



Quando lo svuotamento ascellare in presenza di LS positivo?

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Randomized clinical trials

Sentinel Node Biopsy Vs Axillary Dissection

	Study	No. pts	Primary endpoint
VERONESI	IEO 0185/000	516	DFS, OS
KRAG	NSABP B-32	5611	DFS, OS
MANSEL	ALMANAC	1031	Morbidity
GILL	SNAC	1088	Morbidity

	VERONESI (TRIAL 0185/000)		KRAG (NSABP B-32)	
	AD	SNB	AD	SNB
False Negative	8.8 %		9.8 %	
OS	96.4%	98.4 %	90.3%	91.8%
DFS	88.9%	92.2%	81.5%	82.4%

The SN approach in breast cancer

- Identifies true pN0 patients
- Permits avoidance of complete axillary dissection in pN0 patients
- Allows planning of adjuvant therapy with minimal morbidity
- A low-morbidity technique - reduces complications associated with complete axillary dissection

Historical contraindications and controversial indications to SNB

- SNB after breast surgery?
- SNB after previous aesthetic surgery?
- SNB after previous SNB?
- SNB after chemotherapy?
- SNB in multicentric disease?
- SNB during pregnancy?
- SNB in male breast cancer?

American Society of Clinical Oncology Guideline Recommendations for Sentinel Lymph Node Biopsy in Early-Stage Breast Cancer

Gary H. Lyman, Armando E. Giuliano, Mark R. Somerfield, Al B. Benson III, Diane C. Bodurka, Harold J. Burstein, Alistair J. Cochran, Hiram S. Cody III, Stephen B. Edge, Sharon Galper, James A. Hayman, Theodore Y. Kim, Cheryl L. Perkins, Donald A. Podoloff, Visa Haran Sivasubramaniam, Roderick R. Turner, Richard Wahl, Donald L. Weaver, Antonio C. Wolff, and Eric P. Winer

Extended indications to SNB

- SNB after breast surgery Yes
- SNB after previous SNB Yes
- SNB after chemotherapy Yes
- SNB in multicentric disease Yes
- SNB during pregnancy Yes
- SNB in male breast cancer Yes

Sentinel Node Biopsy...

“works well in a wide range of settings, is sufficiently robust to withstand variations in technique, increases staging accuracy by allowing enhanced pathologic analysis, has less morbidity than complete axillary lymph node dissection, and gives local control comparable of that of axillary dissection”

Cody HS. Sentinel node biopsy for breast cancer: does anybody not need one? Ann Surg Oncol 2003

Sentinel Node Biopsy...

Safely replaces the routine application of AD, and SNB spares nearly two-thirds of clinically node-negative breast cancer patients from unnecessary AD

Articles

Sentinel-lymph-node biopsy as a staging procedure in breast cancer: update of a randomised controlled study ➔

Umberto Veronesi, Giovanni Paganelli, Giuseppe Viale, Alberto Luini, Stefano Zurrida, Viviana Galimberti, Mattia Intra, Paolo Veronesi, Patrick Maisonneuve, Giovanna Gatti, Giovanni Mazzarol, Concetta De Cicco, Gianfranco Manfredi, Julia Rodríguez Fernández

Summary

Background In women with breast cancer, sentinel-lymph-node biopsy (SLNB) provides information that allows surgeons to avoid axillary-lymph-node dissection (ALND) if the SLN does not have metastasis, and has a favourable effect on quality of life. Results of our previous trial showed that SLNB accurately screens the ALN for metastasis in breast cancers of diameter 2 mm or less. We aimed to update this trial with results from longer follow-up.

Lancet Oncol 2006; 7: 983-90

Published Online
November 17, 2006
DOI:10.1016/S1470-2045(06)70947-0

POSITIVE SENTINEL NODE.....



No axillary dissection?

What do prospective
randomized trials tell
us?

Axillary dissection versus no axillary dissection in patients with sentinel node micrometastases (IBCSG 23-01): a phase 3 randomised controlled trial

Viviana Galimberti, Bernard F Cole, Stefano Zurrada, Giuseppe Viale, Alberto Luini, Paolo Veronesi, Paola Baratella, Camelia Chifu, Manuela Sargenti, Mattia Intra, Oreste Gentilini, Mauro G Mastropasqua, Giovanni Mazzarol, Samuele Massarut, Jean-Rémi Garbay, Janez Zgajnar, Hanne Galatius, Angelo Recalcati, David Littlejohn, Monika Bamert, Marco Colleoni, Karen N Price, Meredith M Regan, Aron Goldhirsch, Alan S Coates, Richard D Gelber, Umberto Veronesi, for the International Breast Cancer Study Group Trial 23-01 investigators

