threshold
Percent with Local Recurrence
20%
18%
16%
14%
12%
10%
8%
6%
4%
2%
0%
Patients At Risk:
204 202 196 193 191 188 184 181 178 178 173
0 6 12 18 24 30 36 42 48 54 60
Time (months)

3.1%
(95% CI:
1.3 - 6.4)

Breast MRI

- Initially required, 2015 amended to allow patients without MRI
- 189 patients (92.6%) had MRI, 15 patients (7.4%) no MRI
- Local Recurrence
  - 3/189 with MRI and 3/15 without MRI

	Estimated 5-year LR (95% CI)	HR (95% CI)	P value
Breast MRI (n=189)	1.7 (0.6 – 5.2)	1.00 (ref)	0.002
No Breast MRI (n=15)	22.6 (7.9 – 55.1)	13.5 (2.7 – 66.9)	

Endocrine Therapy

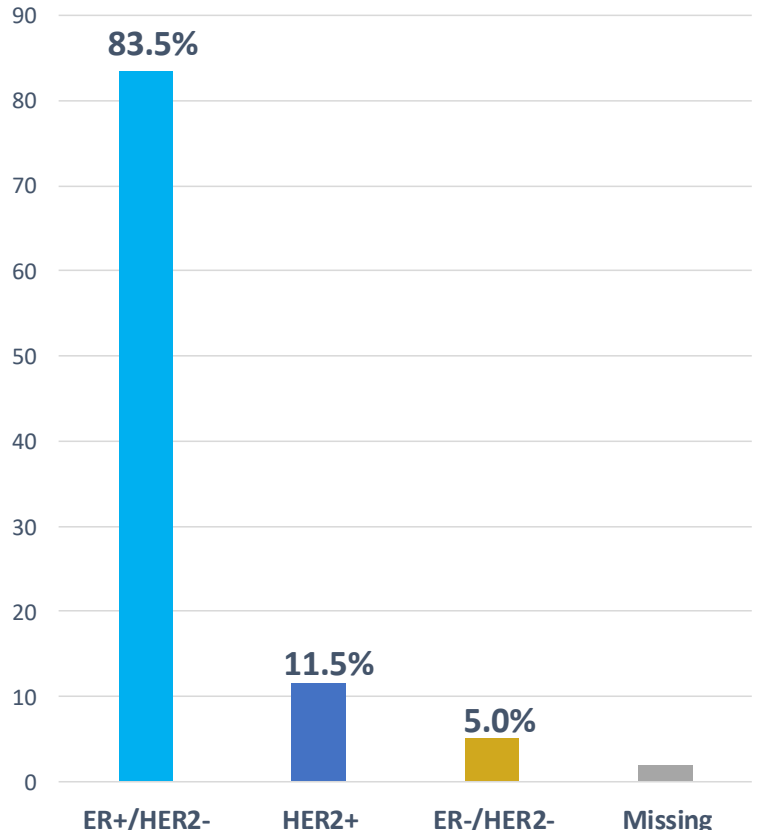
- 195 patients with at least 1 ER+ lesion

Characteristic	Estimated 5-year LR (95%CI)	# of patients with local recurrence	HR (95% CI)	P value
Adjuvant Endocrine Therapy (n=175)	1.9 (1.0 – 5.6)	3	1.0 (ref)	0.025
No Adjuvant Endocrine Therapy (n=20)	12.5 (3.3 – 41.5)	2	7.7 (1.3 – 46.3)	

Conclusions

- Multiple ipsilateral lumpectomy (followed by whole breast radiation plus boosts to the lumpectomy cavities) is reasonable

Tumor Biology



LR by tumor biology

Tumor biology	LR	5-yr est LR	95% CI
ER+/HER2-	4/167	2.6%	1.0-6.8
HER2+	0/23	NE	NE
ER-/HER2-	1/10	10.0%	1.5-52.7

*1 of the events was in a patient missing tumor biology information

Potential application? DAPHNe

- 97 patients treated with neoadjuvant THP
  - 92 without additional pre-operative therapy
- Patients and providers accepted a de-escalated regimen without additional cytotoxic therapy if pCR was achieved

- BCT rates among the 92 treated with THP alone

DAPHNe

Characteristic	N= 53
Potential for tumor downsizing and BCT	28(52.8%)
Tumor to breast size ratio	24(45.2%)
Nipple retraction	2(3.8%)
Tumor location	2(3.8%)
Contraindication to BCT	25(47.2%)
Multifocal/multicentric disease	16(30.2%)
Extensive calcifications	7(13.2%)
Contraindication to radiation	2(3.8%)

Figure 1

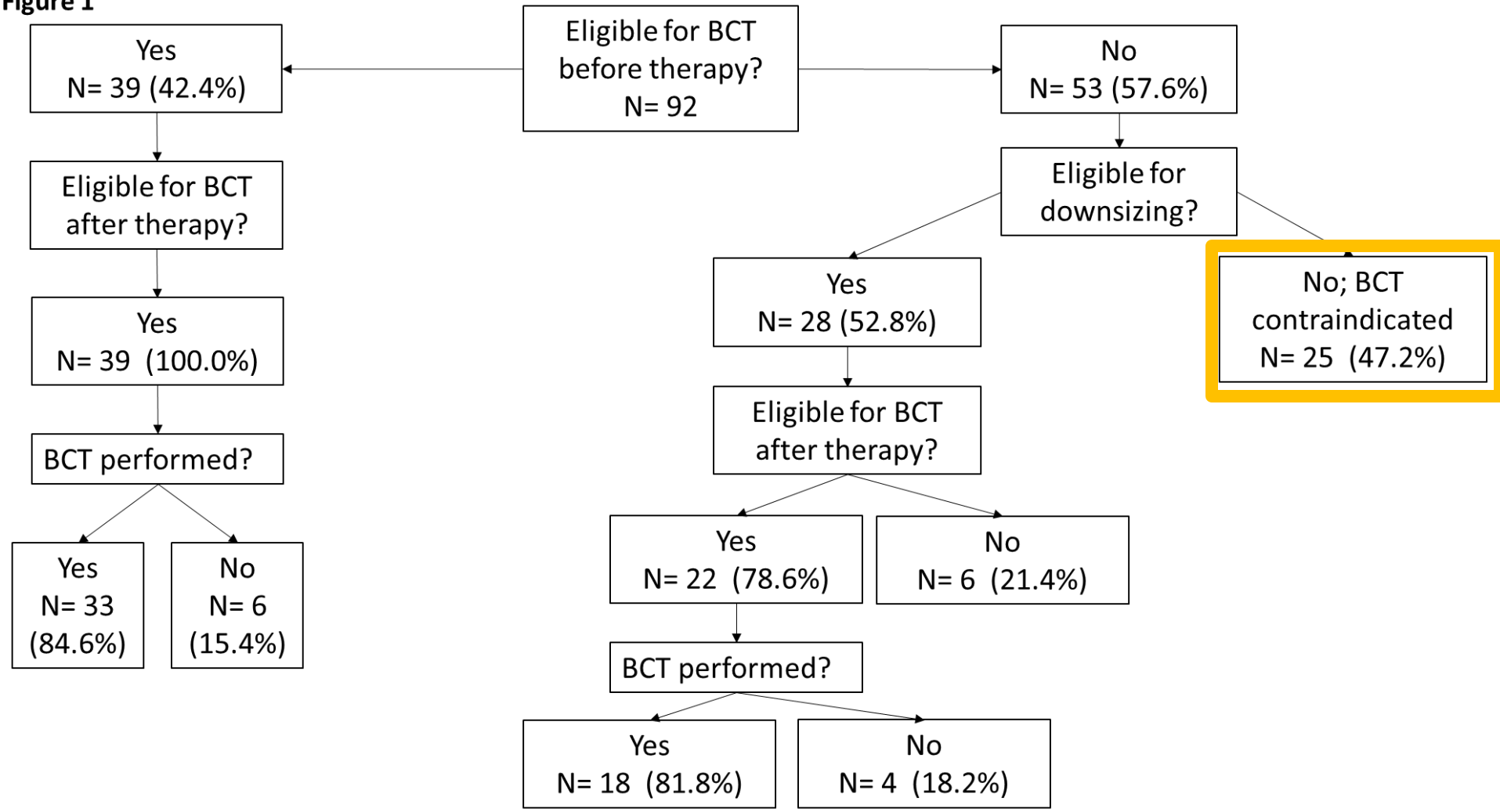
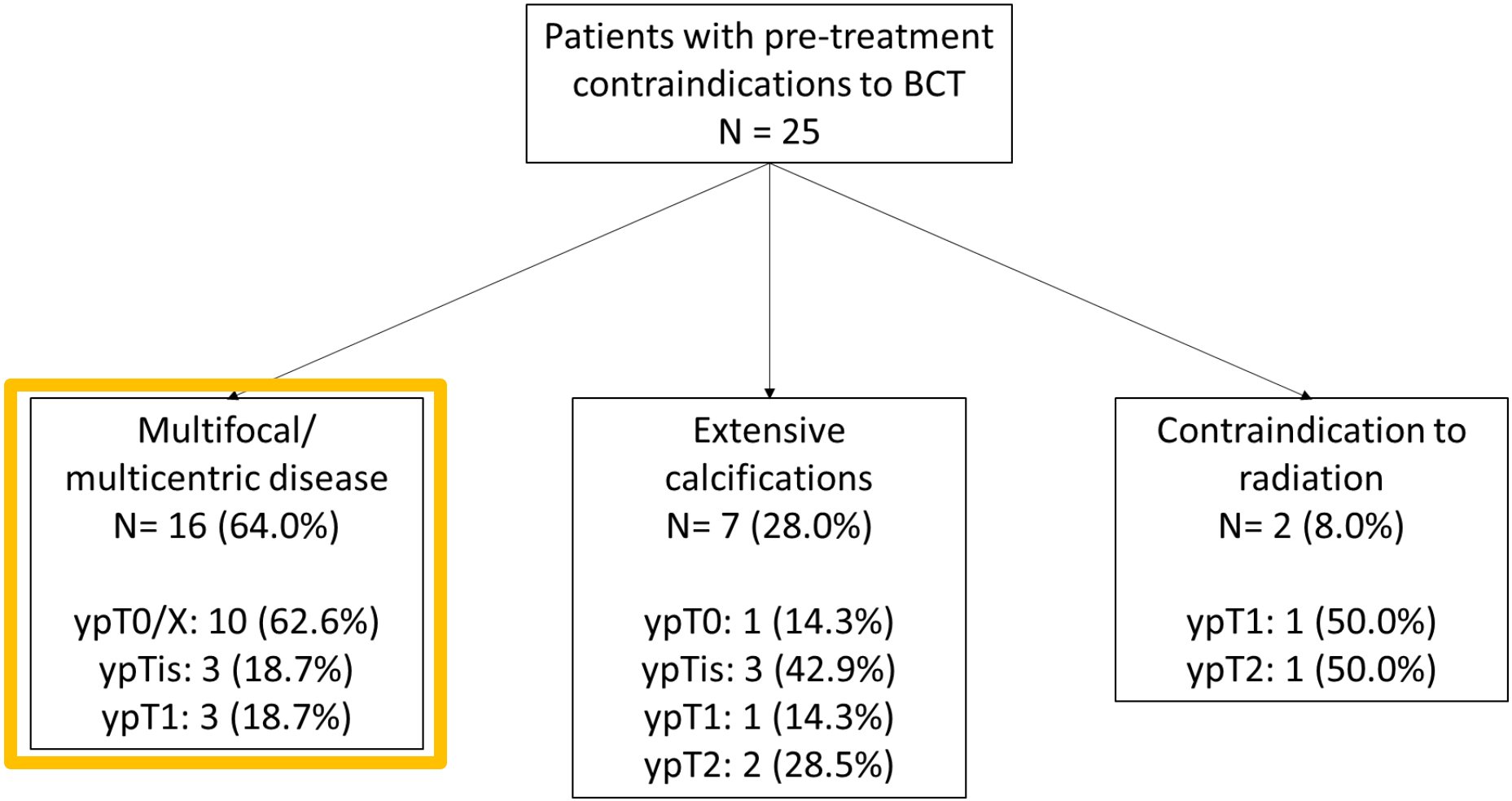

