Trending breast clinical trials

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Surgical Update 2024

UNIVERSITY OF CAPE TOWN
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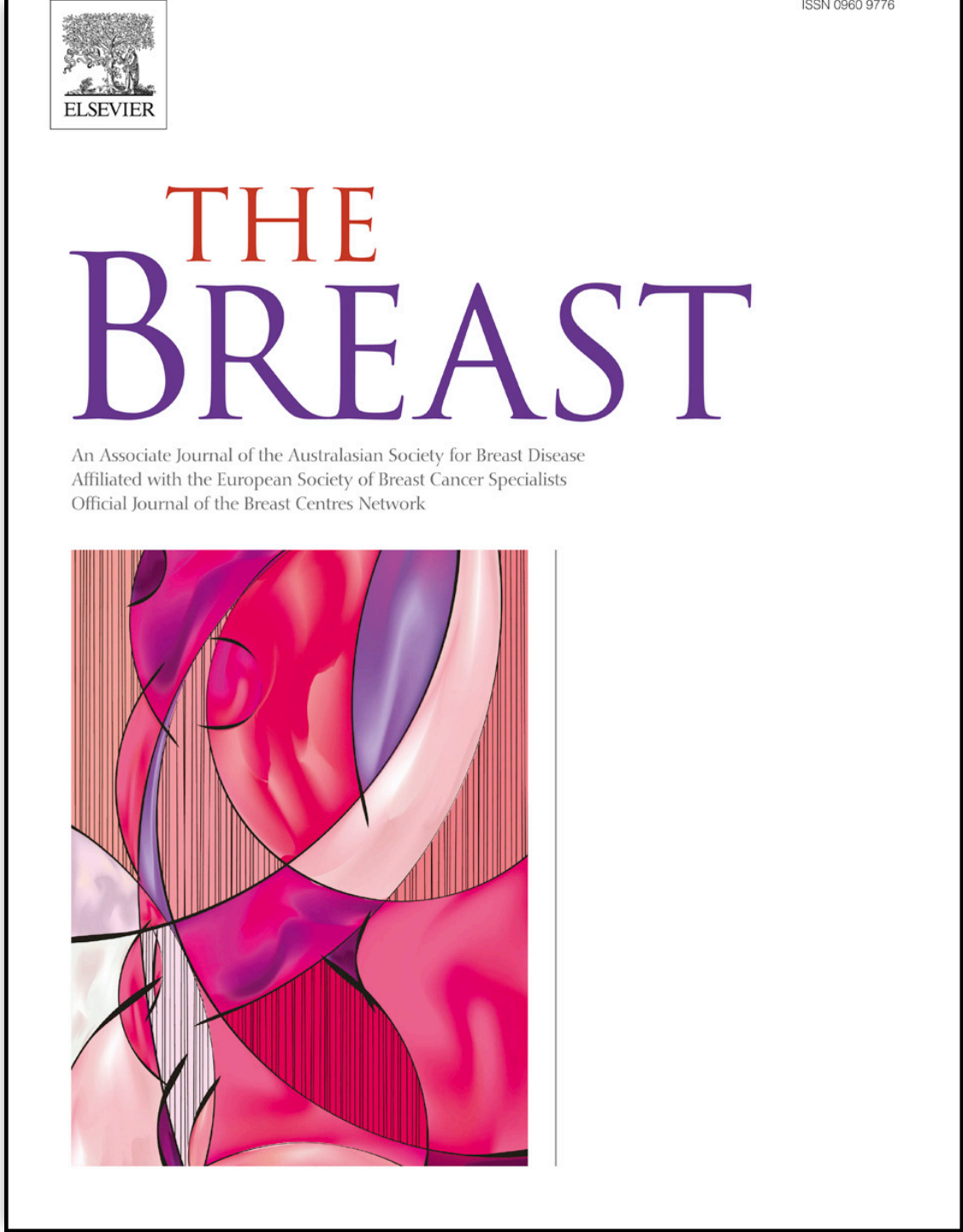
- Breast cancer highlights from 2023: Knowledge to guide practice and future research
- Maria-Joao Cardoso, Philip Poortmans, Elżbieta Senkus, Oreste D. Gentilini, Nehmat Houssami

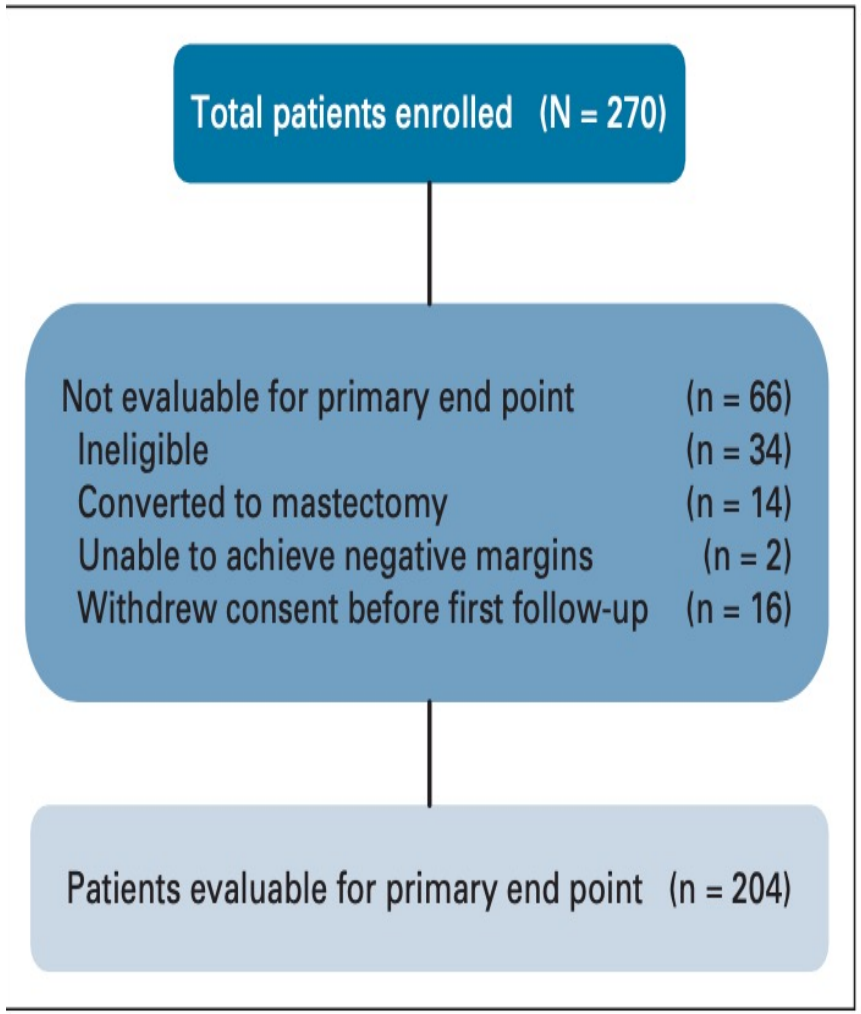


Local Recurrence After Breast-Conserving Therapy in Patients With Multiple Ipsilateral Breast Cancer: Results From ACOSOG Z11102 (Alliance)

