NACT – Kirurgiske aspekter

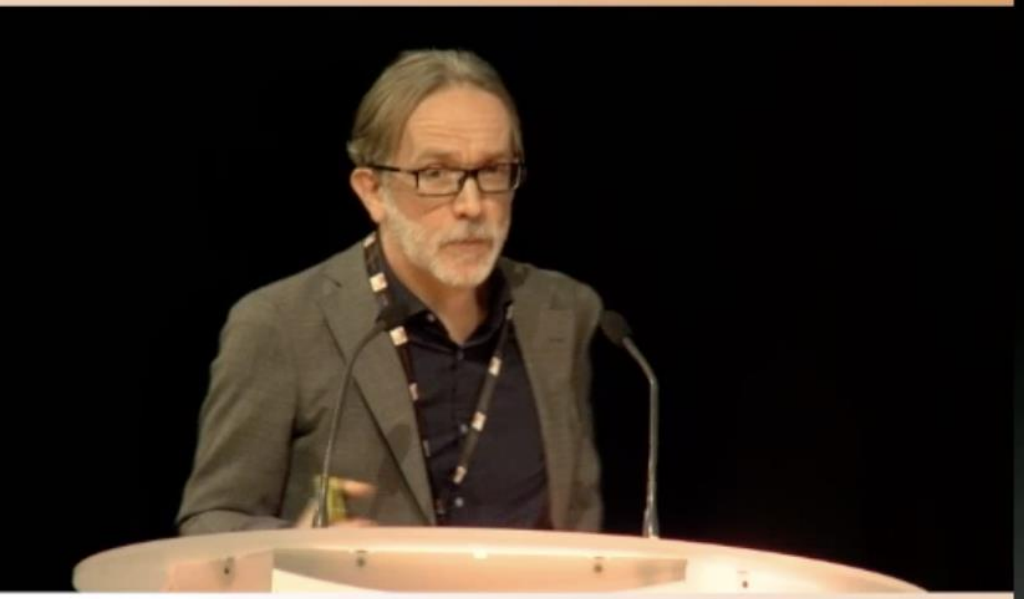
Kirurgisk Udvalg, DBCG

Outline

- Indications for NACT
- Local control after NACT and BCS
- Suboptimal converting to BCS after NACT
  - Prediction of pCR
  - Involved margins
  - Microcalcifications
- Treatment of the axilla after NACT

Indications for NACT according to the DBCG guidelines

- cT2: (2,0 cm < tumor <= 5.0 cm), cN0-N1, and non-lobulær type invasive breast cancer, if chemotherapy indicated:
  - ER negative, HER2 negative
  - HER2 positive
  - ER positive, premenopausal



WHAT DO SURGEONS WANT FROM NACT ?

Offer more conservative surgery

..and more successful conservative surgery

Avoid

- mastectomy for pCR
- node clearance for pCR

Facilitate pathway

Orbs 2019

Ask the panel a question....

#ORBSQ&A

Long-term outcomes for neoadjuvant versus adjuvant chemotherapy in early breast cancer: meta-analysis of individual patient data from ten randomised trials

*Early Breast Cancer Trialists' Collaborative Group (EBCTCG)**

- Treated 1983-2002

	Trials (n)*	Women (n)	Deaths (n)†
No anthracycline or taxane[8,11,12,17]‡	4	918	315
Anthracycline, no taxane[9,10,14–16]	5	2936	1163
Anthracycline and taxane[13]	1	902	126
Total	10	4756	1604

Lancet Oncol 2018; 19: 27–39

Published Online
December 11, 2017
http://dx.doi.org/10.1016/S1470-2045(17)30777-5

See Comment page 2

*Full list of members in the appendix (pp 19–24) or at https://www.ctsu.ox.ac.uk/research/ebctcg

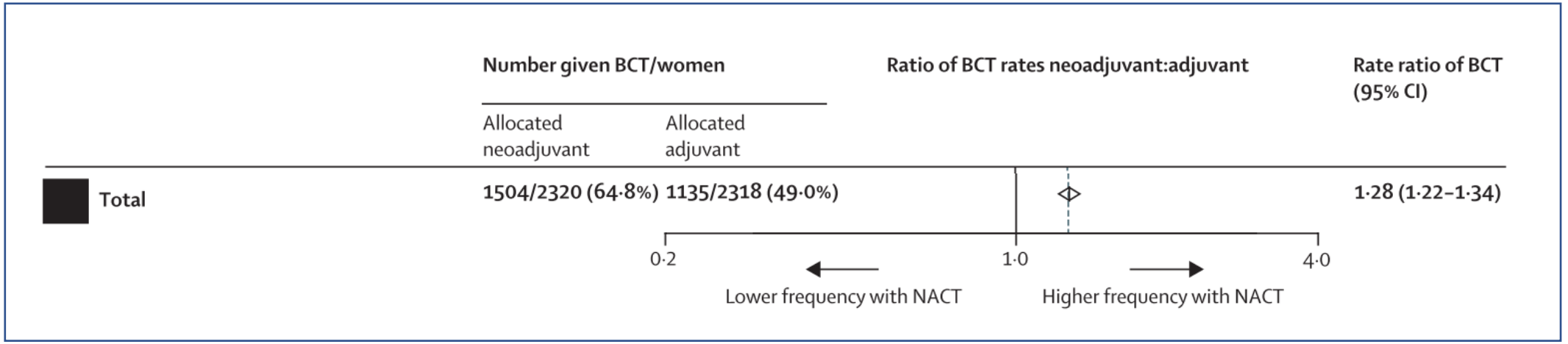
Correspondence to:
EBCTCG Secretariat, Medical Research Council Population Health Research Unit, Nuffield Department of Population Health, Oxford OX3 7LF, UK
bc.overview@ndph.ox.ac.uk