Eligible for BCT before therapy? N= 92
Yes N= 39 (42.4%)
Eligible for BCT after therapy?
Yes N= 39 (100.0%)
BCT performed?
Yes N= 33 (84.6%)
No N= 6 (15.4%)
No N= 53 (57.6%)
Eligible for downsizing?
Yes N= 28 (52.8%)
Eligible for BCT after therapy?
Yes N= 22 (78.6%)
No N= 6 (21.4%)
BCT performed?
Yes N= 18 (81.8%)
No N= 4 (18.2%)
No; BCT contraindicated N= 25 (47.2%)

Figure 2


Patients with pre-treatment contraindications to BCT
N = 25
Multifocal/ multicentric disease
N= 16 (64.0%)
ypT0/X: 10 (62.6%)
ypTis: 3 (18.7%)
ypT1: 3 (18.7%)
Extensive calcifications
N= 7 (28.0%)
ypT0: 1 (14.3%)
ypTis: 3 (42.9%)
ypT1: 1 (14.3%)
ypT2: 2 (28.5%)
Contraindication to radiation
N= 2 (8.0%)
ypT1: 1 (50.0%)
ypT2: 1 (50.0%)

Implications

- THP alone does not seem to negatively impact BCT

ECOG-ACRIN
cancer research group
Reshaping the future of patient care

- Although Z11102 was upfront surgery setting (NAC-treated patients excluded), may consider multiple lumpectomy for patients with multifocal tumors and high pCR rates

Axillary Surgery Updates

Axillary surgery after NAC Historical Perspective

- NAC can downstage the axilla
- NSABP B-18 and B-27

> 80% nodal clinical response rate

> 40% nodal pathologic complete response rate

NSABP B-27

- Some patients SLNB → ALND
- Identification of sentinel node: 84.8%
- FN rate 10.7% (15/70)
- Several large clinical trials subsequently examined SLNB for patients who presented with cN1 disease but converted to cN0 after NAC

Table 3. Status of Sentinel Nodes and Nonsentinel Nodes in Patients Who Underwent Sentinel Node Biopsy Followed by Axillary Node Dissection (n = 343)

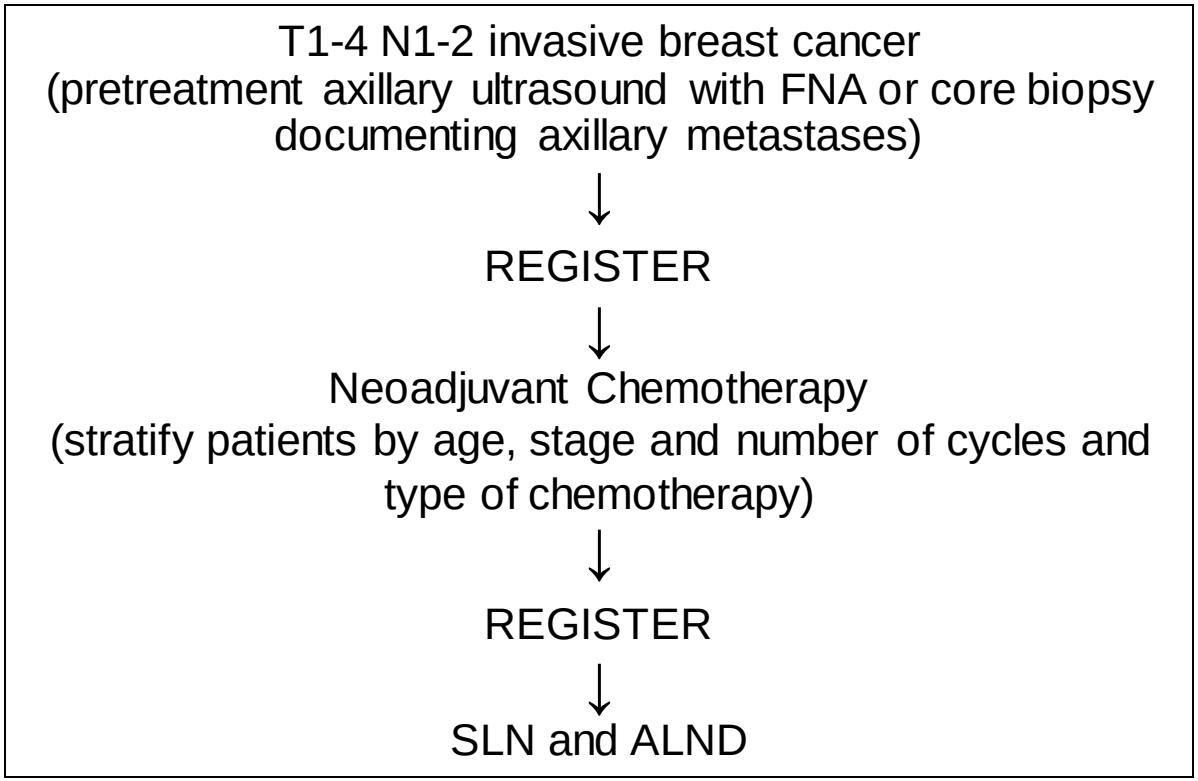
	Nonsentinel Nodes (status)		
	Positive	Negative	All
Sentinel nodes (status)			
Positive	55	70	125
Negative	15*	203	218
Total	70	273	343

*False-negative rate, 10.7% (15/140; 95% CI, 5.6% to 15.8%); overall accuracy, 95.6% (328/343; 95% CI, 95.6% to 97.8%); negative predictive value, 93.1% (203/218; 95% CI, 89.8% to 96.5%); positive predictive value, 100% (by definition).

