

Progetto **CANOA**
CARCINOMA
MAMMARIO:
QUALI NOVITÀ PER IL 2014?

“Saper leggere” uno studio clinico per migliorare la pratica clinica

Coordinatori scientifici:
Stefania Gori
Giovanni L. Pappagallo

La biopsia del linfonodo sentinella:
prima o dopo la chemioterapia neoadiuvante?

**Lo studio SENTINA
(SENTinel
NeoAdjuvant)**

Laura Orlando
UOC Oncologia Medica &
Breast Unit
Osp. A. Perrino
Brindisi

Ospedaletto di Pescantina
21-22 Marzo 2014

Sentinel-lymph-node biopsy in patients with breast cancer before and after neoadjuvant chemotherapy (SENTINA): a prospective, multicentre cohort study

Thorsten Kuehn, Ingo Bauerfeind, Tanja Fehm, Barbara Fleige, Maik Hausschild, Gisela Helms, Annette Lebeau, Cornelia Liedtke, Gunter von Minckwitz, Valentina Nekljudova, Sabine Schmatloch, Peter Schrenk, Annette Staebler, Michael Untch

Background

- Sentinel –node-biopsy replaced axillary node dissection as staging procedure.
- Preoperative chemotherapy is established for locally advanced, large tumors and also early breast cancer.
- Timing of sentinel-node biopsy in the neoadjuvant setting is controversial.
- The best surgical approach of clinically positive nodes downstaged to clinically negative nodes after neoadjuvant CT is unclear.
- Nodal stage after neoadjuvant CT reflects prognosis better than clinical nodal stage.

Lancet Oncology, Vol. 14, 2013

La biopsia del linfonodo sentinella: prima o dopo la chemioterapia neoadiuvante?

Two main questions:

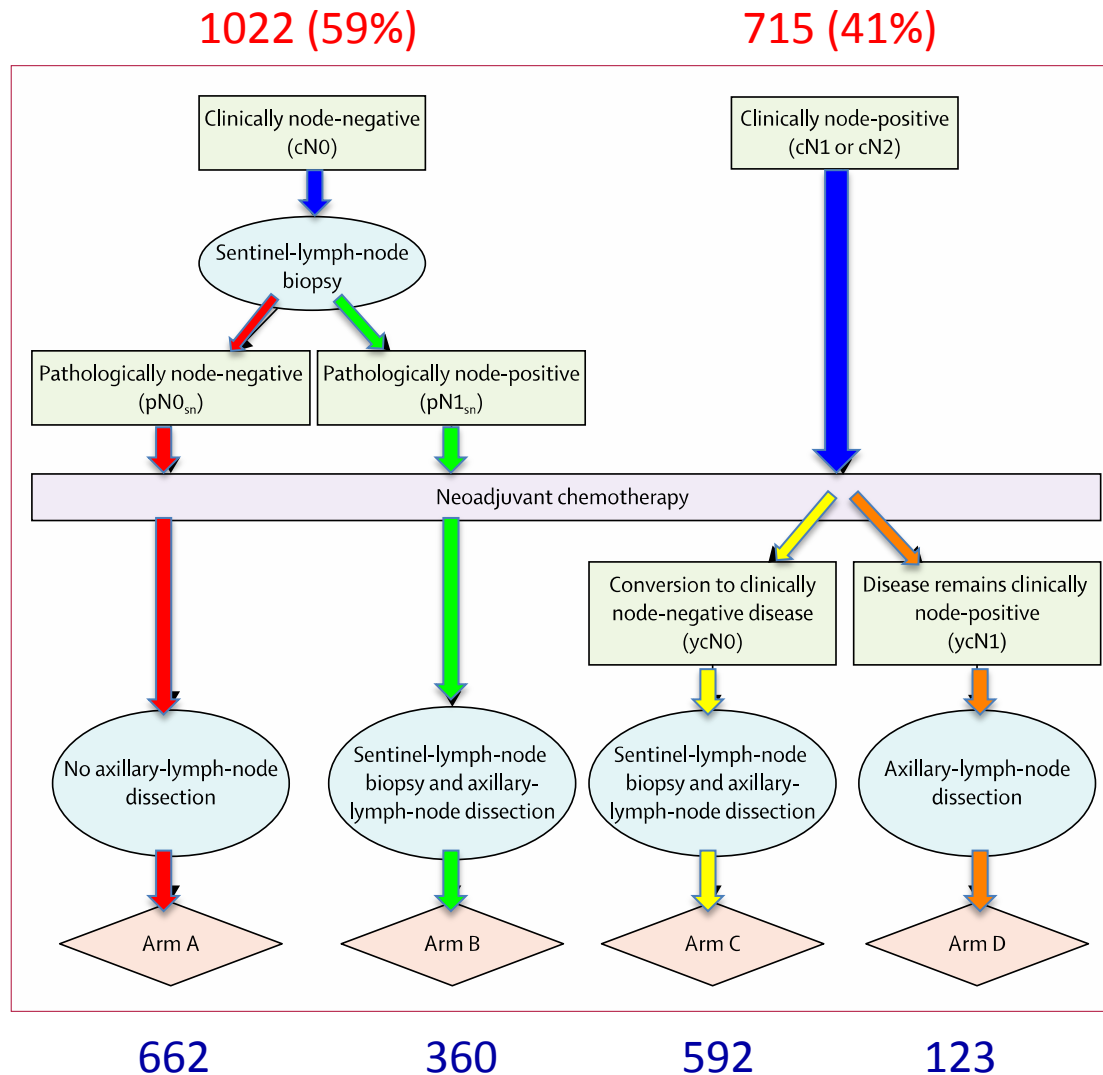
- Feasibility (detection rate)
(63-100%,)
- Accuracy (false-negative rate)
(0-39%)