See Online for appendix

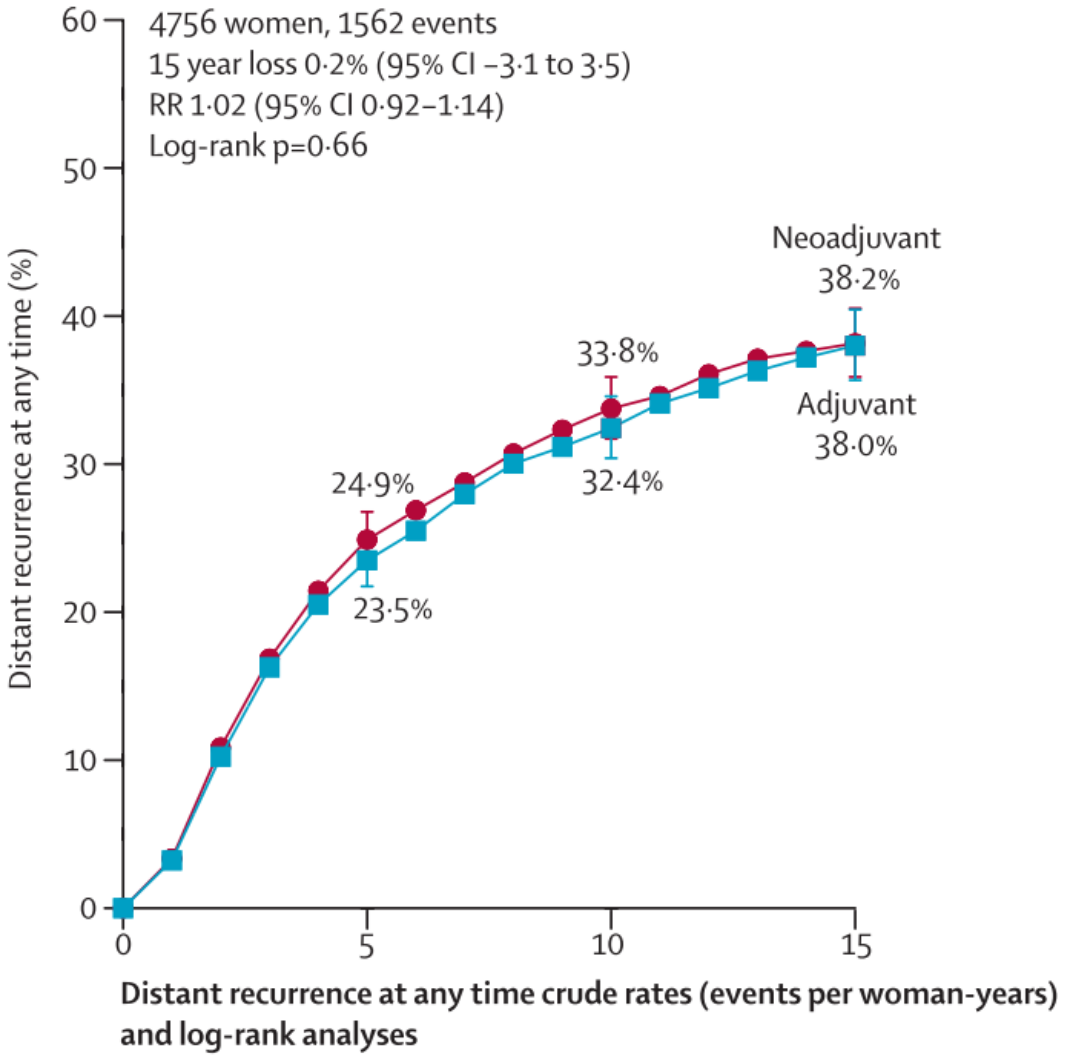
Breast-conserving surgery after NACT

- 65% after NACT
- 49% in patients randomized to adjuv. CT

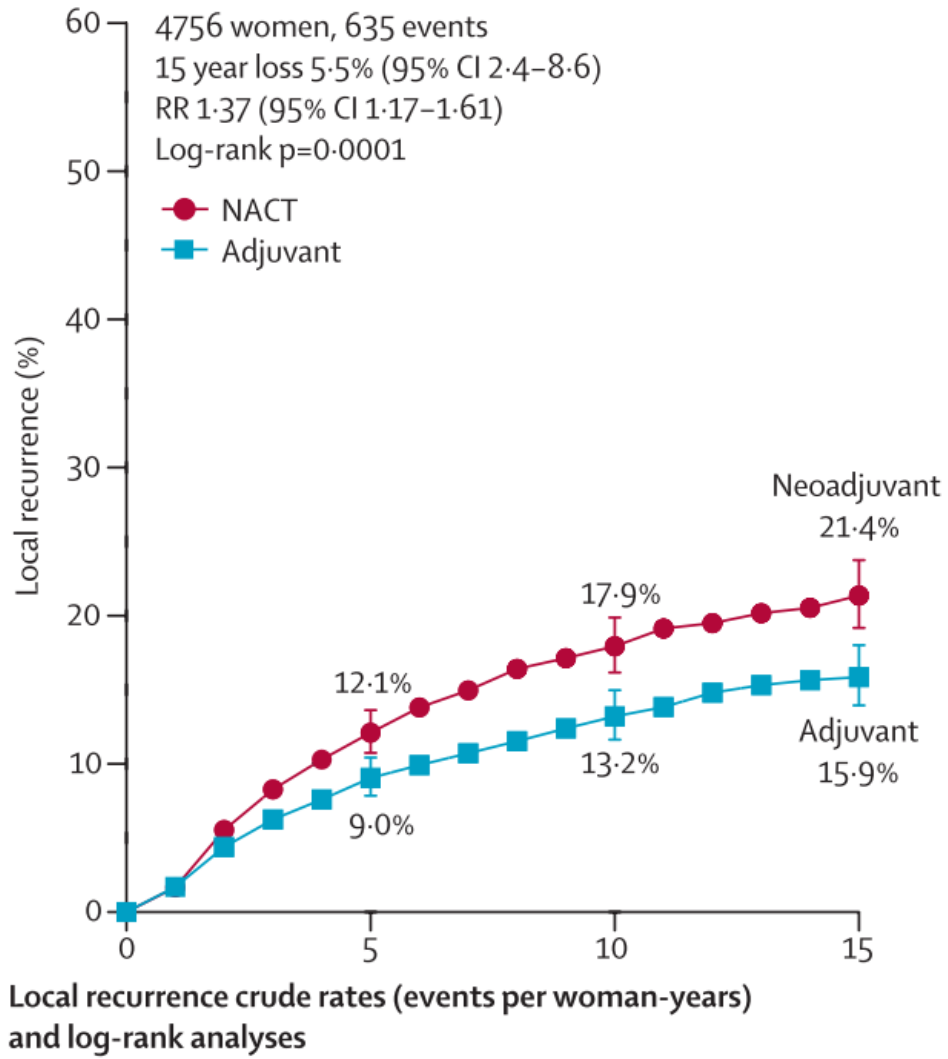
	Clinical response				
	Complete*	Partial†	Stable or progressive disease‡	Unknown	Total
All women					
Breast-conserving	452 (83%)	541 (68%)	246 (42%)	265 (68%)	1504 (65%)
Mastectomy	92 (17%)	258 (32%)	342 (58%)	124 (32%)	816 (35%)
Unknown	2 (NA)	4 (NA)	10 (NA)	51 (NA)	67 (NA)
Total response§	546/1947 (28%)	803/1947 (41%)	598/1947 (31%)	440 (NA)	2387 (100%)



Lancet Oncol 2018; 19: 27–39

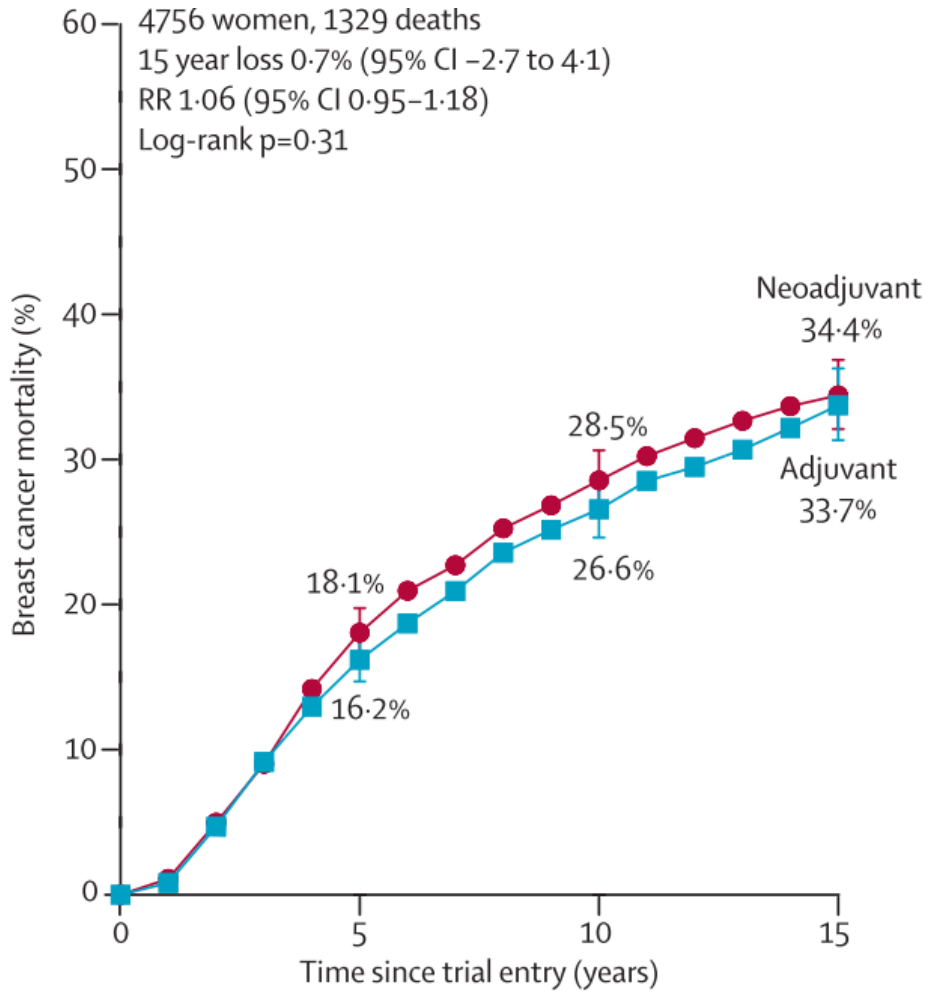


Distant recurrence at any time crude rates (events per woman-years) and log-rank analyses

