

Global Breast Cancer Conference 2015
4th International Breast Cancer Symposium
Symposium 2

Neoadjuvant therapy and axillary staging

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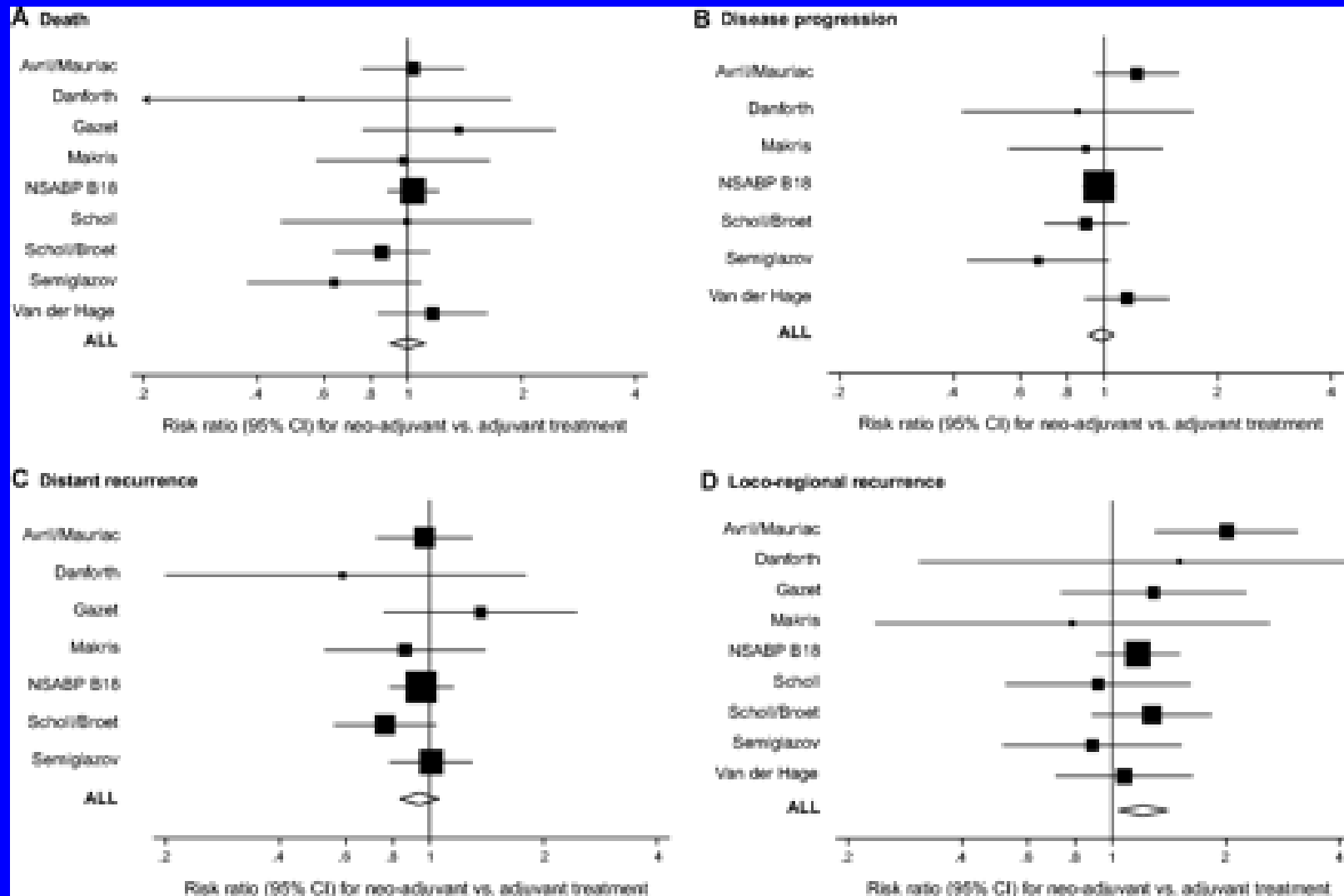
Memorial Sloan-Kettering Cancer Center