Xing Y, *Br J Surg* 2006; Kelly A, *Acad Radiol* 2009; Van Deurzen Ch, *Eur J Cancer* 2009

Study Design

- Four-arm, prospective, cohort study
- 103 centres in Germany and Austria
- Pts enrolled: scheduled for neoadjuvant CT (six cycles of an anthracyclines-based regimen)

Studio SENTINA: four-arm, prospective cohort study



OUTCOMES

- PRIMARY

ACCURACY of sentinel node biopsy (AS FALSE-NEGATIVE RATE) IN ARM C
(cN+ → ycNo → **SNB during surgery**)

Definition of False negative rate:
$$\frac{\text{n}^\circ \text{ pts Sent neg and ALD pos}}{\text{n}^\circ \text{ pts ALD pos}}$$

OUTCOMES

- **SECONDARY**

DETECTION RATE of sentinel node biopsy

a) BEFORE AND AFTER NEOADJ. CT in ARM B
(cN0 with **pN1 SNB** → **SNB** and ALD during surgery)

b) AFTER NEOADJ. CT in ARM C
(cN+ → ycNo → **SNB** and ALD during surgery)

ACCURACY RATE (FALSE-NEGATIVE RATE) of second sentinel node biopsy in
ARM B

Procedures

- **CLINICAL ASSESSMENT**

- Palpation
- Axillary ultrasound
- Fine needle aspiration or core biopsy not mandatory

- **SNB**

- Radiocolloid alone
- Bleu dye alone
- Combined
- Periareolar
- Peritumoral
- Subcutaneous

Patient and tumor features

	Arm A, cNO pNO _{sn} (n=662)	Arm B, cNO pN1 _{sn} (n=360)	Arm C, cN+ ycNO (n=592)	Arm D, cN+ ycN+ (n=123)	p
Age (years)	0.27
Mean	49	49	50	51	..
Median (range)	48 (20–75)	48 (26–78)	49 (22–98)	50 (29–87)	..
Clinical tumour size before NACT	0.014
≤20 mm	19 (3%)	12 (3%)	21 (4%)	8 (7%)	..
>20 to ≤50 mm	499 (75%)	256 (71%)	472 (80%)	93 (76%)	..
>50 mm	27 (4%)	22 (6%)	46 (8%)	16 (13%)	..
Unknown	117 (18%)	70 (19%)	53 (9%)	6 (5%)	..
Grading	<0.0001
G1	33 (5%)	17 (5%)	14 (2%)	5 (4%)	..
G2	213 (32%)	171 (48%)	216 (36%)	46 (37%)	..
G3	315 (48%)	123 (34%)	258 (44%)	48 (39%)	..
Unknown	101 (15%)	49 (14%)	104 (18%)	24 (20%)	..
ER/PR status	<0.0001
Both negative	260 (39%)	73 (20%)	213 (36%)	45 (37%)	..
One or both positive	336 (51%)	256 (71%)	319 (54%)	61 (50%)	..
Unknown	66 (10%)	31 (9%)	60 (10%)	17 (14%)	..

