IS POSTMASTECTOMY RADIATION NEEDED IN PATIENTS WITH NODAL PCR FOLLOWING NEOADJUVANT CHEMOTHERAPY?

CON

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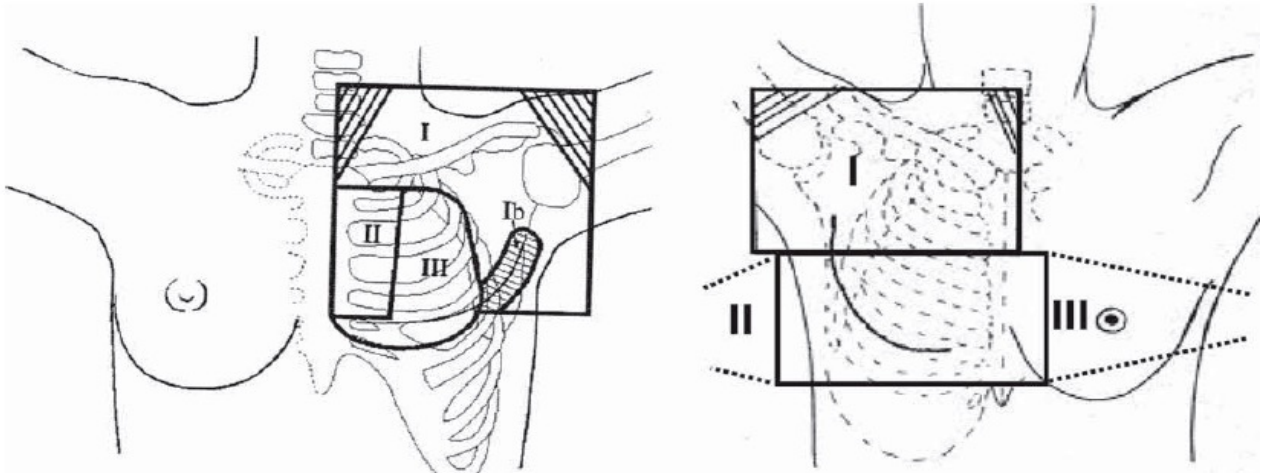
Disclosures

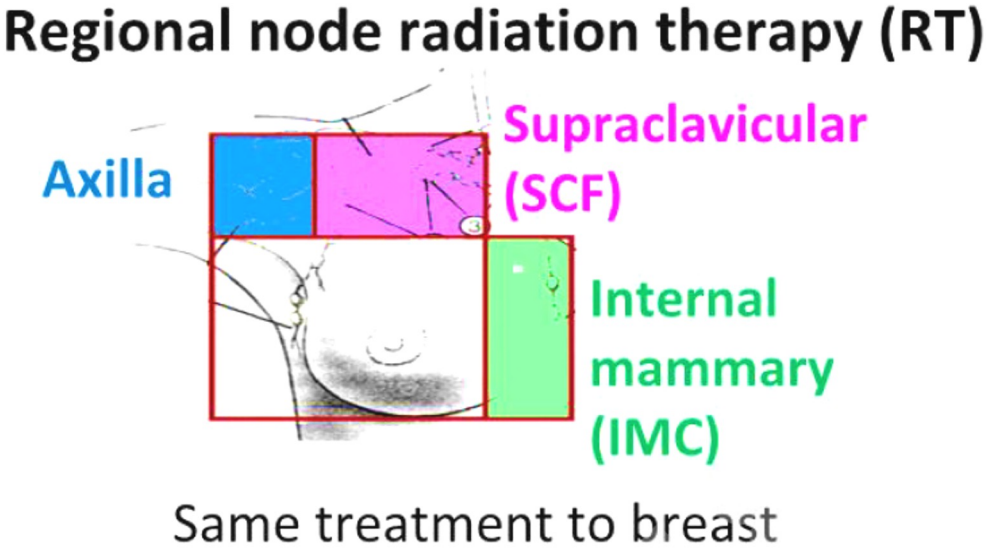
- Emory
- NCI
- Genentech
- Pfizer
- Varian
- V Foundation
- BioAscend
- MJH Life Sciences
- OncoHealth
- There will be no discussion of off-label drug or device use or references to proprietary technology

CN1 PATIENTS → YPN0

IS POSTMASTECTOMY RADIATION NECESSARY WHEN CN1 BECOMES YPNO DISEASE?

TRADITIONAL BREAST, POSTMASTECTOMY (PMRT), AND REGIONAL NODAL IRRADIATION (RNI) FIELDS





Comprehensive all or nothing RNI approach
Mostly in patients with N+ disease

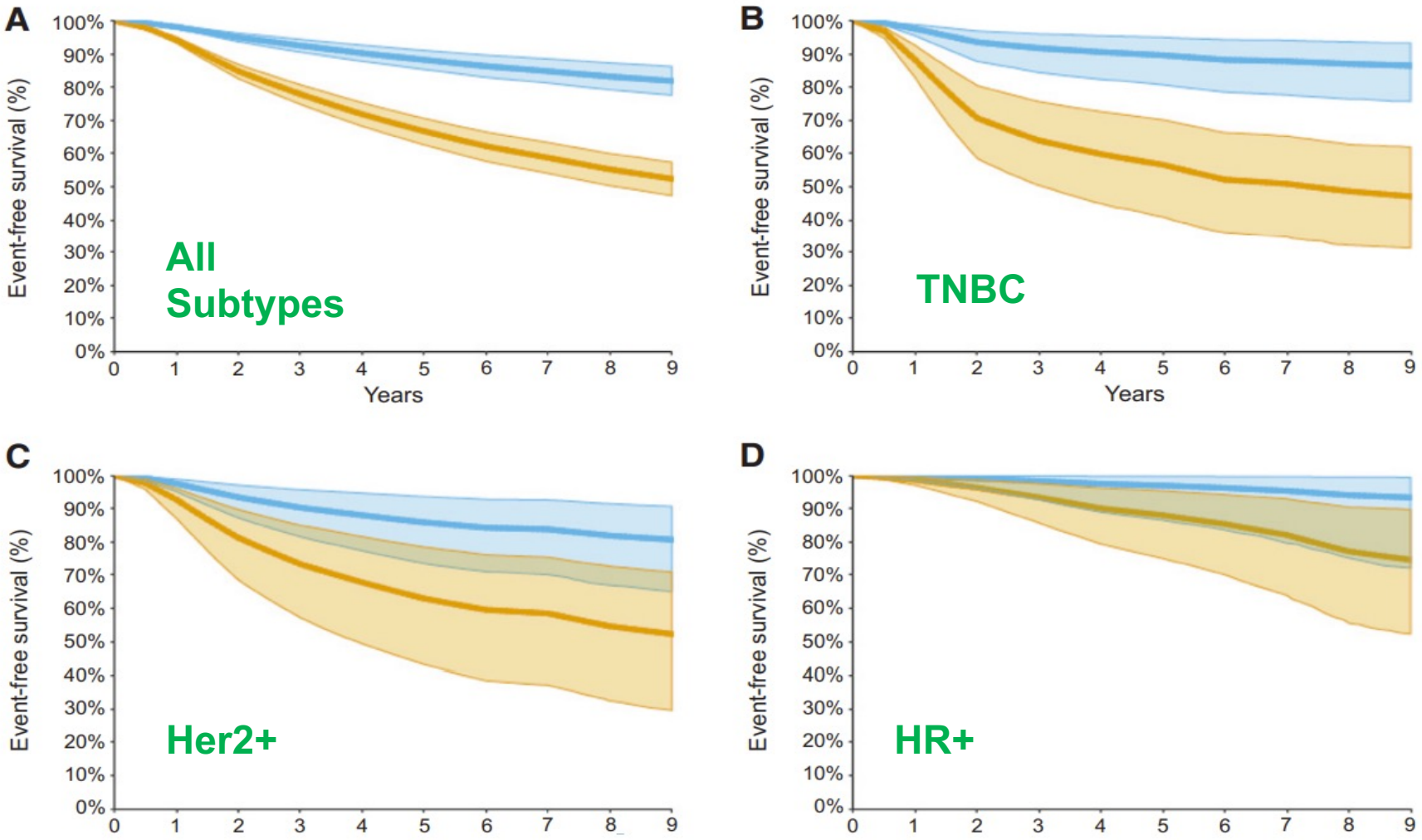
PMRT AND RNI TOXICITY

- Poor cosmetic outcomes particularly within reconstructed breast
- Increases risk of impaired shoulder mobility
- Increases risk of lymphedema
- Small increased risk of secondary malignancies
- Increased risk of cardiac disease and pulmonary toxicities seen in older studies appear to be mitigated with improvements in modern treatment planning

