The SENOMAC trial

Results, implementation and open questions

Prof. Jana de Boniface, MD PhD

Consultant Breast Surgeon, Capio St. Göran's Hospital

Clinical Professor, Dept. of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

1–2 Sentinel Lymph Node Metastases: Omission of Axillary Dissection

IBCSG 23-01

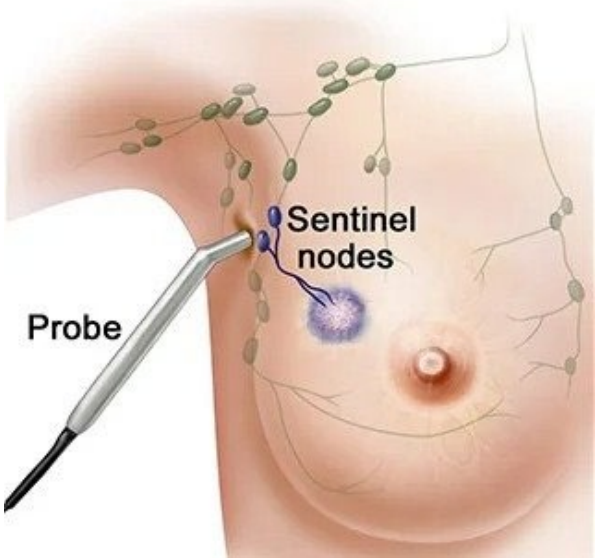
The ACOSOG Z0011 (Alliance) Randomized Clinical Trial

EORTC 10981-22023 AMAROS

OTOASOR trial

SINODAR ONE

the SENOMAC trial



1–2 Sentinel Lymph Node Metastases: Omission of Axillary Dissection

IBCSG 23-01

The ACOSOG Z0011 (Alliance) Randomized Clinical Trial

EORTC 10981-22023 AMAROS

OTOASOR trial

SINODAR ONE

th

Equal survival outcomes but half the risk of postoperative arm lymphoedema

Sentinel Lymph Node Metastases: Omission of Axillary Dissection

ACOSOG Z0011 (N=813)

- T1–2
- **No gross extranodal disease**
- Non–SLN metastases 27%

Few available RT plans
High tangents
Protocol-violating nodal RT

SINODAR-ONE (N=889)

- T1–2
- ≤ 2 **macro**metastatic nodes
- No palpable/visible nodes
- BCS + **mastectomy** (N=218)
- **Age** 40–75 years
- Non–SLN metastases 44%

Sentinel Lymph Node Macrometastases: Axillary Dissection or Axillary Radiotherapy?

AMAROS (N=1425)

- T1–2 ***up to 3 cm*** *until 2008*
- **Statistical power was never achieved (18 instead of 52 axillary recurrences after 10 years)**
- Non-SLN metastases 33%

OTOASOR (N=474)

- T1–2 ***up to 3 cm***
- Number of allowed SLN+ not specified (results: mean 1.36)
- No palpable nodes = cN0
- BCS + **mastectomy** (N=74)
- Non-SLN metastases 38.5%

SENOMAC Eligibility Criteria

- 1–2 sentinel lymph node **macro**metastases
- T1–**3**
- cN0 on palpation but **positive ultrasound** + FNA allowed
- **Extranodal extension** allowed
- All adult ages
- **Male** and female
- **Mastectomy** and breast conservation

SENOMAC Trial Design

- Prospective 1:1 randomized clinical non-inferiority trial
  - → **Standard of Care**: Completion axillary dissection
  - → **Intervention**: No completion axillary dissection
- Primary endpoint: Overall Survival (Non-Inferiority Margin 2.5%)
  - → Upper limit of the Confidence Interval HR<1.44
- Target accrual 3000 patients
  - → 190 events required for statistical power
- **Secondary endpoint: Recurrence-Free Survival**
  - → 190 events required to show Non-Inferiority by 4.1% (Upper CI <1.44)

SABCS SAN ANTONIO BREAST CANCER SYMPOSIUM®
DECEMBER 5-9, 2023 | @SABCSSanAntonio

Recurrence-free survival following sentinel node-positive breast cancer without completion axillary lymph node dissection – first results from the international randomized SENOMAC trial

Jana de Boniface, M.D., Ph.D., Associate Professor
Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden
Breast Unit, Capio St. Göran's Hospital, Stockholm Sweden

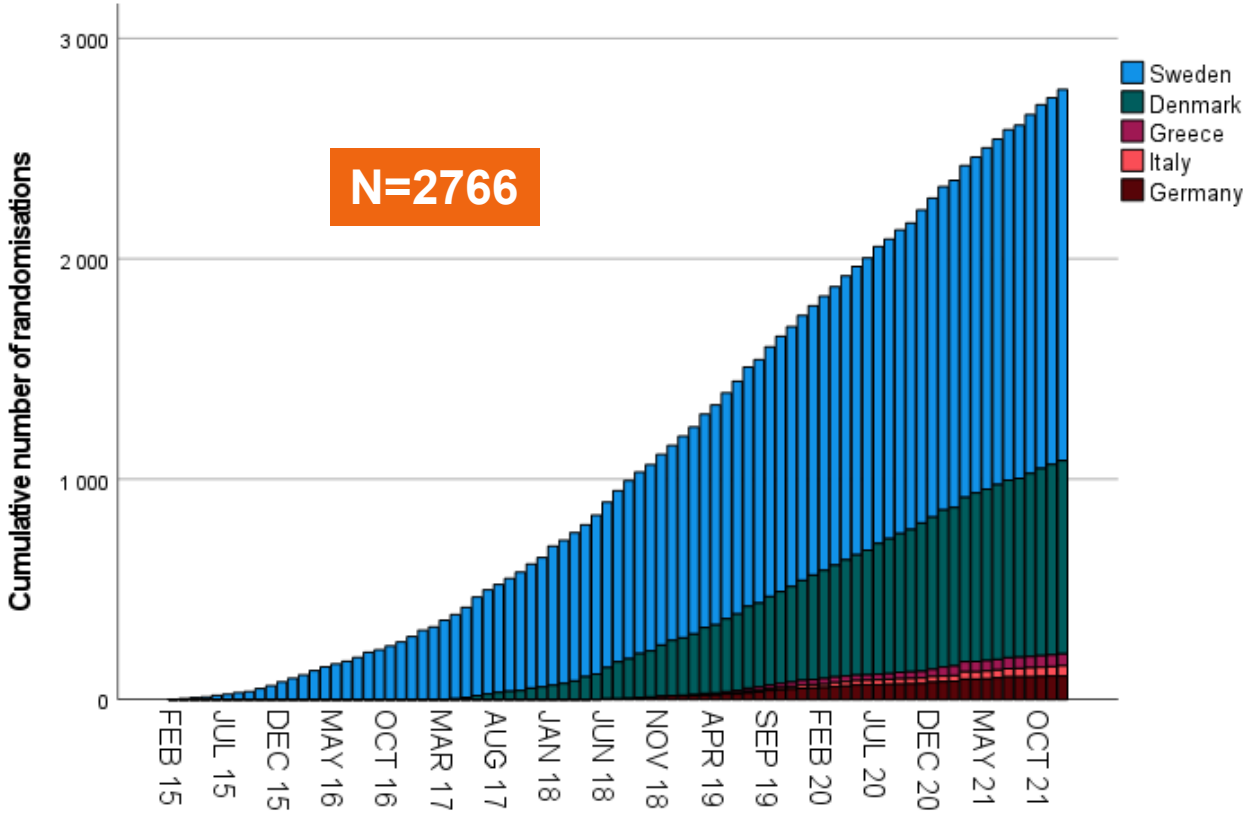
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 4, 2024 VOL. 390 NO. 13

Omitting Axillary Dissection in Breast Cancer with Sentinel-Node Metastases

J. de Boniface, T. Filtenborg Tvedskov, L. Rydén, R. Szulkin, T. Reimer, T. Kühn, M. Kontos, O.D. Gentilini, R. Olofsson Bagge, M. Sund, D. Lundstedt, M. Appelgren, J. Ahlgren, S. Norenstedt, F. Celebioglu, H. Sackey, I. Scheel Andersen, U. Hoyer, P.F. Nyman, E. Vikhe Patil, E. Wieslander, H. Dahl Nissen, S. Alkner, Y. Andersson, B.V. Offersen, L. Bergkvist, J. Frisell, and P. Christiansen, for the SENOMAC Trialists' Group*

Enrolment


N=2766
Cumulative number of randomisations
3 000
2 000
1 000
0
Sweden
Denmark
Greece
Italy
Germany
FEB 15
JUL 15
DEC 15
MAY 16
OCT 16
MAR 17
AUG 17
JAN 18
JUN 18
NOV 18
APR 19
SEP 19
FEB 20
JUL 20
DEC 20
MAY 21
OCT 21

Results: Population

- Per-protocol population N=2540
  - → **Standard of Care** N=1205
  - → **Intervention** N=1335
- Median follow-up 47 months (2-95)
- Median age 61 years (20-94)
  - → Age 65 years or above in 1025 patients (40%)
- Ten male patients (0.4%)
- 55 patients with SLN biopsy before neoadjuvant therapy (early years)