Judy C. Boughey, MD[1]; Kari M. Rosenkranz, MD[2]; Karla V. Ballman, PhD[3]; Linda McCall, MS[4]; Bruce G. Haffty, MD[5]; Laurie W. Cuttino, MD[6]; Charlotte D. Kubicky, MD[7]; Huong T. Le-Petross, MD[8]; Armando E. Giuliano, MD[9]; Kimberly J. Van Zee, MS, MD[10]; Kelly K. Hunt, MD[8]; Olwen M. Hahn, MD[11]; Lisa A. Carey, MD[12]; and Ann H. Partridge, MD, MPH[13]

- BCT is the preferred Tx for unifocal BC
- ? Oncological safety of MIBC
- Phase 2, single arm, prospective trial- Evaluate the oncological outcomes in patients undergoing BCT for MIBC

American Society of Clinical Oncology Volume 41, Issue 17



- Nov 2012- Aug 2016
- Women > 40yrs , Median age 61
- 2 to 3 foci biopsy proven (1 site) cT2N0-1 BC
- Lumpectomy – clear margin. Whole breast RT with boost to all excision beds
- Median f/up 66mo
- End point- cumulative incidence of LR at 5 yrs with a priori rate clinical acceptability of <8%

TABLE 1. Patient and Tumor Characteristics of Patients Enrolled on Z11102 Clinical Trial

Characteristic	Preamendment 5 (n = 103)	Postamendment 5 (n = 101)	Total (n = 204)
No. of malignant lesions at registration, No. (%)			
2	100 (97.1)	97 (96.1)	197 (96.6)
3	3 (2.9)	4 (4.0)	7 (3.4)
Shortest distance between lesions on imaging			
No.	102	100	202
Mean (SD)	4.1 (2.3)	4.7 (2.3)	4.4 (2.3)
Median	3.4	4.5	4.0
Q1-Q3	2.5-5.0	2.8-5.8	2.5-5.4
Range	2.0-14.0	2.0-15.0	2.0-15.0
Clinical T category, No. (%)			
T1	61 (59.2)	60 (59.4)	121 (59.3)
T2	42 (40.8)	41 (40.6)	83 (40.7)
Clinical N category, No. (%)			
N0	99 (96.1)	96 (95.0)	195 (95.6)
N1	4 (3.9)	5 (5.0)	9 (4.4)
Histology, No. (%)			
All ductal	68 (66.0)	51 (50.5)	119 (58.3)
All lobular	5 (4.9)	11 (10.9)	16 (7.8)
DCIS/ductal	23 (22.3)	23 (22.8)	46 (22.5)
DCIS/lobular	1 (1.0)	4 (4.0)	5 (2.5)
Ductal/lobular	6 (5.8)	12 (11.9)	18 (8.8)
Highest histologic grade on biopsy, No. (%)			
G1 (low)	27 (26.2)	26 (25.7)	53 (26.0)
G2 (intermediate)	45 (43.7)	51 (50.5)	96 (47.1)
G3 (high)	29 (28.2)	23 (22.8)	52 (25.5)
GX (grade cannot be assessed)	2 (1.9)	1 (1.0)	3 (1.5)

(continued on following page)

- Maximum tumour 5cm
- (3cm) 2cm of normal tissue
- Disease extent limited to 2 quadrants
- Preop MMG/ +- USS
- Preop MRI- amended May 2015 (optional)
- Excluded –contralateral BC, BRCA, implants
- ER 83.5% HER2 11.5% TPN 5%
- SLNB 84% ANC 5% SLNB-ANC 8%
- No. of lumpectomies 1 =30%, 2= 68%, 3= 2%

Results

- 6 pts developed LR - 3.1% - lower than predicted
- Age, MIBC, ER, HER2, T/N staging were not assoc with LR risk.
- None of HER2 pts developed LR
- 20 pts ER+ didn't receive ET, the 5 yr LR incidence was 12.5% vs 1.9% (ET)
- Breast MRI was done in 92.6% & 7.4 % no MRI (n=15)
- MRI detected 42% of NBL not seen on MMG/USS
- LR rate without MRI 22.6% vs 1.7% with MRI