Patient and tumor features

	Arm A, cN0 pN0 _{sn} (n=662)	Arm B, cN0 pN1 _{sn} (n=360)	Arm C, cN+ ycN0 (n=592)	Arm D, cN+ ycN+ (n=123)	p
HER2 status	0.0021
Negative	461 (70%)	236 (66%)	359 (61%)	80 (65%)	..
Positive	134 (20%)	92 (26%)	173 (29%)	26 (21%)	..
Unknown	67 (10%)	32 (9%)	60 (10%)	17 (14%)	..
Lymphovascular invasion	<0.0001
No	512 (77%)	241 (67%)	372 (63%)	62 (50%)	..
Yes	38 (6%)	68 (19%)	130 (22%)	45 (37%)	..
Unknown	112 (17%)	51 (14%)	90 (15%)	16 (13%)	..
Histological tumour type	0.022
Ductal invasive	521 (79%)	275 (76%)	476 (80%)	91 (74%)	..
Lobular invasive	41 (6%)	42 (12%)	35 (6%)	11 (9%)	..
Other	45 (7%)	18 (5%)	37 (6%)	10 (8%)	..
Unknown	55 (8%)	25 (7%)	44 (7%)	11 (9%)	..

Procedures of SNB

	Arms A and B, before NACT (n=1022)	Arm B, after NACT (n=360)	Arm C, after NACT (n=592)	Total (n=1974)
Tracer				
Radiocolloid alone	580 (57%)	238 (66%)	389 (66%)	1207 (61%)
Blue dye alone	7 (1%)	5 (1%)	7 (1%)	19 (1%)
Combined	401 (39%)	105 (29%)	164 (28%)	670 (34%)
Unknown	34 (3%)	12 (3%)	32 (5%)	78 (4%)
Injection site, multiple choice				
Periareolar	606 (59%)	230 (64%)	396 (67%)	1232 (62%)
Peritumoral	342 (33%)	125 (35%)	207 (35%)	674 (34%)
Subcutaneous	433 (42%)	128 (36%)	276 (47%)	837 (42%)
Median injected dose (MBq)	89.8	95.0	100	94.0
Protocol				
1 day	334 (33%)	97 (27%)	143 (24%)	574 (29%)
2 days	676 (66%)	227 (63%)	415 (70%)	1318 (67%)
Unknown	12 (1.2%)	36 (10%)	34 (6%)	82 (4%)

Data are number of patients (%), unless otherwise stated. NACT=neoadjuvant chemotherapy.

Table 2: Technical aspects of sentinel-lymph-node biopsy procedures in the trial

Clinical results after neoadjuvant CT

	ypN0	ypN+	ypN+ sent only
ARM B (n. 259)	155 (70.8%)	64 (29.2%)	45 (70.3%)
ARM C (n. 474)	248 (52.3%)	226 (47.7%)	131 (58%)