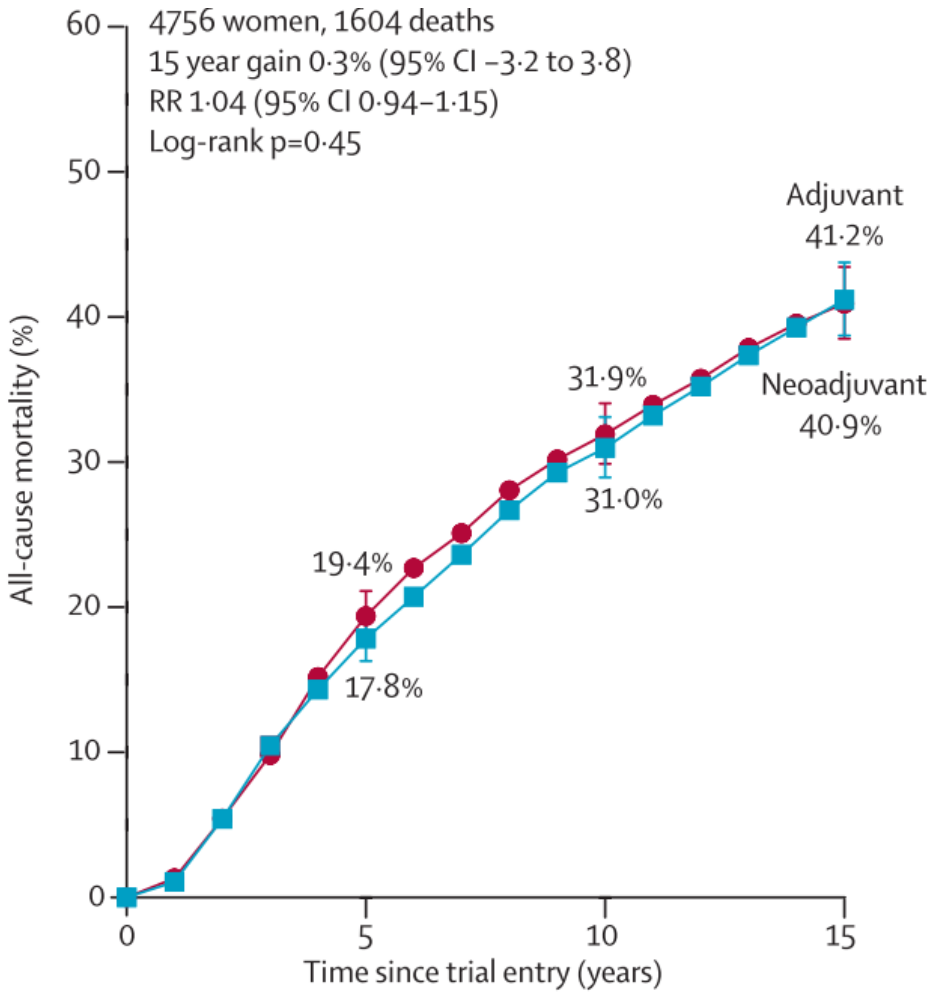


Local recurrence crude rates (events per woman-years) and log-rank analyses

Lancet Oncol 2018; 19: 27–39

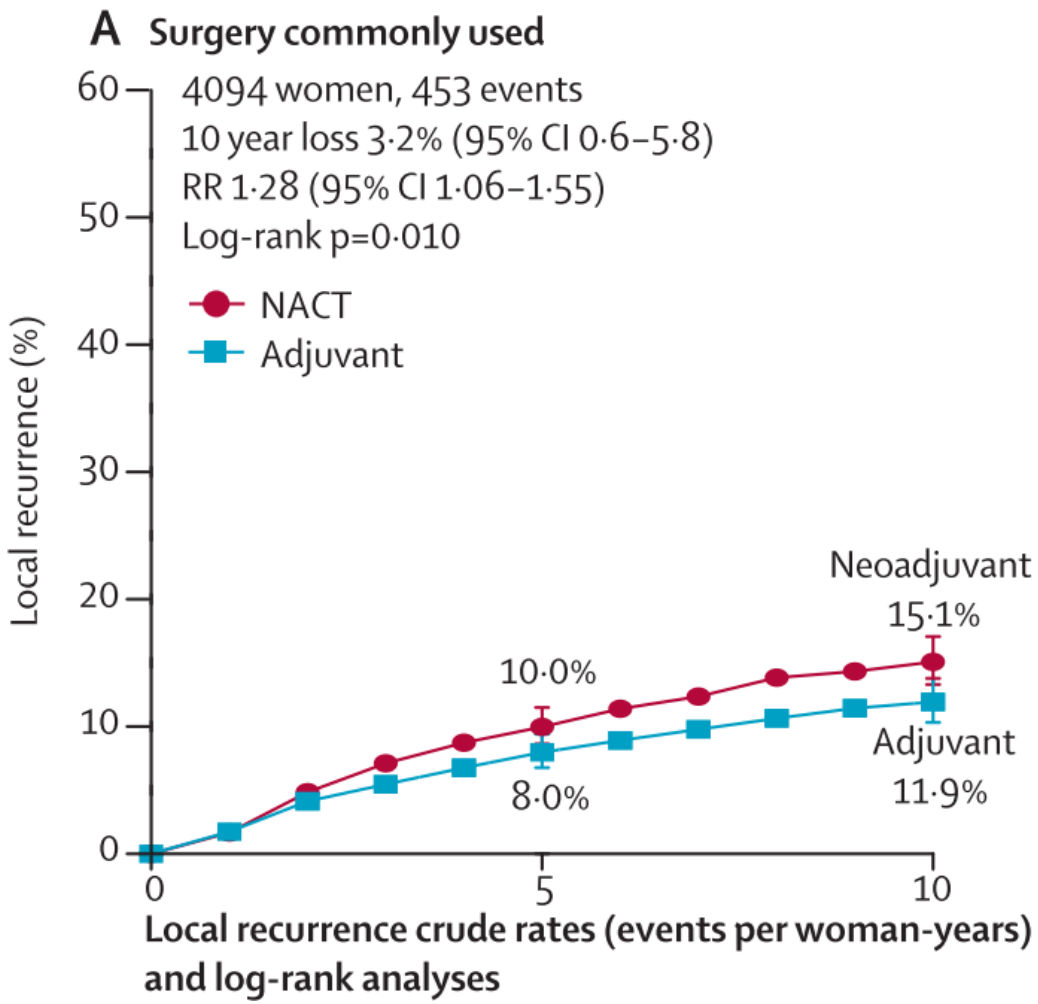


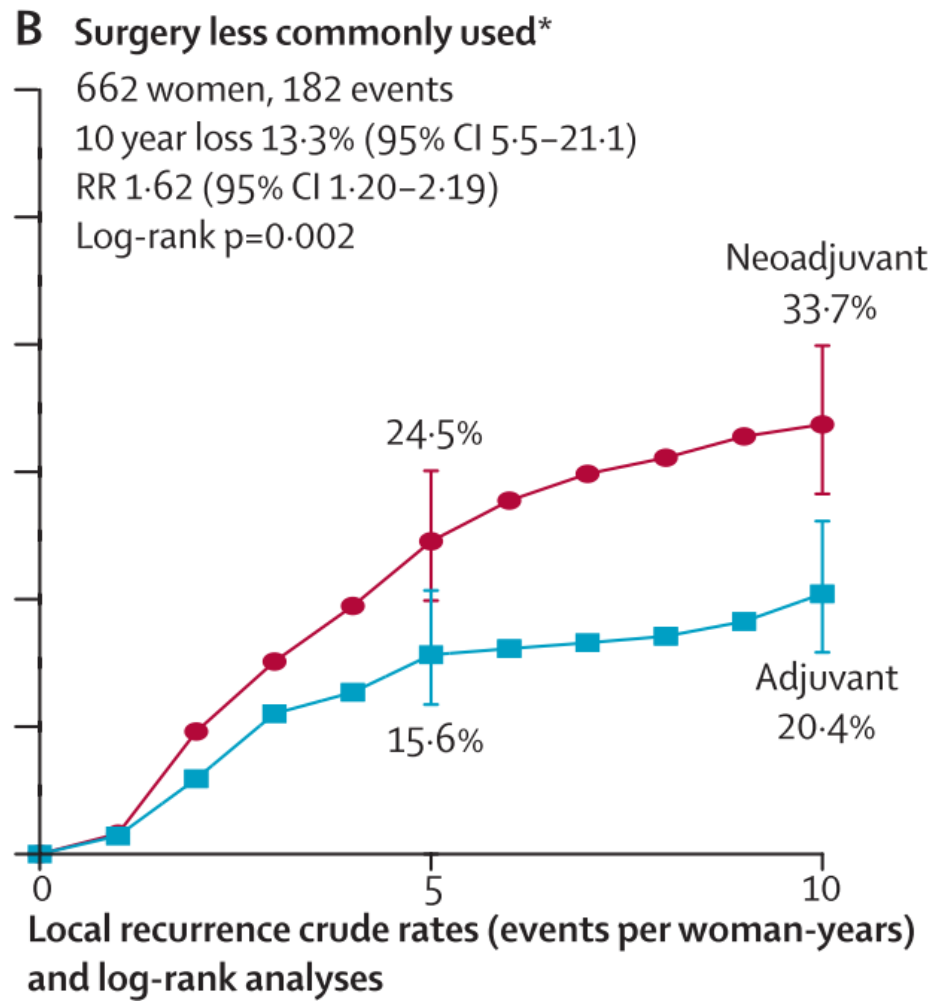
Breast cancer mortality crude rates (events per woman-years) and log-rank analyses



Any death crude rates (events per woman-years) and log-rank analyses

Lancet Oncol 2018; 19: 27–39





Lancet Oncol 2018; 19: 27–39

Systematic review

Meta-analysis of neoadjuvant therapy and its impact in facilitating breast conservation in operable breast cancer

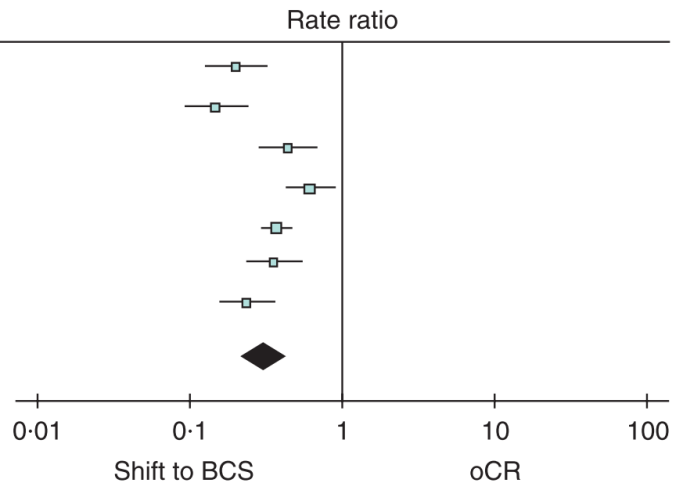
A. Karakatsanis[1,5], M. K. Tasoulis[5], F. Wärnberg[1], G. Nilsson[2,3,4] and F. MacNeill[5]

	Eligibility for BCS (%)				
	Before NAT	After NAT	oCR (%)	BCS performed (%)	Shift to BCS (%)
CALGB 40601	41·4	63·7	63·7	49·0	12·9
CALGB 40603	54·2	68·1	68·1	47·3	−10·9
CHER-LOB	43·8	n.a.	89·9	64·7	39·7
IMPACT	43·6	61·8	34·6	41·5	32·3
NeoALTTO	29·8	46·9	75·4	43·6	28·2
TEAM IIA	61·8	75	64·6	65·7	23·1
TRYPHAENA	46·2	n.a.	92	58·7	21·9
Pooled values	43·3 (41·3, 45·9)	60·4 (57·8, 62·9)	74·8 (72·5, 77·0)	51·8 (49·5, 54·2)	16·6 (14·4,19·0)