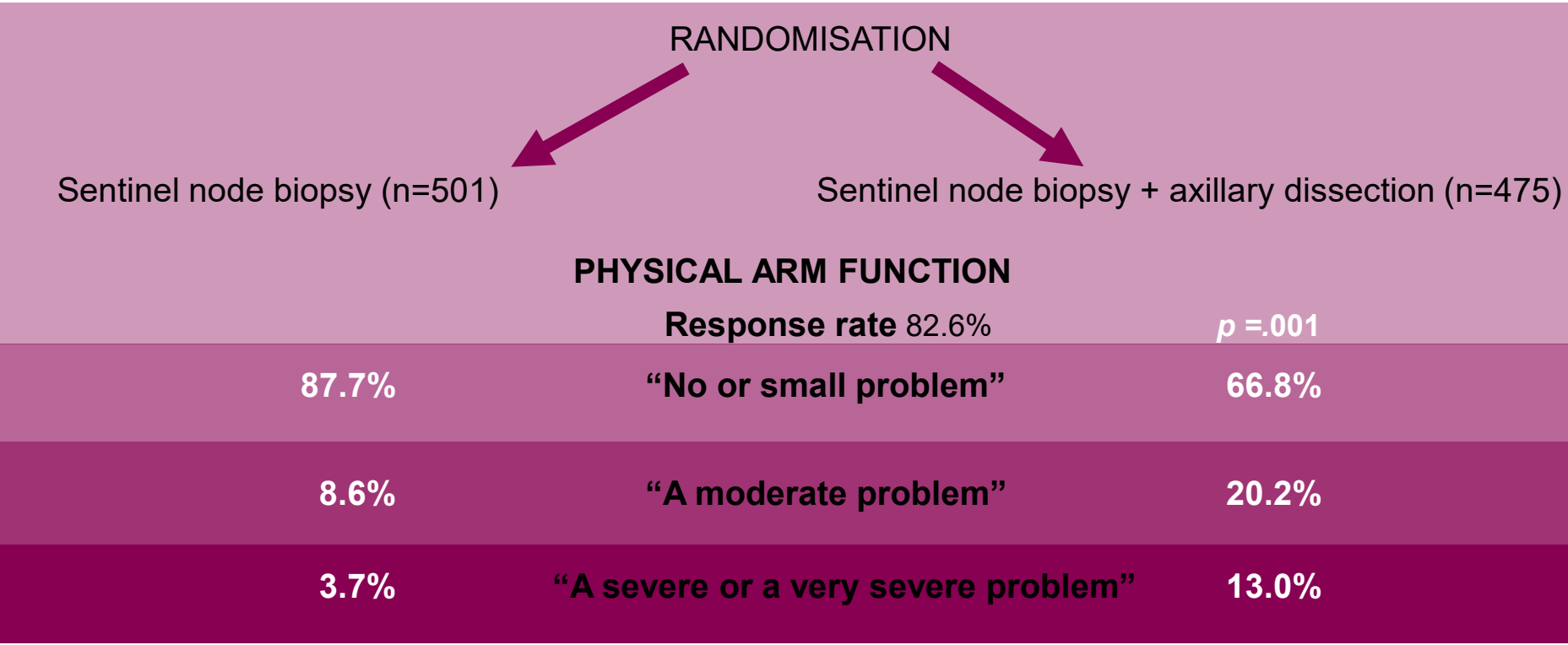
Results: Tumor

- Median tumor size 20 mm (0.2–155 mm)
  → T3 in 147 patients (5.8%)
- Lobular carcinoma in 504 patients (19.8%)
- Estrogen receptor positive & HER2 negative in 2200 patients (86.6%)

Results: Axilla

- 1 sentinel lymph node macrometastasis in 2151 patients (84.7%)
- Extranodal extension in 870 patients (34.3%)
- Removed lymph nodes median 15 (1–51) *versus* 2 (1–15)

Patient-reported outcomes at one year follow-up in the randomized SENOMAC trial



Appelgren et al. 2022, The Breast 63, 16-23

Karolinska Institutet

Results: Axillary Dissection

- Non-sentinel lymph node (SLN) metastases on axillary dissection in 403 patients (34.5%)
  - If 1 SLN met: 31.3%
  - If 2 SLN met: 51.3%
- Pathological nodal stage (**primary surgery**)

	Standard of Care	Intervention
pN1	1016 (84.3%)	1311 (98.2%)
pN2	**116 (9.6%)**	7 (0.5%)
pN3	**35 (2.9%)**	0 (0%)

Results: Treatment

- Mastectomy in 920 patients (36.2%)
- Systemic treatment in all but 27 patients
  - → Chemotherapy N=1649 (64.9%)
  - → Endocrine treatment N=2335 (91.9%)
  - → HER2-targeted therapy N=224 (8.8%)
- Adjuvant radiotherapy including nodal target volumes in
  - **Standard of Care** N=1058 (88.4%)
  - **Intervention** N=1192 (89.9%)

Recurrence-Free Survival

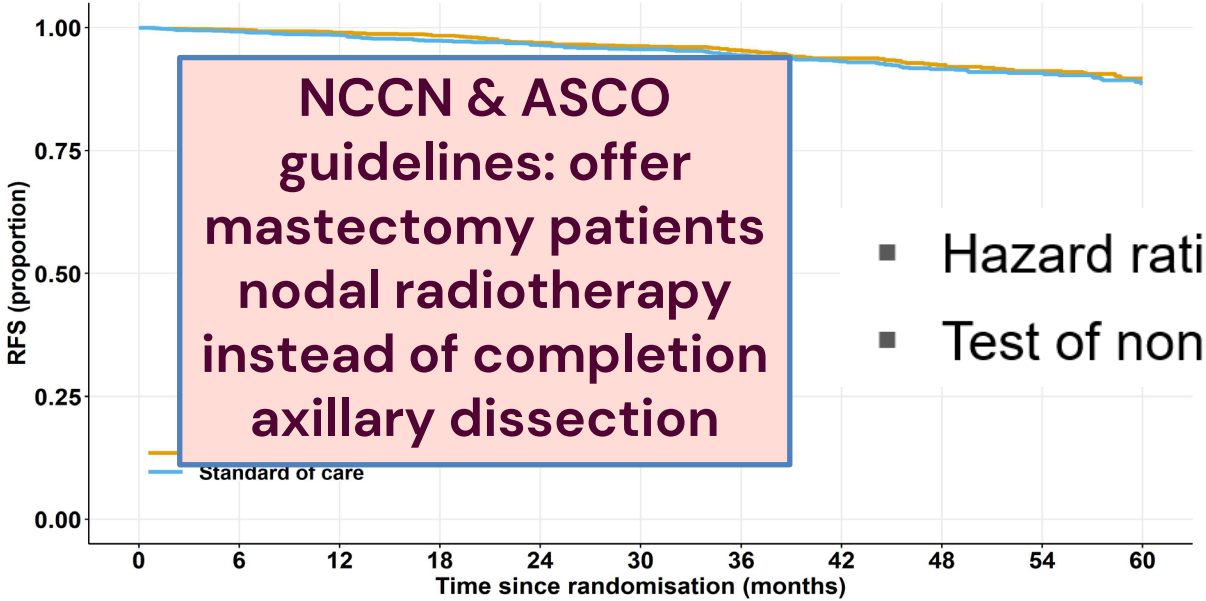
- 191 Recurrence-Free Survival (RFS) events
  - → **Standard of Care** N=96 (8.0%)
  - → **Intervention** N=95 (7.1%)

- Estimated 5-year RFS
  - → **Standard of Care** 88.7% (86.3-91.1)
  - → **Intervention** 89.7% (87.5-91.9)

Table 2. Recurrence-free Survival Analyses (Per-Protocol Population).*

Variable	Sentinel-Node Biopsy Only (N = 1335)	Completion Axillary-Lymph-Node Dissection (N = 1205)
Recurrence — no. (%)		
Local	12 (0.9)	10 (0.8)
Regional	6 (0.4)	6 (0.5)
Distant	44 (3.3)	53 (4.4)
Death — no. (%)	62 (4.6)	69 (5.7)
Cause of death — no./total no. (%)		
Breast cancer	24/62 (39)	31/69 (45)
Other cause	30/62 (48)	30/69 (43)
Unknown	8/62 (13)	8/69 (12)
Recurrence or death as first event — no. (%)		
No	1240 (92.9)	1109 (92.0)
Yes	95 (7.1)	96 (8.0)

Recurrence-Free Survival



NCCN & ASCO guidelines: offer mastectomy patients nodal radiotherapy instead of completion axillary dissection

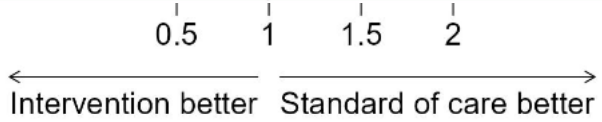
- Hazard ratio 0.89 (0.66-1.19)
- Test of non-inferiority p<0.001

Number at risk

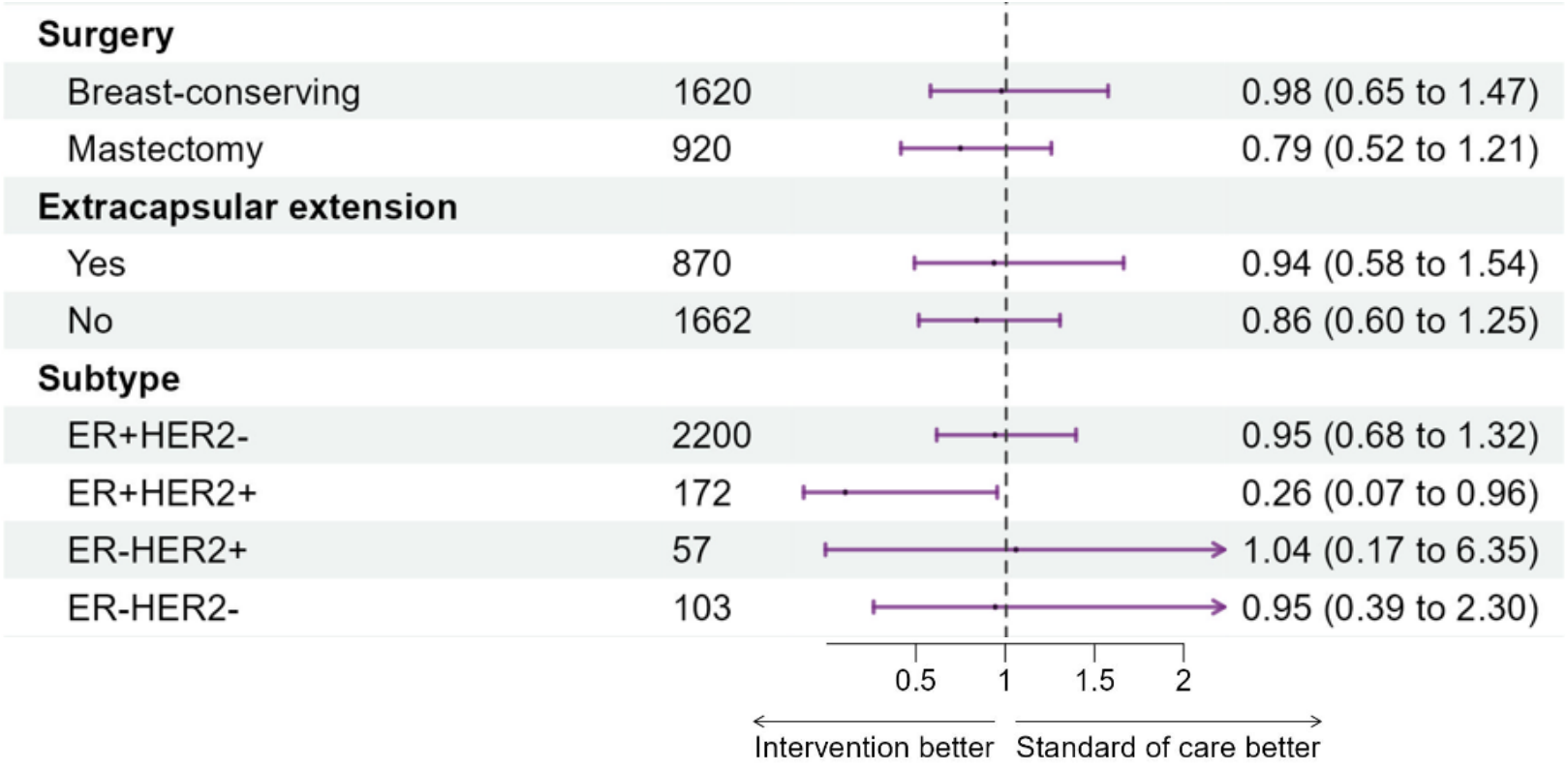
	1335	1276	1069	832	577	307
	1205	1159	1009	772	544	274

