Università degli Studi d

Anno Accademico 20

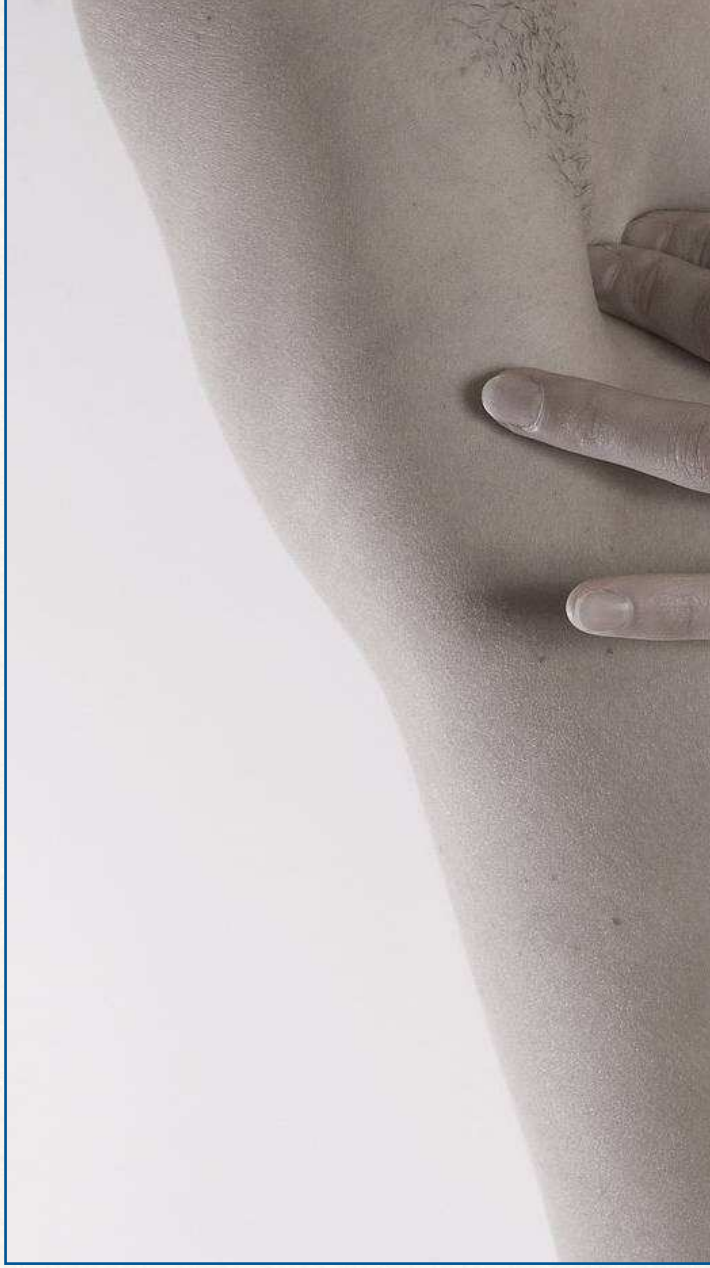
FOCUS-ON: CHEMIOTERAPIA PRE-OPERATORIA (NEOADIUV

ownstaging delle metastasi ascella

zione dell’indicazione chirurgica sull’ascella dopo chemioterapia neoadiuvante

ADJUVANT CHEMOTHERAPY:

