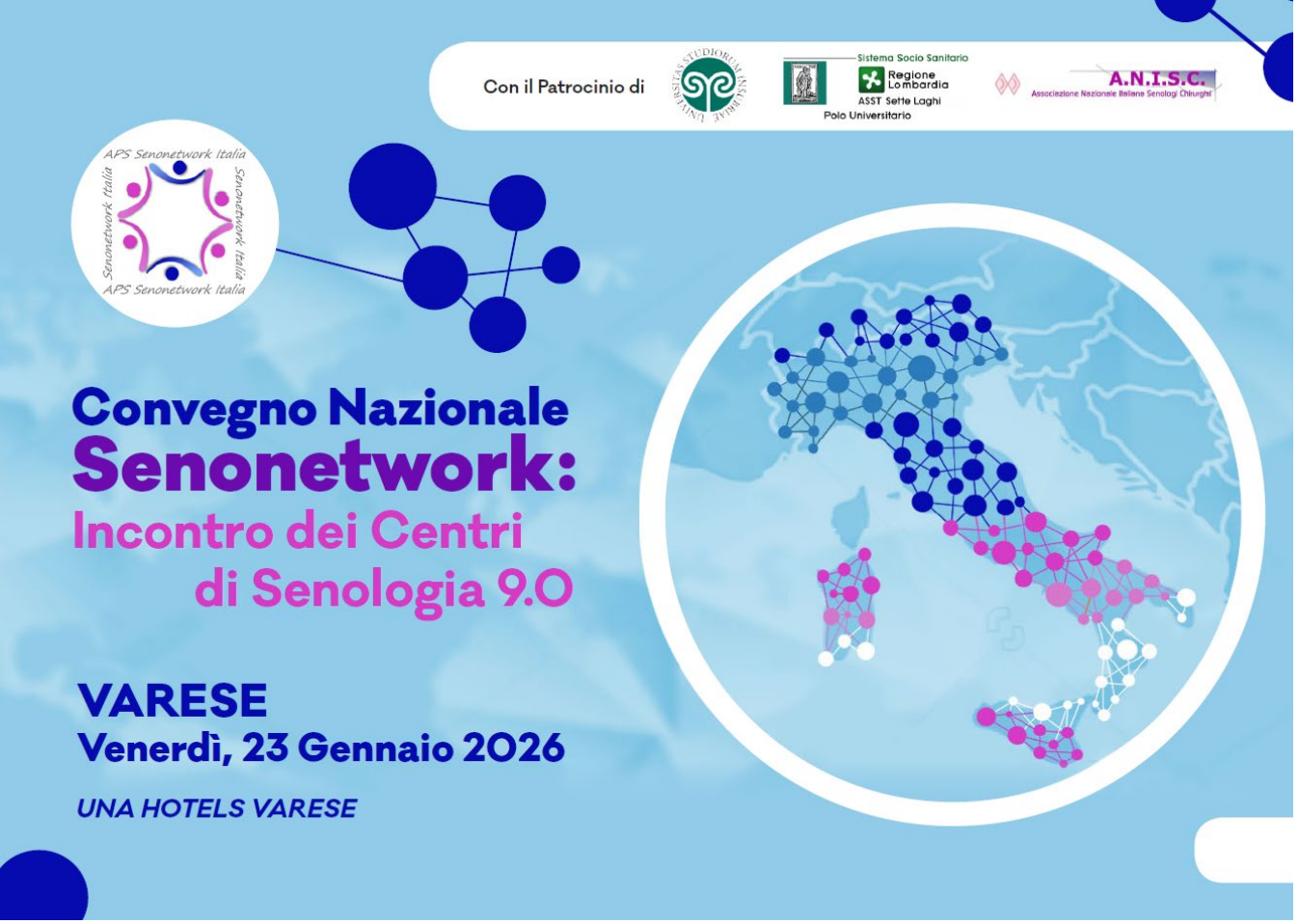

I dati di EUBREAST

Prof. Oreste D. Gentilini M.D.
Università Vita-Salute San Raffaele
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Chairman of EUBREAST ETS www.eubreast.org

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OSPEDALE SAN RAFFAELE

EU-BREAST

EUropean **B**reast Cancer **R**Esearch
Association of **S**urgical **T**rialists

EUBREAST

Purpose

- To promote international no-profit cooperation of independent academic breast cancer research
- Neutral scientific forum in which members can develop and carry out research projects
- Surgical treatment of BC is the main focus of the Association, especially with the aim of finding the best treatment with minor side effects
- To broaden collaboration with other scientific networks or entities
- Fundraising to support the activities within the purposes

EUBREAST

A gap analysis of opportunities and priorities for breast surgical research

non-profit initiative EUBREAST European Breast Cancer Research Association of Surgical Trialists (EUBREAST) in September, 2018. EUBREAST offers an independent scientific forum for its members to

Breast Surgery, San Raffaele University and Research Hospital, 20132, Milano, Italy (ODG); Department of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm, Sweden (JDB); Department of Surgery, Breast Unit, Goran's Hospital, Stockholm, Sweden (JDB); Department of Surgical Oncology, Institut de Cancerologie du Ouest, Nantes, France (J-MC);

Gentilini O et al. Lancet Oncol 2019

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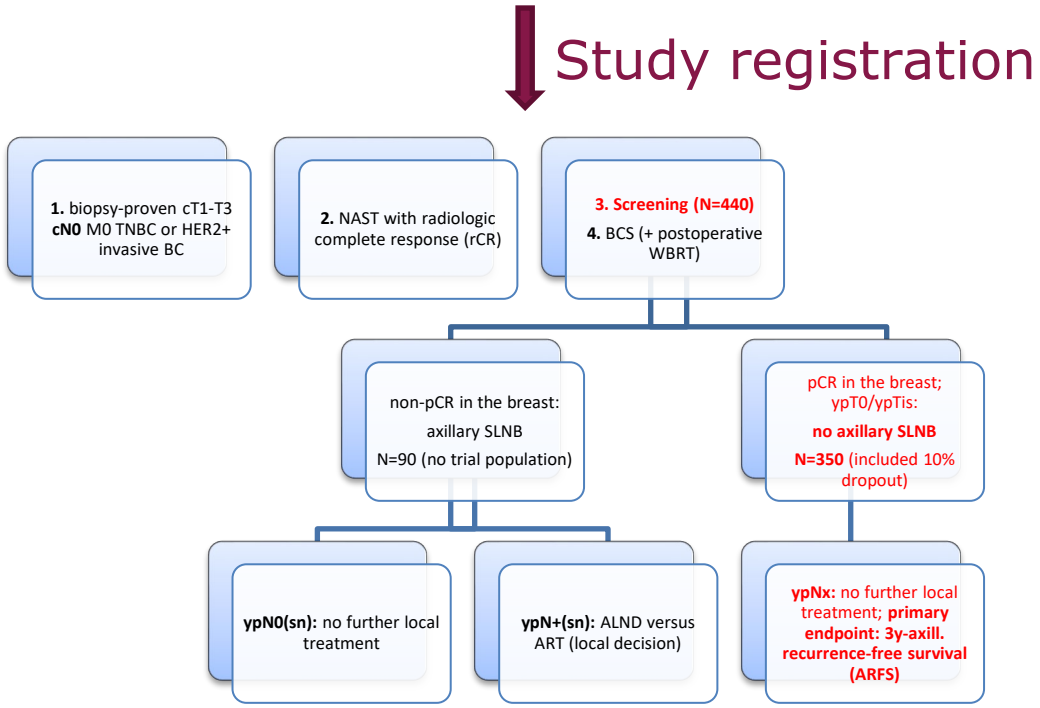
EUBREAST-01 flow chart (Amendment #3)

