

VI ZOOM Journal Club 2016

Bologna, 17 Febbraio 2017

NH Hotel De La Gare



IV Sessione - Radioterapia dopo CT neoadiuvante

Moderatori: Marina Guenzi, Alessandra Huscher

15.00 Rapporteur: Alessandra Fozza

15.15 Discussant: Icro Meattini

15.30 Caso clinico: Antonino Daidone

CT neoadjuvante

- ✓ NAC can permit inoperable cases (clinical stage IIIB-C) to become operable
- ✓ NAC provides an in vivo assessment of the tumor's response to chemotherapy agents and is an avenue to test the efficacy of new systemic agents in clinical trial settings
- ✓ Achieving a pCR (eradication of all invasive disease in the breast and in the lymphnodes) is prognostic for survival. The magnitude of this benefit is strongest in women with triple-negative and HER2positive hormone receptor-negative breast cancers

Radioterapia dopo CT neoadiuvante

One of the most challenging problems facing breast cancer radiation oncologists to day is deciding **which patient** with breast cancer treated with NAC followed by surgery (BCS or mastectomy) **will benefit from locoregional RT** (PMRT and NODAL RT)

Radioterapia dopo CT neoadiuvante

2016

Chemotherapy response and survival of inflammatory breast cancer by hormone receptor- and HER2-de subtypes approximation: an analysis from the Database

The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer

Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

sis

The role of postmastectomy radiotherapy in clinically node-positive, stage II-III breast cancer patients with pathological negative nodes after neoadjuvant chemotherapy: an analysis from the NCDB

Clinical outcomes according to molecular subtypes in stage II-III breast cancer patients treated with neoadjuvant chemotherapy followed by surgery and radiotherapy

Local radiotherapy alone following neoadjuvant chemotherapy and surgery in combined clinical stage II and III breast cancer

Patterns of Local-|
Following Neoadju
Cancer: Results From

Lymphovascular space invasion and lack of downstaging after neoadjuvant chemotherapy are strong predictors of adverse outcome in young women with locally advanced breast cancer

ACU

Body mass index and treatment outcomes

Evaluation of mastectomy with irradiation of latissimus dorsi breast reconst

following neoadjuvant therapy in women aged 45 y or younger: Evidence from a historic cohort

Primary systemic treatment and concomitant low dose radiotherapy for breast cancer: Final results of a prospective phase II study

Radioterapia dopo CT neoadiuvante

1) NACT → MASTECTOMIA → ruolo RT LOCOREGIONALE

2) NACT → CH → RT: risultati per SOTTOTIPI MOLECOLARI

3) NACT → CH con SLNB + ALND → RT: variability in practice

Radioterapia dopo CT neoadiuvante

1) NACT → MASTECTOMIA → ruolo RT LOCOREGIONALE

2) NACT → CH → RT: risultati per SOTTOTIPI MOLECOLARI

3) NACT → CH con SLNB + ALND → RT: variability in practice

The role of postmastectomy radiotherapy in clinically node-positive, stage II-III breast cancer patients with pathological negative nodes after neoadjuvant chemotherapy: an analysis from the NCDB

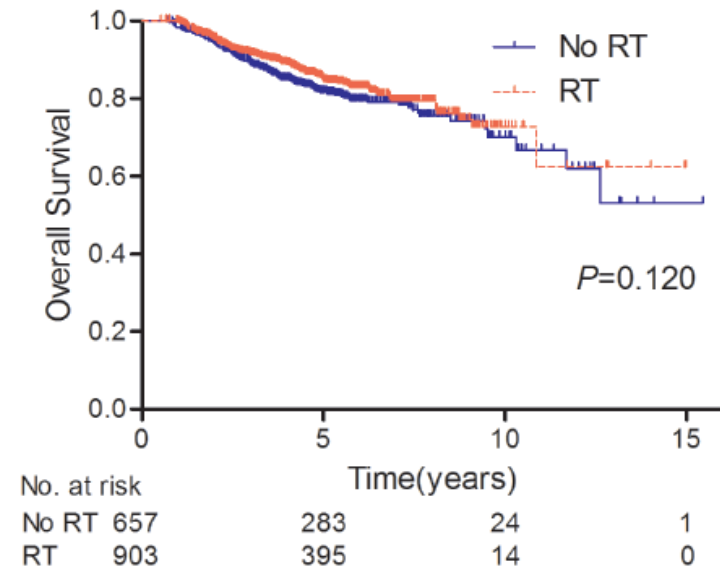
Jieqiong Liu^{1,2,*}, Kai Mao^{3,4,*}, Shuai Jiang⁵, Wen Jiang⁶, Kai Chen^{1,2}, Betty Y.S. Kim⁷, Qiang Liu¹ and Lisa K. Jacobs²

1560 cN+ stage II-III breast cancer pts: NAC and mastectomy → ypN0 (1998-2009 NCDB)

- ✓ Effects of **PMRT** on **OS** for the **entire cohort** and **multiple subgroups analysis**
- ✓ Imputation and propensity score matching as sensitivity analyses to minimize biases

903 (57.9%) PMRT
657 (42.1%) NO PMRT
Median FU 56 months

**5-year OS rates
not significantly different**



(84.6% for PMRT vs 81.7% for NO PMRT, $P = 0.120$, HR 1.57, 95% CI 0.839-2.943)

The role of postmastectomy radiotherapy in clinically node-positive, stage II-III breast cancer patients with pathological negative nodes after neoadjuvant chemotherapy: an analysis from the NCDB

PATIENT CHARACTERISTICS

Table 1: Characteristics of the whole study population (n = 1560)

Characteristics	No PMRT (n = 657)		PMRT (n = 903)		P
	No.	%	No.	%	
Age, years					NS
Median (range)	50 (20-86)		50 (22-88)		
≤40	143	21.8	203	22.5	
41-60	386	58.7	545	60.3	
>60	128	19.5	155	17.2	
Race					NS
White	494	75.2	693	76.7	
Black	121	18.4	162	17.9	
Asian or other	42	6.4	48	5.3	
Insurance status					NS
Not insured	31	4.7	49	5.4	
Private insurance	426	64.8	620	68.7	
Public insurance	186	28.3	227	25.1	
Unknown	14	2.1	7	0.8	
Chalson/Devo score					<0.001
0	552	84.0	797	88.3	
1	44	6.7	83	9.2	
2	10	1.5	7	0.8	
Unknown	51	7.8	16	1.8	
Year of diagnosis					<0.001
1998-2003	90	13.7	56	6.2	
2004-2009	567	86.3	847	93.8	

Histological type					
Ductal	540	82.2	718	79.6	NS
Lobular	50	7.6	61	6.7	
Other	67	10.2	124	13.7	
No. of nodes examined					0.009
Median (range)	11 (1-46)		12 (1-46)		
1-10	317	48.2	379	42.0	
>10	320	48.7	507	56.1	
Unknown	20	3.0	17	1.9	
Clinical T-stage					<0.001
T1	79	12.0	55	6.1	
T2	276	42.0	254	28.1	
T3	170	25.9	279	30.9	
T4	132	20.1	315	34.9	
Clinical N-stage					<0.001
N1	530	80.7	651	72.1	
N2	90	13.7	161	17.8	
N3	37	5.6	91	10.1	
Clinical AJCC stage					<0.001
II	325	49.5	231	25.6	
III	332	50.5	672	74.4	
Pathologic T-stage (after NAC)					NS
T0/Tis	277	42.2	399	44.2	
T1	221	33.6	315	34.9	
T2	159	24.2	189	20.9	
Histologic grade					NS
Well or moderately	161	24.5	199	22.0	
Poorly or undifferentiated	413	62.9	613	67.9	
Unknown	83	12.6	91	10.1	
ER*					<0.001
Negative	330	50.2	503	55.7	
Positive	208	31.7	331	36.7	
Unknown	119	18.1	69	7.6	
PR*					<0.001
Negative	379	57.7	563	62.3	
Positive	159	24.2	270	29.9	
Unknown	119	18.1	70	7.8	
Chemotherapy type					<0.001
Single-agent	13	2.0	4	0.4	
Multi-agent	588	89.5	881	97.6	
Unknown if single or multi-	56	8.5	18	2.0	
Hormone therapy					<0.001
No	449	68.3	539	59.7	
Yes	181	27.5	335	37.1	
Unknown	27	4.1	29	3.2	

The role of postmastectomy radiotherapy in clinically node-positive, stage II-III breast cancer patients with pathological negative nodes after neoadjuvant chemotherapy: an analysis from the NCDB

PMRT no difference in OS by MULTIVARIATE ANALYSIS

(PMRT vs no PMRT: HR 0.820, 95% CI 0.630-1.068)

Table 2: Multivariate analysis of OS for the whole study population (n = 1560)

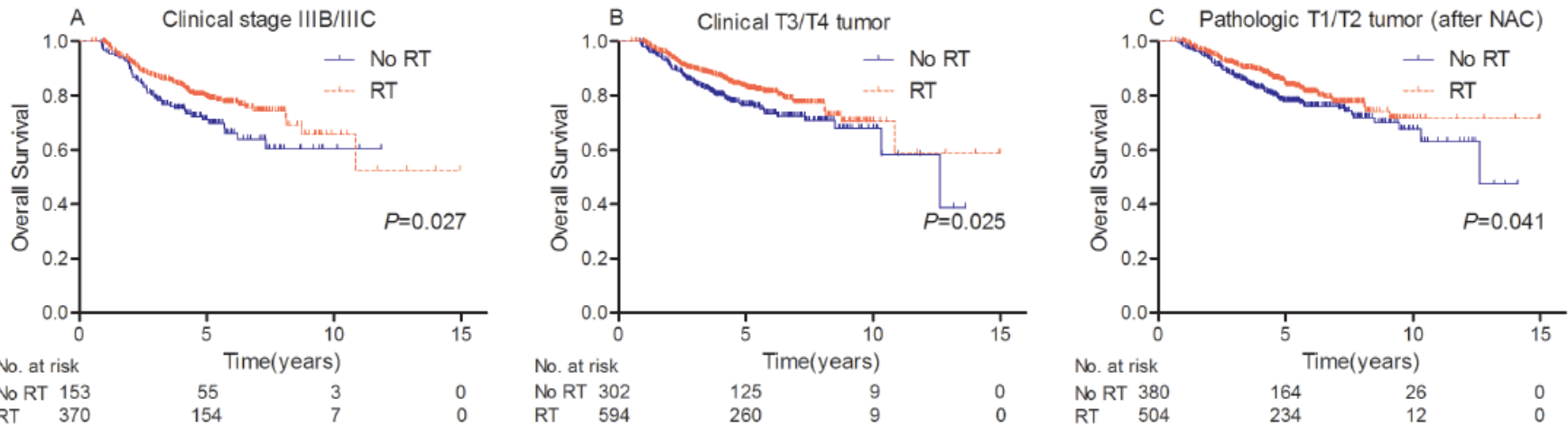
Factors	HR	95% CI	P
Age, years			
≤40	Reference		
41-60	1.209	0.857-1.706	0.281
>60	1.692	1.122-2.553	0.012
Race			
White	Reference		
Black	0.965	0.701-1.329	0.829
Asian or other	0.394	0.174-0.894	0.026
Insurance status			
Private insurance	Reference		
Public insurance	1.468	1.093-1.971	0.011
Not insured	1.155	0.645-2.068	0.627
Unknown	1.176	0.423-3.270	0.756
Histologic grade			
Well differentiated	Reference		
Moderately differentiated	9.749	1.331-71.425	0.025
Poorly or undifferentiated	7.760	1.066-56.489	0.043
Unknown	9.221	1.239-68.657	0.030
Examined regional nodes number			
0-10	Reference		
>10	0.770	0.598-0.991	0.043
Unkown	1.196	0.576-2.482	0.631

Factors	HR	95% CI	P
Clinical T-stage			
T1	Reference		
T2	0.692	0.419-1.141	0.149
T3	1.575	0.784-3.167	0.202
T4	2.808	1.395-5.649	0.004
Clinical AJCC stage			
II	Reference		
III	2.193	1.197-4.017	0.011
Pathologic T-stage (after NAC)			
T0/Tis	Reference		
T1	1.275	0.943-1.724	0.115
T2	1.599	1.160-2.205	0.004
Hormone therapy			
No	Reference		
Yes	0.647	0.441-0.951	0.027
Unknown	0.618	0.300-1.273	0.192
PMRT			
No	Reference		
Yes	0.820	0.630-1.068	0.141

The role of postmastectomy radiotherapy in clinically node-positive, stage II-III breast cancer patients with pathological negative nodes after neoadjuvant chemotherapy: an analysis from the NCDB

On SUBGROUP ANALYSES **PMRT** significantly **improved OS** in:

- ✓ clinical stage IIIB/IIIC disease (cT4 cN0-2/cN3)
- ✓ T3/T4 tumor
- ✓ residual invasive breast cancer after NAC ($P < 0.05$).