Subgroup analyses

Subgroup	N	HR (95% CI)
PP population	**2540**	**0.89 (0.66 to 1.19)**
Age		
<65 years	1515	0.77 (0.49 to 1.20)
≥65 years	1025	1.02 (0.69 to 1.51)
T stage		
T1-2	2393	0.94 (0.69 to 1.28)
T3	147	0.47 (0.16 to 1.39)
Number of macrometastases		
1	2151	0.92 (0.67 to 1.27)
2	389	0.79 (0.39 to 1.59)
Tumor type		
Lobular	504	0.91 (0.47 to 1.76)
Non-lobular	2036	0.88 (0.64 to 1.23)



Subgroup analyses



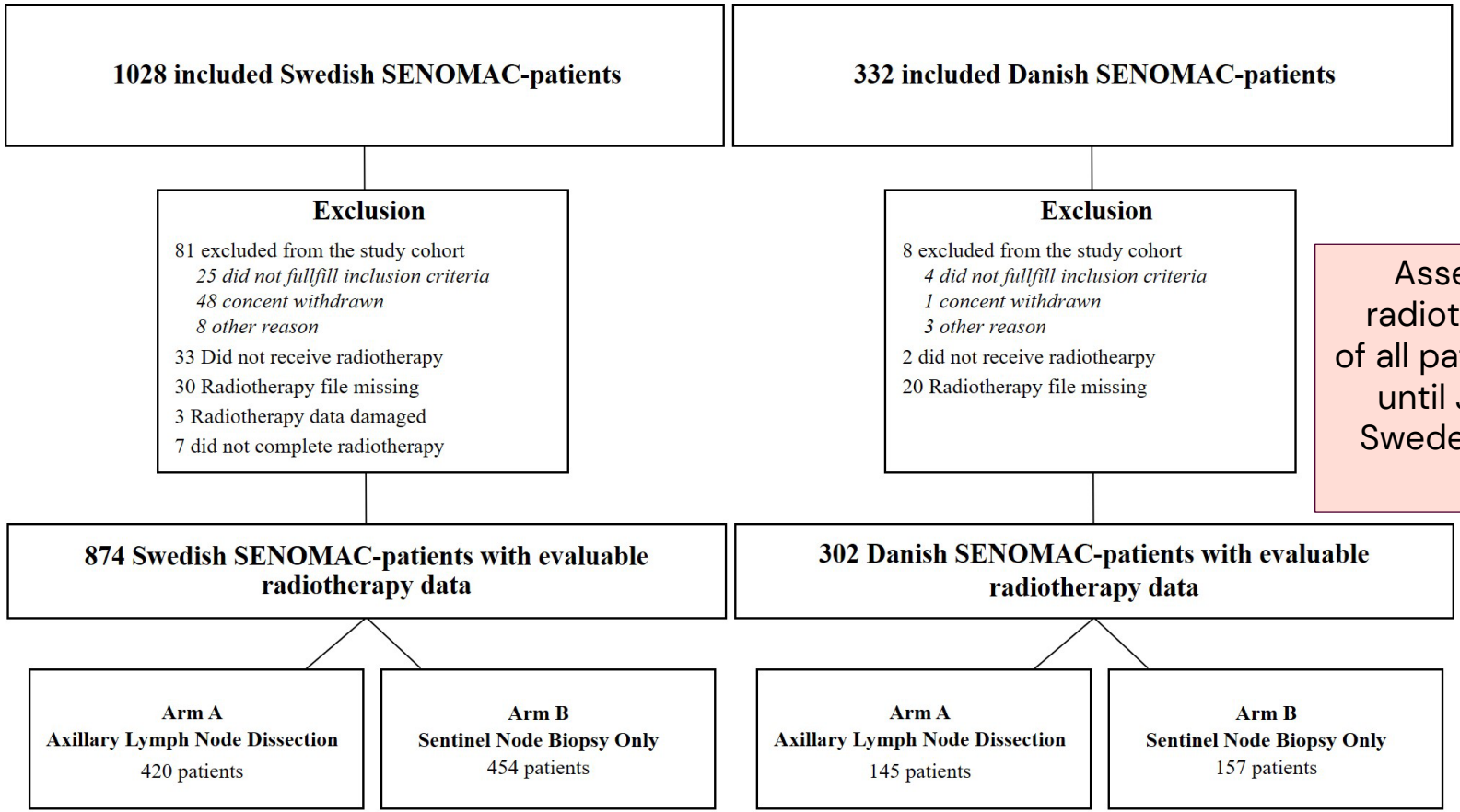
Radiotherapy

- Radiotherapy according to national guidelines
  → Indication, target, dose, volume delineation, boost
- Radiotherapy to remaining breast after breast-conserving surgery mandatory
- Indications for nodal radiotherapy vary by country
- Inclusion of axillary target volumes varies (especially level I)

Guidelines for nodal radiotherapy

	Indication	Internal Mammary Nodes	Axillary level I	Delineation
Sweden	pN1 (macro)	pN2 pN1+central or medial tumour	Regional variation	One common CTV/PTV
Denmark	pN1 (macro)	pN1+	<10 nodes ≥6 macromets	Separate nodal levels

Radiotherapy quality assessment



Assessment of radiotherapy plans of all patients included until June 2019 in Sweden & Denmark
N=1176

Source data verification:
Case Report Form (CRF) *versus* Radiotherapy Plan

- Excellent agreement regarding **Yes/No**
  - → RT to breast/thoracic wall (99.3%)
  - → RT to nodal target volumes (96.6%)

- Good agreement in detailed nodal target volumes
  - → **Exclusion** of axillary level I (CRF) confirmed in 77%
  - → **Inclusion** of axillary level I (CRF) confirmed in 81%

Inclusion of axillary level I

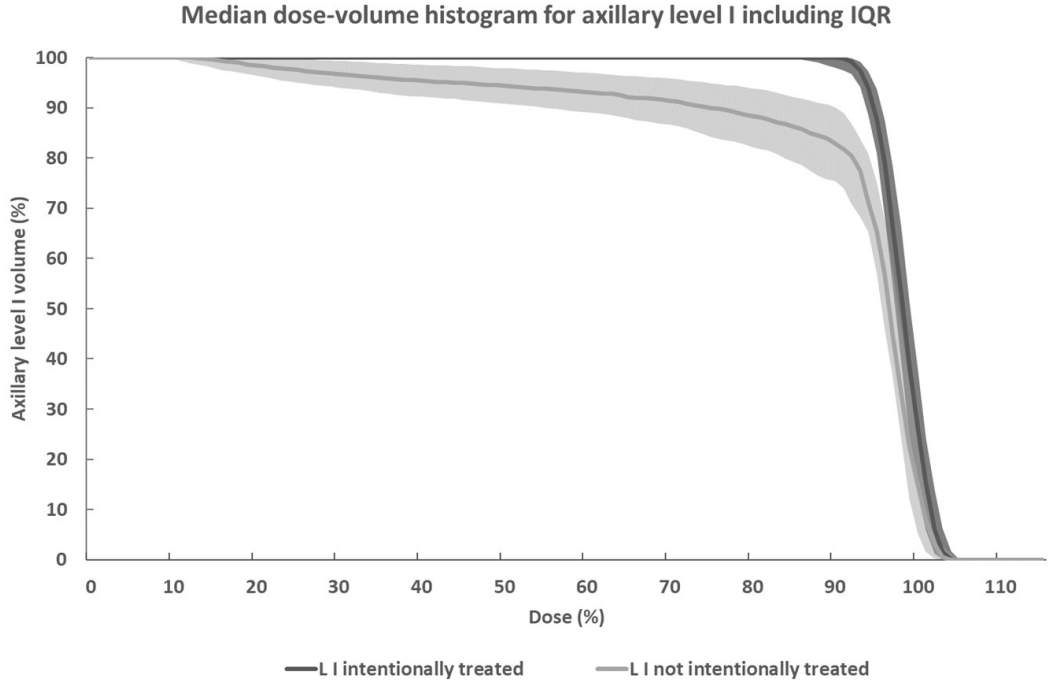
Sweden			Denmark		
Axillary dissection N=420	**SLNB only** N=454	p	**Axillary dissection** N=145	**SLNB only** N=157	p
37%	40%	0.300	14%	97%	<0.001

→ Detailed re-delineation/re-assessment of 270 patients

How much dose reaches axillary level I?

Received dose to axillary level I

- If level I intentionally **included**, full dose to 100% of level I
- If level I **not** intentionally **included**, full dose to >80% of level I



Dose to humeral head increases with inclusion of axillary level I

- If level I **not** intentionally **included,** ≥50% of the humeral head received **6%** of the prescribed dose

- If level I intentionally **included**: ≥50% of the humeral head received **13%** of the prescribed dose

Is omission of axillary dissection safe in cNO T1–3 breast cancer?

