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## **SUNY – YÖK Joint International Public Health and Medical Sciences Conference**

**“Innovative Cancer Research Translating Clinical and Population Research into New  
Approaches to Treatment and Enhanced Prevention, Early Detection, and Quality Care”**

**April 15 – April 17, 2015**

# Locoregional Breast Cancer Treatment after neoadjuvant chemotherapy

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**İstanbul Üniversitesi**  
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**İstanbul Üniversitesi**  
**ONKOLOJİ ENSTİTÜSÜ**

Istanbul - 1982

# NAC in Istanbul University Institute of Oncology

- About 30% of newly diagnosed non-metastatic breast cancer cases treated with NAC
- Clinic and Pathologic N +
- Pts w/ large tumors desiring BCS
- T4 cases



GBG

GERMAN  
BREAST  
GROUP



Heilung  
durch ...

Trials on neoadjuvant (primary, preoperative) chemotherapy

clinically T $\geq$ 2cm, Sono $\geq$ 1cm; N0-2, M0 incl. T4	▪ <b><u>GeparSepto</u></b> : Paclitaxel-EC vs nab-Paclitaxel-EC
clinically T $\geq$ 2cm, Sono $\geq$ 1cm; N0-2, M0 excl. T4	▪ <b><u>Genevieve</u></b> : Triple Neg or Luminal B/Her2 normal: Cabazitaxel vs. Paclitaxel
Sono >1,5cm; M0 incl. T4	▪ <b><u>NeoPHOEBE</u></b> only Her2+: Trastuzumab +/- BKM 120
Mamma-Ca duringr <b>Pregnancy</b> : register retrospectivly and prospectivly: <u>BCP</u> Mamma-Ca in <b>Males</b> : <u>MALE</u>	

# NAC – pathologic change

- NAC changes
  - The pathologic extent 80–90 %
  - Pos. Lymph node (s) convert to neg. 20–40 %
    - Her-2 positive tx with trastuzumab 70 %

Hoffman, Lancet Oncol, 2012

Rastogi, JCO, 2008

Dominici, Cancer, 2010



# Can NAC change the local tx?

- Surgery after NAC
  - Breast conserving surgery could be done [init. Mastectomy candidates]
  - Sentinel lymph node dissection
    - Could be done after NAC [tc99m+blue dye and 2 nodes should removed]
    - But still is not an accepted alternative to ALND [ALLIANCE A011202]
- Radiotherapy after NAC
  - Could lymphatic radiotherapy be omitted in conserved breast?
  - Could Postmastectomy radiotherapy be omitted ?

# Source of information

- Retrospective studies mostly from MDACC
- Combined analyses NSABP B18-B27
  - Prospective cohort





# Predictors of Locoregional Recurrence After Neoadjuvant Chemotherapy: Results From Combined Analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27

*Eleftherios P. Mamounas, Stewart J. Anderson, James J. Dignam, Harry D. Bear, Thomas B. Julian, Charles E. Geyer Jr, Alphonse Taghian, D. Lawrence Wickerham, and Norman Wolmark*

- Combined analysis of Prospective cohort
  - Neoadjuvant
  - No PMRT
  - No lymphatic RT for BCS
  - ?Receptor status?
  - ?Grades?

n

**Table 1.** Distribution of Selected Patient and Tumor Characteristics in NSABP B-18 and B-27 at Random Assignment (before neoadjuvant chemotherapy)

Characteristic	NSABP Trial (%)	
	B-18 (neoadjuvant AC arm) (n = 742)	B-27 (all three arms) (n = 2,346)
Patient age at random assignment, years		
< 50	51	57
≥ 50	49	43
Clinical tumor size at random assignment, cm		
cT1 (≤ 2.0)	28	14
cT2 (2.1-5.0)	59	57
cT3 (> 5)	13	29
Clinical nodal status at random assignment		
cN0	73	70
cN1	27	30
Combined clinical stage at random assignment		
cT1-2N0	65	51
cT1-2N1	22	20
cT3N0	8	19
cT3N1	5	10

Abbreviations: AC, doxorubicin/cyclophosphamide; NSABP, National Surgical Adjuvant Breast and Bowel Project.



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- Median follow-up: 11,7 years
- Mastectomy + No PMRT (n=1,947)  
LRR 12.6% (9.0% local; 3.6% regional)
- Lumpectomy plus breast only XRT (n=1,100)  
LRR 10.3% (8.1% local; 2.2% regional).