Trial	Weight (%)	Rate ratio
CALGB 40601[17]	13·6	0·20 (0·13, 0·31)
CALGB 40603[15]	13·2	0·15 (0·09, 0·24)
CHER-LOB[19]	13·9	0·44 (0·29, 0·67)
IMPACT[23]	14·8	0·62 (0·43, 0·89)
NeoALTTO[20]	16·4	0·37 (0·30, 0·47)
TEAM IIA[24]	14·1	0·36 (0·24, 0·54)
TRYPHAENA[22]	14·1	0·24 (0·16, 0·36)
Total	100·0	0.31 (0.22, 0.44)

Heterogeneity: $\tau^2=0{\cdot}16$; $\chi^2=33{\cdot}04$, 6 d.f., $P<0{\cdot}001$; $I^2=82\%$

Test for overall effect: $Z=6{\cdot}82$, $P<0{\cdot}001$

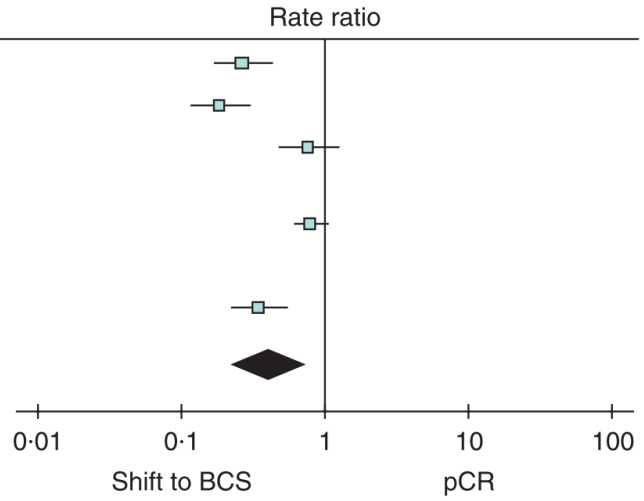


c Shift to BCS *versus* oCR

Trial	Weight (%)	Rate ratio
CALGB 40601[17]	19·6	0·27 (0·17, 0·42)
CALGB 40603[15]	19·5	0·19 (0·12, 0·30)
CHER-LOB[19]	19·6	0·79 (0·50, 1·24)
IMPACT[23]		Not estimable
NeoALTTO[20]	21·3	0·81 (0·62, 1·04)
TEAM IIA[24]		Not estimable
TRYPHAENA[22]	20·0	0·35 (0·23, 0·54)
Total	100·0	0·41 (0·23, 0·74)

Heterogeneity: $\tau^2=0{\cdot}40$; $\chi^2=43{\cdot}58$, 4 d.f., $P<0{\cdot}001$; $I^2=91\%$

Test for overall effect: $Z=2{\cdot}96$, $P=0{\cdot}003$



d Shift to BCS *versus* pCR

BJS 2018; 105: 469–481

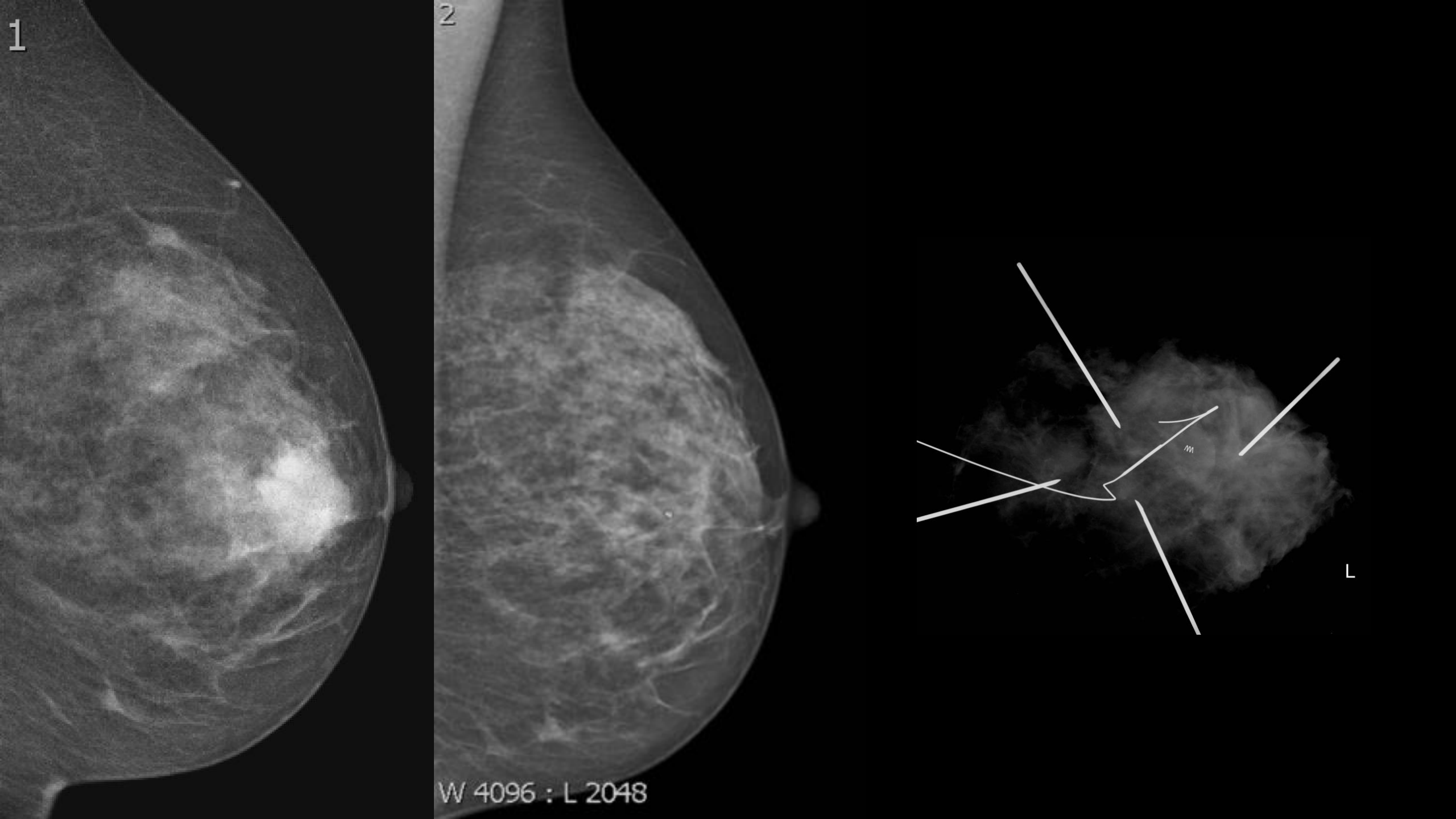
POOLED RESULTS RCT'S

pCR (47.9%)

- CALGB 40601
- CALGB 40603
- CHER-LOB
- IMPACT
- NeoALTTO
- TEAM IIA
- TRYPHAENA

	pCR	*No pCR*
BCS performed	76.9%	23.1%
Mastectomy performed	29.7%	70.3%

British Journal Surgery 2018; 105: 469–481


1
2
W 4096 : L 2048
L

Predicting pCR

World J Surg (2019) 43:2254–2261
https://doi.org/10.1007/s00268-019-05032-9

World Journal of Surgery

Check for updates

SCIENTIFIC REVIEW

MRI Performance in Detecting pCR After Neoadjuvant Chemotherapy by Molecular Subtype of Breast Cancer

Nancy Yu[1] · Vivian W. Y. Leung[1] · Sarkis Meterissian[1,2,3,4]

