



# Management of axilla «In **all** aspects»

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## Clinical negative axilla

ALND vs. Axillary RT  
N= 658, All BCS, < 3 cm tumor

15-year survival  
73,8 % vs 75,5 %  
Axillary recurrences  
1 % vs. 3 % (p= 0.04)



Clinically negative axilla SLNB is trustable and less toxic than ALND

NSABP B-32, ALMANAC, Milan

Ongoing trials SOUND < 2cm tm  
INSEMA < 5 cm  
USG only vs. SLNB

Brito, E cancer 2013

Louis-Sylvestre, JCO, 2004

# Axilla current management-Invasive cancer

- Clinical negative axilla (palpation, mamography/USG, possibly PET)
  - SLNB is current standard
- Clinical positive Axilla
  - ALND (at beginning or after neoadj. ypN+ (even micro)  
or
  - US Bx (clips for node) , try to avoid ALND in ypN0 (sn) (after neoadj.) in case of RT



# Every SN + has not same axillary burden

The probability to find additional lymph node at ALND

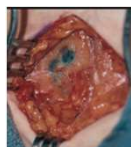
SLN status	ITC	Micro	Macro
	0 %	13 %	27 - 32 %
			<p><b>ECE</b> vs no ECE            20% vs 3 % had additional <math>\geq 4</math> positive nodes at ALND</p> <p>Pts with <b>ECE</b>            if the ECE &lt; 2mm vs &gt; 2mm            9 % vs <b>33 %</b> had additional <math>\geq 4</math> positive nodes at ALND</p>

Chu, Ann Surg, 1999

Galimberti,  
Lancet Oncol,  
2013

Gooch, Ann Surg Oncol, 2014

Giuliano, Ann Surg 2016



## Further tx after of Axilla 1-2 sentinel node + in cN0

4 RCT				
	IBCSG 23-01	ACOSOG Z0011	AMAROS	OTOASOR
No of ptnts	931	856	1425	474
Ptnt characteristics	Only micromet 95 % 1 node+ ITC + No ECE	Micro 40 % (ITC+) Macro 60 % Gross ECE – Matted node –	ITC 12% Micro 29% Macro 59% ECE ?	ITC 6 % Micro 34 % Macro 60 % ECE ?
Surgery	BCS Mastectomy 9 % BCS + PBI 19 %	BCS 100 %	BCS Mastectomy 11%	BCS Mastectomy 17 %
Randomization	ALND vs. SLND	ALND vs. SLND	ALND vs Axillary RT	ALND vs. Axillary RT
FU	9,7 years	9,3 years	6.1 years	8 years

# Further tx after of Axilla 1-2 sentinel node + in cN0



IBCSG 23-01	
No of ptnts	931 [target 1960]
Ptnt	Only micromet 95 % 1 node+ ITC + No ECE
Surg.	BCS Mastectomy 9 % BCS + PBI 19 %
Rand.	ALND vs. SLND
FU	9,7 years

ALND



SLND



Motor  
neuropathy  
9 % vs 3%

10 y DFS  
74.9 % vs 76.8 %

Sensory  
neuropathy  
19 % vs 13%

Lymphoedema  
13 % vs 4%

Low accrual !  
Mastectomy RT details !  
Breast tangents could incl. axilla !

1 micromet ALND is not  
necessary in case of breast RT

Galimberti, Lancet Oncol 2018



# Further tx after of Axilla 1-2 sentinel node + in cN0



## ACOSOG Z0011

No of ptnts	856 [Target 1900]
Ptnt	Micro 40 % (ITC+) Macro 60 % Gross ECE – Matted node –
Surg.	BCS 100 %
Rand.	ALND vs. SLND
FU	9,3 years

ALND



SLND



Med FU 9.3 years

10 y OS  
83,6 % vs 86,3 %

10 y DFS  
78,2 % vs 80,2 %

Ten year LRR 6,2 %

Ten year LRR 5,3 %

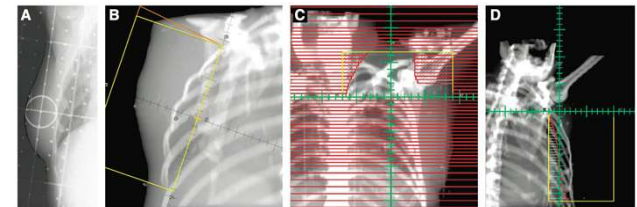
Between 5 - 10 y reg rec  
0 vs 1

228 patients' detailed RT fields:

- 104/389 (26.7%) ALND
  - 61 of 104 (59%) received some form of lymphatic RT
    - SCV n=22 (21%)
    - PAB (posterior axillary boost) n=6 (6%)
    - High tangents n=33 (32%)
- 124/404 (30.7%) SLND
  - 73 of 124 (59%) received some form of lymphatic RT
    - SCV n=21 (17%)
    - PAB n=12 (10%)
    - high tangents n=40 (32%)

Major protocol violation

Major protocol violation



60 % of both arm recieved some form of lymphatic RT

Jagsi, JCO, 2014      Guiliano, JAMA, 2017



# Further tx after of Axilla 1-2 sentinel node + in cN0



**Mastectomy**  
26 % in ALND arm  
42 % in Ax RT arm  
also recieved CWRT

5 y axillary recurrence rates  
0.54 % vs 1.03 %

Less lymphedema  
with Axillary RT

	AMAROS
No of ptnts	1425
Ptnt	ITC 12% Micro 29% Macro 59% ECE -
Surg.	BCS Mastectomy 11%
Rand.	ALND vs Axillary RT
FU	6.1 years



# SLNB in special circumstances-1

- DCIS
  - Pure DCIS SLNB is not necessary
  - If biopsy / excision showed microinv
  - mastectomy due to ext DCIS SLNB indicated
- Multi-focal / multi-sentric tumor
  - Meta-analysis 96 % Ident. Rate  
7.7 % FNR

# SLNB in special circumstances-2

- SLNB for previously operated cases

- 692
  - 301 after prev. SLNB
  - 361 after ALND
  - 30 without any surg

- ID rate 65,3 %
  - 80 % prev SLNB
  - 52 % prev ALND

- Aberrant drenage 43 %
  - 69 % prev ALND
  - 17 % prev SLNB

Not a standard approach but  
could give useful info esp.  
prev SLNB cases

# SLNB in special circumstances-3



- SLNB after neoadjuvant systemic chemotherapy

Study	Population cN1-N2	Biopsy required	cN0 post NAC	Identification rate	False-negative rate
SENTINA	592	No *	100% *	80%	14%
ACOSOG Z1071	689	Yes	83%	93%	13%
SN FNAC Study	153	Yes	Unknown *	88%	13% **

\* Ultrasound performed in all patients

\*\* False-negative rate excluding immunohistochemically detected isolated tumor cells

Abbreviations: SLNB, sentinel lymph node biopsy; NAC, neoadjuvant chemotherapy; SENTINA, Sentinel Neoadjuvant; ACOSOG Node Biopsy Following Neoadjuvant Chemotherapy

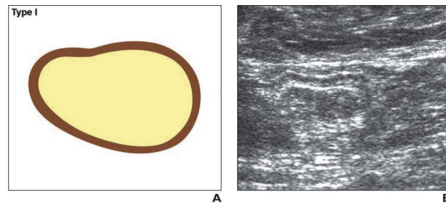
# SLNB in special circumstances-3

- SLNB after neoadjuvant systemic chemotherapy

## Axillary Ultrasound Identifies Residual Nodal Disease After Chemotherapy: Results From the American College of Surgeons Oncology Group Z1071 Trial (Alliance)