- Yes, at least if nodal radiotherapy is provided
- The turn has now come to radiotherapy to be de-escalated

Next step: de-escalation of nodal radiotherapy

Open access Protocol

BMJ Open

Protocol for the T-REX-trial: tailored regional external beam radiotherapy in clinically node-negative breast cancer patients with 1-2 sentinel node macrometastases – an open, multicentre, randomised non-inferiority phase 3 trial

Sara Alkner ,[1,2] Jana de Boniface,[3,4] Dan Lundstedt,[5] Ingvil Mjaaland,[6] Lisa Ryden,[1] Johan Vikstrom,[6] Pär-Ola Bendahl,[1] Erik Holmberg,[5] Helena Sackey,[3,7] Elinore Wieslander,[2] Per Karlsson[5]

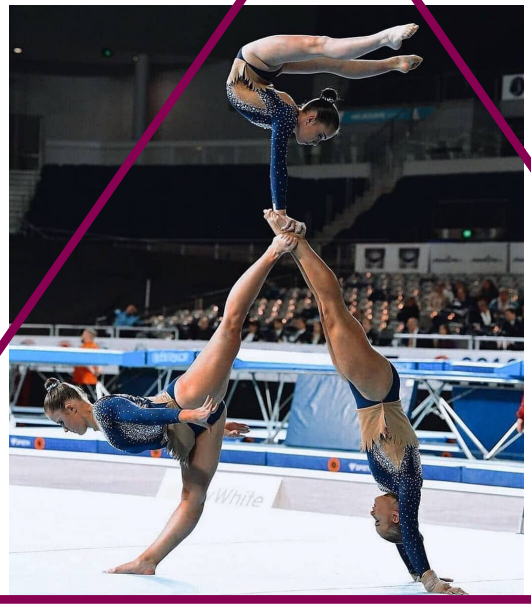
Is omission of axillary dissection safe in cN0 T1-3 breast cancer?

- Yes, if nodal radiotherapy is provided
- The turn has now come to radiotherapy to be de-escalated
- Remaining issues regard lack of staging details
  - → Only axillary dissection can identify pN2-3 patients for potential intensification of adjuvant therapies, follow-up and diagnostics
  - → De-escalation of axillary surgery requires a re-take on risk categorisation from anatomical to biological

High nodal burden

Omission of axillary lymph node dissection implies less staging information

Survival & recurrence

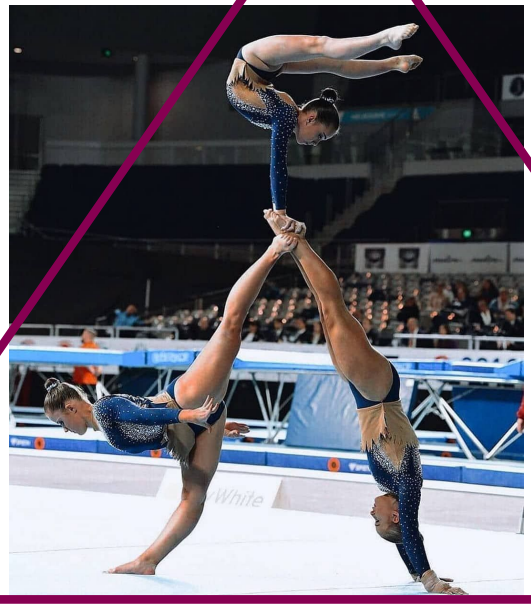


Quality of survivorship

Staging information

Survival & recurrence

Further treatment & management



Quality of survivorship

Staging information

Problem #1: abemaciclib

- 41 mm ER+HER2- breast cancer grade 2
- Clinically NO
- 2 macrometastases on sentinel lymph node biopsy

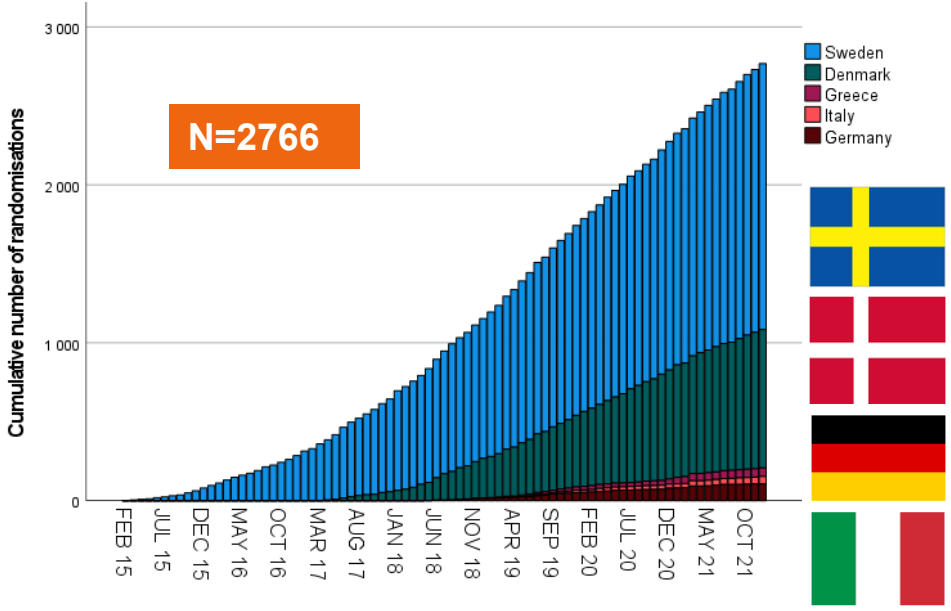
→ Axillary lymph node dissection?

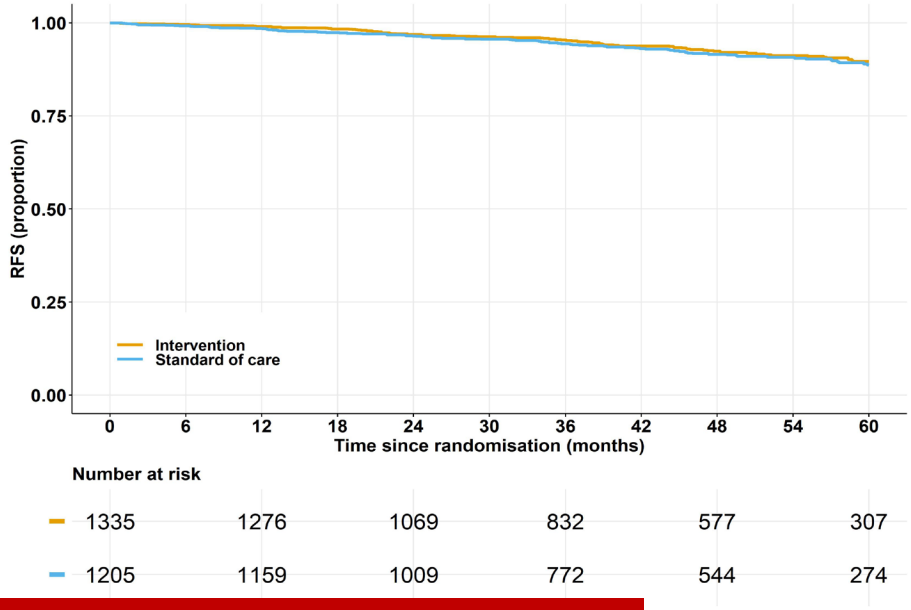
monarchE Trial
(Harbeck 2021, Rugo 2022, Johnston 2023, Rastogi 2024)

Indication for CDK4/6 inhibitor abemaciclib in…
- **Grade 1 or 2**
- **Tumour size <5 cm**

…only in case of high nodal burden (pN2-3)

The SENOMAC trial





monarchE selection: ER+HER2-, grade 1-2, tumour <5 cm (N=1705)
+ assigned to completion axillary dissection (N=802)

Number needed to treat / diagnose (dissect) / harm

Number of people who need to undergo

- abemaciclib treatment for 2 years to avoid one negative event at 5 years (iDFS)
- axillary dissection to find one individual with ≥4 nodal metastases (pN2-3)
- axillary dissection to have one individual develop arm-related complications

AMAROS trial
5-year arm lymphoedema rate
Arm lymphoedema treatment within 5 years

SENOMAC trial
Patient-reported arm problems at 1 year
(Lymph-ICF)

Bartels et al, J Clin Oncol 2022; Appelgren et al, The Breast, 2022

Number Needed to Treat: 13 patients

Absolute benefit 5-year iDFS in cohort 1 of monarchE *(Rastogi, 2024)*: 7.9%

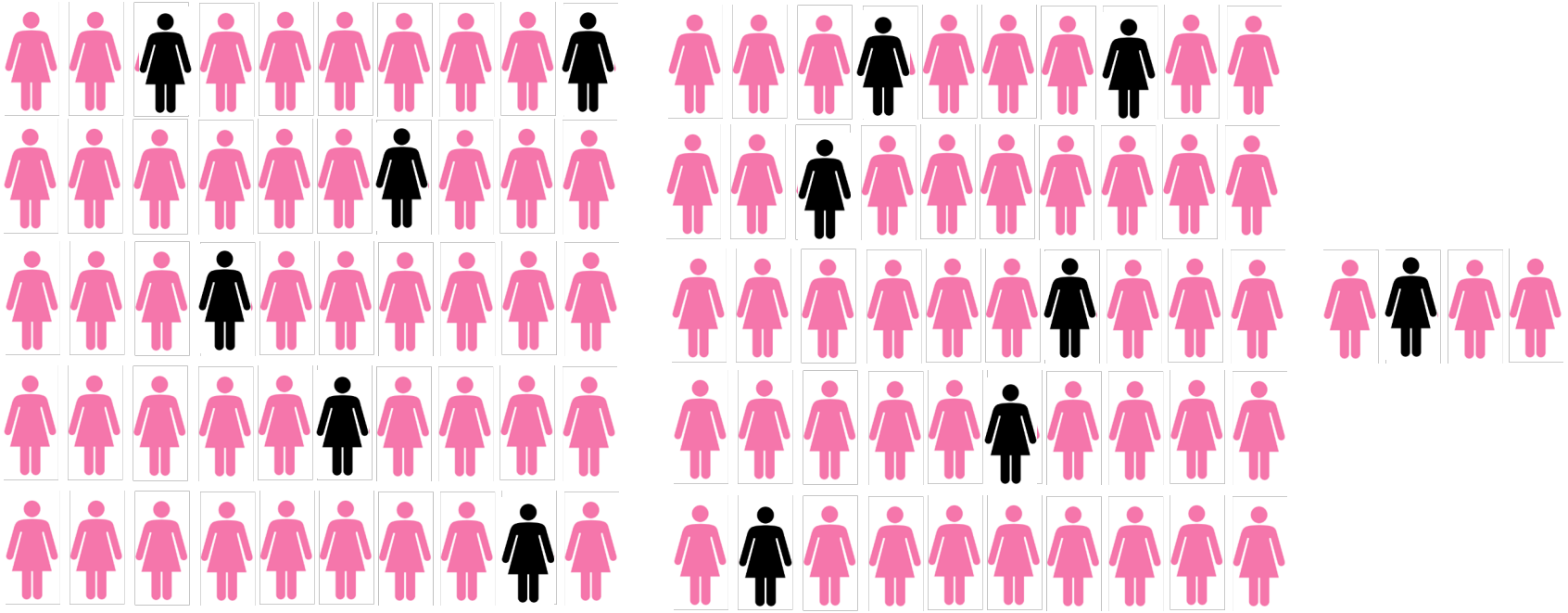
Number Needed to Dissect for identification of pN2-3: 8 patients