Torres et al. JCO 2020; 38(20); 2299-2309

TUMOR SUBTYPE, PCR, AND EFS

pCR is prognostic particularly in patients with triple negative and Her2+ disease



Blue: pCR group
Yellow: Residual disease (RD) group

Spring et al. CCR 2020; 26:2838-48

PREDICTORS OF LRR IN NSABP B-18 AND B-27

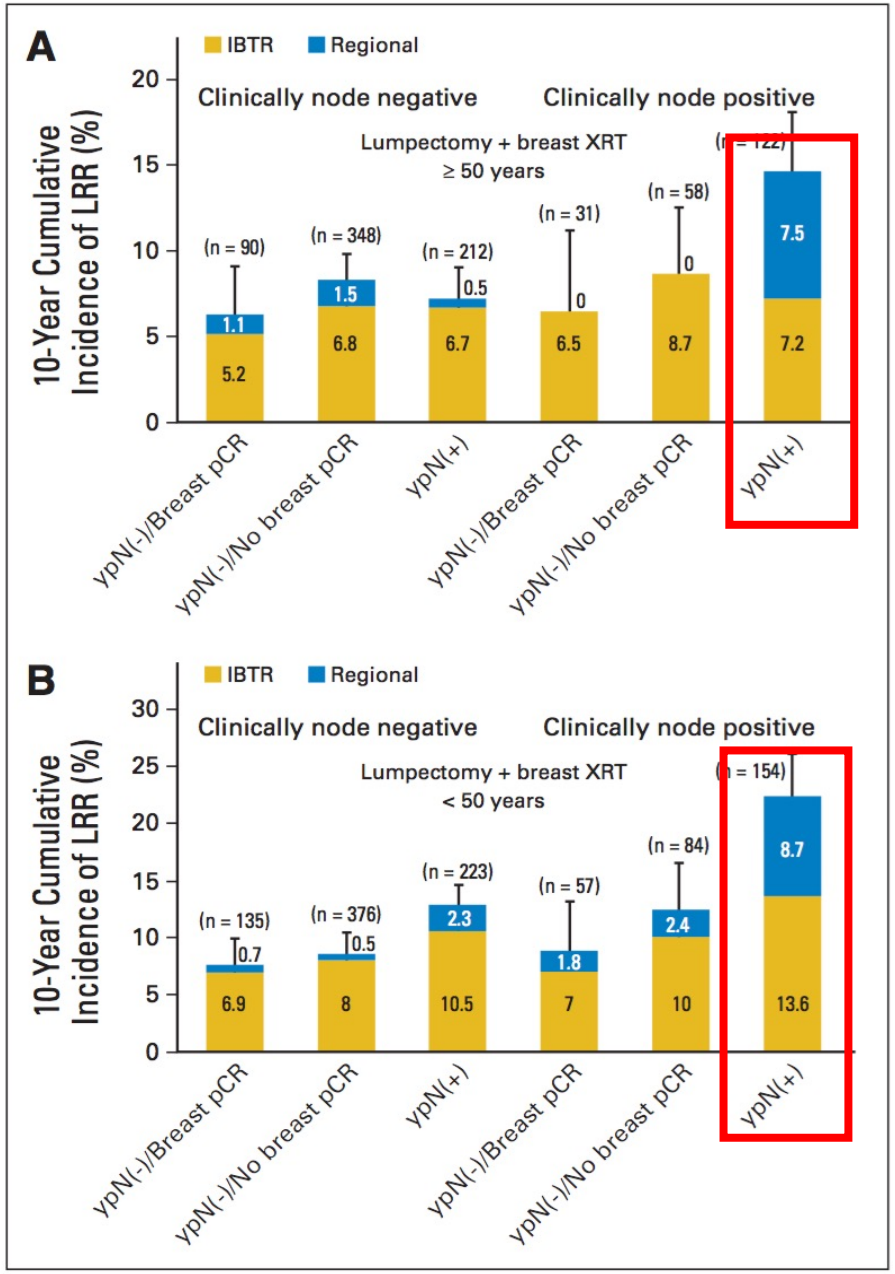
Table 2. Multivariate Analysis of Independent Predictors of 10-Year LRR in the Combined Data Set*

Variable	HR	95% CI	*P*
Age ≥ 50 *v* < 50 years†	0.78	0.63 to 0.98	.03
Clinical tumor size > 5 *v* ≤ 5 cm†	1.51	1.19 to 1.91	< .001
Clinical nodal status cN(+) *v* cN(−)†	1.61	1.28 to 2.02	< .001
Nodal/breast pathologic status			< .001
ypN(−)/no breast pCR *v* ypN(−)/breast pCR†	1.55	1.01 to 2.39	
→ ypN(+) *v* ypN(−)/breast pCR†	2.71	1.79 to 4.09	