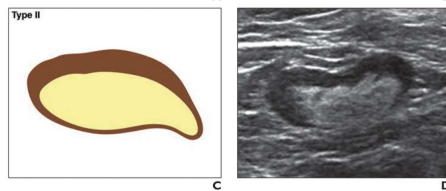


Tip I no visible cortex

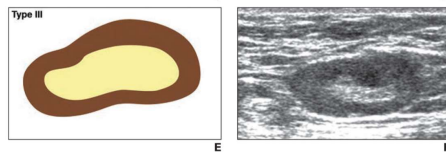


Type I-II  
56 % +

Tip II, hypoecho cortex < 3 mm

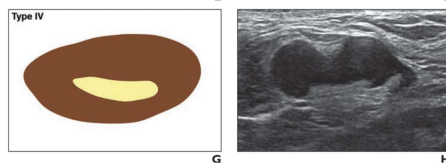


Tip III, hypoecho cortex > 3 mm



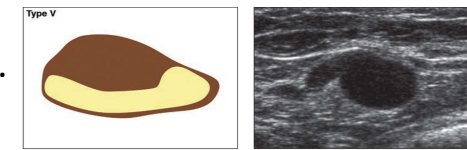
Type III  
59 % +

Tip IV, Generalized lobulated hypo ech cortex



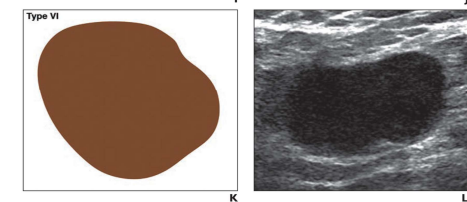
Type IV  
79 % +

Tip V focal hypo cort. lobulation



Type V  
68 % +

Tip VI Total hypo with no hilum



Type 6  
80 % +

# SLNB in special circumstances-3

- SLNB after neoadjuvant systemic chemotherapy



## SLNB False-Negative Rate

Study	Number SLNs removed			P value	Tracer used		P value
	1	2	≥3		Single tracer	Dual tracer	
SENTINA	24%	19%	7%	0.008	16%	9%	0.15
ACOSOG Z1071	-	21%	9%	.007	20%	11%	.05
SN FNAC study*	18%	5%**			16%	5%	

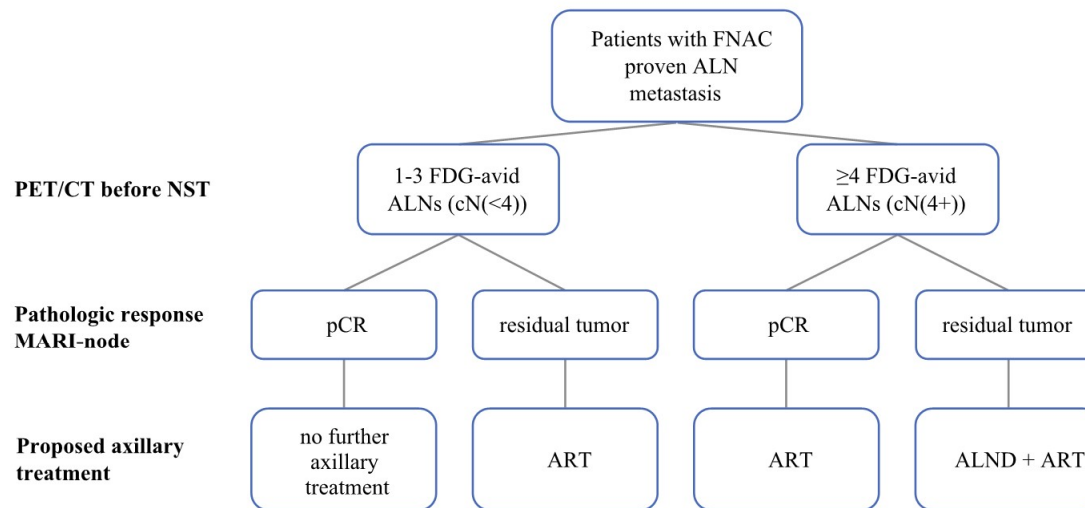
The current standard is ALND in all sn + patients



Ongoing trial  
ALLIANCE A011202  
(kind of neoadj Z0011 )  
ypN+ (sn)  
ALND vs Axillary RT