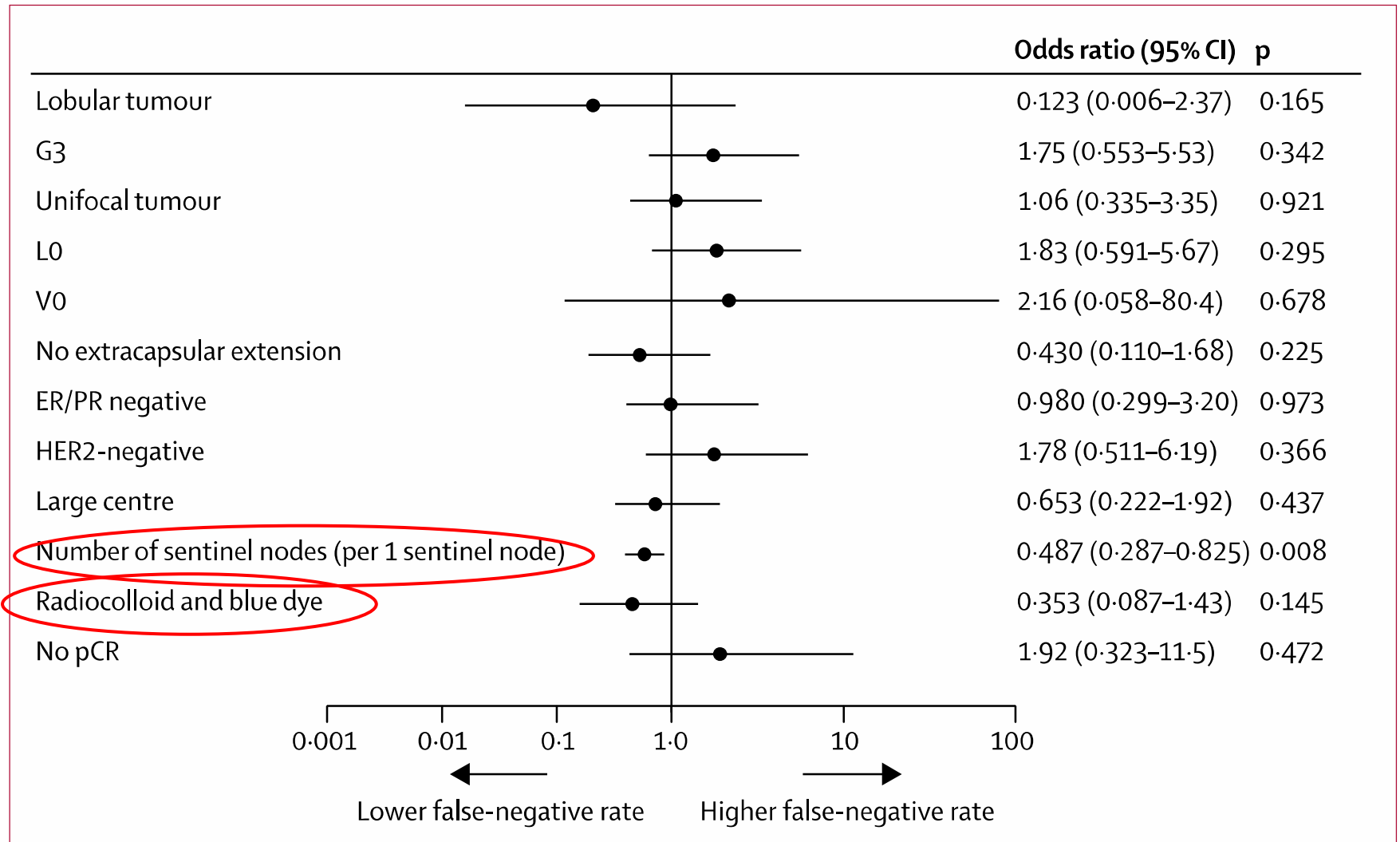
ACCURACY RATE FOR SNB AFTER CT and ALD (arm B and arm C) in ypN+ pts

	Arm B (n=64)	Arm C (n=226)
Overall false-negative rate (n/N; 95% CI)	51.6% (33/64; 38.7-64.2)	14.2% (32/226; 9.9-19.4)
False-negative rate, according to number of sentinel nodes removed		
1	66.7% (16/24)	24.3% (17/70)
2	53.8% (7/13)	18.5% (10/54)
3	50.0% (5/10)	7.3% (3/41)
4	50.0% (3/6)	0.0% (0/28)
5	18.2% (2/11)	6.1% (2/33)
False-negative rate, according to detection technique		
Radiocolloid alone	46.2% (18/39)	16.0% (23/144)
Radiocolloid and blue dye	60.9% (14/25)	8.6% (6/70)

Data are rate (number of patients), unless otherwise stated.

Table 4: False-negative rate of sentinel-lymph-node resection in patients with positive nodes, according to selected factors

Multivariate regression analysis for false-negative rate (arm C)