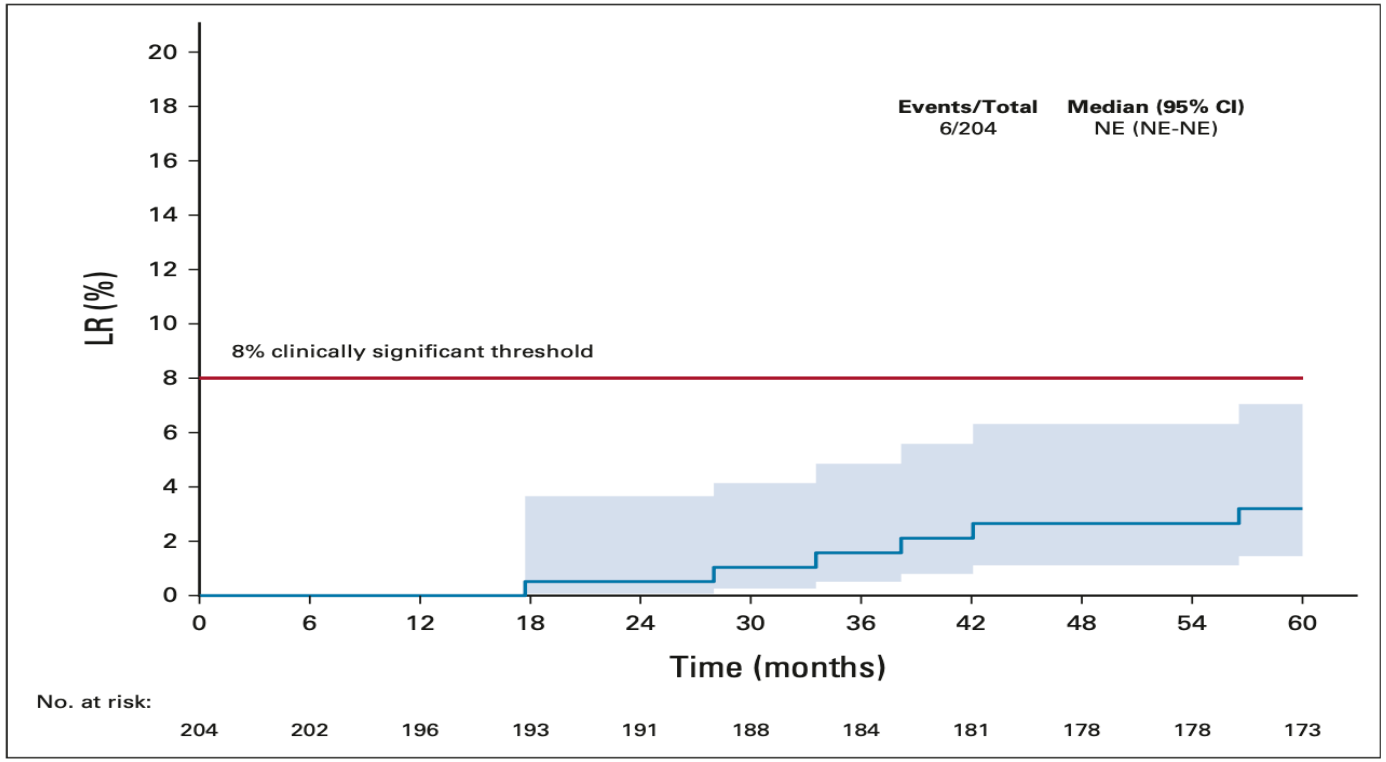


FIG 2. Cumulative incidence of LR after breast-conserving surgery with whole breast radiation in multiple ipsilateral breast cancer. Shaded region is the 95% confidence interval for the cumulative incidence curve. LR, local recurrence; NE, not estimable.

- Advances in systemic Rx, high quality digital imaging, targeted surgical resection, assessment of margins, LR rates are low making it acceptable to Rx MIBC with BCT

JAMA Oncology November 2023 Volume 9, Number 11

JAMA Oncology | Original Investigation

Sentinel Lymph Node Biopsy vs No Axillary Surgery in Patients With Small Breast Cancer and Negative Results on Ultrasonography of Axillary Lymph Nodes
The SOUND Randomized Clinical Trial

Oreste Davide Gentilini, MD; Edoardo Botteri, PhD; Claudia Sangalli, BSc; Viviana Galimberti, MD; Mauro Porpiglia, MD; Roberto Agresti, MD; Alberto Luini, MD; Giuseppe Viale, MD; Enrico Cassano, MD; Nickolas Peradze, MD; Antonio Toesca, MD; Giulia Massari, MD; Virgilio Sacchini, MD; Elisabetta Munzone, MD; Maria Cristina Leonardi, MD; Francesca Cattadori, MD; Rosa Di Micco, PhD; Emanuela Esposito, PhD; Adele Sgarella, MD; Silvia Cattaneo, MD; Massimo Busani, MD; Massimo Dessena, MD; Anna Bianchi, MD; Elisabetta Cretella, MD; Francisco Ripoll Orts, MD; Michael Mueller, MD; Corrado Tinterri, MD; Badir Jorge Chahuan Manzur, MD; Chiara Benedetto, PhD; Paolo Veronesi, MD; for the SOUND Trial Group

- SLNB is standard of care for axillary node staging in early BC
- ? Questioned since surgery for examination of axillary nodes is not performed with curative intent
- Is omission of axillary surgery noninferior to SLNB in patients with small BC & negative results on preoperative axillary LN USS?

Methods

- Prospective noninferiority phase 3 RCT
- Italy, Switzerland, Spain & Chile (Feb 2013 – June 2017)
- 1463-women of any age with BC up to 2cm - 1405
- Negative preoperative axillary USS
- Outcomes - 1. Distant disease- free survival (DDFS) @ 5 yrs
- 2. Cumulative incidence of distant recurrences, axillary recurrences, DFS, OS, and Adjuvant Rx recommendations

Table 1. Baseline Patient and Tumor Characteristics

Characteristic	Patients, No. (%) SLNB (n = 708)	No axillary surgery (n = 697)
Age at surgery, y		
<40	10 (1.4)	10 (1.4)
40-49	114 (16.1)	128 (18.4)
50-64	324 (45.8)	298 (42.8)
≥65	260 (36.7)	261 (37.4)
Median (IQR)	60 (52-68)	60 (51-68)
Menopausal status[a]		
Premenopausal	145 (20.6)	154 (22.3)
Perimenopausal or postmenopausal	558 (79.4)	538 (77.7)
Histotype		
Ductal	551 (77.8)	543 (77.9)
Lobular	61 (8.6)	59 (8.5)
Tubular	27 (3.8)	33 (4.7)
Other	69 (9.7)	62 (8.9)
Pathological tumor size		
pT1mic or pT1a	71 (10.0)	61 (8.8)
pT1b	251 (35.5)	240 (34.4)
pT1c	355 (50.1)	361 (51.8)
pT2	31 (4.4)	35 (5.0)
Median (IQR), cm	1.1 (0.8-1.5)	1.1 (0.8-1.5)
No. of positive SLNs		
0	599 (84.6)	12 (1.7)
1	83 (11.7)	10 (1.4)
≥2	14 (2.0)	0
SLNB not performed	12 (1.7)	675 (96.8)
No. of positive LNs		
0	599 (84.6)	12 (1.7)
1-3	93 (13.1)	9 (1.3)
4-9	2 (0.3)	1 (0.1)
≥10	2 (0.3)	0
[illegible]	[illegible]	[illegible]
Pathological node status		
pNx	12 (1.7)	675 (96.8)
pN0	584 (82.5)	12 (1.7)
pN0(i+)	15 (2.1)	0
pN1mi	36 (5.1)	4 (0.6)
pN1	57 (8.1)	5 (0.7)
pN2	4 (0.6)	1 (0.1)
Grade[b]		
1	194 (27.7)	204 (29.9)
2	377 (53.8)	356 (52.2)
3	130 (18.5)	122 (17.9)
ER status		
0	56 (7.9)	44 (6.3)
>0	652 (92.1)	653 (93.7)
PgR status		
0	108 (15.3)	95 (13.6)
>0	600 (84.7)	602 (86.4)