Plewskie, JAMA Oncol, 2017

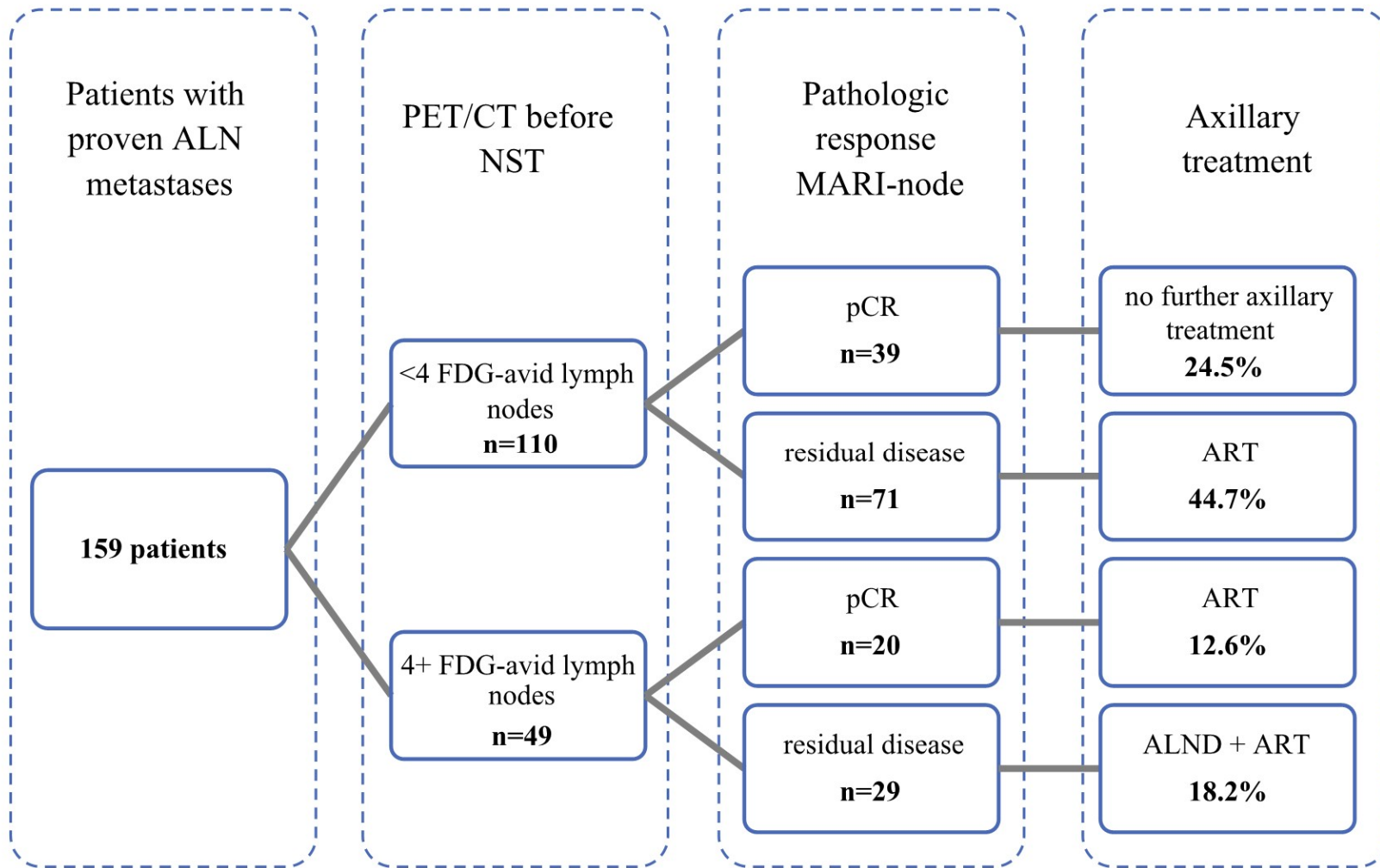
# Major Reduction in Axillary Lymph Node Dissections After Neoadjuvant Systemic Therapy for Node-Positive Breast Cancer by combining PET/CT and the MARI Procedure



**FIG. 1** Axillary treatment protocol at the Netherlands Cancer Institute for patients presenting with axillary disease before neoadjuvant systemic therapy (NST). FNAC, fine-needle aspiration cytology; ALN, axillary lymph node; PET/CT, positron emission tomography combined with computed tomography; MARI, marking

axillary lymph nodes with radioactive iodine seeds; pCR, pathologic complete response; ALND, axillary lymph node dissection; ART, axillary radiotherapy





Current standard is RT

Current standard is ALND + RT

Van der Noordoaa, Ann Surg Oncol, 2018

# Further tx after of Axilla 1-2 sentinel node + in cN0

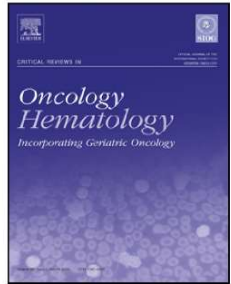


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## Critical Reviews in Oncology/Hematology

journal homepage: [www.elsevier.com/locate/critrevonc](http://www.elsevier.com/locate/critrevonc)



Adjuvant nodal radiotherapy in the era of sentinel node biopsy staging of breast cancer: A review of published guidelines and prospective trials and their implications on clinical practice



Yazid Belkacemi <sup>a,\*</sup>, Pauline T. Truong <sup>b</sup>, Atif J. Khan <sup>c</sup>, Fady Geara <sup>d</sup>,  
Alphonse G. Taghian <sup>e</sup>, Meena S. Moran <sup>f</sup>



# Lymphatic RT in adjuvant setting

Results of published trials evaluating nodal irradiation according to extent of axillary nodal involvement.

