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The OPBC05/EUBREAST-14R/ICARO study

Are nodal isolated tumor cells (ITCs) after neoadjuvant chemotherapy an indication for axillary dissection?

ONCOPLASTIC BREAST CONSORTIUM

Speaker: **Giacomo Montagna, MD, MPH**
Breast Service, Department of Surgery, Memorial Sloan Kettering Cancer Center

Giacomo Montagna MD, MPH, Alison Laws MD, MPH, Massimo Ferrucci MD, PhD, Mary M. Mrdutt MD, MS, Susie X. Xun MD, Sung Gwe Ahn MD, PhD, Mariacarla Andreozzi PhD, Suleyman Bademler MD, Hakan Balbaloglu MD, Nora Balint-Lahat MD, Maggie Banys-Paluchowski MD PhD, Daniel Meirelles Barbano MD, PhD, Andrea V. Barrio MD, Nuran Bese MD, Jean François Boileau MD, MSc, Judy Boughey MD, Marissa Boyle MD, Flavia Vidal Cabero MD, MSc, Daniela Cocco MD, Fabio Corsi MD, Angelena Crown MD, Elco de Bree MD, PhD, Maria del Mar Vernet-Tomas MD, Christine Deutschmann MD, Emilia J. Diego MD, Nina Ditsch MD, Claire Eden MD, Ruth Eller MD, Emanuela Esposito MD, PhD, Oluwadamilola Fayanju MD, MPHS, Franziska Fick MD, Forian Fitzal MD, Meghan R. Flanagan MD, MPH, Damiano Gentile MD, Oreste D. Gentilini MD, Maite Goldschmidt MSc, Mehmet Ali Gulcelik MD, Callie Hlavin, MD, MPH, Martin Heidinger MD, Jörg Heil MD, PhD, Justyna Jelinska MD, PhD, Güldeniz Karadeniz Cakmak MD, FEBS, Susan Kesmodel MD, Natalia Krawczyk MD, Henry M. Kuerer MD, PhD, Thorsten Kühn MD, PhD, Sherko Kümmel MD PhD, Cornelia Leo MD, Julie Loesch MD, Francesco Milardi MD, Dawid Murawa MD, PhD, Tracy Ann Moo MD, Tehillah S. Menes MD, Valentina Nekljudova PhD, Lisa A. Newman MD MPH, Daniele Passeri MD, PhD, Jessica M. Pastoriza MD, Andraz Perhavec MD, PhD, Melissa Pilewskie MD, Nina Pislar MD, Natália Polidorio MD, PhD, Fiorita Poulakaki MD, PhD, Avina Rami, Fabian Riedel MD, Nicola Rocco MD PhD, Jai Min Ryu MD, PhD, Freya R. Schnabel MD, Alexandra Schulz MSc, Emily L. Siegel MD, Colin Simonson MD, Christian Singer MD, PhD, Leonardo Soares MD, PhD, Varadan Sevilimedu, MBBS, DrPH, Christoph Tausch MD, Ekaterini Christina Tampaki MD, PhD, Athanasios Tampakis MD, PhD, Marios Konstantinos Tasoulis MD, PhD, M. Umit Ugurlu MD, Cihan Uras MD, Cicero Urban, MD, PhD, Astrid Botty Van den Bruele MD, Annemiek van Hemert MSc , Glenn Vergauwen MD, PhD, Denise Vorburger MD, Fredrik Wärnberg, Anna Weiss MD, Austin D. Williams MD, MSEd, Kerstin Wimmer MD, PhD, Stephanie M Wong MD, MPH, Steven G. Woodward MD, Tae-Kyung Robyn Yoo MD, Jennifer Q. Zhang MD, Firdos M. Ziauddin MD, Tari King MD, Hasan Karanlik MD, Neslihan Cabioğlu MD, Marie-Jeanne Vrancken Peeters MD, PhD, Monica Morrow MD, Walter P. Weber, MD

Disclosure Information

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Speaker: Giacomo Montagna, MD

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Background: Nodal Burden in Patients with Residual Nodal Disease After NAC

- Patients with a positive sentinel lymph node (SLN) after neoadjuvant chemotherapy (NAC) have a high residual nodal burden, and axillary lymph node dissection (ALND) is currently considered standard of care

	ACOSOG Z1071	SN FNAC	MSKCC
Micromets	164/273 **(60.1%)**	3/8 **(37%)**	34/61 **(56%)**
Macromets		28/44 **(64%)**	75/121 **(62%)**

Boughey J et al. JAMA 2013
Boileau JF et al. JCO 2015
Moo TA et al. ASO 2018
Moo TA et al. ASO 2021

Residual Isolated Tumor Cells

- Residual isolated tumor cells (ITCs) are found in ~1.5% of patients undergoing neoadjuvant chemotherapy
- Data on the likelihood of finding additional positive lymph nodes in patients with residual ITCs are scarce, and the benefit of ALND is unclear