*This **improvement in OS** remained significant after sensitivity analyses for the propensity score-matched pts*

The role of postmastectomy radiotherapy in clinically node-positive, stage II-III breast cancer patients with pathological negative nodes after neoadjuvant chemotherapy: an analysis from the NCDB

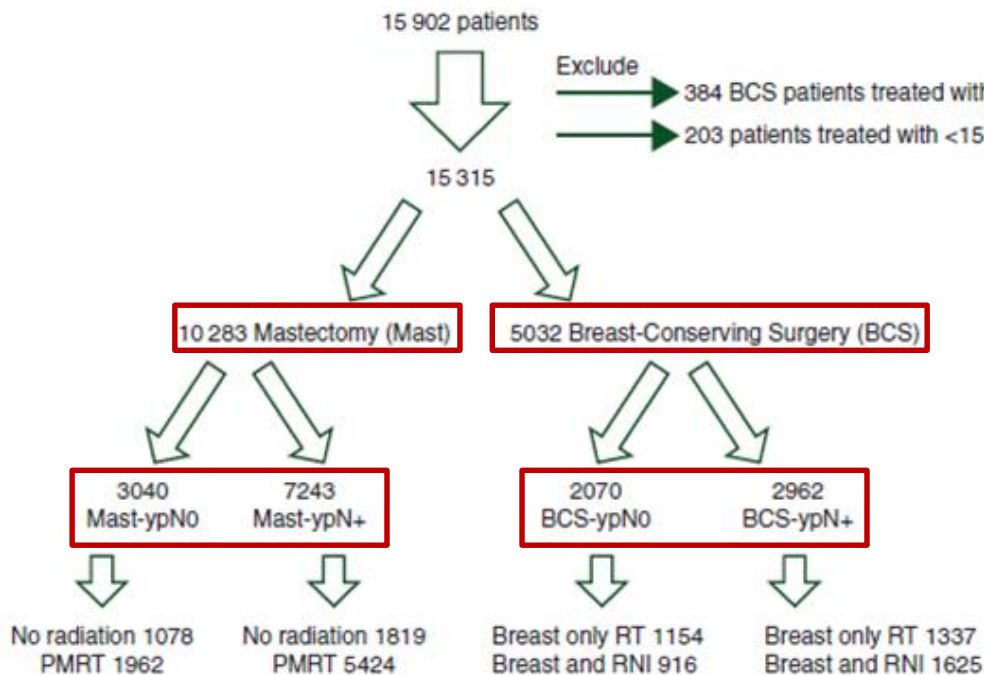
CONCLUSIONS:

- PMRT showed a heterogeneous effect in **cN+ stage II-III** breast cancer patients with **ypN0 following NAC**
- **PMRT improved OS** for patients with **clinical stage IIIB/IIIC** disease, **T3/T4 tumor**, or **residual invasive breast tumor after NAC**
- In the absence of definitive conclusions from prospective studies (including ongoing NSABP B-51 trial) these findings may help **identify specific groups** of women who could **benefit from PMRT** after NAC

The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis

C. G. Rusthoven^{1*}, R. A. Rabinovitch¹, B. L. Jones¹, M. Koshy^{2,3}, A. Amini¹, N. Yeh¹, M. W. Jackson¹ & C. M. Fisher¹

Women in the NCDB with **cT1-3 cN1** M0 breast cancer
Receiving Neoadjuvant Chemotherapy (NAC) and definitive surgery from 2003-2011



Mastectomy pts primary end point:

- OS with **PMRT(+/-RNI)** vs **no PMRT**
- **Secondary end point OS by RNI**

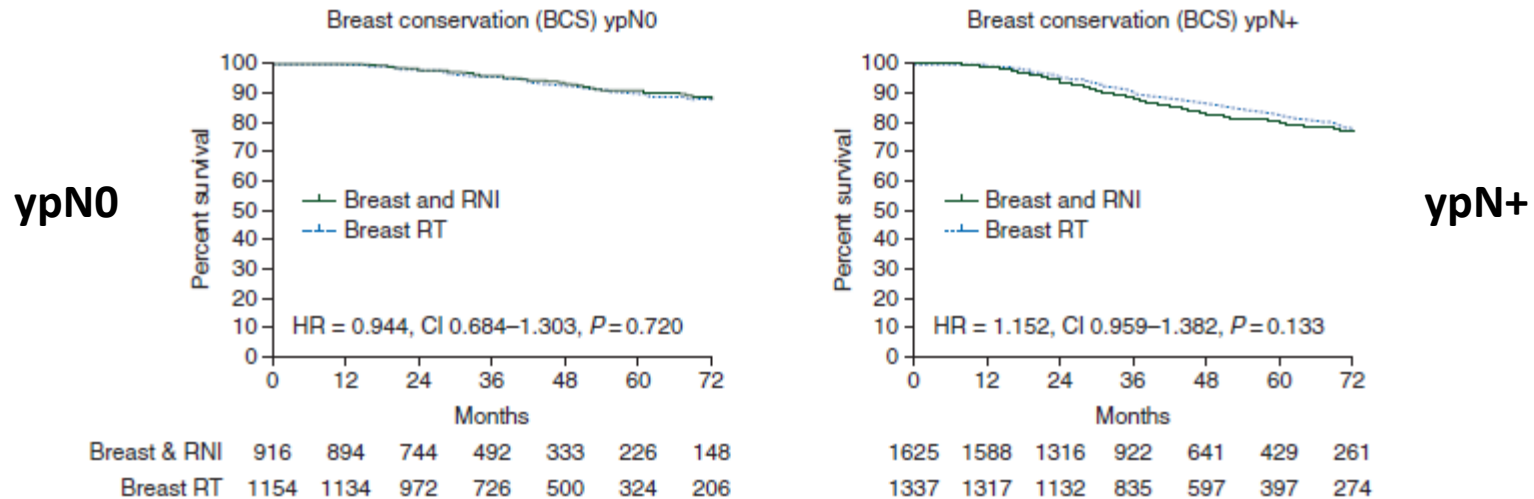
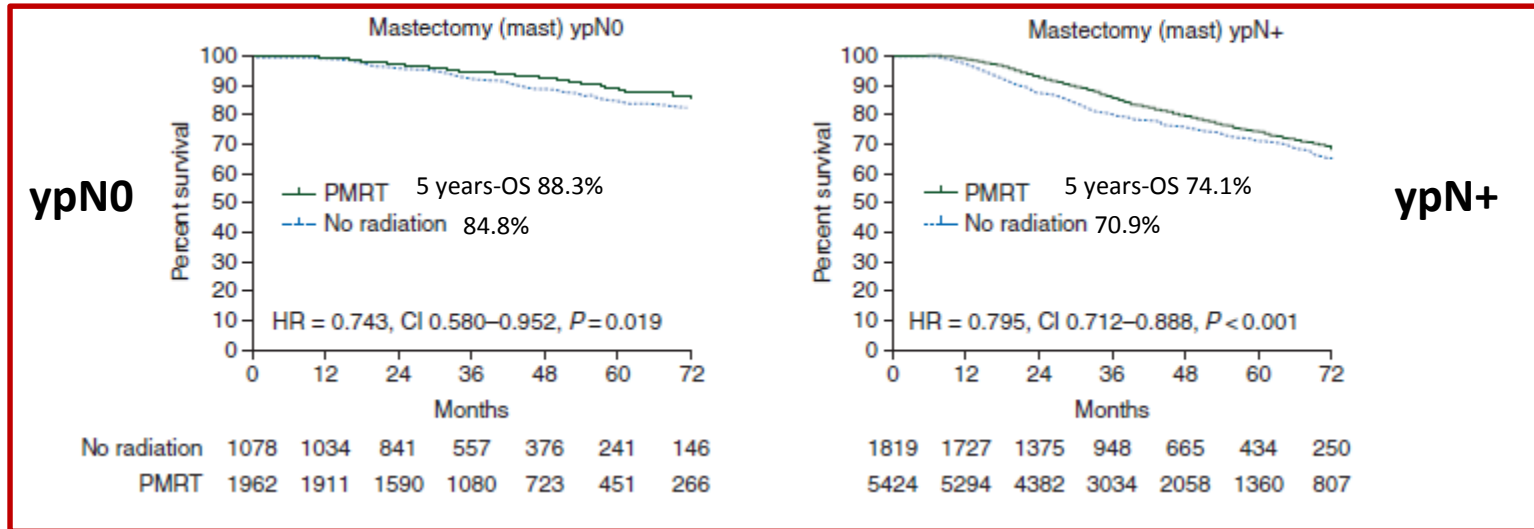
BCS pts primary end point:

- OS with **breast RT alone** vs **breast RT + RNI**

- ✓ No RT quality control data
- ✓ No data of specific types of ChT or HT agents

The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis

OS univariate analysis: RT



The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis

OS multivariate analysis

Table 2. Multivariate survival analysis

	Mastectomy/ypN0 (3040)				Mastectomy/ypN-positive (7243)				Breast conservation/ypN0 (2070)				Breast conservation/ypN-positive (2962)						
	HR	Low	High	P	HR	Low	High	P	HR	Low	High	P	HR	Low	High	P			
Radiation																			
No RT	1				No RT	1				Breast	1				Breast	1			
PMRT	0.729	0.566	0.939	0.015	PMRT	0.772	0.689	0.866	<0.001	Br and RNI	0.969	0.699	1.344	0.851	Br and RNI	1.037	0.862	1.248	0.700
Age																			
<50	1				<50	1				<50	1				<50	1			
≥50	1.477	1.149	1.898	0.002	≥50	1.164	1.050	1.289	0.004	≥50	1.159	0.836	1.606	0.375	≥50	1.145	0.948	1.384	0.160
Race																			
White	1				White	1				White	1				White	1			
Black	1.010	0.746	1.368	0.950	Black	1.456	1.293	1.641	<0.001	Black	0.612	0.401	0.935	0.023	Black	1.181	0.952	1.464	0.131
Other	0.246	0.078	0.770	0.016	Other	0.929	0.713	1.211	0.586	Other	0.890	0.411	1.926	0.767	Other	0.845	0.484	1.477	0.555
Unknown	0.398	0.056	2.852	0.359	Unknown	0.871	0.514	1.477	0.608	Unknown	0.974	0.238	3.994	0.971	Unknown	1.724	0.800	3.718	0.165
Year of Dx																			
Per year	1.041	0.969	1.118	0.273	Per Year	1.026	0.999	1.055	0.060	Per Year	1.106	1.002	1.221	0.046	Per Year	1.015	0.965	1.067	0.567
Grade																			
1	1				1	1				1	1				1	1			
2	1.015	0.479	2.152	0.969	2	1.365	0.998	1.868	0.052	2	0.977	0.296	3.227	0.970	2	3.600	1.325	9.783	0.012
3	1.302	0.628	2.702	0.478	3	2.465	1.810	3.356	<0.001	3	1.281	0.396	4.138	0.679	3	6.208	2.299	16.765	<0.001
Unknown	1.545	0.684	3.490	0.295	Unknown	1.599	1.118	2.287	0.010	Unknown	0.260	0.043	1.582	0.144	Unknown	3.190	1.075	9.460	0.037
Ax LN Sx																			
≤4 LNs	1				≤4 LNs	1				≤4 LNs	1				≤4 LNs	1			
5-9	1.013	0.706	1.454	0.944	5-9	1.170	0.952	1.439	0.136	5-9	0.982	0.617	1.561	0.937	5-9	0.890	0.626	1.266	0.517
≥10	0.894	0.666	1.200	0.455	≥10	0.925	0.774	1.105	0.391	≥10	0.874	0.606	1.259	0.469	≥10	0.883	0.665	1.173	0.392
Unknown	0.443	0.139	1.417	0.170	Unknown	0.815	0.531	1.248	0.347	Unknown	1.722	0.868	3.413	0.120	Unknown	0.631	0.310	1.285	0.204
cT stage																			
1	1				1	1				1	1				1	1			
2	0.765	0.502	1.165	0.213	2	1.384	1.148	1.667	0.001	2	1.539	0.838	2.825	0.164	2	1.519	1.139	2.025	0.004
3	1.180	0.779	1.787	0.434	3	1.816	1.508	2.186	<0.001	3	2.279	1.204	4.312	0.011	3	1.721	1.242	2.384	0.001
ypN stage																			
1	-	-	-	-	1	1				1	-	-	-	-	1	1			
2	-	-	-	-	2	1.921	1.706	2.164	<0.001	2	-	-	-	-	2	2.701	2.176	3.353	<0.001
3	-	-	-	-	3	3.267	2.845	3.753	<0.001	3	-	-	-	-	3	3.211	2.346	4.395	<0.001
In-breast																			
Path CR	1				Path CR	1				Path CR	1				Path CR	1			
Residual	2.154	1.599	2.903	<0.001	Residual	1.519	1.164	1.981	0.002	Residual	2.288	1.574	3.326	<0.001	Residual	1.255	0.847	1.860	0.258
ER/HT																			
ER+/HT+	1				ER+/HT+	1				ER+/HT+	1				ER+/HT+	1			
ER+/HT-	1.434	0.803	2.560	0.223	ER+/HT-	1.678	1.344	2.096	<0.001	ER+/HT-	2.531	1.104	5.802	0.028	ER+/HT-	1.551	0.934	2.578	0.090
ER-	1.816	1.336	2.467	<0.001	ER-	3.255	2.879	3.680	<0.001	ER-	2.588	1.679	3.988	<0.001	ER-	3.405	2.702	4.291	<0.001
Unknown	1.346	0.777	2.334	0.289	Unknown	2.011	1.658	2.439	<0.001	Unknown	2.322	1.167	4.623	0.016	Unknown	2.225	1.545	3.203	<0.001
Comorbidity																			
0	1				0	1				0	1				0	1			
1	1.227	0.799	1.883	0.350	1	1.283	1.088	1.513	0.003	1	1.413	0.824	2.424	0.209	1	1.183	0.878	1.595	0.270
≥2	2.426	0.988	5.958	0.053	≥2	1.578	1.081	2.304	0.018	≥2	0.963	0.130	7.144	0.971	≥2	1.144	0.505	2.594	0.747

Improvement in OS significant also after sensitivity analyses for the propensity score-matching

The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis

OS impact of PMRT and RNI subgroups analysis

Table 3. Overall survival impact of PMRT and RNI by subgroup

Mastectomy/ypN0	N (Events) Total	N (Events) PMRT	N (Events) No RT	Multivariate analysis				Interaction P
				HR w/PMRT	Low	High	P	
Axillary surgery								
≤4 LNs	832 (68)	519 (42)	313 (26)	0.916	0.557	1.507	0.730	0.151
5–9 LNs	570 (53)	368 (33)	202 (20)	0.750	0.403	1.394	0.363	
≥10 LNs	1570 (135)	1027 (74)	543 (61)	0.626	0.442	0.887	0.008	
In-breast response								
Path CR	1274 (61)	834 (37)	440 (24)	0.770	0.445	1.335	0.352	0.614
Residual	1766 (198)	1128 (114)	638 (84)	0.713	0.534	0.951	0.021	
Clinical T stage								
cT1–2	1834 (124)	1070 (58)	764 (66)	0.620	0.433	0.889	0.009	0.529
cT3	1206 (135)	892 (93)	314 (42)	0.782	0.540	1.133	0.194	
Age								
<50	1696 (115)	1127 (69)	569 (46)	0.752	0.510	1.109	0.150	0.909
≥50	1344 (144)	835 (82)	509 (62)	0.705	0.502	0.990	0.044	

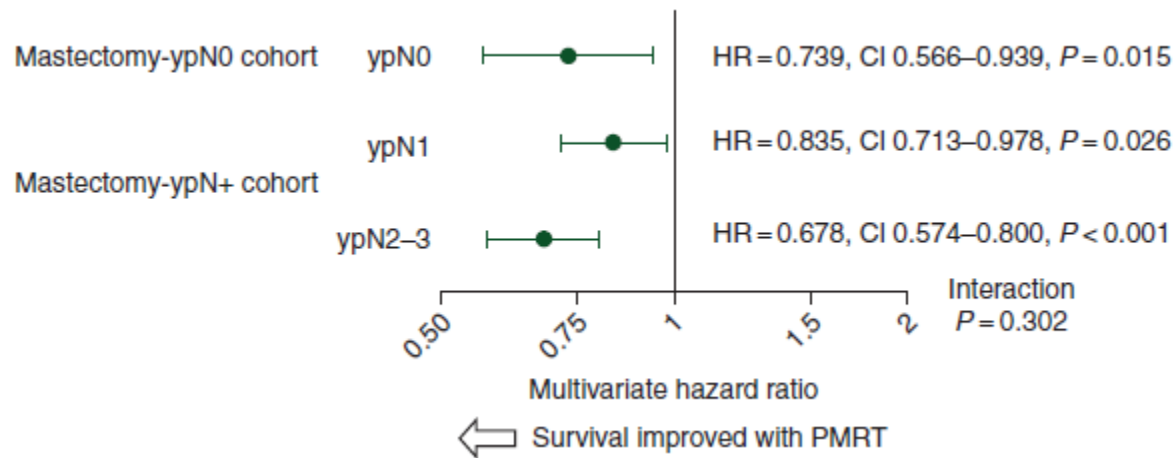
Mastectomy/ypN+	Total	PMRT	No RT	HR w/PMRT	Low	High	P	Interaction P
Axillary surgery								
≤4 LNs	770 (142)	539 (98)	231 (44)	0.899	0.621	1.302	0.574	0.460
5–9 LNs	1234 (256)	920 (184)	314 (72)	0.887	0.667	1.179	0.408	
≥10 LNs	5125 (1121)	3871 (805)	1254 (316)	0.737	0.644	0.843	0.000	
yp Nodal stage								
ypN1	4504 (736)	3186 (493)	1318 (243)	0.835	0.713	0.978	0.026	0.083
ypN2–3	2739 (808)	2238 (611)	501 (197)	0.678	0.574	0.800	<0.001	
In-breast response								
Path CR	406 (58)	273 (19)	133 (39)	0.865	0.471	1.589	0.641	0.518
Residual	6837 (1486)	5151 (421)	1686 (1065)	0.767	0.682	0.862	<0.001	
Clinical T stage								
cT1–2	4323 (797)	3087 (559)	1236 (238)	0.839	0.716	0.983	0.030	0.020
cT3	2920 (747)	2337 (545)	583 (202)	0.691	0.585	0.817	<0.001	
Age								
<50	3697 (704)	2818 (517)	879 (187)	0.784	0.659	0.933	0.006	0.662
≥50	3546 (840)	2606 (587)	940 (253)	0.754	0.646	0.879	<0.001	

Mast-ypN0

Mast-ypN+

The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis

Forest plot: survival impact of PMRT by ypN stage.



Improved OS with PMRT in each pathologic nodal subgroup (ypN0, ypN1, and ypN2–3)

The impact of postmastectomy and regional nodal radiation after neoadjuvant chemotherapy for clinically lymph node-positive breast cancer: a National Cancer Database (NCDB) analysis

CONCLUSIONS:

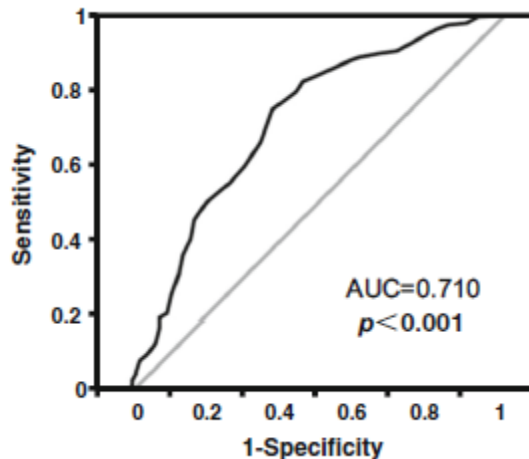
- After mastectomy a **significant OS advantage** was observed with **PMRT** for **all pathologic nodal subgroups**
- **No OS benefit** was observed with the addition of **RNI to breast RT**
- Potential differences in LRC and DFS were not evaluable

Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

Fei Xin^{1,2,3} · Yue Yu^{1,2,3} · Zheng-Jun Yang^{1,2,3} · Li-Kun Hou^{1,2,3} · Jie-Fei Mao^{1,2,3} · Li Xia^{1,2,3} · Xin Wang^{1,2,3} · Xu-Chen Cao^{1,2,3}

275 stage I-III breast: NAC (2006 -2009) → mastectomy + DLA (≥10N) → PMRT

- ✓ End point: **OS** and **DFS**
- ✓ Prognostic value of the **number of Negative LN (NLNs)**
- ✓ The **number of NLNs** would give some indications on **PMRT** in **ypN1**



- ✓ The **median number** of the total removed lymph nodes was **22 (13-78)**
- ✓ The **median number** of NLNs was **16 (0-60)**
- ✓ **13** was the **optimal cutoff** point of NLNs (area under ROC curve =0.710, $p<0.001$)

Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

Clinicopathological features with the number of NLNs

Variables	Number	0–13 NLNs	13–60 NLNs	<i>p</i> value
Age (years)				0.841
≤40	46 (16.7 %)	18 (6.5 %)	28 (10.2 %)	
>40	229 (83.3 %)	86 (31.3 %)	143 (52 %)	
Menopausal status				0.093
Premenopausal	150 (54.5 %)	50 (18.2 %)	100 (36.3 %)	
Postmenopausal	125 (45.5 %)	54 (19.7 %)	71 (25.8 %)	
BMI				0.128
Normal	143 (52 %)	62 (22.5 %)	81 (29.5 %)	
Overweight	101 (36.7 %)	31 (11.3 %)	70 (25.4 %)	
Obesity	31 (11.3 %)	11 (4 %)	20 (7.3 %)	
Stages before NAC				<0.001
Stage I-II	132 (48 %)	29 (10.5 %)	103 (37.5 %)	
Stage III	143 (52 %)	75 (27.3 %)	68 (24.7 %)	
Response to chemotherapy				0.091
cCR	51 (18.6 %)	14 (5.1 %)	37 (13.5 %)	
Non-cCR	224 (81.4 %)	90 (32.7 %)	134 (48.7 %)	
Chemotherapy regimens				0.221
Include T and (or) E regimens	258 (93.8 %)	160 (58.2 %)	98 (35.6 %)	
Others	17 (6.2 %)	8 (2.9 %)	9 (3.3 %)	
The chemotherapy cycles before surgery				0.682
1 or 2 cycles	111 (40.4 %)	42 (15.3 %)	69 (25.1 %)	
3 or 4 cycles	129 (46.9 %)	50 (18.2 %)	79 (28.7 %)	
5 or 6 cycles	35 (12.7 %)	15 (5.5 %)	20 (7.2 %)	
Histological type				0.328
IDC	250 (90.9 %)	95 (34.5 %)	155 (56.4 %)	
Others	25 (9.1 %)	12 (4.4 %)	13 (4.7 %)	
Ki-67 levels				0.892
≤14 %	57 (20.7 %)	22 (8 %)	35 (12.7 %)	
>14 %	218 (79.3 %)	82 (29.8 %)	136 (49.5 %)	

Variables	Number	0–13 NLNs	13–60 NLNs	<i>p</i> value
Breast cancer subtype				0.744
Luminal A	40 (14.5 %)	13 (4.7 %)	27 (9.8 %)	
Luminal B	117 (42.5 %)	47 (17.1 %)	70 (25.4 %)	
Erb-B2 overexpression	41 (14.9 %)	17 (6.2 %)	24 (8.7 %)	
Basal-like	77 (28 %)	27 (9.8 %)	50 (18.2 %)	
Pathological tumor size				<0.05
ypT0-T1	95 (34.5 %)	30 (10.9 %)	65 (23.6 %)	
ypT2	135 (49.1 %)	48 (17.5 %)	87 (31.6 %)	
ypT3-T4	45 (16.4 %)	26 (9.5 %)	19 (6.9 %)	
Pathological nodal stage				<0.001
ypN0-N1	145 (52.7 %)	23 (8.4 %)	122 (44.3 %)	
ypN2	58 (21.1 %)	24 (8.7 %)	34 (12.4 %)	
ypN3	72 (26.2 %)	60 (21.8 %)	12 (4.4 %)	
Pathological stage after NAC				<0.001
Stage 0-II	139 (50.5 %)	19 (6.9 %)	120 (43.6 %)	
Stage III	136 (49.5 %)	85 (30.9 %)	51 (18.6 %)	

Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

Clinicopathological features with the different ypN

Variables	Number	ypN0-N1	ypN2	ypN3	p value
Age (years)					0.193
≤40	46 (16.7 %)	23 (8.4 %)	14 (5.1 %)	9 (3.2 %)	
>40	229 (83.3 %)	122 (44.4 %)	44 (16 %)	63 (22.9 %)	
Menopausal status					0.079
Premenopausal	150 (54.5 %)	81 (29.5 %)	37 (13.5 %)	32 (11.5 %)	
Postmenopausal	125 (45.5 %)	64 (23.3 %)	21 (7.6 %)	40 (14.6 %)	
BMI					0.066
Normal	143 (52 %)	71 (25.8 %)	39 (14.2 %)	33 (12 %)	
Overweight	101 (36.7 %)	56 (20.4 %)	17 (6.2 %)	28 (10.1 %)	
Obesity	31 (11.3 %)	18 (6.5 %)	2 (0.7 %)	11 (4 %)	
Stages before NAC					<0.001
Stage I-II	132 (48 %)	89 (32.4 %)	23 (8.4 %)	20 (7.2 %)	
Stage III	143 (52 %)	56 (20.4 %)	35 (12.7 %)	52 (18.9 %)	
Response to chemotherapy					<0.001
cCR	51 (18.5 %)	39 (14.2 %)	4 (1.5 %)	8 (2.8 %)	
Non-cCR	224 (81.5 %)	106 (38.5 %)	54 (19.6 %)	64 (23.4 %)	
Chemotherapy regimens					0.331
T and (or) E regimens	258 (93.8 %)	139 (50.5 %)	53 (19.3 %)	66 (24 %)	
Others	17 (6.2 %)	6 (2.2 %)	5 (1.8 %)	6 (2.2 %)	
The chemotherapy cycles before surgery					0.576
1 or 2 cycles	111 (40.4 %)	57 (20.7 %)	21 (7.7 %)	33 (12 %)	
3 or 4 cycles	129 (46.9 %)	69 (25.1 %)	27 (9.8 %)	33 (12 %)	
5 or 6 cycles	35 (12.7 %)	19 (6.9 %)	10 (3.6 %)	6 (2.2 %)	
Histological type					0.058
IDC	250 (90.9 %)	137 (49.8 %)	52 (18.9 %)	61 (22.2 %)	
Others	25 (9.1 %)	8 (2.9 %)	6 (2.2 %)	11 (4 %)	
Ki-67 levels					<0.05
≤14 %	57 (20.7 %)	41 (14.9 %)	7 (2.5 %)	9 (3.3 %)	
>14 %	218 (79.3 %)	104 (37.8 %)	51 (18.5 %)	63 (22.8 %)	
Breast cancer subtype					<0.05
Luminal A	40 (14.5 %)	27 (9.8 %)	9 (3.3 %)	4 (1.4 %)	
Luminal B	117 (42.5 %)	49 (17.8 %)	28 (10.2 %)	40 (14.5 %)	
Erb-B2 overexpression	41 (14.9 %)	20 (7.3 %)	10 (3.6 %)	11 (4 %)	
Basal-like	77 (28 %)	49 (17.8 %)	11 (4 %)	17 (6.2 %)	
Pathological tumor size					<0.00
ypT0-T1	95 (34.5 %)	66 (24 %)	17 (6.2 %)	12 (4.3 %)	
ypT2	135 (49.1 %)	67 (24.4 %)	27 (9.8 %)	41 (14.9 %)	
ypT3-T4	45 (16.4 %)	12 (4.4 %)	14 (5.1 %)	19 (6.9 %)	
Pathological stage after NAC					<0.00
Stage 0-II	139 (50.5 %)	136 (49.5 %)	2 (0.7 %)	1 (0.3 %)	
Stage III	136 (49.5 %)	9 (3.3 %)	56 (20.4 %)	71 (25.8 %)	

Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

OS and DFS UNIVARIATE ANALYSIS of prognostic factors

Characteristic	OS			DFS		
	HR	95% CI	p value	HR	95% CI	p value
Age (years)						
≤40	1					
>40	0.674	0.369–1.231	0.199	0.626	0.392–0.999	<0.05
Menopausal status						
Premenopausal	1			1		
Postmenopausal	1.094	0.652–1.837	0.734	1.008	0.676–1.503	0.969
BMI						
Normal	1			1		
Overweight	1.396	0.801–2.433	0.239	1.001	0.654	0.996
Obesity	1.252	0.567–2.744	0.578	0.761	0.387–1.499	0.43
Primary stage						
Stage I-II	1			1		
Stage III	3.118	1.751–5.553	<0.001	2.895	1.872–4.478	<0.001
Response to chemotherapy						
cCR	1			1		
Non-cCR	1.067	0.565–2.015	0.841	1.359	0.814	0.241
Chemotherapy regimens						
CEF	1			1		
TB/TEC	1.398	0.658–2.972	0.384	1.186	0.689–2.044	0.538
Others	3.038	1.503–8.764	0.058	2.581	1.168–5.707	0.067
The chemotherapy cycles before surgery						
1 or 2 cycles	1			1		
3 or 4 cycles	1.278	0.713–2.290	0.41	0.995	0.648–1.527	0.981
5 or 6 cycles	2.709	1.323–5.547	0.059	1.428	0.807–2.711	0.205
Histological type						

Characteristic	OS			DFS		
	HR	95% CI	p value	HR	95% CI	p value
Histological type						
IDC	1			1		
Others	0.892	0.356–2.231	0.807	0.847	0.411–1.748	0.654
Ki-67 levels						
≤14 %	1			1		
>14 %	1.209	0.611–2.393	0.586	1.278	0.489–1.249	0.303
Breast cancer subtype						
Luminal A	1			1		
Luminal B	0.789	0.340–1.892	0.58	0.976	0.505–1.887	0.944
Erb-B2 overexpression	2.481	1.060–5.806	<0.05	2.283	1.1128–4.618	<0.05
Basal-like	1.462	0.615–3.307	0.409	1.489	0.761–2.913	0.245
Pathological tumor size						
ypT0-T1	1			1		
ypT2	2.105	1.031–4.378	<0.05	3.158	1.851–5.389	<0.001
ypT3-T4	4.46	2.419–8.223	<0.001	4.826	2.984–7.923	<0.001
Pathological nodal stage						
ypN0-N1	1			1		
ypN2	2.015	1.013–4.378	<0.05	3.158	1.851–5.389	<0.001
ypN3	4.46	2.419–8.223	<0.001	4.826	2.984–7.923	<0.001
PMRT						
No	1			1		
Yes	0.842	0.409–1.448	0.535	0.799	0.531–1.203	0.282
Number of NLNs						
0–13 NLNs	1			1		
14–60 NLNs	0.266	0.155–0.458	<0.001	0.289	0.192–0.435	<0.001

Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

OS and DFS MULTIVARIATE ANALYSIS of prognostic factors

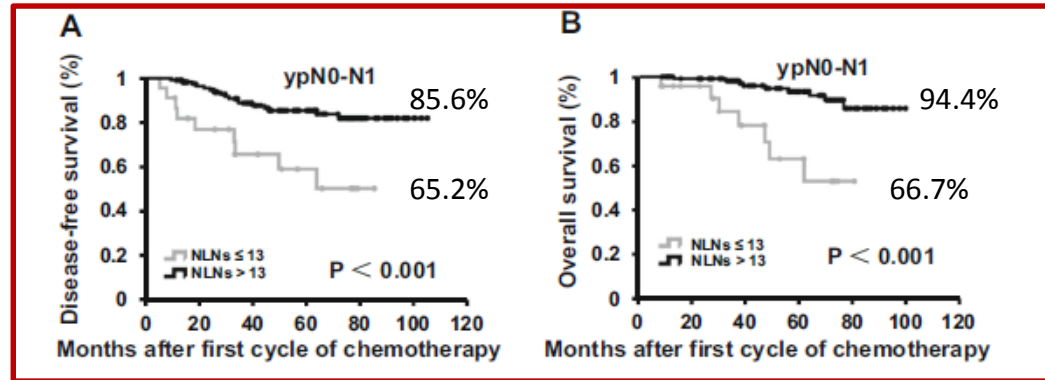
Characteristics	OS			DFS		
	HR	95% CI	<i>p</i> value	HR	95% CI	<i>p</i> value
Age				0.500	0.310–0.807	<0.05
Primary stage	2.008	1.093–3.687	<0.05	1.995	1.256–3.168	<0.05
Breast cancer subtype	1.367	1.059–1.765	<0.05	1.274	1.049–1.548	<0.05
Pathological tumor size				1.001	0.605–1.656	0.997
Pathological nodal stage	1.410	0.963–2.064	0.078	1.590	1.197–2.111	<0.05
Number of NLNs	0.393	0.194–0.793	<0.05	0.460	0.278–0.763	<0.05

Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

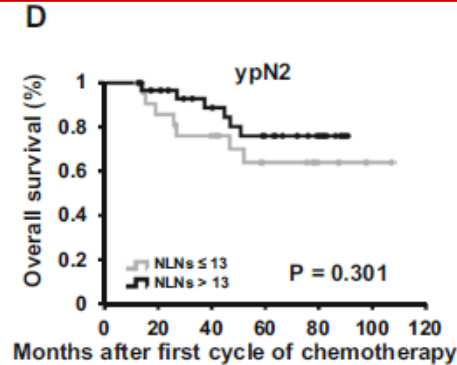
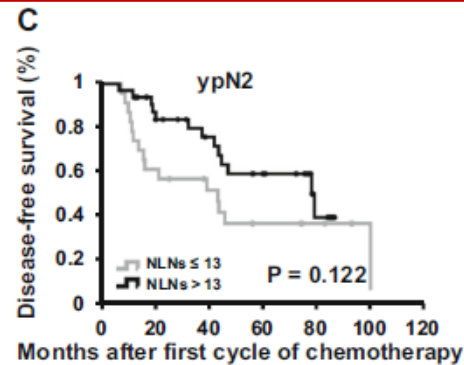
Impact of the NLNs on the DFS and OS of different ypN

NLNs >13

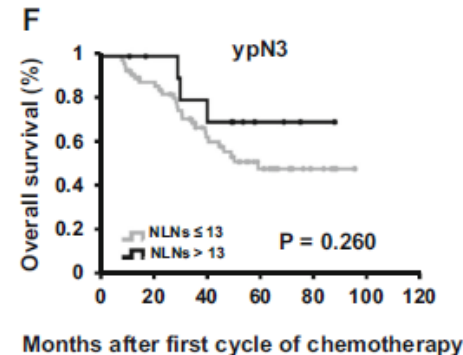
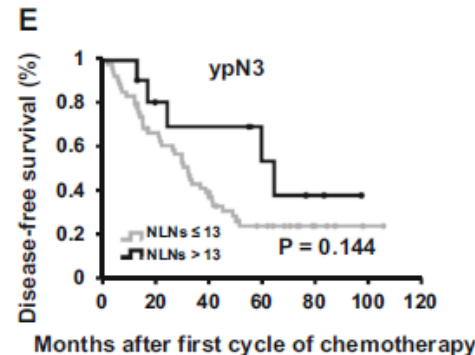
NLNs ≤13



5-year DFS

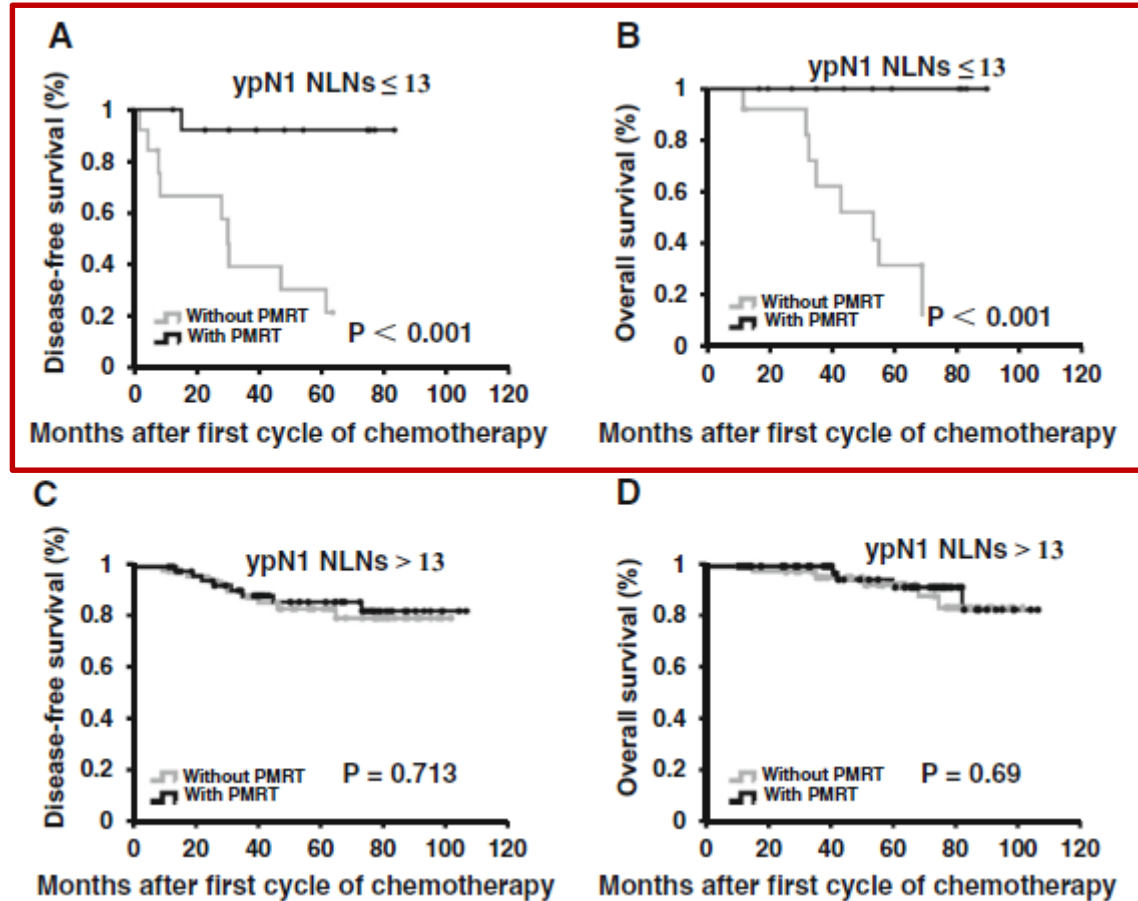


5-year OS



Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

Impact of the PMRT on the DFS and OS of ypN1 patients



5-year DFS

5 year-OS

Number of negative lymph nodes as a prognostic factor for ypN0-N1 breast cancer patients undergoing neoadjuvant chemotherapy

CONCLUSIONS:

- The **number of NLNs** is a **prognostic indicator in ypN0-N1** patients
- Patients **ypN1 with less number of NLNs** will benefit from **PMRT**

Radioterapia dopo CT neoadiuvante

1) NACT → MASTECTOMIA → ruolo RT LOCOREGIONALE

2) NACT → CH → RT: risultati per *SOTTOTIPI MOLECOLARI*

3) NACT → CH con SLNB + ALND → RT: variability in practice

Clinical outcomes according to molecular subtypes in stage II–III breast cancer patients treated with neoadjuvant chemotherapy followed by surgery and radiotherapy

Hakyoung KIM,¹ Won PARK,¹ Seung Jae HUH,¹ Doo Ho CHOI,¹ Jae Myoung NOH,¹

329 clinical stage II–III breast cancer: NAC + surgery + RT (2007-2011)

End point: OS, DFS, pCR

Table 1 Patients, tumors and treatment characteristics (n = 329)

Characteristics	Number of patients	%
Age (years; median [range])	44 (24–69)	
Age group (years)		
≤40	116	35.3
>40	213	64.7
Clinical T stage		
T1–T2	175	53.2
T3–T4	154	46.8
Clinical N stage		
N0	11	3.4
N1	134	40.7
N2	108	32.8
N3	76	23.1
Hormonal receptor status		
Positive	172	52.3
Negative	157	47.7
HER2/neu receptor status		
Positive	96	29.2
negative	233	70.8
Molecular subtypes		
Luminal A	108	32.8
Luminal B	64	19.5
HER2-enriched	55	16.7
Triple-negative	102	31.0

Characteristics	Number of patients	%
Ki-67 status		
–		
Negative	174	52.9
Positive	155	47.1
Type of surgery		
BCS	211	64.1
MRM	118	35.9
Median number of sampled LN (range)	16 (1–47)	
Number of sampled LN		
<10	68	20.7
≥10	261	79.3
Pathology		
IDC	311	94.5
ILC	6	1.9
Others	12	3.6

Characteristics	Number of patients	%
Pathologic T stage		
ypT0-is	79	24.0
ypT1	106	32.2
ypT2	79	24.0
ypT3	56	17.0
ypT4	9	2.8
Pathologic N stage		
ypN0	138	41.9
ypN1	97	29.5
ypN2	49	14.9
ypN3	45	13.7
Histologic grade		
Grade 1	49	14.9
Grade 2	153	46.5
Grade 3	77	23.4
Unknown	50	15.2
LVSI		
No	204	62.0
Yes	125	38.0
ECE		
No	210	63.8
Yes	119	36.2
Resection margin		
Negative	231	70.2
Close (≤3 mm)	89	27.1
Positive	9	2.7
AJCC stage		
0	66	20.1
I	46	14.0
II	97	29.5
IIIA, B	75	22.8
IIIC	45	13.6

PATIENT CHARACTERISTICS

Clinical outcomes according to molecular subtypes in stage II–III breast cancer patients treated with neoadjuvant chemotherapy followed by surgery and radiotherapy

Luminal A (HR+ HER2- Ki-67-)
 Luminal B (HR+ and HER2+ or HR+ HER2- Ki-67+)
 HER2 enriched (HR- HER2+)
 Triple negative (HR- HER2-)

Pathologic characteristics according to molecular subtypes (*n* = 329)