Proportion of pN2-3 in SENOMAC: 12.6%

Number Needed to Dissect for benefit of abemaciclib: 104 patients

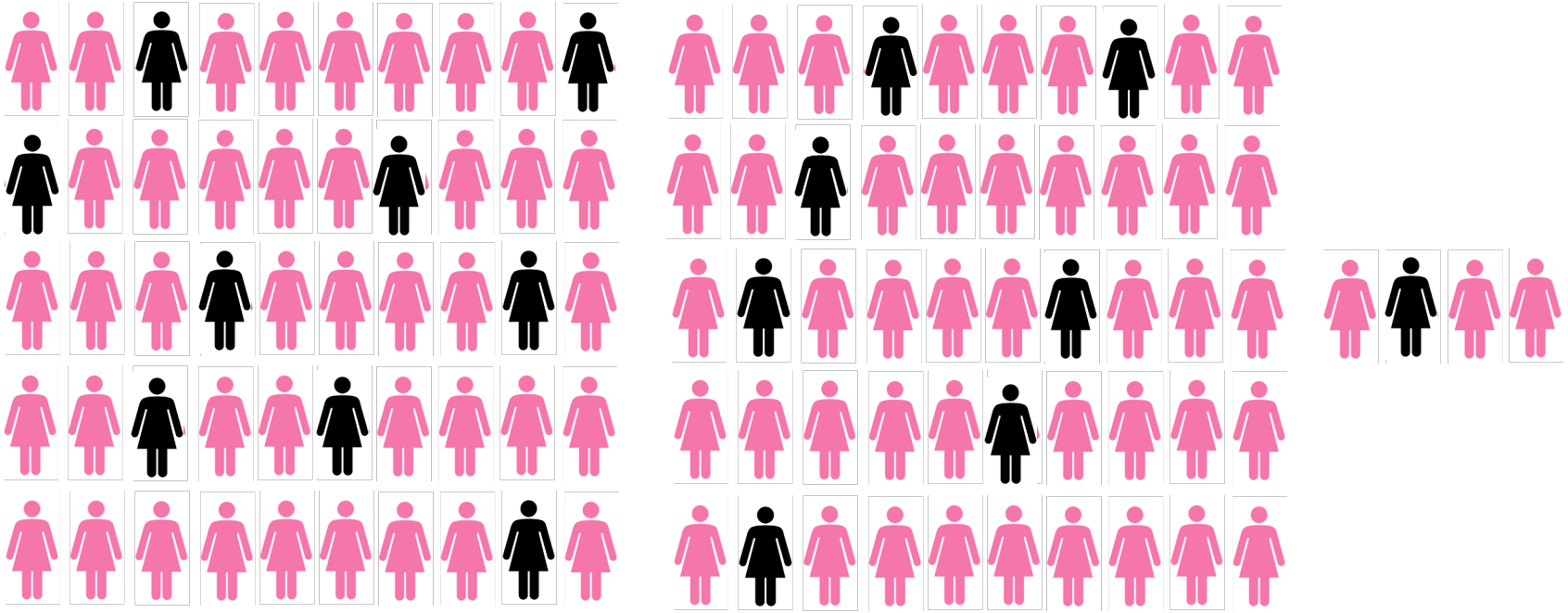
AMAROS trial: arm lymphoedema at 5 years

24.5% after completion axillary dissection vs. 11.9% after axillary radiotherapy, NNH 8



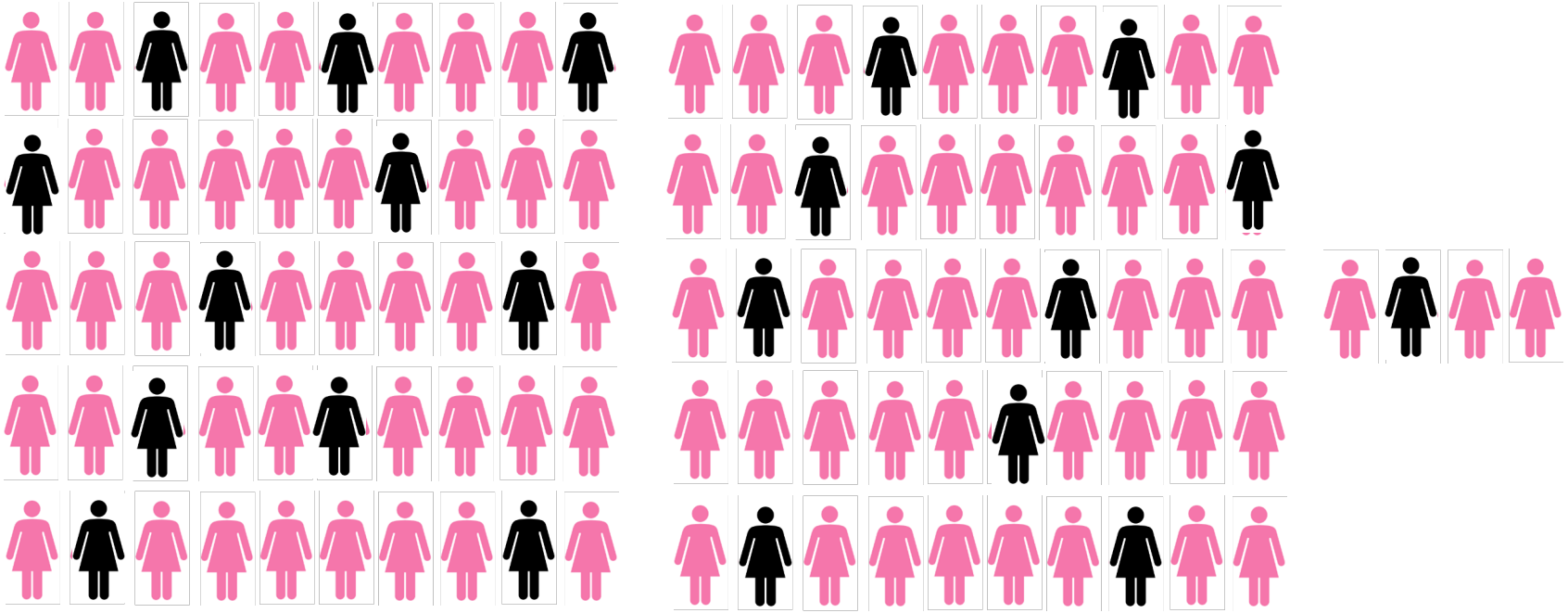
AMAROS trial: *treatment* for arm lymphoedema within 5 years

36.0% after completion axillary dissection vs. 20.2% after axillary radiotherapy, NNH 6



SENOMAC trial: patient-reported moderate-severe arm problems

33.2% after completion axillary dissection vs. 12.3% after omission, NNH 5



Completion axillary lymph node dissection for the identification of pN2–3 status as an indication for adjuvant CDK4/6 inhibitor treatment: a post-hoc analysis of the randomised, phase 3 SENOMAC trial

*Jana de Boniface, Matilda Appelgren, Robert Szulkin, Sara Alkner, Yvette Andersson, Leif Bergkvist, Jan Frisell, Oreste Davide Gentilini, Michalis Kontos, Thorsten Kühn, Dan Lundstedt, Birgitte Vrou Offersen, Roger Olofsson Bagge, Toralf Reimer, Malin Sund, Peer Christiansen, Lisa Rydén, Tove Filtenborg Tvedskov, on behalf of the SENOMAC Trialists' Group**

Summary

Background In luminal breast cancer, adjuvant CDK4/6 inhibitors (eg, abemaciclib) improve invasive disease-free survival. In patients with T1–2, grade 1–2 tumours, and one or two sentinel lymph node metastases, completion axillary lymph node dissection (cALND) is the only prognostic tool available that can reveal four or more nodal metastases (pN2–3), which is the only indication for adjuvant abemaciclib in this setting. However, this technique can lead to substantial arm morbidity in patients. We aimed to pragmatically describe the potential benefit and harm of this strategy on the individual patient level in patients from the ongoing SENOMAC trial.

Lancet Oncol 2024

Published Online
August 6, 2024
https://doi.org/10.1016/
S1470-2045(24)00350-4

See Online/Comment
https://doi.org/10.1016/

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Ribociclib plus Endocrine Therapy in Early Breast Cancer

D. Slamon, O. Lipatov, Z. Nowecki, N. McAndrew, B. Kukielka-Budny, D. Stroyakovskiy, D.A. Yardley, C.-S. Huang, P.A. Fasching, J. Crown, A. Bardia, S. Chia, S.-A. Im, M. Ruiz-Borrego, S. Loi, B. Xu, S. Hurvitz, C. Barrios, M. Untch, R. Moroose, F. Visco, K. Afenjar, R. Fresco, I. Severin, Y. Ji, F. Ghaznawi, Z. Li, J.P. Zarate, A. Chakravartty, T. Taran, and G. Hortobagyi

N Engl J Med 2024;390:1080-91.
DOI: 10.1056/NEJMoa2305488

Problem #2: chemotherapy indication

Does the lack of detailed axillary staging information affect adjuvant treatment?