Professor of Clinical Surgery

Weill Cornell Medical College

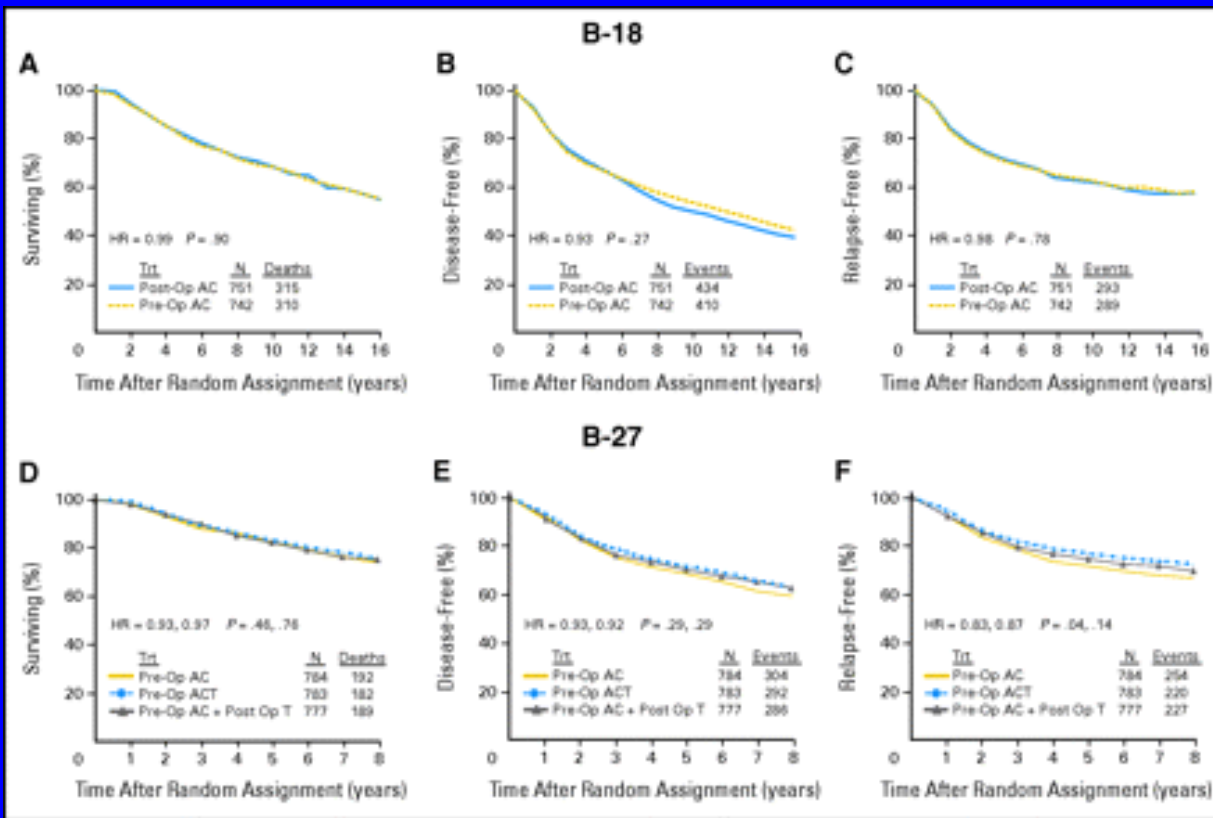
Neoadjuvant rx (chemo or endocrine)

Meta-analysis of 9 trials



B-18 and B-27 update

Survival, DFS, RFS



- no difference between pre- and post-op chemo
- the addition of docetaxel to AC significantly increased pCR, but did not affect survival

NSABP B-18

Breast conservation done

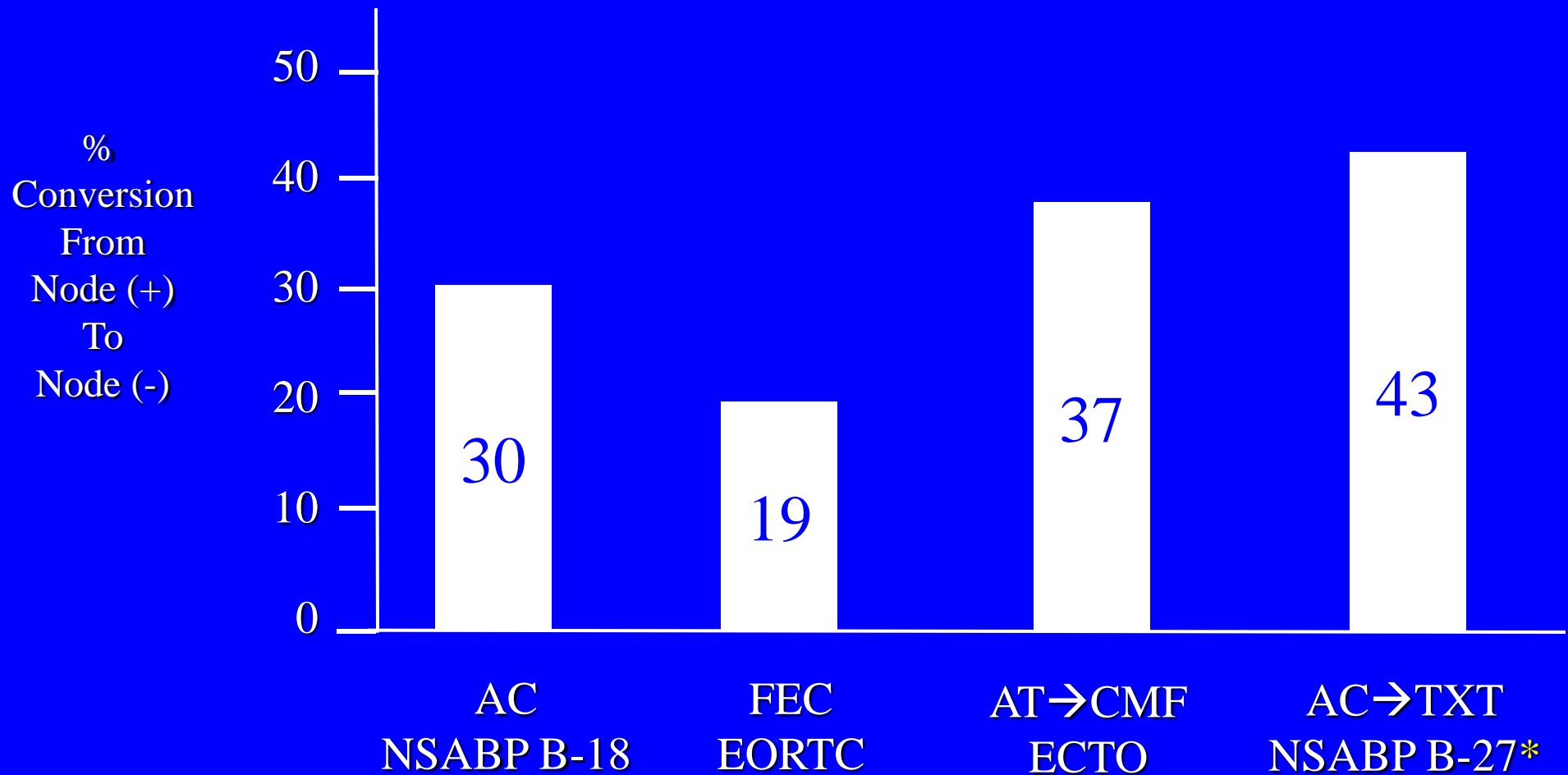
Tumor size	Surgery first % BCT	Chemo first % BCT
T1 (≤ 2.0 cm)	79%	81%
T2 (2.1-5.0 cm)	63%	71%
T3 (> 5 cm)	8%	22%
All patients	60%	67% p=0.002