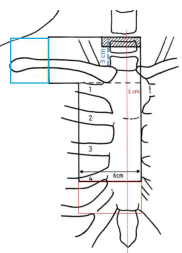
Criteria	Randomized trials of nodal irradiation			
Trials	MA20 trial ( <a href="#">Whelan et al., 2015</a> ) BCS N = 1832	EORTC ( <a href="#">Poortmans et al., 2015</a> ) BCS/TM * N = 4004	French trial TM ( <a href="#">Hennequin et al., 2013</a> ) N = 1334	German Metaanalysis N = 7170 ( <a href="#">Budach et al., 2013</a> )
Inclusion criteria and radiation parameters in the trials				
RT volumes	WBI + IMC + SCN + ALN vs. WBI alone	WBI/CWI + IMC + SCN vs. WBI/CWI alone	All patients had CWI + SCN and randomized to IMC RT vs no IMC Rt	-
Dose to RNI	Breast and IMC: 50 Gy in 25 fr (80% of the dose to IMC) # SCN and ALN: 45 or 50 Gy in 25 fr	IMC and SCN: 50 Gy in 25 fr	50 Gy in 25 fr to IMC	-
Benefit with RNI according to pN status				
Rate of pN0	10%	44%	25%	33%
Benefit in pN0	Unknown due to small sample	Benefit in Inner/central tumors	No Benefit	<i>Benefit: DFS, DMFS, OS</i>
Micrometastasis in SLN	ND	ND	ND	-
Macrometastasis in SLN	Unknown among pN1a (85%)	Unknown among pN1a (43%)	Unknown among pN1a (75%)	-
Rate of pN+	90%	56%	75%	67%
Impact of RNI on outcome	Benefit:  - LRRFS - DFS, - DMFS - Trend for OS	Benefit:  - DFS - DMFS - Trend for OS	No Benefit	Benefit:  - DFS, - DMFS - OS

Belkacemi, Crit.Rev. Oncol/Hematol, 2017

ORIGINAL ARTICLE

### Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer

P.M. Poortmans, H. Struikmans, L. C. S. Marnitz, I. Barill N. Weidner, G. v H. Bartelink, and V



n Limbergen, V. Budach, gon, M. Valli, K. De Winter, .. Rodenhuis, H. Marsiglia, r, A. Kuten, R. Arriagada, IORTC Radiation Oncology ps\*

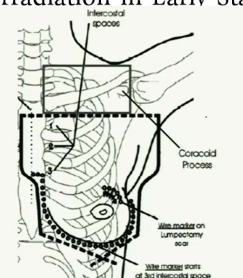
- Any Lung toxicity (fibrosis, dispne, pneumonia)
  - 4.3 % [LNI] – 1.3 % p < 0.0001
- Cardiac toxicity
  - 0,3 % [LNI] – % 0,4 p = NS
- Lymphedema
  - % 12 [LNI] – %10,5 p=NS
- No performance impairment with LNI

Poortmans, NEJM, 2015

### The NEW ENGLAND JOURNAL of MEDICINE

### Regional Nodal Irradiation in Early-Stage Breast Cancer

Timothy J. Whelan, B.M., B.Ch Boon H. Chua, M.B., B.S., Ph.D., Ab Pierre Rousseau, M.D., Andre Maureen C. Nolan, M.D., Kathleen I. Pritchard, M.D., Kai Bingshu E. Chen, Ph.D