WNSTAGING IN cN0



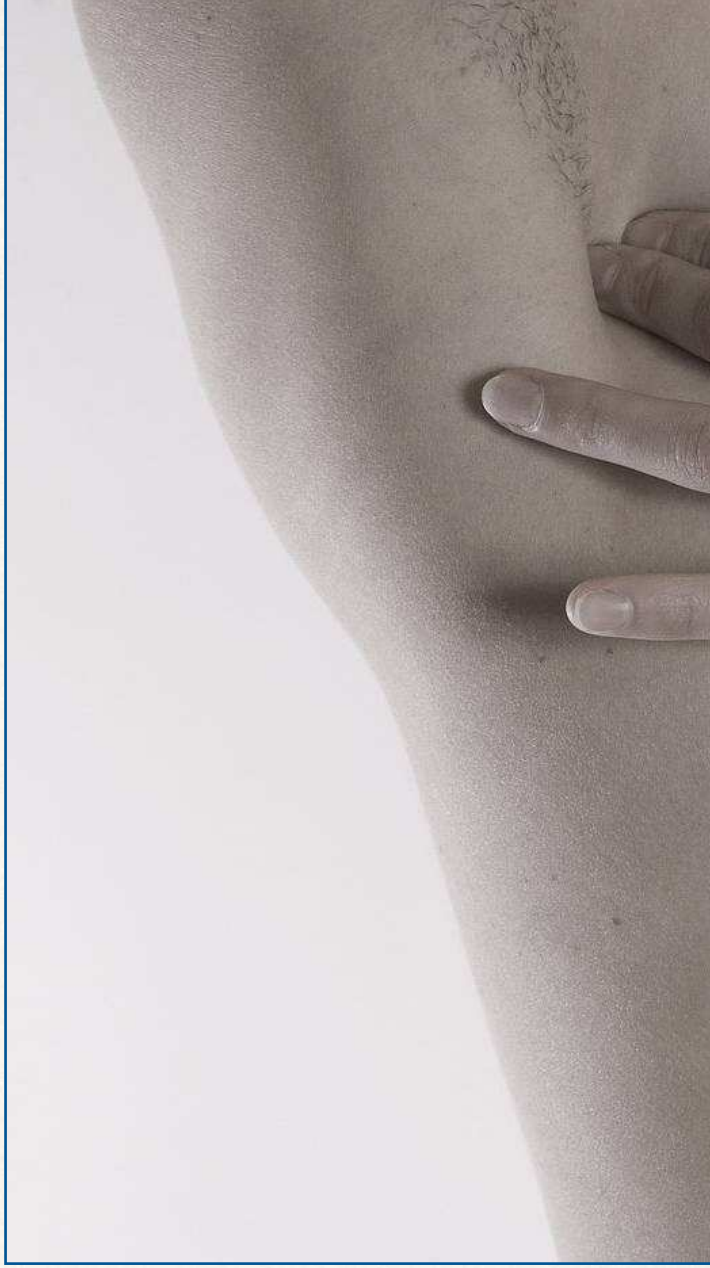
POSITIVE	NAC (575 pz)	No NAC (3171 pz)	
T 1	12.7 %	19.0 %	p= .0,2
T 2	**20.5 %**	**36.5 %**	p < 0.0001
T 3	30.4 %	51.4 %	p 0.04

3746 Patients cN0 extensively

DADJUVANT CHEMOTHERAPY:

LB IN cN0

	NAC (575 pz)	No NAC (3171 pz)	
	97.4 %	**98.7 %**	p= .017
R	**5.9 %**	**4.1 %**	p= .39
R regional ecurrence at w of 47 months	**1.2 %**	**0.9 %**	ns



SLNB surgery after chemotherapy is as accurate for axillary stag as SLNB surgery prior to chemotherapy in cN0

DADJUVANT CHEMOTHERAPY:

WNSTAGING IN cN1/2

Nodal pCR

P B-18 (1997) – 185 pz cN+ doxorubicina e cyclophosfamide % risposta clinica linfonodale - 73% completa - 16% parziale	32%
RER (1999) – 191 pz cN+	23%
ESSEY (2005) – 403 pz cN+ ce free survival CR: 67% al pCR: 60% (p<0,0001) urvival CR: 93% al pCR: 72% (p<0,0001)	22%
WMANN (2007) – 32 pz N+ → NAC → SLNB+ALND	32,5%

Nodal

SN FNAC study (2015) – 153 pz Biopsy proven node-positive T0-3, N1-2 NAC → SLNB+ALND -IHC use was mandatory -SLN metasteses of any size were considered positive (including ITC)	30,
SWEDISH Trial (2015) – 195 pz Biopsy proven node-positive T0-3, N1-2 NAC → SLNB+ALND Clinically node-negative axyllary status after NAC was not mandatory	33,
Netherlands Cancer Register retrospective study (2005-2008) – 1347 pz cN+	22

OADJUVANT CHEMOTHERAPY:

WNSTAGING IN cN1/2

Nodal pCR

COSOG Z1071 ALLIANCE (2013) – 525 pz cN1-cN2 NAC → SLNB+ALND	41,0%

C et al. Sentinel lymph node surgery after neoadjuvant chemotherapy in patients with node-positive
cer: the American College of Surgeons Oncology Group (ACOSOG) Z1071 clinical trial. JAMA 2013