Table 1. Baseline Patient and Tumor Characteristics (continued)

Characteristic	Patients, No. (%) SLNB (n = 708)	No axillary surgery (n = 697)
Ki-67 index[c]		
<20	455 (64.4)	439 (63.2)
≥20	252 (35.6)	256 (36.8)
Median (IQR)	15 (10-23)	15 (10-24)
ERBB2 overexpression		
Not overexpressed	660 (93.2)	650 (93.3)
Overexpressed	48 (6.8)	47 (6.7)
Surrogate subtype		
Luminal *ERBB2*-negative	617 (87.1)	617 (88.5)
ERBB2-enriched	48 (6.8)	47 (6.7)
Triple-negative	43 (6.1)	33 (4.7)

Abbreviations: ER, estrogen receptor; LN, lymph node; PgR, progesterone receptor; SLN, sentinel lymph node; SLNB, sentinel lymph node biopsy.

[a] Frequencies do not sum to total due to missing data. Percentages were based on 703 patients in the SLNB group and 692 patients in the no axillary surgery group.

[b] Frequencies do not sum to total due to missing data. Percentages were based on 701 patients in the SLNB group and 682 patients in the no axillary surgery group.

[c] Frequencies do not sum to total due to missing data. Percentages were based on 707 patients in the SLNB group and 695 patients in the no axillary surgery group.

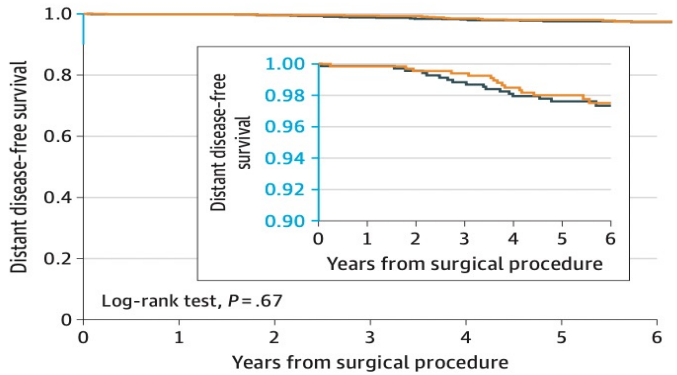
Table 3. Summary of First Events, Deaths, and Follow-Up Time

Outcome	Events, No. (%)	
	SLNB (n = 708)	No axillary surgery (n = 697)
First events		
Ipsilateral breast recurrence	7 (1.0)	6 (0.9)
Axillary recurrence	3 (0.4)	5 (0.7)
Ipsilateral breast and axillary recurrence	2 (0.3)	0
Distant metastasis	13 (1.8)	14 (2.0)
Contralateral breast cancer	5 (0.7)	7 (1.0)
Nonbreast primary tumors	17 (2.4)	22 (3.2)
Death from breast cancer	0	0
Death from cause other than breast cancer	5 (0.7)	6 (0.9)
Death from unknown cause	1 (0.1)	1 (0.1)
Follow-up, median (IQR), y	5.7 (5.0-6.8)	5.7 (5.0-6.6)
All deaths, cause		
Breast cancer	7 (1.0)	4 (0.6)
Cause other than breast cancer	10 (1.4)	12 (1.7)
Unknown cause	4 (0.6)	2 (0.3)
Follow-up, median (IQR), y	5.8 (5.0-6.9)	5.8 (5.0-6.8)

Abbreviation: SLNB, sentinel lymph node biopsy.

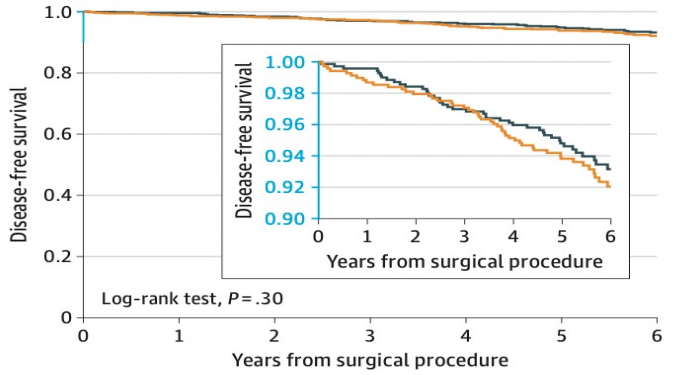
Figure 2. Kaplan-Meier Estimates of Distant Disease-Free Survival, Disease-Free Survival, and Overall Survival

A Distant disease-free survival



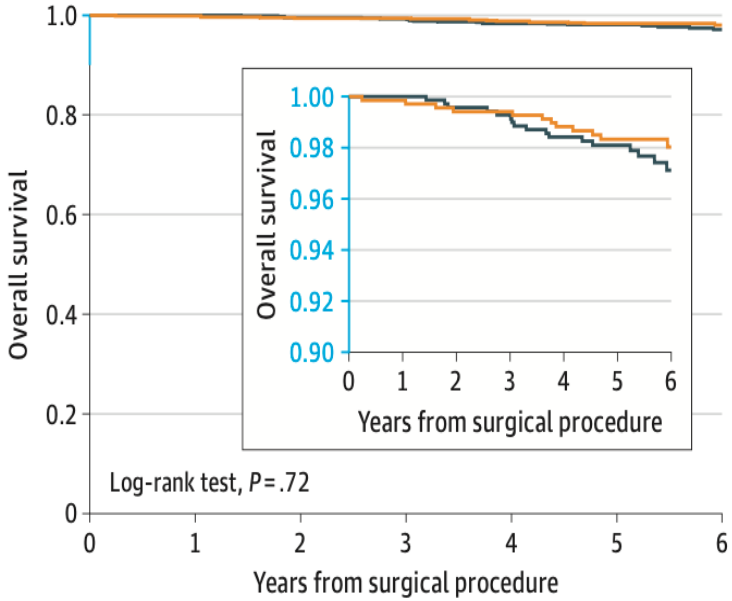
No. at risk							
SLNB	708	702	694	684	657	532	303
No SLNB	697	684	675	669	640	512	289

B Disease-free survival



No. at risk							
SLNB	708	702	694	684	657	532	303
No SLNB	697	684	675	669	640	512	289

C Overall survival



No. at risk							
SLNB	708	705	702	700	673	550	317
No SLNB	697	693	688	687	663	531	310

SLNB indicates sentinel lymph node biopsy.