N=350 per protocol
(31/Dec/2024: N=411 for screening)



EUBREAST-01 flow chart (Amendment #3)

N=350 per protocol
(31/Dec/2024: N=411 for screening)

↓ Study registration

Primary and secondary results? > expected for January 2028

SAN ANTONIO BREAST CANCER SYMPOSIUM®
UT Health San Antonio Mays Cancer Center
AACR American Association for Cancer Research
DECEMBER 9–12, 2025
HENRY B. GONZALEZ CONVENTION CENTER • SAN ANTONIO, TX

More versus less invasive axillary surgical staging procedures in breast cancer patients converting from a clinically node-positive to a clinically node-negative stage through neoadjuvant chemotherapy - primary endpoint analysis of the international prospective multicenter AXSANA/EUBREAST 3(R) study

Kühn T [1, 2], Banys-Paluchowski M, Ditsch N, Stickeler E, Hauptmann M, Schroth J, Karadeniz Cakmak G, Hahn M, Thill M, Reimer T, Fröhlich S, Schmidt E, Lux MP, Kolberg HC, Rubio IT, Gasparri ML, Kontos M, Bonci EA, Niinikoski L, Murawa D, Pinto D, Peintinger F, Schlichting E, Nina H, Valiyeva Qanimat H, Vanhoeij M, Rebaza L, Aktas Sezen B, Jursik K, Kadayaprath G, Dostalek L, Kothari A, Perhavec A, Ivanov T, Zippel D, Thongvitokomarn S, Adamczyk B, Gurleyik MG, Watermann D, Porpiglia M, Grasshoff ST, Loibl S, Krug D, Lebeau A, Di Micco R, Gentilini OD, de Boniface J, Hartmann S and the AXSANA Study Group

[1] Department of Gynecology and Obstetrics, University of Ulm, Germany
[2] Breast Center, Die Filderklinik gGmbH, Filderstadt Germany

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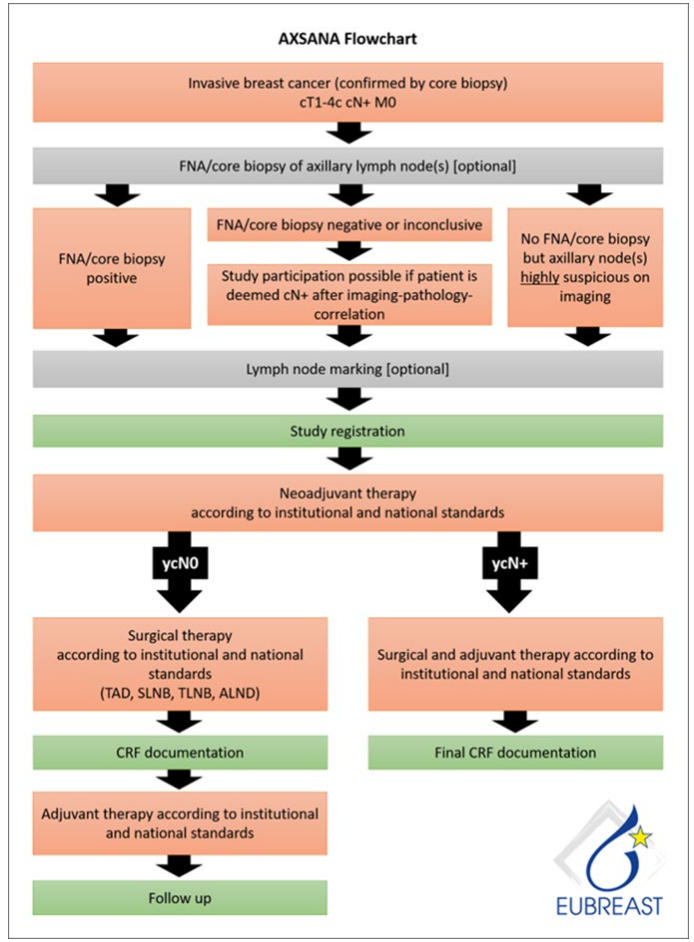
UNIVERSITÄTS KLINIKUM ulm
Die Filderklinik
AGO-B BREAST STUDY GROUP
GBG GERMAN BREAST GROUP

AXSANA Study

- Ongoing, international, multicentric, non-interventional prospective registry
- In cN+ ⟶ ycN0 treated with different staging procedures after NACT according to the physician`s choice (ALND/SLNB/TADTLNB)
- (Neo-) Adjuvant systemic and locoregional treatment according to institutional and national guidelines



Co primary endpoints

- Axillary recurrence-free survival
- Invasive breast cancer-specific disease-free survival
- QoL and arm morbidity

Aims of this analysis

The majority of axillary recurrences occur early

Assessment of

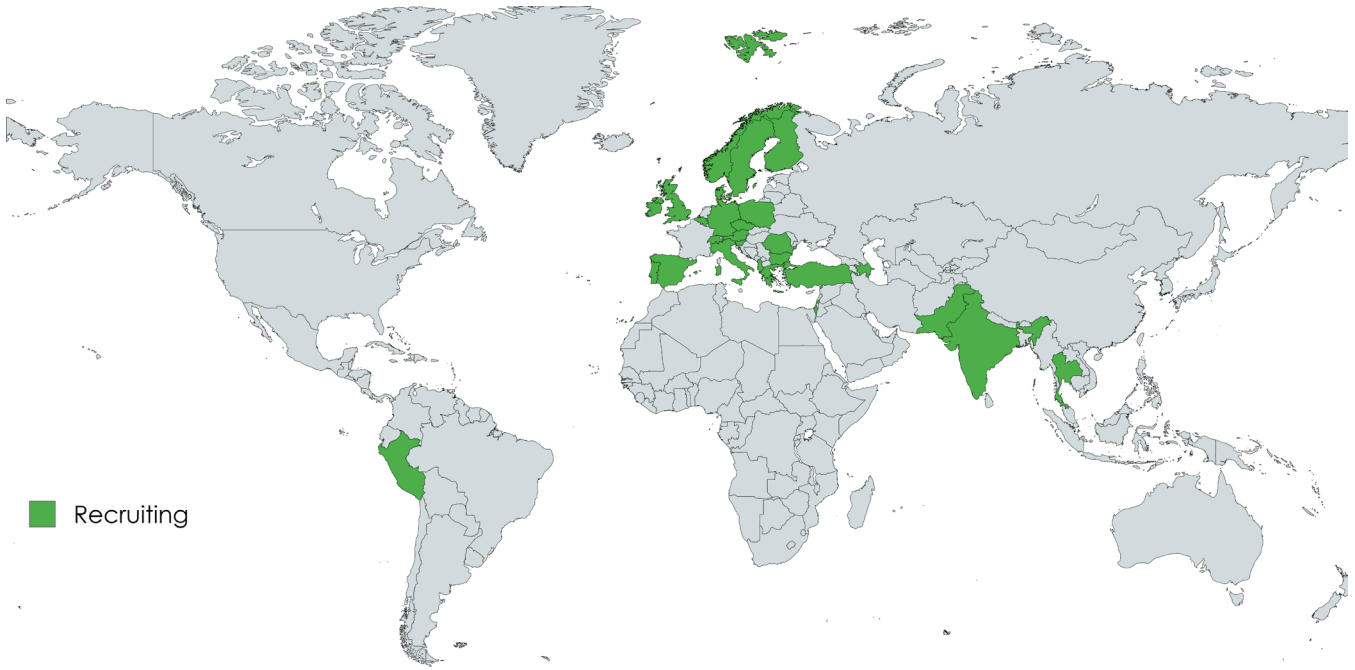
- 3-year axillary recurrence rates ALND vs less invasive procedures
- 3-year axillary recurrence rates SLNB vs TAD
- Local, regional, distant recurrences, and overall survival