NSABP B-18

Axillary node downstaging

	Surgery first (n=743)	Chemo first (n=735)
1-3 nodes+	30%	24%
4-9 nodes+	17%	12%
>10 nodes+	10%	4%
Overall node+	57%	41%
		p<0.001

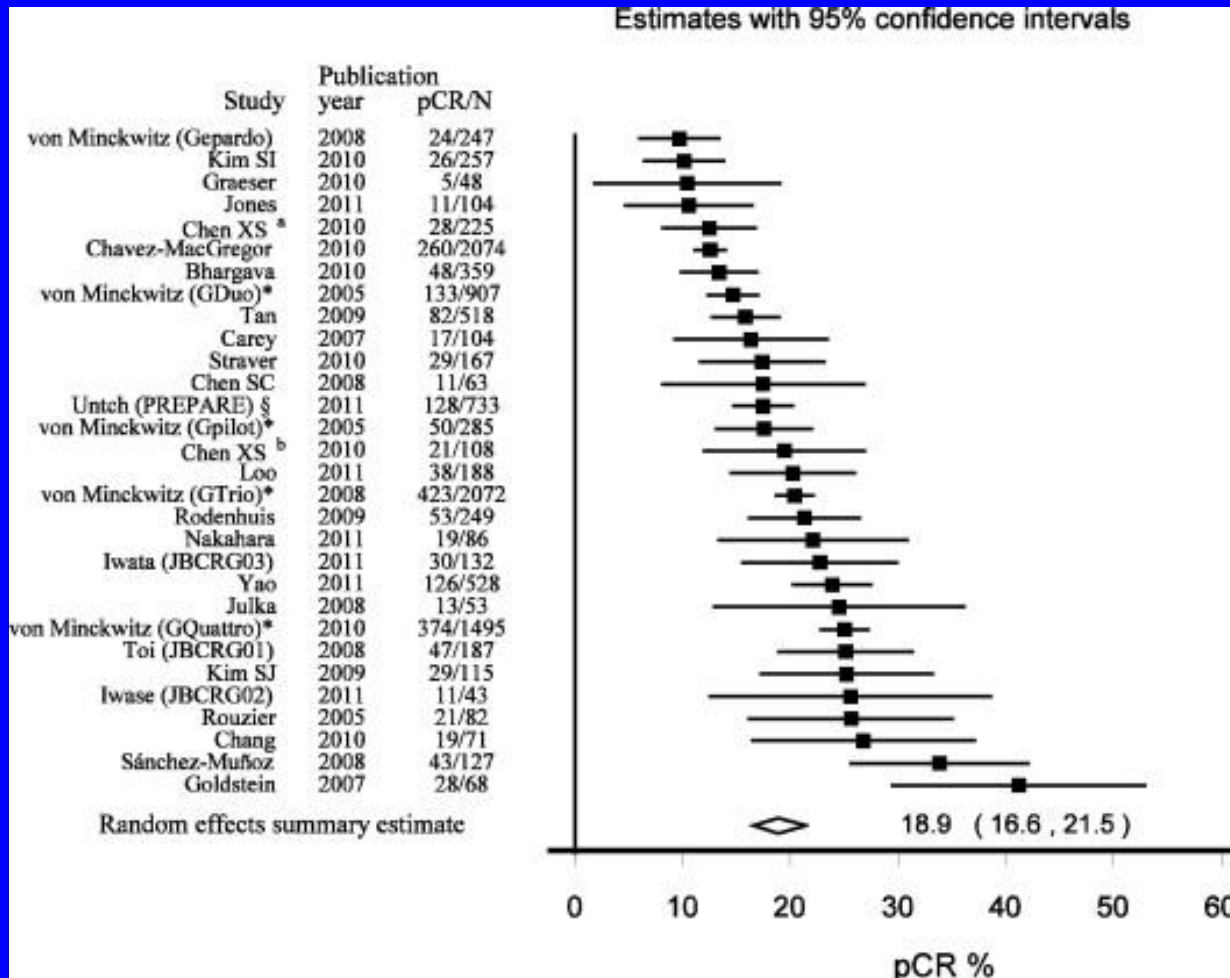
Axillary node downstaging 4 randomized trials