Conclusions

- Z11 – ANC was the standard of care in the presence of +ve SLNB.
- Now with better systemic Rx, it is no longer necessary.
- SOUND– omission of axillary surgery is noninferior to SLNB in early BC & negative axillary USS.

Limitations

- Definition of negative Axillary LN vs suspicious.
- 57 pts – doubtful node on USS- FNA – to exclude nodal metastasis
- SLNB – pts with nodal mets (13.7% +ve nodes : 5.1% micro mets, 8.6% macro mets & 0.6 % > 4 nodes +ve) had to undergo ANC – further randomized. ? Frozen section.
- 114 pts (16%) randomized to No axillary procedure received ELIOT as full dose/ intraoperative boost.
- ? Mastectomy patients (9) ANC
- Radiotherapy not standardized

Effect of Peritumoral Infiltration of Local Anesthetic Before Surgery on Survival in Early Breast Cancer

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- Preventing metastases by using perioperative interventions has not been adequately explored.
- Local anaesthesia blocks voltage-gated sodium channels and thereby prevents activation of pro-metastatic pathways.
- Open-label, multicentre randomized trial to test the impact of presurgical, peritumoral in- filtration of local anaesthesia on disease-free survival (DFS).

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Methods

- Women with early breast cancer planned for upfront surgery
- without prior neoadjuvant treatment
- randomly assigned to receive peritumoral injection of 0.5% lidocaine < 4.5 mg/kg body weight) around all 6 tumour surfaces, 7-10 minutes before surgery ([LA] arm) or no LA arm).
- Operable BC, cT2N1, no mets, ECOG 0 - 1583
- Participants received standard postoperative adjuvant treatment.
- Primary and secondary end points were DFS and overall survival (OS), respectively.

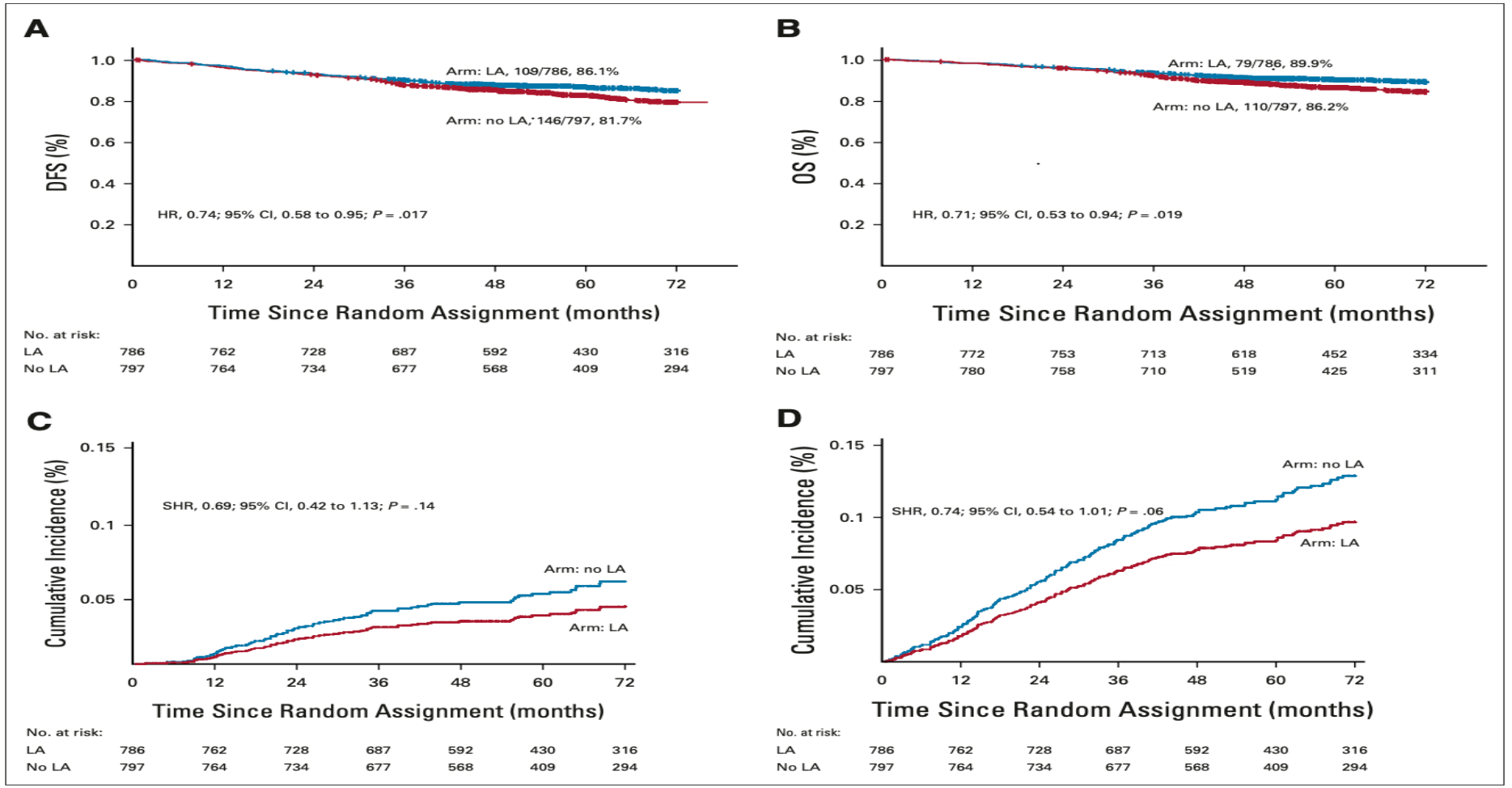
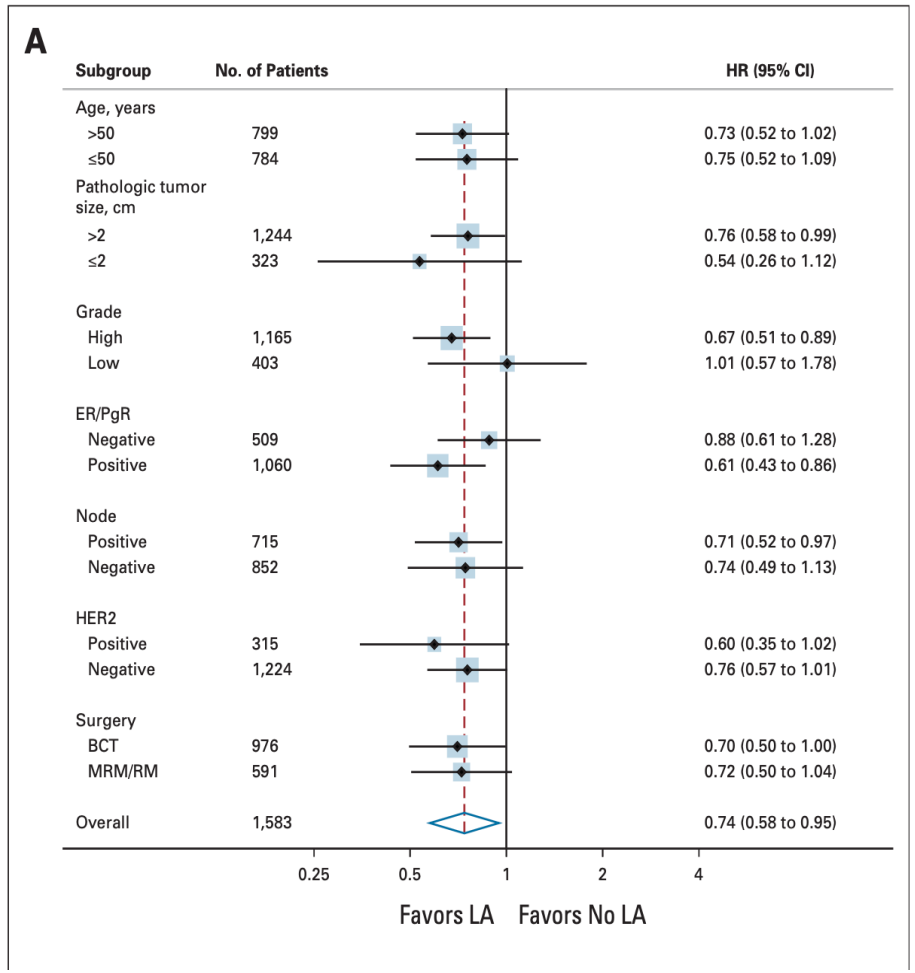