Slide adapted from B. Hilty

Mamounas JCO 2005

ACOSOG Z1071



ACOSOG Z1071
SLN identification rate

Patients	N	SLN identified	SLN identification rate (%)	CI
All patients	689	639	92.7	90.5 - 94.6
cN1	651	605	92.9	90.7 - 94.8
cN2	38	34	89.5	75.2 - 97.1

ACOSOG Z1071
False negative rate (FNR)

FNR among patients with cN1 disease and <u>at least 2 SLNs examined</u>

$$\text{FNR} = \frac{\textbf{\# pts SLN - / ALND +}}{\textbf{Total \# pts SLN + or ALND +}}$$

310 patients had residual nodal disease

39 of these patients had negative SLNs

FNR = 12.6%

SLNB for patients who presented with cN1 disease but converted to cN0 after NAC

	Identification rate	False negative rate
NSABP B-27, 2005	85%	10.7%
GANEA 1, 2009	81.5%	15%
ACOSOG Z1071, 2013	92.9%	12.6%
SENTINA (Arm C), 2013	80.1%	14.2%
SN FNAC, 2015	87.6%	9.6%

- Largely negative trials!
- FNR >10%

Mamounas JCO 2005, Classe JCO 2009, Boughey JAMA 2013, Kuehn Lancet Oncol 2013, Boileau JCO 2015

10% FNR

- Somewhat arbitrary acceptable cutoff
  - B-32 = 10%
- Only SN FNAC (with IHC) met this cutoff
  - 8.4% overall population
- Community was committed to decreasing morbidity and adopting SLNB in this setting

ACOSOG Z1071 Technical factors

	310 patients	p Value
Mapping Agent		
Blue dye only Radiolabeled colloid only Both blue dye and radiolabeled colloid	2/9 (22.2%) 10/50 (20.0%) 27/251 (10.8%)	p=0.05
Number of SLN Examined		
2	19/90 (21.1%)	
≥3	20/220 (9.1%)	p=0.007
Clinical T Stage		
T0, Tis, T1, T2 T3, T4	32/225 (14.2%) 7/85 (8.2%)	p=0.18

Slide courtesy of K Hunt

Boughey et al. *JAMA* 2013

Method	Study	FNR
Mapping agent	Z1071	Single 20.3% Dual 10.8%
	SENTINA	Single 16% Dual 8.6%
	SN FNAC	Single 16% Dual 5.2%
Number of lymph nodes obtained	Z1071	2 nodes 21.1% 3 or more 9.1%
	SENTINA	1 node 24.3% 2 nodes 18.5% 3 or more 7.3%
	SN FNAC	1 node 18.2% 2 nodes 4.9%
Pathologic Evaluation	Z1071	H&E 11.3% IHC 8.7%
	SN FNAC	H&E 13.3% IHC 8.4%
Localization/ identification of the clipped node	Z1071	6.8%

Boughey et al. *Ann Surg* 2015; Kuehn et al *Lancet Oncol* 2013; Boileau et al *JCO* 2015; Boughey et al. *Ann Surg* 2016

Study	Years	N	Median Follow-up	Axillary recurrence	Distant recurrence	Special notes
Milan	2000-2010 123	70 123	61 months 9.2 years	0 2 (1.6%)	12.8% (absolute) 10.6% (absolute)	-No tracer requirement -Required only 1 SLN obtained -74.3% had < 3 SLNs obtained
Mayo	2009-2019	159	34 months	1 (0.6%)	NR	-Required only 1 SLN obtained
McGill	2013-2018	60	36 months	0	13.7% (5-yr)	-Required dual tracer -Median of 4 SLNs obtained
MSKCC	2013-2019	234	40 months	1 (0.4%)	6.1% (4-yr)	-Required dual tracer -At least 3 SLNs obtained in all patients

N= patients who presented with pretreatment cN1 disease, were pN0 and treated with SLNB alone

Galimberti *EJSO* 2016; Kahler-Ribeiro-Fontana *EJSO* 2021; Piltin *ASO* 2020; Wong *ASO* 2020; Barrio *JAMA Oncol* 2021

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Galimberti *EJSO* 2016; Kahler-Ribeiro-Fontana *EJSO* 2021; Piltin *ASO* 2020; Wong *ASO* 2020; Barrio *JAMA Oncol* 2021

AXILLARY RECURRENCE IS RARE IN PATIENTS UNDERGOING SENTINEL LYMPH NODE BIOPSY FOLLOWING NEOADJUVANT CHEMOTHERAPY IN INITIALLY CLINICALLY NODE-POSITIVE BREAST CANCER: EARLY RESULTS OF THE NEOSENTITURK-TRIAL/MF18-03

N Cabioğlu[1], H Karanlık[2], MA Gulcelik[3], A Igci[4], M Müslümanoğlu[1], HB Koçer[5], C Uras[6], GG Akgul[7], M Tukenmez[1], S Bademler[8], S Ilgun[7], DC Trablus[9], GK Çakmak[9], A Dag[10], N Yildirim[4], B Zengel[11], ES Oran[12], K Senol[13], S Emiroglu[1], U Ugurlu[14], H Kara[6], B Citgez[15], YE Ersoy[15], I Joranl[13], A Celik[17], E Dilege[18], Y Bolukbasi[19], N Karaman[20], G Basaran[21], B Yigit[22], A Soydor[4], AK Polat[23], G Sakman[24], S Ozbas[25], A Albnok[26], E Ozkurt[7], S Gokoz[13], G Ercan[17], B Celik[18], L Zer[27], A Akcan[28], E Baran[15], IA Ozemir[29], L Yeniay[30], Z Utkan[31], L Dogan[32], M Dogan[32], M Velidedeoglu[33], F Calikoglu[17], B Ozcinar[1], A Kebudi[34], K Atahan[35], V Valiyeva[36], S Yormaz[37], F Erozgen[38], A Sevinc[39], C Arici[40], E Varol[31], HG Kilic[1], O Agcaoglu[18], B Goktepe[38], S Ergun[31], P Alakbarova[36], T Yildirim[14], B Mollavelioglu[40], B Kilic[2], E Arikan[5], M Akinci[38], S Aksoy[28], FL Balci[40], S Onder[41], A Soran[42], A Aydiner[43], K Ibis[44], and V Ozmen[7]

[1]...e, Surgery and [41]Pathology, and Institute of Oncology, [2]Surgical Oncology and [43]Radiation and [44]Medical Oncology , Istanbul; [3]Gulhane Education and Research Hospital, Surgery, Ankara; [4]American Hospital, Surgery, Istanbul; [5]Sakarya University, Faculty of M...kul, [7]Istanbul Florence Nightingale Hospital, Surgery, Istanbul; [8]Bahcesehir University, School of Medicine, Surgery, Istanbul; [9]Zonguldak Bulent Ecevit University, Faculty of Medicine, Zonguldak; [10]Mersin University, Faculty of Medicine, Surgery, Mersin; [11]Izm...kura City Hospital, Istanbul; [12]Uludag University, Faculty of Medicine, Surgery,Bursa; [13]Marmara University, Faculty of Medicine, Surgery, Istanbul; [15]Uskudar University, Memorial Hospital, Surgery, Istanbul; [16]Bezmialem Vakif University, Medical Faculty, Surge...versity, Faculty of Medicine, Surgery and ...smidiye Sisli Etfal Training and Research ...Samsun; [24]Cukurova University, Faculty ...istanbul; [26]Erciyes University, Faculty of M...il; [29]Ege University, Faculty of Medicine, S...icine, Surgery, Istanbul; [35]Izmir Ataturk Tra...linic, Breast Surgery, Baki, AZERBAIJAN; ...ir; [42]Akdeniz University, Faculty of Medici

Türkiye Meme Hastalıkları Dernekleri Federasyonu

Breast Health Working Group International

Table 2. Axillary (AR) and locoregional recurrences (LRR)

	All (n=2390)	SLNB (n=1433)	ALND (n=957)		SLNB (-) (n=1032)	SLNB (+) (n=401)		ALND (-) (n=160)	ALND (+) (n=797)	
	n(%)	n(%)	n(%)	P*	n(%)	n(%)	P*	n(%)	n(%)	P*
AR				0.45			0.564			0.520
Yes	7(0.3)	3(0.2)	4(0.4)		3(0.3)	0(0)		1(0.6)	3(0.4)	
No	2383 (99.7)	1430 (99.8)	953 (99.6)		1029 (99.7)	401 (100)		159 (99.4)	794 (99.6)	
LRR				0.18			0.999			0.179
Yes	15(0.6)	6(0.4)	9(0.9)		5(0.5)	1(0.2)		3(1.9)	6(0.8)	
No	2375 (99.4)	1427 (99.6)	948 (99.1)		1027 (99.5)	400 (99.8)		157 (98.1)	791 (99.2)	
LR after BCT^				0.999			0.459			0.999
Yes	14 (1.2)	9 (1.1)	5 (1.3)		8 (1.4)	1(0.5)		1 (1.4)	4 (1.2)	
No	1181 (98.8)	789 (98.9)	392 (98.7)		583 (98.6)	206 (99.5)		69 (98.6)	323 (98.8)	
LR after MST				0.403			0.999			0.366
Yes	13(1.1)	5(0.8)	8(1.4)		4(0.9)	1(0.5)		0(0)	8(1.7)	
No	1182 (98.9)	630 (99.2)	552 (98.6)		437 (99.1)	193 (99.5)		90(100)	462 (98.2)	

Axillary recurrences (AR) were seen at a median of 12 months IQR (25, 75) (range, 12-27) months after the surgery.

Of 7 cases with AR, 4 had synchronous local recurrences in breast (n=3) or mastectomy (n=1), and 3 of them also had lung (n=2) or liver/bone (n=1) metastases in addition to AR.

All patients (except 1 case: luminal-B HER2-) with AR were found to have HER2(+) or TNBC.

All cases had residual invasive cancer in the breast surgical specimen.

Long Term Outcome in Patients with Nodal-Positive Breast Cancer Treated with Sentinel Lymph Node Biopsy Alone After Neoadjuvant Chemotherapy

Sue Zann Lim[1,2], Tae-Kyung Yoo[1], Sae Byul Lee[1], Jisun Kim[1], Il Yong Chung[1], Beom Seok Ko[1], Jong Won Lee[1], Byung Ho Son[1], Sei-Hyun Ahn[1], Seonok Kim[3] and Hee Jeong Kim[1]

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of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea.