Axillary clearance and chemotherapy rates in ER+HER2– breast cancer: secondary analysis of the SENOMAC trial

Tove Filtenborg Tvedskov,[a,b,*] Robert Szulkin,[c,d] Sara Alkner,[e,f] Yvette Andersson,[g,h] Leif Bergkvist,[h] Jan Frisell,[i,j] Oreste Davide Gentilini,[k,l] Michalis Kontos,[m] Thorsten Kühn,[n,o] Dan Lundstedt,[p,q] Birgitte Vrou Offersen,[r,s] Roger Olofsson Bagge,[t,u] Toralf Reimer,[v] Malin Sund,[w,x] Lisa Rydén,[y,z] Peer Christiansen,[aa,ab,ad] and Jana de Boniface,[j,ac,ad] on behalf of the SENOMAC Trialists' Group

The Lancet Regional Health - Europe 2024;47: 101083

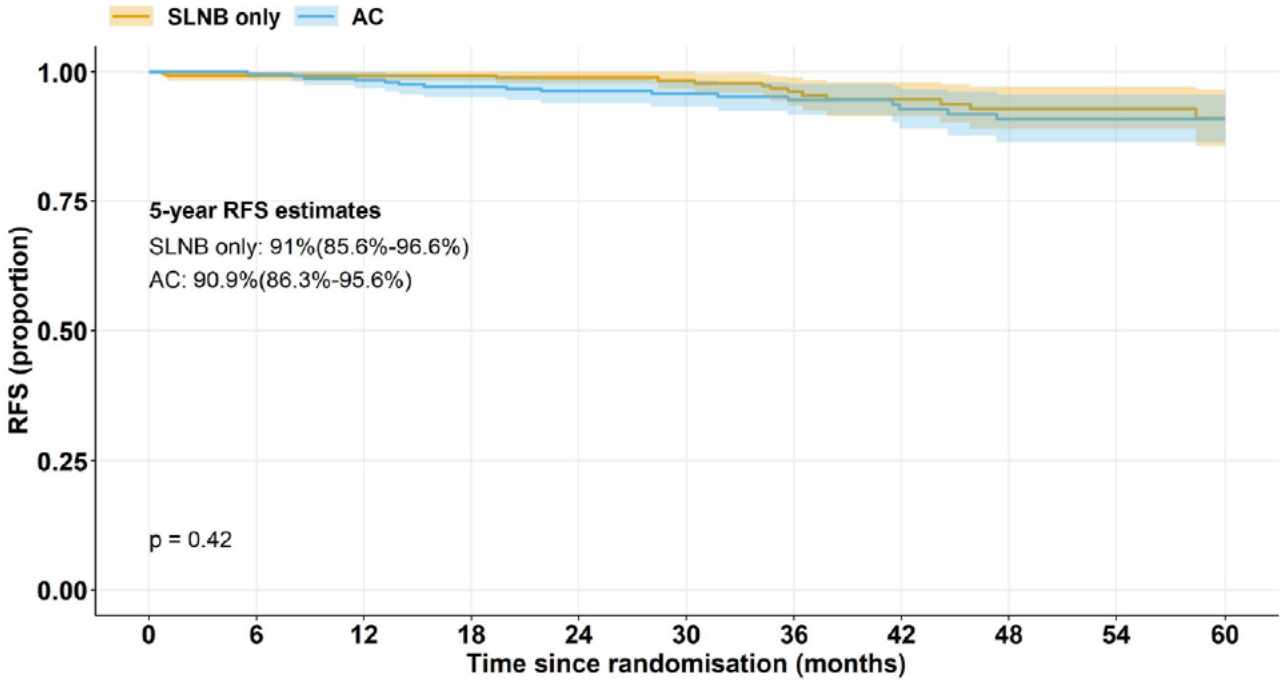
Published Online xxx

https://doi.org/10.1016/j.lanepe.2024.101083

	Completion AC	SLNB only	Total	p-value
Total number of patients, N	1010	1158	2168	
Adjuvant chemotherapy, N (%)				0.092
Yes	623 (61.7)	673 (58.1)	1296 (59.8)	
No	379 (37.5)	477 (41.2)	856 (39.5)	
Missing	8 (0.8)	8 (0.7)	16 (0.7)	
Duration of chemotherapy, weeks[a]				0.815
Mean (SD)	16.34 (4.10)	16.42 (3.87)	16.38 (3.98)	
Median [min–max]	17.37 [0.00–30.40]	17.37 [0.00–52.11]	17.37 [0.00–52.11]	
Missing (%)	23 (3.7)	26 (3.9)	49 (3.8)	

Postmenopausal patients (≥50 years)

- Chemotherapy in 54.9% after axillary clearance, 48.8% after SLNB (p=0.0151)
- Sweden: 61.1% received chemotherapy, no difference between groups
  - → RxPonder not yet implemented due to requirement of OncotypeDX
  - → Optima trial results (Prosigna/PAM50) awaited
- Denmark: 37.1% received chemotherapy, 44.4% versus 30.4% (p<0.001)
  - → PSI score requires number of axillary metastases



Number at risk (number of events)

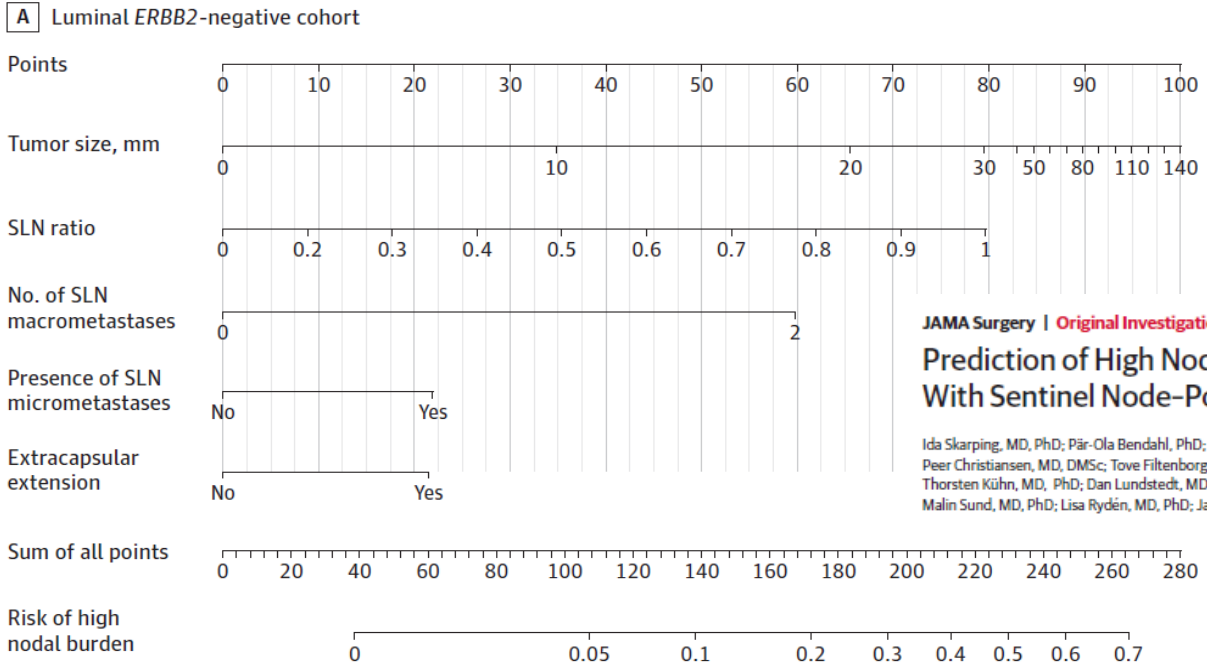
SLNB only	287 (0)	276 (2)	226 (3)	149 (8)	90 (12)	30 (13)
AC	252 (0)	242 (4)	212 (9)	146 (12)	86 (16)	31 (16)

What information do we need from axillary staging?

- pN0 *versus* pN+
  - → SLNB would be enough in all patients → no surgery if imaging+/FNA+
- 1-2 *versus* ≥3 positive SLNs: **surgeon perspective**
  - → Max 2 positive SLNs allowed in Z0011, SINODAR-ONE, SENOMAC
  - → Few patients with ≥3 positive SLNs in AMAROS, INSEMA
- pN1 *versus* pN2-3 (high nodal burden): **oncologist perspective**

Nomogram: risk of pN2–3 (SENOMAC)

Figure 2. Nomogram for Predicting the Probability of High Nodal Burden



JAMA Surgery | Original Investigation

Prediction of High Nodal Burden in Patients With Sentinel Node–Positive Luminal *ERBB2*-Negative Breast Cancer

Ida Skarping, MD, PhD; Pär-Ola Bendahl, PhD; Robert Szulkin, PhD; Sara Alkner, MD, PhD; Yvette Andersson, MD, PhD; Leif Bergkvist, MD, PhD; Peer Christiansen, MD, DMSc; Tove Filtenborg Tvedskov, MD, PhD; Jan Frisell, MD, PhD; Oreste D. Gentilini, MD; Michalis Kontos, MD; Thorsten Kühn, MD, PhD; Dan Lundstedt, MD, PhD; Birgitte Vrou Offersen, MD, PhD; Roger Olofsson Bagge, MD, PhD; Toralf Reimer, MD, PhD; Malin Sund, MD, PhD; Lisa Rydén, MD, PhD; Jana de Boniface, MD, PhD

Skarping et al, JAMA Surg 2024, doi:10.1001/jamasurg.2024.3944

Welcome to the High Nodal Burden Calculator

Nomogram for the Prediction of High Nodal Burden (≥pN2) in Patients With ER+ HER2neu/ ERBB2-negative Breast Cancer and 1-2 Sentinel Lymph Node Macrometastases

Please enter the following data. All fields are mandatory.