The Lancet Oncology April 2013

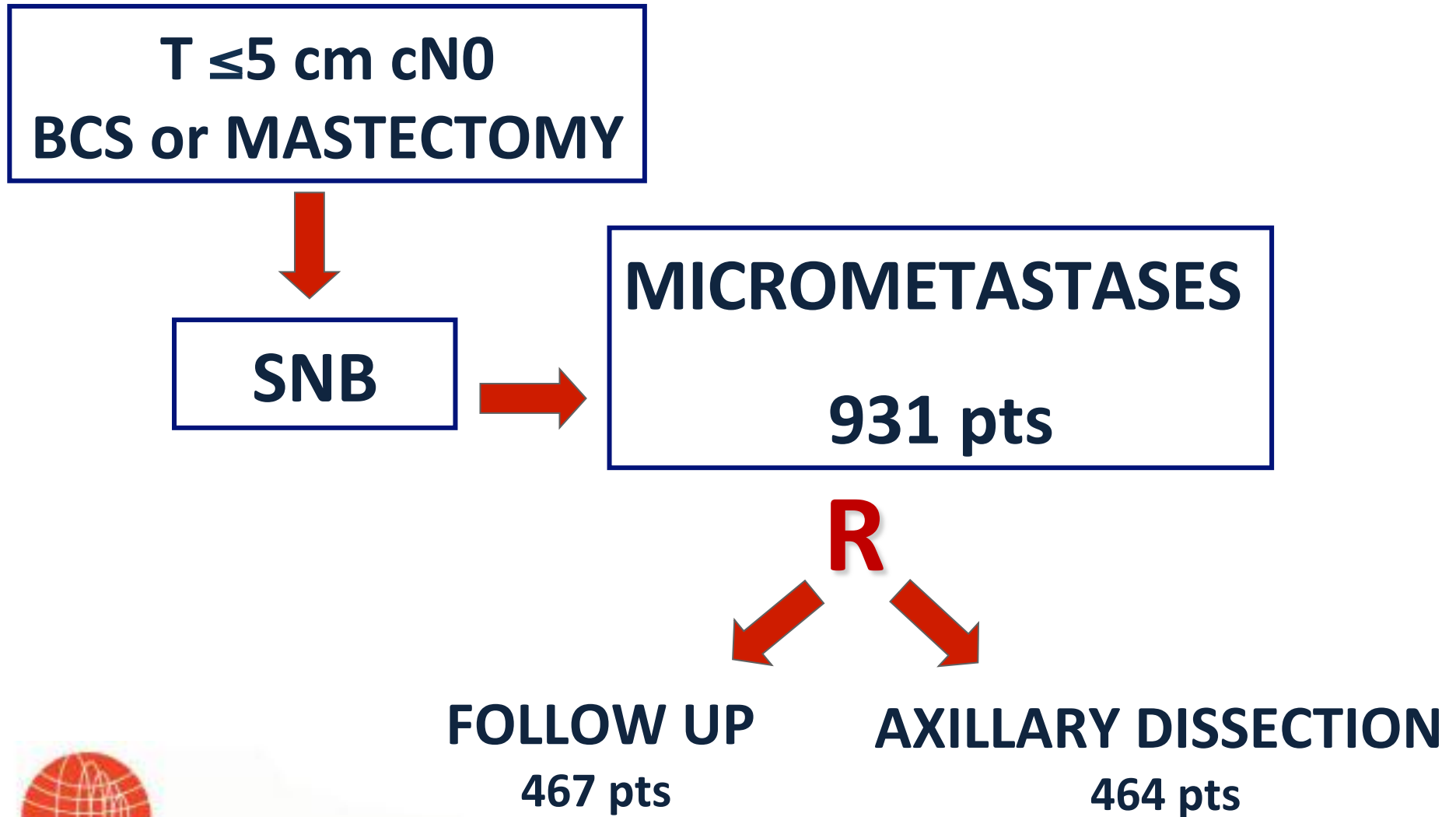


International Breast Cancer Study Group

IBCSG

Trial 23-01

Apr 2001 - Feb 2010

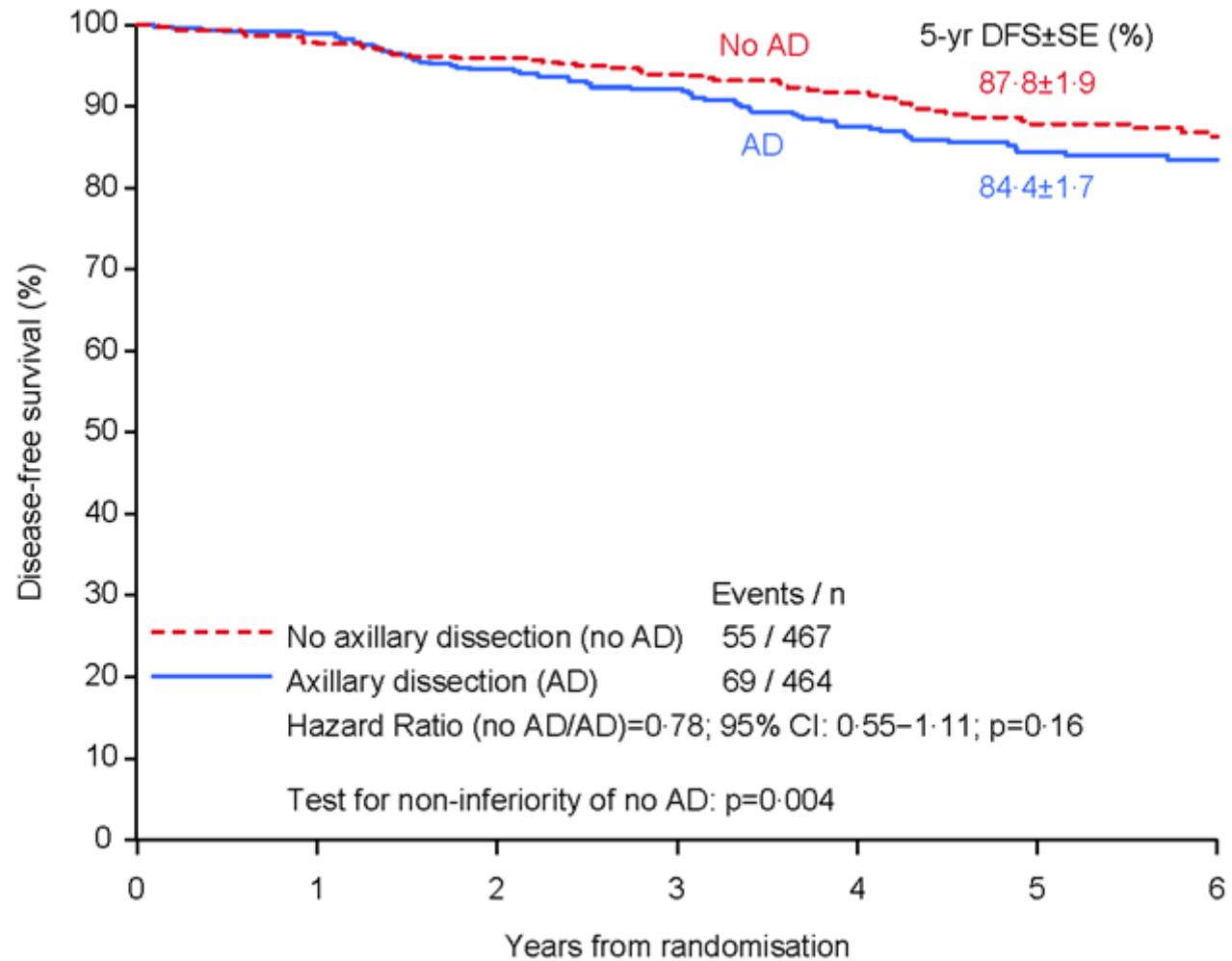


Patient characteristics	AD (n=464)	No AD (n=467)	Total (n=931)
Age (years) <i>Median (range)</i>	53 (28 – 81)	54 (26 – 81)	54 (26 – 81)
Pre-operative SNB			
<i>No</i>	287 (62%)	286 (61%)	573 (62%)
<i>Yes</i>	177 (38%)	181 (39%)	358 (38%)
Pathologic tumour size			
<i><2 cm</i>	316 (68%)	322 (69%)	638 (69%)
<i>2 – 2.9 cm</i>	106 (23%)	112 (24%)	218 (23%)
<i>>= 3</i>	35 (8%)	28 (6%)	63 (7%)
<i>Unknown</i>	7 (2%)	5 (1%)	12 (1%)
Oestrogen receptor status			
<i>Negative</i>	51 (11%)	40 (9%)	91 (10%)
<i>Positive</i>	409 (88%)	425 (91%)	834 (90%)
<i>Unknown</i>	4 (<1%)	2 (<1%)	6 (<1%)
Progesterone receptor status			
<i>Negative</i>	108 (23%)	115 (25%)	223 (24%)
<i>Positive</i>	352 (76%)	350 (75%)	702 (75%)
<i>Unknown</i>	4 (<1%)	2 (<1%)	6 (<1%)

Patient characteristics	AD (n=464)	No AD (n=467)	Total (n=931)
Local treatment			
<i>Mastectomy</i>	44 (9%)	42 (9%)	86 (9%)