*Assuming 30% nodal down-staging with neoadjuvant AC

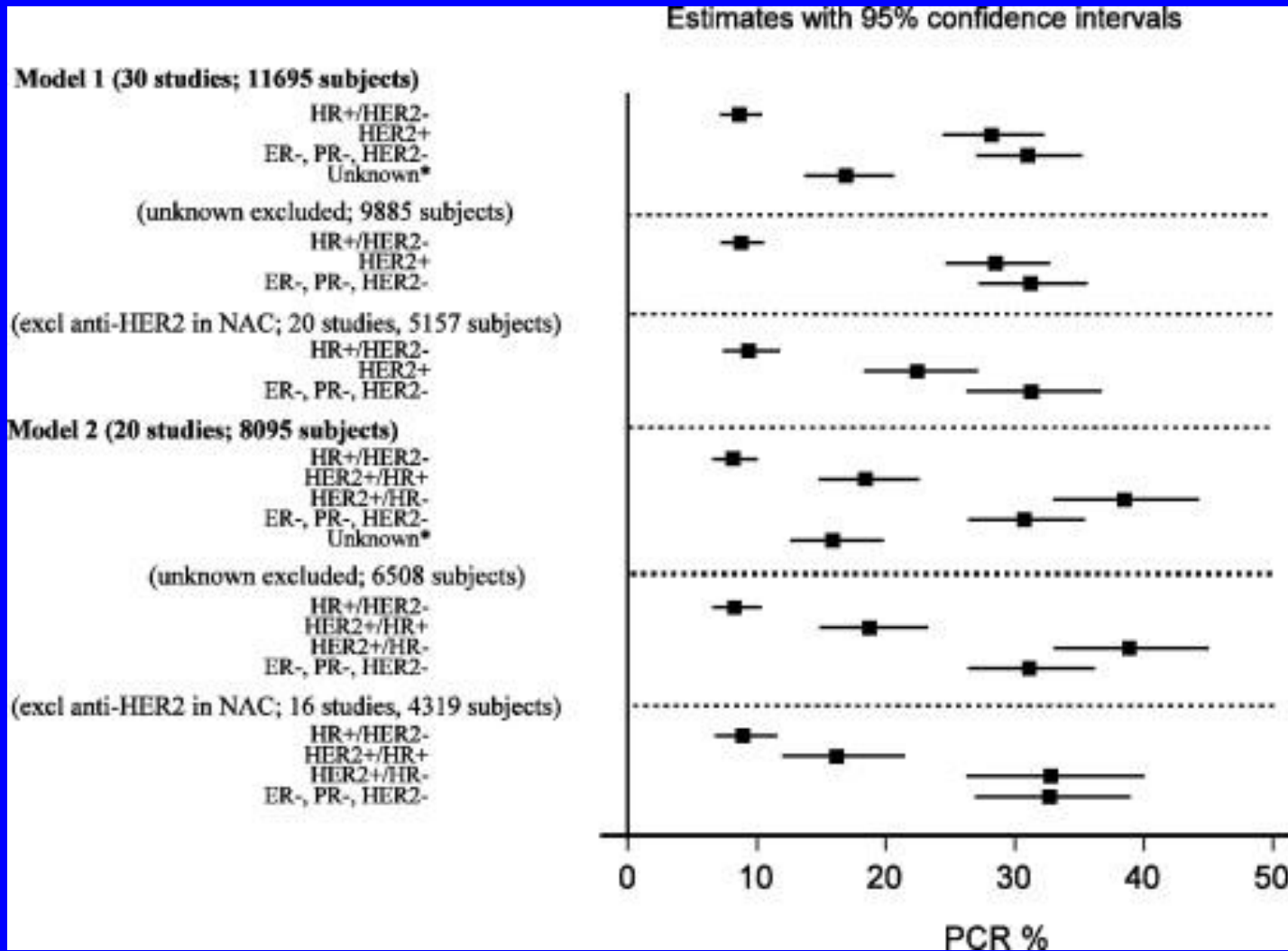
Neoadjuvant chemotherapy

Importance of tumor subtype



- 30 studies
- pCR by tumor subtype
- 11,695 patients
- pCR = 18.9%

Neoadjuvant chemotherapy Response by tumor subtype



- model 1 (30)
 - HR+/her2-
 - HR+/her2+
 - HR-/her2-
- model 2 (20)
 - HR+/her2-
 - HR+/her2+
 - HR-/her2+
 - HR-/her2-

Sentinel node

Before or after NAC?

	PRO	CON
SLN biopsy <u>before</u> NAC	- more accurate staging	- 2 operations -unnecessary ALND for 1/3 of node-positive pts
SLN biopsy <u>after</u> NAC	- 1 operation - ALND avoided for 1/3 of node-positive pts	- less accurate staging

Sentinel node

Does better staging change treatment?