ASAN Medical Center

Results

1. 902 patients with clinically stage N1 (cN1) cancer treated with NAC and turned cN0 were identified
2. 477 (52.9%) patients achieved complete pathological response in the axilla (ypN0), while the remaining 425 (47.1%) patients still have metastasis in the axillary lymph nodes. 133 (14.7%) patients had ypN0i or ypN1mi disease.
3. In the ypN0 cohort, most patients underwent SLNB only (n=314, 65.8%), while about one-third of the cohort had ALND (n=163, 34.2%). (Table 1)
4. Clinical and histopathological features were comparable between these 2 groups, except for clinical T staging (cT). (Table 1) We noted that significantly more patients in the ALND group had T3-4 tumour as compared to the SLNB group.
5. In the SLNB only group, median number of SLN and non SLN harvested were both 2, but the range were 1-7 and 0-8 respectively. In the ALND group, median number of total lymph node was 11 (range 2-35).
6. At a median follow up of 65 months, ARR was 3.2% in the SLNB only group and 1.8% in the ALND group (p=0.398). (Table 2)
7. DFS and OS were significantly worse in patients with ALND as compared to patients with SLNB alone (p=0.010 & 0.031 respectively). (Figure 1)
8. Due to the uneven distribution of patients based on cT stage between SLNB and ALND group, we did a subgroup analysis and showed that in the cT1-2 subgroup (n=377), there was no statistically significant difference in DFS and OS (p=0.239 and 0.669 respectively) between SLNB and ALND group. (Figure 2)
9. In the ypN0i and ypN1mi cohort, at a median follow up of 66 months, ARR was 12.1% in the SLNB group and 4.0% in the ALND group (p=0.095). (Table 2)
10. There was no significant difference in DFS and OS between the SLNB and ALND group (p=0.475 and 0.254). (Figure 4)

Ways to optimize SLNB after NAC

"TAD"

- Targeted Axillary Dissection (TAD)
- Retrieving the clipped lymph node and performing SLNB

- Clipped node is not the SLN 23% of the time

- Only factor associated with clipped node NOT retrieved as a SLN was ≥4 abnormal nodes on ultrasound (41% of the time vs 17% of the time if 1-3 nodes abnormal, P=.004)
- No difference by tumor subtype – sample size issue ?

Caudle et al. *JCO* 2016

Clipping and ensuring the clipped, biopsy-proven lymph node is removed with SLNB provides the lowest FNR

	Study	FNR
Localization/ identification of the clipped node	ACOSOG Z1071	6.8% (95% CI 1.9%-16.5%)
	MARI*	7% (95% CI 2%-16%)
	TAD@	2% (95% CI 0.05%-10.7%)
	RISAS@	3.5% (95% CI 1.38%-7.16%)

*included removing the clipped node only @included removing the clipped node and performing SLNB

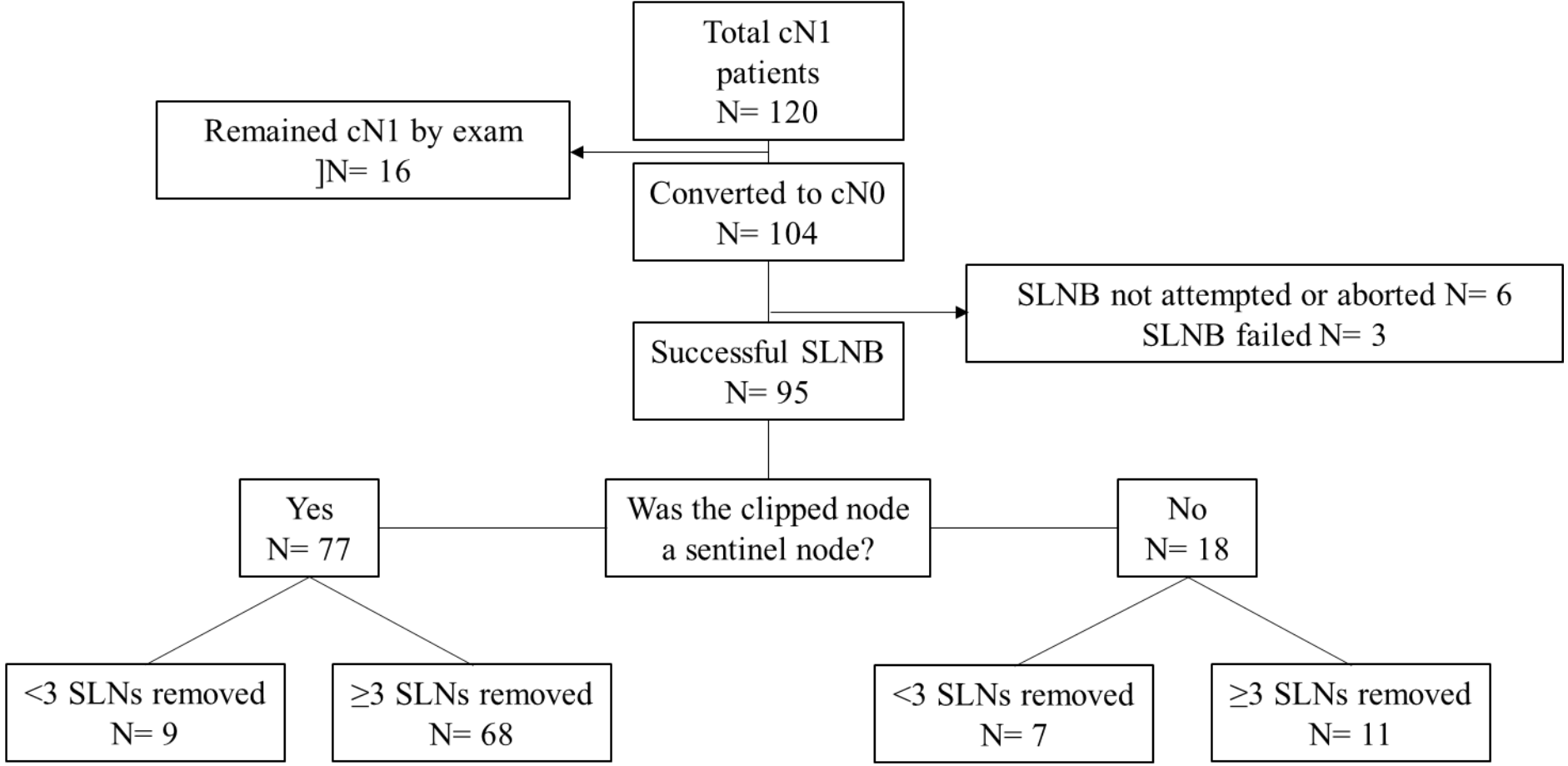
Boughey Ann Surg 2016, Donker Ann Surg 2015; Caudle JCO 2016; Simons SABCS 2020

Debate around "TAD"

- Without a doubt, TAD is the most accurate way to determine nodal status after NAC (provides the lower FNR)

- But what FNR corresponds to a change in management? What FNR is needed for acceptable or better oncological outcomes???

DFCI Experience



Clipped node was a non-sentinel lymph node 19% of the time

1 patient cLN was positive while all other SLNs were negative
2 patients cLN were negative while other SLNs were positive

Weiss et al. *ASO* 2022

DFCI Experience

- cLN was a non-SLN 19% of the time overall
- Only once did the cLN pathology change management
- HR+ patient – ALND, but radiation and systemic therapy recommendations did not change

Weiss et al. *ASO* 2022

Debate around "TAD"

- Without a doubt, TAD is the most accurate way to determine nodal status after NAC (provides the lower FNR)

- But what FNR corresponds to a change in management? What FNR is needed for acceptable or better oncological outcomes???

San Antonio Breast Cancer Symposium®, December 6-10, 2022

EUBREAST NETWORK
EUROPEAN BREAST CANCER RESEARCH ASSOCIATION OF SURGICAL TRIALISTS

ONCOPLASTIC BREAST CONSORTIUM

The OPBC-04/EUBREAST-06/OMA Study

Oncological Outcomes Following Sentinel Lymph Node Biopsy (SLNB) or Targeted Axillary Dissection (TAD) in Breast Cancer Patients Downstaging From Node Positive To Node Negative with Neoadjuvant Chemotherapy

Giacomo Montagna, MD, MPH, Mary Mrdutt, MD, Susie X. Sun, MD, Callie Hlavin, MD, Emilia Diego, MD, Stephanie M. Wong, MD, MPH, Andrea V. Barrio, MD, Astrid Botty, MD, Neslihan Cabioglu, MD, PhD, Varadan Sevilimedu, MBBS, DrPH, Laura Rosenberger, MD, MS, Shelley Hwang, MD, Abigail Ingham, MBchB, Bärbel Papassotiropoulos, MD, Bich Doan Nguyen-Sträuli, MD, Christian Kurzeder, MD, Danilo Diaz Aybar, MD, Denise Vorburger, MD, Dieter Michael Matlac, MD, Edvin Ostapenko, MD, Fabian Riedel, MD, Florian Fitzal, MD, Francesco Meani, MD, Franziska Fick, MD, Jaqueline Sagasser, MD, Jörg Heil MD, PhD, Hasan Karanlık, MD, Konstantin J. Dedes, MD, Laszlo Romics, MD, PhD, Maggie Banys-Paluchowski, MD, PhD, Mahmut Muslumanoglu, MD, Maria Del Rosario Cueva Perez, MD, Marcelo Chavez Diaz, MD, Martin Heidinger, MD, Mathias K. Fehr, MD, Mattea Reinisch, MD, Mustafa Tukenmez, MD, Nadia Maggi, MD, Nicola Rocco, MD, PhD, Nina Ditsch, MD, Oreste Davide Gentilini, MD, Regis R. Paulinelli, MD, PhD, Sebastian Sole Zarhi, MD, Sherko Kümmel, MD, PhD, Simona Bruzas, MD, Simona di Lascio, MD, Tamara Parissenti, MD, Tanya L. Hoskin, MS, Uwe Güth, MD, Valentina Ovalle, MD, Christoph Tausch, MD, Henry M. Kuerer, MD, PhD, Abigail S. Caudle, MD, Jean-Francois Boileau, MD, MSc, Judy C. Boughey, MD, Thorsten Kühn, MD, PhD, Monica Morrow, MD and Walter P. Weber, MD