<i>Breast conserving surgery</i>	420 (91%)	425 (91%)	845 (91%)
RT on breast conservative surgery			
<i>No RT</i>	10 (2%)	12 (3%)	22 (3%)
<i>Intraoperative only</i>	79 (19%)	80 (19%)	159 (19%)
<i>Postoperative only</i>	293 (70%)	297 (70%)	590 (70%)
<i>Combination RT</i>	36 (9%)	35 (8%)	71 (8%)
<i>Unspecified RT</i>	2 (<1%)	1 (<1%)	3 (<1%)
Systemic therapy			
<i>Any systemic therapy</i>	441 (95%)	451 (97%)	892 (96%)
<i>Hormonal therapy only</i>	292 (63%)	315 (67%)	607 (65%)
<i>Chemotherapy only</i>	42 (9%)	33 (7%)	75 (8%)
<i>Combination therapy</i>	107 (23%)	103 (22%)	210 (23%)

Disease free survival events	AD (n=464)	No AD (n=467)	Total (n=931)
Total	69 (15%)	55 (12%)	124 (13%)
Breast cancer events			
<i>Local</i>	10 (2%)	8 (2%)	18 (2%)
<i>Regional</i>	1 (<1%)	5 (1%)	6 (1%)
<i>Distant</i>	34 (7%)	25 (5%)	59 (6%)
<i>Contralateral breast</i>	3 (<1%)	9 (2%)	12 (1%)
Non breast cancer events			
<i>Second (non breast) primary</i>	20 (4%)	6 (1%)	26 (3%)
<i>Death without prior cancer event</i>	1 (<1%)	2 (<1%)	3 (<1%)
Deaths	19 (4%)	17 (4%)	36 (4%)