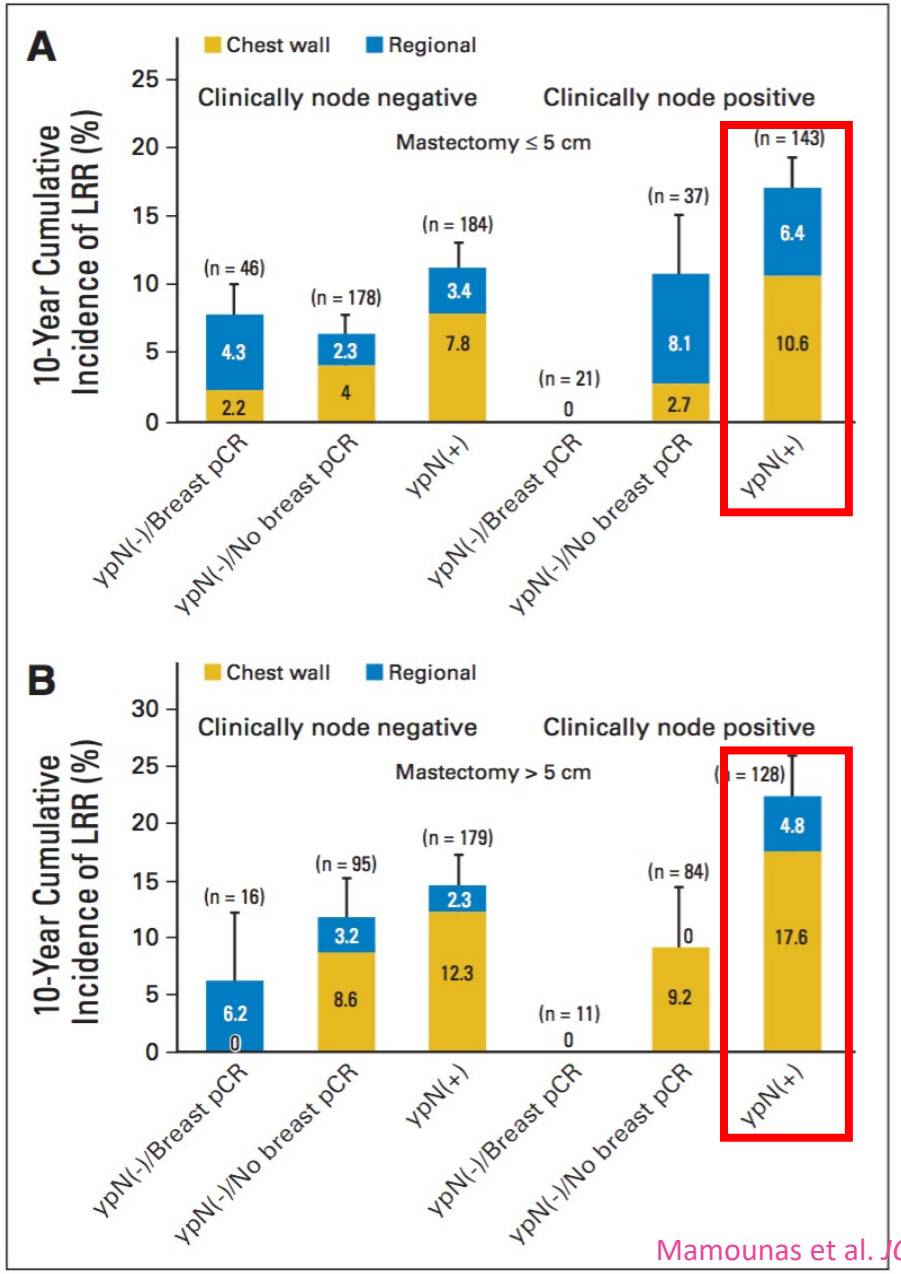
Mamounas et al. *JCO* 2012

NSABP B-18
NSABP B-27

Lumpectomy



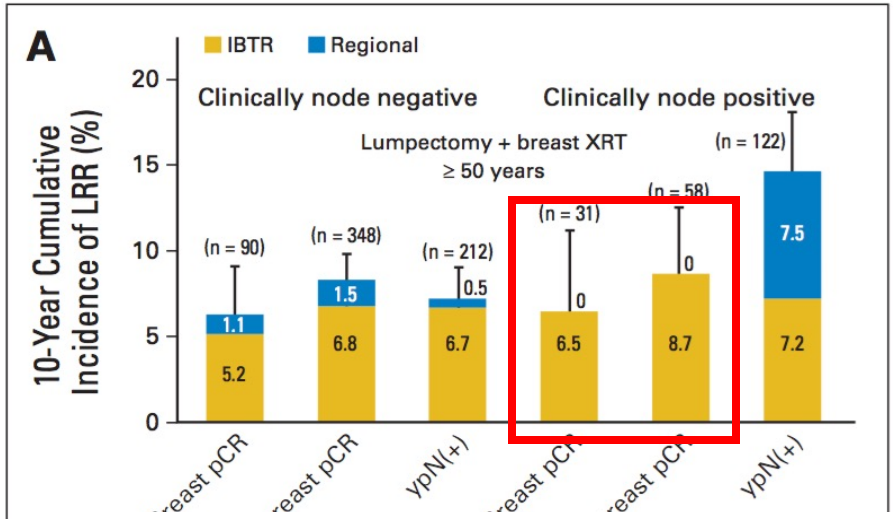
Mastectomy

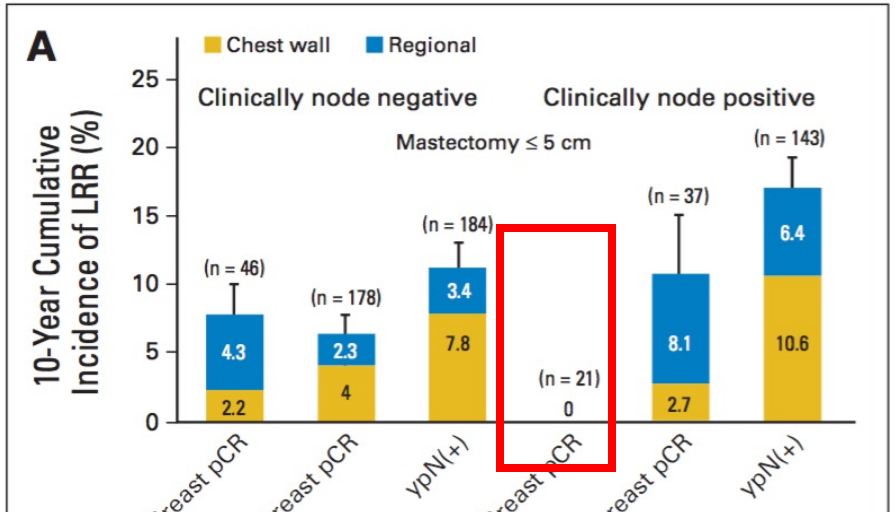


Mamounas et al. *JCO* 2012: 30(32):3960-66

Lumpectomy

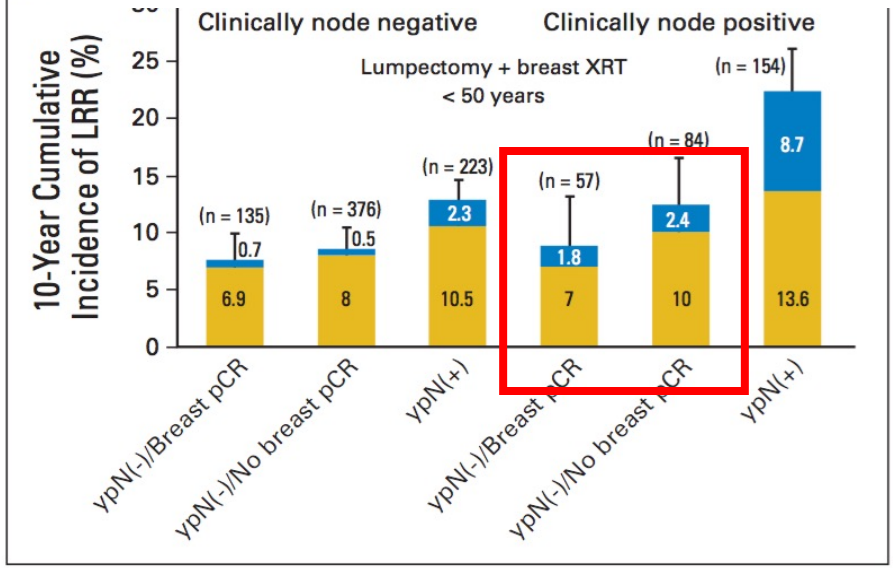
Mastectomy

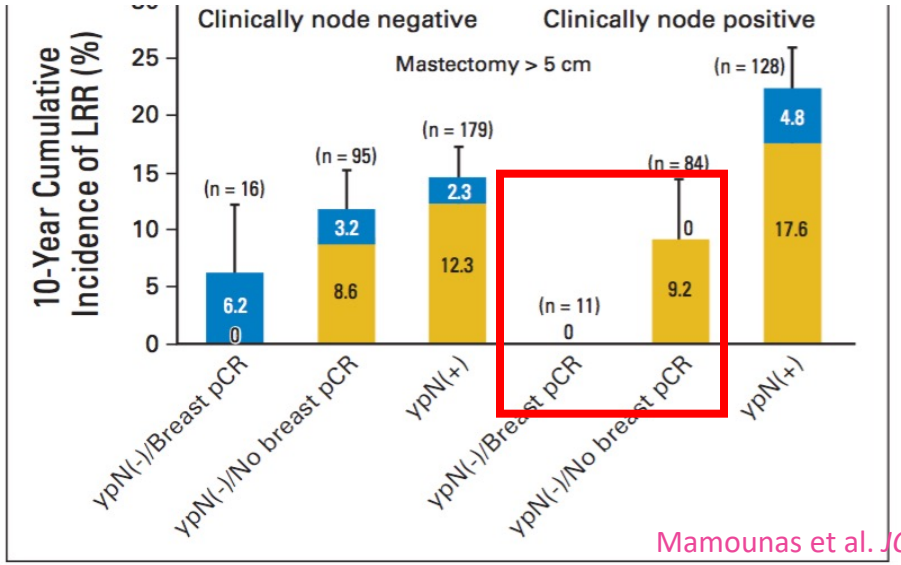




NSABP B-18
NSABP B-27

In cN1 patients who become ypN0, 10-year LRR is 0-12% depending on age, breast response, and type of surgery





Mamounas et al. *JCO* 2012: 30(32):3960-66

Loco-regional Irradiation in Patients with Biopsy-proven Axillary Node Involvement at Presentation Who Become Pathologically Node-negative After Neoadjuvant Chemotherapy: Primary Outcomes of NRG Oncology/NSABP B-51/RTOG 1304

Eleftherios P. Mamounas[1*], Hanna Bandos[2], Julia R. White[3*], Thomas B. Julian[4], Atif J. Khan[5], Simona F. Shaitelman[6], Mylin A. Torres[7], Frank A. Vicini[8], Patricia A. Ganz[9], Susan A. McCloskey[10], Peter C. Lucas[11,12], Nilendu Gupta[3], X. Allen Li[13], Beryl McCormick[5], Saumil Gandhi[6], Rahul D. Tendulkar[14], Vivek S. Kavadi,[15], Masahiko Okamoto[16], Samantha Andrews Seaward[17], William J. Irvin, Jr.[18], Jolinta Lin [7], Robert Mutter[19], Thierry M. Muanza[20], Andrew A. Muskovitz[21], Reshma Jagsi[22], Anna C. Weiss[23,24], Walter J. Curran, Jr.[7], and Norman Wolmark[12]

*These authors contributed equally.