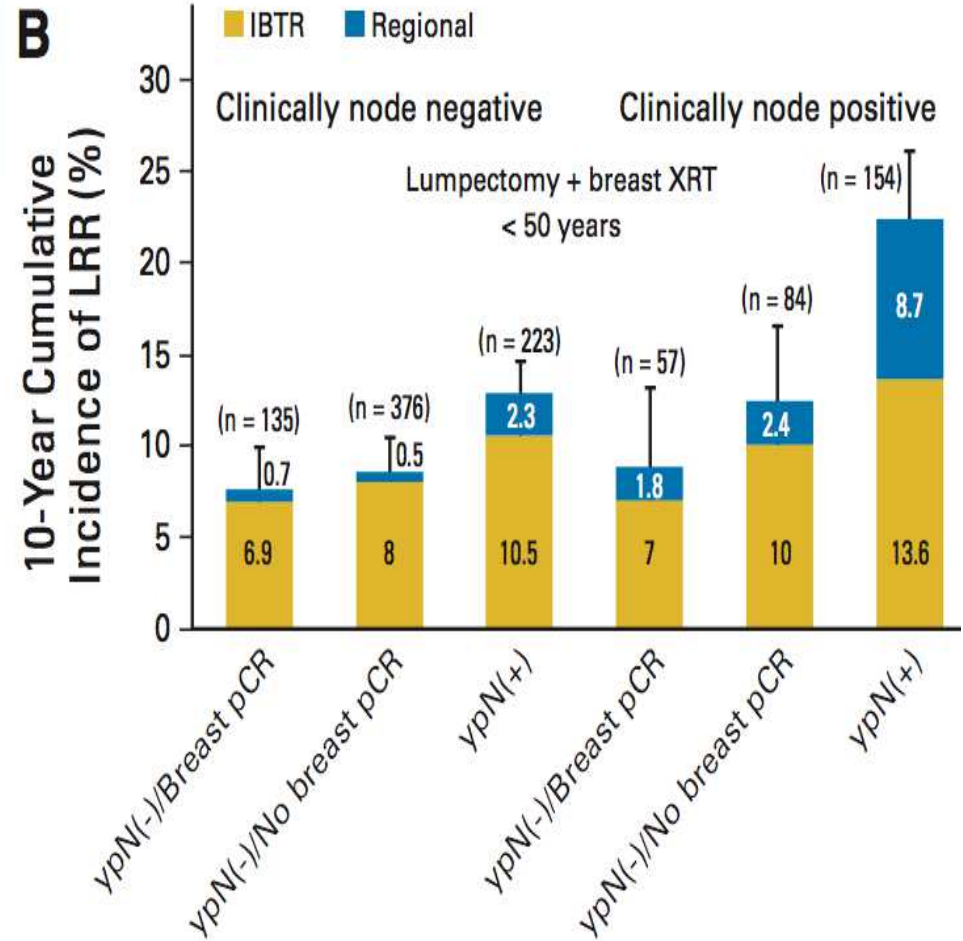
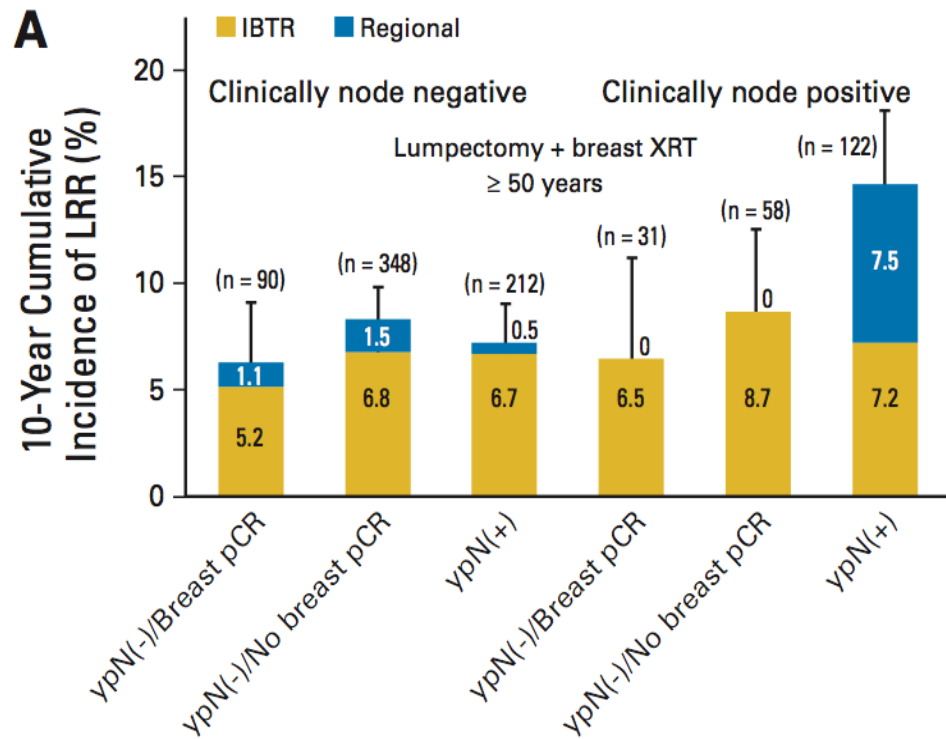