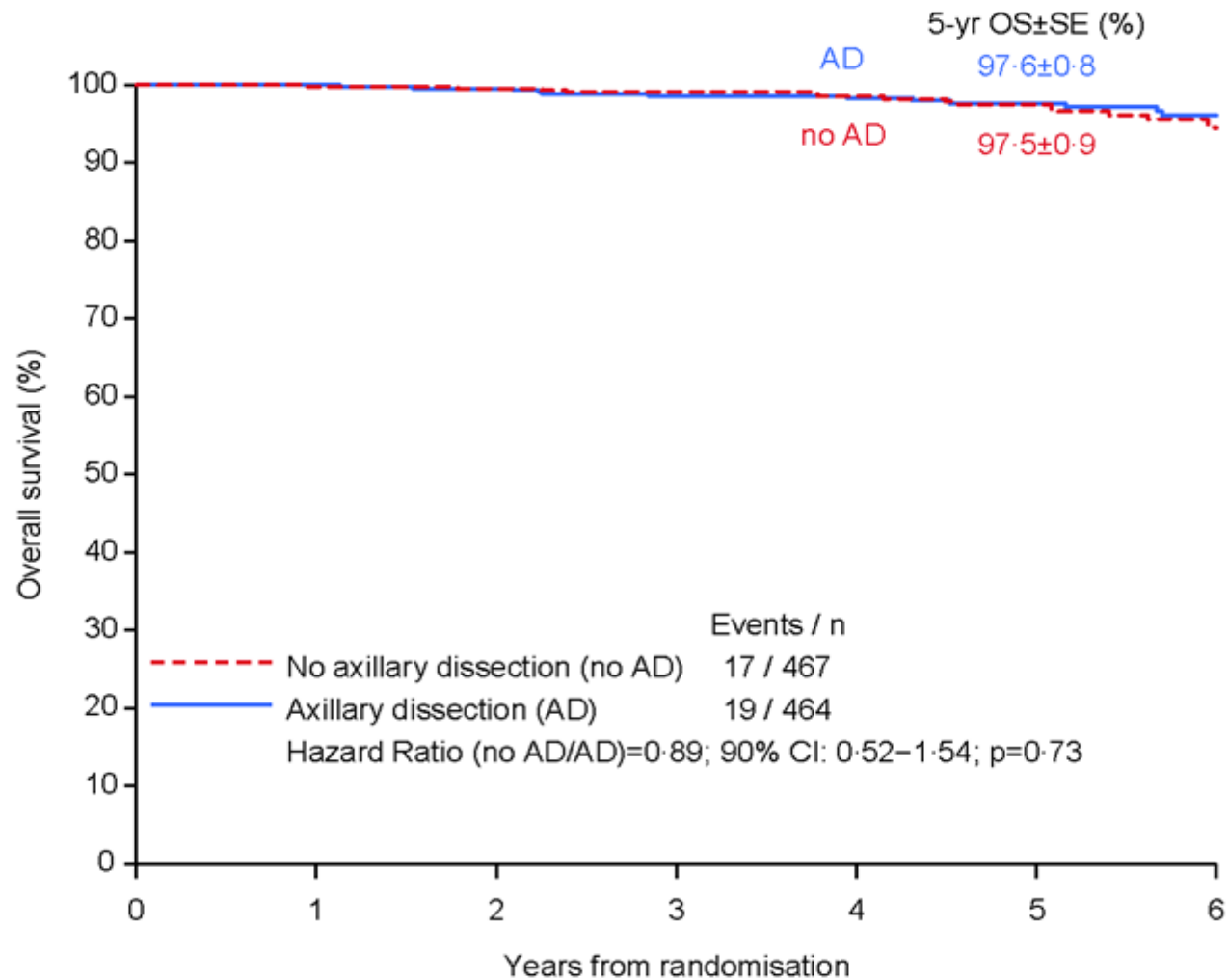
DISEASE-FREE SURVIVAL



Number at risk

	0	1	2	3	4	5	6
No AD	467	454	431	360	292	210	158
AD	464	453	421	350	281	206	156

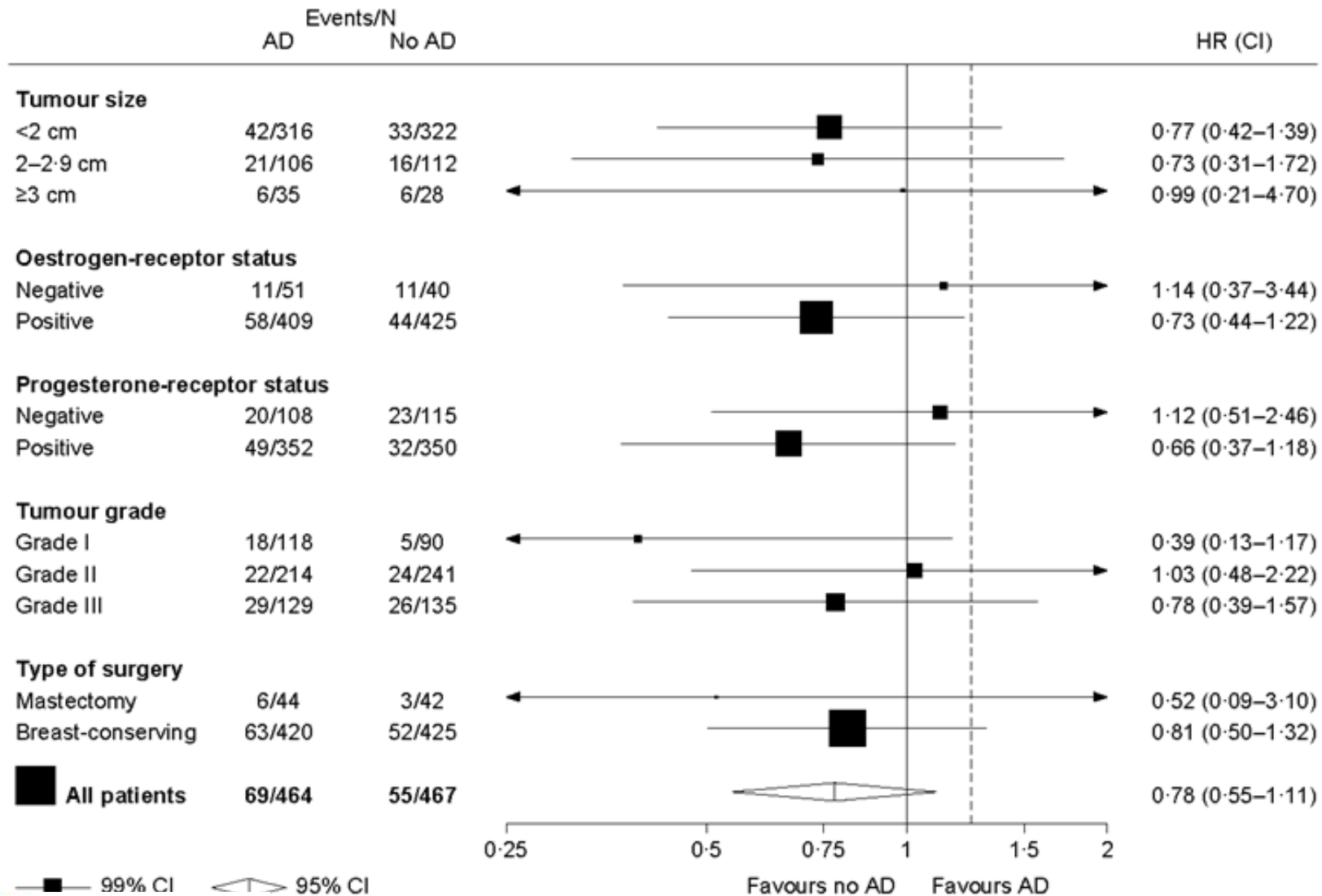
OVERALL SURVIVAL



Number at risk

	0	1	2	3	4	5	6
No AD	467	463	448	380	315	235	174
AD	464	458	444	375	312	234	178

23-01 Subgroup analysis



IBCSG 23-01 trial

- ✓ “Not giving AD to patients with 1 or more SN micrometastases has no adverse influence on DFS or OS”
- ✓ This is level 1 evidence in favour of the San Gallen 2011 recommendation that axillary dissection should not be performed if the sentinel node contains only micrometastases

What about no AD in pts scheduled for mastectomy?

- ✓ In Trial 23.01 only 9% of cases had mastectomy
- ✓ So no conclusions on mastectomy

**Out-trial IEO:
No AD in 90 mastectomy pts with SN micrometastases
(from 2003-2011)**

All patients (N=90)	No.	%
Age (years)		
<i>Median (range)</i>	45	31-76
<i><40</i>	17	18.9
<i>40-49</i>	43	47.8
<i>50-59</i>	17	18.9
<i>≥ 60</i>	13	14.4
Menopausal status		
<i>Pre</i>	63	70
<i>Post</i>	27	30
Surgery		
<i>Mastectomy + SNB</i>	35	38.9
<i>NSM + SNB</i>	55	61.1
Histology		
<i>Ductal carcinoma</i>	76	84.4
<i>Lobular carcinoma</i>	6	6.7
<i>Others carcinoma</i>	8	8.9

Out-trial IEO:
No AD in 90 mastectomy pts with SN micrometastases

All patients (N=90)	No	%
pT		
<i>1mic</i>	2	2.2
<i>1a-b</i>	7	7.8
<i>1c</i>	27	30.0
<i>2</i>	47	52.2
<i>3</i>	5	5.6
<i>4</i>	1	1.1
<i>X</i>	1	1.1
Grade		
<i>G1</i>	14	15.5
<i>G2</i>	42	46.7
<i>G3</i>	34	37.8
Molecular subtype		
<i>LUM A</i>	20	22.2
<i>LUM B-</i>	47	52.2
<i>LUM B+</i>	11	12.2
<i>HER 2+</i>	7	7.8
<i>Triple Neg</i>	5	5.6