- The “>3 nodes” argument
 - SLN biopsy after NAC fails to identify pts with >3 positive nodes, denying them the benefit of axillary and supraclavicular RT
- Response
 - post-chemo RT is usually based on clinical stage pre-chemo
 - cN0 pre-chemo = low risk of local relapse
 - SLN+ post-chemo have ALND (+/-RT)

SLN biopsy after neoadjuvant chemo

Systematic review of 27 studies 2148 patients* 2000-2009	SLN found	SLN false negative (SLN-/axilla+)
	90.5% (88-92)	10.5% (8-14)

*23 single center, 4 multicenter:

- 1) Neoadjuvant chemo
- 2) SLN biopsy
- 3) Backup ALND

SLN biopsy after neoadjuvant chemo

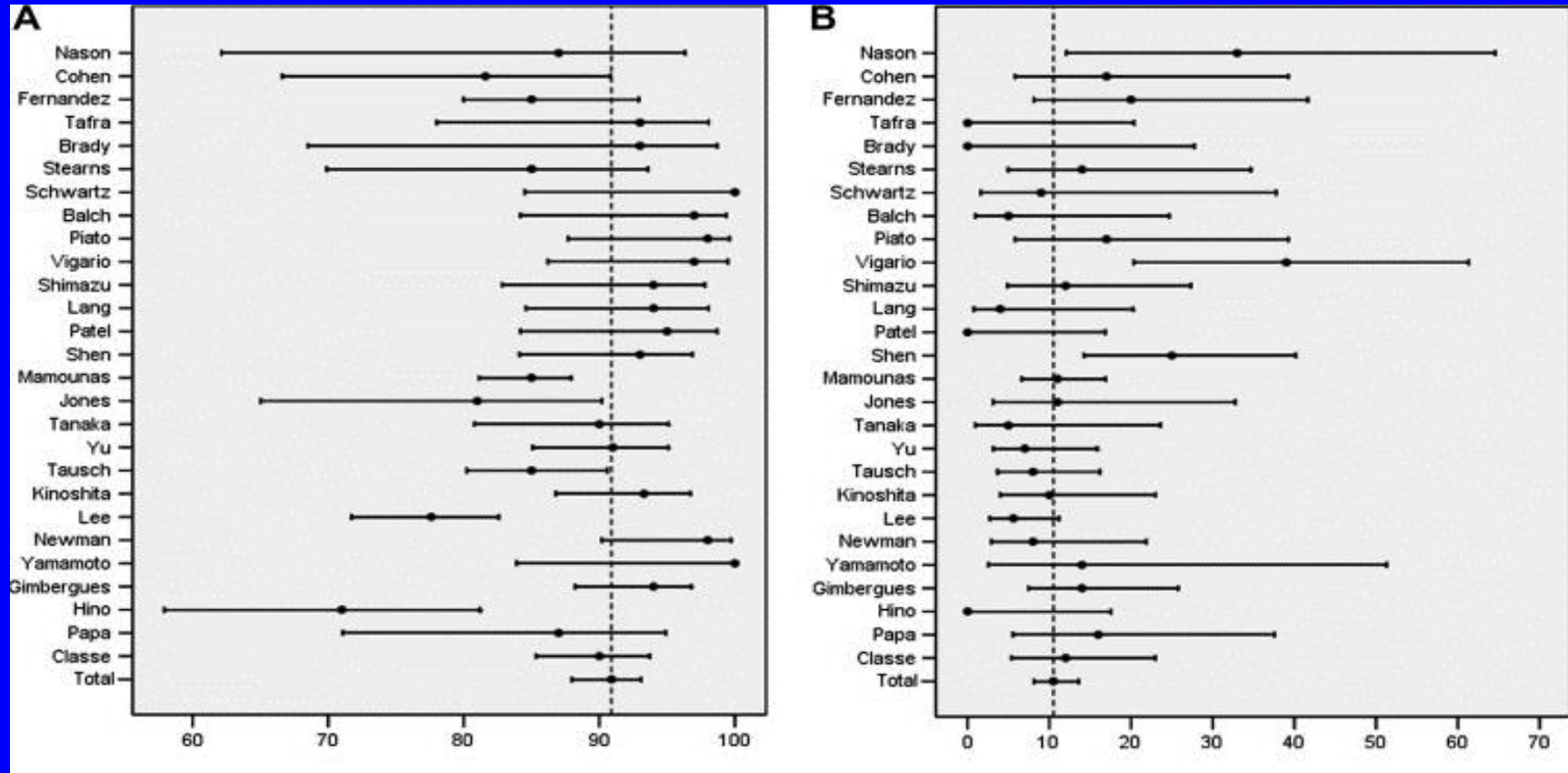
Success rate

False-negative rate

2000



2009



SLN biopsy after chemo: cN1*

2000-2008 19 studies of SLN biopsy following neoadjuvant chemo	# pts with cN1 axillae	SLN found	SLN false-neg	Pathologic CR (axilla)
	793	85%	11%	35%

