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VENUE OF THE CONFERENCE: VÁRKERT BAZÁR



# CURRENT VIEW ON MANAGEMENT OF AXILLA IN PATIENTS WITH EARLY BREAST CANCER

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- **De-escalating of surgery in last few years after presentation of ACOSOG Z0011, IBCSG Trial 23-01**
- **More radiotherapy? AMAROS, OTOASOR, MA 20, EORTC 22922**
- **Should we translate results of these trials on our patients? Should we predict number of positive lymph nodes?**
- **Current questions of treating axila**

**Do we need SLNB in low risk patients?**

**Treatment of axilla (RNI/ALND) or nothing in patients with 1-2 involved SN?**

**What to do in patients with mastectomy and involved SN?**

**What to do in patients with  $\geq 3$  positive sentinel nodes?**



## The aim of the study

- to evaluate the involvement of SN and NSN
- applicability of the Z0011 criteria to our patients
- to identify the predictive factors of NSN involvement

## Type of study: a retrospective cohort study

- 1393 patients selected for SLNB between 2010-2014
- 43 patients were excluded after neoadjuvant CHT or identification failure

## Methodology

- SLNB – combined method (radiocolloid + blue dye)
- SN – frozen section H&E, serial sections, IHC
- Univariable and multivariable statistical analysis of data



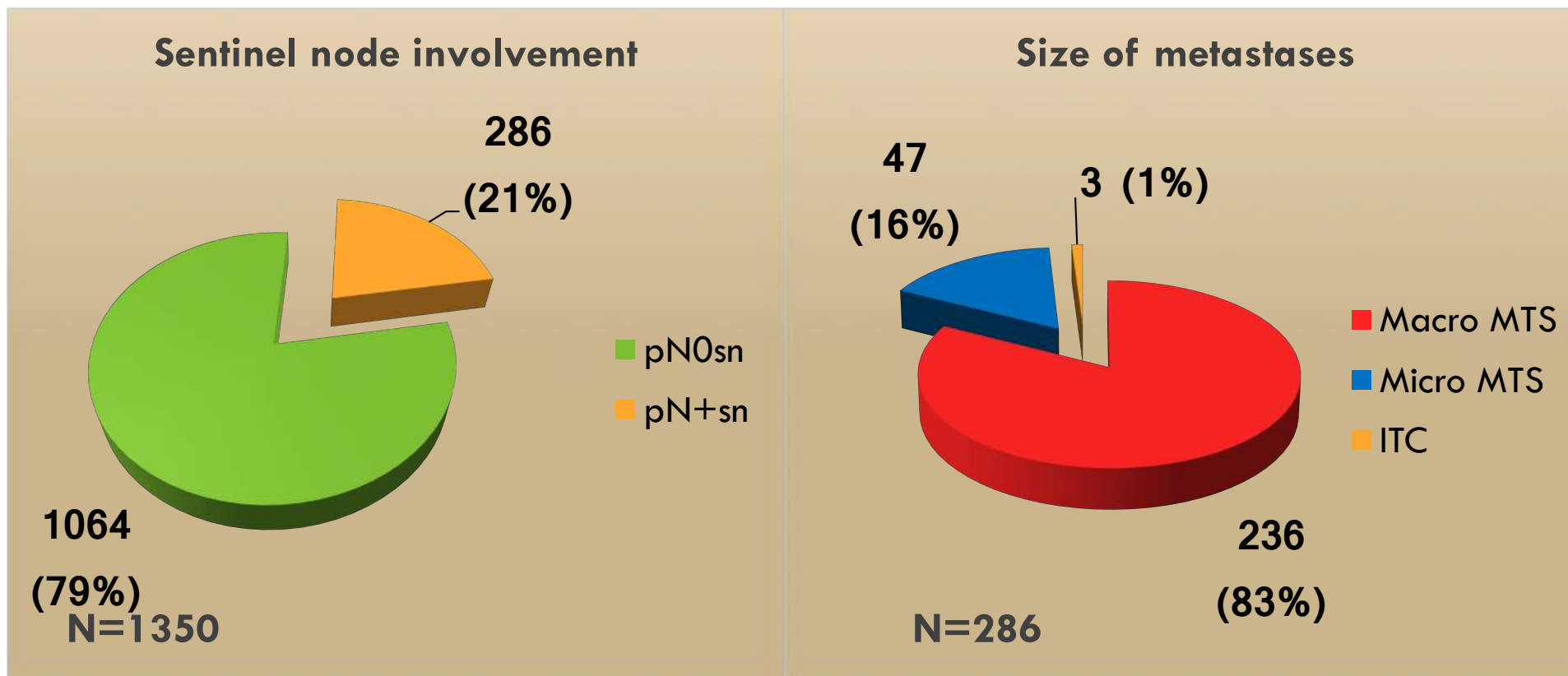
# Predictive factors of non-SN involvement



Clinical	Histological - TU	Histological - SN
Age	Type of tumor	Size of MTS
Palpability	Grading	Ratio of positive-to-removed SN
Multicentricity/unicentricity	Lympho-vascular invasion	Perinodal invasion
Tumor size	ER, PR, Ki67, Her2	Number of involved nodes
Positivity by frozen section	Molecular subtype	