Out-trial IEO:
No AD in 90 mastectomy pts with SN micrometastases

All patients (N=90)	No	%
RT treatment		
<i>Locoregional RT</i>	2	2.2
Systemic treatment		
<i>Only HT</i>	58	64.5
<i>Only CT</i>	11	12.2
<i>HT+CT</i>	21	2.3

Out-trial IEO: No AD in 90 mastectomy pts with SN micrometastases

All patients (N=90)	No	%.
First Event		
<i>Axillary LN mts</i>	1	1.1
<i>Regional LN mts</i>	1	1.1
<i>Contralateral BC</i>	1	1.1
<i>Liver mts</i>	2	2.2
<i>Liver + Bone mts</i>	1	1.1
<i>Brain mts</i>	1	1.1
<i>Other primary cancer</i>	1	1.1
<i>Death (unknown cause)</i>	1	1.1
TOTAL	9	10
Follow up (months)		
<i>Median (range)</i>	28 (5-115)	

ORIGINAL ARTICLE – BREAST ONCOLOGY

Characteristics and Outcomes of Sentinel Node–Positive Breast Cancer Patients after Total Mastectomy without Axillary-Specific Treatment

Sarah Milgrom, MD¹, Hiram Cody, MD, FACS², Lee Tan, MD³, Monica Morrow, MD, FACS², Catherine Pesce, MD², Jeremy Setton, MD¹, Katherine Rogers, BA¹, Brittany Arnold, BA¹, Anne Eaton, MS⁴, Jeffrey Catalano, BA³, Beryl McCormick, MD, FACR¹, Simon Powell, MD, PhD¹, and Alice Ho, MD¹

Conclusions: ✓ 210 pts received mastectomy; 325 pts received BCS
✓ “early-stage breast cancer patients with minimal sentinel node disease experience excellent outcomes without AD [even if] they undergo total mastectomy”
✓ Median follow-up 57.8 months
✓ DFS - OS 94.7% - 97.8% in TM
✓ DFS - OS 90.1% - 92.6% in BCS

No AD in mastectomy

It seems possible, therefore, that axillary dissection may also be abandoned in mastectomy patients with limited sentinel node involvement

Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis

A Randomized Clinical Trial

Armando E. Giuliano, MD

Kelly K. Hunt, MD

Karla V. Ballman, PhD

Peter D. Beitsch, MD

Pat W. Whitworth, MD

Peter W. Blumencranz, MD

A. Marilyn Leitch, MD

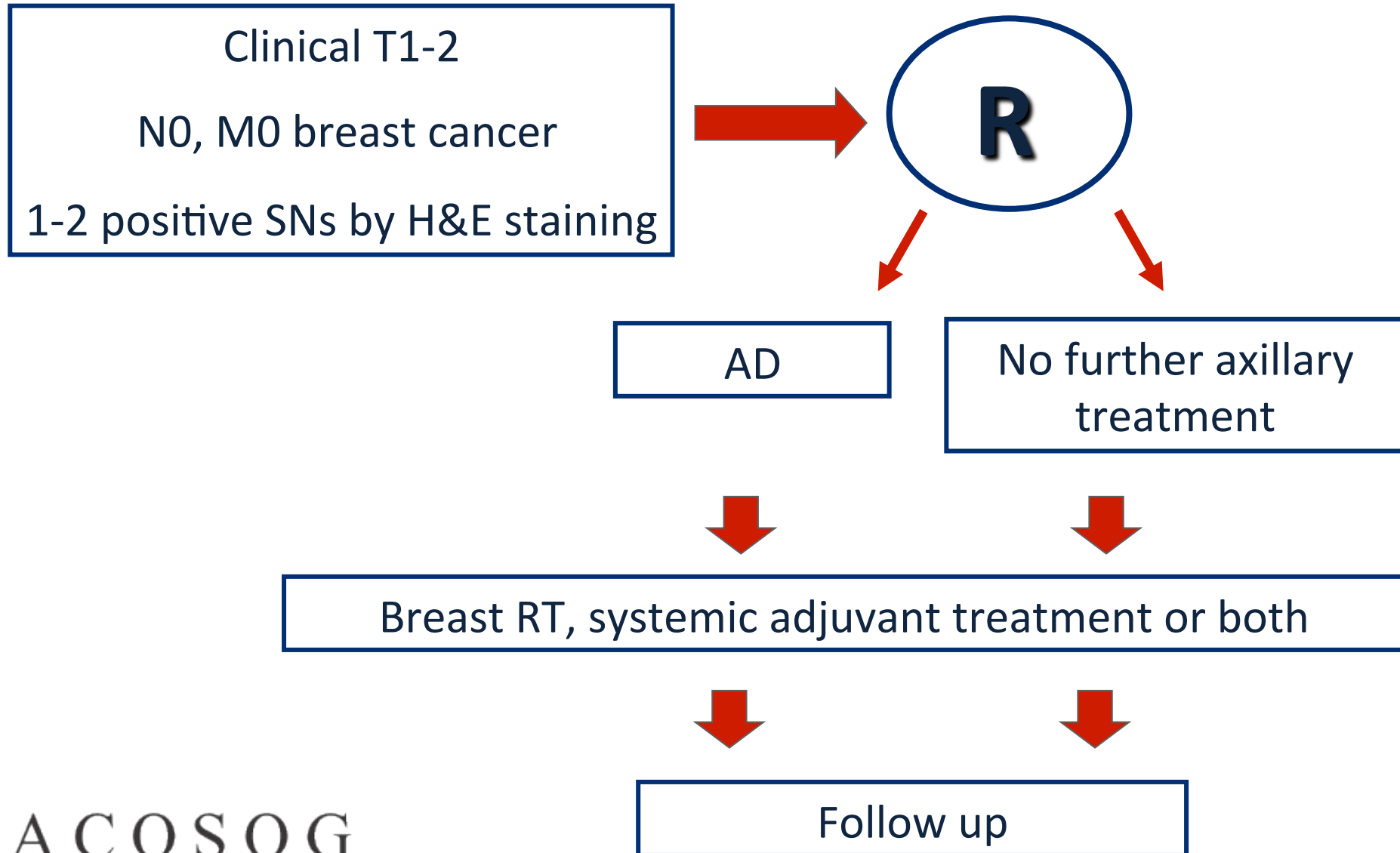
Sukamal Saha, MD

Linda M. McCall, MS

Monica Morrow, MD

Trial Z0011

(Closed 12/04 at n=891)