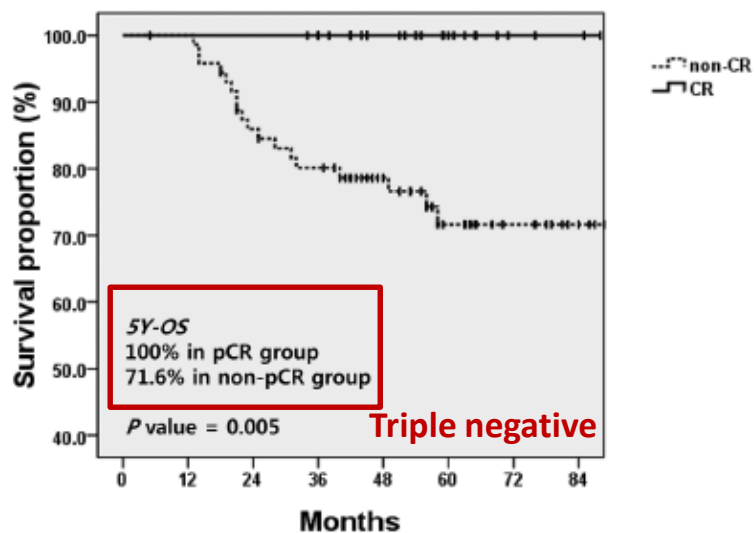
Characteristics	Luminal A (<i>n</i> = 108)	Luminal B (<i>n</i> = 64)	HER2 (<i>n</i> = 55)	Triple-negative (<i>n</i> = 102)	<i>P</i> value
EGFR status [†]					
Negative	100 (92.6%)	51 (79.7%)	31 (56.4%)	11 (10.8%)	< 0.001
Positive	5 (4.6%)	9 (14.1%)	22 (40.0%)	87 (85.3%)	
Ki-67 status					
Negative	108 (100.0%)	20 (31.3%)	16 (29.1%)	30 (29.4%)	< 0.001
Positive	0 (0.0%)	44 (68.8%)	39 (70.9%)	72 (70.6%)	
Pathologic T					
ypT0-is	7 (6.5%)	8 (12.5%)	27 (49.1%)	37 (36.3%)	< 0.001
ypT1-4	101 (93.5%)	56 (87.5%)	28 (50.9%)	65 (63.7%)	
Pathologic N					
ypN0	24 (22.2%)	22 (34.4%)	37 (67.3%)	55 (53.9%)	< 0.001
ypN1-3	84 (77.8%)	42 (35.6%)	18 (32.7%)	47 (46.1%)	
Pathologic CR					
No	103 (95.4%)	57 (89.1%)	31 (56.4%)	72 (70.6%)	< 0.001
Yes	5 (4.6%)	7 (10.9%)	24 (43.6%)	30 (29.4%)	

Survivals in pathologic response according to molecular subtypes (*n* = 329)

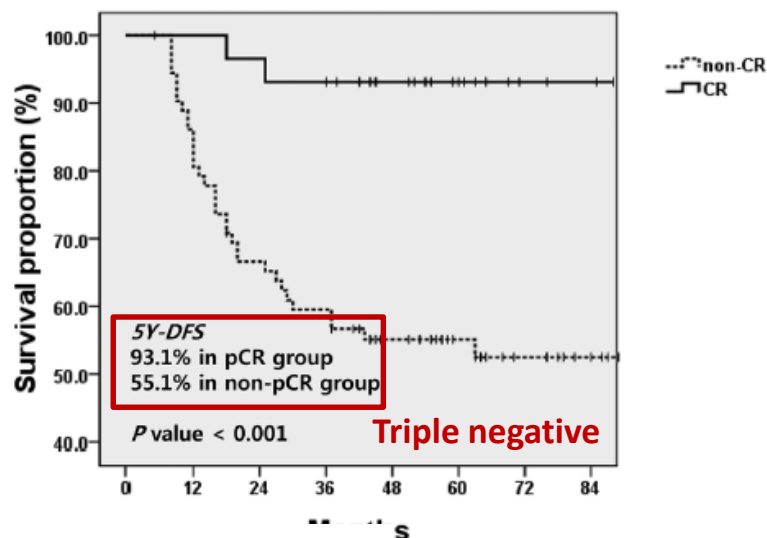
Characteristics	Luminal A (<i>n</i> = 108)	Luminal B (<i>n</i> = 64)	HER2-enriched (<i>n</i> = 55)	Triple-negative (<i>n</i> = 102)	<i>P</i> value
5-Year OS 89%					
All patients	92.8%	96.5%	89.3%	79.4%	0.007
Non-pCR (<i>n</i> = 263)	92.4%	96.1%	79.1%	71.6%	< 0.001
pCR (<i>n</i> = 66)	100%	100%	100%	100%	-
5-Year DFS 73%					
All patients	80.1%	70.6%	74.6%	65.9%	0.03
Non-pCR (<i>n</i> = 263)	80.2%	69.1%	73.1%	55.1%	< 0.001
pCR (<i>n</i> = 66)	80.0%	85.7%	78.0%	93.1%	0.602

Clinical outcomes according to molecular subtypes in stage II–III breast cancer patients treated with neoadjuvant chemotherapy followed by surgery and radiotherapy

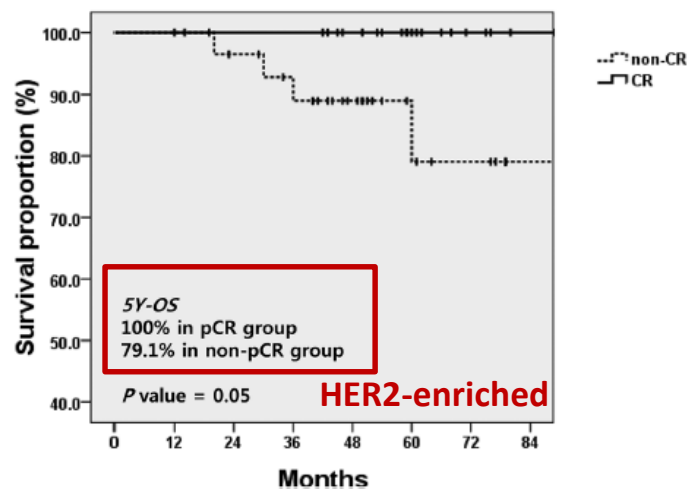
A Overall Survival



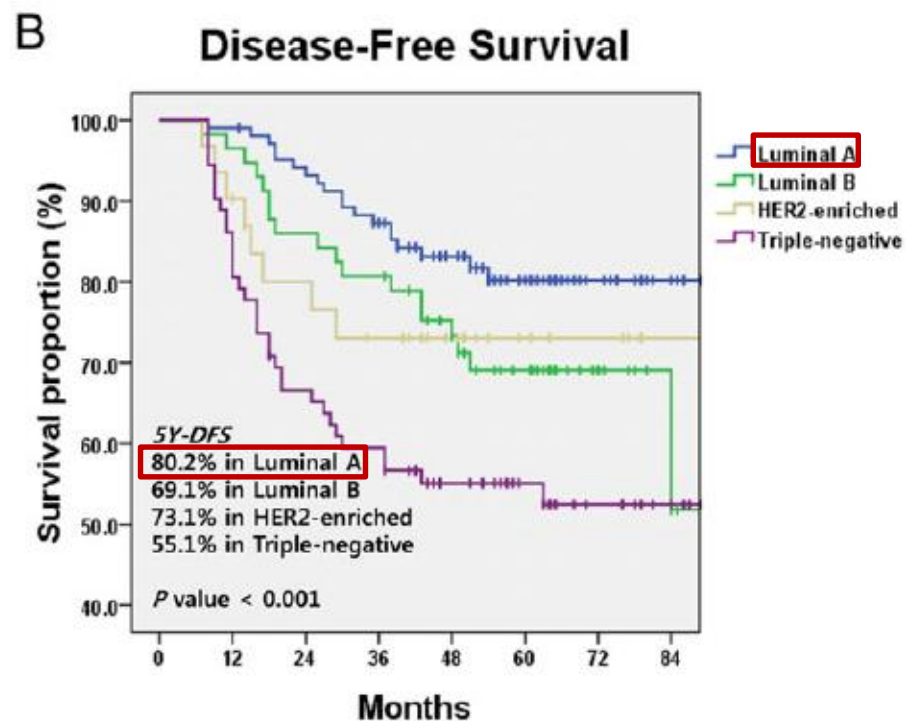
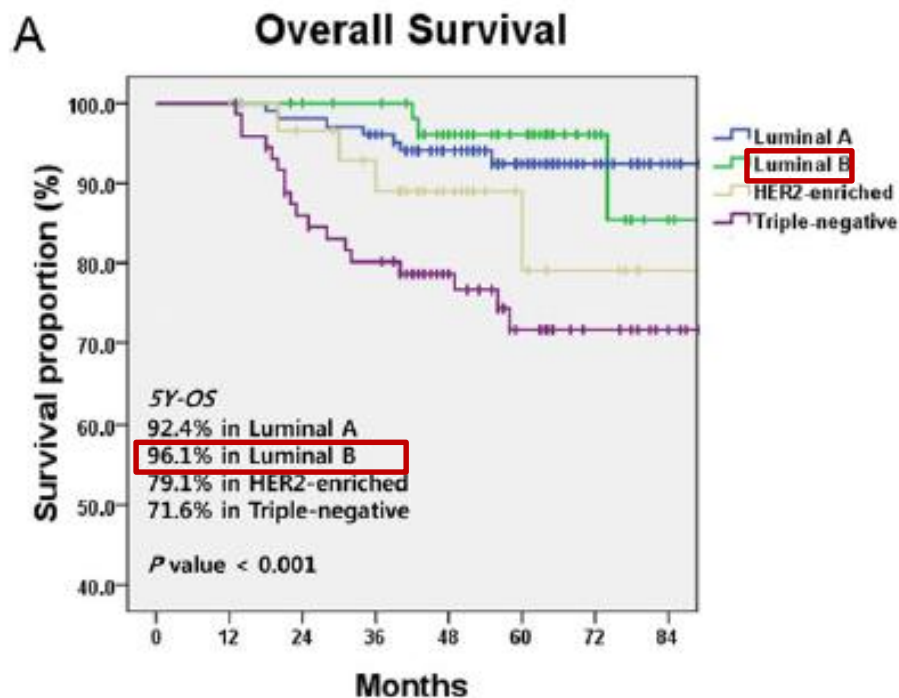
B Disease-Free Survival



C Overall Survival



Clinical outcomes according to molecular subtypes in stage II–III breast cancer patients treated with neoadjuvant chemotherapy followed by surgery and radiotherapy



Clinical outcomes according to molecular subtypes in stage II–III breast cancer patients treated with neoadjuvant chemotherapy followed by surgery and radiotherapy

CONCLUSIONS:

- The **non-pCR group** showed **significantly decreased 5-year OS and DFS** rates compared to the pCR group especially in **triple negative** and **HER2-enriched** breast cancer patients.
- A **significant difference in survival rates and molecular subtypes** was found in patients who **failed to attain pCR**

Chemotherapy response and survival of inflammatory breast cancer by hormone receptor- and HER2-defined molecular subtypes approximation: an analysis from the National Cancer Database

Received: 2 September 2016 / Accepted: 29 September 2016

Jieqiong Liu^{1,2} · Kai Chen^{1,2} · Wen Jiang³ · Kai Mao⁴ · Shunrong Li¹ · Min Ji Kim⁵ · Qiang Liu¹ · Lisa K. Jacobs²

✓ **Primary endpoint : OS**

OS curves were constructed using the Kaplan–Meier method and compared among subtypes and patients with or without pCR using the log-rank test

✓ **Impact of HR and HER2 defined subtypes on survival of IBC**

✓ **Determine whether sensitivity to NAC varies with subtypes in a large IBC population (breast pCR or breast and node pCR)**

Chemotherapy response and survival of inflammatory breast cancer by hormone receptor- and HER2-defined molecular subtypes approximation: an analysis from the National Cancer Database

PATIENT CHARACTERISTICS

Table 1 Patient clinicopathologic characteristics by subtype (n = 593)