# Sentinel node involvement

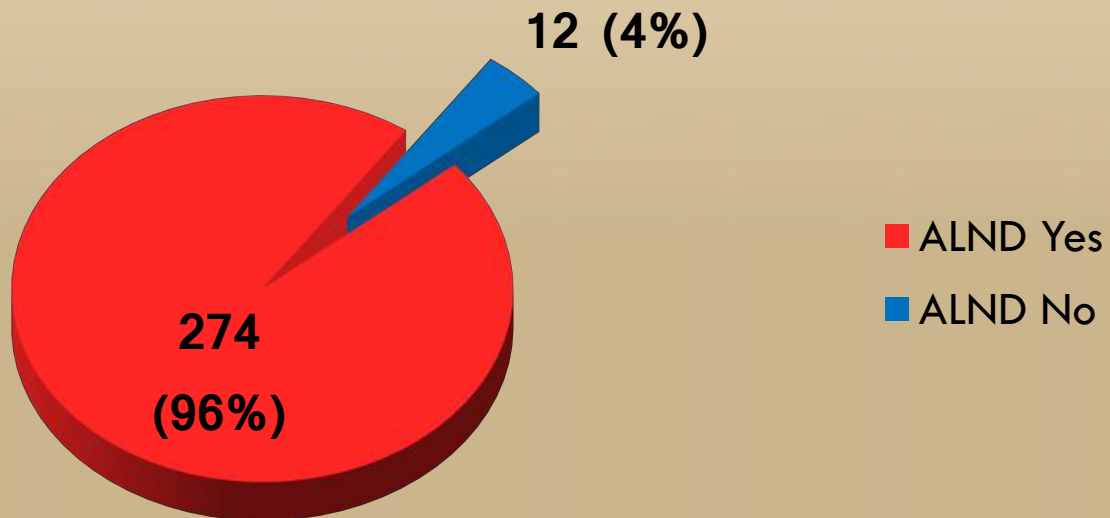




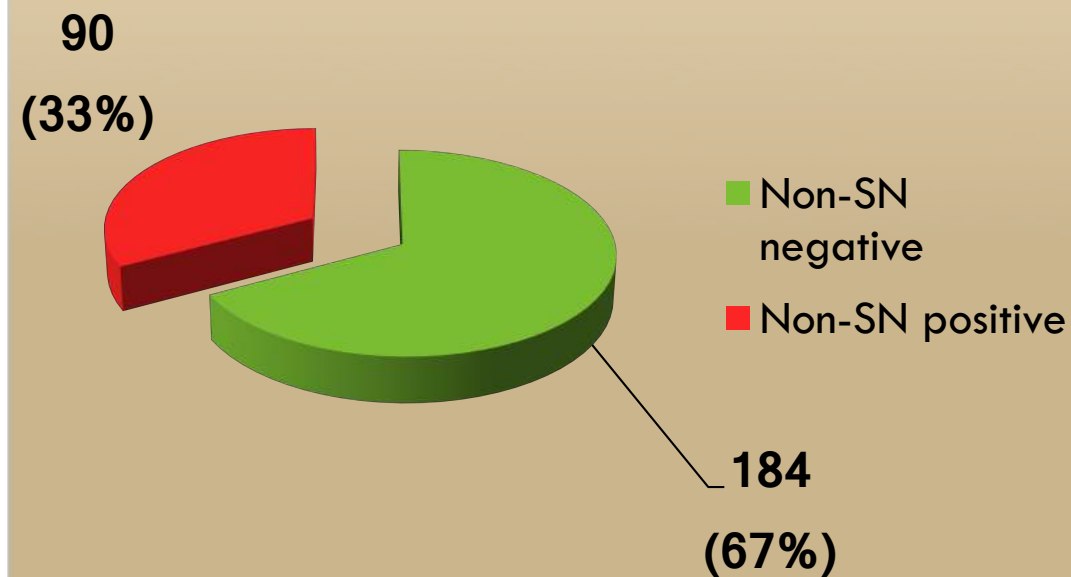
# Non-sentinel node involvement



## Axillary lymph node dissection



## Non-sentinel node involvement



N=286



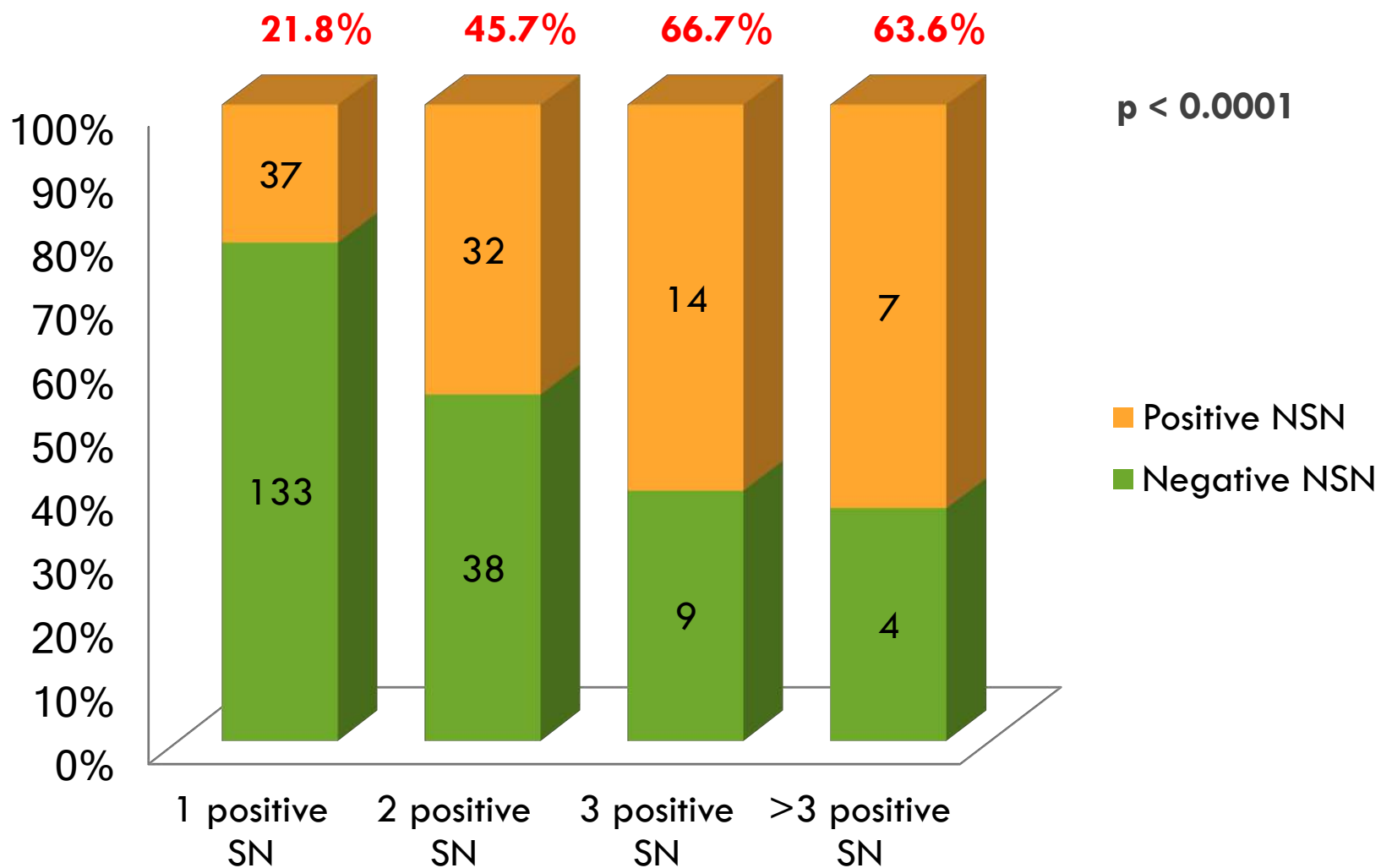
# Univariable analysis of predictive factors of NSN involvement



- **Number of involved SN** **p < 0.0001**
- **Ratio of positive-to-removed SN** **p < 0.0001**
- **Positivity of SN in frozen section** **p = 0.0019**
- **Lympho-vascular invasion of TU** **p = 0.0038**
- **Size of MTS in SN** **p = 0.012**
- **Size of TU** **p = 0.0298**
  
- **Multicentricity/Multifocality** **p = 0.07**
- **High level of Ki67** **p = 0.0916**



# NSN involvement for the variable Number of positive SN







# Multivariable logistic regression analysis

## Variables involved in the prediction model



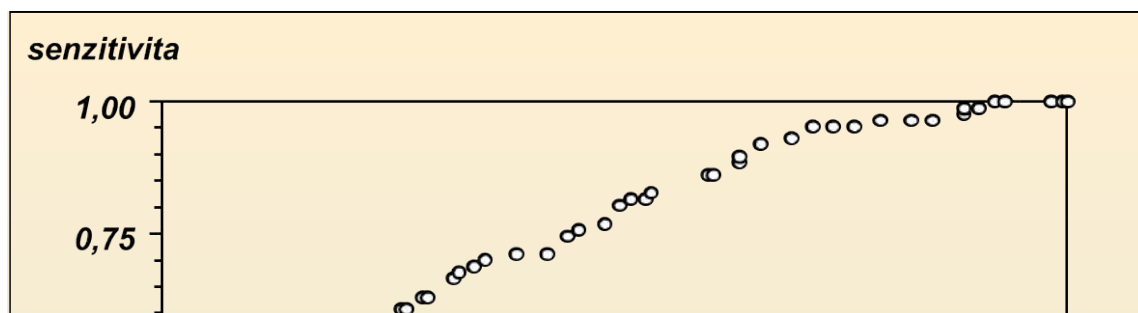
	OR	CI interval 95%		P
<b>Size of metastases in SN</b>	<b>2.88</b>	<b>1.02</b>	<b>8.13</b>	<b>0.0451</b>
Tumor size	1.53	0.86	2.72	0.1472
Perinodal infiltration	1.09	0.42	2.82	0.8585
Multicentricity/multifocality	1.51	0.70	3.28	0.2968
<b>Ratio positive-to-removed SN</b>	<b>7.82</b>	<b>2.61</b>	<b>23.40</b>	<b>0.0002</b>
<b>Lympho-vascular invasion</b>	<b>2.24</b>	<b>1.10</b>	<b>4.56</b>	<b>0.0265</b>
Invasive lobular carcinoma	1.91	0.84	4.33	0.1231
Positivity of PR	0.58	0.29	1.15	0.1186
High level of Ki67	1.46	0.77	2.79	0.2466





# ROC curve

(Receiver Operating Characteristic curve)



Other models	Original population AUC

**USELESS for decision of ALND after Z0011**

**But might be useful for indication of RNI?**

- **AUC** (area under ROC curve) = **74.16%** , 95% CI (67,9-80,5)

Cut threshold	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	% correct
0.6	25.29	95.4	73.33	71.86	72.03
0.3	71.26	58.05	45.93	80.16	62.45



# Applicability of Z0011 study criteria on our cohort



**Of 286 patients – 196 (68.5%) met Z0011 criteria**

**Of 186 with ALND 52 (27.5 %) had NSN involvement**



# Prospective randomised studies Z0011 and IBCSG 23-01



## ACOSOG Z0011

- 5/1999-12/2004
- T<5cm, BCS, cN0, SU 1-2 posit., WBI, NO: neo HT/CHT, extranodal extension
- SLNB - 436/ SLNB + ALND 420
- Follow-up 6.3 y.
- DFS SLNB – 83.9% / ALND – 82.2%
- OS SLNB – 92.5% / ALND – 91.8%
- Axillary recurrence  
SLNB 0.9% (4) / ALND 0.5% (2)

(Giuliano A et al., JAMA, 2011, 2017)

## IBCSG 23-01

- 4/2001 - 2/2010.
- T<5cm, BCS/ME, cN0, SU 1-2 N1mi, ITC, NO: makroMTS, extracapsular extension
- SLNB – 467 / SLNB + ALND 464
- Follow-up 5 r. (3.6-7.3)
- DFS SLNB – 87.8% / ALND – 84.4%
- OS SLNB – 97.5% / ALND – 97.6%
- Axillary recurrence <1%/1%

(Galimberti V et al., Lancet Oncol, 2013)



## ACOSOG Z011

- closed early
- **21% / 17%** lost to follow -up
- „Low risk“ patients
- only BCS + WBI
- disproportion in microMTS arms
- **97%** of patients had adjuvant therapy
- relatively short follow-up
- RT standardization
- **50%** high tangents, **18.9%** third field on axilla

(Kühn T., Poortmans P.M.P, Breast Care 2011)

(Gatzemeier W., Mann G.B., The Breast, 2013)

(Jagsi R., Chcdha M., Moni J. Et al, JCO, 2014)

## IBCSG 23-01

- closed early
- **93%** patients TU < 3cm
- **69%** MTS in SN < 1mm
- Relatively short follow-up

## MIRROR

- No adjuvant TH
- ↑5 r. AR pN0 **1.2** vs. pN1mi **6.2%**

(Boer et al., N Engl J Med, 2009)





Ann Surg. 2016 Sep;264(3):413-20. doi: 10.1097/SLA.0000000000001863.

## Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients With Sentinel Lymph Node Metastases: Long-term Follow-up From the American College of Surgeons Oncology Group (Alliance) ACOSOG Z0011 Randomized Trial.

Giuliano AE<sup>1</sup>, Ballman K, McCall L, Beitsch P, Whitworth PW, Blumencranz P, Leitch AM, Saha S, Morrow M, Hunt KK.

Giuliano et al.