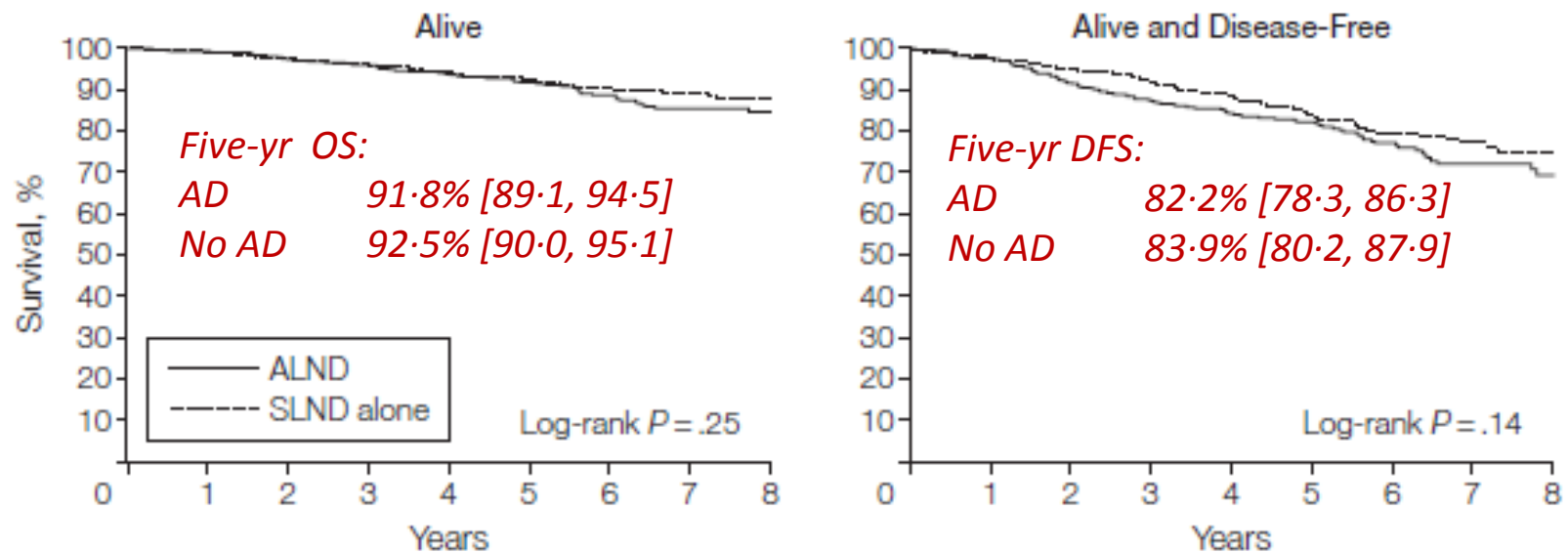


ACOSOG

American College of Surgeons Oncology Group

OS and DFS in trial Z0011

Survival of the ALND Group compared with SLND-Alone Group



No. at risk	0	1	2	3	4	5	6	7	8	0	1	2	3	4	5	6	7	8
ALND	420	408	398	391	378	313	223	141	74	420	369	335	310	286	226	152	83	37
SLND alone	436	421	411	403	387	326	226	142	74	436	395	363	337	307	231	147	81	36

ALND indicates axillary lymph node dissection; SLND, sentinel lymph node dissection.

20011 conclusion

“it is time to abandon AD in early BC pts with a positive SN provided they receive systemic adjuvant treatment and whole breast RT”

Criticisms of Z0011

Criticisms

- ✓ Trial closed recruiting only half projected number of pts
- ✓ Might not have power to detect a small difference in outcomes between groups
- ✓ Axillary recurrence rate in the no AD arm double that in the AD arm
- ✓ Non-inferiority criterion too lax (5-yr survival in the no AD arm assumed not less than 75% of that in the AD arm)
- ✓ No AD = no information on any additional axillary involvement that may change adjuvant treatment

Rebuttals

- ✓ **No difference in 5-yr OS**
- ✓ **No difference in 5-yr DFS**
- ✓ **Excellent OS and DFS in no AD group**
- ✓ **In fact OS and DFS non significantly better in no AD arm**
- ✓ **Low rate of axillary disease in no AD arm**
- ✓ **Data indicate that complete axillary information almost never changes adjuvant treatment**

Axillary failure rates in comparison to percentage with other axillary nodes involved

Trial	RT/ Systemic therapy	Additional +ve nodes at AD	Axillary failure, (no AD)	Ratio
NSABP B04 (2002)	0/0	40%	18.5%	2.2
NSABP B32 (2010)	82/84%	9.8%	0.7%	14
ACOSOG Z0011 (2011)	89/97%	27.4%	0.9%	30
IBCSG 2301 (2013)	71/96%	13%	1.0%	13

Fisher B, NEJM 2002;347:567
Krag D, Lancet Oncol 2010;11:927

Galimberti V, Lancet Oncol 2013;14:297
Giuliano A, JAMA 2011;305:589



TAKE HOME MESSAGE

- ✓ For most patients with early breast cancer and a clinically negative axilla, a positive SN should not be further treated
- ✓ CAUTION: the decision should continue to consider all the relevant factors including patient age, comorbidities, and also patient preference



NEW QUESTION

**DO WE EVEN NEED TO
PERFORM SENTINEL NODE
BIOPSY?**

Sentinel node vs Observation after axillary Ultra-souND

SOUND

Trial

A multicentric randomized trial comparing sentinel node biopsy vs. observation only (no SNB) in patients with small breast cancer and negative preoperative axillary assessment with US

(IEO S637/311)

Study design

Tumor <2 cm

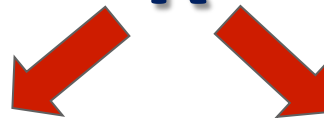
Any age

Negative axilla on US

(or negative FNAC of axillary node suspicious on US)