# The omission of lymphatic RT in BCS



- NSABP B18-B27
- Prospective



# The omission of lymphatic RT in BCS



Ten year LRR with preoperative chemotherapy and with Post BCS plus only breast RT %		
	<u>≥ 50 years</u>	
	cN0	cN1
ypN(1-3+)	5.9	11.4
ypN(4+)	11.3	19.6
	< 50 years	
ypN(1-3+)	12	21.1
ypN(4+)	15.6	24



# No PMRT after NAC

## Stage IIA [cT0-1 N1 or T2N0]

- cT2N0
- MDACC
- pCR (no inv. dis.) 0 % LRR without PMRT

McGuire, IJROBP, 2007

Settle, IJROBP, 2009





# No PMRT after NAC

## Stage IIA [cT0-1 N1 or T2N0]

- cT1N1
- MDACC
- <35-40
- LVSI
- ECE
- TN

Absence of these      ypN1-3 + 4-5%LRR





# No PMRT after NAC Stage II

- cT1-2N0-1
- MDACC n=181 no PMRT

## 5 y LRR

- ypN0 1 %
- ypN1-3+ 5,4 %
- ypN  $\geq$  4 + 20 % **p=0,03**
  
- LVSI -- 2 %
- LVSI + 15,4 % **p=0,006**



# No PMRT after NAC Stage IIA

- cT1-2N0
- **NSABP trial**
  - 10 y LRR
  - ypN0 6,5 %
  - ypN1-3+ 11,2 %
  - ypN  $\geq$  4 + 11,1 %





# No PMRT after NAC

## Stage IIB [cT2N1 / T3N0]

- cT2N1 / T3N0
- <35 y all pts should receive PMRT



# No PMRT after NAC

## Stage IIB [cT2N1 / T3N0]

- cT1-2N1

- **NSABP trial**

10 y LRR without PMRT

- pCR 0 %
- ypN0 (no breast pCR)+ 10,8 %
- ypN1-3+ 14,4 %
- ypN  $\geq$  4 + 19,5 %



# No PMRT after NAC

## Stage IIB [cT2N1 / T3N0]

- cT3N0

- MDACC

- 5 y LRR

with PMRT

4 %

Without PMRT

24 %

$p < 0.001$





# No PMRT after NAC

## Stage IIB [cT2N1 / T3N0]

- cT3N0

- NSABP

10 y LRR without PMRT

- pCR 6,2 %
- ypN0 (no breast pCR)+ 10,6 %
- ypN1-3+ 10,6 %
- ypN  $\geq$  4 + 19,5 %



# No PMRT after NAC

## Stage IIIA [cT3N1 / T0-3N2]

- stage III
- MDACC

• pCR	with PMRT	Without PMRT	
• 10 y LRR	7,3 %	33,3 %	p=0,04
• 10 y DMFS	87,9 %	40,7 %	p=0,0006
• 10 y OS	77 %	33,3%	



# No PMRT after NAC

## Stage IIIA [cT3N1 / T0-3N2]

- cT3N1

- NSABP

10 y LRR without PMRT

- pCR 0 %
- ypN0 (no breast pCR)+ 9,2 %
- ypN1-3+ 14,7 %
- ypN  $\geq$  4 + 27,2 %