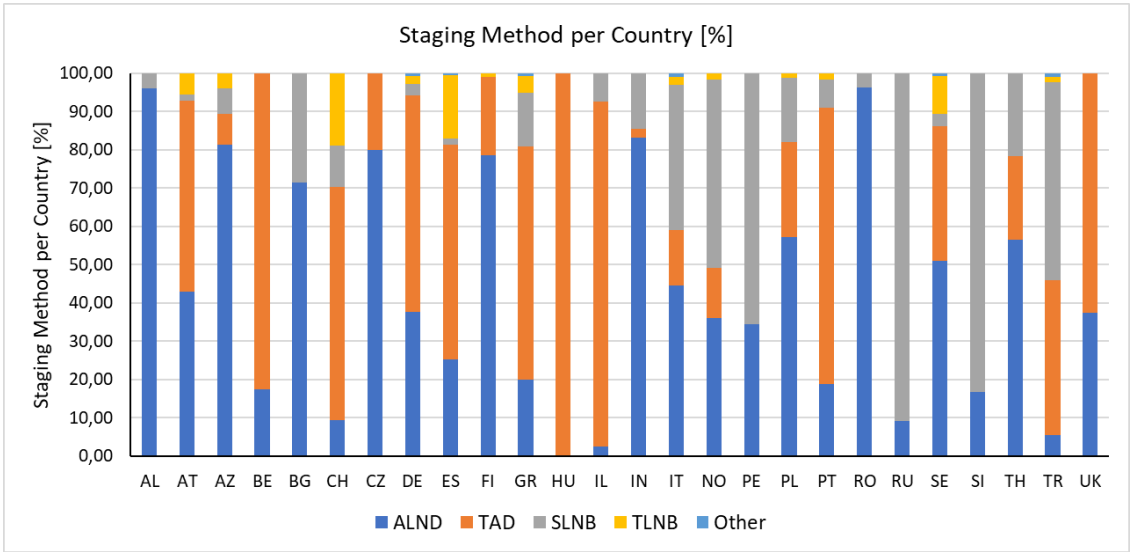
Methods

- Less invasive axillary staging (SLNB/TAD) is considered non-inferior to ALND at 3 years if axillary recurrence-free survival is above 97 % based on the lower bound of a one-sided 95% confidence interval
- Cox proportional hazards regression models were used to detect differences between the groups. Variables with at least one category with a p-value < 0.05 in univariate Cox models were included in the multivariate analyses
- Kaplan-Meier curves were generated and stratified by the axillary staging procedure
- 100 % of the datasets are monitored (>15.000 queries solved). Only complete datasets were used for analyses. Less than 6% of values were missing for any variable used in the analyses. Missing data were multiply imputed.

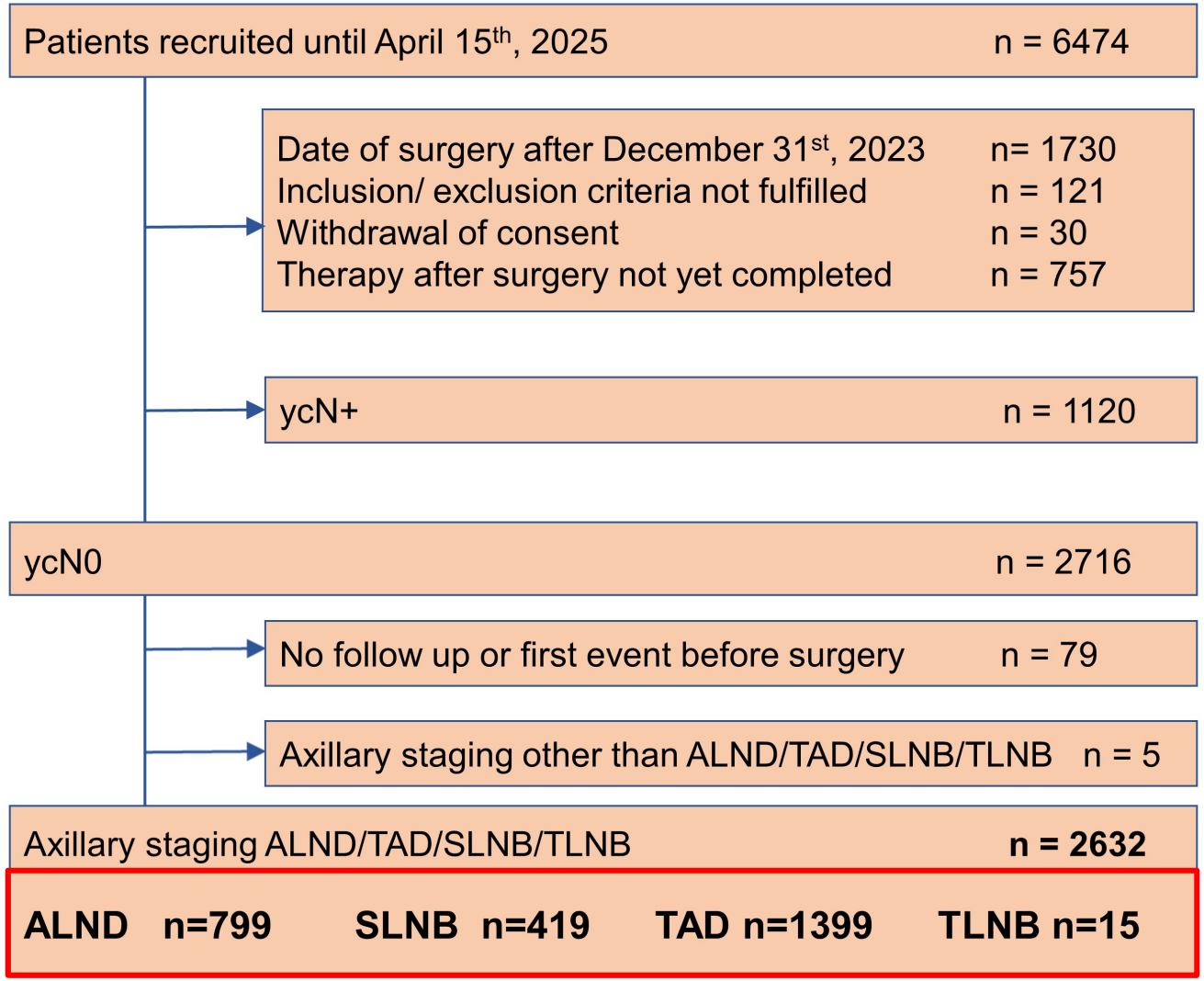
Trial Status

- The trial includes patients from 288 study sites
- 26 countries





Consort Diagramm



- ypN0 and ypN+ included
- Median Follow-up 2 years
- Range: 1.07 – 4.45 years
- 17.4 % with ≥ 3 years Follow-up
- Nodal pCR-Rate: 51.1 %

Regional treatment characteristics

Information on Radiotherapy (RT) available (N=2475) (aRT = axillary RT: Level I and II included in target volume)		Staging procedure			
		ALND (%)	TAD/SLNB (%)	TAD (%)	SLNB (%)
ypN0 (sn/tln) (n=1522)	aRT	232 (47.2)	548 (53.2)	380 (49.0)	168 (65.9)
	No aRT	260 (52.8)	482 (46.8)	395 (51.0)	87 (34.1)
ypN+ (sn/tln) (n=953)	cALND + aRT	171 (63.8)	287 (41.9)	219 (40.0)	68 (49.3)
	cALND, no aRT	97 (36.2)	179 (26.1)	151 (27.6)	28 (20.3)
	No cALND + aRT	-	160 (23.4)	124 (22.7)	36 (26.1)
	No cALND, no aRT	-	59 (8.6)	53 (9.7)	6 (4.3)