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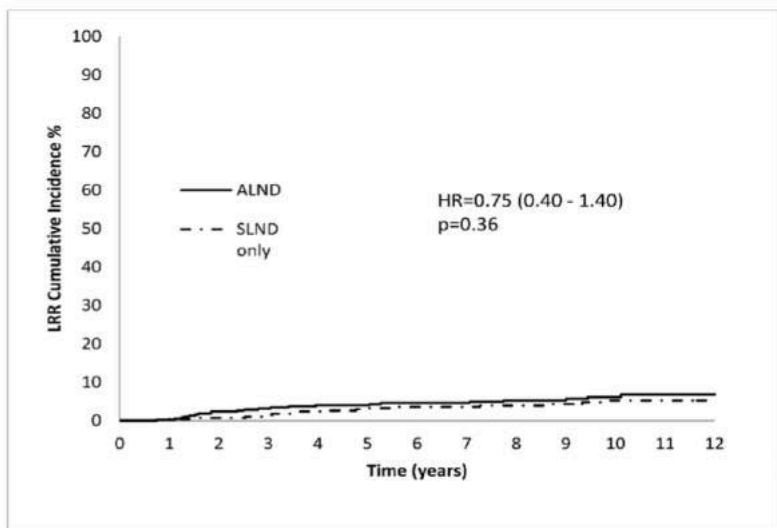
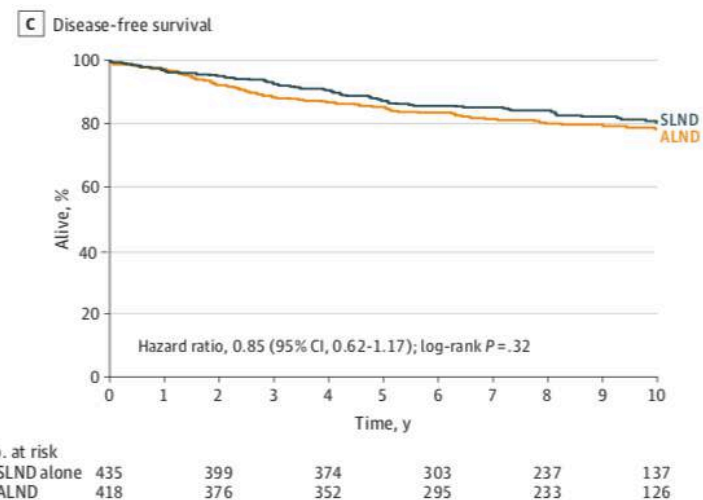


Figure 2. Cumulative Incidence of Locoregional Recurrence by Treatment Arm



No. at risk	0	1	2	3	4	5	6	7	8	9	10
SLND alone	435	399	374	303	237	137					
ALND	418	376	352	295	233	126					

statistically significant difference in local recurrence-free survival ( $P = 0.13$ ). The cumulative incidence of nodal recurrences at 10 years was 0.5% in the ALND arm and 1.5% in the SLND alone arm ( $P = 0.28$ ). Ten-year cumulative locoregional recurrence was 6.2% with ALND and 5.3% with SLND alone ( $P = 0.36$ ).



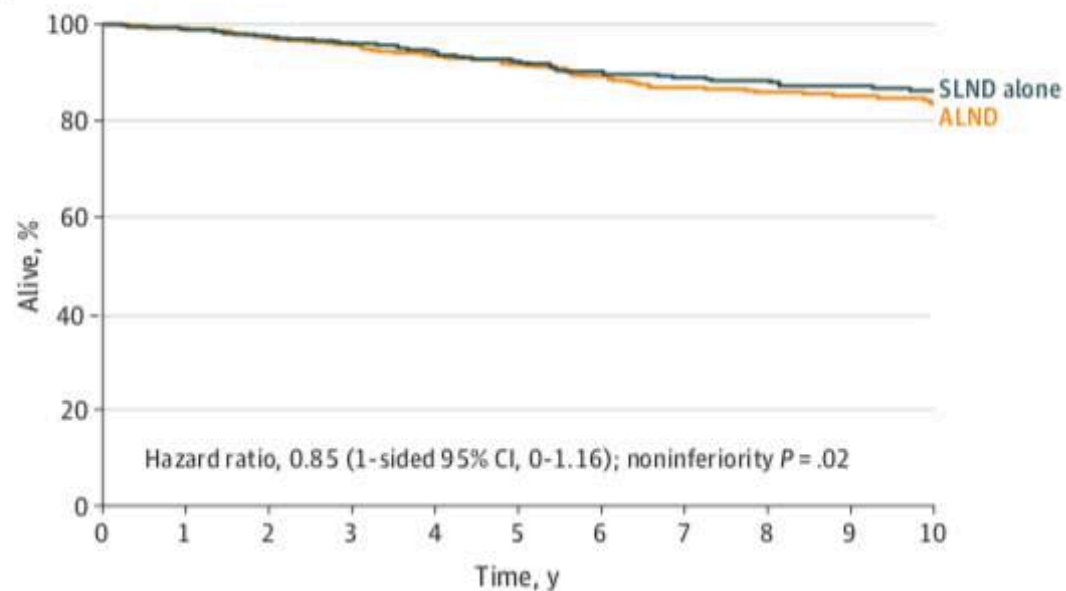


JAMA | Original Investigation

## Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis The ACOSOG Z0011 (Alliance) Randomized Clinical Trial

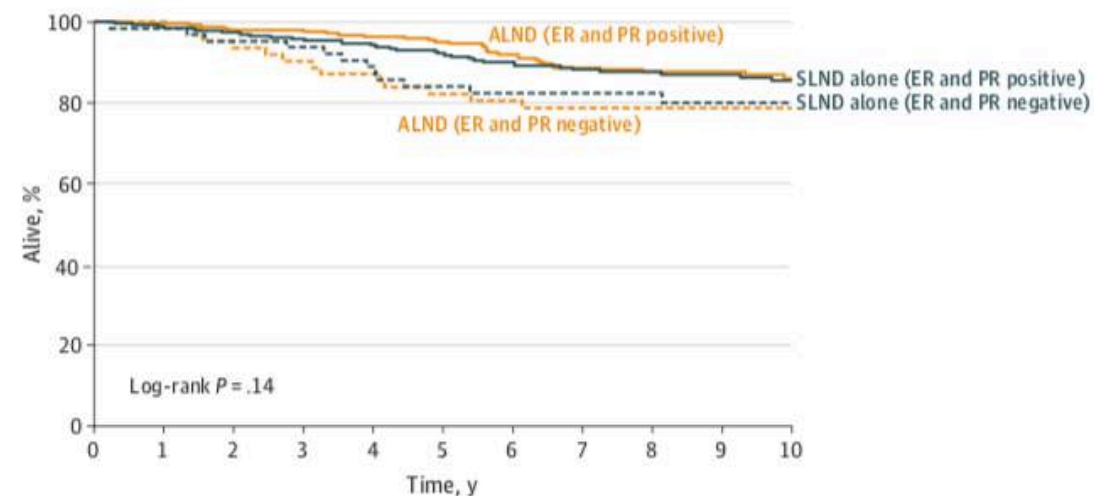
Armando E. Giuliano, MD; Karla V. Ballman, PhD; Linda McCall, MS; Peter D. Beitsch, MD; Meghan B. Brennan, RN, ONP, PhD; Pond R. Kelemen, MD; David W. Ollila, MD; Nora M. Hansen, MD; Pat W. Whitworth, MD; Peter W. Blumencranz, MD; A. Marilyn Leitch, MD; Sukamal Saha, MD; Kelly K. Hunt, MD; Monica Morrow, MD

**A** Overall survival



No. at risk	0	1	2	3	4	5	6	7	8	9	10
SLND alone	436	411	391	317	246	146					
ALND	420	398	381	317	248	134					

**B** Overall survival by estrogen receptor (ER) and progesterone receptor (PR) status



No. at risk	0	1	2	3	4	5	6	7	8	9	10
SLND alone											
ER and PR Negative	64	60	56	45	37	19					
ER and PR Positive	270	254	240	196	147	92					
ALND											
ER and PR Negative	63	58	54	45	31	19					
ER and PR Positive	256	243	238	201	163	85					



## POsitive Sentinel NOde: Adjuvant Therapy Alone Versus Adjuvant Therapy Plus Clearance or Axillary Radiotherapy

### PATIENT POPULATION

Women  $\geq 18$  years  
T1 or T2 unilateral breast cancer  
Pre-operative axillary ultrasound  
BCS/Mastectomy + 1-2 sentinel node macrometastases

### STRATIFICATION

Institution  
Age (<50,  $\geq 50$ )  
BCS/Mastectomy  
ER (positive, negative)  
Number of positive nodes (1, 2)  
OSNA (yes, no)

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ARM 1:  
Adjuvant therapy alone

ARM 2:  
Adjuvant therapy plus  
Axillary treatment (ALND or ART)

Accrual target 1900 patients  
Primary endpoint axillary recurrence (5 years)  
Estimated completion 2023

ALND: Axillary Lymph Node Dissection  
BCS: Breast Conserving Surgery  
ART: Axillary Radiotherapy  
SN: Sentinel Node

- All patients will receive adjuvant systemic therapy (chemotherapy and/or endocrine therapy) with or without HER2 targeted treatment.
- All patients may receive breast/chest wall RT.
- 5 years follow-up



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Editorial

POSNOC: A Randomised Trial Looking at Axillary Treatment in Women with One or Two Sentinel Nodes with Macrometastases

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Received 7 July 2015; accepted 17 July 2015





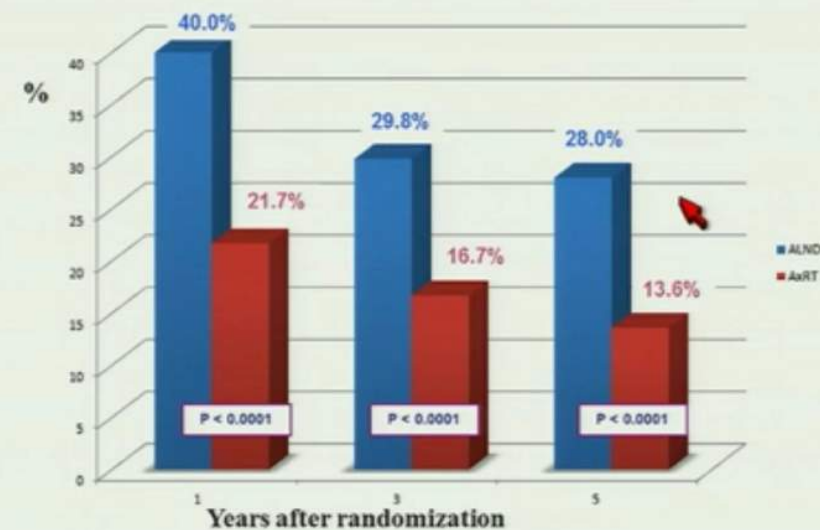


# AMAROS - After Mapping of the Axilla: Radiotherapy Or Surgery?



- EORTC, prospective, multicenter, 2001-2010
- T1-T2N0,
- pN1sn → random ALND/ART (50Gy v 25 fr., 5 weeks)
- 4806 p. : 744 – ALND/ 681 – ART
- **60% macrometastases**
- median follow- up 6.1 r.
  
