GBG 104 / EUBREAST-01

Omission of sentinel lymph node biopsy in triple-negative and HER2-positive breast cancer patients with radiologic and pathologic complete response in the breast after neoadjuvant systemic therapy: a single-arm, prospective surgical trial.

(NCT04101851)

Conflict of Interest

- **Founding member of EUBREAST**

- **Funding of the trial in Germany:**
  - Else Kröner-Fresenius-Stiftung
  - Deutsche Gesellschaft für Senologie
  - Universitäts-Frauenklinik Rostock

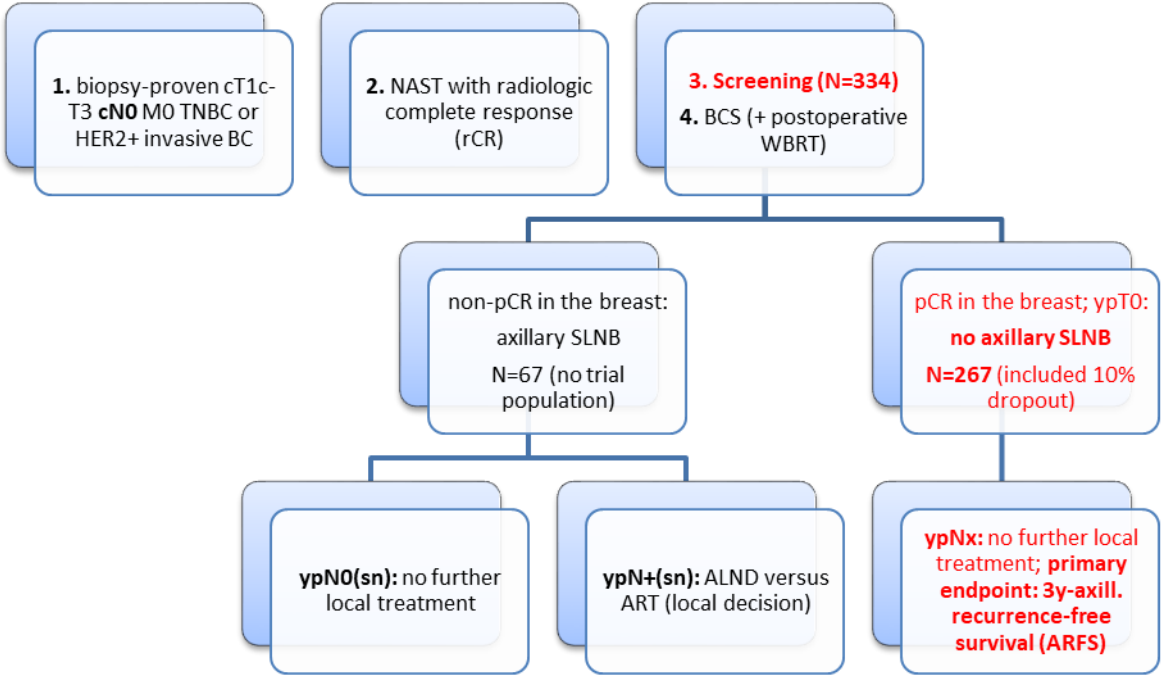
Governance

- **Sponsorship: University Medicine of Rostock**
  - Germany / Austria
- **Study chairs:**
  - Prof. Toralf Reimer (Rostock) and Dr. Oreste Gentilini (Mailand)
- **Statistician: Edoardo Botteri (San Raffaele Hospital, Mailand and Norwegian Cancer Registry, Oslo)**
- **Data Management and Monitoring GBG**

Rationale

- NAST is the standard approach for TNBC and HER2-positive BC
- The highest rates of breast pCR were seen in these two subtypes
- The highest rates of axillary nodal pCR (ypN0) were described for these two subtypes
- designed as uncontrolled, single-arm study comparable with the APT trial → robust and reliable results in a short period of time (saving both time and resources which are needed to conduct a randomized trial)

Study Design: N=267 per protocol



Planned subgroup analysis: TNBC vs. HER2-positive

Background for EUBREAST-01

Tab.: List of trials with axillary interventions after NAST reporting outcomes regarding ypN+ rate with respect to initial cN status and breast pCR.

Study for ypN+ rate in cN0 patients with breast pCR (N) after NAST	**ER+/ HER2-**	**HER2+**	**TNBC**
Barron [2018] N=5,377	n.d.	1.6%	1.6%
Samiei [2018] N=986	6.7%	ER+/HER2+: 1.6% ER-/HER2+: 0%	1.5%
Tadros [2017] N=116	n.d.	0%	0%
Van der Noordaa [2020] N=89	0%	0%	0%

Primary objective

- Primary endpoint 3-year rate of axillary recurrence-free survival (ARFS) after breast-conserving surgery (no SLNB arm)
- An acceptable 3-year ARFS for optimally treated patients with initially cN0/iN0 status and NAST is considered to be ≥98.5%
- A clinical non-relevant magnitude of up to 2 points is defined for this population, so that a 3-year ARFS of ≤96% is unacceptable for the non-SLNB group (experimental arm)

Sample size calculation

- **Sample size calculation:**
  - Alternate hazard rate 0.00504
  - Null hazard rate 0.01361
  - Test significance level, α 0.05
  - Power (%) 95
  - Accrual period (years) 2
  - Follow-up (years) of last patient enrolled 3
  - Dropout hazard rate 0.03512
  - 1-sided or 2-sided test? 2-sided

  Required sample size: N=267

Secondary Objectives

- 5-year invasive disease-free survival
- 5-year overall survival
- 5-year locoregional disease-free survival
- 5-year distant disease-free survival
- 5-year ipsilateral axillary recurrence rate
- Diagnostic accuracy of imaging methods for pathologic complete response (breast pCR) after NAST

Main Inclusion Criteria 1

- Histologically confirmed unilateral primary invasive carcinoma of the breast (core biopsy). Multifocal or multicentric tumors are allowed if BCS is planned.
- Age at diagnosis at least 18 years
- Imaging techniques with estimated tumor stage between cT1c-T3 prior to NAST
- Triple-negative or HER2-positive invasive breast cancer
- Clinically and sonographically tumor-free axilla prior to core biopsy (cN0/iN0)

Main Inclusion Criteria 2

- In cases with cN0 and iN+, a negative core biopsy or fine needle aspiration (FNA) biopsy of the sonographically suspected lymph node is required
- No evidence for distant metastasis (M0)
- Standard NAST with radiologic complete response (rCR)
- Planned BCS with postoperative external whole-breast irradiation (conventional fractionation or hypofractionation)

Main Exclusion Criteria

- Histologically non-invasive breast carcinoma
- Hormone receptor-positive/HER2-negative disease (triple-positive tumors are allowed)
- cT4 or iT4 tumors
- Pregnant or lactating patients
- No radiological complete response at the end of NAST
- Planned total mastectomy after NAST
- Male patients

Timelines / Sites

- Recruitment start Q1 / 2021
- Recruitment end Q4 / 2022
- Primary analysis Q4 / 2025
- 5-year analysis Q4 / 2027

Study sites:

Germany: 30

Italy: 10-15 (EC vote pending)

Austria: 2 (EC vote approved)

Sweden: 1-3 (EC vote approved)

Recruitment (19.02.2021) n = 4

- First-patient-in: 13-JAN-2021
- Initiierte Zentren in D: n = 14

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HERZLICHEN DANK!