Detection rate

-high PRE CT

-low AFTER CT

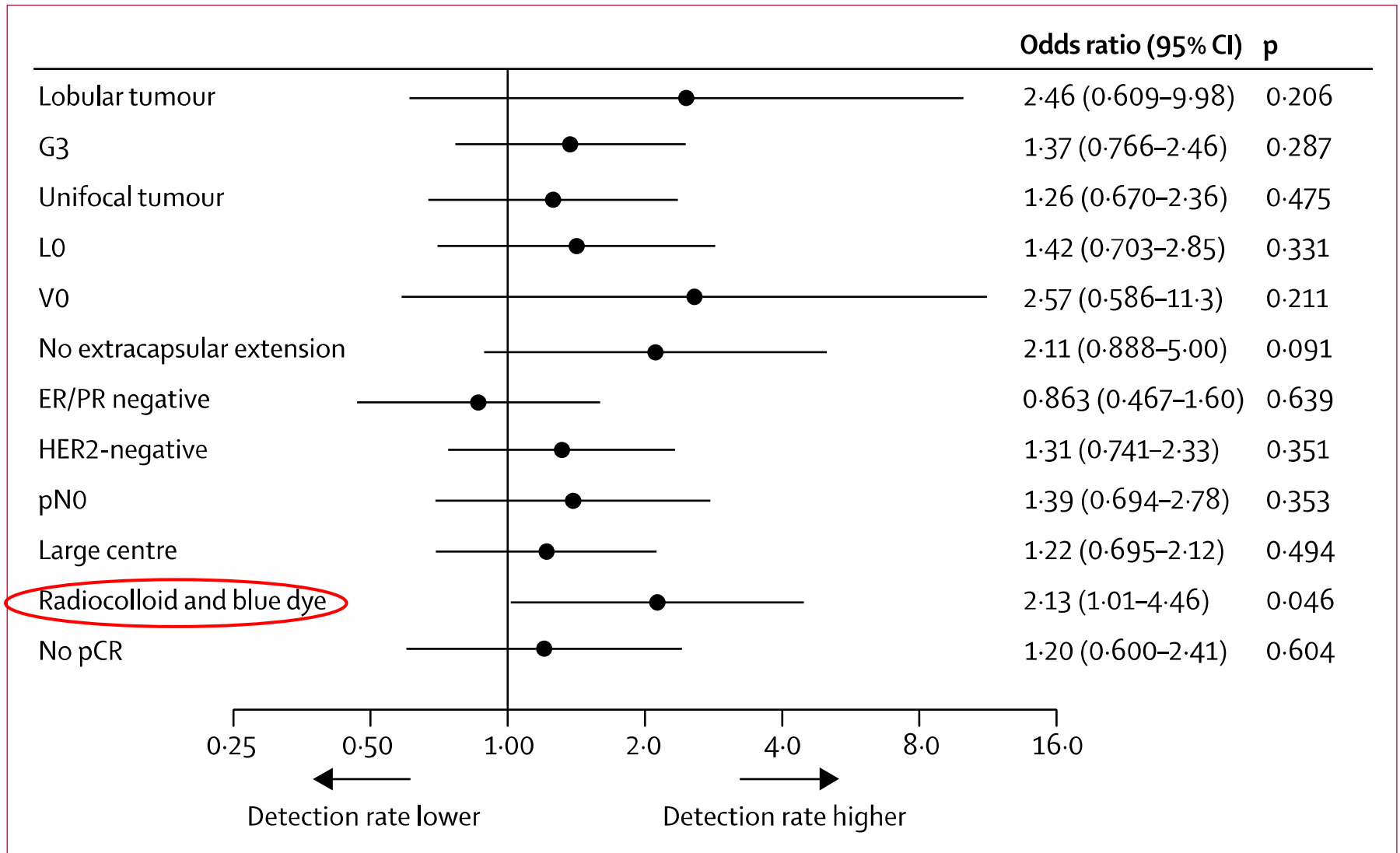
-lower after CT and a previous SNB

	SNB pre		SNB post		p
	Arms A and B	Arm B	Arm C		
Hot spot on lymphoscintigraphy	1014/1022 (99%)	236/360 (66%)	476/592 (80%)		<0.0001
Overall surgical detection rate (n/N; 95% CI)	99.1% (1013/1022; 98.3-99.6)	60.8% (219/360; 55.6-65.9)	80.1% (474/592; 76.6-83.2)		<0.0001
Overall surgical detection rate with radiocolloid alone	98.8% (573/580; 97.5-99.5)	52.9% (126/238; 46.4-59.4)	77.4% (301/389; 72.9-81.4)		..
Overall surgical detection rate with radiocolloid and blue dye	99.5% (399/401; 98.2-99.9)	76.2% (80/105; 66.9-84.0)	87.8% (144/164; 81.8-92.4)		..
Sentinel lymph nodes removed					
0	9/1022 (1%)	141/360 (39%)	118/592 (20%)		..
1	284/1022 (28%)	96/360 (27%)	142/592 (24%)		..
2	294/1022 (29%)	56/360 (16%)	131/592 (22%)		..
3	186/1022 (18%)	22/360 (6%)	81/592 (14%)		..
4	114/1022 (11%)	20/360 (6%)	59/592 (10%)		..
>4	135/1022 (13%)	25/360 (7%)	61/592 (10%)		..
At least one sentinel node removed					
All patients	Mean 2.7, median 2.0	Mean 2.4, median 2.0	Mean 2.7, median 2.0		<0.0001
Radiocolloid alone	Mean 2.6, median 2.0	Mean 2.3, median 2.0	Mean 2.6, median 2.0		0.012
Radiocolloid and blue dye	Mean 2.8, median 2.0	Mean 2.6, median 2.0	Mean 2.9, median 3.0		0.059