- **5 r. AR: ALND 0.54% (4/744)**  
**ART 1.03% (7/681)**  
pN0sn 0.8% (25/3131)
  
- OS: EA 93.3% / ART 92.5% p=0.338
- DFS: EA 86.9% / ART 82.6% p= 0.178
- QOL – no difference

## Lymphedema: clinical observation and/or treatment



# Eight-year follow up result of the OTOASOR trial: The Optimal Treatment Of the Axilla – Surgery Or Radiotherapy after positive sentinel lymph node biopsy in early-stage breast cancer:

## A randomized, single centre, phase III, non-inferiority trial

Á. Sávolt<sup>a,\*</sup>, G. Péley<sup>b,†</sup>, C. Polgár<sup>c</sup>, N. Udvarhelyi<sup>d</sup>,  
G. Rubovszky<sup>d</sup>, E. Kovács<sup>e</sup>, B. Győrffy<sup>f</sup>, M. Kásler<sup>a</sup>, Z. Mátrai<sup>a</sup>

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Available online 16 January 2017

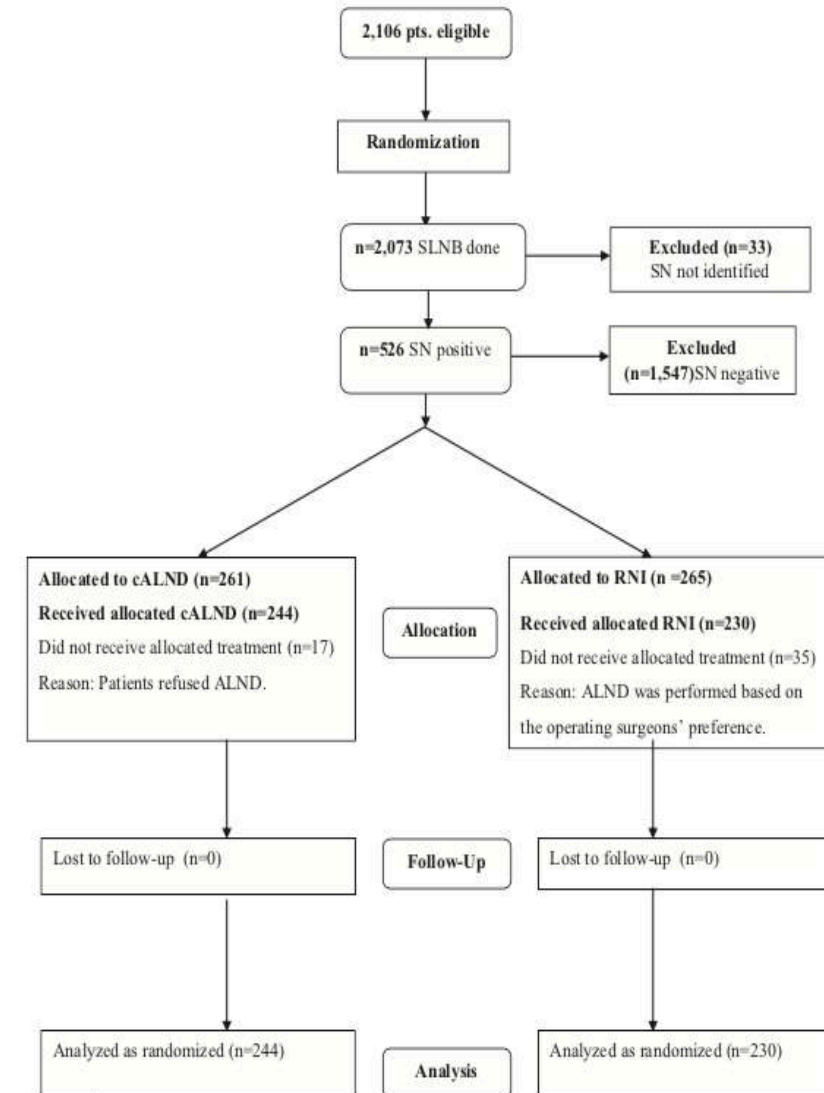


Figure 1. Patients flow chart of study protocol and number of enrolled cases SLNB – sentinel lymph node biopsy, cALND – completion axillary lymph node dissection, RNI – regional nodal irradiation.



- **St. Gallen 2013-17** – ALND is not recommended (ACOSOG Z0011)  
ALND if  $\geq 3$  involved SN, ME if no RT
  
- **NCCN 2019** – ALND is not recommended (ACOSOG Z0011)
  
- **ASCO 2014** – ALND is not recommended (ACOSOG Z0011)
  
  
  
  
  
  
  
  
  
  
- **NICE Guideline 2018** – offer ALND or RT to patients with  $\geq 1$  MacroMTS in SN,  
discuss risks / benefits of no ALND (ACOSOG Z0011)
  
  
- **ESMO 2015** – may not need ALND (IBCSG 23-01, Z0011)  
□ results need to be confirmed and cannot be extended



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Version 2018.1

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FORSCHEN  
LEHREN  
HEILEN

# Axillary Lymph Node Dissection I



□ St. G

□ NCCN

□ ASCO

□ NICE  
2018

□ ESMO

## ■ Axillary lymph node dissection

- To improve survival
- For Staging
- For local control

## ■ Axillary lymph node dissection

- N+\*\* (pre-surgery) without neoadjuvant systemic therapy
- DCIS
- SN + ( cT1/2 cN\*0; < 3 SN +, BCS + tangential radiation field, no subsequent axillary radiation, adequate systemic therapy)
- SN + (mic)
- SN (i+)
- SN + and mastectomy (no radiotherapy of the chestwall)
- SN + and mastectomy (radiotherapy of the chestwall)
  - Only if T1, T2 and 1-2 pos. SLN

## ■ Axillary lymph node dissection indicated, but not feasible

- Irradiation according to AMAROS-trial

\* Study participation recommended \*\* histologically proven

	Oxford LoE	GR	AGO
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3 D -

3 A -

2a A +/-

2a B +

2b B -

1b B +/-

1b A --

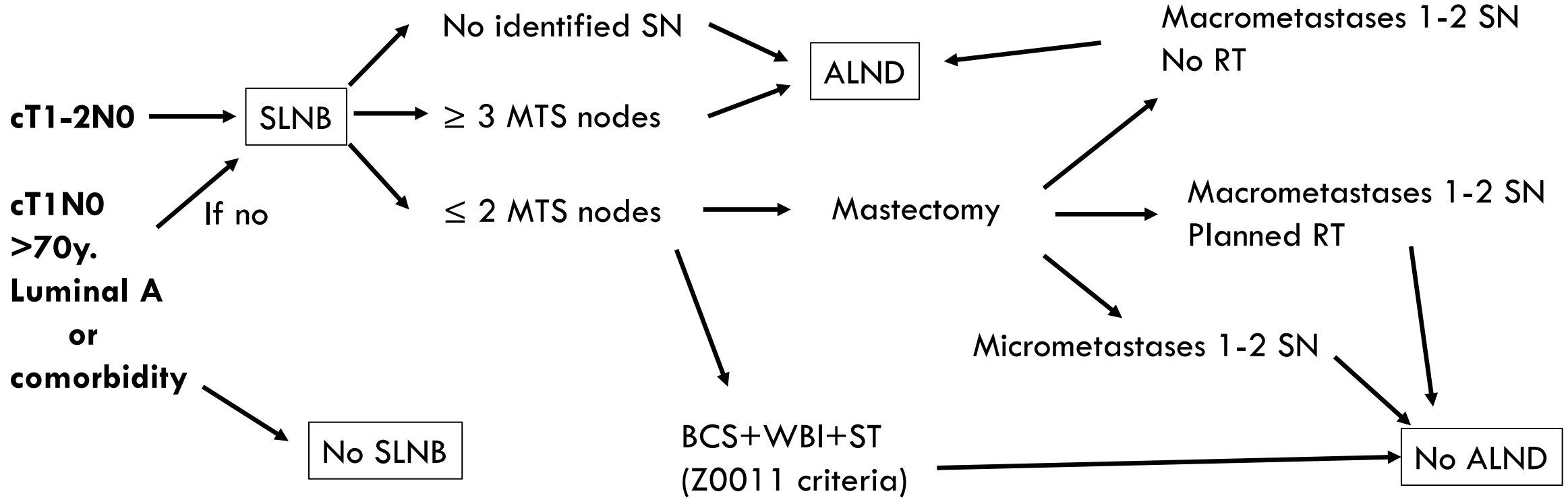
2b B --

1b B +

5 D +/-

1b B +





Since 2014 – first “low risk” patients, ER+, PR+

Since 2018 – ER-, PR- patients

Since 2015 – selective approach to low risk patients with cT1, >70 y., Luminal A,





# Still current questions



- **Do we need SLNB in low risk patients?**
- **Treatment of axilla (AxRT/ALND) or nothing?**
- **What to do in patients with mastectomy?**
- **What to do with 3 positive sentinel nodes?**



## Viewpoints and debate

# Abandoning sentinel lymph node biopsy in early breast cancer? A new trial in progress at the European Institute of Oncology of Milan (SOUND: Sentinel node vs Observation after axillary UltraSouND)

Oreste Gentilini\*, Umberto Veronesi

*Division of Breast Surgery, European Institute of Oncology, Milano, Italy*

### Exclusion Criteria:

- synchronous distant metastases
- previous malignancy
- bilateral breast cancer
- multicentric or multifocal breast cancer
- previous primary systemic therapy
- pregnancy or breastfeeding
- pre-operative diagnosis (cytology or histology) of axillary lymph node metastases
- pre-operative radiological evidence of multiple involved or suspicious nodes
- patients with psychiatric, addictive, or any disorder, which compromises ability to give informed consent for participation in this study.