Patient characteristics ALND vs SLNB/TAD

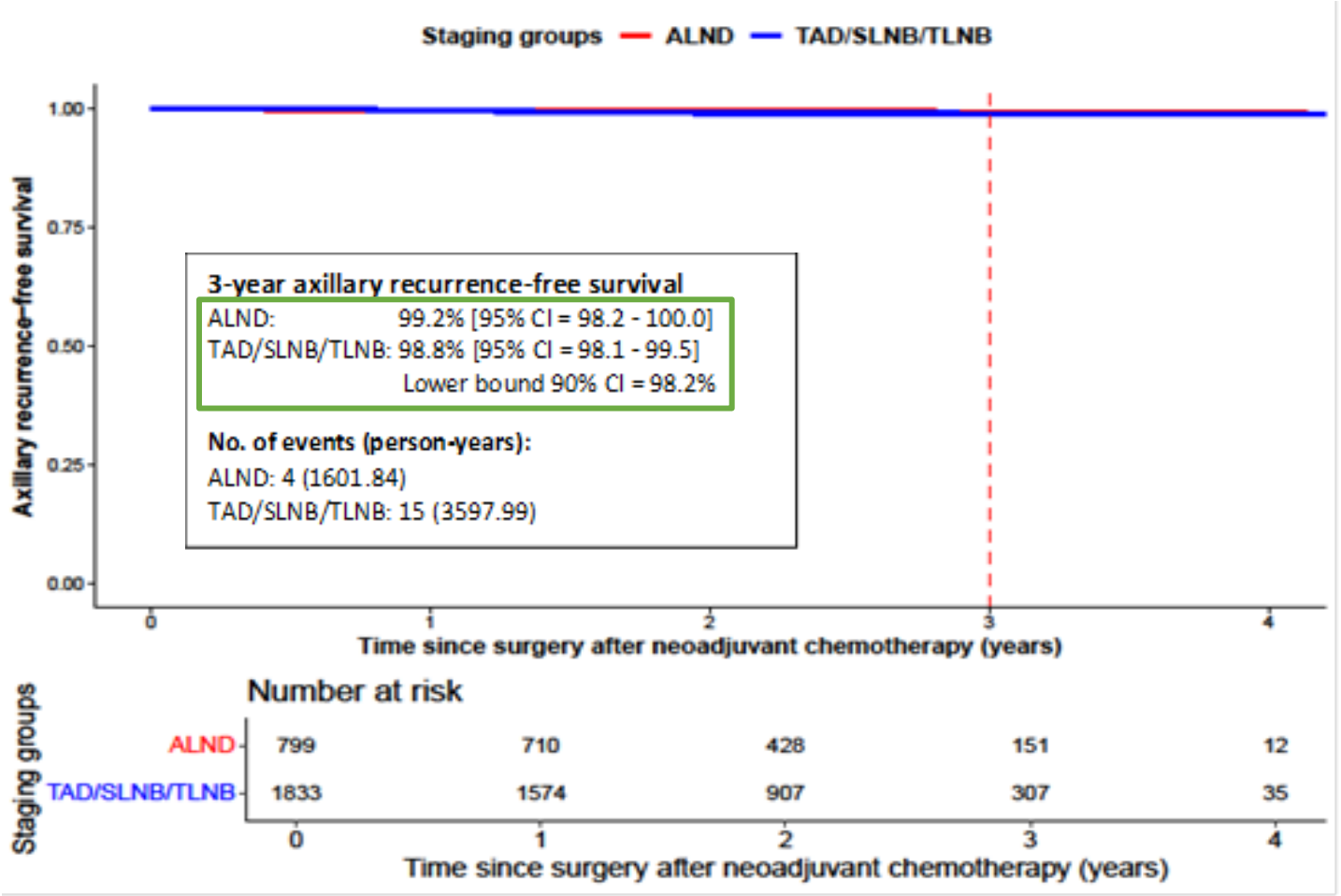
Characteristic	Overall (n/%) (n = 2632)	ALND (n/%) (n = 799)	TAD/TLNB/SLNB (n/%) (n= 1833)	p-value
Clinical tumor stage at diagnosis cT1 cT2 cT3 cT4	 580 (22.0) 1670 (63.4) 317 (12.0) 65 (2.5)	 131 (16.4) 497 (62.2) 127 (15.9) 44 (5.5)	 449 (24.5) 1173 (64.0) 190 (10.4) 21 (1.1)	<0.001
Number of suspicious nodes 1-3 ≥ 4	2138 (81.8) 476 (18.2)	501 (63.4) 289 (36.6)	1637 (89.7) 187 (10.3)	<0.001
Median size of the largest suspicious node, mm (IQR)	17 (10)	18 (12)	16 (9)	<0.001
Type of breast surgery BCS Mastectomy	 1732 (66.4) 876 (33.6)	 427 (54.3) 359 (45.7)	 1305 (71.6) 517 (28.4)	<0.001
Axillary Radiotherapy Yes No	 1406 (56.5) 1084 (43.5)	 403 (53.0) 357 (47.0)	 1003 (58.0) 727 (42.0)	0.024
Tumor Stage after NACT ypN+ ypN0	 983 (37.4) 1648 (62.6)	 275 (34.4) 524 (65.6)	 708 (38.6) 1124 (61.4)	0.044

No significant differences

- Median age
- Tumor subtype, histological type, grading
- Breast pCR
- CHT regimen, breast/cheast wall radiotherapy and adjuvant systemic therapy