Tumor size (mm), assessed with histopathology	27
Number of sentinel lymph nodes with macrometastases (>2 mm)	1
Presence of sentinel lymph node micrometastases (>0.2 mm but ≤2 mm and/or >200 cells)	No
Total number of excised sentinel lymph nodes with metastases (micro- and macrometastases)	1
Number of excised sentinel lymph nodes	3
Presence of extracapsular extension in any sentinel lymph node metastases	No

Calculate Reset

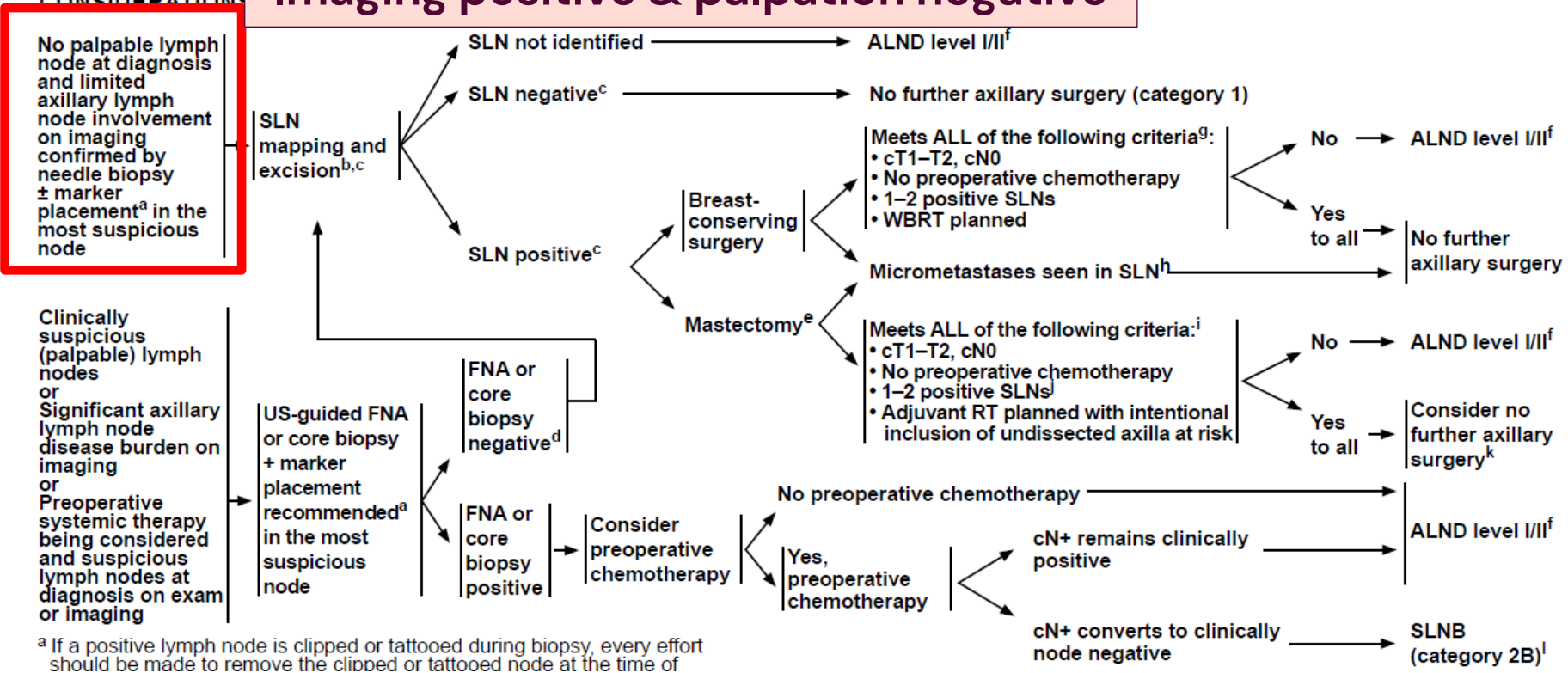
Your result

The probability of high nodal burden in the ipsilateral axilla is 4%. This translates to that 4 out of 100 patients with the characteristics entered by you will be identified to have high nodal burden (in total four or more metastatic axillary nodes, i.e. sentinel lymph node metastases included) if subjected to a completion axillary lymph node dissection.

Problem #3: open questions

- SENOMAC was open to patients with a positive axillary ultrasound and positive fine needle aspiration cytology
  → N=36
- ACOSOG Z0011 did not require a negative axillary ultrasound
  → Still not standard of care in the US

Imaging positive & palpation negative



[a] If a positive lymph node is clipped or tattooed during biopsy, every effort should be made to remove the clipped or tattooed node at the time of

National Comprehensive Cancer Network

NCCN Guidelines Version 2.2024

CONSIDERATIONS

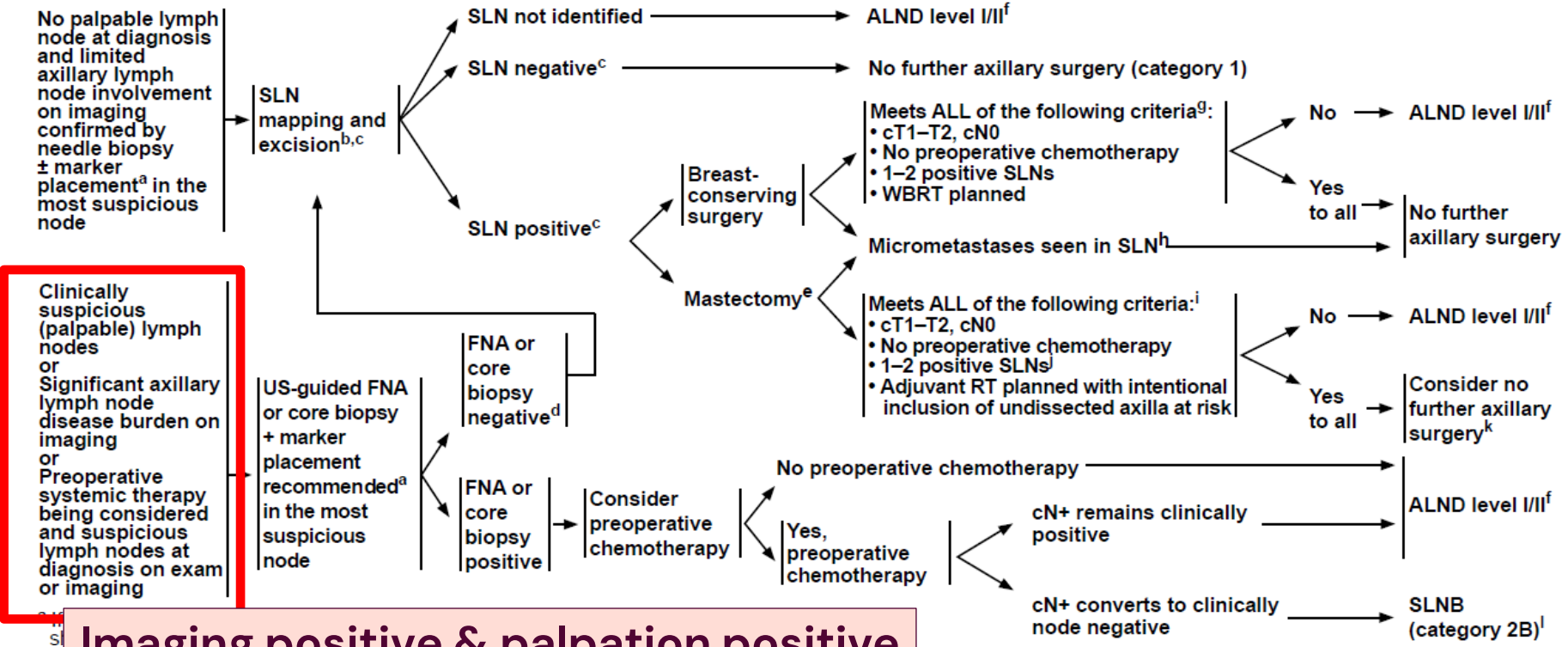
No palpable lymph node at diagnosis and limited axillary lymph node involvement on imaging confirmed by needle biopsy ± marker placement[a] in the most suspicious node

Clinically suspicious (palpable) lymph nodes
or
Significant axillary lymph node disease burden on imaging
or
Preoperative systemic therapy being considered and suspicious lymph nodes at diagnosis on exam or imaging

cN+ converts to clinically node negative → SLNB (category 2B)[l]

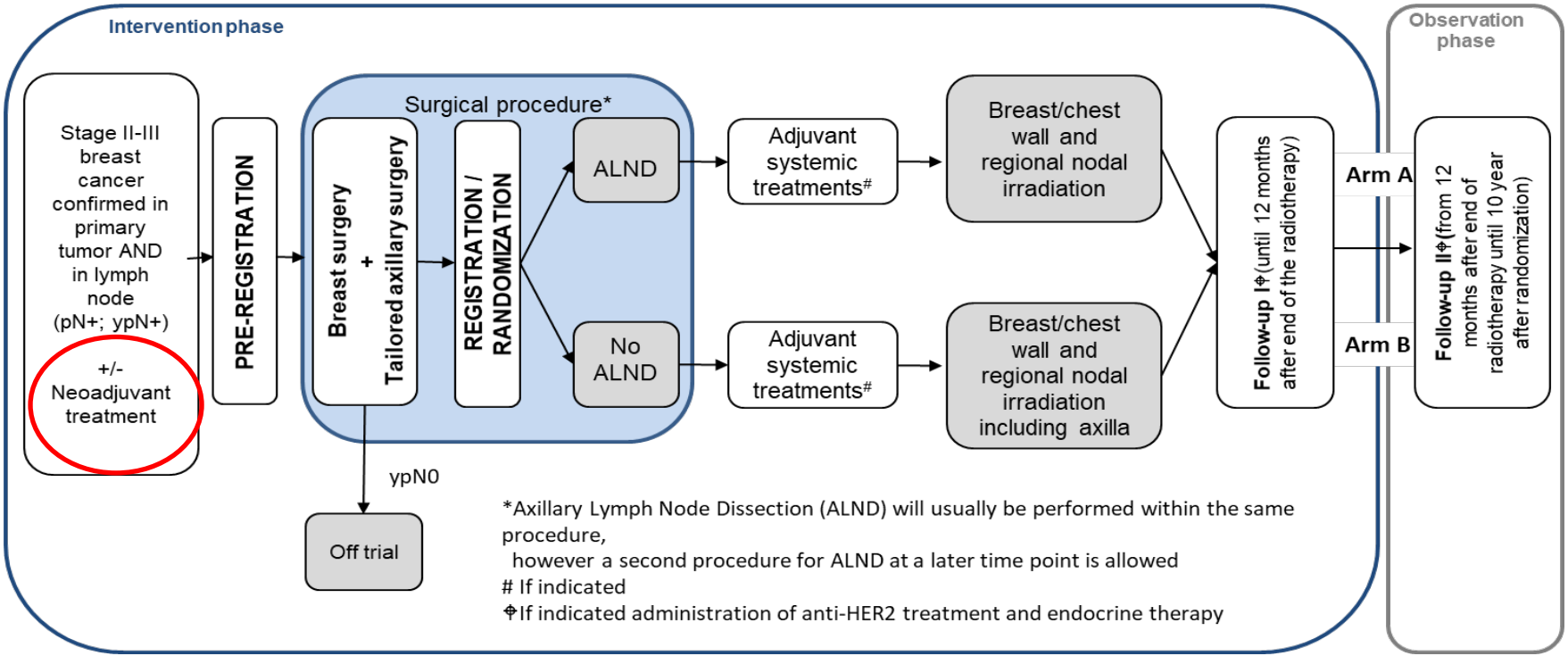
[a] If a positive lymph node is clipped or tattooed during biopsy, every effort should be made to remove the clipped or tattooed node at the time of