## Trial SOUND

Sentinel node vs Observation after axillary Ultra-souND

- Patients with breast cancer  $\leq 2.0$  cm
  - Any age
- Candidates to Breast Conserving Surgery
- Negative preoperative axillary assessment (negative ultra-sound of the axilla or negative FNAC of a single doubtful axillary lymph node)



**Randomization**



SNB policy

No axillary surgery





# St. Gallen/Vienna 2019: A Brief Summary of the Consensus Discussion on the Optimal Primary Breast Cancer Treatment



Marija Balic<sup>a</sup> Christoph Thomssen<sup>b</sup> Rachel Würstlein<sup>c</sup> Michael Gnant<sup>d</sup>  
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Forgoing SLNB in low risk patients (T1, luminal A, >70 years) or comorbidity  
- YES 56%, NO 40% (USG is mandatory 80%)

Application of the Z0011 criteria in clinical practise

- 29% - AxRT in all cases
- 25% - AxRT in aggressive histology (TNBC),
- 42% no AxRT

Mastectomy - omit ALND 1-2 positive nodes

- TNBC, RNI planned – YES 71% NO 23%
- ER+ HER2+, RNI planned – YES 83%
- AxRT in accordance with AMAROS - YES 48%, 8% depends on tumor biology  
- 17% insisted on following ALND
- Absence of RNI – ALND must be done YES 66%





**SERC (2014)** – no ALND or ALND in patients with cN0 and  $\geq 1$  MTS in SN (**no limit on involved nodes**)

**SENOMAC (2015)** – no ALND or ALND in patients with cN0 and  $\geq 2$  MTS SU (**+ cT3, Mastectomy**)

**INSEMA (2015)** – patients  $\leq$  cT2N0 - **SLNB or no-SLNB**

**if  $\leq 3$  MTS SU** - randomization on ALND or no-ALND

**BOOG 2013-07 (2015)** – no axillary therapy or ALND or RT in patients with  $\leq 3$  macro MTS SN

(patients after mastectomy and SLNB)

- terminated due slow accrual rate

# Restricted Axillary Staging in Clinically and Sonographically Node-Negative Early Invasive Breast Cancer (c/iT1–2) in the Context of Breast Conserving Therapy: First Results Following Commencement of the Intergroup-Sentinel-Mamma (INSEMA) Trial

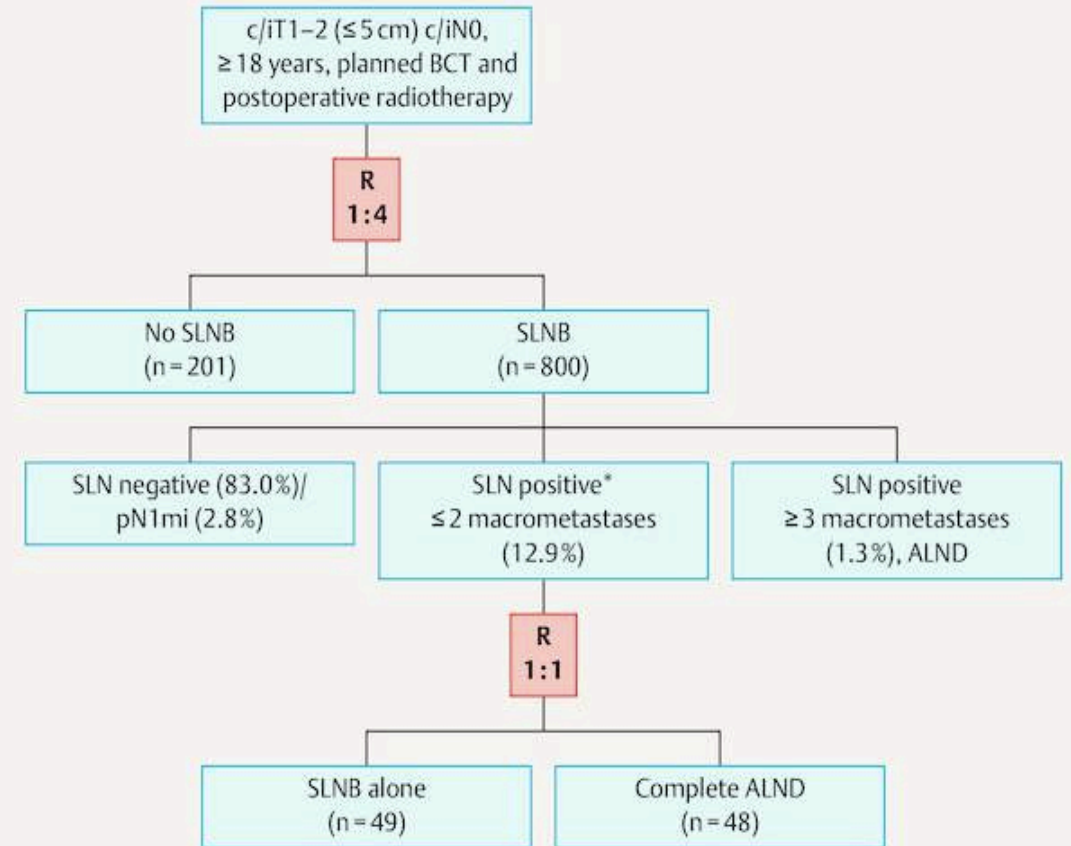
T. Reimer<sup>1</sup>, A. Stachs<sup>1</sup>, V. Nekljudova<sup>2</sup>, S. Loibl<sup>2</sup>, S. Hartmann<sup>1</sup>,  
K. Wolter<sup>3</sup>, G. Hildebrandt<sup>3</sup>, B. Gerber<sup>1</sup>

## Essential inclusion criteria for the INSEMA trial (recent changes according to protocol amendment #4 from 15.09.2016 in bold type):

- Histologically confirmed unilateral invasive breast carcinoma (punch biopsy, Mammotome biopsy or **open biopsy** possible)
- **Age ≥ 18 years**
- Tumour size clinically and radiologically ≤ 5 cm (iT1/iT2) independent of hormone receptor and HER2 status
- Clinically and sonographically tumour-free axillary lymph nodes before biopsy (c/iN0); if cN0/iN+ negative core biopsy or fine needle aspiration of suspicious lymph node required
- No suspicion of distant metastases
- Planned BCT with postoperative whole-breast irradiation and adequate systemic therapy

## Essential exclusion criteria for the INSEMA trial:

- History of carcinoma in the previous 5 years
- Invasive breast cancer treated with neoadjuvant therapy
- c/iT3-T4 tumours
- Planned mastectomy
- Planned exclusive intraoperative partial breast irradiation (e.g. INTRABEAM) or exclusive postoperative partial breast irradiation (e.g. multi-catheter technique); both methods allowed as boost
- Pregnancy and breastfeeding
- Male breast cancer



\* According to protocol amendment #4 changed to ≤ 3 macrometastases. Direct inclusion of patients in the randomization is then possible for all trial centres.

| Fig. 1 Flow chart of the INSEMA trial showing the distribution after recruitment of 1001 patients. |



# Conclusion

- Most of our patients didn't profit from ALND (67% had negative NSN)
- 68.5 % met Z0011 criteria – 27.5% had NSN involvement
- ALND no better LRR, DFS and OS in selected group of patients
- Since 2014 – selective approach to patients with pN1
  
- More results awaited from POSNOC, SERC, SENOMAC, INSEMA, SOUND
- Continue of reduction of axillary surgery is expected
  
- Low-risk patients            spared of ALND and RNI (only WBI)
- High-risk patients         Discuss RNI
  