	ACOSOG Z1071	SN FNAC	MSKCC	OVERALL
ITCs	4/11	4/7	1/6	**9/24 (37.5%)**

- As a consequence, surgical management of the axilla in these patients is not standardized

Wong SM et al. ASO 2019
Burstein HJ et al. Ann Onc 2021

Aims

- To determine how often additional positive LNs are found in patients with residual ITCs
- To evaluate rates of axillary and any invasive recurrence
- To compare outcomes in patients treated with and without ALND

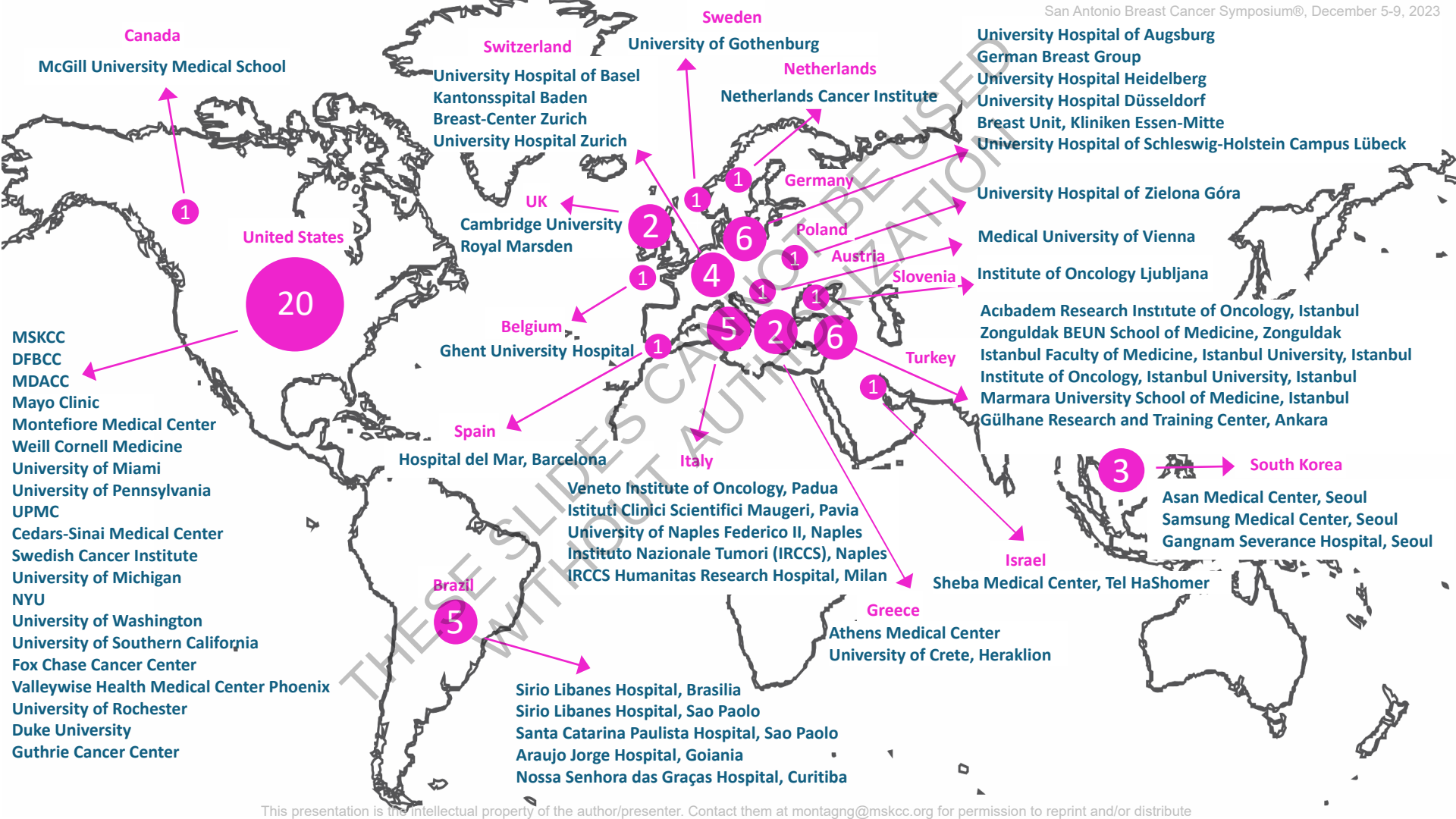
Study Population

Inclusion criteria

- T1-4 N0-3 BC patients
- Surgery after NAC with detection of ITCs [ypN0(i+)] at frozen section or final pathology
- SLNB performed with dual-tracer mapping *or* TAD *or* MARI for N+ and with single tracer for N0
- Detection of ITCs by H&E or IHC

Exclusion criteria

- No SLNB/TAD
- Inflammatory breast cancer
- Stage IV
- NET
- Detection by OSNA (quantitative measurement of target mRNA) due to lack of standardized cut-off