* cN1 = N+ upfront on px or US

SLN biopsy

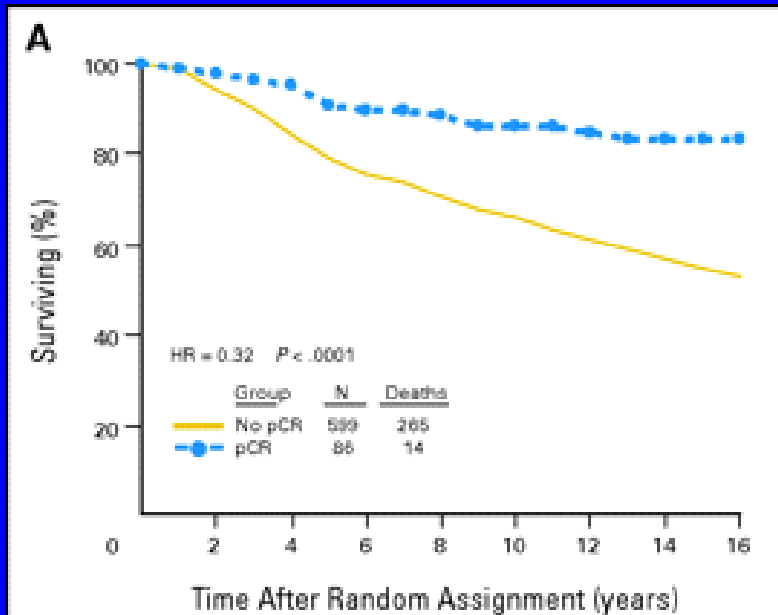
NSABP B-27 vs B-32

	# pts	SLN found	SLN false-neg
B-27* SLN biopsy after chemo	428	89%	10.7%
B-32** SLN biopsy upfront	720	97%	9.7%

*JCO 2005;23:2694-2702 ** Lancet Oncol 2007;8:881-8

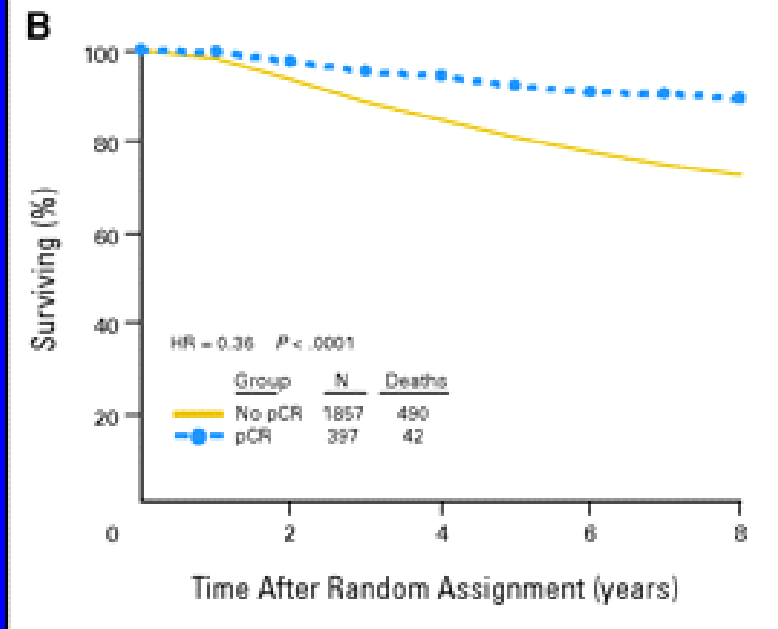
B-18 and B-27 update Survival by response

B-18



- survival is better for patients with pCR

B-27



Neoadjuvant Response to treatment

- for patients with proven axillary metastases who receive NAC
 - HER-2+ disease is responsive
 - 74% axillary pCR¹
 - ER+ disease is unresponsive
 - <10% axillary pCR²
- responders to NAC do better than non-responders BUT
 - treatments which improve response may not improve survival
 - non-responders do not benefit from a change in treatment

ACOSOG Z1071

SLN 2014

ACOSOG Z1071

- 708 pts (2009-2011) with cT0-4, N1-2, M0 disease
- all had neoadjuvant chemo, *then* SLNB/ALND
- SLN identified 92.5%
- pathologic CR 40%

SLN 2014

ACOSOG 1071

- False negative rate by # of SLN removed
 - 1 SLN 31.5%
 - 2 SLN 21%
 - ≥ 2 SLN 12.6%
 - ≥ 3 SLN 9.1%

- False negative rate by mapping technique
 - Dye or isotope alone 20.3%
 - Dye plus isotope 10.8%

SENTINA trial

SENTINA trial

prospective cohort study (n=1737)

- cN0: *SLNB before chemo*
 - Arm A: SLN-, no further axillary surgery
 - Arm B: SLN+, chemo, then re-SLNB/ALND
- if cN1-2: *SLNB after chemo*
 - Arm C: if converted to cN0, SLNB/ALND
 - Arm D: if still cN1-2, ALND