FIG 2. (A) Kaplan-Meier estimates of DFS and corresponding HR in the local anesthetics group (arm: LA) and the no local anesthetics group (arm: no LA). (B) Kaplan-Meier estimates of OS and corresponding HR in the local anesthetics group (arm: LA) and the no local anesthetics group (arm: no LA). (C) Kaplan-Meier estimates of locoregional recurrences: competing risk analysis. (D) Kaplan-Meier estimates of distant recurrences: competing risk analysis. DFS, disease-free survival; HR, hazard ratio; LA, local anesthetics; OS, overall survival; SHR, subdistribution HR.



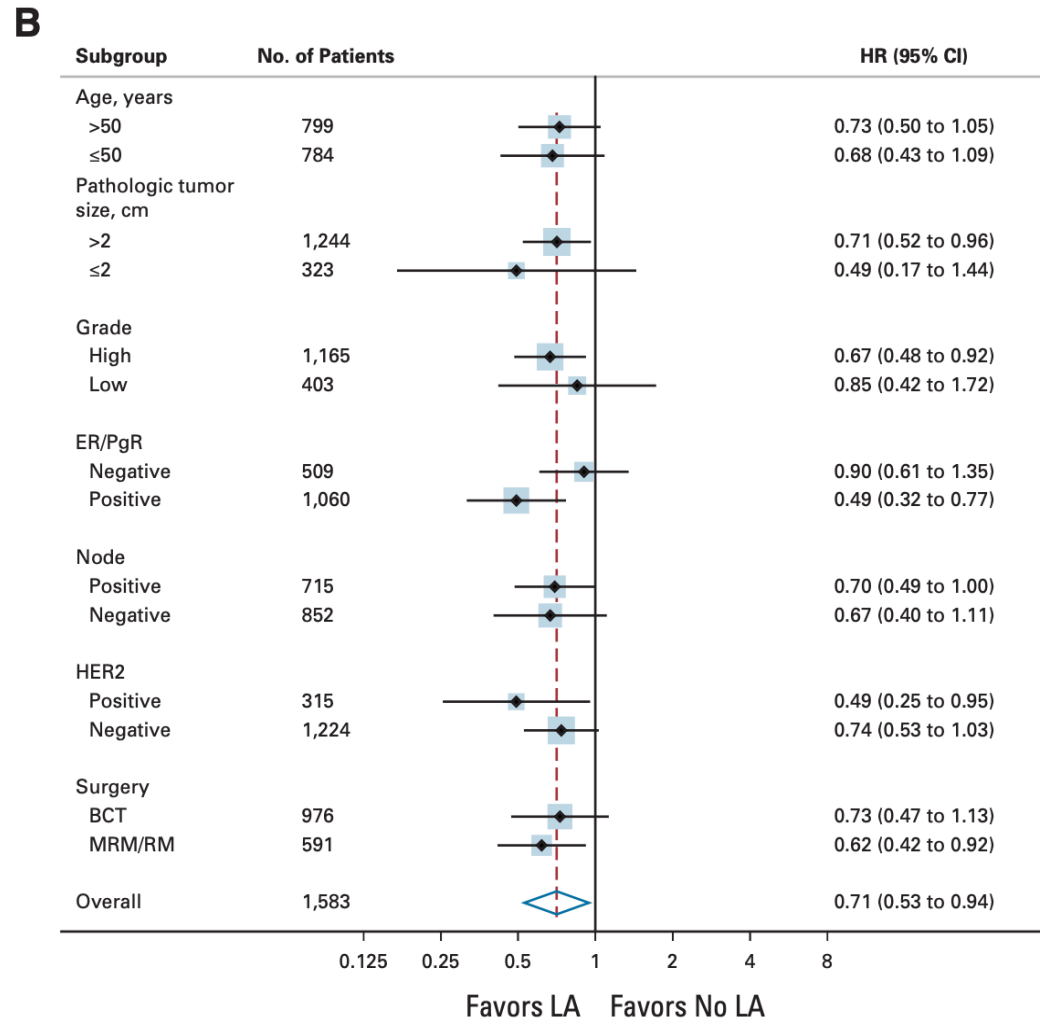


FIG 3. (Continued). (A) DFS according to subgroup (forest plot). The subgroups were determined according to prespecified stratification factors and known prognostic factors. The size of the squares corresponds to the number of patients with event. The diamond incorporates the point estimate and the 95% CI of the overall effect. (B) OS according to subgroup (forest plot). The subgroups were determined according to prespecified stratification factors and known prognostic factors. The size of the squares corresponds to the number of patients with event. The diamond incorporates the point estimate and the 95% CI of the overall effect. BCT, breast conserving treatment; DFS, disease-free survival; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HR, hazard ratio; MRM, modified radical mastectomy; OS, overall survival; PgR, progesterone receptor; RM, radical mastectomy.

- Peritumoral infiltration of Lidocaine before surgery significantly increases DFS and OS.
- The benefit was evident in all subgroups based on T, LN mets, age, type of Sx (BCS / MX), HR status.
- The reduction was seen in locoregional recurrences as well as distant mets.
- Downside- No placebo control. Not blinded.
- ? Lidocaine pharma kinetics have antimetastatic effect.– could explore this theory in other solid tumours.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Omitting Radiotherapy after Breast-Conserving Surgery in Luminal A Breast Cancer

T.J. Whelan, S. Smith, S. Parpia, A.W. Fyles, A. Bane, F.-F. Liu, E. Rakovitch, L. Chang, C. Stevens, J. Bowen, S. Provencher, V. Théberge, A.M. Mulligan, Z. Kos, M.A. Akra, K.D. Voduc, T. Hijal, I.S. Dayes, G. Pond, J.R. Wright, T.O. Nielsen, and M.N. Levine, for the LUMINA Study Investigators*

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- Adjuvant RT is prescribed after BCT to reduce the risk of LR.