Triplo negative	49.9%
HER2-positive	64.7%
Ormono-pos HER2-neg	22.1%

Boughey C et al.Tumor biology correlates with rates of breast conserving surgery and pathologic co
response after neoadjuvant chemotherapy for breast cancer: findings from the ACOSOG Z1071 (Alli
prospective multicenter trial. Ann Surg. 2014

ADJUVANT CHEMOTHERAPY:

WNSTAGING IN cN1/2

dal pcR in Her2+

1997 - **NSABP B-18** (1523 pz; TN-Her2+)

2010 - **DOMINICI** (CT+Trastuzumab)

astuz. (**sottogruppo ER-**)

- 2010 - **NOAH**
- 2012 - **NeoALTTO**
- 2012 - **NeoSphere**
- 2013 - **NSABP B-41**

2014 - **LI** (255 pz; CT+/-Trastuz.)

ER- e Trastuz.

ypN0	ypN+(1-3ln)	ypN+(>3l
40%		
70%		
38%(38%)		
28%(36%)		
23%(36%)		
49%(65%)		
52,9%	27,4%	19,7%
79,6%	**18,5%**	**1,9%**

ADJUVANT CHEMOTHERAPY:
NB IN cN1/2

hemotherapy, the axilla often has more fibrosis, making evaluation
nage and surgical dissection more challenging.

SOG Z1071 ALLIANCE (2013) – 525 pz cT0-4, cN1-cN2. M0

→ NAC (anthracycline and taxane)

→ SLNB+ALND

z cN1 and 2 or more LNS excised + ALND 215 pCR (41,0%)		
TS in SLN only	FNR 12,6%	
TS in SLN + others LN		
S no in LNS but in other LN		
ng: **BD + RC** only BD or RC	FNR **10,8%** 20,3%	**P=0.052**
ination:	FNR **9,1%**	

Goal: FNR <10%

"Using two mapping agents with different molecular size and transit is an important surgical standard that shou be adhered to for SLN surg after chemotherapy."

"Until further data are availa we recommended that SLN surgery after chemotherapy not be performed in patient with clinically evident residu

ADJUVANT CHEMOTHERAPY:
NB IN cN1/2

hemotherapy, the axilla often has more fibrosis, making evaluation
nage and surgical dissection more challenging.

AC study (2013) – 153 pz biopsy proven node-positive T0-3 N1-2

→ NAC (anthracycline, taxane, both)
→ SLNB+ALND

Nodal pCR: 30.3

e was mandatory
etasteses of any size were considered positive (including ITC)

FNR → 8,4% (with an average of 2.7 SLNs removed)

A low FNR (8.4%) of SLN after NAC ca be achieved with mandatory use of IHC for SLN evaluation.

SLN metastases of any size including micrometastases an ITC , should be considered positive.

This is the most convenient and inclusive method to decrease the FNR of SLNB below the threshold of 10%.

The FNR was decreased with the use of dual traces and when > one SLN was removed.

→ 89,6%

e IR of SLNB after NAC (89.6%) was slightly
erior to 90%.

N.of SLNs removed	FNR
1	18.2%
2 or more	4.9%
Method of mapping	
Isotope only	16.0%
Dual trace (isotope+blue)	5.2%
Definition of SLN pos	
Any size	8.4%
> 0.2 mm	13.3%

ADJUVANT CHEMOTHERAPY:

NB IN cN1/2

hemotherapy, the axilla often has more fibrosis, making evaluation
nage and surgical dissection more challenging.

DISH trial biopsy-proven node-positive T1-4d N1-2
5 pz
→ NAC
→ SLND + ALND

r node-negative axillary status after NAC was not mandatory.

77.9% **80.7% with dual tracer**

14.1% **4 % with 2 or more SLN removed**

10.3% with any size of posiyive SLN (ITC and micro/macro mts)

sitive in 52%, almost 66% of whom had nal nonSLNs-positive

pCR 33.3% (66/195)

To optimized IR and FNR, dual mapping should be metod of choise.