# No PMRT after NAC Stage IIIB [cT4 N0-2]

- MDACC

5 y LRR without PMRT

42 %



# St Gallen 2015

## Neo-Adjuvant Chemotherapy

Approach to RT after neo-adjuvant therapy:

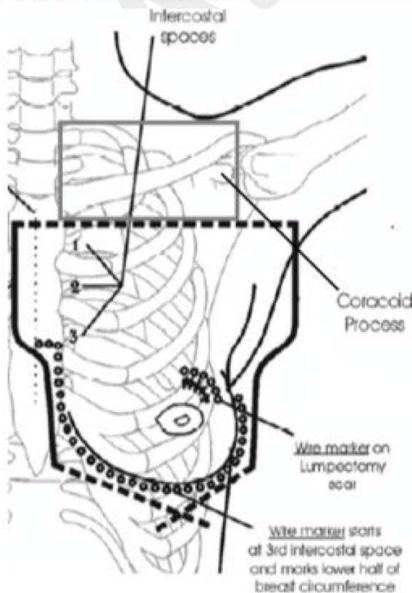
- Should follow the stage before neo-adjuvant therapy? **68.3/22/9.8** 1Y/ 2N/ 9A
- Should follow the stage after neo-adjuvant therapy? 24.4/**65.9**/9.8 1Y/ 2N/ 9A



# The omission of lymphatic RT in BCS -Conclusion

## MA 20: Methods

### WBI + RNI



Courtesy T. Whelan & I. Olivetto

Contact at jyarnold@icr.ac.uk for permission to reprint and/or distribute.

FU: 62 months

DFS [HR, **0.68**; p=**0.003**

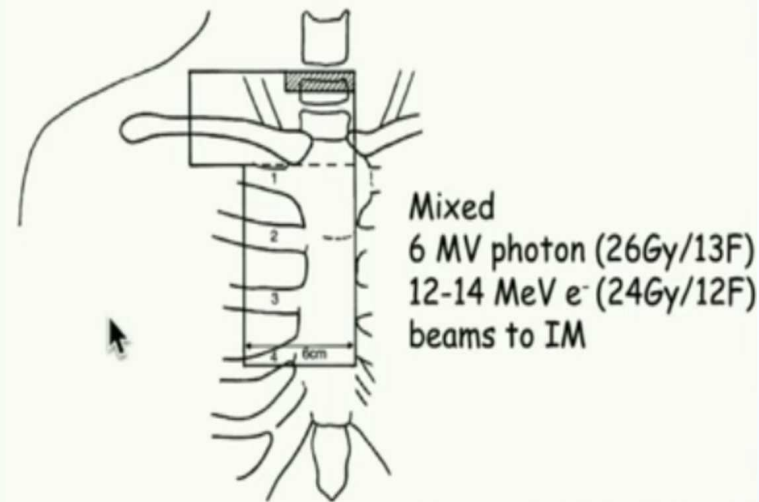
5y risk 89.7% - 84%]

OS [HR, **0.76**; p=**0.07**

5y risk 92.3% 90,7%]

San Antonio Breast Cancer Symposium - December 9-12, 2014

## Recommended MS-IM RT Technique in EORTC Trial



Poortmans, EJC, 2003, 39; 2035-42

FU: 130 months

OS [HR, **0.87**; p=**0.055**

10y risk 82.3% 80,7%]

DFS [HR, **0.89**; p=**0.044**

10y risk 72.1% - 69.1%]

MFS [HR, **0.86**; p=**0.02**

10y risk 78% - 75%]

How /  
should  
these  
results  
from  
adjuvant  
studies  
affect  
NAC ?

Courtesy of Yarnold, SABC 2014

# Conclusion

- Patients with clinical T3-T4 tumors, pathological non-complete responders in the axilla, and younger patients (<35) with cT2N1 or worse disease should be treated with RT according to retrospective data.
- Selected patients (cT1-2 cN1 and >40 years old) with a pathological complete response (ypT0, ypTis, ypN0) after NAC could perhaps be followed without PMRT and without regional irradiation in the BCS



# Conclusion

- NSABP B51/Radiotherapy Oncology Group (RTOG) 1304 study, the randomized study of omission the PMRT and lymphatic RT in BCS
- SLNB + radiotherapy vs. ALND+RT after NAC. Phase 3 randomized (ALLIANCE A011202) is still accruing pts.