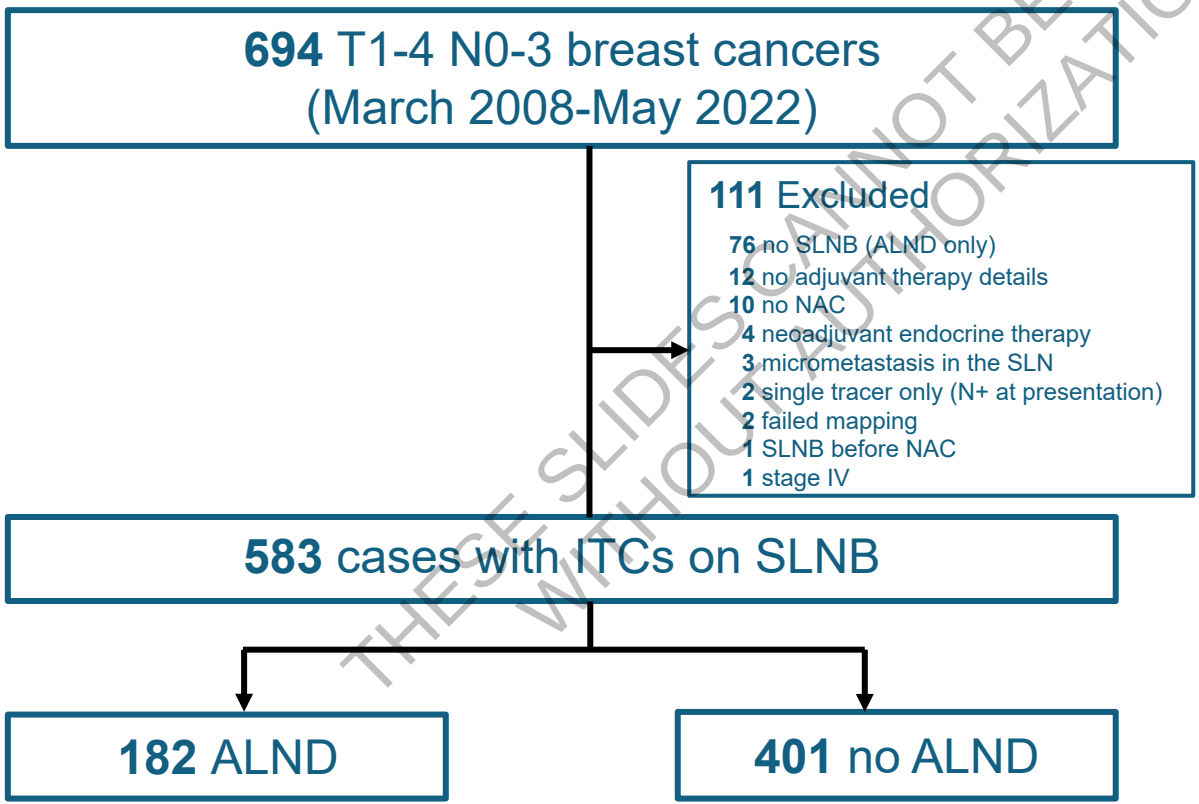
Data Collection

- Clinical and treatment variables, including pathologic characteristics of the primary tumor, surgery, radiation, and systemic therapy were collected from institutional databases

Statistical Analysis

- Clinicopathologic characteristics were compared between surgical groups using the Wilcoxon rank sum test, Pearson's Chi-squared test, and Fisher's exact test
- Competing risk analysis was performed to assess the cumulative incidence rates of axillary recurrence and any invasive recurrence (locoregional or distant)
- 5-year cumulative incidence rates were compared between patients treated with and without ALND using Gray's test

Flow Diagram



Median follow-up
3.2 years

Clinical Characteristics

	Overall n = 583	No ALND n = 401	ALND n = 182	p value
Age, years (IQR)	48 (41, 57)	48 (40, 57)	49 (43, 58)	0.11
Race/Ethnicity				0.5
Asian	11%	10%	13%	
Black	5%	6%	3%	
Hispanic	5%	6%	4%	
White	77%	76%	77%	
Other/unknown	2%	3%	2%	
Clinical T stage				0.15
1	16%	17%	15%	
2	57%	55%	62%	
3	23%	25%	19%	
4	3%	3%	4%	
X	0.2%	0%	0.5%	
Clinical N stage				**<0.001**
0	26%	30%	16%	
1	64%	63%	67%	
2	8%	5%	13%	
3	2%	2%	4%	