If only one SLN can be accurately identified and retrieved, a completion ALND should be considere

*** pre NAC marking of the citologically verified lym node**

*** selecting only patients with sonographically unsuspicious lymph nodes for SLNB after NAC**

*** broadering the definition of SLN metastasis after to include ITC**

all have the potential of further decreasing the F

ADJUVANT CHEMOTHERAPY:
NB IN cN1/2

hemotherapy, the axilla often has more fibrosis, making evaluation
nage and surgical dissection more challenging.

cN1/2 → NAC → cN0 → SLNB + ALND

- 2013 - **ACOSOG-Z1071** (701 pz)
- 2013 - **SENTINA** (1737 pz)
- 2015 - **SN-FNAC** (153 pz)
- 2014 - **Metanalisi FU** (2471 pz)
- 2016 - **Metanalisi ELHAGE** (3398 pz)
- 2015 - **Swedish study** (195 pz)

IR	FNR	FNR(1)	FNR(>2)	FN
	12,6%		8,7%	10
80,1%	14,2%	24,3%	<10%	8
87,6%	8,4%	18,2%	4,9%	5
89%	14% 8%IHC			
90,9%	13%			
77,9%	14,1%			

2 or more SLN **dual tracer**

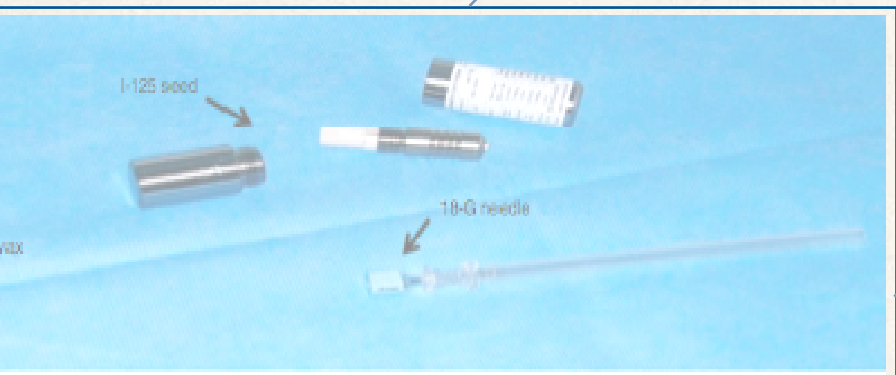
J, Mittendorf EA, et al.: Sentinel lymph node surgery after neoadjuvant
ents with node-positive breast cancer: the ACOSOG Z1071 (Alliance)
013, 310:1455–1461. 10.1001/jama.2013.278932
, Fehm T, et al.: Sentinel-lymph-node biopsy in patients with breast
er neoadjuvant chemotherapy (SENTINA): a prospective, multicenter
Oncol. 2013, 14:609–618. 10.1016/S1470-2045(13)70166-9
Basik M, et al.: Sentinel node biopsy after neoadjuvant chemotherapy in
positive breast cancer: the SN FNAC study. J Clin Oncol. 2015, 33:258–
1.55.7827
J, et al.: Feasibility and accuracy of sentinel lymph node biopsy in
ve breast cancer after neoadjuvant chemotherapy: a meta-analysis. PLoS
. 10.1371/journal.pone.0105316
eadon H, El Tokhy O, et al.: Is sentinel lymph node biopsy a viable

cellari metastatici:

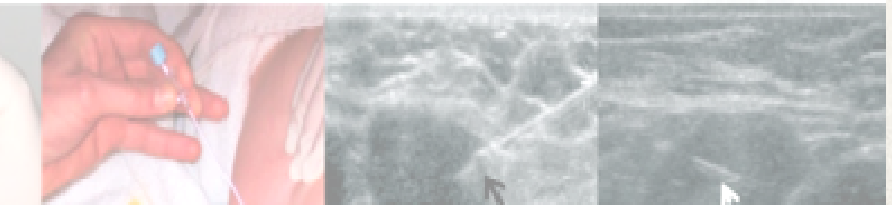
are l'accuratezza della stadiazione ascellare dopo
oterapia neoadiuvante in pazienti cN+ alla diagnosi

CCN 2017: indicato posizionamento di **clip o tatuaggio** di onodo metastatico per eventuale successivo reperimento.