  RT is inconvenient, costly & associated with both short-term and long-term side effects.

- Can they use clinicopathologic factors and molecular subtypes to see in whom to omit RT ?

Methods

- Prospective cohort study, Multicenter
- Women > 55 yrs (median 67)
- 500 eligible
- BCT for T1N0, 1mm margin, IDC GR1 /2, Luminal A -Ki67 index < 13.25%
- Had to receive Adjuvant ET
- Calculated cumulative incidence @ 5 yrs < 5% - acceptable risk for LR
- F/up 5yrs – recurrent invasive or in situ cancer in ipsilateral breast

N ENGL J MED 389;7 NEJM.ORG AUGUST 17, 2023

The New England Journal of Medicine

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	All Patients (N = 500)
Age	
Median (IQR) — yr	67.1 (62.9–71.6)
Distribution — no. (%)	
55 to <60 yr	61 (12)
60 to <65 yr	138 (28)
65 to <70 yr	136 (27)
70 to <75 yr	107 (21)
75 to <80 yr	42 (8)
≥80 yr	16 (3)
Tumor size	
Median (IQR) — cm	1.0 (0.7–1.4)
Distribution — no. (%)	
≤0.5 cm	39 (8)
0.5–1.0 cm	217 (43)
1.1–2.0 cm	244 (49)
Tumor grade — no. (%)	
1	330 (66)
2	170 (34)
Histologic cancer type — no. (%)	
Ductal	437 (87)
Tubular	25 (5)
Mucinous	26 (5)
Other	12 (2)

* Percentages may not total 100 because of rounding. IQR denotes interquartile range.

- 59% Aromatase Inhibitor 41% Tamoxifen
- 82.7% were still on ET at 5yrs
- LR = 10 pts (invasive) – 6 true/ marginal recurrence & 4 elsewhere in the ipsilateral breast
- Cumulative incidence @ 5yrs was 2.3%

- Contralateral BC = 8, CI 1.9%

- Disease free survival – 11 recurrences, 7 contralateral BC, 23 second primary cancers, 6 deaths (47 overall).
- 5 yr DFS of 89%
- Of total deaths – 1 was related to BC = DFS 97.2%

CONCLUSIONS

RT CAN BE OMITTED AFTER BCS IN > 55 YEARS OF AGE

T1N0 GRADE 1 OR 2

LUMINAL A

Artificial intelligence-supported screen reading versus standard double reading in the Mammography Screening with Artificial Intelligence trial (MASAI): a clinical safety analysis of a randomised, controlled, non-inferiority, single-blinded, screening accuracy study

Kristina Lång, Viktoria Josefsson, Anna-Maria Larsson, Stefan Larsson, Charlotte Högberg, Hanna Sartor, Solveig Hofvind, Ingvar Andersson, Aldana Rosso

- Can we use AI to improve mammography screening accuracy?
- And reduce screen reading workload?
- RCT- population based, 40-80yrs, (general & moderate hereditary risk of BC), Sweden
- The AI system (Transpara version 1.7.0)