Pathological Characteristics

	Overall n = 583	No ALND n = 401	ALND n = 182	p value
Tumor differentiation				0.13
Well	6%	8%	3%	
Moderately	39%	39%	40%	
Poorly	54%	53%	57%	
unknown	49	27	22	
Histology				**0.02**
Ductal	89%	88%	92%	
Lobular or mixed	9%	11%	5%	
Other	2%	2%	3%	
unknown	2	1	1	
Receptor subtype				0.6
HR+/HER2-	41%	40%	43%	
HR+/HER2+	28%	27%	29%	
HR-/HER2+	10%	10%	10%	
HR-/HER2-	21%	22%	18%	
LVI				**<0.001**
Yes	29%	24%	38%	

Axillary Staging Characteristics

	Overall n = 583	No ALND n = 401	ALND n = 182	p value
Staging technique (cN+ only)	**n = 433**			
SLNB with dual tracer mapping	58%	52%	69%	**< 0.001**
TAD	34%	37%	28%	
MARI	8%	11%	3%	
Entire cohort (cN0 and cN+)				
# of SLNs removed (mean, min, max)	3.3 (0, 16)	3.5 (1, 16)	2.8 (0, 10)	**< 0.001**
# of SLNs with ITCs (mean, min, max)	1.2 (0, 6)	1.2 (0, 6)	1.2 (0, 6)	0.6
ITCs detected on frozen section				**< 0.001**
Yes	25%	8%	62%	
Not performed/unknown	20	11	9	
Total # of LNs removed (mean, min, max)	7 (1,37)	4 (1, 16)	15 (4, 37)	**< 0.001**

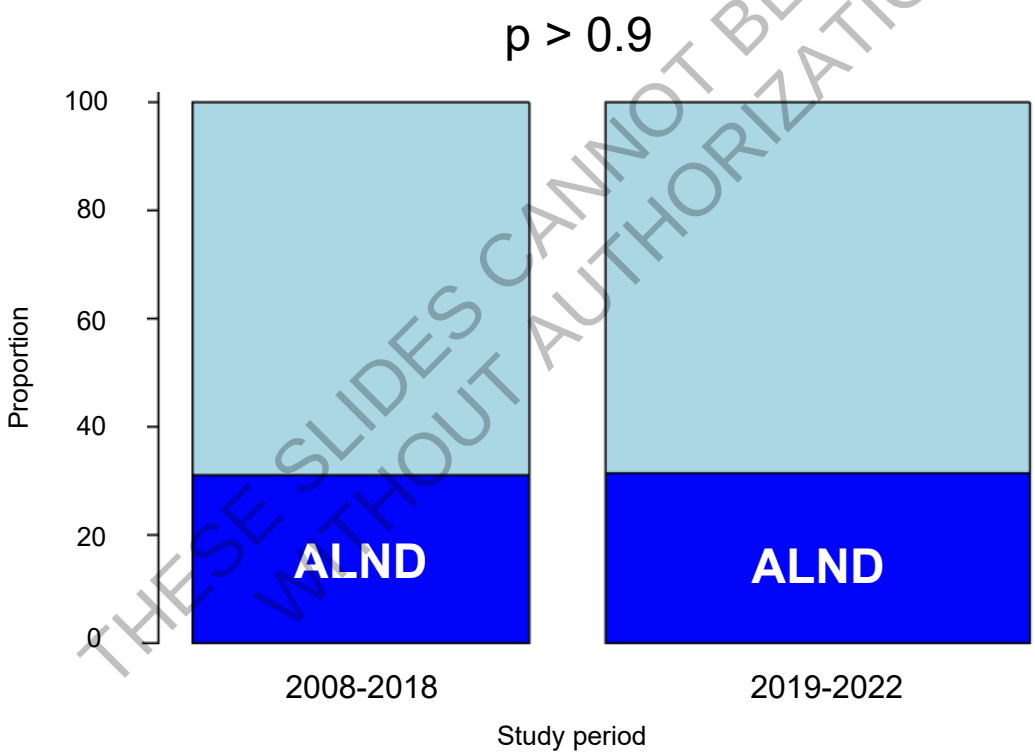
Treatment Characteristics

	Overall n = 583	No ALND n = 401	ALND n = 182	p value
NAC regimen				
HER2-	**n = 362**			0.8
AC-T	79%	78%	81%	
AC-T + Carbo	6.6%	6.0%	8.1%	
AC-T + Carbo with pembrolizumab	2.8%	2.8%	2.7%	
Anthracycline-free regimen	2.8%	3.2%	1.8%	
Other	8.6%	9.6%	6.3%	
HER2+	**n = 221**			0.068
AC-TH	22%	20%	27%	
AC-THP	29%	29%	31%	
TC-H	1.8%	1.3%	2.8%	
TC-HP	30%	36%	18%	
Other	16.5%	13.7%	18%	