SENTINA trial

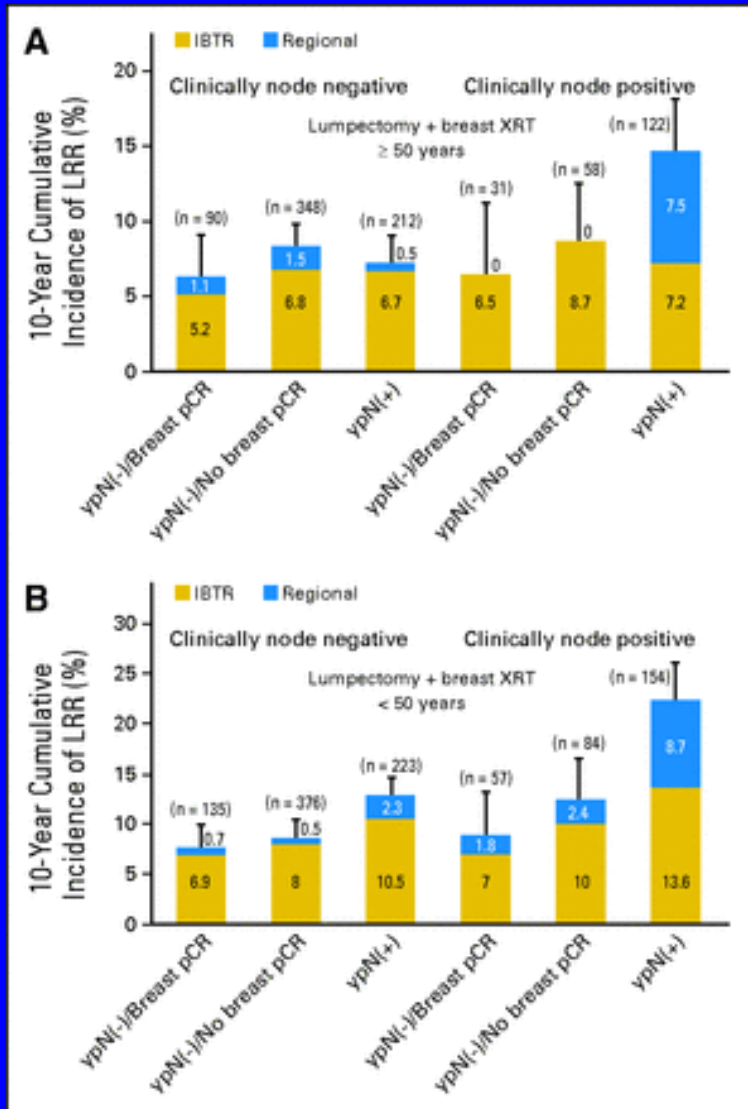
Outcome 1737 pts 103 institutions	Arms A+B cN0 SLNB upfront n=1022	Arm B cN0/SLN+ SLNB upfront chemo re-SLNB/ALND n=360	Arm C cN1-2 Chemo upfront SLNB/ALND n=592
Success (SLN found)	99%	61%	80%
False negative (SLN-/axilla+)	-	52%	14%

SENTINA trial

- False negative rate by # of SLN removed
 - 1 SLN 24%
 - 2 SLN 18%
 - 3 SLN 7%
- False negative rate by mapping technique
 - Isotope 16%
 - Isotope+dye 8.6%

NASBP B-18 and B-27

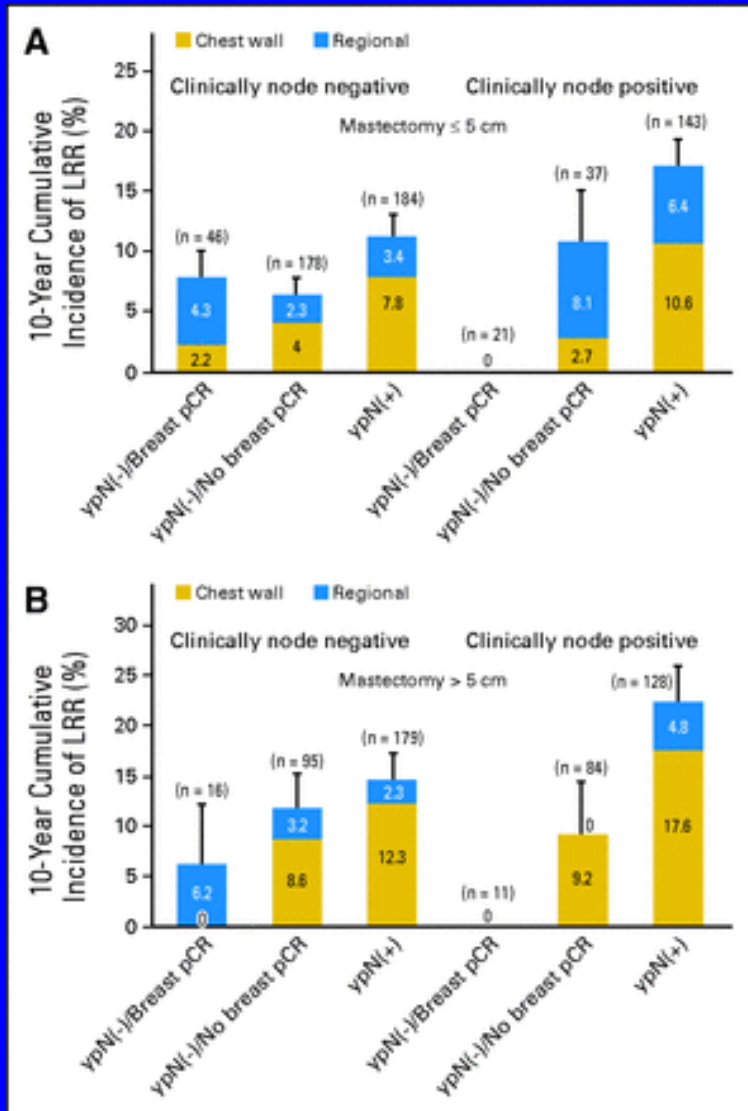
patterns of LRR: BCT+WBRT



- by clinical node status
- by age
- by PCR in breast
 - absence of invasive tumor
- by PCR in nodes