R



Sentinel Node Biopsy

+/- Axillary Dissection
N=780

Observation

N=780

RATIONALE FOR NOT DOING SNB

- ✓ SNB has lost much of its importance: we don't do AD when the SN is negative, micrometastatic, and now even when its positive
- ✓ Advancing imaging technology can identify increasingly smaller axillary involvement and may be used for axillary staging
- ✓ Adjuvant treatment recommendations increasingly depend on primary tumor biology not axillary status

Primary Endpoint

- ✓ DDFS (distant disease free survival)

Secondary Endpoints

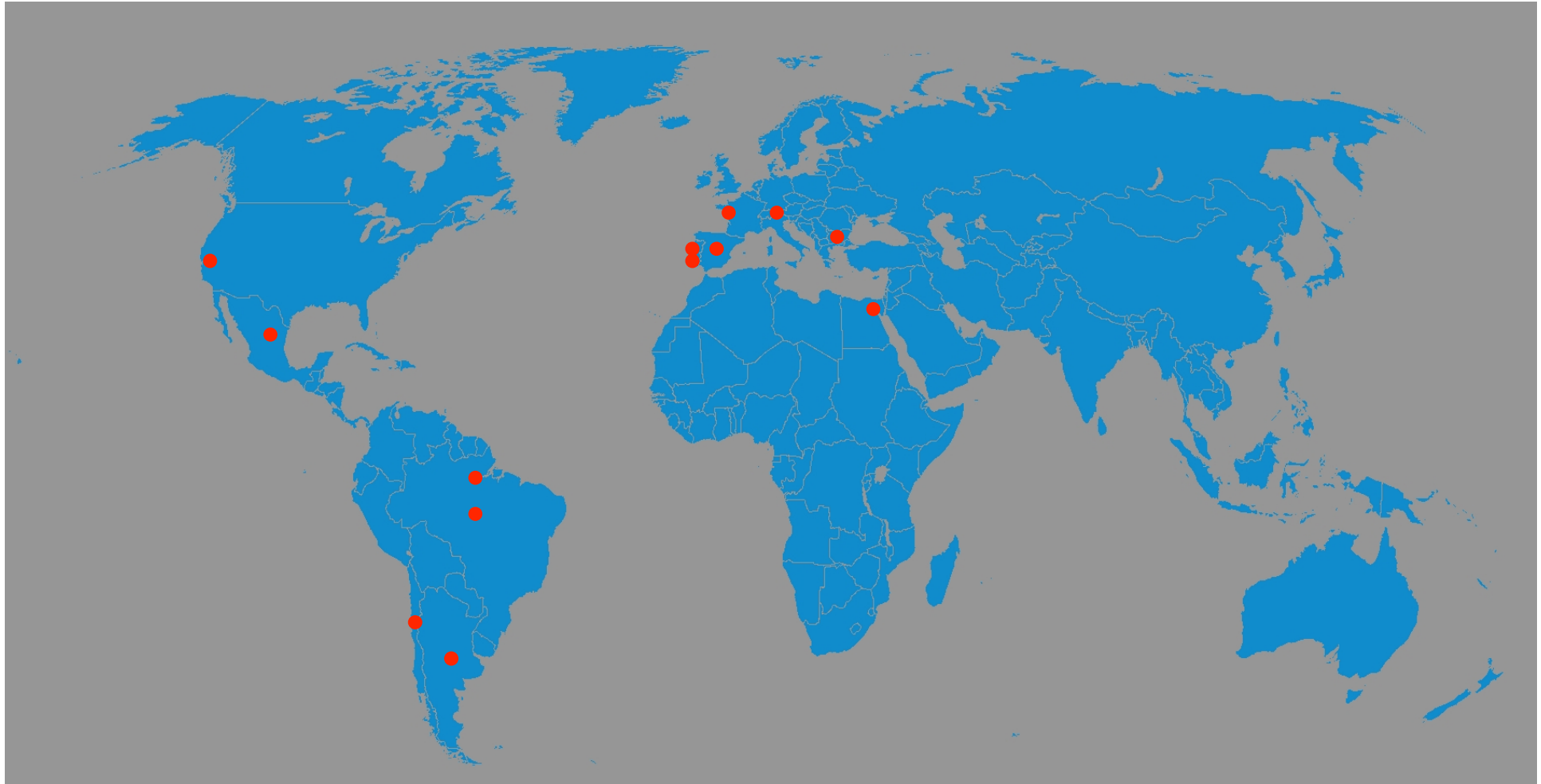
- ✓ Axillary recurrences
- ✓ DFS and OS
- ✓ Quality of life
- ✓ Type of adjuvant treatment

BRESCIA
CAGLIARI
COMO VALDUCE
COMO S.ANNA
COMO - GRAVEDONA
CREMONA
DESIO
LECCO
MILANO INT
MANTOVA
VARESE
PAVIA
ROZZANO 1
ROZZANO 2
PADOVA 1
PADOVA 2
CONEGLIANO VENETO
PIACENZA
FORLI'
RAVENNA
CARPI
RIMINI
NAPOLI
Napoli 2
ANCONA
TORINO
TORINO
BOLZANO
FIRENZE
ISERNIA
BARI
RIONERO IN VULTURE



Recruitment started
February 2012

WORLD CENTRES INTERESTED IN SOUND



SAN PAOLO, JUIZ DE FORA (Brazil); CALIFORNIA USA; LISBON, OPORTO (Portugal); VALENCIA (Spain); BELLINZONA, LUGANO GENEVA, BERN (Switzerland); ATHENS; ROSARIO (Argentina); SANTIAGO (Chile); MEXICO CITY; TEL HASHOMER (Israel)