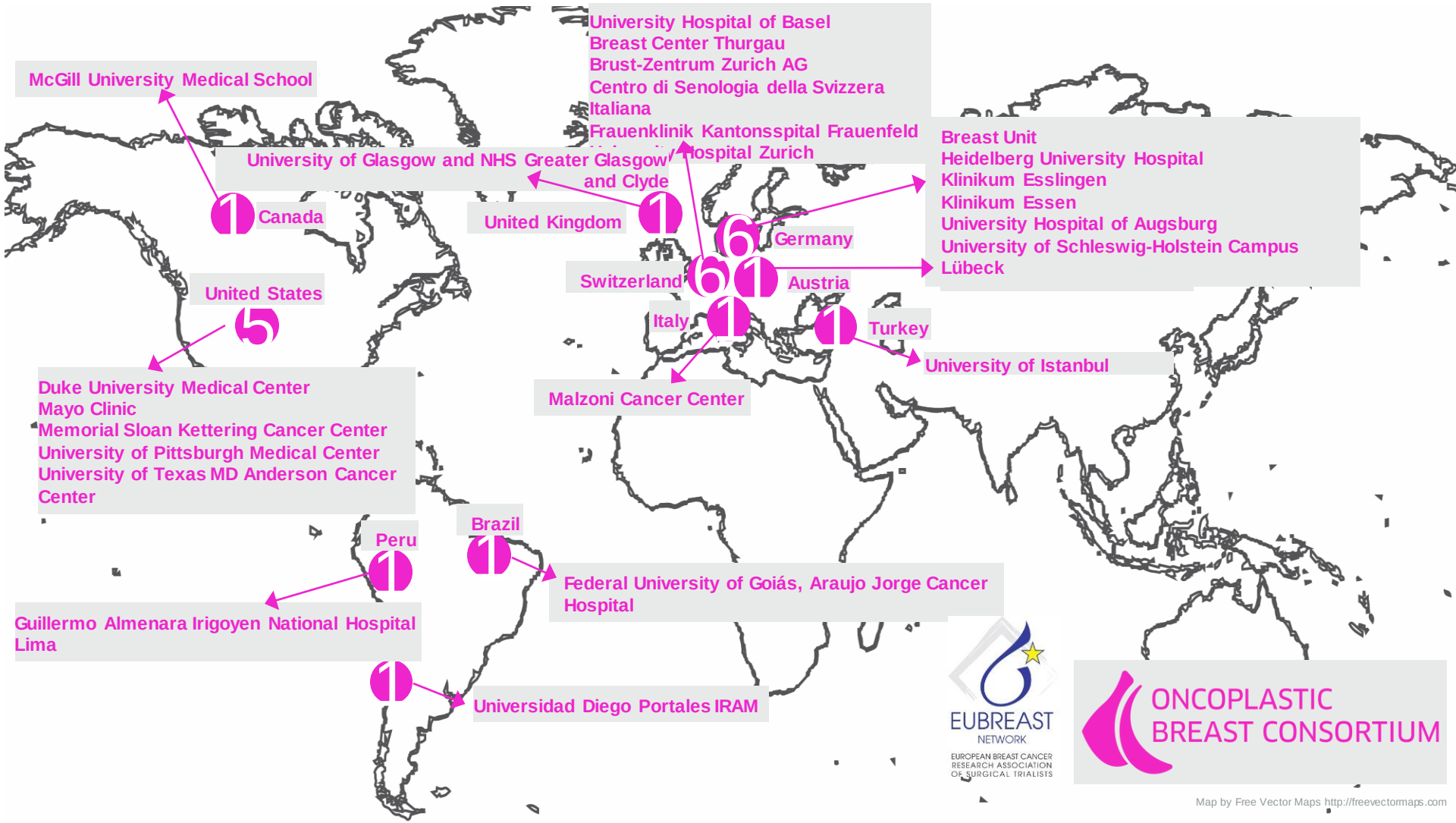
Study Population

Inclusion criteria

- T1-4
- Biopsy-proven nodal metastases (N1-3)
- Nodal pathologic complete response (pCR)
- SLNB performed with dual-tracer mapping *or*
- TAD (image-guided localization of the sampled node in combination with the SLNB procedure with or without dual mapping)
- A minimum of 10 cases per institution

Exclusion criteria

- ALND
- Inflammatory breast cancer
- Stage IV
- < 1-year follow-up


McGill University Medical School
1
Canada
University Hospital of Basel
Breast Center Thurgau
Brust-Zentrum Zurich AG
Centro di Senologia della Svizzera Italiana
Frauenklinik Kantonsspital Frauenfeld
Hospital Zurich
University of Glasgow and NHS Greater Glasgow and Clyde
1
United Kingdom
6
Germany
Breast Unit
Heidelberg University Hospital
Klinikum Esslingen
Klinikum Essen
University Hospital of Augsburg
University of Schleswig-Holstein Campus Lübeck
6
Switzerland
1
Austria
United States
5
Duke University Medical Center
Mayo Clinic
Memorial Sloan Kettering Cancer Center
University of Pittsburgh Medical Center
University of Texas MD Anderson Cancer Center
Italy
1
Malzoni Cancer Center
1
Turkey
University of Istanbul
Brazil
1
Federal University of Goiás, Araujo Jorge Cancer Hospital
Peru
1
Guillermo Almenara Irigoyen National Hospital Lima
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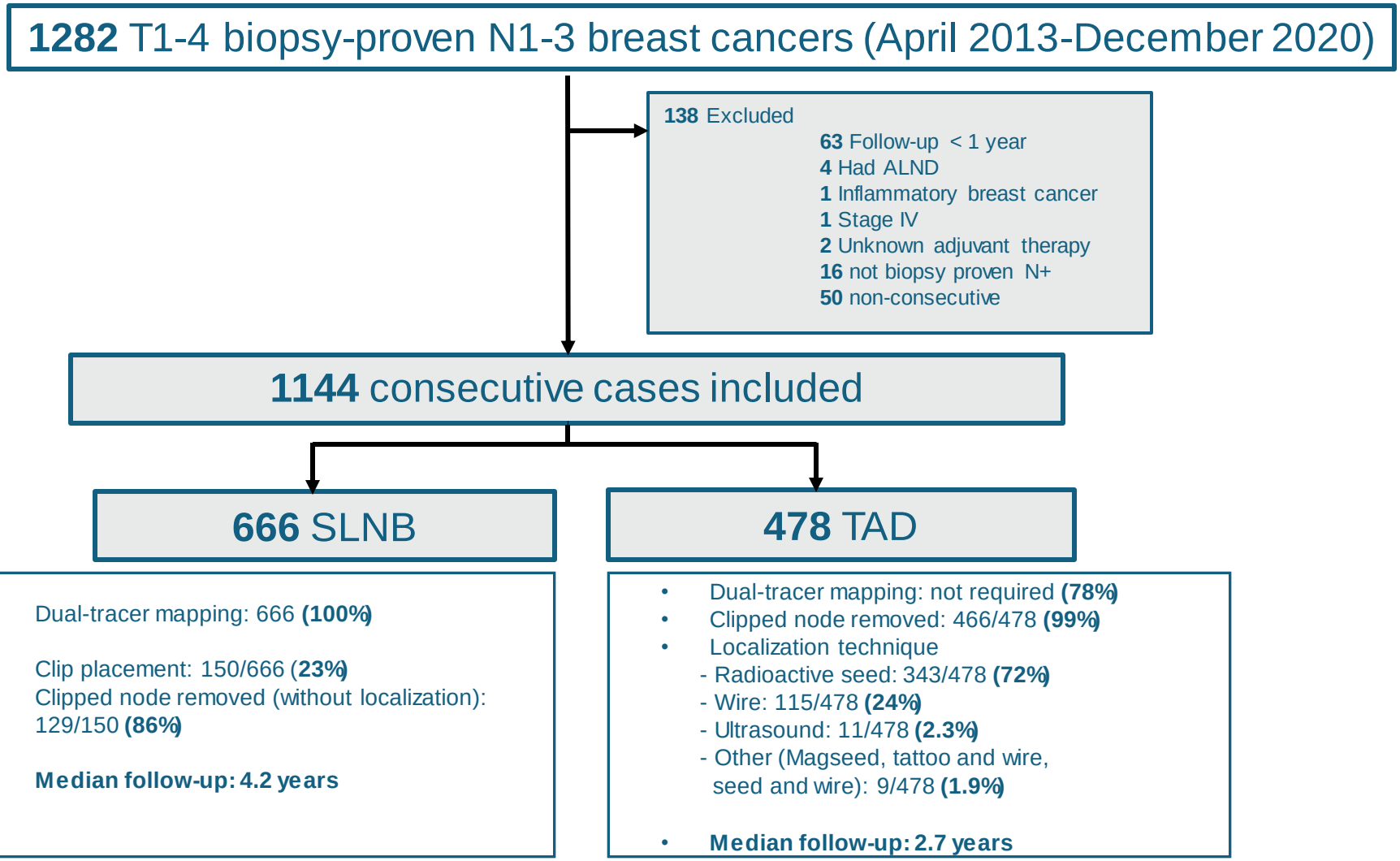
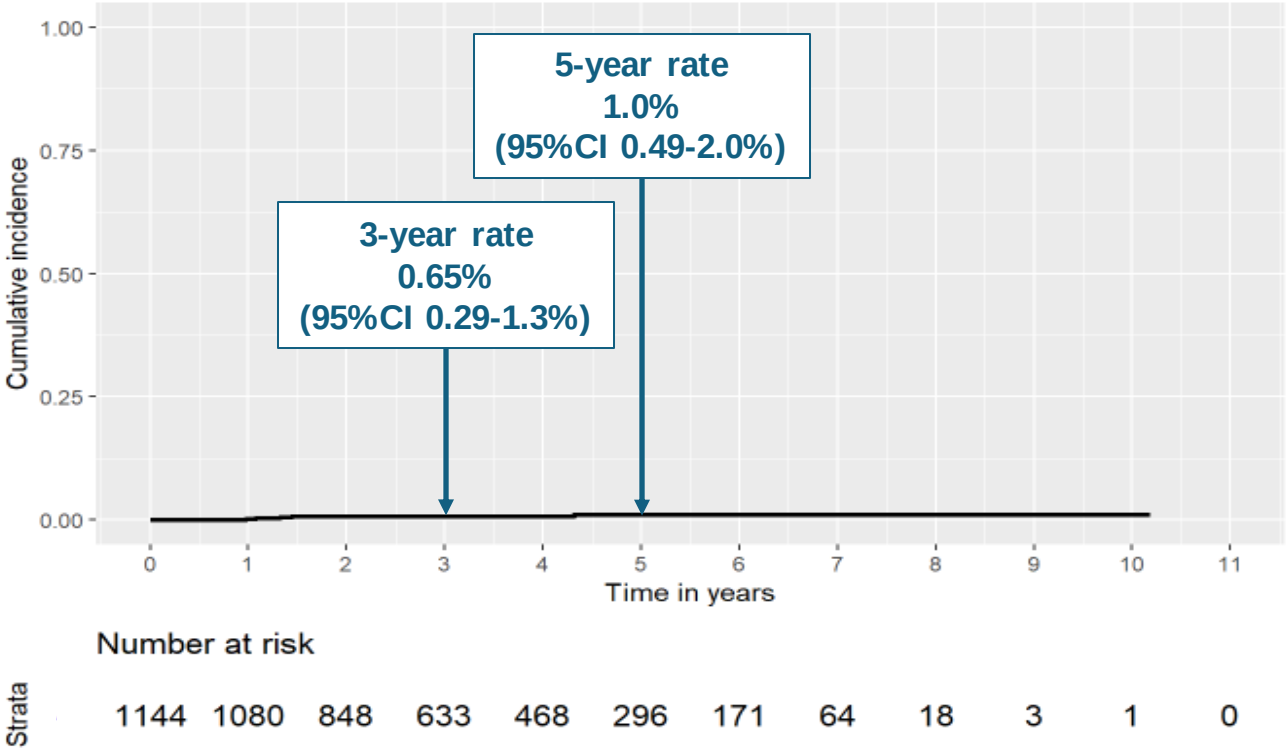
Map by Free Vector Maps http://freevectormaps.com