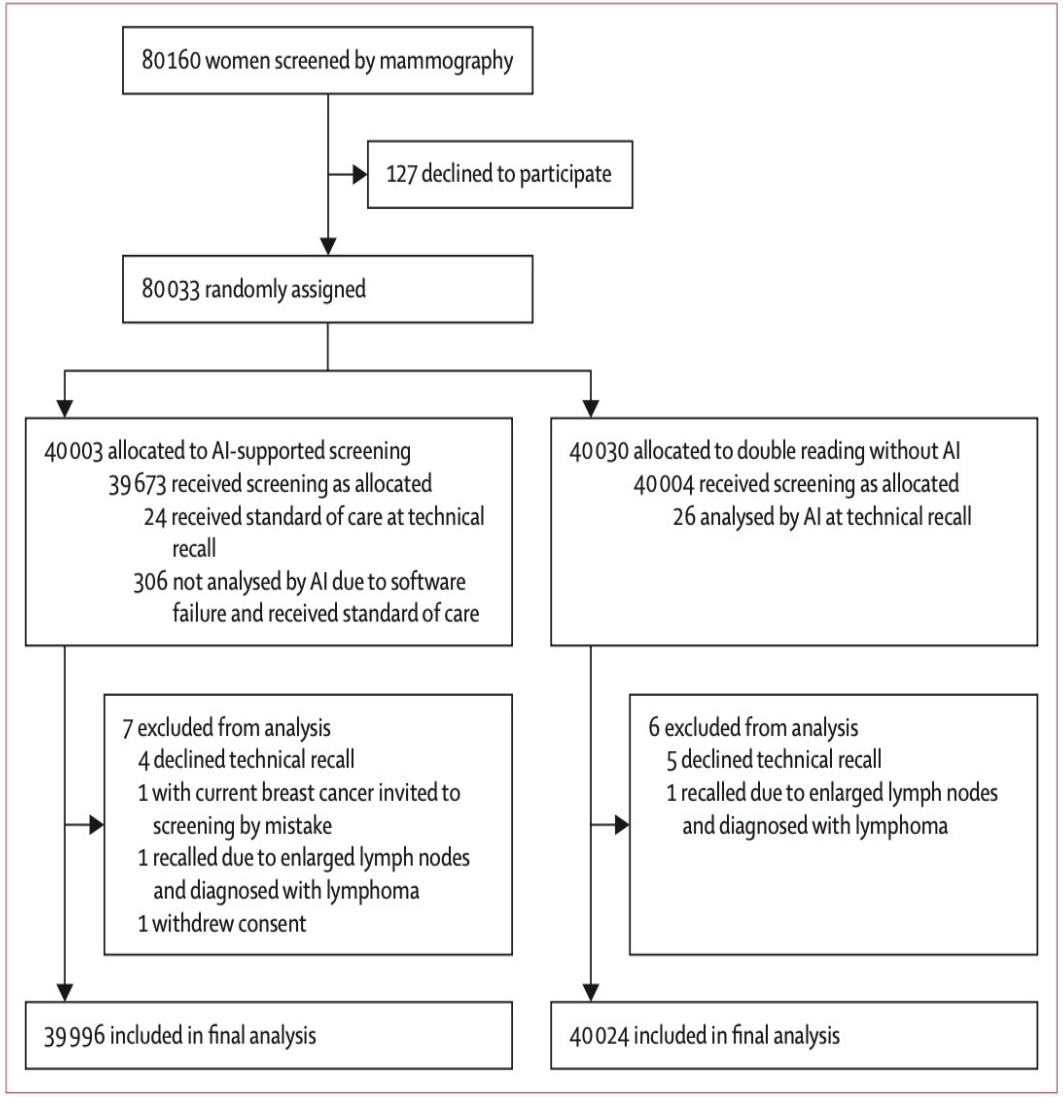

Figure 2: **Trial profile**
AI=artificial intelligence.

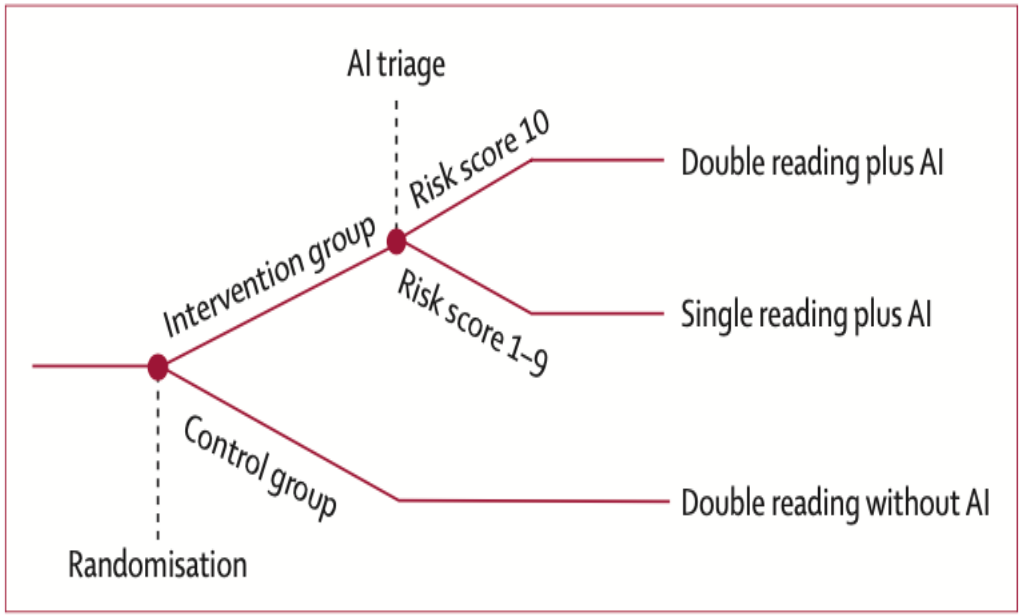

Figure 1: **Overview of trial intervention**
AI=artificial intelligence.

	Intervention group (n=39 996)	Control group (n=40 024)
Early screening performance		
Number of recalls	861	817
Recall rate, %	2·2% (2·0–2·3)	2·0% (1·9–2·2)
Number of screen-detected cancers	244	203
Cancer-detection rate, per 1000 participants screened	6·1 (5·4–6·9)	5·1 (4·4–5·8)
False positive rate, %	1·5% (1·4–1·7)	1·5% (1·4–1·7)
Positive predictive value of recall, %	28·3% (25·3–31·5)	24·8% (21·9–28·0)
Workload		
Number of screen readings	46 345	83 231
Number of consensus meetings	1584	1576
Consensus meeting rate	4·0% (3·8–4·2)	3·9% (3·8–4·1)

Data are n or point estimate (95% CI).

Table 2: **Early screening performance and workload measures, modified intention-to-treat population**

- AI-supported MMG can be considered safe.
- Resulted in similar rate of screen detected cancers, without increasing recalls, False positives.
- While reducing screen reading workload.

THANK YOU