- **Discuss patients on MDT before and after surgery**

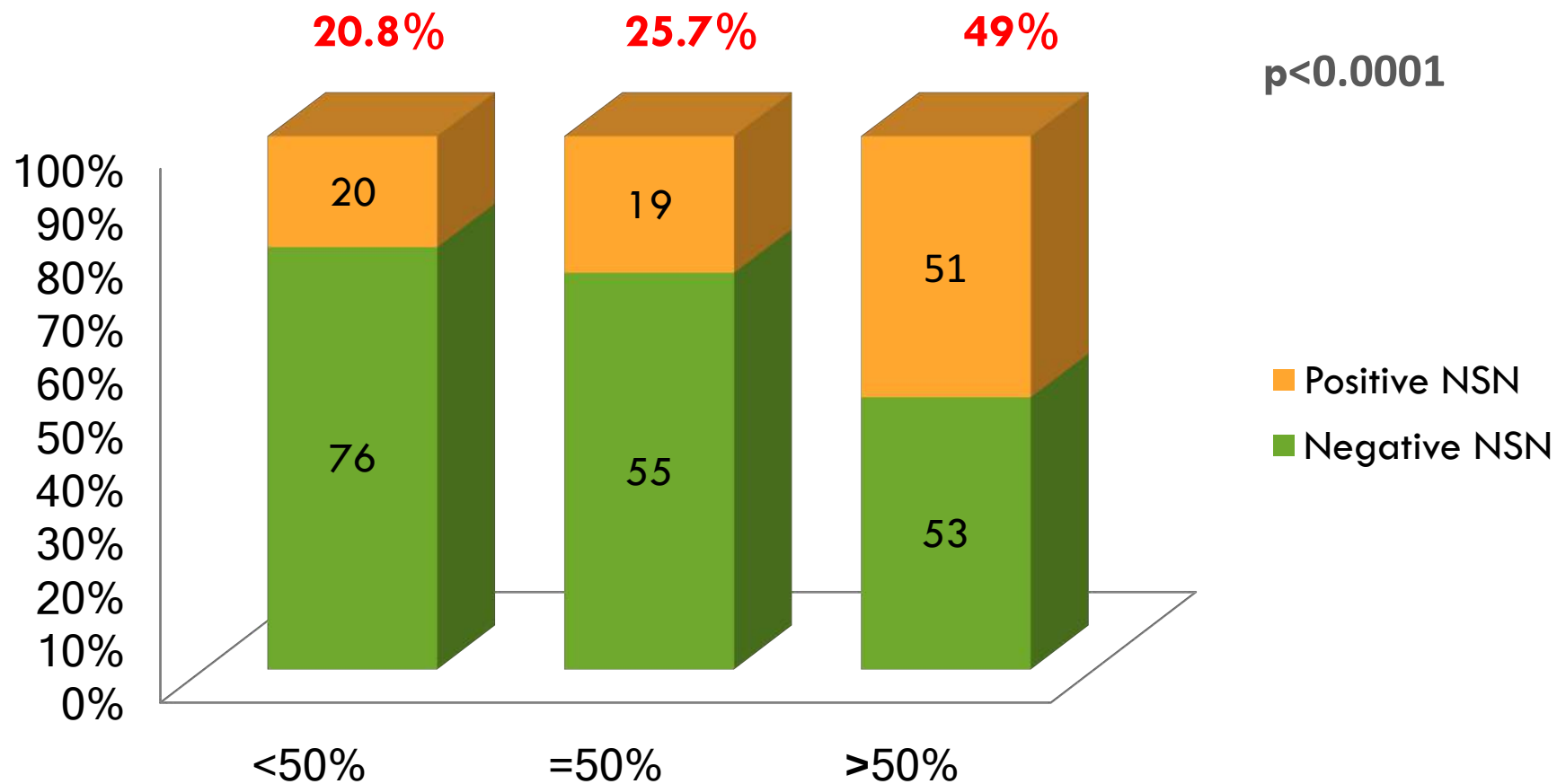


# Thank you for attention!





# NSN involvement for the variable Ratio of positive-to-removed SN





# Conclusion

**NSN involvement was found in approximately 33% of our patients with early BC**

**Significant predictors in the logistic regression model:**

- ▣ Ratio of positive-to-removed SN
- ▣ Size of MTS (Macrometastases) in SN
- ▣ Lympho-vascular invasion

**More than XY% of patients met criteria of Z0011**

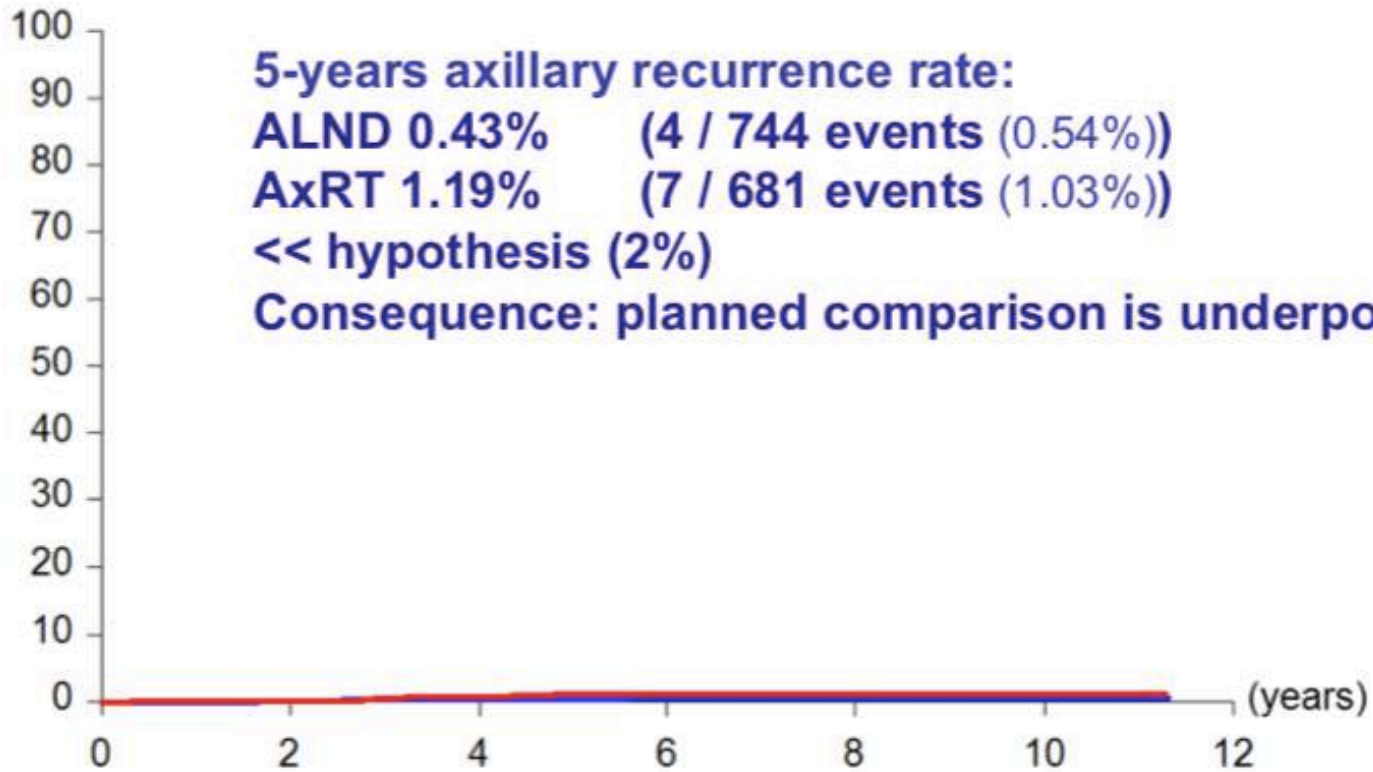
**Since 2014 we changed internal guideline according to Z0011 criteria**

**Patient registry**

**Patients with higher risk of extensive nodal involvement are indicated to ALND**



# Axillary recurrence rate



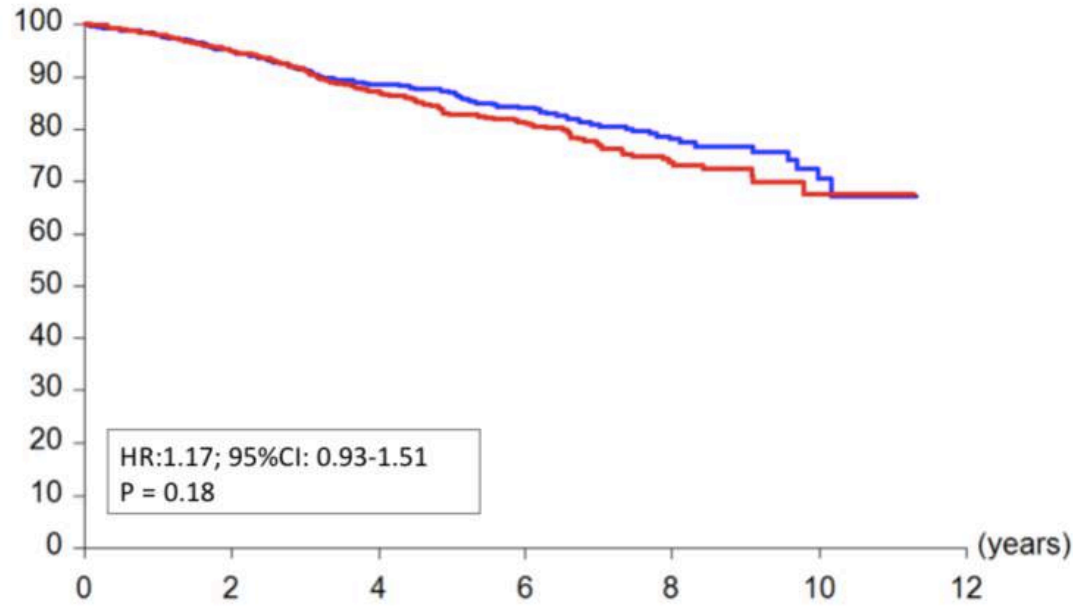
O	N	Number of patients at risk :					
4	744	707	550	349	156	38	— ALND
7	681	659	503	314	151	29	— AxRT