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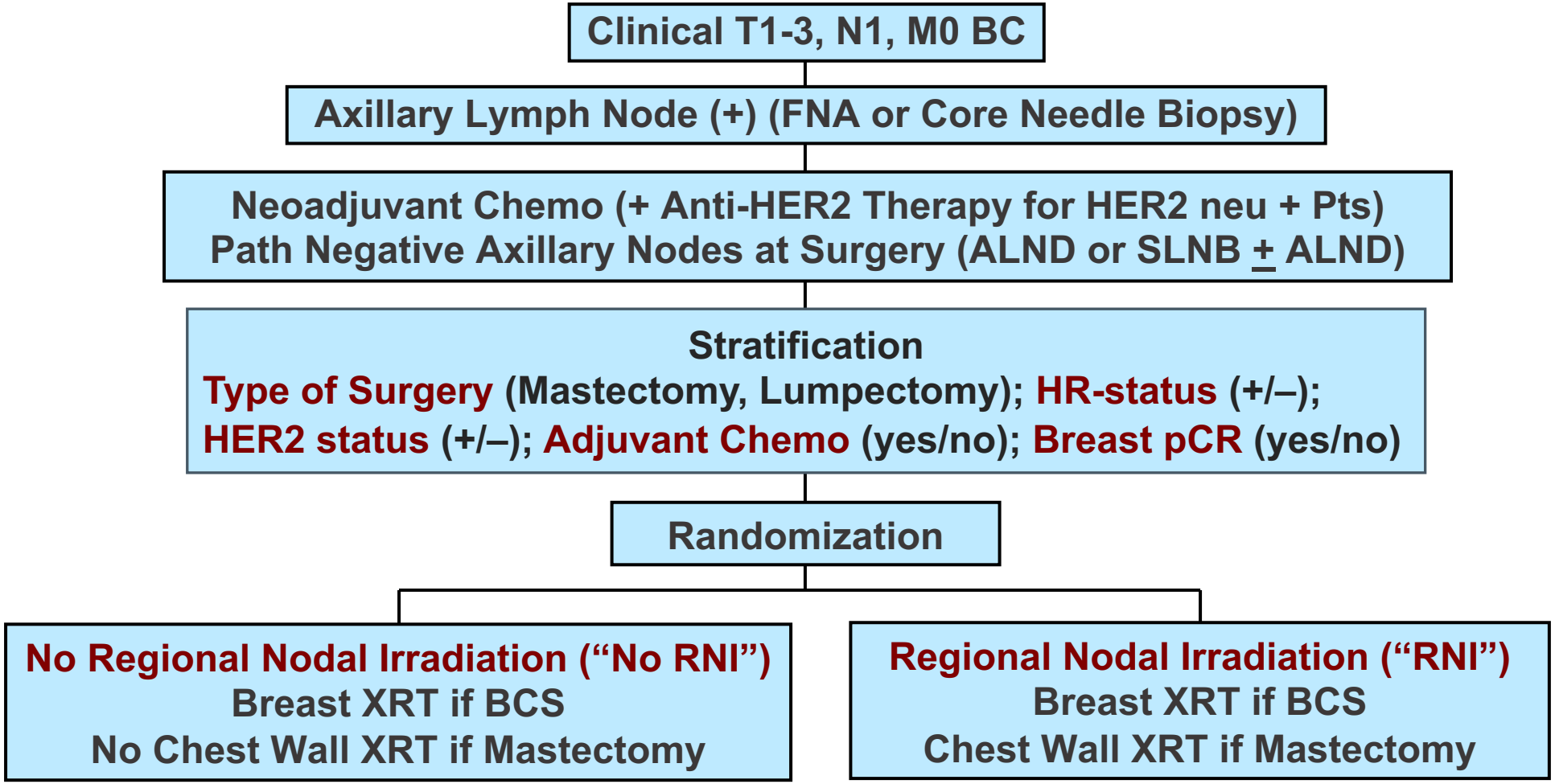
NSAPB B-51/RTOG 1304



FNA: Fine Needle Aspiration; ALND: Axillary Lymph Node Dissection; SLNB: Sentinel Lymph Node Biopsy; XRT: Radiation; BCS: Breast Conserving Surgery

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Statistical Considerations

- Primary endpoint – invasive BC recurrence-free interval (IBCRFI)
- Study was designed to have 80% power to detect 35% reduction in annual IBCRFI rate (4.6% abs. risk reduction in 5-yr cumulative rate)
- Per protocol, final analysis was to occur after 172 events or 10 years after study initiation
- Reported time-driven analysis, prespecified in the protocol
- Median Follow-up Time: 59.5 months (IQR 40.7-74.1)

Baseline Characteristics

Characteristic		No RNI (%) n=821	RNI (%) n=820
Age	**Median**	52 years	52 years
	≤ 49 yrs	40	41
	50-59 yrs	32	33
	≥ 60 yrs	28	26
Race	Asian	8	6
	Black/African American	17	18
	White	69	69
	Unknown/Other	6	6
Ethnicity	Hispanic or Latino	14	14
	Not Hispanic or Latino	83	82
	Unknown	3	3
Clinical Tumor Size	T1	21	21
	T2	59	61
	T3	20	18

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Baseline Characteristics

Characteristic		No RNI (%) n=821	RNI (%) n=820
Tumor Subtype	Triple-negative ER+ and/or PR+/HER2- ER- and PR-/HER2+ ER+ and/or PR+/HER2+	21 22 25 31	23 20 24 33
Breast Surgery	Lumpectomy Mastectomy	58 42	58 42
Axillary Surgery	SLNB ALND (+/-SLNB)	55 45	56 44
pCR in Breast	No Yes	22 78	21 79
Adjuvant Chemotherapy	No Yes	100 <1	99 1

56% Her2+
22% TNBC

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Axillary Surgery	SLNB ALND (+/-SLNB)	55 45	56 44
pCR in Breast	No Yes	22 78	21 79
Adjuvant Chemotherapy	No Yes	100 <1	99 1

60% Her2+
20% TNBC

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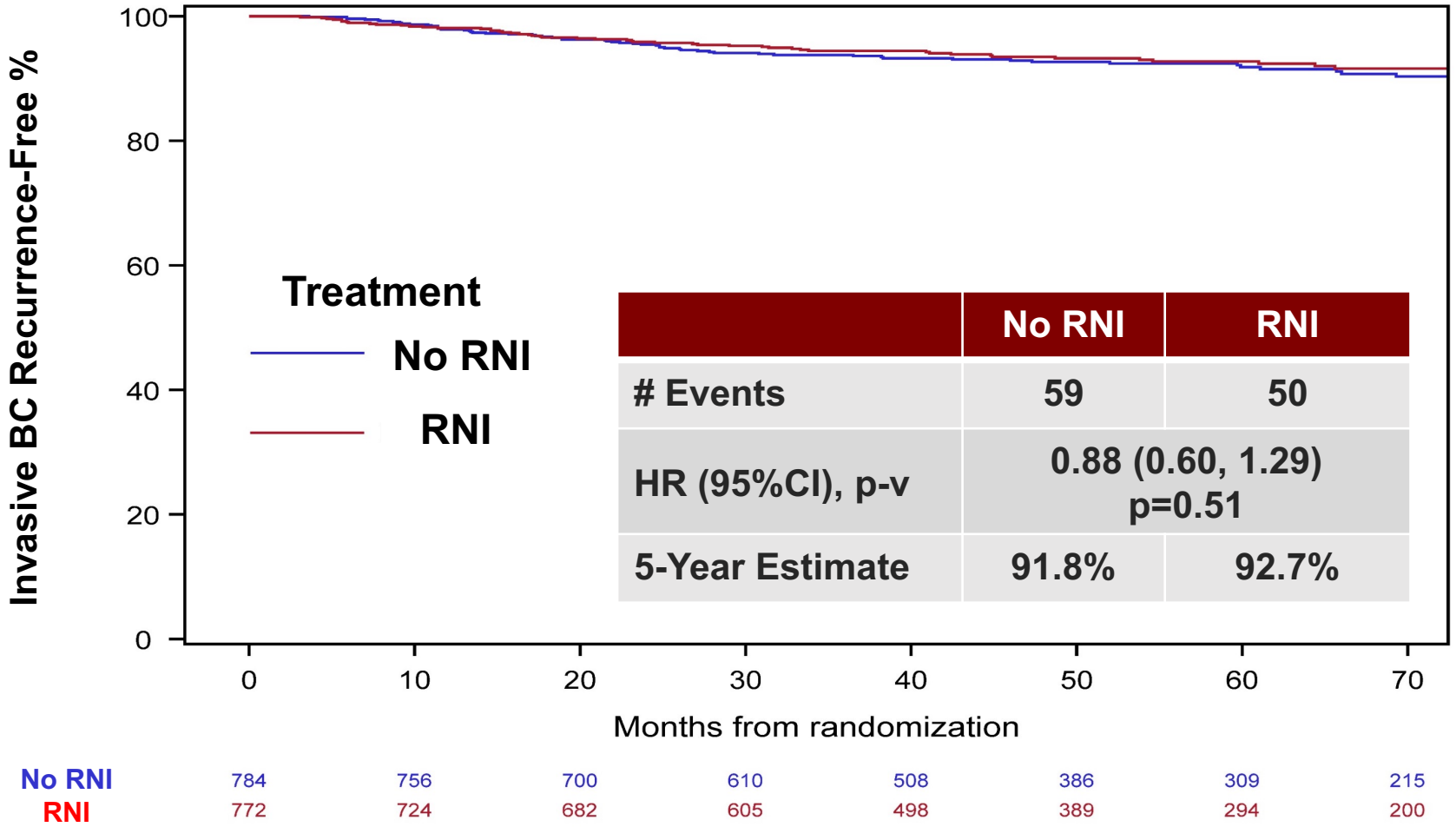
Primary Endpoint