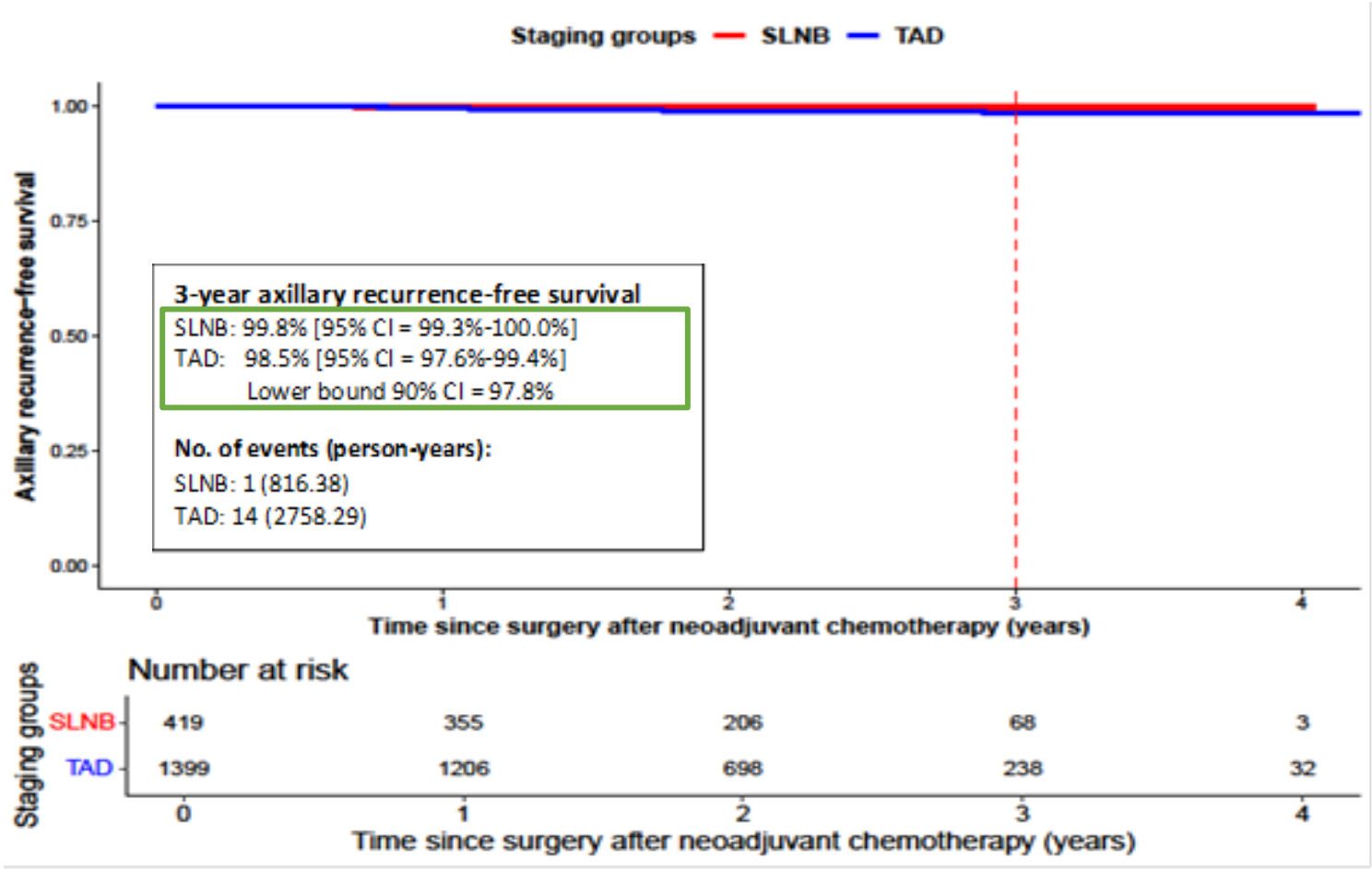
ALND vs TAD / SLNB /TLNB (3-year axillary disease-free survival) (unadjusted)

Axillary Recurrence-Free Survival in 2632 Patients with Initial Node-Positive Breast Cancer: ALND vs. TAD/SLNB/TLNB after Neoadjuvant Chemotherapy



TAD vs SLNB (3-year axillary recurrence-free survival) (unadjusted)

Axillary Recurrence-Free Survival in 1818 Patients with Initial Node-Positive Breast Cancer: SLNB vs. TAD after Neoadjuvant Chemotherapy



Conclusions

- The AXSANA study, a quality-assured, prospective, international, multicenter study reflecting real-world data, confirmed that axillary recurrence-free survival following TAD/SLNB is excellent and not inferior to ALND at 3 years
- No difference was observed between TAD and SLNB
- Findings were independent of the initial tumor stage or subtype
- Higher initial risk was associated with more distant events, but not with increased regional failures
- Less invasive staging procedures (TAD/SLNB) are safe concerning regional control for patients who convert from cN+ to ycN0
- Regional radiotherapy is currently heterogenous. More data to optimize and standardize target volumes are required.
- Further follow-up is needed to assess the effect of the staging accuracy of different procedures on BCSS

Low volume nodal involvement after neoadjuvant therapy

Axillary dissection for low-volume nodal involvement after neoadjuvant therapy in breast cancer: multicentre AXSANA cohort study

Thorsten Kühn[1,2,*], Maggie Banys-Paluchowski[3], Nina Ditsch[4], Elmar Stickeler[5], Michael Hauptmann[6], Jennifer Schroth[6], Guldeniz Karadeniz Cakmak[7], Markus Hahn[8], Marc Thill[9], Toralf Reimer[10], Sarah Fröhlich[10], Esther Schmidt[10], Kristina Wihlfahrt[11], Tomasz Berger[12], Timo Basali[13], Franziska Ruf[3], Angelika Rief[14], Michael Patrick Lux[15,16], Hans-Christian Kolberg[17], Isabel Teresa Rubio[18], Maria Luisa Gasparri[19,20], Michalis Kontos[21], Eduard-Alexandru Bonci[22,23], Laura Niinikoski[24], Dawid Murawa[25,26], David Pinto[27], Florentia Peintinger[14,28], Ellen Schlichting[29], Helidon Nina[30], Hagigat Valiyeva Qanimat[31], Marian Vanhoeij[32], Lia Pamela Rebaza[33], Bilge Aktas Sezen[34], Katharina Jursik[34], Geeta Kadayaprath[35], Lukas Dostalek[36], Ashutosh Kothari[37], Andraz Perhavec[38], Tsvetomir Ivanov[39], Douglas Zippel[40], Sarun Thongvitokomarn[41], Meryem Gunay Gurleyik[42], Dirk Watermann[43], Mauro Porpiglia[44], Annette Lebeau[45,46], Rosa Di Micco[47], Oreste Davide Gentilini[47,48], Jana de Boniface[49,50], Steffi Hartmann[10] and the AXSANA Study Group

Kuehn et al. BJS 2025

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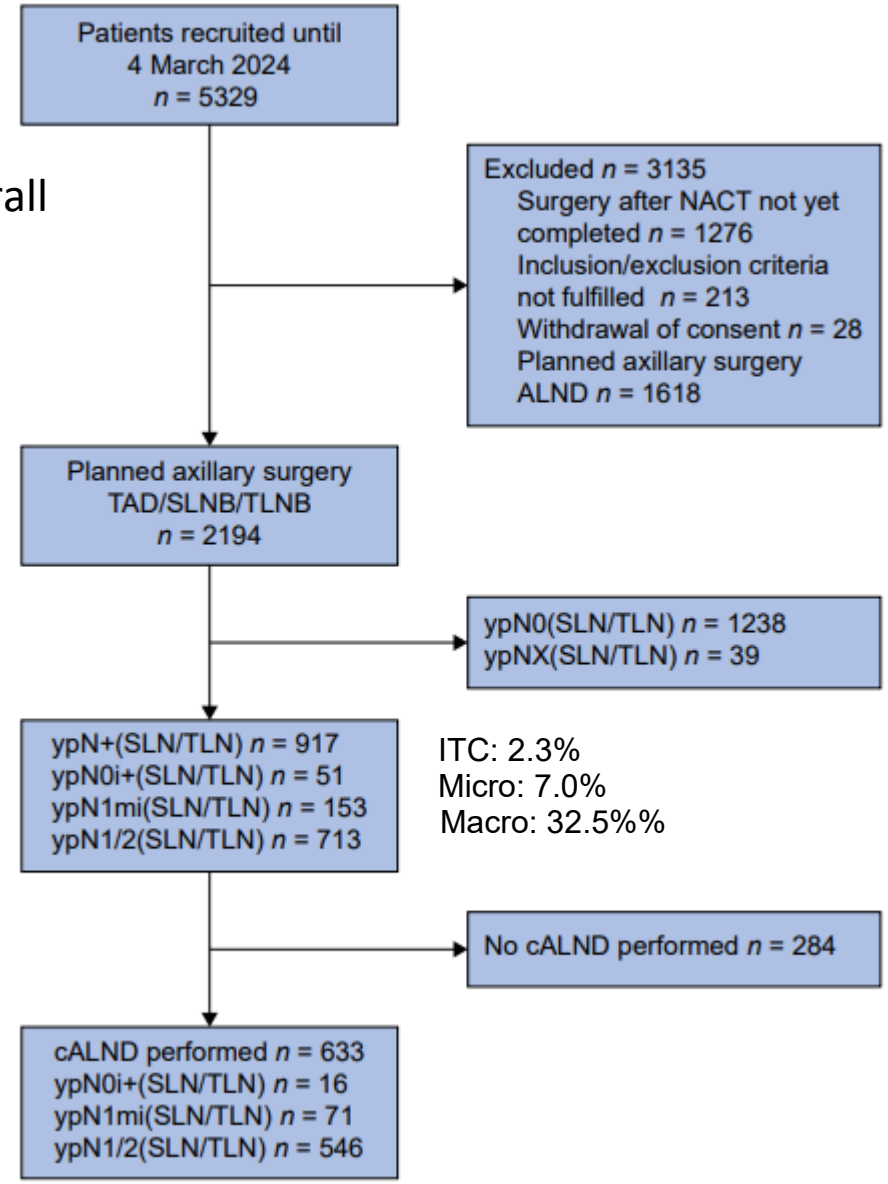
Low volume nodal involvement after neoadjuvant therapy

cALND was performed in 69.0% overall
In 76.6% with macrometastases
In 46.4% with micrometastases
In 31.4% with ITCs