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

Table 3: Detection of sentinel lymph nodes, according to selected factors

Detection rate: multivariate regression analysis in arm C



Sentinel Lymph Node Biopsy After Neoadjuvant Chemotherapy for Advanced Breast Cancer: Results of Ganglion Sentinelle et Chimiothérapie Neoadjuvante, a French Prospective Multicentric Study

Jean-Marc Classe, Virginie Bordes, Loic Campion, Herve Mignotte, François Dravet, Jean Leveque, Christine Sagan, Pierre François Dupre, Gilles Body, and Sylvia Giard

Table 2. Sentinel Lymph Node Detection Rate

Patient Group	Detection Rate				False-Negative Rate			
	%	No. of Patients	Total Patients	χ^2 P	%	No. of Patients	Total Patients	χ^2 P
All patients, n = 195	90.1	176	195		11.5	6	52	
N0 patients, n = 130	94.6	123	130	.008	9.4	3	32	.66
N1 patients, n = 65	81.5	53	65		15	3	20	

NOTE. N0 indicates patients with axilla clinically free of involved nodes; N1 indicates patients with clinical axillary suspicious nodes not fixed.

SENTINA TRIAL: Conclusions

- Detection rate and accuracy rate of SNB are low for patients who convert during neoadjuvant CT from an initially positive axillary status to clinically negative disease (80% and 14.2% respectively) (**arm C**).
- The accuracy rate of SNB is especially unfavourable in patients with only one or two harvested sentinel lymph nodes after neoadjuvant chemotherapy (**arm C**).
- Addition of blue dye might improve the detection and accuracy rate of sentinel-lymph-node biopsy.
- A second SNB after neoadjuvant CT, in patients with previous SNB before systemic treatment, is not a good clinical option, with false negative rate of 51.6% (**arm B**).

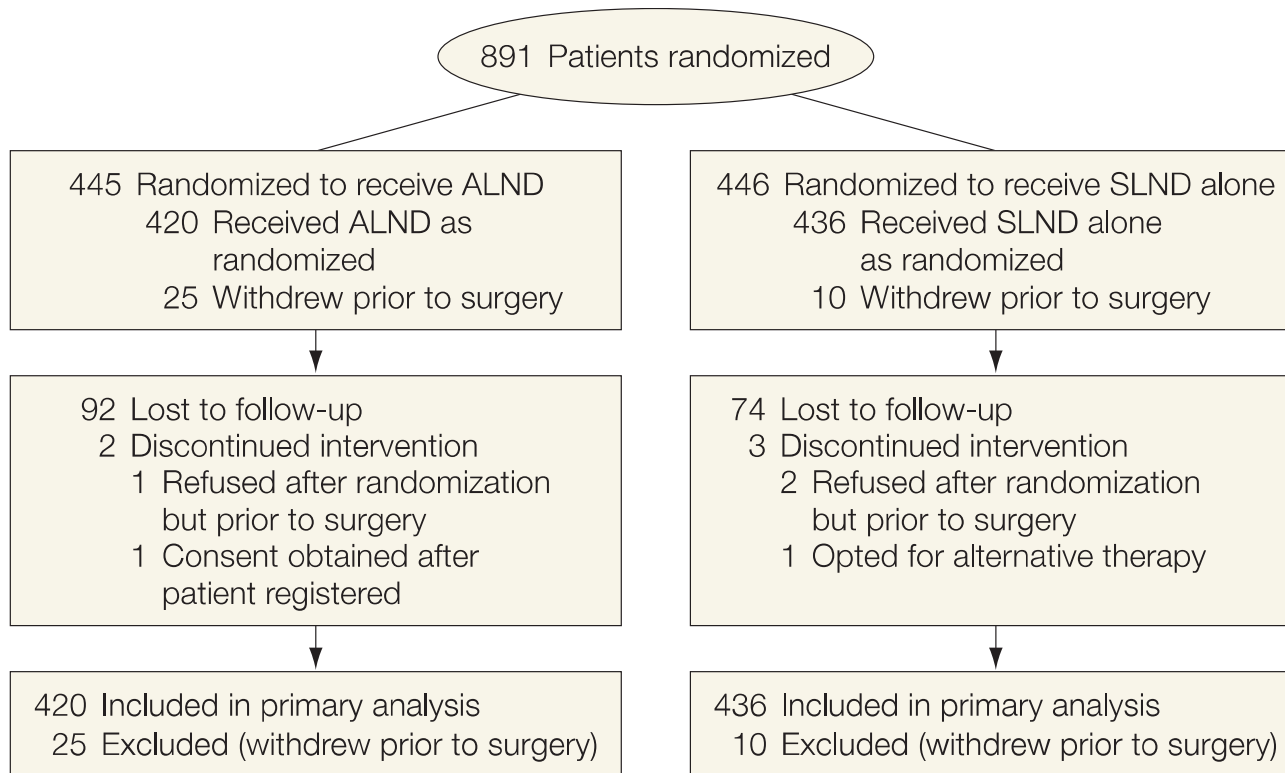
- SNB before neoadjuvant CT is feasible (99%) (**arm A and arm B**) (no data on accuracy).