CONSIDERATIONS FOR SURGICAL AXILLARY STAGING



Imaging positive & palpation positive

TAXIS trial


Intervention phase
Observation phase
Stage II-III breast cancer confirmed in primary tumor AND in lymph node (pN+; ypN+)
+/- Neoadjuvant treatment
PRE-REGISTRATION
Surgical procedure*
Breast surgery + Tailored axillary surgery
REGISTRATION / RANDOMIZATION
ALND
No ALND
Adjuvant systemic treatments#
Adjuvant systemic treatments#
Breast/chest wall and regional nodal irradiation
Breast/chest wall and regional nodal irradiation including axilla
Follow-up IΦ (until 12 months after end of the radiotherapy)
Arm A
Arm B
Follow-up IIΦ (from 12 months after end of radiotherapy until 10 year after randomization)
ypN0
Off trial
*Axillary Lymph Node Dissection (ALND) will usually be performed within the same procedure,
however a second procedure for ALND at a later time point is allowed
If indicated
ΦIf indicated administration of anti-HER2 treatment and endocrine therapy

Patient selection for neoadjuvant treatment: Who has a reasonable chance to de-escalate?

Axillary pCR

- 60% in HER2+ ER-
- 45% in HER2+ ER+
- 48% in triple-negative
- 35% in high-proliferative ER+
- 13% in low-proliferative ER+

JAMA Surgery | Original Investigation

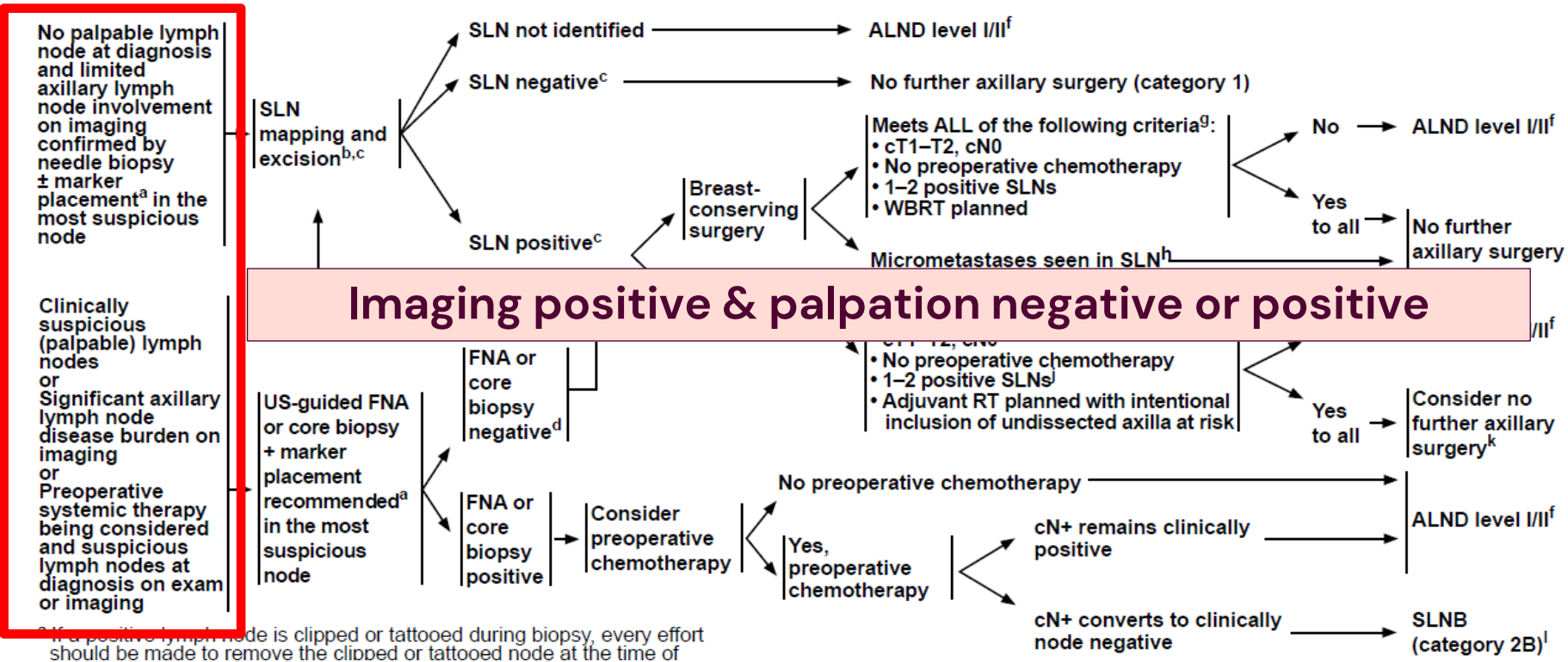
Axillary Pathologic Complete Response After Neoadjuvant Systemic Therapy by Breast Cancer Subtype in Patients With Initially Clinically Node-Positive Disease

A Systematic Review and Meta-analysis

Sanaz Samiei, MD; Janine M. Simons, MD, PhD; Sanne M. E. Engelen, MD, PhD; Regina G. H. Beets-Tan, MD, PhD; Jean-Marc Classe, MD, PhD; Marjolein L. Smidt, MD, PhD; and the EUBREAST Group

JAMA Surg. doi:10.1001/jamasurg.2021.0891
Published online April 21, 2021.

CONSIDERATIONS FOR SURGICAL AXILLARY STAGING



Imaging positive & palpation negative or positive

[a] If a positive lymph node is clipped or tattooed during biopsy, every effort should be made to remove the clipped or tattooed node at the time of

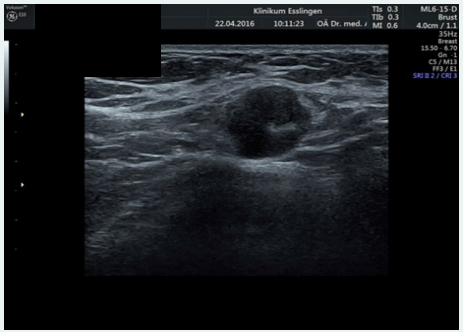
Primary axillary surgery in clinical node positivity
SENOMAC–ULTRA trial

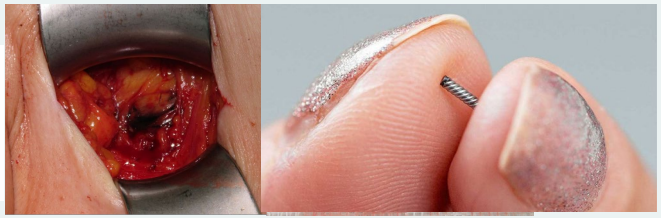
cT1-3
i/cN+ FNA+
Primary surgery

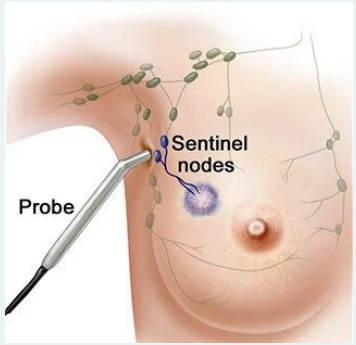
Randomisation
1:1

Upfront axillary dissection

Targeted axillary dissection (TAD)







Karolinska Institutet

SENOMAC-ULTRA

- International randomised non-inferiority trial
  - → Primary endpoint recurrence-free survival (RFS)
  - → Non-inferiority margin 4.5% at 5 years
  - → N=1380
- Start December 2025/January 2026
  - → Sweden
  - → Denmark
  - → Finland
  - → Taiwan
  - → South Korea
  - → Norway, USA, Japan, Spain…

SENOMAC-ULTRA Team: Jana de Boniface, Lisa Rydén, Sara Alkner, Malin Sund, Per Karlsson, Tuomo Meretoja, Birgitte Offersen, Tove Filtenborg Tvedskov, Elinor Wieslander, Henrik Dahl Nissen, Chiun-Sheng Huang, Sung-Hsin Kuo, Trine Tramm, Karin Dembrower, Steven Nash, Robert Szulkin, Tanja Spanic

Thank you!

Capio S:t Görans Sjukhus

Karolinska Institutet

Vetenskapsrådet

EUBREAST NETWORK

CANCERFONDEN

NORDIC CANCER UNION

BRÖSTCANCER FÖRBUNDET

SENOMAC Trialists:
Jana de Boniface, Jan Frisell, Leif Bergkvist, Yvette Andersson, Dan Lundstedt, Roger Olofsson Bagge, Sara Alkner, Lisa Rydén, Malin Sund, Peer Christiansen, Tove Filtenborg Tvedskov, Birgitte Vrou Offersen, Thorsten Kühn, Toralf Reimer, Oreste Gentilini, Michalis Kontos
Radiotherapy quality control:
Henrik Dahl Nissen
Elinor Wieslander
Statistical analysis:
Robert Szulkin
Patient-reported outcomes:
Matilda Appelgren
SENOMAC nomogram:
Ida Skarping
Pär-Ola Bendahl


KAROLINSKA INSTITUTET
ANNO 1810
Karolinska
Institutet