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Low volume nodal involvement after neoadjuvant therapy

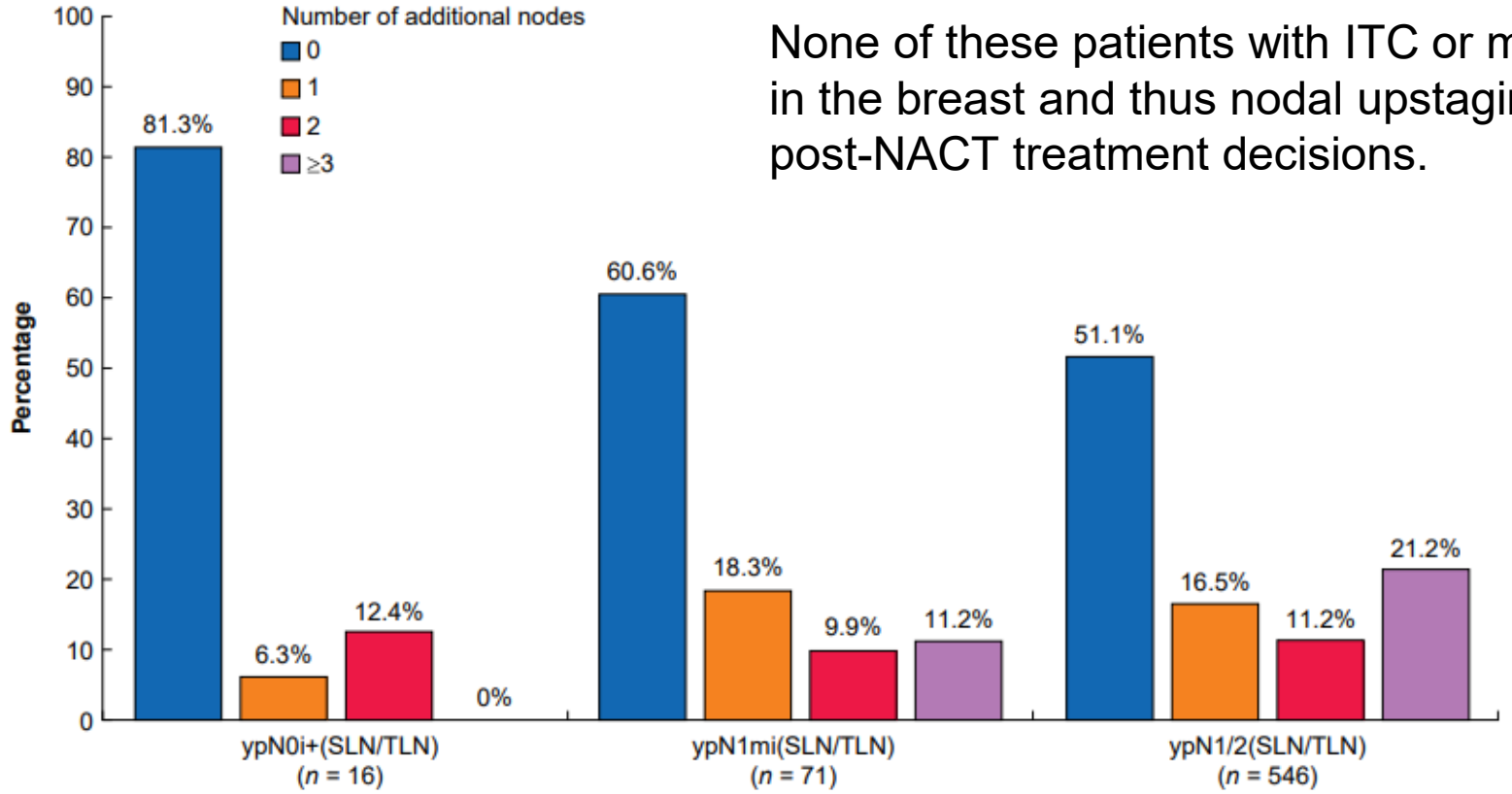

Fig. 2 Frequency and number of additional metastatic non-sentinel/non-target lymph nodes by cALND

cALND, completion axillary lymph node dissection; SLN, sentinel lymph node; TLN, target lymph node.

None of these patients with ITC or micromets had a pCR in the breast and thus nodal upstaging had no impact on post-NACT treatment decisions.

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Low volume nodal involvement after neoadjuvant therapy

Conclusion: Despite substantial additional nodal involvement in low-volume SLN/TLN disease, cALND does not provide clinically meaningful information for post-NACT systemic treatment modifications and should not be encouraged for diagnostic purposes alone.

Kuehn et al. BJS 2025

Low volume nodal involvement after neoadjuvant therapy

Implications for clinical management in routine practice:
consider to omit frozen sections of the sentinel node
and to make decision according to final pathology report on permanent sections.

Presenter's opinion

Recruiting

International Prospective REgistry on Pre-pectorAl Breast REconstruction (I-PREPARE)

ClinicalTrials.gov ID NCT05817175

- PI: Oreste D.Gentilini
- Sponsor: EUBREAST ETS Italy

- I-PREPARE is an **international, multicentric, prospective** cohort study.
- The study started in 2023
- Study duration: 4 years (2y recruitment+ 2y follow-up)

Study Start (Actual)
2023-10-16

Primary Completion (Estimated)
2027-09-10

Study Completion (Estimated)
2027-09-10

Enrollment (Estimated)
1236

Study Type
Observational

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Primary endpoint

Implant-loss at three months: defined as the unplanned removal or loss of the implant as a result of infection or other complication.