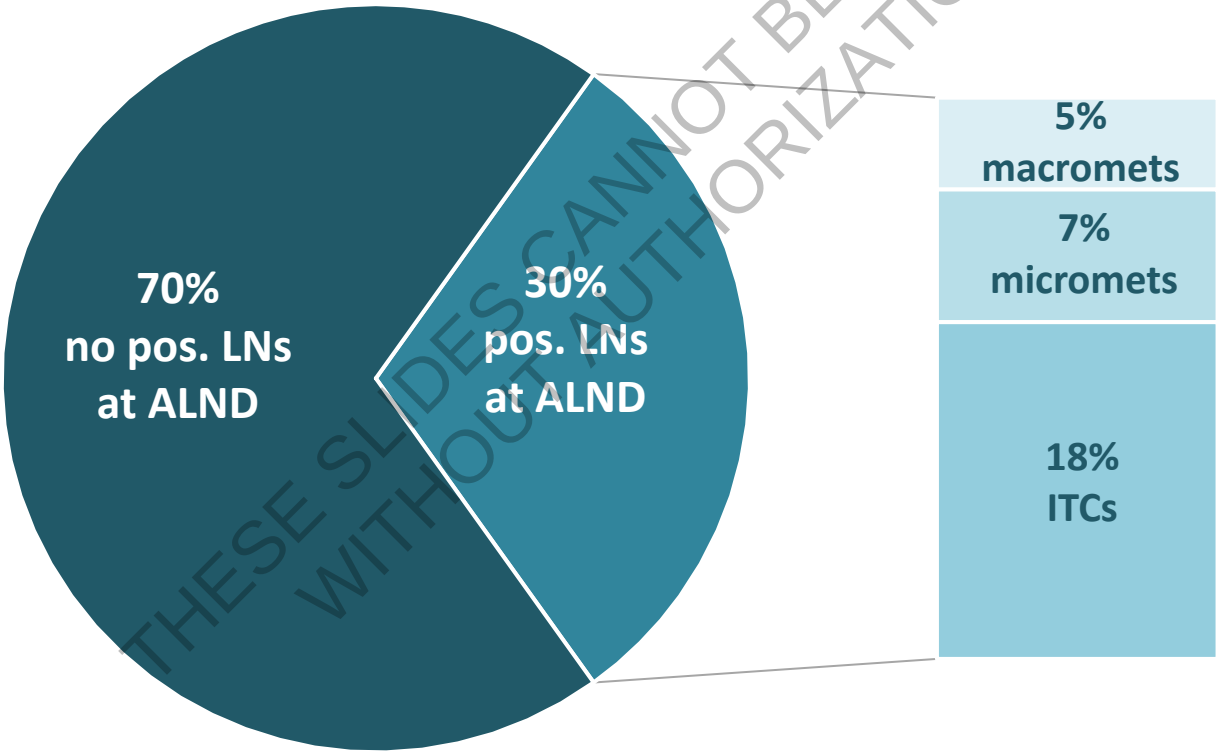
Treatment Characteristics

	Overall n = 583	No ALND n = 401	ALND n = 182	p value
Type of breast surgery				0.13
Breast conservation	46%	48%	41%	
Mastectomy	54%	52%	59%	
Radiation therapy (RT)				
Breast (n = 267)	98%	97%	100%	0.3
Chest wall (n = 316)	82%	78%	89%	**0.024**
Nodal RT				**0.038**
Yes	77%	75%	82%	