Flow Diagram

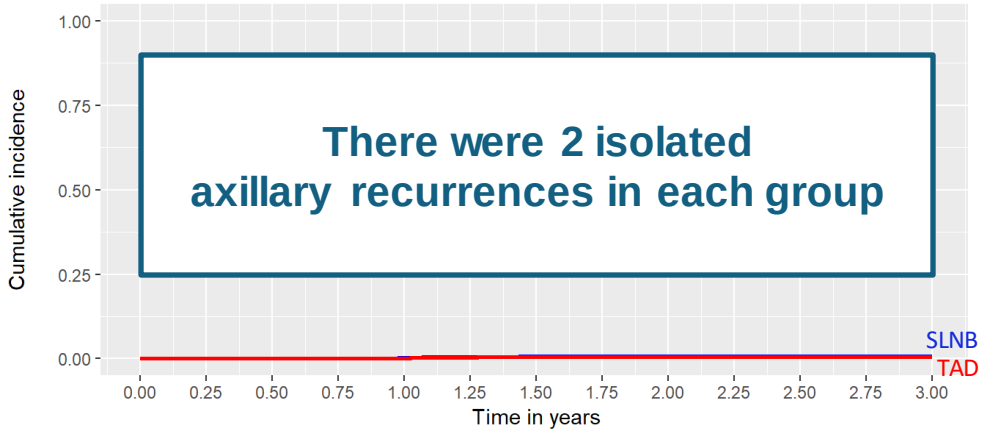


Any Axillary Recurrence



Any Axillary Recurrence (TAD vs SLNB)

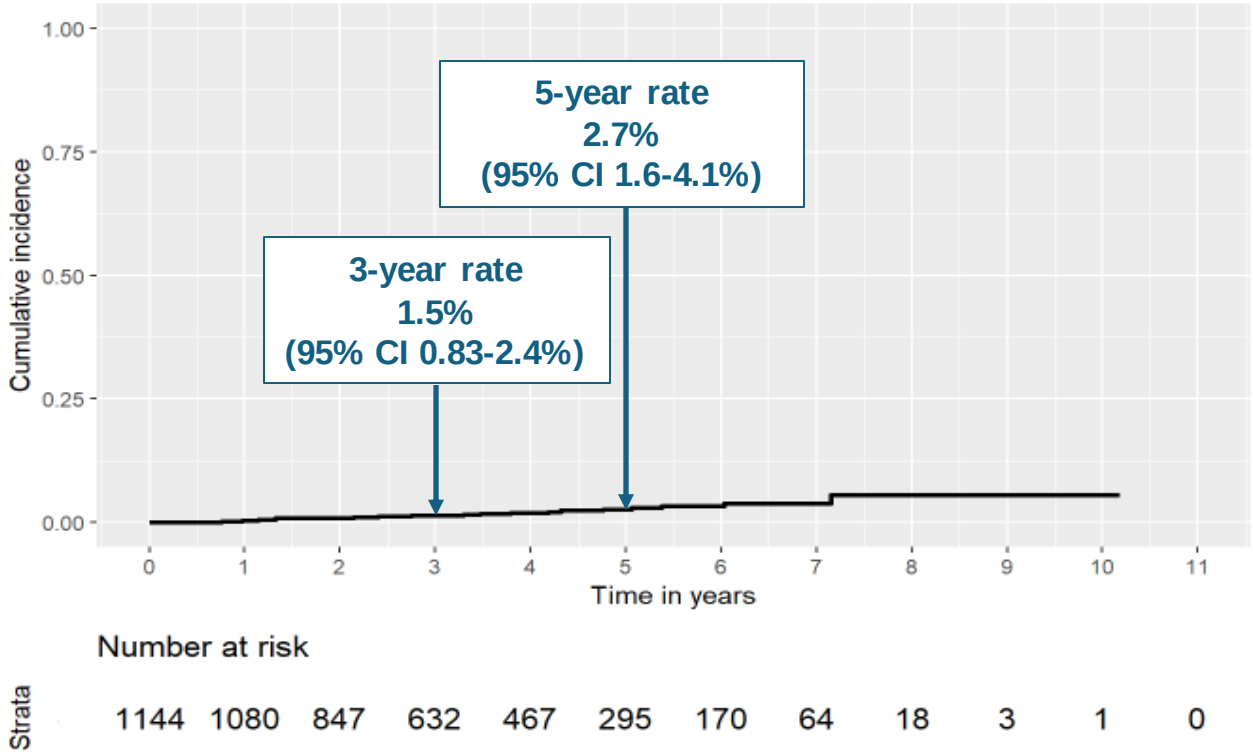
3-year rate of any axillary recurrence TAD vs SLNB (0.5% vs 0.8%, p = 0.55)