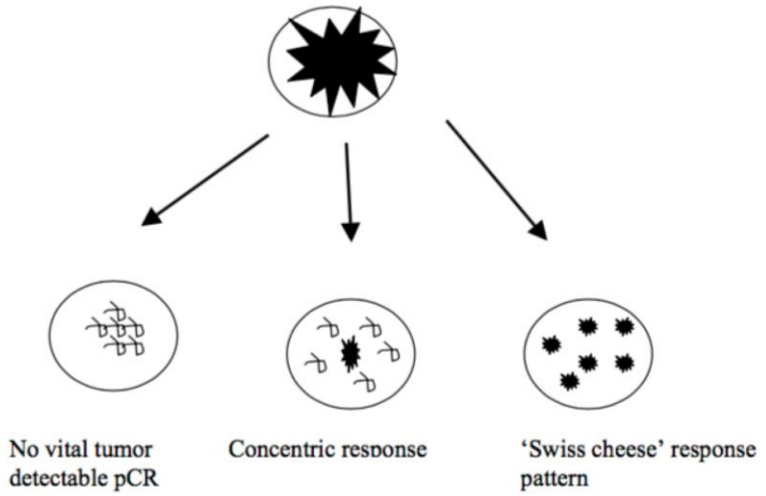
- Review 10 studies

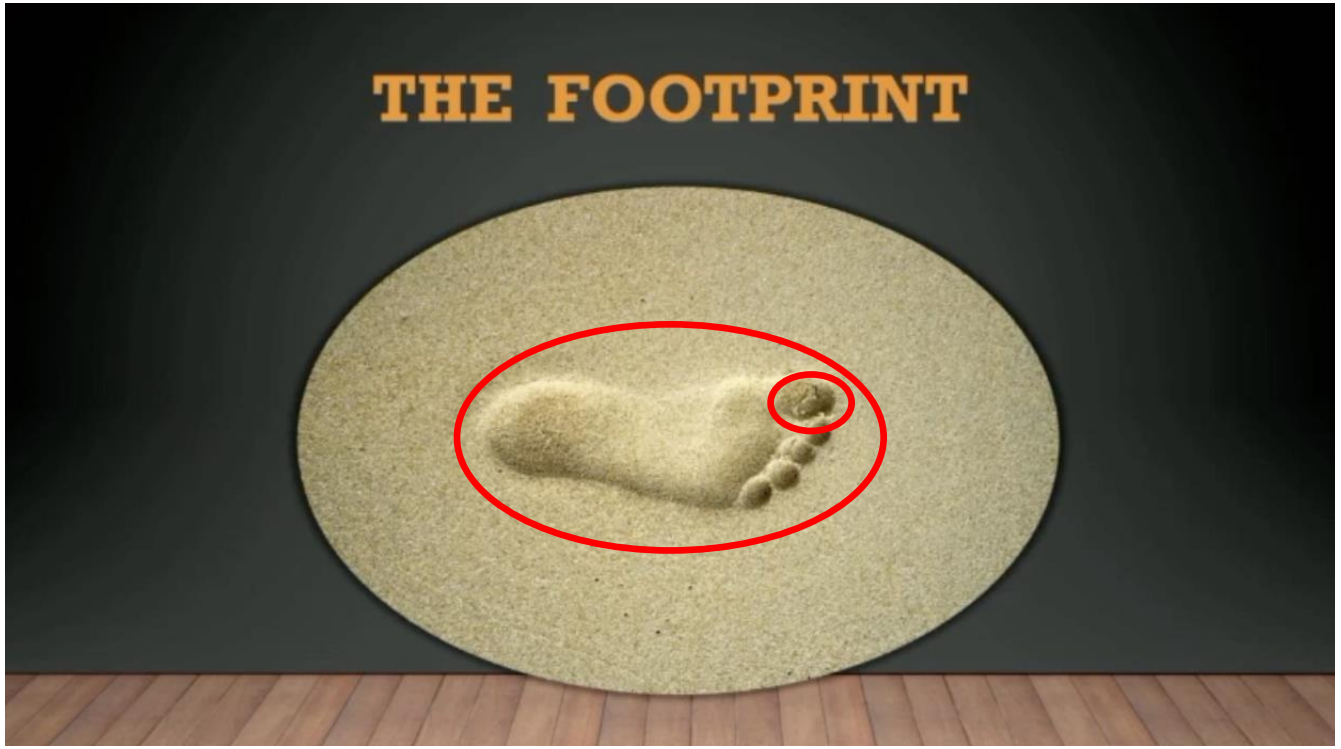
	PPV (% rCR = pCR)	NPV
Overall	50%	90%
Triple Neg / Her2 +	80-90%	90%
ER+	33%	80-90%

World J Surg (2019) 43:2254–2261

Involved margins after NACT

In pCR it's easy but what to do in partial response?





Ann Surg Oncol (2017) 24:1507–1515
DOI 10.1245/s10434-016-5760-8

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

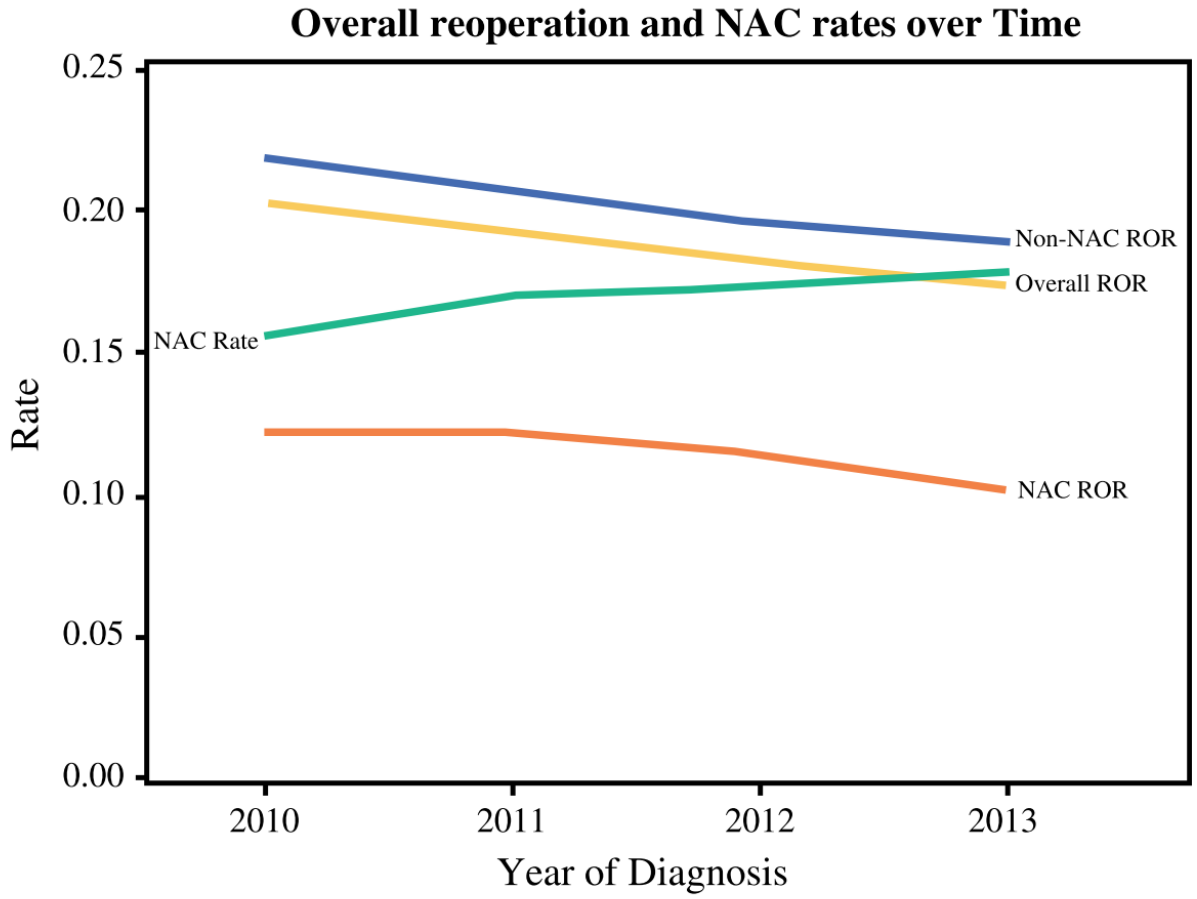
CrossMark

ORIGINAL ARTICLE – BREAST ONCOLOGY

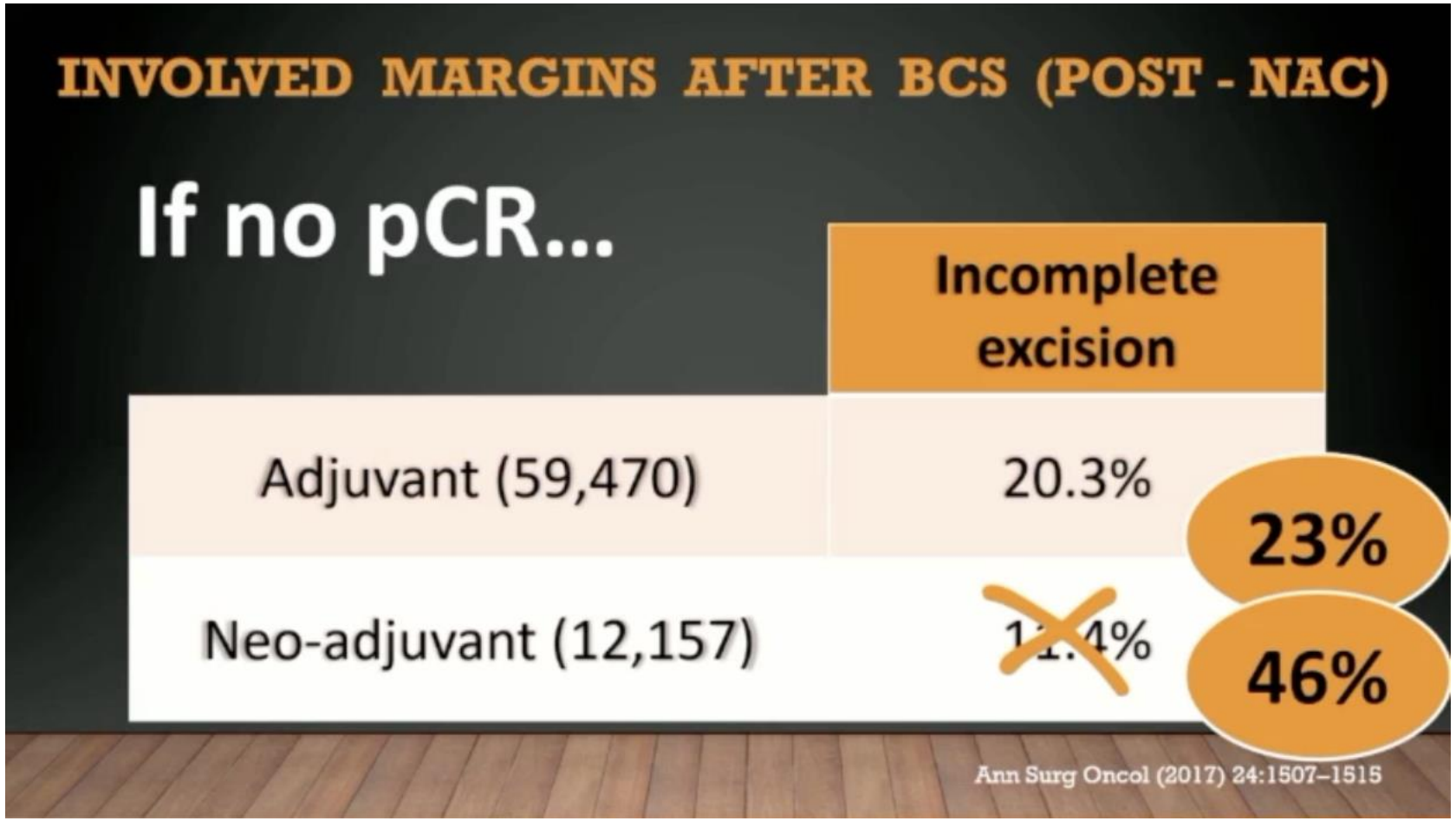
Fewer Reoperations After Lumpectomy for Breast Cancer with Neoadjuvant Rather than Adjuvant Chemotherapy: A Report from the National Cancer Database