# AMAROS - After Mapping of the Axilla: Radiotherapy Or Surgery?

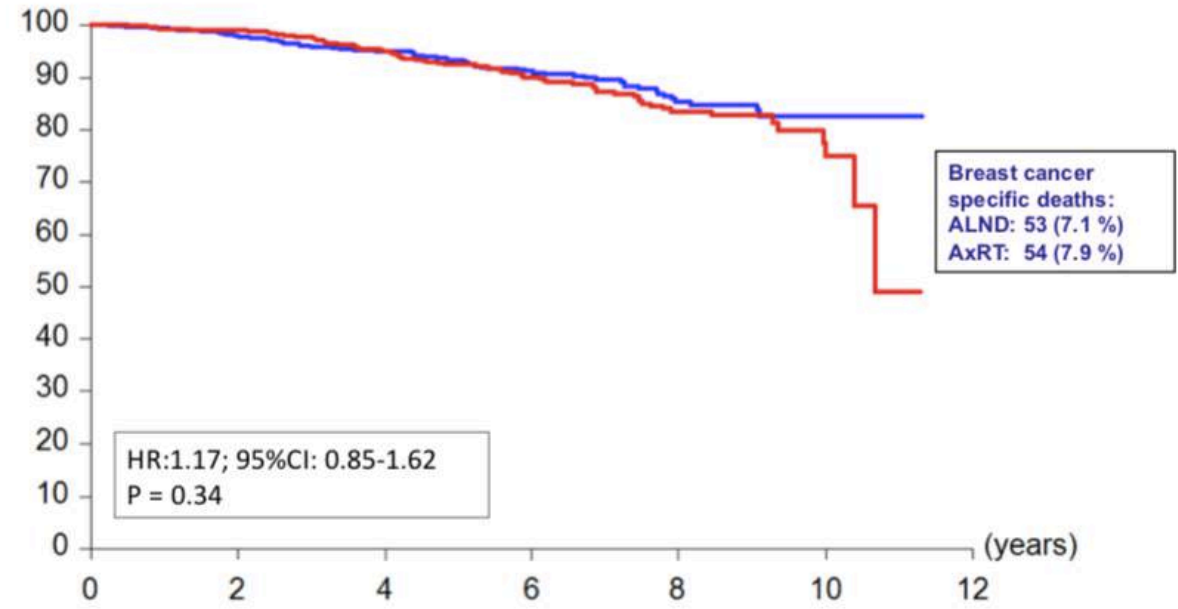


## Disease-free survival



O	N	Number of patients at risk :					
124	744	686	511	322	140	33	— ALND
134	681	633	468	284	131	24	— AxRT

## Overall survival



O	N	Number of patients at risk :					
71	744	708	552	352	157	38	— ALND
76	681	661	505	316	151	29	— AxRT

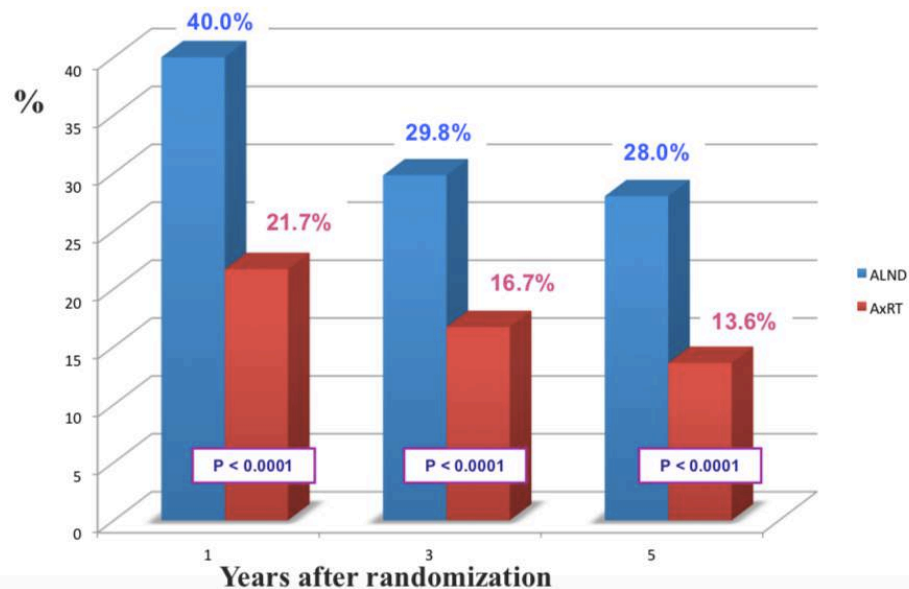




# AMAROS - After Mapping of the Axilla: Radiotherapy Or Surgery - Lymfedém



## Lymphedema: clinical observation and/or treatment



	Axillary lymph node dissection	Axillary radiotherapy	p value
<b>Clinical sign of lymphoedema in the ipsilateral arm</b>			
Baseline	3/655 (<1%)	0/586 (0%)	0.25
1 year	114/410 (28%)	62/410 (15%)	<0.0001
3 years	84/373 (23%)	47/341 (14%)	0.003
5 years	76/328 (23%)	31/286 (11%)	<0.0001
<b>Arm circumference increase &gt;10% of the ipsilateral upper or lower arm, or both</b>			
Baseline	33/655 (5%)	24/586 (4%)	0.497
1 year	32/410 (8%)	24/410 (6%)	0.332
3 years	38/373 (10%)	22/341 (6%)	0.080
5 years	43/328 (13%)	16/286 (5%)	0.0009

Data are n/N (%), unless otherwise specified.



**We don't need to predict NSN involvement any more**

**We need to predict who will reccure**



# Pooled long-term outcomes from two randomized trials of axillary node sampling with axillary radiotherapy *versus* axillary node clearance in patients with operable node-positive breast cancer



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**Background:** The aim was to determine long-term overall, breast cancer-specific and metastasis-free survival as well as axillary relapse rate from a pooled analysis of two randomized trials in women with operable breast cancer. These trials compared axillary node sampling (ANS), combined with axillary radiotherapy (AXRT) if the sampled nodes were involved, with axillary node clearance (ANC).

**Methods:** Data from two clinical trials at the Edinburgh Breast Unit that randomized patients between 1980 and 1995 were pooled. Long-term survival was analysed using Kaplan–Meier curves and Cox regression, with separate analyses for patients with node-positive (ANS + AXRT *versus* ANC) and node-negative (ANS *versus* ANC) disease.

**Results:** Of 855 women randomized, 799 were included in the present analysis after a median follow-up of 19.4 years. Some 301 patients (37.7 per cent) had node-positive disease. There was no evidence of a breast cancer survival advantage for ANS *versus* ANC in patients with node-negative disease (hazard ratio (HR) 0.88, 95 per cent c.i. 0.58 to 1.34;  $P = 0.557$ ), or for ANS + AXRT *versus* ANC in those with node-positive breast cancer (HR 1.07, 0.77 to 1.50;  $P = 0.688$ ). There was no metastasis-free survival advantage for ANS *versus* ANC in patients with node-negative tumours (HR 1.03, 0.70 to 1.51;  $P = 0.877$ ), or ANS + AXRT *versus* ANC in those with node-positive disease (HR 1.03, 0.75 to 1.43;  $P = 0.847$ ). Node-negative patients who underwent ANS had a higher risk of axillary recurrence than those who had ANC (HR 3.53, 1.29 to 9.63;  $P = 0.014$ ). Similarly, among women with node-positive tumours, the risk of axillary recurrence was greater after ANS + AXRT than ANC (HR 2.64, 1.00 to 6.95;  $P = 0.049$ ).

**Conclusion:** Despite a higher rate of axillary recurrence with ANS combined with radiotherapy to the axilla, ANC did not improve overall, breast cancer-specific or metastasis-free survival. Axillary recurrence is thus not a satisfactory endpoint when comparing axillary treatments.



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## Surgeon Attitudes Toward the Omission of Axillary Dissection in Early Breast Cancer.

Morrow M<sup>1</sup>, Jagsi R<sup>2</sup>, McLeod MC<sup>3</sup>, Shumway D<sup>2</sup>, Katz SJ<sup>4</sup>.

### ⊕ Author information

#### Abstract

**IMPORTANCE:** The American College of Surgeons Oncology Group (ACOSOG) Z0011 study demonstrated the safety of sentinel node biopsy alone in clinically node-negative women with metastases in 1 or 2 sentinel nodes treated with breast conservation. Little is known about surgeon perspectives regarding when axillary lymph node dissection (ALND) can be omitted.

**OBJECTIVES:** To determine surgeon acceptance of ACOSOG Z0011 findings, identify characteristics associated with acceptance of ACOSOG Z0011 results, and examine the association between acceptance of the Society of Surgical Oncology and American Society for Radiation Oncology negative margin of no ink on tumor and surgeon preference for ALND.

**DESIGN, SETTING, AND PARTICIPANTS:** A survey was sent to 488 surgeons treating a population-based sample of women with early-stage breast cancer (N = 5080). The study was conducted from July 1, 2013, to August 31, 2015.

**MAIN OUTCOMES AND MEASURES:** Surgeons were categorized as having low, intermediate, or high propensity for ALND according to the outer quartiles of ALND scale distribution. A multivariable linear regression model was used to confirm independent associations.

**RESULTS:** Of the 488 surgeons invited to participate, 376 (77.0%) responded and 359 provided complete information regarding propensity for ALND derived from 5 clinical scenarios. Mean surgeon age was 53.7 (range, 31-80) years; 277 (73.7%) were male; 142 (37.8%) treated 20 or fewer breast cancers annually and 108 (28.7%) treated more than 50. One hundred seventy-five (49.0%) recommended ALND for 1 macrometastasis. Of low-propensity surgeons who recommended ALND, only 1 (1.1%) approved ALND for any nodal metastases compared with 69 (38.6%) and 85 (95.5%) of selective and high-propensity surgeons ( $P < .001$ ), respectively. In multivariable analysis, lower ALND propensity was significantly associated with higher breast cancer volume (21-50: -0.19; 95% CI, -0.39 to 0.02; >51: -0.48; 95% CI, -0.71 to -0.24;  $P < .001$ ), recommendation of a minimal margin width (1-5 mm: -0.10; 95% CI, -0.43 to 0.22; no ink on tumor: -0.53; 95% CI, -0.82 to -0.24;  $P < .001$ ), participation in a multidisciplinary tumor board (1%-9%: -0.25; 95% CI, -0.55 to 0.05; >9%: -0.37; 95% CI, -0.63 to -0.11;  $P = .02$ ), and Los Angeles Surveillance, Epidemiology, and End Results site (-0.18; 95% CI, -0.35 to -0.01;  $P = .04$ ).

**CONCLUSIONS AND RELEVANCE:** This study shows substantial variation in surgeon acceptance of more limited surgery for breast cancer, which is associated with higher breast cancer volume and multidisciplinary interactions, suggesting the potential for overtreatment of many patients and the need for education targeting lower-volume breast surgeons.