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Sample size calculation

We will use **a single-arm design** to assess the safety of PPBR based on the primary outcome of **implant loss rate at 3 months.**

It is expected that the **implant loss rate will be 9% or lower** based on previous literature (Potter S. et al.), **12% or greater will be regarded as unacceptably high**. The assessment will be based on 1,112 patients. For this sample size calculation, power was set to 90%, and the two- sided alpha was set to 0.05. Allowing for a 10% loss to follow-up at 3 months, we aim at recruiting **1.236 patients.**

A single interim analysis is pre-specified after two-thirds of enrolment (740 evaluable patients, 814 allowing for 10% loss to follow-up)

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EUBREAST App

EUBREAST App

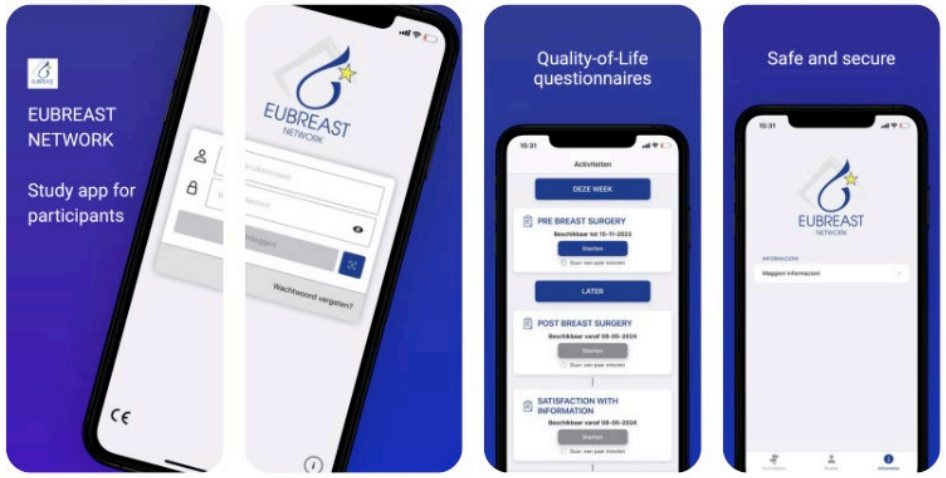
Physician Registration:

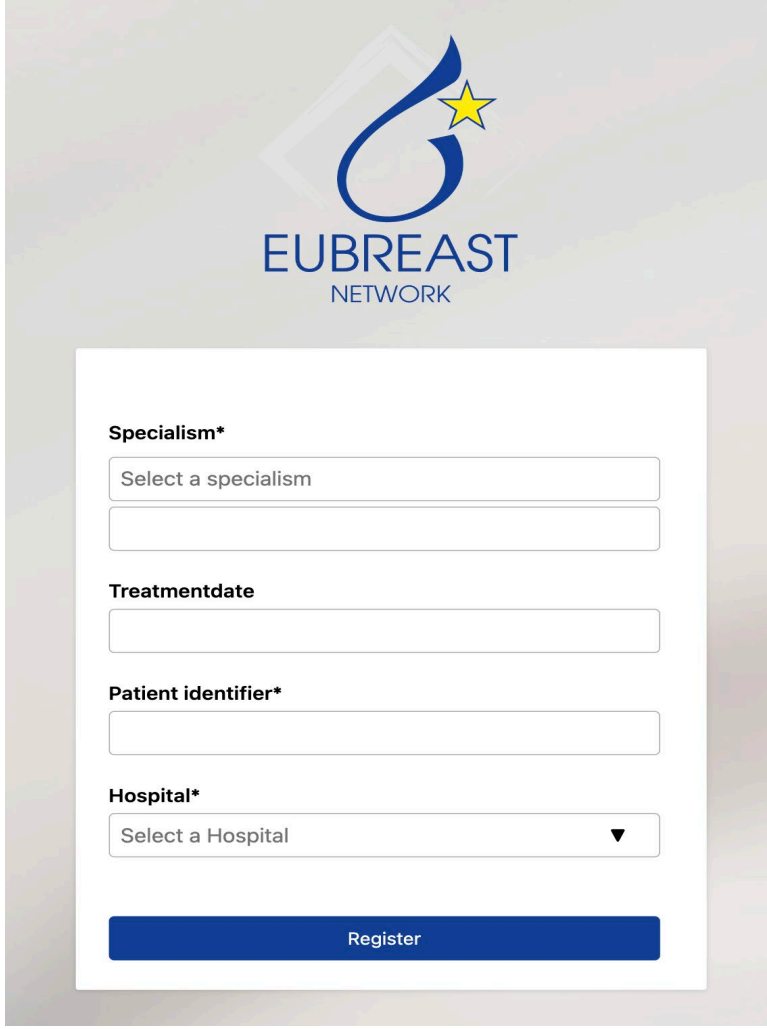
- **Inform** Patient about study and participation.
- **Register** patients through a dedicated registration page.
- Generates a unique **QR code** for each patient.

Patient App Access:

- **Download** the EUBREAST App on Android or iOS.
- **QR code scan** for automatic, secure, and anonymous login.

seline **questionnaire**





BRIGHTFISH

LOGEX

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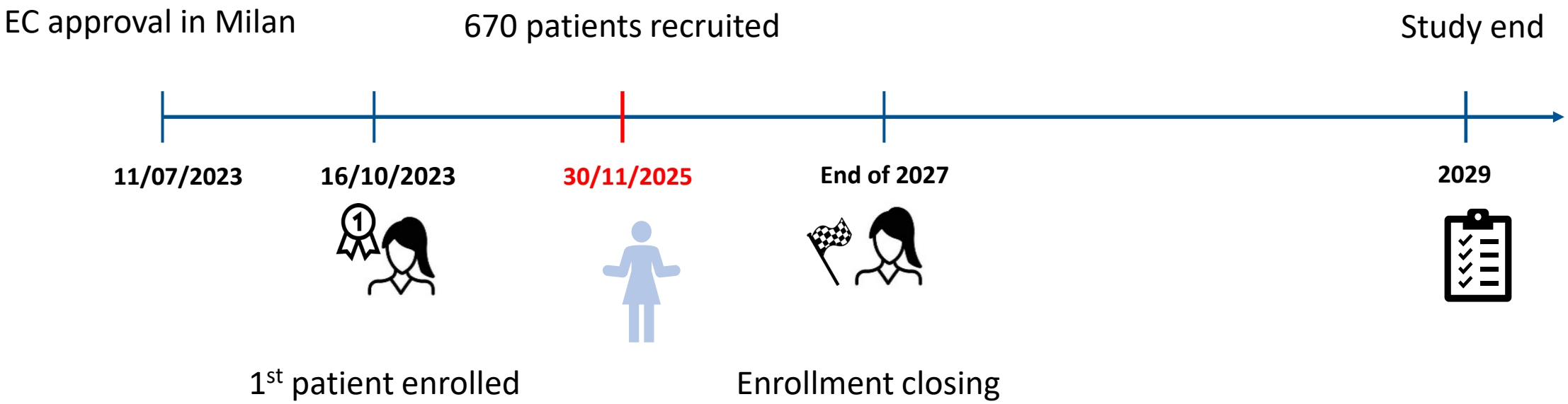
Current status