	HR-/HER2-defined subtypes								P
	HR+/HER2-		HR+/HER2+		HR-/HER2+		Triple negative		
	No.	%	No.	%	No.	%	No.	%	
Age									0.994
Median (range)	55 (23-90)		52.5 (27-88)		54 (22-90)		56.5 (27-90)		
≤40 year	27	11.7	12	12.2	14	12.5	19	12.5	
>40 year	204	88.3	86	87.8	98	87.5	133	87.5	
Race									0.052
White	205	88.7	79	80.6	95	84.8	117	77.0	
Black	18	7.8	16	16.3	11	9.8	27	17.8	
Asian or other	8	3.5	3	3.1	6	5.4	8	5.2	
Facility type									0.682
Community	33	14.3	16	16.3	15	13.4	19	12.5	
Comprehensive	123	53.2	59	60.2	64	57.1	92	60.5	
Academic/research	75	32.5	23	23.5	33	29.5	41	27.0	
Insurance status									0.698
Not insured	17	7.4	4	4.1	7	6.3	12	7.9	
Private insurance	123	53.3	58	59.2	58	51.8	70	46.1	
Public insurance	89	38.4	34	34.7	46	41.0	67	44.0	
Unknown	2	0.9	2	2.0	1	0.9	3	2.0	
Charlson/Deyo score									0.780
0	194	84.0	80	81.6	96	85.7	124	81.6	
1	27	11.7	14	14.3	15	13.4	24	15.8	
2	10	4.3	4	4.1	1	0.9	4	2.6	
Histologic grade									<0.001
Well/moderately	75	32.5	32	32.7	14	12.5	13	8.5	
Poorly/undifferentiated	113	48.9	45	45.9	72	64.3	105	69.1	
Unknown	43	18.6	21	21.4	26	23.2	34	22.4	
Regional nodes examined									0.005
Median (range)	10 (0-52)		9 (0-33)		10 (0-45)		8 (0-87)		
0	18	7.8	17	17.4	13	11.6	31	20.4	
1-10	93	40.3	33	33.7	47	42.0	58	38.2	
>10	109	47.2	36	36.7	45	40.2	55	36.2	
Unknown	11	4.8	12	12.2	7	6.2	8	5.2	
N stage									0.411
N0	47	20.4	23	23.5	20	17.9	29	19.1	
N1	105	45.5	46	46.9	56	50.0	60	39.5	
N2	42	18.2	15	15.3	22	19.6	32	21.1	
N3	27	11.7	8	8.2	12	10.7	27	17.8	
Unknown	10	4.2	6	6.1	2	1.8	4	2.6	
AJCC stage									0.097
IIIB	203	87.9	90	91.8	99	88.4	124	81.6	
IIIC	28	12.1	8	8.2	13	11.6	28	18.4	
Lymphovascular invasion									0.594
Negative	45	19.5	21	21.4	16	14.3	34	22.4	
Positive	123	53.2	45	45.9	60	53.6	72	47.4	
Unknown	63	27.3	32	32.7	36	32.1	46	30.2	
Surgery									0.427
No	21	9.1	12	12.2	12	10.7	21	13.8	

593 IBCs (2010-2011) from NCDB
 women ≥18 years cT4d cN0-3 cM0
 Median FU 24 months

4 subtypes:

- 1) HR+/HER2- (Luminal A) 231 pts (39%)
- 2) HR+/HER2+ (Luminal B) 98 pts (16%)
- 3) HR-/HER2+ (HER2 like) 112 pts (19%)
- 4) HR-/HER2- (triple negative) 152 pts (26%)

	HR-/HER2-defined subtypes								P
	HR+/HER2-		HR+/HER2+		HR-/HER2+		Triple negative		
	No.	%	No.	%	No.	%	No.	%	
Yes	210	90.9	86	87.8	100	89.3	131	86.2	0.246
Margin status									
Negative	172	74.5	73	74.5	93	83.0	112	73.7	
Positive	25	10.8	8	8.2	6	5.4	14	9.2	
Unknown	13	5.6	5	5.1	1	0.9	5	3.3	0.251
Radiotherapy									
No	53	22.9	26	26.5	39	34.8	39	25.7	
Yes	177	76.6	71	72.5	72	64.3	110	72.4	0.068
Unknown	1	0.4	1	1.0	1	0.9	3	1.9	
Hormone therapy									
No	52	22.5	25	25.5	107	95.5	144	94.7	<0.001
Yes	175	75.8	70	71.4		3.6	5	3.3	
Unknown	4	1.7	3	3.1	1	0.9	3	2.0	
(Neo)adjuvant chemotherapy									
No	15	6.5	1	1.0	2	1.8	7	4.6	0.068
Yes	216	93.5	97	99.0	110	98.2	145	95.4	

Chemotherapy response and survival of inflammatory breast cancer by hormone receptor- and HER2-defined molecular subtypes approximation: an analysis from the National Cancer Database

pCR

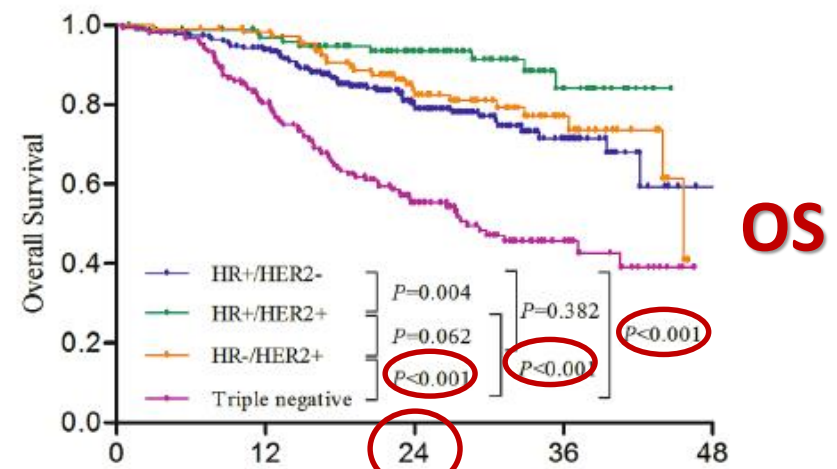
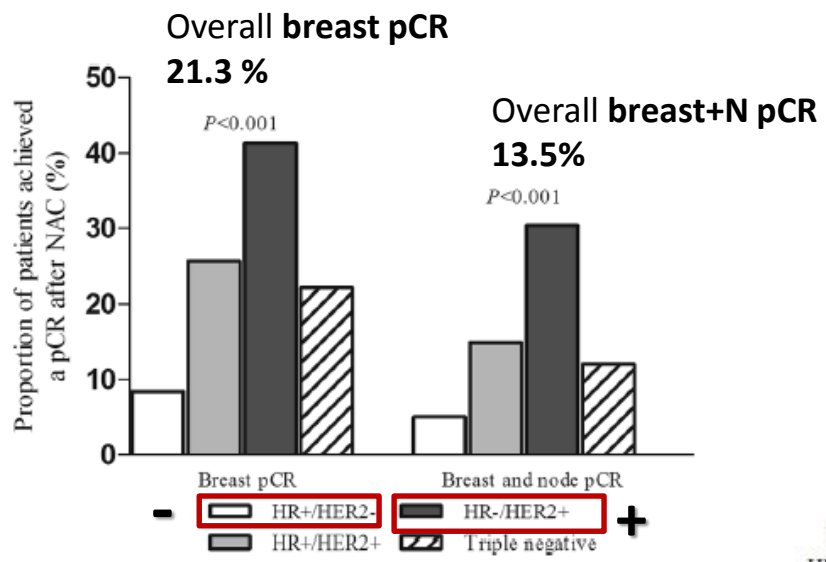


Fig. 2 Difference of pCR rate (breast pCR and breast and node pCR) among distinct HR-/HER2-defined breast cancer subtypes

No. at risk	Follow-up Time (months)				
	0	12	24	36	48
HR+/HER2-	231	204	115	34	1
HR+/HER2+	98	91	63	18	0
HR-/HER2+	112	106	65	23	0
Triple negative	152	116	63	19	0

Cumulative 2-year and 4-year OS rates of different HR-/HER2-defined subtypes

OS rate (%)	HR-/HER2-defined subtypes			
	HR+/HER2-	HR+/HER2+	HR-/HER2+	Triple negative
2-year	80.3 (95 % CI 74.0–85.2)	93.5 (95 % CI 86.0–97.0)	83.9 (95 % CI 75.0–89.9)	55.3 (95 % CI 46.6–63.2)
4-year	59.1 (95 % CI 39.2–74.5)	84.2 (95 % CI 68.5–92.5)	38.4 (95 % CI 5.5–72.9)	38.8 (95 % CI 27.1–50.3)

Chemotherapy response and survival of inflammatory breast cancer by hormone receptor- and HER2-defined molecular subtypes approximation: an analysis from the National Cancer Database

Impact of receptor-defined molecular subtype and other clinicopathologic or treatment factors on OS by multivariate survival analysis (n = 593)

Factors	Hazard ratio	95 % CI	P
Charlson/Deyo score			
0	Reference		
1	1.413	0.884–2.258	0.149
2	3.402	1.804–6.276	<0.001
Surgery/margin status			
Surgery, negative margin	Reference		
Surgery, positive margin	1.986	1.155–3.416	0.013
Surgery, unknown margin	1.086	0.456–2.588	0.852
No surgery	3.268	1.844–5.792	<0.001
Radiotherapy			
No	Reference		
Yes	0.543	0.375–0.787	0.001
Unknown	0.159	0.021–1.216	0.076
Hormone therapy			
No	Reference		
Yes	0.548	0.369–0.812	0.003
Unknown	0.164	0.020–1.323	0.090
AJCC stage			
IIIB	Reference		
IIIC	1.558	1.020–2.381	0.040
Regional nodes examined			
0	Reference		
1–10	1.641	0.947–2.842	0.077
>10	1.364	0.744–2.503	0.315
Unknown	1.080	0.472–2.474	0.855

OS multivariate analysis

Molecular subtype			
HR+/HER2–	Reference		
HR+/HER2+	0.304	0.147–0.630	0.001
HR–/HER2+	0.407	0.222–0.746	0.004
Triple negative	1.321	0.820–2.123	0.253
Molecular subtype			
HR+/HER2–	3.287	1.587–6.806	0.001
HR+/HER2+	Reference		
HR–/HER2+	1.337	0.578–3.095	0.497
Triple negative	4.343	2.044–9.227	<0.001
Molecular subtype			
HR+/HER2–	0.757	0.470–1.220	0.253
HR+/HER2+	0.230	0.108–0.489	<0.001
HR–/HER2+	0.308	0.186–0.509	<0.001
Triple negative	Reference		



Chemotherapy response and survival of inflammatory breast cancer by hormone receptor- and HER2-defined molecular subtypes approximation: an analysis from the National Cancer Database

CONCLUSIONS:

- ✓ **IBC** is an aggressive heterogeneous disease with **distinct molecular subtypes** associated with **differential prognostic outcomes and sensitivities to NAC**
- ✓ **IBC HR-positive disease** was **not associated** with **favorable prognosis**
- ✓ **IBC HER2-positive status** was **not correlated with unfavorable OS**
- ✓ **Triple-negative** and **Luminal A** are **independent predictors for suboptimal OS** in IBC
- ✓ The need to address the aggressive biology of IBC and to identify novel **individualized IBC-specific therapies for different subtypes**