Jeffrey Landercasper, MD, FACS[1,2], Barbara Bennie, PhD[3], Benjamin M. Parsons, DO[4], Leah L. Dietrich, MD[4], Caprice C. Greenberg, MD, MPH, FACS[5], Lee G. Wilke, MD, FACS[5], and Jared H. Linebarger, MD, FACS[2,6]

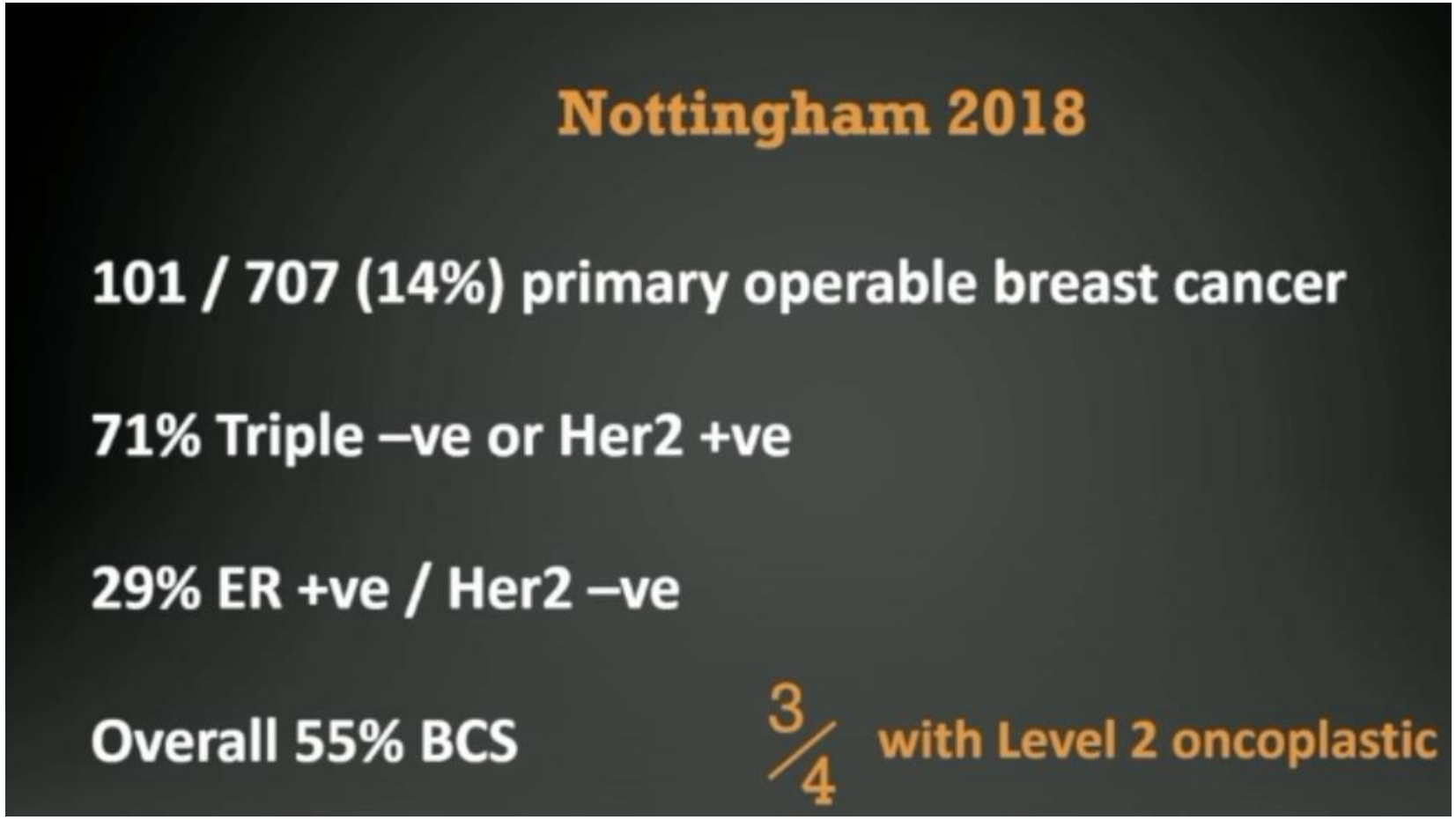
	Incomplete excision
Adjuvant (59470)	20.3%
NACT (12177)	11.4%

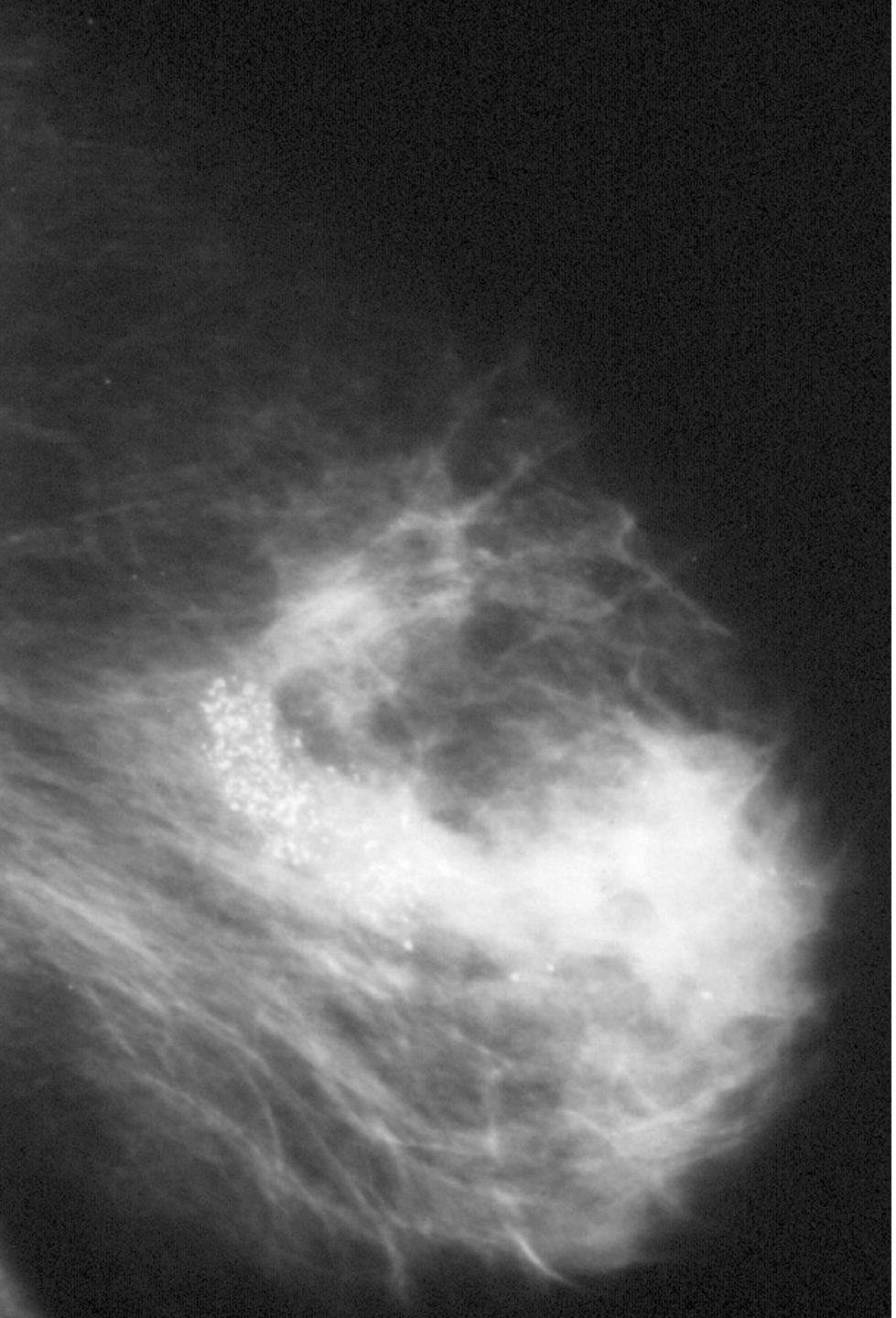


	Reoperation odds Ratio
Comparing NAC to no NAC	
(reference level no NAC)	
1 Stage 1 to 3	
2 Stage 1	
3 Stage 2	
4 Stage 3	
Comparing NAC to no NAC within subtype	
(reference level no NAC, subtype fixed)	
5 Luminal A: NAC yes vs no	
6 Luminal B1: NAC yes vs no	
7 Luminal B2: NAC yes vs no	
8 Triple Neg: NA yes vs no	
9 Her 2 type: NAC yes vs no	