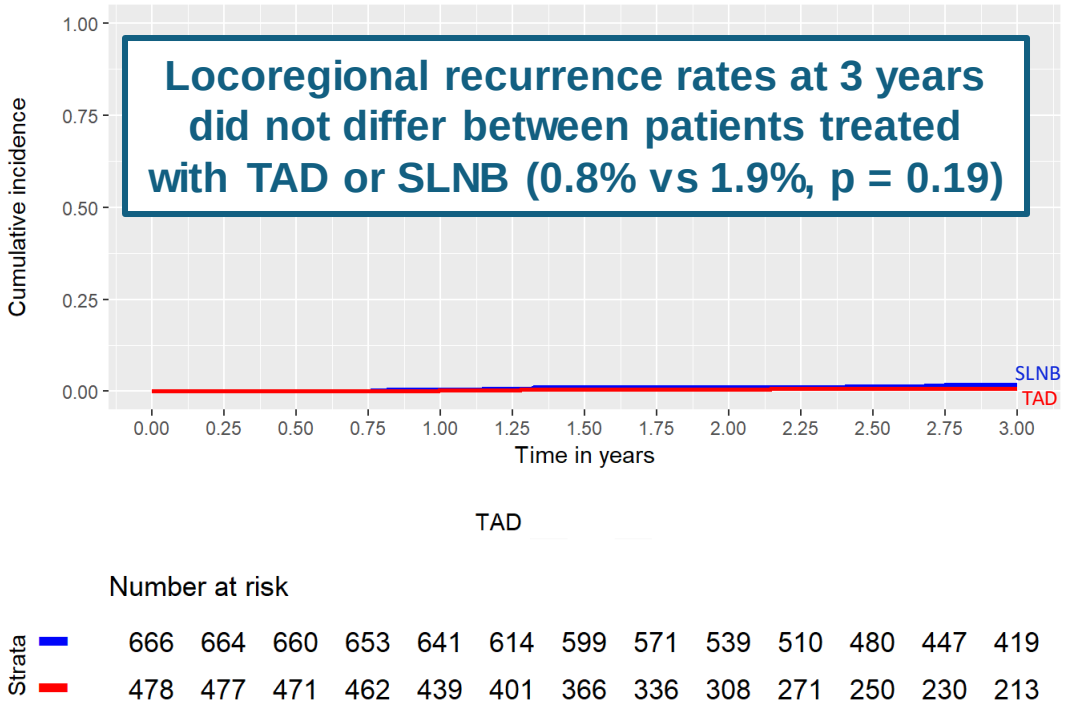
Number at risk

Strata													
	666	664	660	653	641	615	600	572	540	511	481	448	420
	478	477	471	462	439	401	366	336	308	271	250	230	213

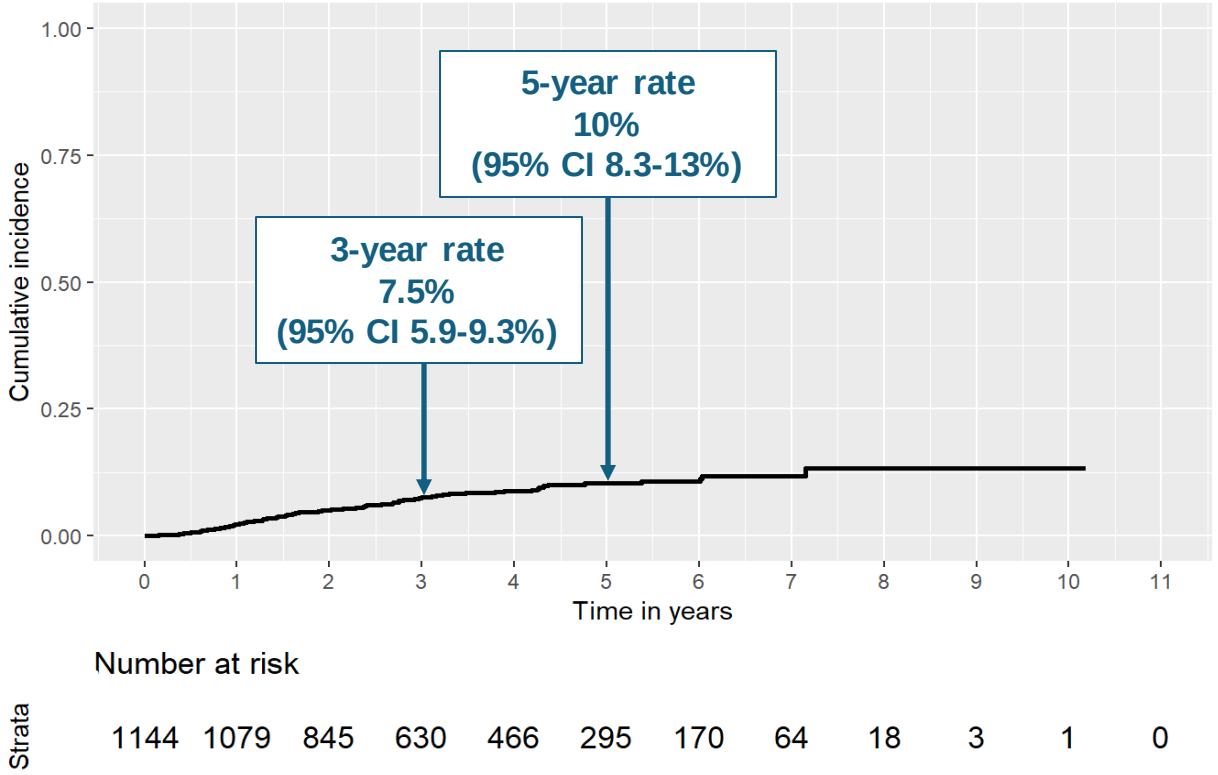
Locoregional Recurrence



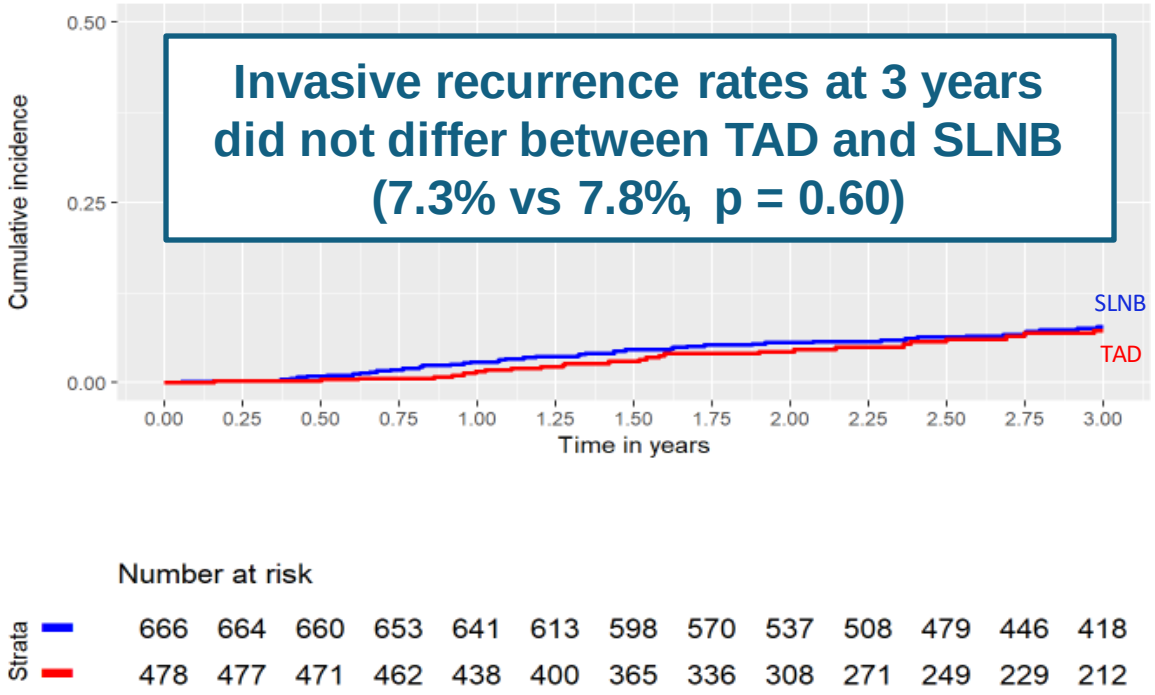
Locoregional Recurrence (TAD vs SLNB)



Any Invasive Recurrence (Locoregional or Distant)



Any Invasive Recurrence (TAD vs SLNB)



Other ways to optimize SLNB after NAC

San Antonio Breast Cancer Symposium® - December 6-10, 2022

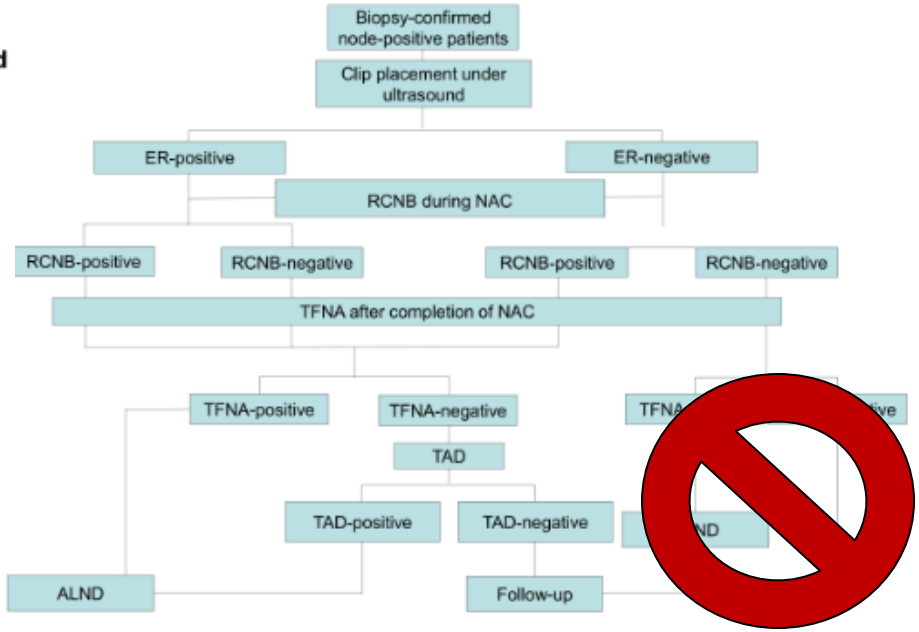
Incorporation of Repeated Core Needle Biopsy and Targeted Fine Needle Aspiration to Optimize Axillary Surgery After Neoadjuvant Chemotherapy in Node-positive Breast Cancer: A Prospective Feasibility Study