NASBP B-18 and B-27

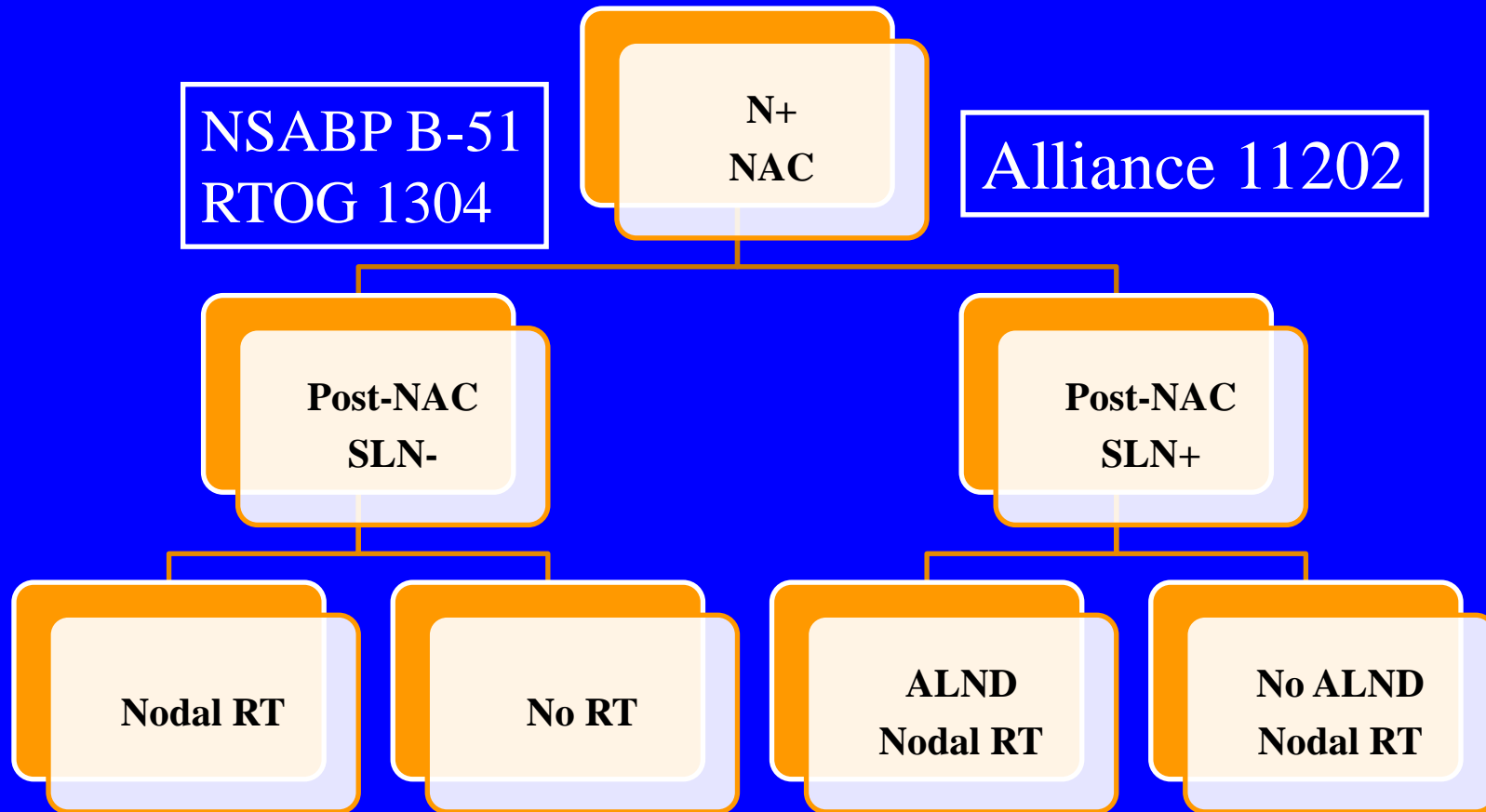
patterns of LRR: mastectomy/no RT



- by clinical node status
- by T size
- by PCR in breast
 - absence of invasive tumor
- by PCR in nodes

SLN 2014

Two new neoadjuvant RCTs



SLN and neoadjuvant

Conclusions I

- axillary staging before NAC is best done by US+/- FNA, not surgery
- SLN biopsy is best done *after* NAC
- present evidence for SLNB post-NAC is sufficient
 - Success rate *somewhat lower* than SLNB in general
 - False negative rate *comparable* to SLNB in general
 - *Technique matters*
 - Remove ≥ 3 SLN
 - Map with dye + isotope

SLN and neoadjuvant Conclusions II

- SLN biopsy is well established BUT
 - next-generation trials in cN0 breast cancer will compare SLNB vs no axillary staging
 - next-generation trials in cN+ breast cancer will compare combinations of ALND and RT