Invasive Breast Cancer Recurrence-free Interval (IBCRFI)



	No RNI	RNI
# Events	59	50
HR (95%CI), p-v	0.88 (0.60, 1.29) p=0.51	
5-Year Estimate	91.8%	92.7%

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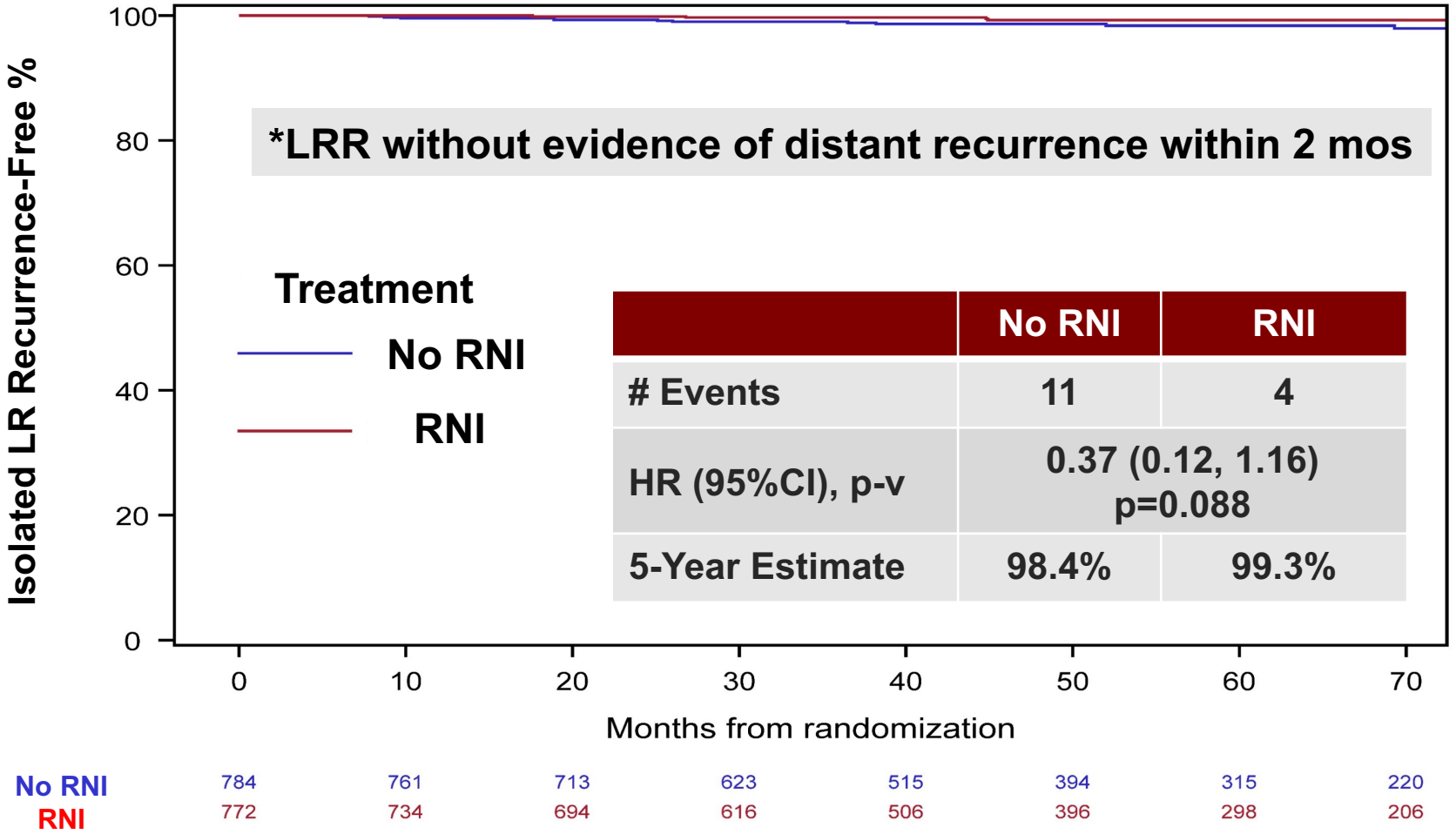
Secondary Endpoints

Isolated Loco-Regional Recurrence-free Interval (ILRRFI)*



	No RNI	RNI
# Events	11	4
HR (95%CI), p-v	0.37 (0.12, 1.16) p=0.088	
5-Year Estimate	98.4%	99.3%

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Secondary Endpoints

Isolated LRRs by Location

Location	No RNI (n=784)	RNI (n=772)
Local	2	4
Regional	8	0
Loco-regional	1	0
Total	11 (1.4%)	4 (0.5%)

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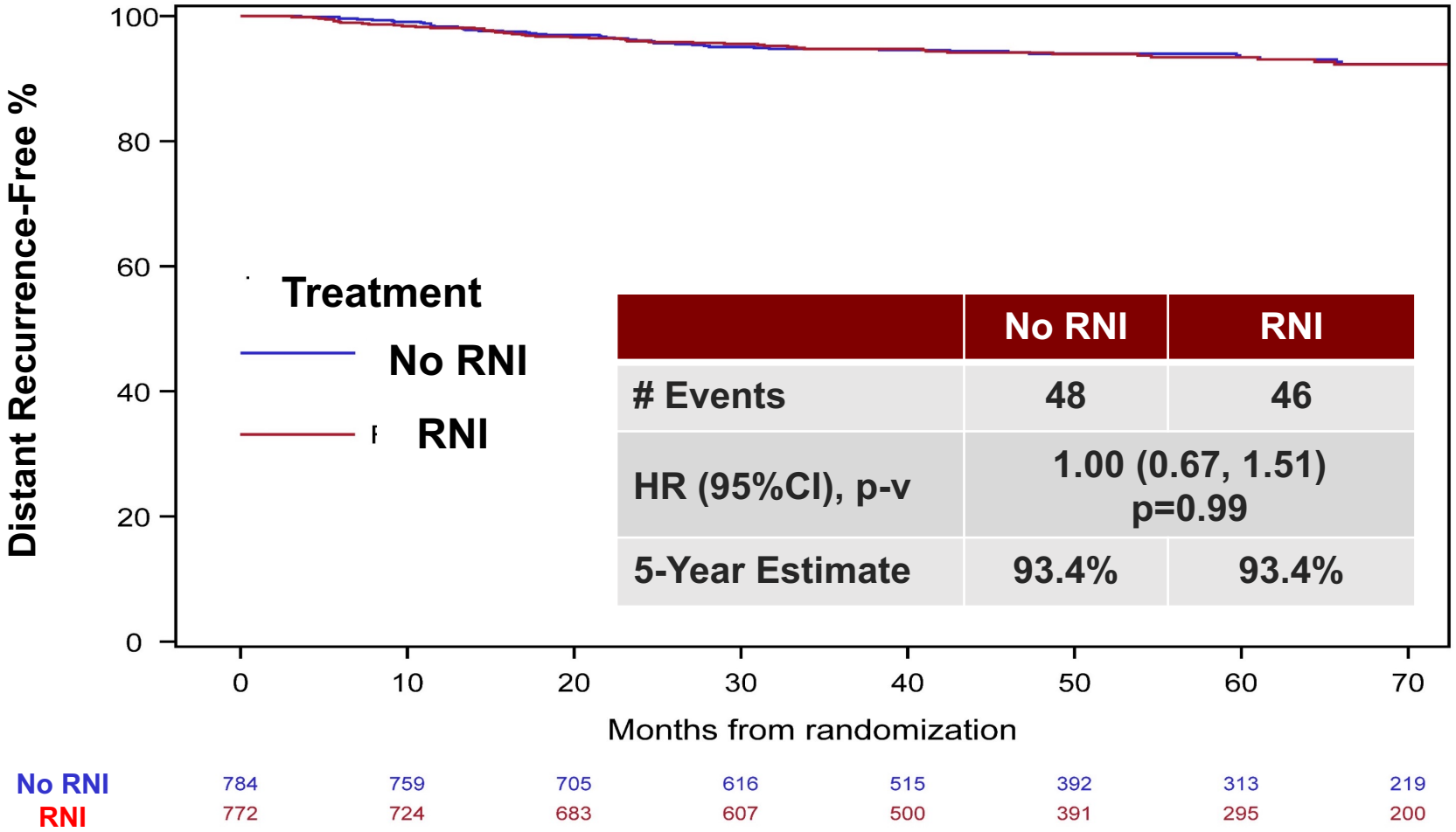
Secondary Endpoints