# Introduction



- Non-SN involvement in **less than 40%** patients with positive SN  
(24-67.5%, median 38%)  
*(a meta-analysis of 56 studies, Van la Parra R. et al., EJSO, 2011)*
- Why to treat healthy nodes in the rest 60%?
- A large number of studies on potential predictive factors specific to the outcome.

# Predictive factors of NSN involvement

## Meta-analysis 56 studies:

- ▣ Detection of mts in H&E
- ▣ **Size of MTS in SN >2 mm**
- ▣ Extranodal invasion
- ▣ >1 positive SN
- ▣ ≤ 1 negative SN
- ▣ **Ratio of positive SN >50%**
- ▣ Size of tumor > 2 cm
- ▣ **Lympho-vascular invasion of TU**

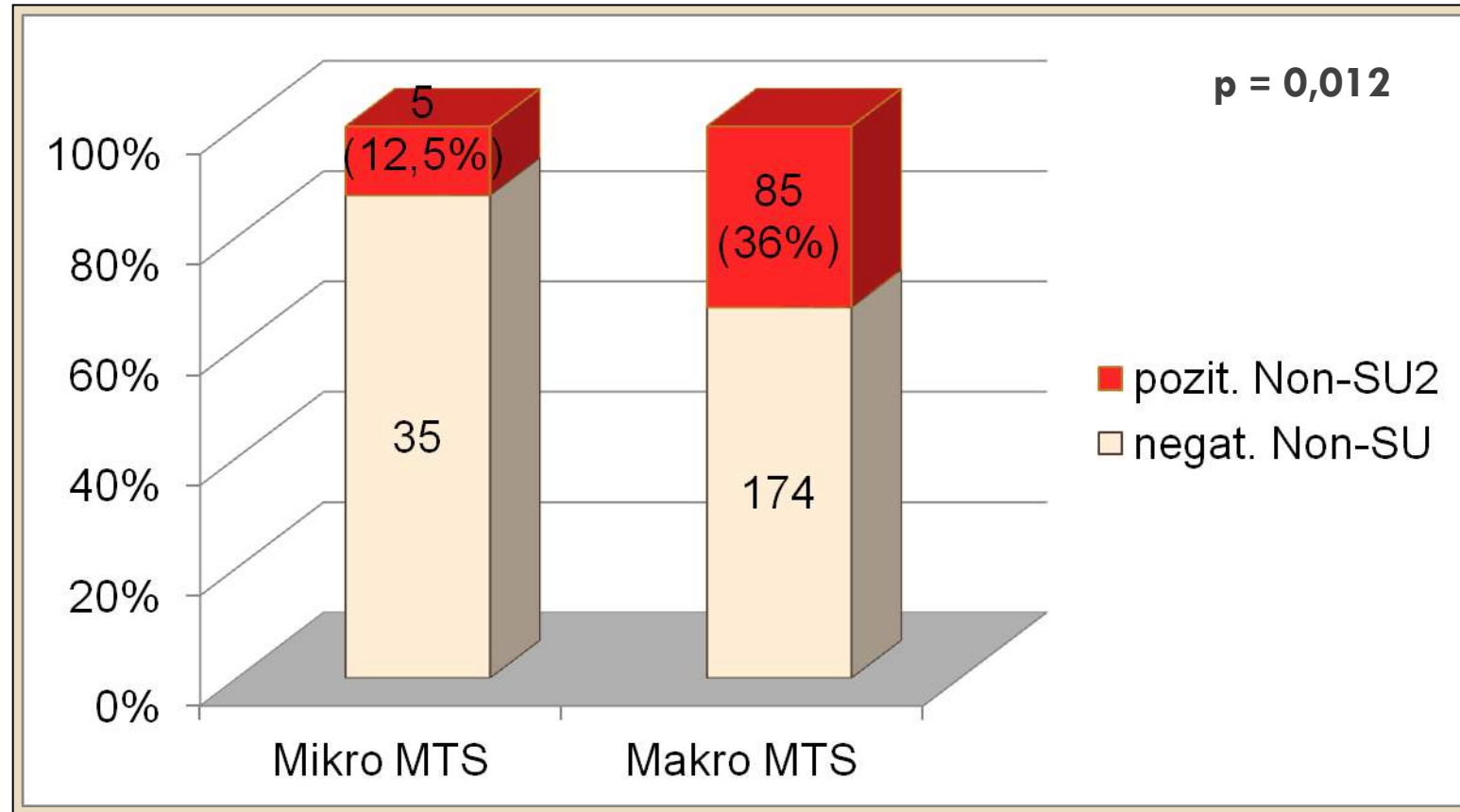
Absolute risks on positive NSNs and 95% CI for all predictors.

		Positive NSN			
		Pooled proportion	95% CI	Pooled OR	95% CI
Method of detection	IHC-only	0.11	0.06–0.16	4.37	2.78–6.86
	Other	0.40	0.36–0.44		
Size of metastasis	≤2 mm	0.17	0.15–0.20	4.22	3.51–5.07
	>2 mm	0.51	0.47–0.55		
ECE	No	0.30	0.26–0.33	4.10	3.16–5.34
	Yes	0.64	0.56–0.72		
No negative SNs	>1	0.24	0.18–0.30	2.66	2.05–3.46
	≤1	0.48	0.44–0.53		
No positive SNs	1	0.33	0.30–0.36	2.60	2.03–3.34
	>1	0.56	0.47–0.66		
Tumour size	≤2 cm	0.30	0.28–0.33	2.41	2.00–2.91
	>2 cm	0.52	0.46–0.57		
Ratio positive SNs	≤50%	0.24	0.19–0.29	2.25	1.63–3.10
	>50%	0.44	0.34–0.54		
LVI	Absent	0.31	0.27–0.35	2.24	1.93–2.59
	Present	0.52	0.48–0.56		
Nuclear grade	≤2	0.41	0.35–0.46	1.51	1.27–1.81
	>2	0.47	0.43–0.50		
Multifocality	Absent	0.37	0.33–0.40	1.40	1.23–1.60
	Present	0.46	0.40–0.52		
No SNs removed	>1	0.37	0.34–0.40	1.34	1.07–1.68
	1	0.44	0.38–0.49		





# Size of metastases in SNs





## Univariate analysis of predictive factors of NSN involvement

	No additional MTS in NSN N=184	Additional MTS in NSN N=90	All patients N=274	P
<b>Frozen section positivity</b>				<b>0,0019</b>
Yes	148	85	233	
No	36	5	41	
<b>Multiplicity of tumor</b>				<b>0,07</b>
Multiplicity	22	19	41	
Unicentricity	162	71	233	
<b>Size of tumor, mm</b>				<b>0,0298</b>
Median	20	22	20	
min-(Q1-Q3)-max	3-(13-24)-130	5-(15-28)-90	3-(14-25)-130	
<b>Ki 67 (≥20%)</b>				<b>0,0916</b>
High value	91	55	146	
Low value	93	35	128	
<b>LVI of primary TU</b>				<b>0,0038</b>
Yes	110	71	181	
No	64	16	80	
Unknown	10	3	13	
<b>Number of involved SN</b>				<b>&lt;0,0001</b>
<b>Ratio of positive-to-removed SN</b>				<b>&lt;0,0001</b>
< 50%	76	20	96	
= 50%	55	19	74	
> 50%	53	51	104	
<b>Size of MTS in SN</b>				<b>0,012</b>



# ACOSOG Z011 a IBCSG 23-01

## ACOSOG Z011

- ukončená predčasne
- **117** centier, **5** rokov
- **166/856** „stratených“ pacientok (**21%** ALND, **17%** SLNB)
- prevažne pacientky s nízkym rizikom
- len BCS + ožiarenie celého prsníka
- **45%** pac. v skupine SNB malo mikro mts vs **37,5%**
- **97%** s adj. syst. terap.
- relatívne krátky follow-up
- informácie o rozsahu ožarovania?

(Kühn T., Poortmans P.M.P, Breast Care 2011)

(Gatzemeier W., Mann G.B., The Breast, 2013)

## IBCSG 23-01

- ukončená predčasne
- **93%** pacietov TU < 3cm
- **69%** MTS v LU < 1mm
- väčšina pacietov z Milána
- relatívne krátky follow-up



# Pozitívna SU – je disekcia vždy nevyhnutná?

	ACOSOG Z011	IBCSG 23-01
	5/1999 - 12/2004	4/2001 - 2/2010.
Pacienti zaradení do štúdie	T<5cm, BCS, cN0, SU 1-2 pozit., WBI, nie:extranod. propagácia, neoadjuv. HT/CHT,	T<5cm, BCS/ME, cN0, SU 1-2 N1mi, ITC, Nie: makroMTS, extranod. propagácia
Výsledný súbor SNB/EA	436/420	467/464
Median age	56/54(24-92)	54 (26-81)
BCS/ME	100%/0	90%/10%
Hormonálny status	ER 83%, PR 68%	ER 90%, PR 75%
Veľkosť TU	<2 cm (69%) <5cm (30%)	<2cm (69%) ≥3cm (7%)
Veľkosť MTS v SU	SLNB <2mm (44,9%) ALND <2 mm (37,5%)	<1mm(69%) 1.1-2mm (29%)
Median Follow-up	6,3 r. (5,2-7,7)	5 r. (3,6-7,3)
Adj. RAT	WBI	97% po BCS
Adj. HT	46%	65%
Adj. CHT	58%	8%
Adj. HT + CHT		23%
MTS v non-SU	27,3%	13%
SNB DFS/OS	83,9/92,5%	87,8%/97,5%
ALND DFS/OS	82,2/91,8%	84,4%/97,6%
Rekurencia v axile	ALND 0,5% (2)/ SLNB 0,9% (4)	<1%/1%