- Clinical impact is unclear.

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

A Randomized Clinical Trial

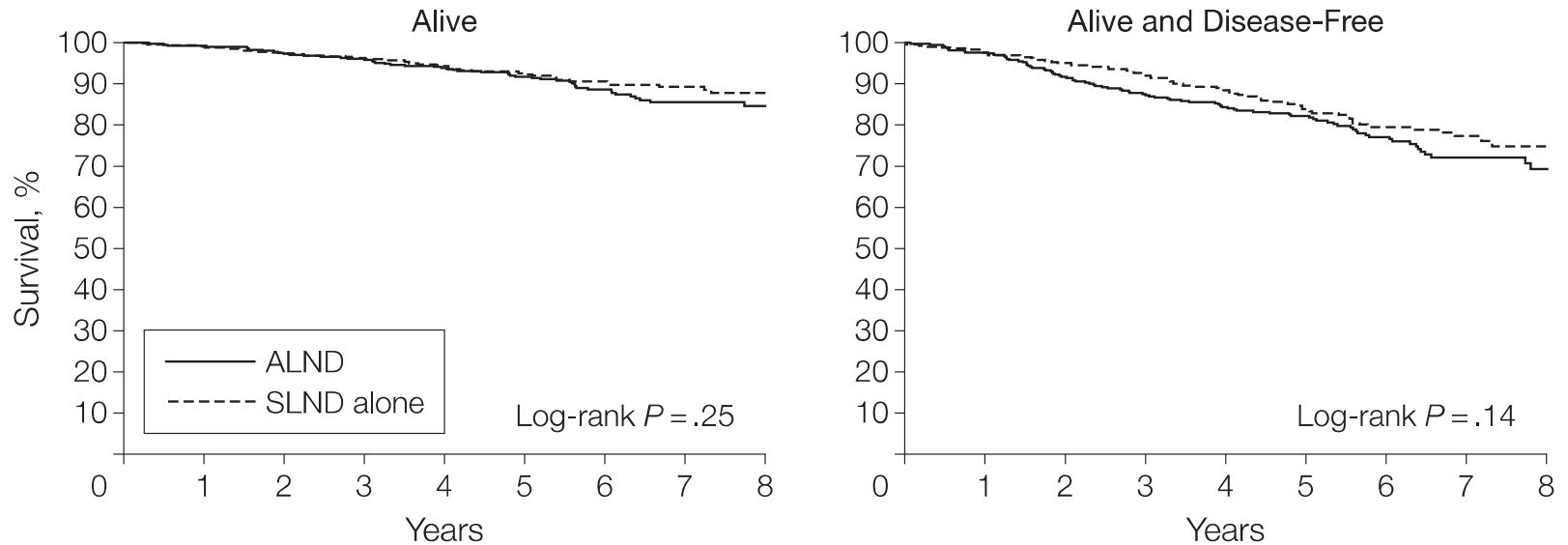
Figure 1. Study Flow



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

A Randomized Clinical Trial

Figure 2. Survival of the ALND Group Compared With SLND-Along 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.