Distant Recurrence-free Interval (DRFI)



	No RNI	RNI
# Events	48	46
HR (95%CI), p-v	1.00 (0.67, 1.51) p=0.99	
5-Year Estimate	93.4%	93.4%

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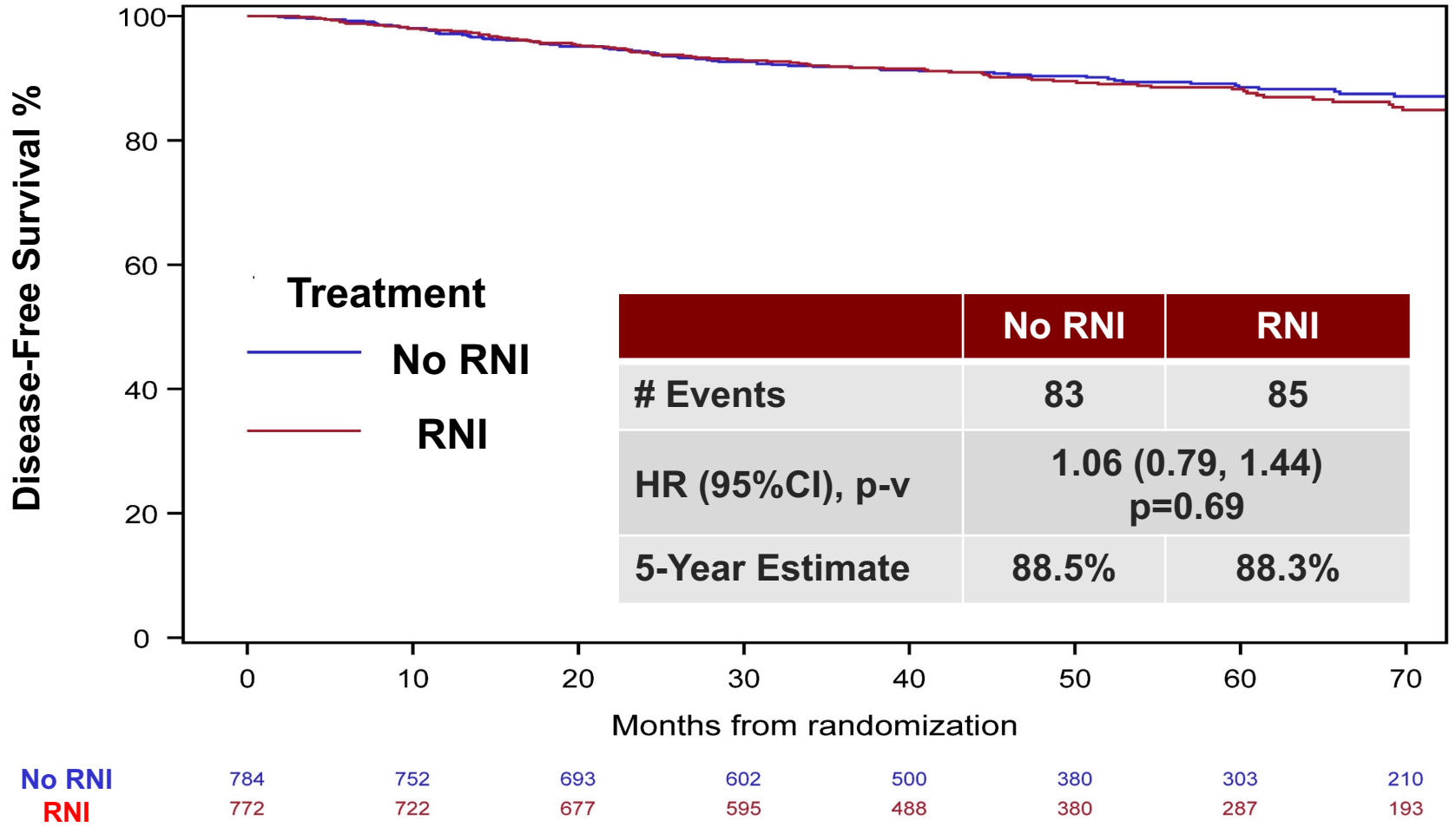
Secondary Endpoints

Disease-free Survival (DFS)



	No RNI	RNI
# Events	83	85
HR (95%CI), p-v	1.06 (0.79, 1.44) p=0.69	
5-Year Estimate	88.5%	88.3%

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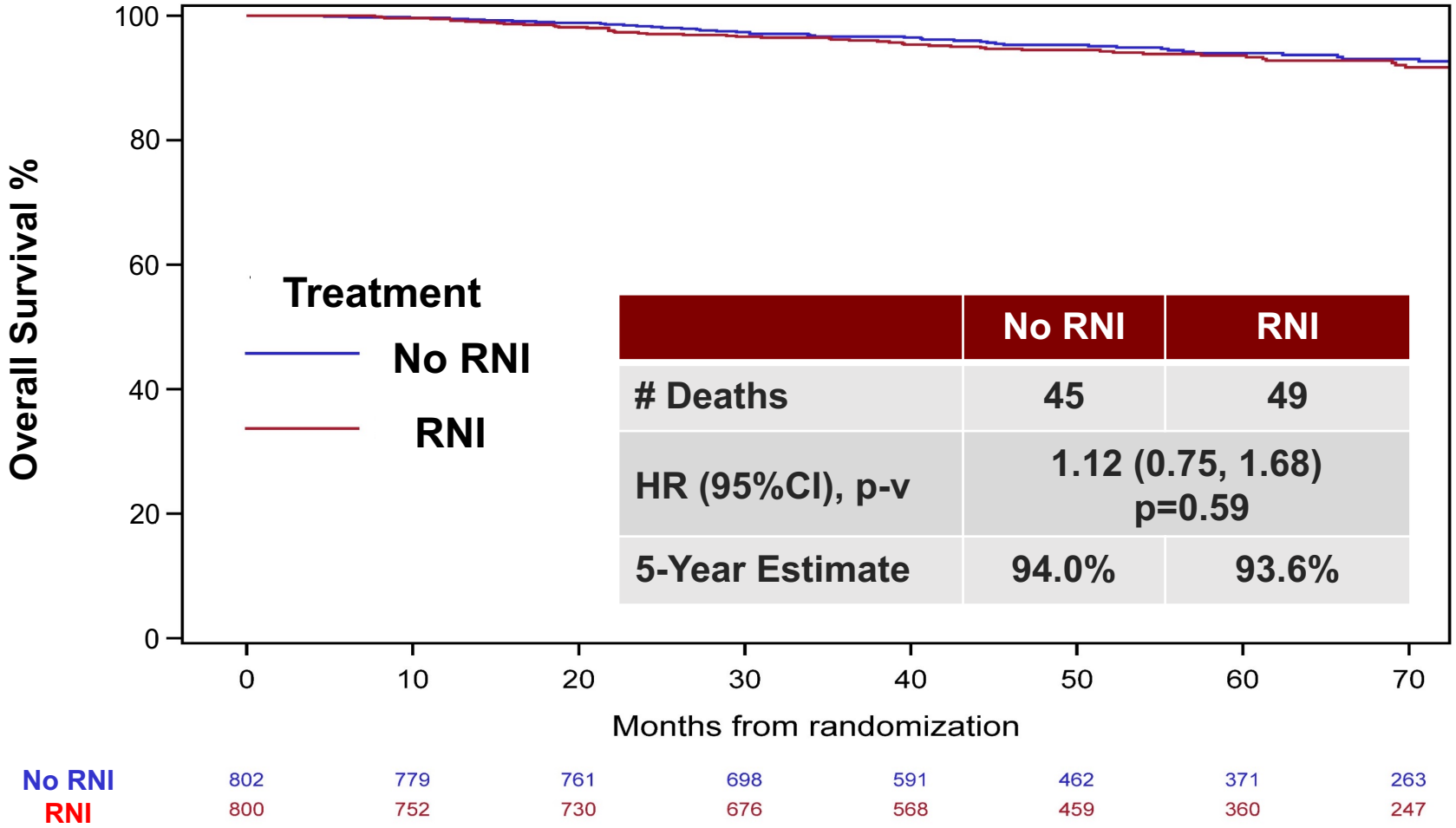
Secondary Endpoints