MARI procedure (BJS,2010) – iodine-125 seed localization in the biopsied positive node → NAC → MARI surgery + ALND



MARI procedure (Ann Surg, 2016)

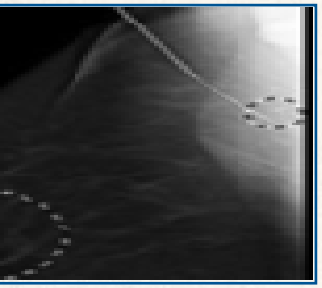


CLIP+WIRE (Ann Surg Onc, 2015) – clip placed in metastatic LN → NAC VS no NAC → SLNB or

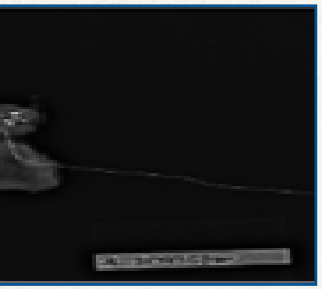
n°	IR (marked LN)
15	100%
100	**97%**
107	circa **97%** wire VS circa

cellari metastatici:

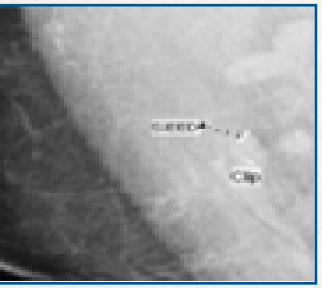
are l'accuratezza della stadiazione ascellare dopo
oterapia neoadiuvante in pazienti cN+ alla diagnosi

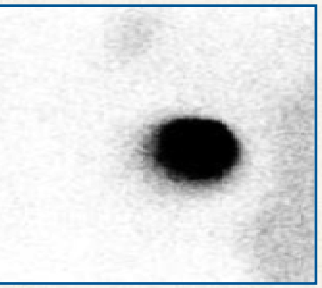


TAD - Targeted Axillary Dissection (JAMA Surg, 2015) – clip placed in metastatic LN → NAC → iodine 125 Seed or wire → SLNB or ALND



TAD – (JCO, 2016) – seed only





ACOSOG Z1071 – (ann Surg, 2016) – clip placed in metastatic LN → NAC → SLNB + ALND → after surgery radiografy of the SLNs resected / axillary dissection

n°	IR	FNR	L clip
12 (10+2)	100%	**0%**	8
208	97,6%	10,1% If only SLNB performed **1,4%** If TAD performed	7
484 no clip in LNmts 203	83% (IR SLN)	13% In pts with no clip in LNmts 19% clip in DA	75

nd DFS in cN1/2

lands Cancer Register 2005 - 2008
pective study (2005-2008) 1347 pz 944 pz follow

NAC FEC x 5 or TAC x 6 +trastuzumab in Her2+
SLNB + ALND

athological axillary nodal status after
nd SLNB + ALND

(ypN0)	22 %
or micromts (ypN1itc/mi)	3.8%
romts (ypN1-3)	74 %

osis of residual axillary diseases after juvant chemotherapy in clinically node-ve breast cancer patients:

ted tumor cell and micro stases carry a better nosis than ometastases

n s.

- globale
- ypN0

OS mean 7.4ys	DFS F
7,4	57,
8,3	71,

nd DFS in cN1/2

ective study 2007 – 2013 median fu 19.5 month (2-65)
ollogically-proven positive SLN → NAC

SLNB	266	ALND
LN positive or non found	187	negative
LN negative	79	positive

1 SLNB negative
0 SLNB + ALND negative

ifference among SLNB negative
SLNB+ALND negative
ALND negative

LNB negative :
nic recurrences
clavicular noder
y recurrence

axillary recurrence: no statistical differences

SLNB after NAC in patients with initial node-positive breast cancer may help identify down-staging to negative nodal status and reduce the surgical morbidity by avoiding the need for standard ALND