Si-Yu Wu, Jian-Wei Li, Ying Zhang, Na Hu, Guang-Yu Liu
Department of Breast Surgery& Department of Ultrasound, Fudan University Shanghai Cancer Centre, contacting e-mail address: drwu1187343296@163.com (Siyu Wu)

Table 2. Diagnostic Accuracy of Repeated Core Needle Biopsy in Breast, Targeted Fine Needle Aspiration and the Combination (N = 87)

	RCNB alone	TFNA alone	Combination
% (95%CI)			
Accuracy	63.2% (52.9-73.6)	74.7% (65.4-84.0)	63.2% (52.9-73.6)
Sensitivity	60.9% (74.0-95.6)	54.3% (39.4-69.3)	95.7% (89.5-100.0)
Specificity	39.0% (23.4-54.6)	97.6% (92.6-100.0)	39.0% (23.4-54.6)
NPV	69.6% (49.2-89.9)	65.6% (53.3-77.8)	88.9% (72.8-100.0)
PPV	60.9% (48.7-73.2)	96.2% (88.2-100.0)	68.8% (57.1-80.4)

Figure 1. A proposed algorithm applying RCNB and TFNA to tailor axillary surgery among patients with biopsy-confirmed node-positive patients in our study.



CONCLUSIONS

Combination of RCNB and TFNA allows for an accurate assessment of nodal response after NAC. These results may facilitate reliable identification of suitable candidates for de-escalation or elimination in axillary surgery.

Implications

- Forthcoming systemic therapy de-escalation trials, SOC algorithms
- Consider re-biopsy if suspicious lymph nodes after NAC
  - If positive, consider additional therapy

Tailoring therapy

- Overall goal
  - Omission of ALND

  AND
  - Safe de-escalation of cytotoxic therapies, then escalate if poor response

- Systemic therapy is often dependent on surgical findings

PD-15-11

Axillary dissection to determine nodal burden to inform systemic therapy recommendations in patients with clinically node-positive breast cancer: Pre-planned substudy of TAXIS (OPBC-03, SAKK 23/16, IBCSG 57-18, ABCSG-53, GBG 101)

Walter P. Weber, MD[1,2]; Zoltan Matrai, MD, PhD[3]; Stefanie Hayoz, PhD[4]; Christoph Tausch, MD[5]; Guido Henke, MD[6,7]; Daniel R. Zwahlen, MD[8]; Günther Gruber, MD[9]; Frank Zimmermann, MD[9,10]; Thomas Ruhstaller, MD[11]; Simone Muenst, MD[2,12]; Markus Ackerknecht, PhD[2,13]; Sherko Kuemmel, MD, PhD[14]; Vesna Bjelic-Radisic, MD[15]; Viktor Smanykó, MD[16]; Conny Vrieling, MD, PhD[17]; Rok Satler, MD[18]; Inna Meyer, MD[19]; Charles Becciolini, MD[20]; Susanne Bucher, MD[21]; Colin Simonson, MD[22]; Peter M. Fehr, MD[23]; Natalie Gabriel, MD[24]; Robert Maráz, MD[25]; Dimitri Sarlos, MD[26]; Konstantin J. Dedes, MD[27]; Cornelia Leo, MD[28]; Gilles Berclaz, MD[29]; Hisham Fansa, MD[30]; Christopher Hager, MD[31]; Klaus Reisenberger, MD[32]; Ákos Sávolt MD, PhD[33]; Christian F. Singer, MD[34]; Roland Reitsamer, MD[35]; Jelena Winkler, MD[36]; Giang Thanh Lam, MD[37]; Mathias K. Fehr, MD[38]; Tatiana Naydina, MD[39]; Magdalena Kohlik, MD[40]; Karine Clerc, MD[41]; Valerijus Ostapenko, MD[42]; Florian Fitzal, MD[43]; Martin Heidinger, MD[1,2]; Nadia Maggi, MD[1,2]; Alexandra Schultz[2,44]; Pagona Markellou, MD[7]; Loïc Lelièvre, MD[45]; Daniel Egle, MD[46]; Jörg Heil, MD[47]; Michael Knauer, MD, PhD[11]; Andreas Mueller, MD[4], Christian Kurzeder, MD[1,2]

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- "Axillary node debulking", followed by RNI vs ALND+RNI
- N=297 upfront surgery patients; N=143 NAC

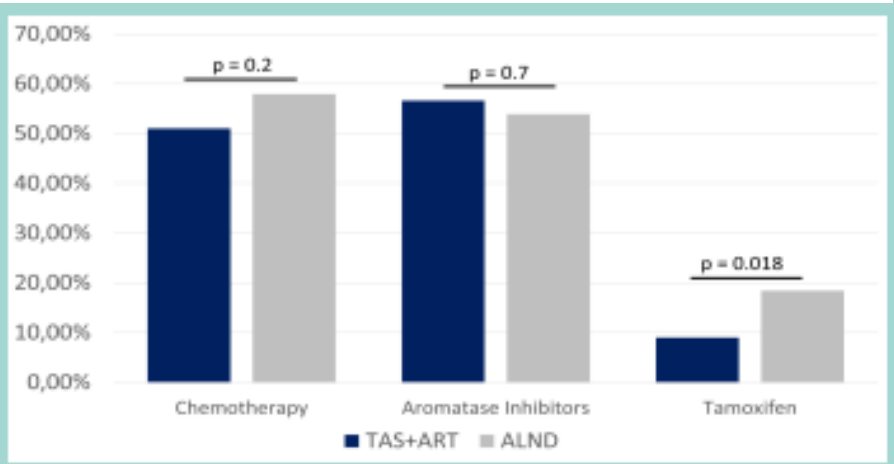


Figure 2. Adjuvant systemic therapy in HR+ / Her2 - patients with upfront surgery using TAS and ART compared to ALND

TAS – tailored axillary surgery; ART – axillary radiotherapy; ALND – axillary lymph node dissection
HR – hormone receptor; Her2 – human epidermal growth factor receptor 2

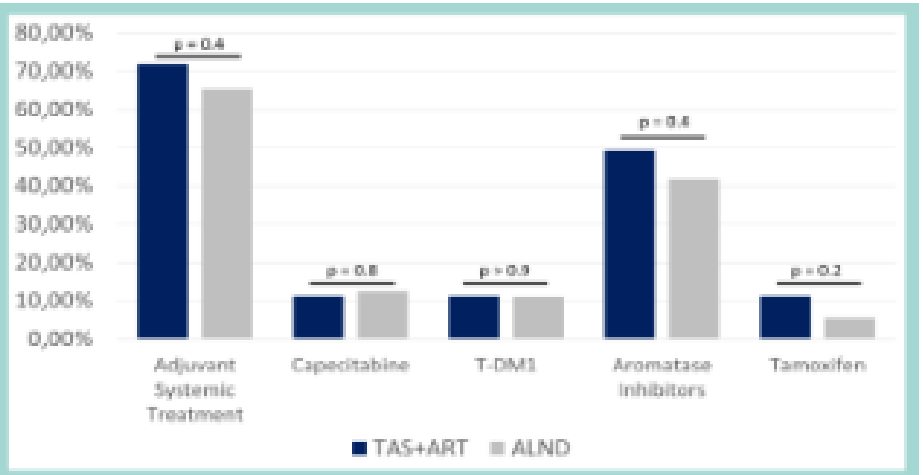


Figure 3. Adjuvant systemic therapy after neoadjuvant systemic treatment using TAS and ART compared to ALND

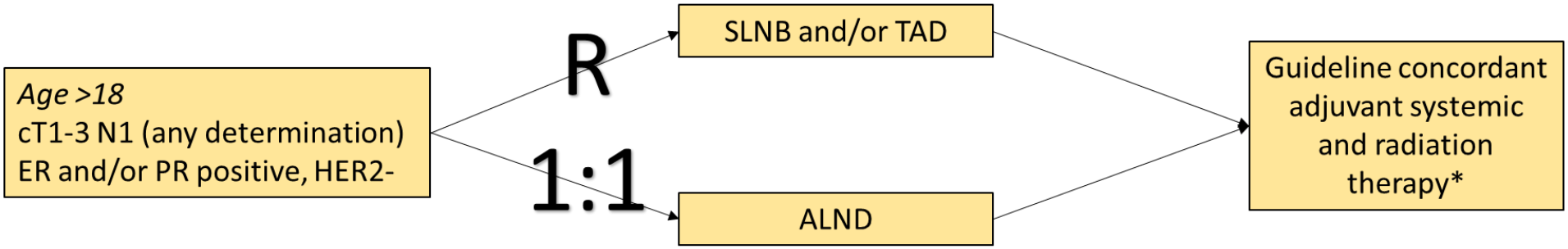
TAS – tailored axillary surgery; ART – axillary radiotherapy; ALND – axillary lymph node dissection

DISCUSSION

- Both, in patients with neoadjuvant systemic treatment and those with upfront surgery, significantly more positive lymph nodes were removed by axillary lymph node dissection compared to tailored axillary surgery.
- However, this did not have a relevant impact on rate and type of adjuvant systemic therapy.

Implications

- Further clinical trials testing omission of ALND (upfront surgery setting)



PI: Weiss, in development

Thank you!

anna_weiss@urmc.rochester.edu