BCC 2013

13th St. Gallen International Breast Cancer Conference 2013

Primary Therapy of Early Breast Cancer
Evidence, Controversies, Consensus

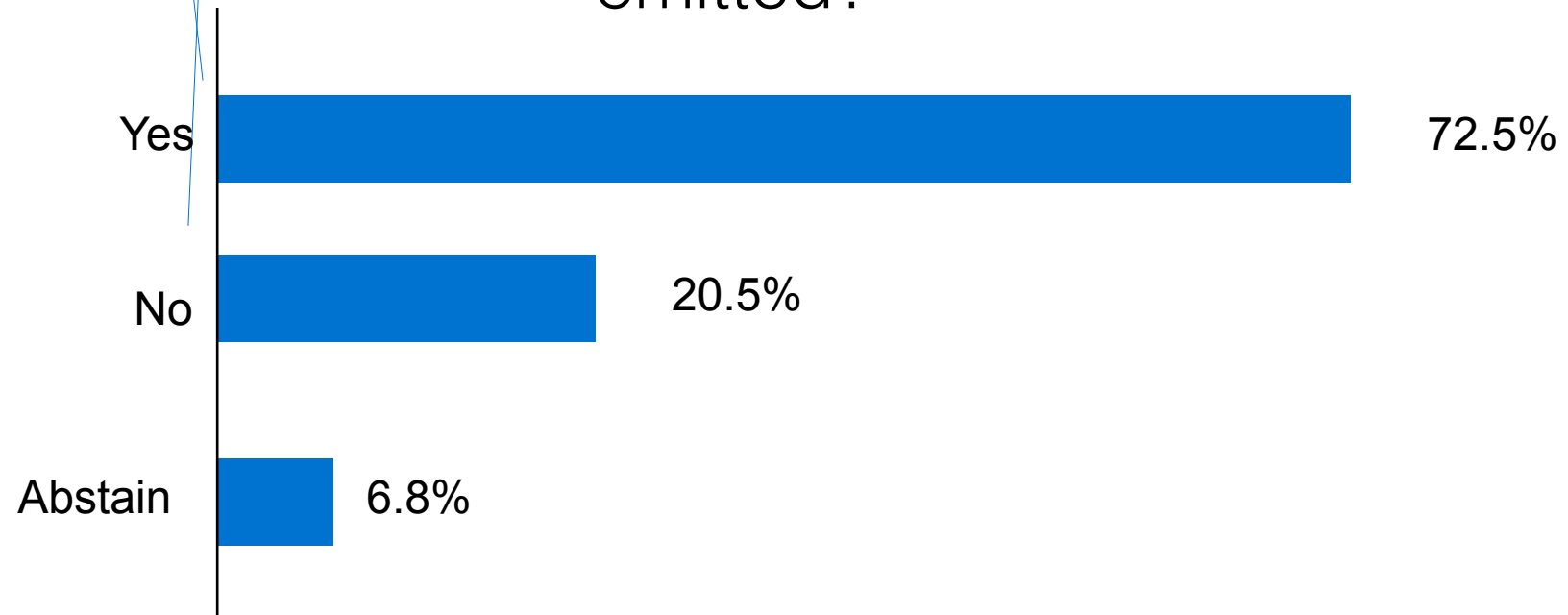
13–16 March 2013, St. Gallen/Switzerland

Recommendations

Axillary surgery?

San Gallen Panel vote

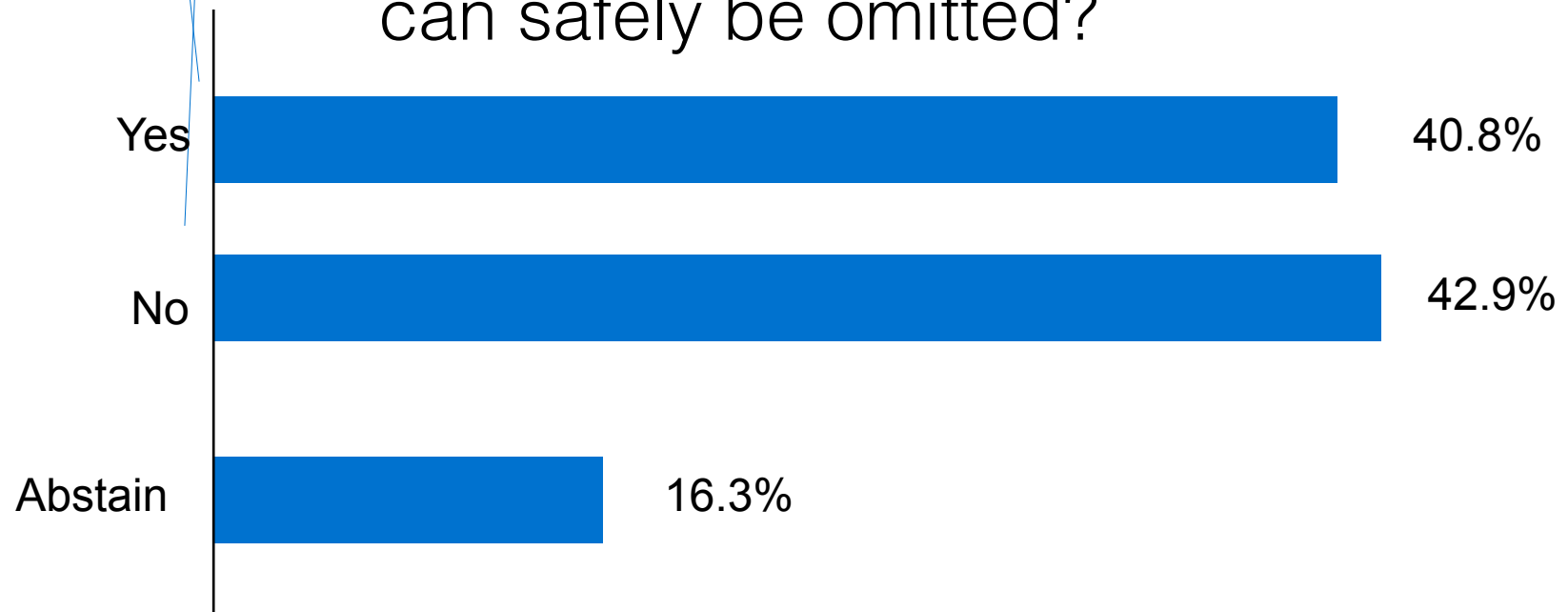
For patients with 1-2 macrometastatic SNs receiving BCS and RT, AD can safely be omitted?



Axillary surgery?

San Gallen Panel vote

For patients with 1-2 macrometastatic SNs receiving Mastectomy and planned RT, AD can safely be omitted?



CONCLUSIONS

- ✓ The SNB story is destined to run and run
- ✓ In a few year's time we will be considering data on the option of no longer doing SNB
- ✓ In the meantime I suggest.....

Conclusions

- ✓ No AD when the SNs are micrometastatic
- ✓ No AD when 1-2 SNs are macrometastatic in early breast cancer patients scheduled for BCS, whole breast RT, and systemic treatment



THANKS