nd DFS in cN1/2

retrospective study
median follow up 61 months

cN0-1-2 → NAC → remained or became cN0 after NAC

LB only with SLN negative

NB + ALND with SLN positive

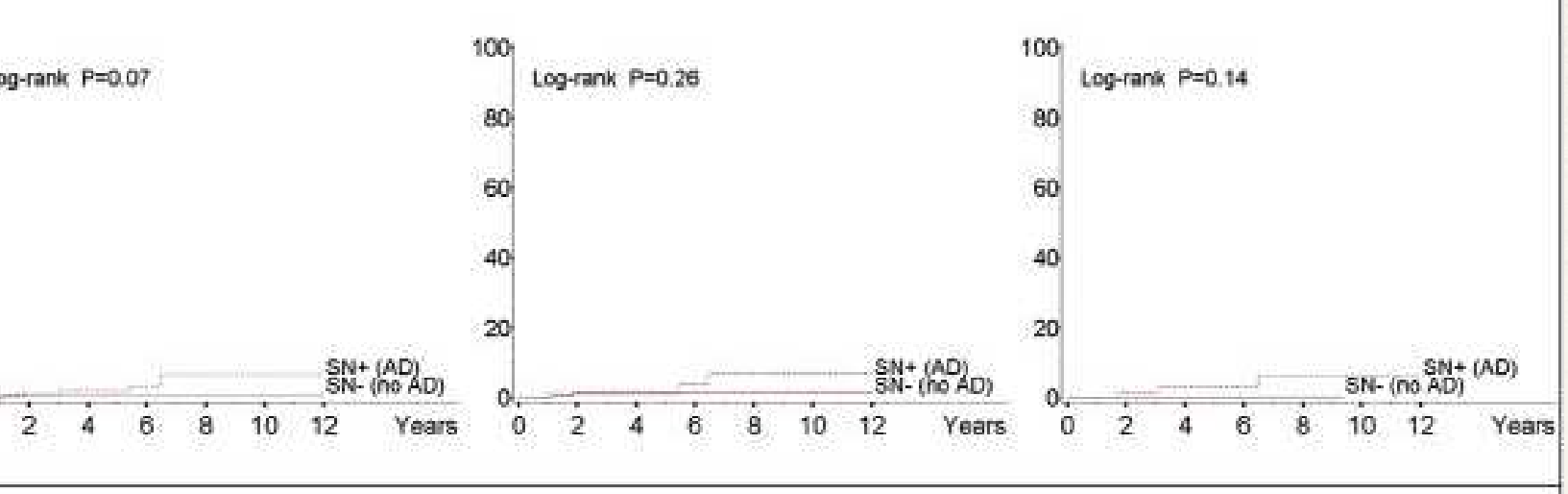
y failure

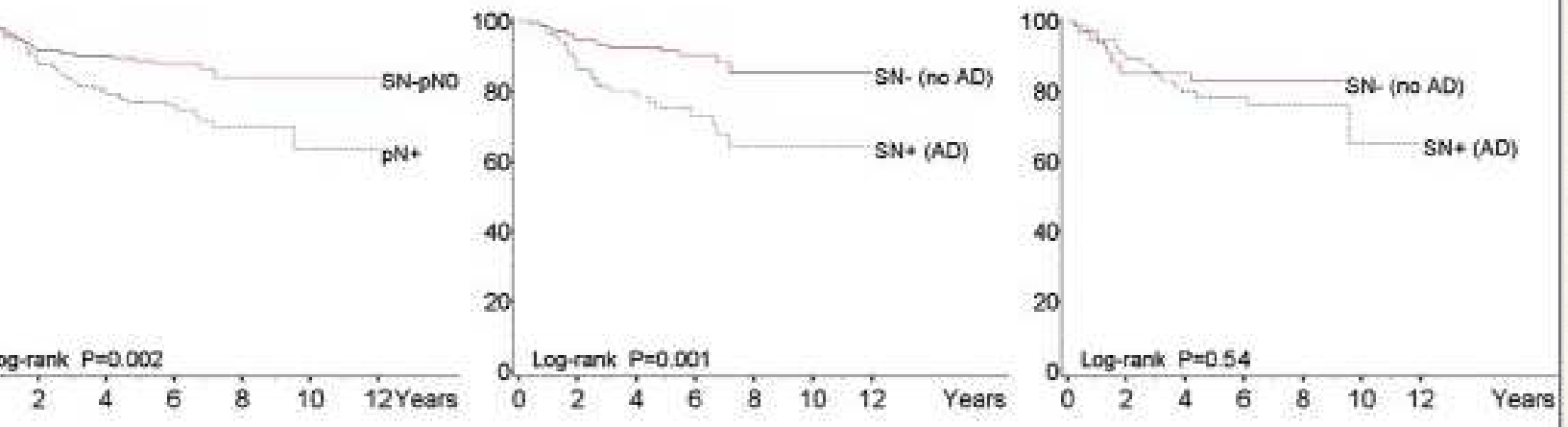
%) axillary deseased after a year
N0 →NAC → SLN negative (no ALND))