INVOLVED MARGINS AFTER BCS (POST - NAC)
If no pCR...
Incomplete excision
Adjuvant (59,470)
20.3%
Neo-adjuvant (12,157)
11.4%
23%
46%
Ann Surg Oncol (2017) 24:1507–1515

The role of oncoplastic surgery after NACT





Microcalcifications and NACT

Ann Surg Oncol (2017) 24:1492–1498
DOI 10.1245/s10434-016-5741-y

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

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ORIGINAL ARTICLE – BREAST ONCOLOGY

Do Calcifications Seen on Mammography After Neoadjuvant Chemotherapy for Breast Cancer Always Need to Be Excised?

Yara Feliciano, MD[1], Anita Mamtani, MD[2], Monica Morrow, MD[3], Michelle M. Stempel, MPH[3], Sujata Patil, PhD[4], and Maxine S. Jochelson, MD[5]

Memorial Sloan Kettering Cancer Center April 2009 - October 2015.

90 patients with pre- and posttreatment MRI and mammograms demonstrating calcifications within the tumor bed either at presentation or after treatment.

TABLE 2 Correlation between changes in calcification on mammogram, changes in enhancement on magnetic resonance imaging (MRI), and rates of pathologic complete response (pCR)

Change in calcifications on mammography	Change in MRI enhancement		pCR *n* (%)
	Resolved *n* (%)	Decreased *n* (%)	
Resolved (*n* = 3)	3 (100)	0 (0)	3 (100)
Decreased (*n* = 15)	5 (33)	10 (67)	4 (27)[a]
No change (*n* = 42)	16 (38)	26 (62)	10 (24)[b]
Increased (*n* = 24)	14 (58)	10 (42)	9 (38)[c]
New (*n* = 6)	2 (33)	4 (67)	3 (50)[d]

[a] 1 of 4 had resolved MRI enhancement; 3 of 4 had decreased MRI enhancement

[b] 9 of 10 had resolved MRI enhancement; 1 of 10 had decreased MRI enhancement

[c] 9 of 9 had resolved MRI enhancement

[d] 1 of 3 had resolved MRI enhancement; 2 of 3 had decreased MRI enhancement

An et al. World Journal of Surgical Oncology (2017) 15:198
DOI 10.1186/s12957-017-1263-8

World Journal of Surgical Oncology

RESEARCH Open Access

Residual microcalcifications after neoadjuvant chemotherapy for locally advanced breast cancer: comparison of the accuracies of mammography and MRI in predicting pathological residual tumor

Yeong Yi An[1], Sung Hun Kim[2] and Bong Joo Kang[2*]

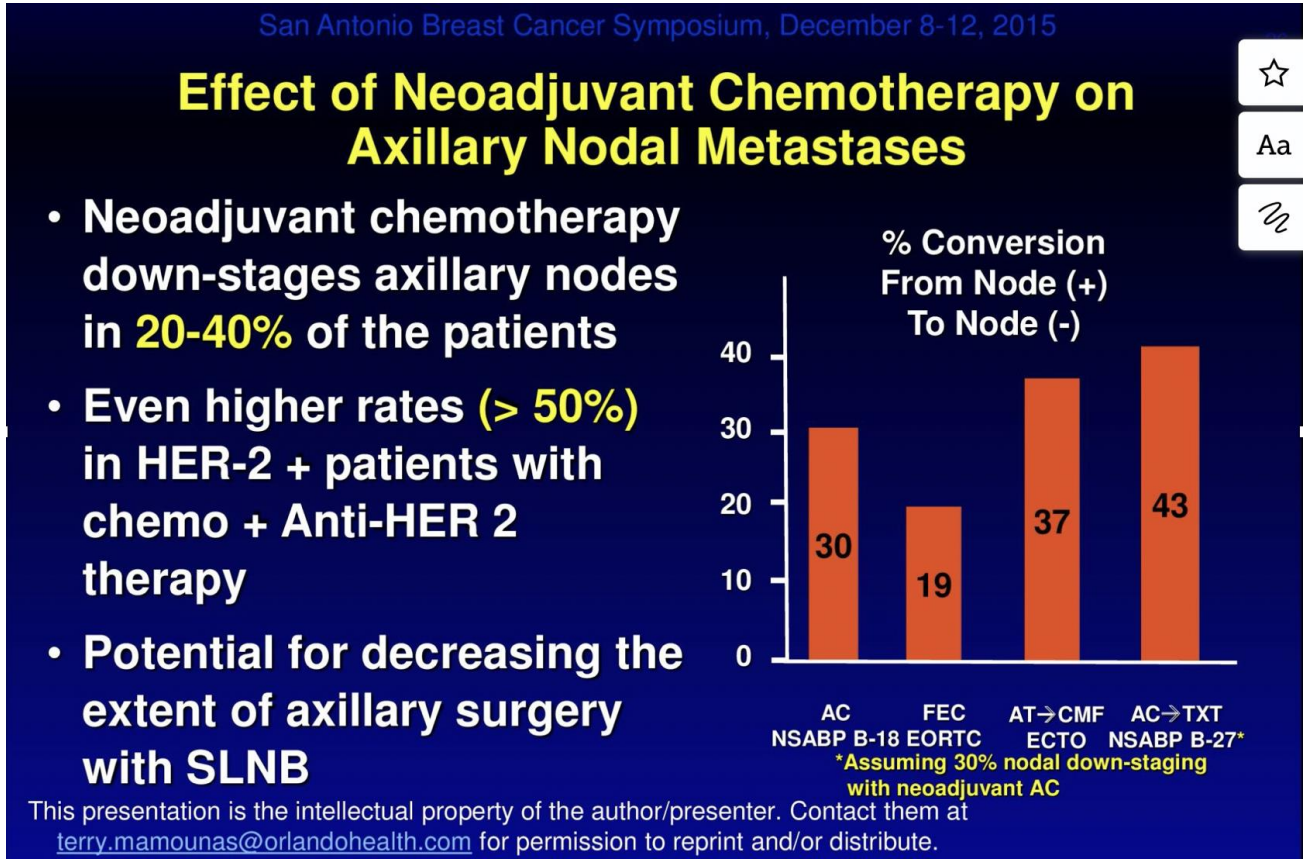
Clinical stage	
IIA	3 (10.3)
IIB	7 (24.1)
IIIA	18 (62.1)
IIIC	1 (3.5)

Table 3 Residual mammographic microcalcifications after NAC correlated with final pathological results

	Benign calcifications (n = 13)	Malignant calcifications (n = 16)	p value
Pathologic responses			0.03
pCR	4 (100.0)	0 (0.0)	
Non-pCR	9 (36.0)	16 (64.0)	

Treatment of the axilla after NACT

Axillary metastatic lymph nodes are converted to node negative in most patients having pCR in the breast



SN after NACT in node positive patients

Study	N	Detection	Nodal pCR
SENTINA (arm C)	474	80%	49%
ACOSOG Z1071	649	93%	41%
SN FNAC	153	88%	30%

Table 3 | False-negative rates for SLNB after conversion to clinically node-negative disease following NACT

Prospective trial	Overall false-negative rate	Stratified by number of SLNs			Stratified by SLN-detection technique	
		1 (%)	2 (%)	≥3 (%)	Single agent (%)	Dual agent (%)
SENTINA (treatment arm C)[58]	14.2 (95% CI 9.9–19.4)	24.3	18.5	7.3	16.0*	8.6
ACOSOG Z1071[57]	12.6% (95% CI 9.9–16.1)	31.5	21	9.1	20.3‡	10.8
SN FNAC[56]	8.4% (95% CI 2.4–14.4)	18.2	4.9§	NR	16.0*	5.2

*With radioactive colloid only. ‡With either radioisotope alone or blue dye alone. §Reported as two or more. Abbreviations: ACOSOG, American College of Surgeons Oncology Group; NACT, neoadjuvant chemotherapy; NR not reported; SLN, sentinel lymph node; SLNB, sentinel lymph-node biopsy.