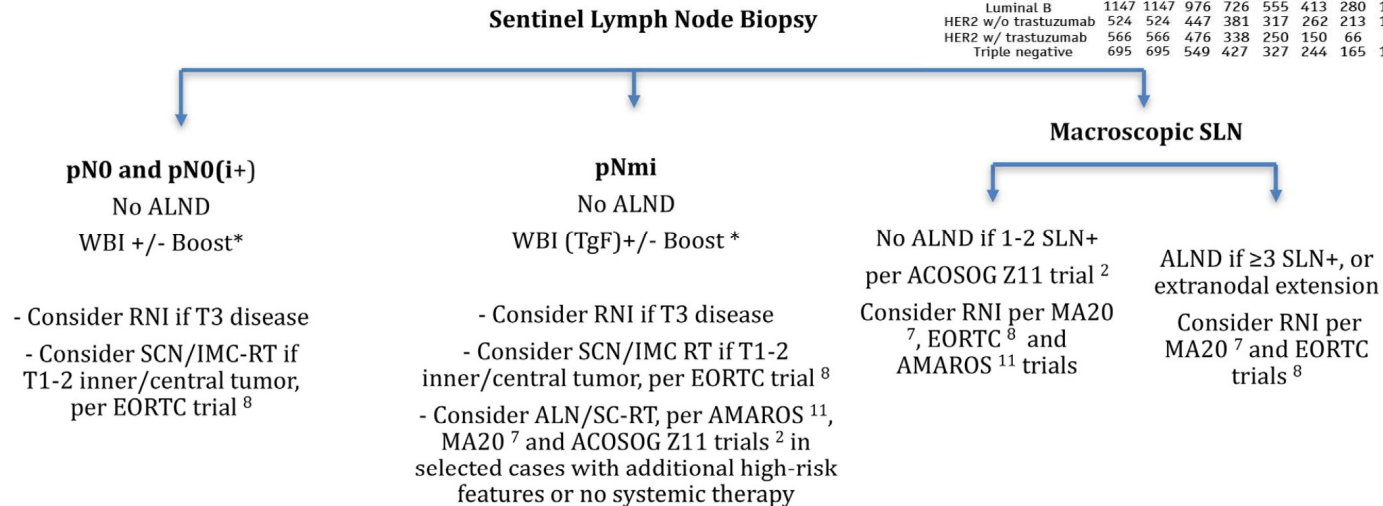
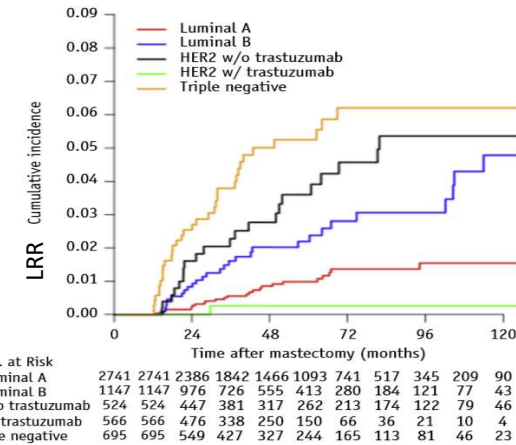
Courtesy T. Whelan & I. Olivetto

ar, M.D., Ida Ackerman, M.D., I.B., B.S., Ph.D., Julia R. White, M.D., chul, M.D., Susan Chafe, M.D., David R. McCready, M.D., Judy-Anne W. Chapman, Ph.D., 0 Study Investigators\*

- Pneumonia
  - 1.2 % [LNI] – 0,2 % p < 0.01
- Cardiac toxicity
  - % 0,4 [LNI] – % 0,9 p = NS
- Lymphedema
  - 8,4 % [LNI] – 4,5 % p=0,001

Whelan, NEJM, 2015

# Further tx after of Axilla 1-2 sentinel node + in cN0



**Fig. 1.** Represents the main options and indications according to nodal involvement and data reported in surgical and radiotherapy randomized trials. ALND: axillary lymph node dissection; SLN: sentinel lymph node; RNI: regional nodal irradiation; pN: pathologic nodal status; WBI: whole breast irradiation; TgF: tangential fields; ST: systemic therapy; SCN-RT: supraclavicular nodal radiotherapy; IMC-RT: Internal mammary chain radiotherapy, ALN/SC-RT: axillary node radiotherapy (including undissected axilla level III).

\*Chest wall irradiation indications should be discussed with consideration of individual patients' clinical and pathologic prognostic factors. 2: Giuliano, A.E., Ann. Surg.; 7: Whelan, T., N. Engl. J. Med.; 8: Poortmans, P., N. Engl. J. Med.; 9: Budach, W., Radiother. Oncol.; 11: Donker, M., Lancet Oncol.

# Conclusion

- cN0 axilla

ALND  $\approx$  Axillary RT

ALND  $\approx$  Sentinel lymph node bx (less toxic) for T1-2 tumor

pN0 lymphatic RT can be considered in selected cases (i.e. T3 cases, inner/centr.)

USG only vs. SLNB (INSEMA and SOUND trials) arguably to decrease RT indications 😊

pN1(sn) most cases had benefit some form of RT

After NAC the SLNB (>2 SN, dual tracer)

if ypN+ ALND indicated --- ALLIANCE A011202 (kind of Neoadj. Z11)

--- NSABP B51 for RT field design after NAC

--- More axilla could be spared MARI ? Need longer FU