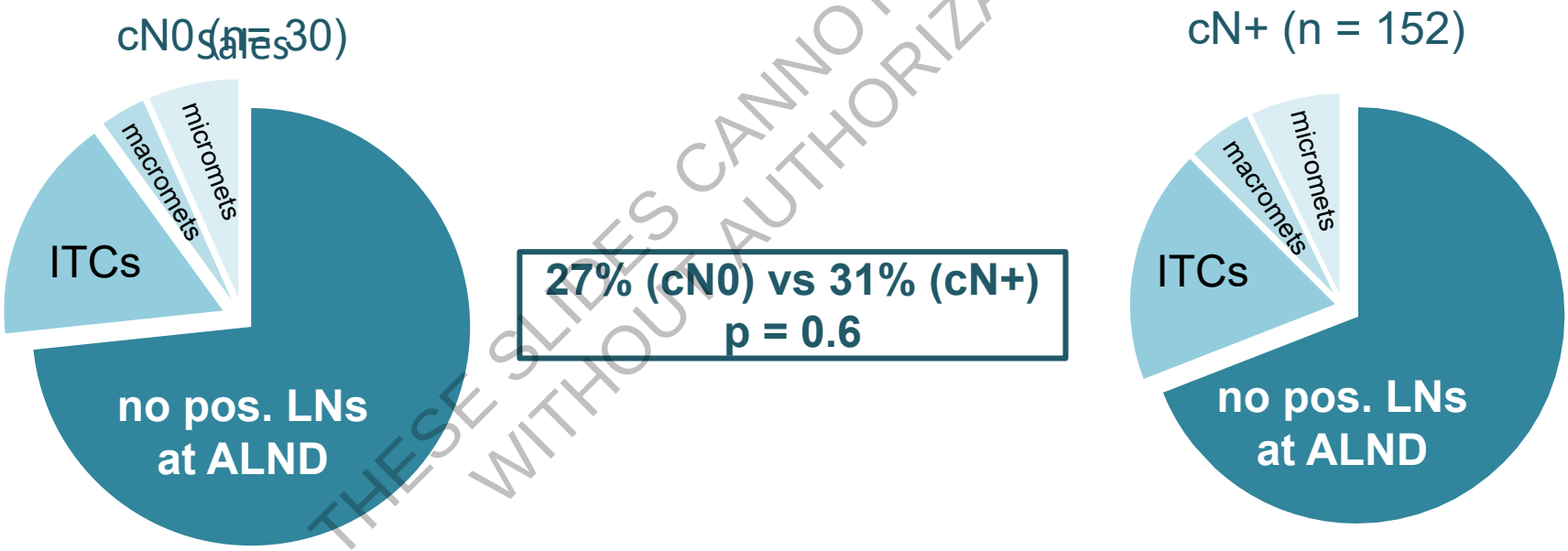
Trend in ALND Over Time



Additional Positive Lymph Nodes in the ALND Group (n=182)

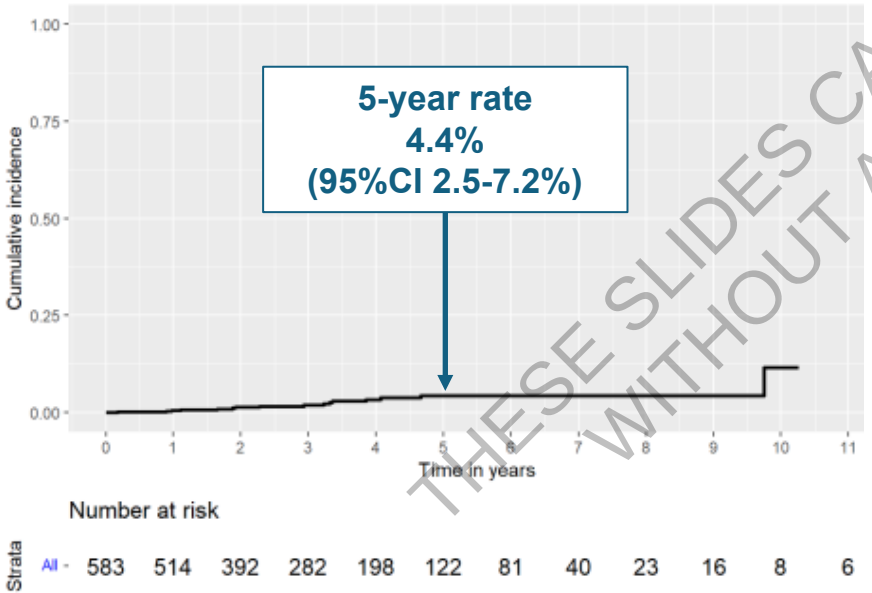


Additional Positive Lymph Nodes at ALND by Nodal Status at Presentation

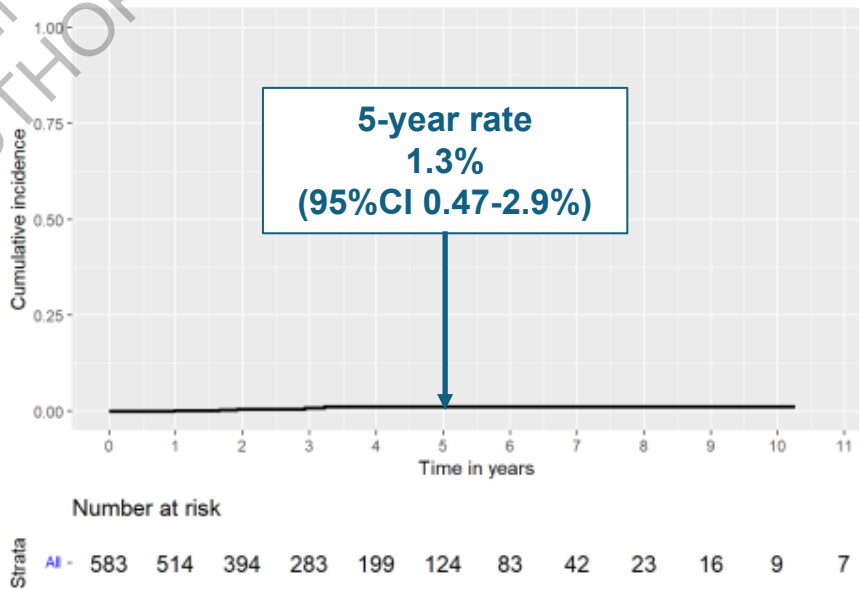


Axillary Recurrence

Any (Isolated or Combined with Local and Distant Recurrence)