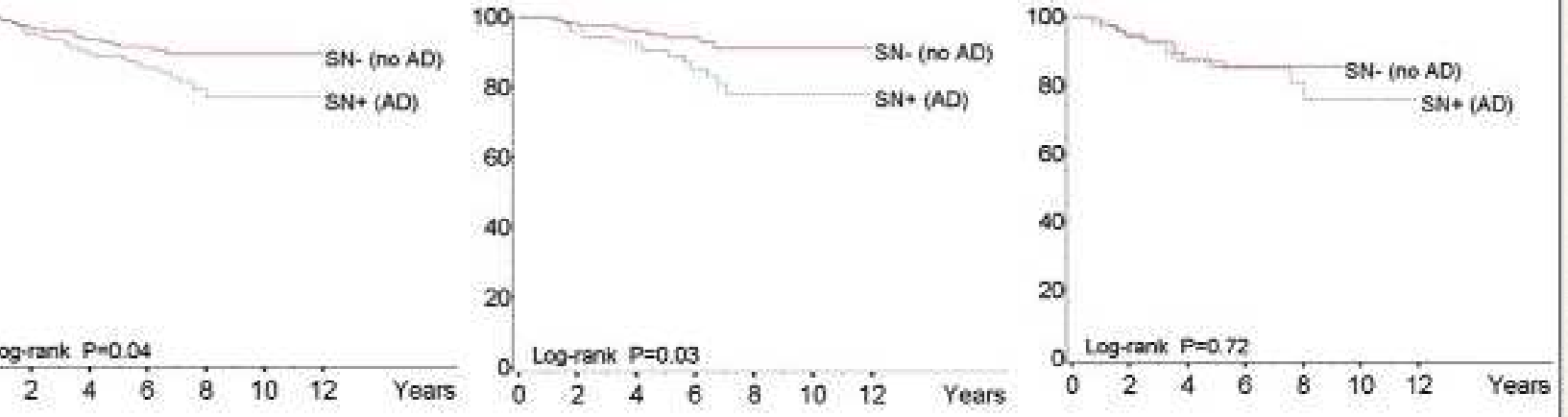
%) axillary desease after 12 years
cN1/2 →NAC → cN0 → SLN positive + ALND (12 positive nodes found)