Overall Survival (OS)



	No RNI	RNI
# Deaths	45	49
HR (95%CI), p-v	1.12 (0.75, 1.68) p=0.59	
5-Year Estimate	94.0%	93.6%

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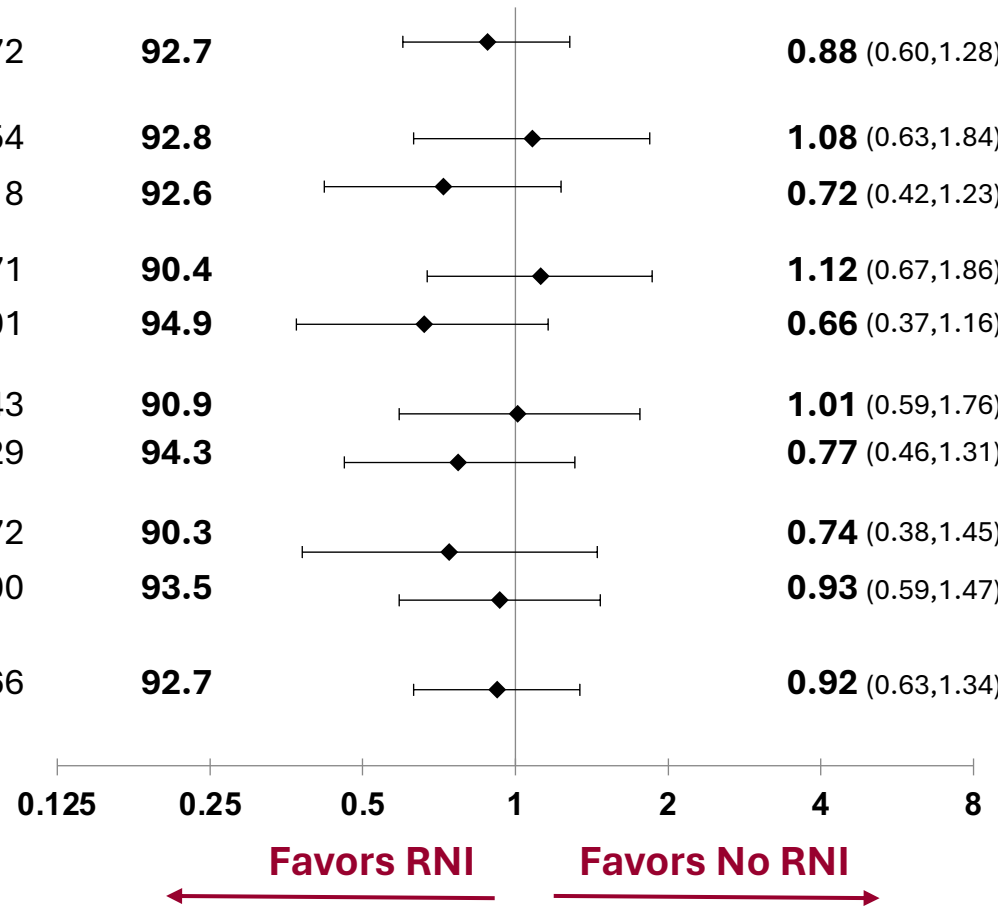
IBCRFI – Subgroup Analysis by Stratification Factors

Variable		No RNI (D/N)	No RNI 5-y est (%)	RNI (D/N)	RNI 5-y est (%)	HR (95% CI)	*P*-interaction
	All patients	59/784	**91.8**	50/772	**92.7**	**0.88** (0.60,1.28)	
Surgery	Lumpectomy	26/454	**93.5**	28/454	**92.8**	**1.08** (0.63,1.84)	**0.28**
	Mastectomy	33/330	**89.5**	22/318	**92.6**	**0.72** (0.42,1.23)	
ER/PR	Negative	28/367	**91.7**	31/371	**90.4**	**1.12** (0.67,1.86)	**0.17**
	Positive	31/417	**92.1**	19/401	**94.9**	**0.66** (0.37,1.16)	
HER2	Negative	25/342	**92.6**	26/343	**90.9**	**1.01** (0.59,1.76)	**0.47**
	Positive	34/442	**91.3**	24/429	**94.3**	**0.77** (0.46,1.31)	
pCR breast	No	20/173	**87.8**	15/172	**90.3**	**0.74** (0.38,1.45)	**0.59**
	Yes	39/611	**93.0**	35/600	**93.5**	**0.93** (0.59,1.47)	
Adjuvant Chemotherapy	No	57/780	**92.1**	50/766	**92.7**	**0.92** (0.63,1.34)	
	Yes	2/4		0/6			



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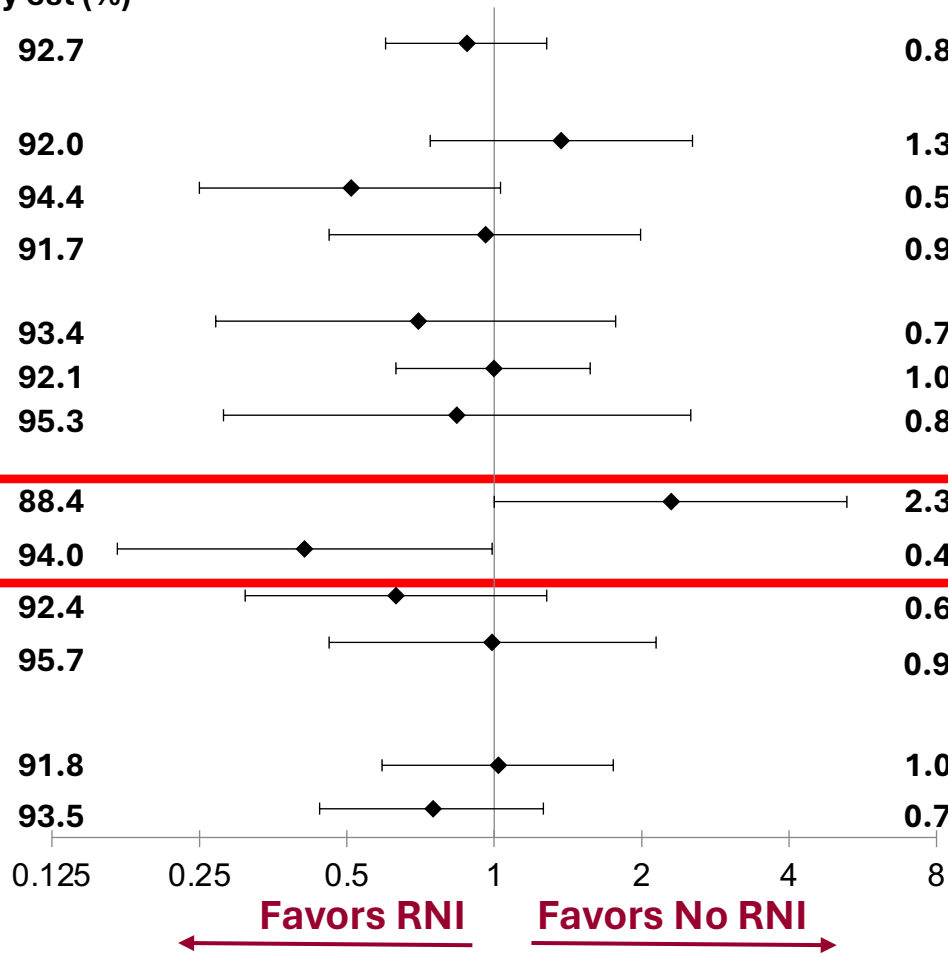
IBCRFI – Exploratory Subgroup Analysis