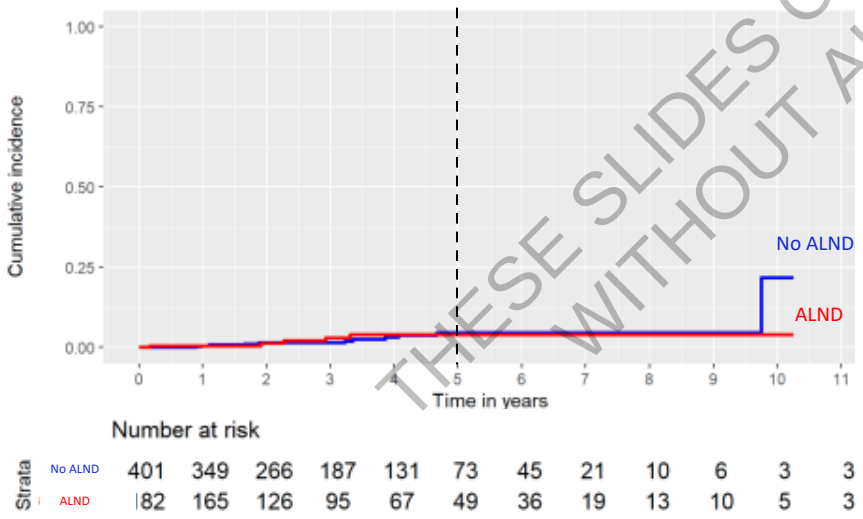
Isolated



Axillary Recurrence (No ALND vs ALND)

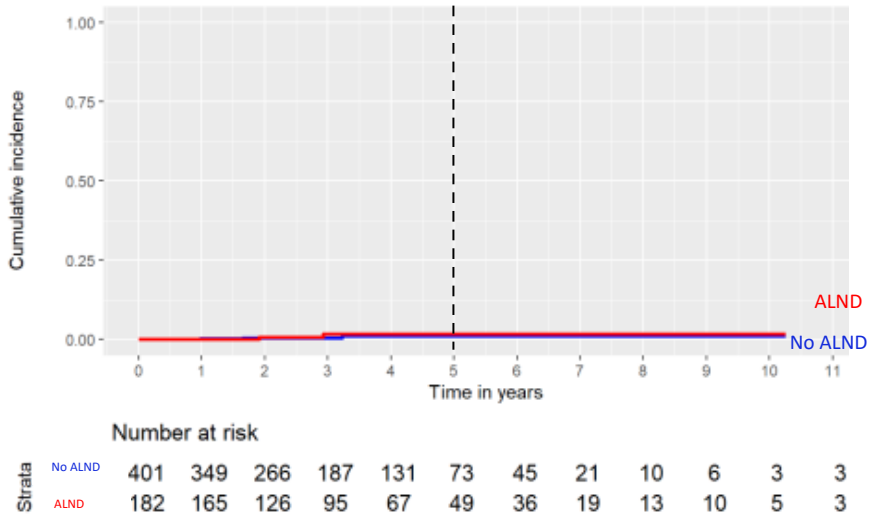
Isolated or Combined with Local and Distant Recurrence