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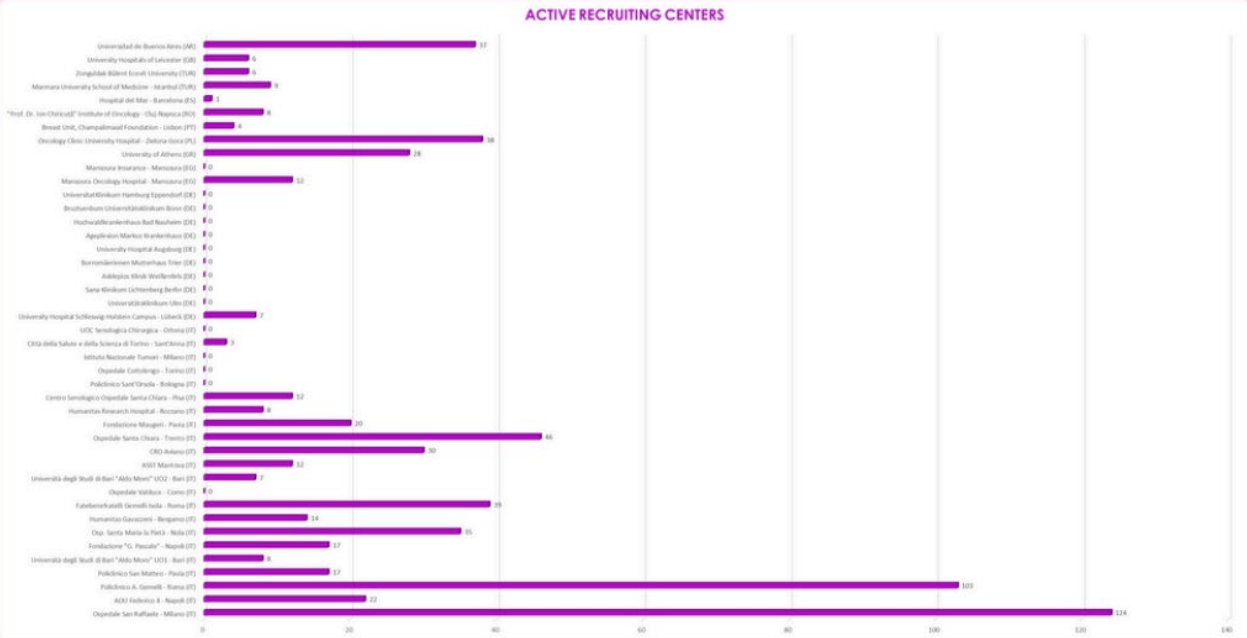
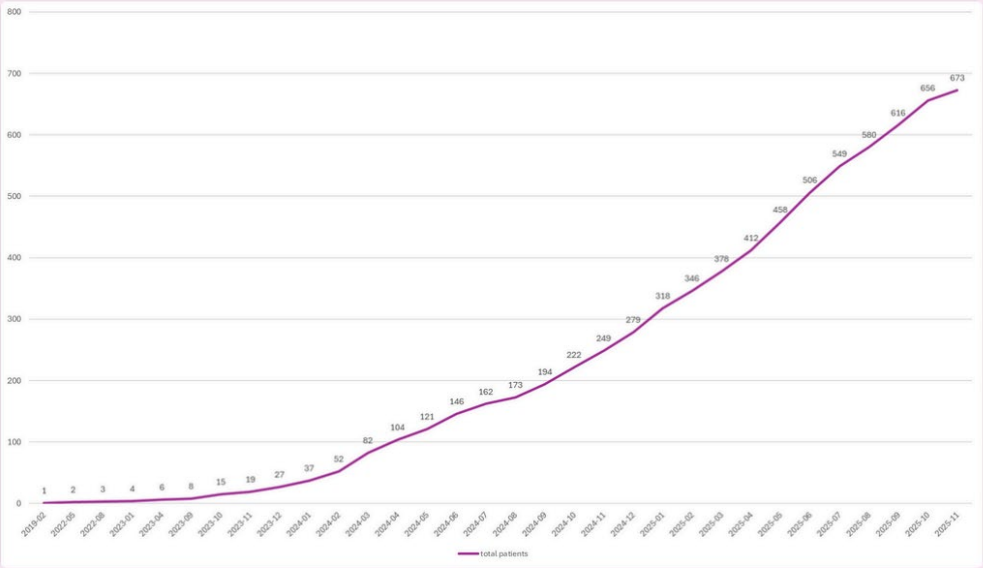
28 centers are actively recruiting patients





Top recruiting centres

1 - IRCCS Ospedale San Raffaele, Milano (Italy) – 124 patients
2 - Fondazione Policlinico Universitario Agostino Gemelli, Roma (Italy) – 103 patients
3 - Ospedale Santa Chiara, Trento (Italy) – 46 patients
4 - Ospedale Fatebenefratelli Isola Tiberina, Roma (Italy) – 39 patients
5 - Oncology Clinic University Hospital, Zielona Gora (Poland) - 38 patients

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Early results

Implant loss rate at 3 months was **2.4% (11/670)**

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MELODY

Current Status 19.01.2026

224 open study sites
27 countries
9562 patients

Country	Site count	Patient count
Germany	102	3120
Korea	23	1573
Turkey	27	995
Sweden	4	675
Denmark	3	513
Switzerland	14	449
France	4	332
Ireland	3	271
Portugal	1	228
Spain	4	224
Norway	3	212
Greece	7	156
Italy	3	140
Poland	1	130

Country	Site count	Patient count
UK	5	124
Pakistan	2	115
Argentinia	2	81
Egypt	2	52
Peru	1	49
Austria	3	36
USA	3	31
Czech Republic	1	21
Andorra	1	16
Venezuela	2	15
Slovakia	1	4
Romania	1	0
South Africa	1	0

Localization Methods 15.01.2026

Localization method	Patient number
Wire	3965
Intraoperative Ultrasound	1623
Magseed Probe	335
Sirius Pintuition Probe	405
Savi Scout Probe	317
LOCalizer	143
Radioactive seed	725
ROLL	267
Carbon suspension	544
LuminoImager	598
Other	313

More than 15.000 patients entered EUBREAST trials in the last 5 years!

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Anything new for 2026?

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LIBRETTO: Peritumoral Lidocaine Injection in BREast cancer: impact on Time TO recurrence and survival (EUBREAST-22)

A prospective randomized phase III open-label multicenter study to evaluate the effect of preoperative peritumoral injection of local anesthetic lidocaine on recurrence risk and survival in early breast cancer (low intervention trial)

Sponsor:
EUBREAST e.V.
Baumreute 37
D-73730 Esslingen, Germany

Representative of Sponsor
Prof. Dr. med. Maggie Banys-Paluchowski
Universitätsklinikum Schleswig-Holstein
Klinik für Frauenheilkunde und Geburtshilfe
Ratzeburger Allee 160
23562 Lübeck, Germany

LUNA trial

- ***L**obular breast cancer:*
- ***U**nderstanding the role of sentinel*
- ***N**ode*
- ***A**ssessment*

Rationale

- **SLNB omission** is supported by SOUND and INSEMA trials for small, low-risk breast cancers
- **Invasive lobular carcinoma** (ILC) was underrepresented (8.6% and 12.7%) → surgeons' reluctancy in omitting SLNB
- SLN metastases are **less detectable** on imaging in ILC → uncertainty regarding axillary de-escalation in this subtype

	FIRST PHASE	SECOND PHASE
Study Design	Retrospective multicenter study	Prospective multicenter study
Population	Patients with **pT1N0 ILC** who underwent SLNB	Patients with **cT1N0 ILC** undergoing SLNB
Data source	Merged prospective databases	Merged prospective databases
Period	January 2020 – December 2024	January 2027 – December 2029

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LUNA trial

- ***L**obular breast cancer:*
- ***U**nderstanding the role of sentinel*
- ***N**ode*
- ***A**ssessment*

A retrospective study on sentinel lymph node positivity in invasive lobular breast cancer

Primary Endpoints

- Rate of SLN positivity in cT1/pT1 ILC
- Benchmark comparison: SOUND: 8.7% macrometastases INSEMA: 11.6% macrometastases

Secondary Endpoints

- Systemic treatment rates (chemotherapy, CDK4/6 inhibitors, ovarian suppression)
- Number of lymph nodes removed
- Associations between SLN involvement and Tumor biology, Clinical and imaging features
- Predictors of high axillary burden (>4 positive nodes)
- Multivariable analyses for SLN positivity AND Indication to chemotherapy

Tertiary Endpoint

- Development of a predictive algorithm integrating clinical, imaging, pathological, and genomic data to estimate nodal status in ILC

Sample Size:

- Expected SLN positivity: 12% → Unacceptable threshold: ≥15%
- One-sided α = 5%, power = 80% →Required sample size: **~800 patients**

Expected Impact

- Provide dedicated evidence on SLN positivity in ILC
- Assess whether SLNB omission can be safely extended to ILC
- Inform future guideline updates and support personalized axillary de-escalation strategies

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International prospective registry on endoscopic nipple-sparing mastectomy

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