Lancet Oncol 2013; 14: 609–18 *JAMA 2013; 310: 1455-61* *JCO 2015; 33: 258-64*

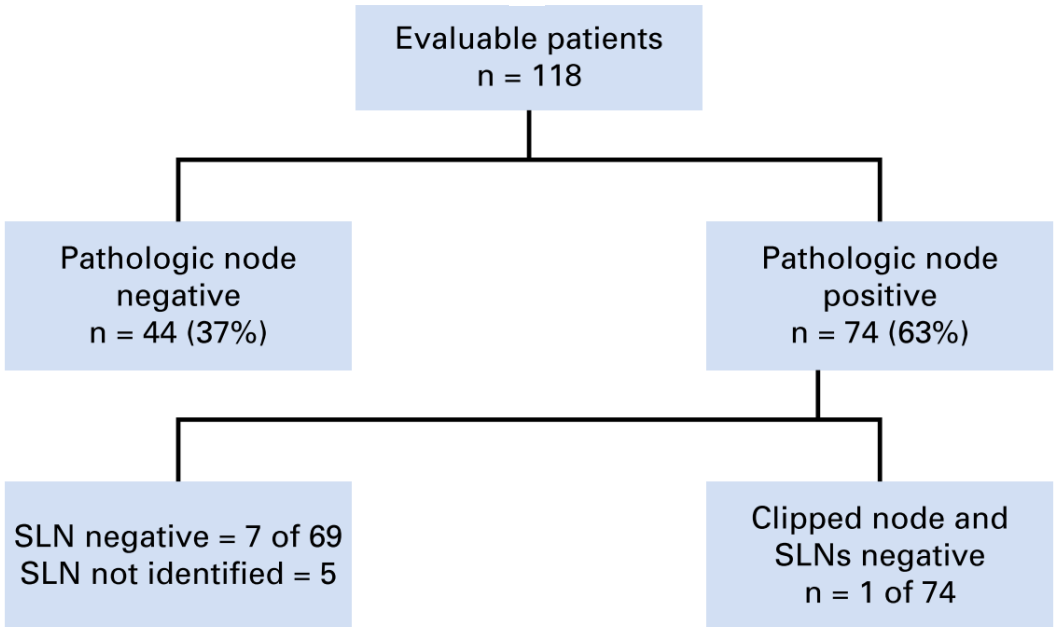
VOLUME 34 · NUMBER 10 · APRIL 1, 2016

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Improved Axillary Evaluation Following Neoadjuvant Therapy for Patients With Node-Positive Breast Cancer Using Selective Evaluation of Clipped Nodes: Implementation of Targeted Axillary Dissection

Abigail S. Caudle, Wei T. Yang, Savitri Krishnamurthy, Elizabeth A. Mittendorf, Dalliah M. Black, Michael Z. Gilcrease, Isabelle Bedrosian, Brian P. Hobbs, Sarah M. DeSnyder, Rosa F. Hwang, Beatriz E. Adrada, Simona F. Shaitelman, Mariana Chavez-MacGregor, Benjamin D. Smith, Rosalind P. Candelaria, Gildy V. Babiera, Basak E. Dogan, Lumarie Santiago, Kelly K. Hunt, and Henry M. Kuerer



False-negative rate
SLN alone = 10.1% (95% CI 4.2 to 19.8)
SLN + evaluation of the clipped node = 1.4% (95% CI, 0.03 to 7.3)
P = .03

Caudle et al. J Clin Oncol 2016; 34:1072-1078.

Ongoing trials: N-positive pre NACT

- GANEA 3 (France)
  - pN+ (clipped node) → NACT → SN + excision clipped node + ALND
  - N=385
  - Outcome: FNR

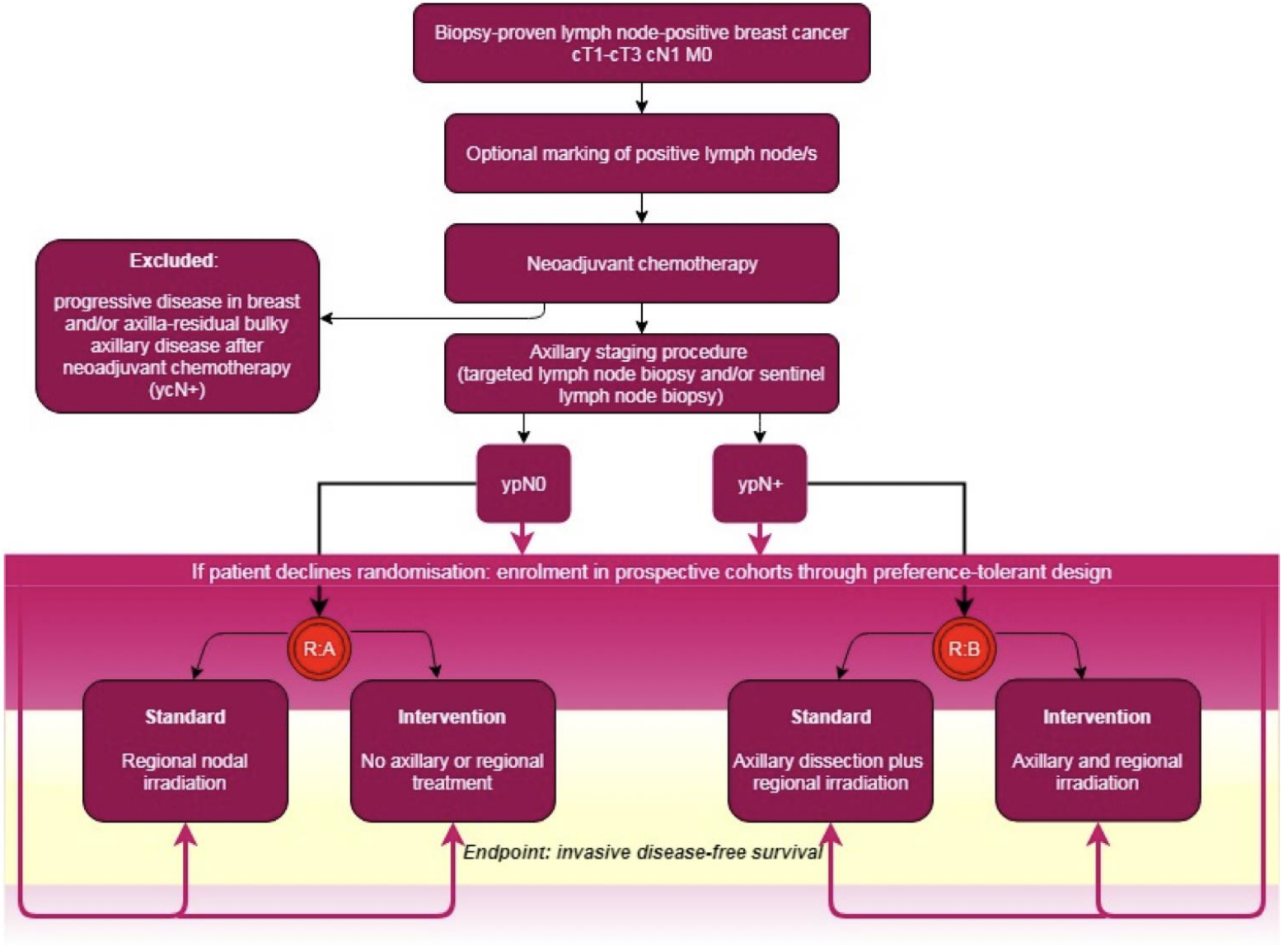
- RISAS - Primary **R**adioactive **I**odine **S**eed Localization in the Axilla in **A**xillary Node Positive Breast Cancer Combined With **S**entinel Node Procedure (the Netherlands)

  - pN+ (iodine seed) → NACT → SN + excision iodine seed + ALND
  - N=200
  - Outcome: Identification rate, FNR

- NSABP B51 (USA)
  - pN+ → NACT → SN (≥2) ypN0
    - → Regional RT
    - → No regional RT
  - N=1636 (71% included)
  - Outcome: recurrence-free interval (IBC-RFI)

- ATNEC (UK)
  - pN+ → NACT → SN (≥2 + clipped node) ypN0
    - → Regional RT/ALND
    - → No regional RT/ALND
  - N=1900 (not started to include)
  - Outcome: 5-yr DFS

- NEONOD 2 (Italia)
  - pN+ → NACT → SN
    - ypN1(mi) No axillary treatment
    - ypN0/ypN0(i+) No axillary treatment
    - ypN1 ALND
  - N=1500
  - Outcome: 5-yr DFS


Biopsy-proven lymph node-positive breast cancer
cT1-cT3 cN1 M0
Optional marking of positive lymph node/s
Neoadjuvant chemotherapy
Excluded:
progressive disease in breast and/or axilla-residual bulky axillary disease after neoadjuvant chemotherapy (ycN+)
Axillary staging procedure
(targeted lymph node biopsy and/or sentinel lymph node biopsy)
ypN0
ypN+
If patient declines randomisation: enrolment in prospective cohorts through preference-tolerant design
R:A
R:B
Standard
Regional nodal irradiation
Intervention
No axillary or regional treatment
Standard
Axillary dissection plus regional irradiation
Intervention
Axillary and regional irradiation
Endpoint: invasive disease-free survival

- ALLIANCE A011 202 (USA)
  - pN+ → NACT → SN ypN1
    - → ALND + regional RT
    - → Axillary RT + regional RT
  - N=2918
  - Outcome: invasive breast cancer recurrence-free interval (IBC-RFI)

- TAXIS trial (Switzerland)
  - pN+ → NACT → SN ypN1
    - ALND + regional RT
    - Axillary RT + regional RT
  - N=1500
  - Outcome: DFS

Tak for opmærksomheden