Variable		No RNI (D/N)	No RNI 5-y est (%)	RNI (D/N)	RNI 5-y est (%)	HR (95% CI)	P-interaction
	All patients	59/784	**91.8**	50/772	**92.7**	**0.88** (0.60,1.28)	
Age	<=49	18/311	**92.8**	24/312	**92.0**	**1.37** (0.74,2.54)	0.09
	50-59	25/257	**90.4**	12/254	**94.4**	**0.51** (0.25,1.03)	
	>= 60	16/216	**92.4**	14/206	**91.7**	**0.96** (0.46,1.99)	
Race	Black	11/135	**92.6**	8/140	**93.4**	**0.70** (0.27,1.77)	0.69
	White	40/543	**91.6**	36/533	**92.1**	**1.00** (0.63,1.57)	
	Other	8/106	**91.8**	6/99	**95.3**	**0.84** (0.28,2.52)	
Tumor Subtype	Triple-negative	8/169	**95.0**	19/188	**88.4**	**2.30** (1.00,5.25)	0.037
	ER/PR+/HER2-	17/173	**90.5**	7/155	**94.0**	**0.41** (0.17,0.99)	
	ER/PR-/HER2+	20/198	**88.8**	12/183	**92.4**	**0.63** (0.31,1.28)	
	ER/PR+/HER2+	14/244	**93.3**	12/246	**95.7**	**0.99** (0.46,2.14)	
Axillary Surgery	Axil +/- SLNB	27/357	**92.0**	25/338	**91.8**	**1.02** (0.59,1.75)	0.42
	SLNB alone	32/427	**91.5**	25/434	**93.5**	**0.75** (0.44,1.26)	



Toxicity

- There were no study-related deaths and no unexpected toxicities

Toxicity	No RNI (%) n=800	RNI (%) n=759
Grade 0-1	58.0	37.2
Grade 2	35.4	52.3
Grade 3	6.5	10.0
Grade 4	0.1	0.5
Radiation Dermatitis (Grade 3)	3.3%	5.7%

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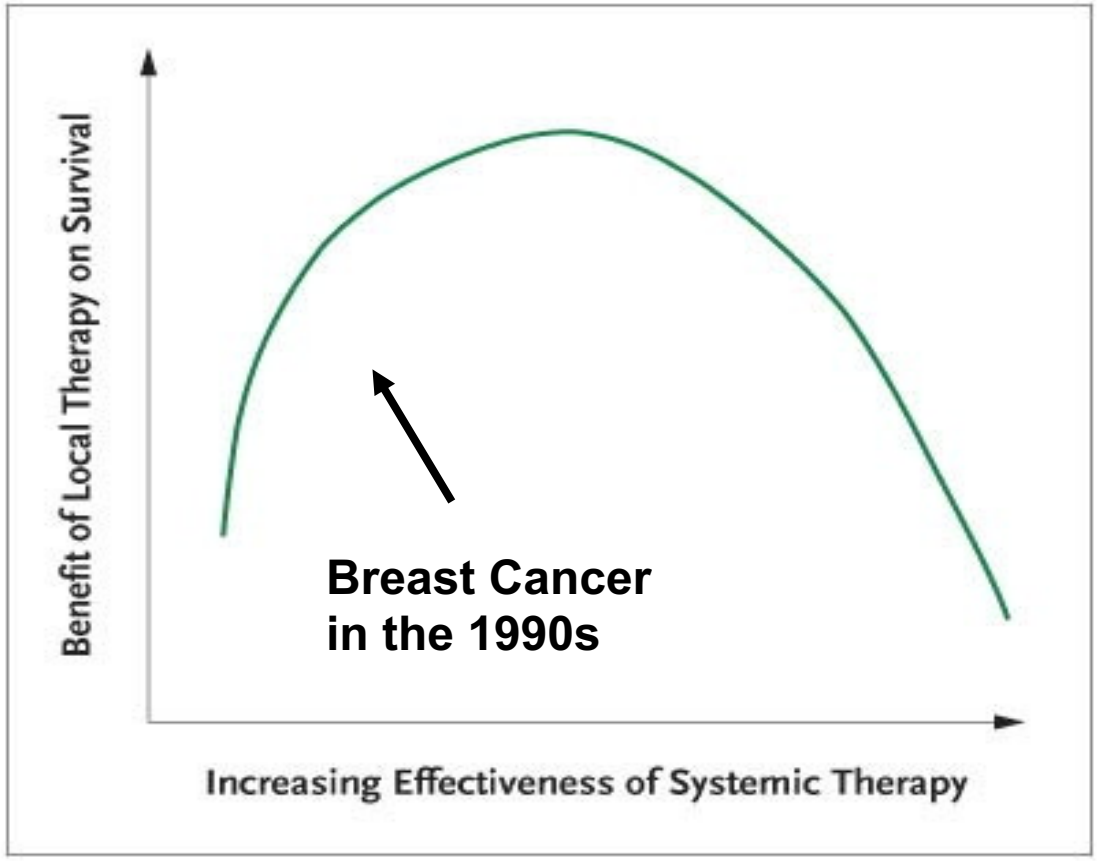
Conclusions

- With a median follow-up of 5 years, regional nodal irradiation does not appear to benefit the following patients with ypN0 disease:
  - Her2+ &
  - Breast pCR &
  - Patients ≥ age 50

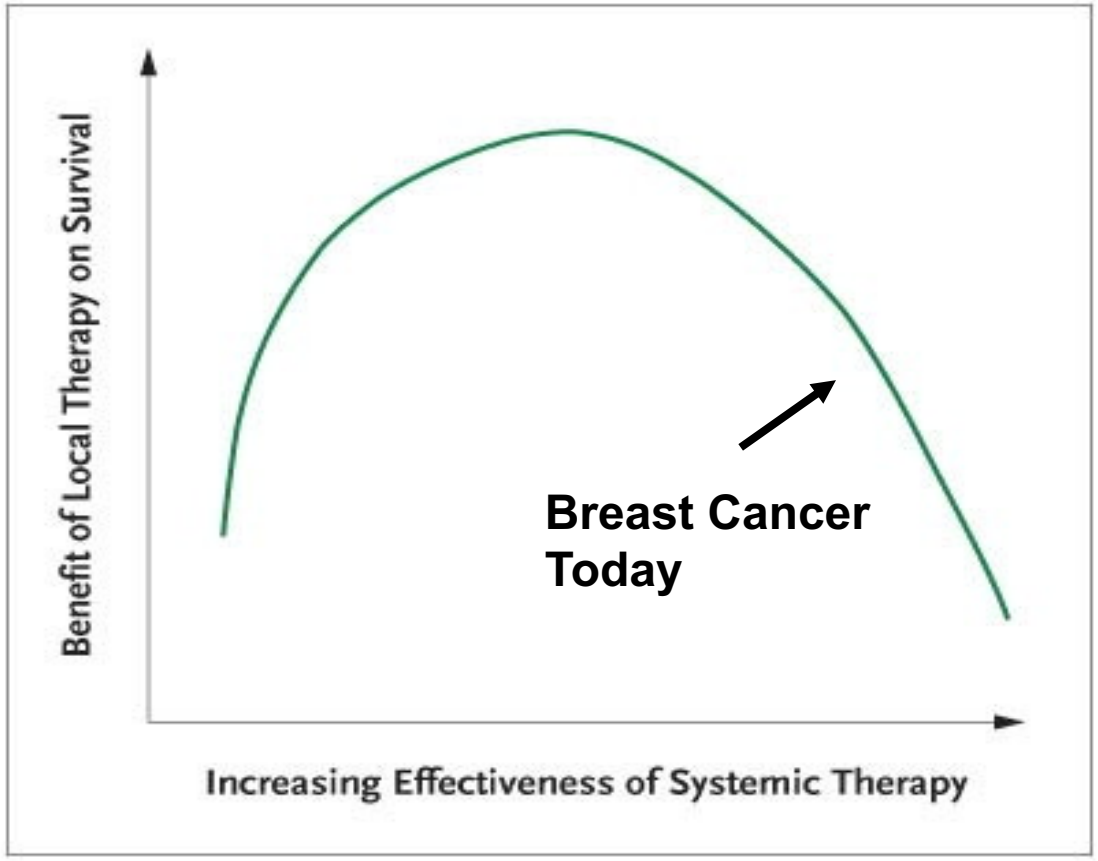
- Other groups were relatively well represented but longer follow-up and further data may indeed confirm irradiation in other patients with ypN0 disease (e.g., premenopausal patients with TNBC) is not needed

Hypothetical Benefit of Improved Local Tumor Control with Increasing Effectiveness of Systemic Therapy



Punglia RS et al. *N Engl J Med.* 2007;356(23):2399-2405.

Hypothetical Benefit of Improved Local Tumor Control with Increasing Effectiveness of Systemic Therapy



Punglia RS et al. *N Engl J Med.* 2007;356(23):2399-2405.

Thank you