5-year rate of any axillary recurrence
no ALND vs ALND
4.6% vs 4.1%, p = 0.8

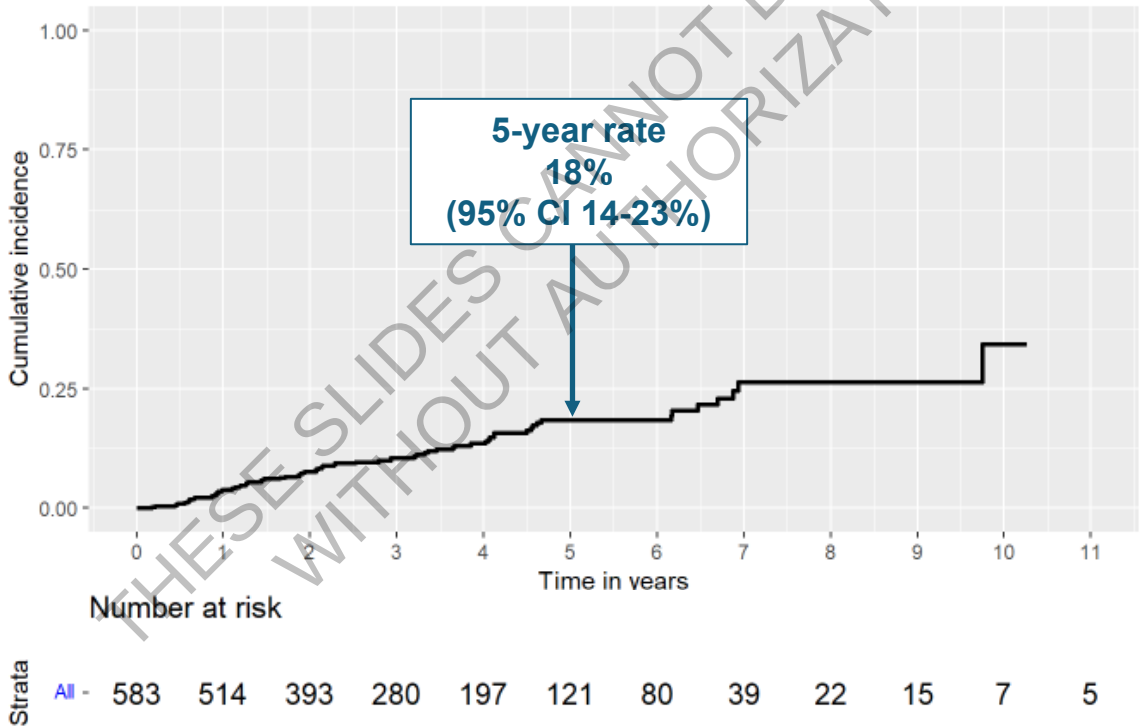


Isolated

5-year rate of isolated axillary recurrence
no ALND vs ALND
1.1% vs 1.7%, p = 0.7

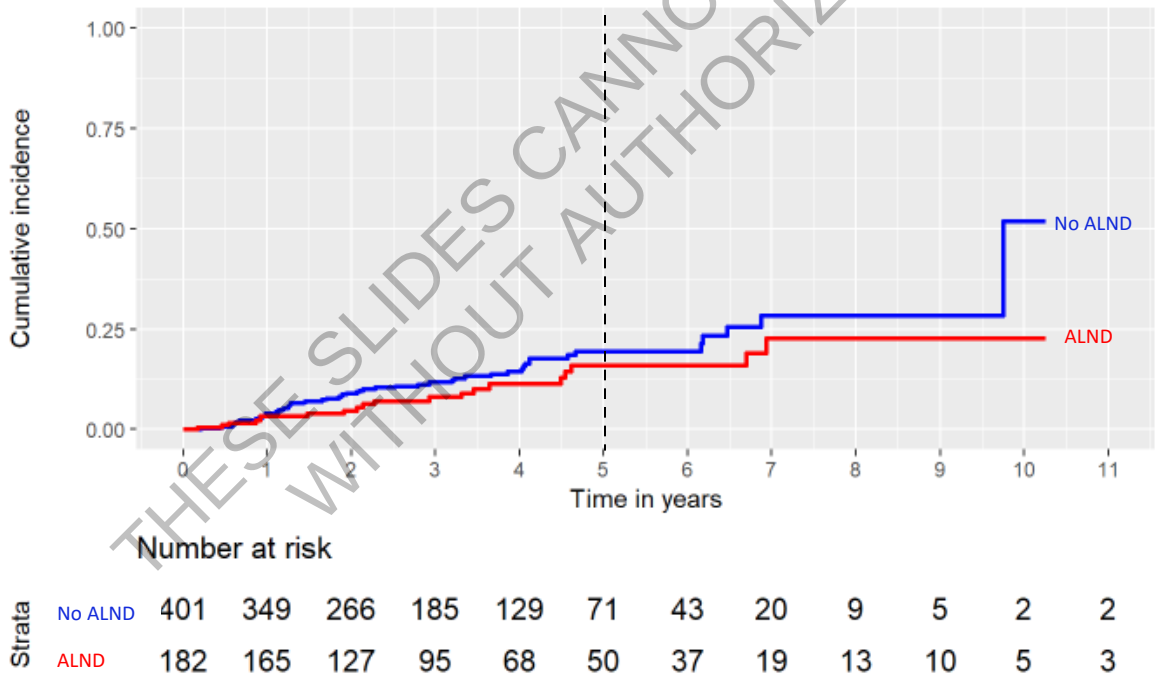


Any Invasive Recurrence (Locoregional or Distant)



Any Invasive Recurrence (No ALND vs ALND)

5-year rate of any invasive recurrence no ALND vs ALND
19% vs 16%, p = 0.13



Strengths and Limitations

Strengths

- First study to compare outcomes in patients with residual ITCs treated with and without ALND
- Large number of patients to examine residual nodal burden in patients with ITCs
- Multicenter
- All settings (public, private academic, and community hospitals)

Limitations

- Retrospective
- Relatively short median follow-up (3.2 years)
- Pathological assessment was not standardized

Conclusions

- The likelihood of finding additional positive lymph nodes in patients with residual ITCs is lower than in patients with residual micro- and macrometastases
  - macrometastases were found at ALND in 5% of cases
  - no impact of nodal status at presentation
- Detection of ITCs on frozen section was strongly associated with ALND
- Rates of axillary and invasive recurrence did not statistically differ based on the use of ALND

Conclusions

- These results do not support routine ALND in patients with residual ITCs after NAC
- Randomized trials (NASBP-B51) will provide further insight to whether nodal RT is needed in this setting