5 yr DFS **5yr OS** **overall 90.7%**

cN0 81.1% cN1 73.4 p= 0.33 **cN0 93.3% cN1 86.3 p= 0**





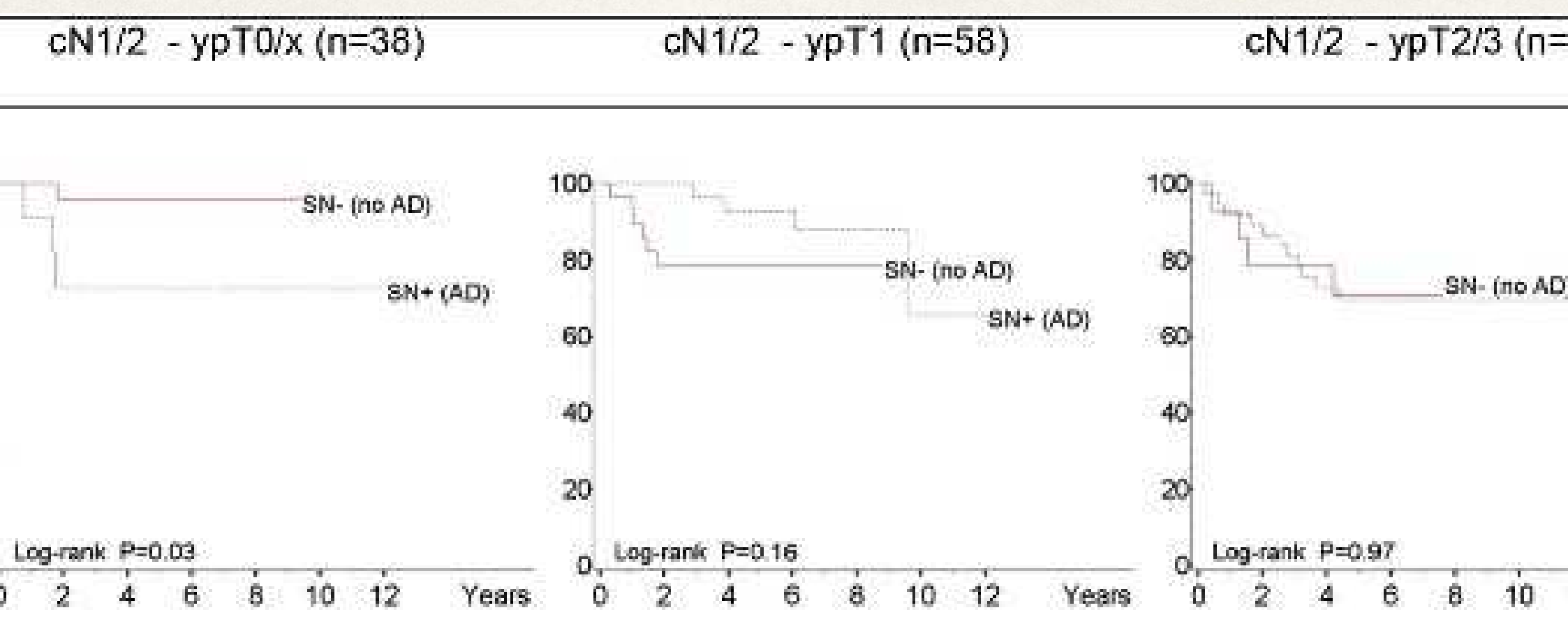


All patients and cN0:
outcome are better in SLN n
than in SLN pos.

cN1/2 :
outcomes for SLN neg and
patient did not differ signific

SLN neg status is not a
favorable prognostic factor

If SLN status no longer pr
outcomes, then a negative
probably no longer indicat
a negative axylla
(suggestin high FNR)



ypT1 and ypT2-3 subgroups, outcomes did not differ between SLN neg and SLN pos patients, s
e SLN no longer predicted better prognosis.

was significantly better in the SLN neg group for patient who had an excellent response to NAC
lary status had its normal prognostic value.

ce of residual breast disesase is such a strongly unfavorable prognostic factor that is overrides
g as a favorable prognostic factor? Or because the FNR is high

nd DFS in cN1/2

SLNB is acceptable in cN1-2 patients who become cN0 after NAC

Particularly in those with no residual disease in the breast

Because SLN status maintains its expexted prognostic role

But also in cases with residual desease, because ALND has no influence on outcomes

à della Salute e della
enza di Torino

2014-Settembre 2017:
e 115 pz sottoposte a CT neoadiuvante

ati i dati relativi alle pazienti operate fino a
bre 2016, per un FU mediano di 21 mesi (87
i

23 pz cN0
ALND
SLNB+ALND 2 mancata migrazione
2 LNS pos
3 SLNB

4 pz cN1-2:
5 ALND
4 SLNB + ALND 1 mancata migrazione

Luminal A	6	T1
Luminal B	28	T2
Her2 +	34	T3
TNBC	19	T4

à della Salute e della
enza di Torino

2014-Settembre 2017:
e …pz sottoposte a CT neoadiuvante

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i

IR 90.4 % 28/31

ownstaging ascellare in cN1/2

30/64 paz 47%

FU mediano 21 mesi (10-40 mesi)

3 recidive locoregionali

1 recidiva linfonodale,
1 recidiva mammaria seguita da mts,

EN QUESTION

ance of residual axillary desease after NAC

le of Regional Node Irradiation in the presence ary pCR

eed for ALND and RNI versus RNI alone in the presence sitive SLNB after NAC

SLN positive

ALND + XRT vs **XRT**

ALLIANCE A11202
mparision of axillary lymph node dissection with ary radiation for patients with node-positive breast cancer treated with chemotherapy

R trial - Eur J Surg Oncol, 2017

SLN negative

NO XRT vs **XRT**

NSABP B-51 / RTOG 1304:
Randomized phase III clinical trial evaluating the role of postmastectomy ch

v to decrease the FNR of SLNB
r NAC in cN1/2

g dual traces

oving ≥2 (3) SLNs

dering the definition of SLN metastasis after NAC to include ITC and micro

IAC marking of the cytologically proven LN positive

cting only patient with unsuspicious LN after NAC

staging of biopsy-proven node-positive patients with NAC could safety per
alone when the index node has been successfully retrieved at surgery
nodal deposits of any size continue to mandate completion ALND

Grazie per l’attenzione

ification by Iodine-125 (**AMELII**):
ibility trial and observational study
ne the knowledge of axillary status.

In progettazione

presso la nostra Breast Unit

ELII-1

re un metodo di marcatura dei linfonodi ascellari
astatici mediante posizionamento di seme
attivo individuabile con Gamma-camera durante
rvento chirurgico.

are il tasso di corrispondenza tra linfonodo
astatico e linfonodo sentinella evidenziato tramite
ia metodica.

ELII-2

azione del metodo di marcatura ed
ificazione del linfonodo metastatico dopo