Radioterapia dopo CT neoadiuvante

1) NACT → MASTECTOMIA → ruolo RT LOCOREGIONALE

2) NACT → CH → RT: risultati per SOTTOTIPI MOLECOLARI

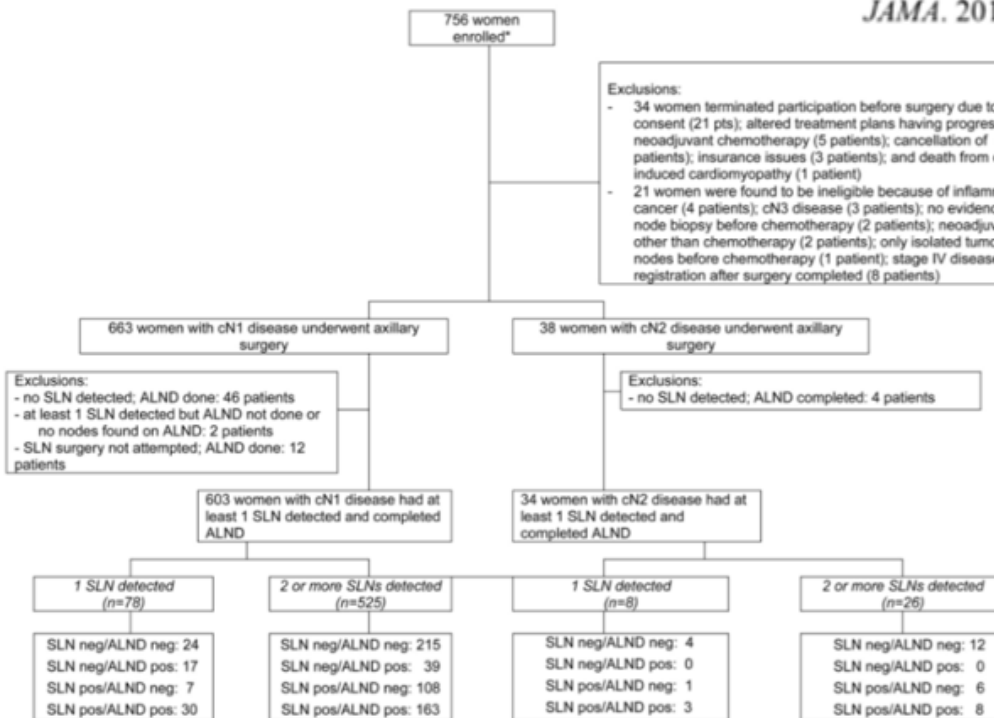
3) NACT → CH con **SLNB + ALND** → RT: **variability in practice**

Patterns of Local-Regional Management Following Neoadjuvant Chemotherapy in Breast Cancer: Results From ACOSOG Z1071 (Alliance)

Bruce G. Haffty, MD,* Linda M. McCall, MS,† Karla V. Ballman, PhD,‡

JAMA. 2013 October 9; 310(14): 1455–1461. doi:10.1001/jama.2013.278932.

- ✓ **Prospective trial**: false negative rate of **SLNB** after **NAC** in **cN+** breast cancer pts
- ✓ **RT at the discretion of treating physicians** (opportunity to evaluate variability in practice)



- 756 cT1-T4 cN1-N2
- 663 cN1(bx) pts SLNB IR 92.7%
→ 40% convertiti ypN0 e 60% (382 pts) ypN+
- 525 pts ≥2 SLN (criterio di elegibilità)
→ 39 pts BLSN neg ma DLA +
→ **FNR 12.6% (39/310)** (cut off FNR <10%)

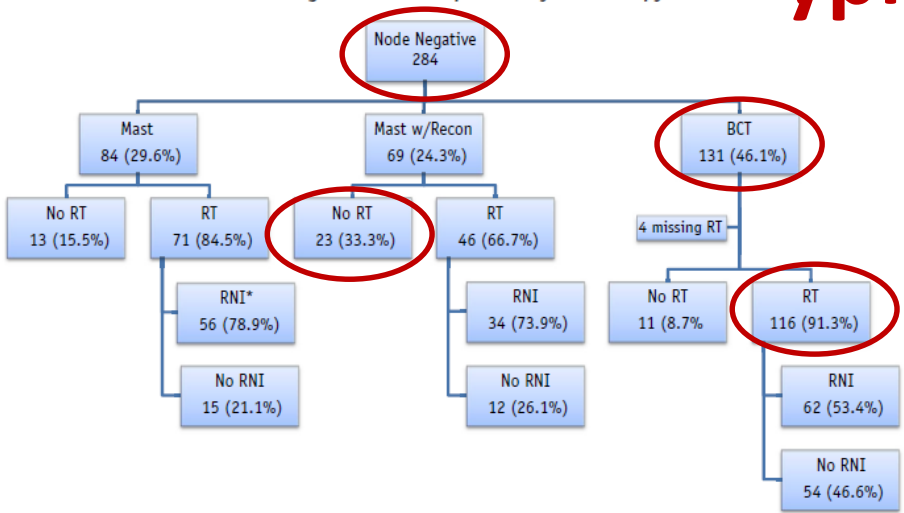
FNR: 1 SLN → 31.5%
2 SLN → 21%
3 SLN → <10%

Patterns of Local-Regional Management Following Neoadjuvant Chemotherapy in Breast Cancer: Results From ACOSOG Z1071 (Alliance)

A

Local-Regional Management From Z1071
Node Negative After Preoperative System Therapy

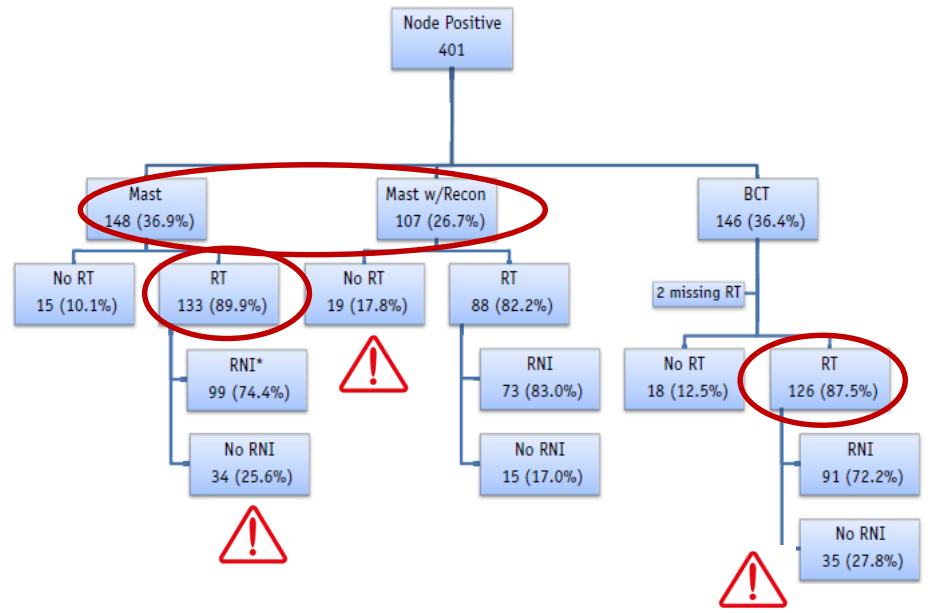
ypN0



B

Local-Regional Management From Z1071
Node Positive After Preoperative System Therapy

ypN+



Patterns of Local-Regional Management Following Neoadjuvant Chemotherapy in Breast Cancer: Results From ACOSOG Z1071 (Alliance)

RT

Table 3 Radiation therapy by surgical approach

Radiation therapy	Received RT	Breast-conserving surgery (N = 277)	Mastectomy without reconstruction (N = 232)	Mastectomy with immediate reconstruction (N = 176)	P value
Breast RT	Yes	242 (89.3%)	NA	NA	NA
	No	29 (10.7%)			
Chest wall RT	Yes	NA	179 (77.2%)	100 (56.8%)	<.0001
	No		53 (22.8%)	76 (43.2%)	
Axillary RT	Yes	64 (23.6%)	64 (27.6%)	57 (32.4%)	.12
	No	207 (76.4%)	168 (72.4%)	119 (67.6%)	
Supraclavicular RT	Yes	134 (49.4%)	121 (52.2%)	82 (46.6%)	.54
	No	137 (50.6%)	111 (47.8%)	94 (53.4%)	
Internal mammary RT	Yes	21 (7.8%)	26 (11.2%)	16 (9.1%)	.41
	No	250 (92.2%)	206 (88.8%)	160 (90.9%)	

Patterns of Local-Regional Management Following Neoadjuvant Chemotherapy in Breast Cancer: Results From ACOSOG Z1071 (Alliance)

Table 4 Axillary radiation

Finding	Axillary radiation received		P value
	Yes	No	
Type of breast surgery			.12
Breast-conserving surgery	64 (34.6%)	207 (41.9%)	
Mastectomy without reconstruction	64 (34.6%)	168 (34.0%)	
Mastectomy with reconstruction	57 (30.8%)	119 (24.1%)	
Unknown	7	6	
Clinical tumor stage at presentation			.85
cT0/Tis	4 (2.1%)	6 (1.2%)	
cT1	26 (13.5%)	63 (12.6%)	
cT2	105 (54.7%)	274 (54.9%)	
cT3	50 (26.0%)	131 (26.2%)	
cT4	7 (3.6%)	25 (5.0%)	
Unknown	0	1	
Clinical nodal stage at presentation			.94
cN1	179 (94.2%)	469 (94.4%)	
cN2	11 (5.8%)	28 (5.6%)	
Unknown	2	3	
Clinical stage			.78
II	127 (66.8%)	326 (65.7%)	
III	63 (33.2%)	170 (34.3%)	
Unknown	2	4	
Pathologic tumor stage at surgery			.025
pT0/is	54 (28.6%)	176 (35.3%)	
pT1	62 (32.8%)	187 (37.5%)	
pT2	55 (29.1%)	93 (18.6%)	
pT3	18 (9.5%)	40 (8.0%)	
pT4	0	3 (0.6%)	
Unknown	3	1	
Pathologic nodal stage at surgery			.002
pN0	62 (32.3%)	222 (44.4%)	
pN1	65 (33.8%)	174 (34.8%)	
pN2	48 (25.0%)	81 (16.2%)	
pN3	17 (8.8%)	23 (4.6%)	
Unknown	0	0	
Approximated tumor subtype			.13
Triple negative	48 (25.0%)	120 (24.0%)	
HER2 positive	48 (25.0%)	163 (32.6%)	
HR positive, HER2 negative	96 (50.0%)	217 (43.4%)	
Unknown	0	0	

Patterns of Local-Regional Management Following Neoadjuvant Chemotherapy in Breast Cancer: Results From ACOSOG Z1071 (Alliance)

CONCLUSIONS:

- Most **clinically node-positive** patients treated with NAC undergoing **mastectomy** receive **RT**
- **RT is less common** in patients undergoing **reconstruction**
- There is wide **variability in RT fields**
- There is a significant need for greater uniformity and guidelines regarding RT following NAC

VI ZOOM Journal Club 2016

Bologna, 17 Febbraio 2017

NH Hotel De La Gare



IV Sessione - Radioterapia dopo CT neoadiuvante

Moderatori: Marina Guenzi, Alessandra Huscher

15.00 Rapporteur: Alessandra Fozza

15.15 Discussant: Icro Meattini

15.30 Caso clinico: Antonino Daidone



...GRAZIE!