

## Background

- Axillary surgery in early breast cancer has become less aggressive. However, the optimal surgical approach for patients undergoing neoadjuvant systemic therapy (NST) in the axilla is still uncertain and depends on response to NST.
- The significance of nodal micrometastases (ypN1mi) after NST remains uncertain, and detecting additional macrometastases could influence post-neoadjuvant treatment decisions.
- Our study aimed to retrospectively analyze the occurrence of ypN1mi in five neoadjuvant GBG/AGO-B trials conducted from 2012 to 2019.

## Patients and Methods

We analyzed data from 3163 out of 3199 early breast cancer patients who underwent breast surgery across five neoadjuvant chemotherapy studies (GeparSepto [GBG 69], GeparOcto [GBG 84], GeparNuevo [GBG 89], GeparX [GBG 88], GeparOla [GBG 90]) to investigate axillary surgeries and ypN1mi incidence, and their correlation with outcome. Baseline characteristics are shown in **Table 1**.

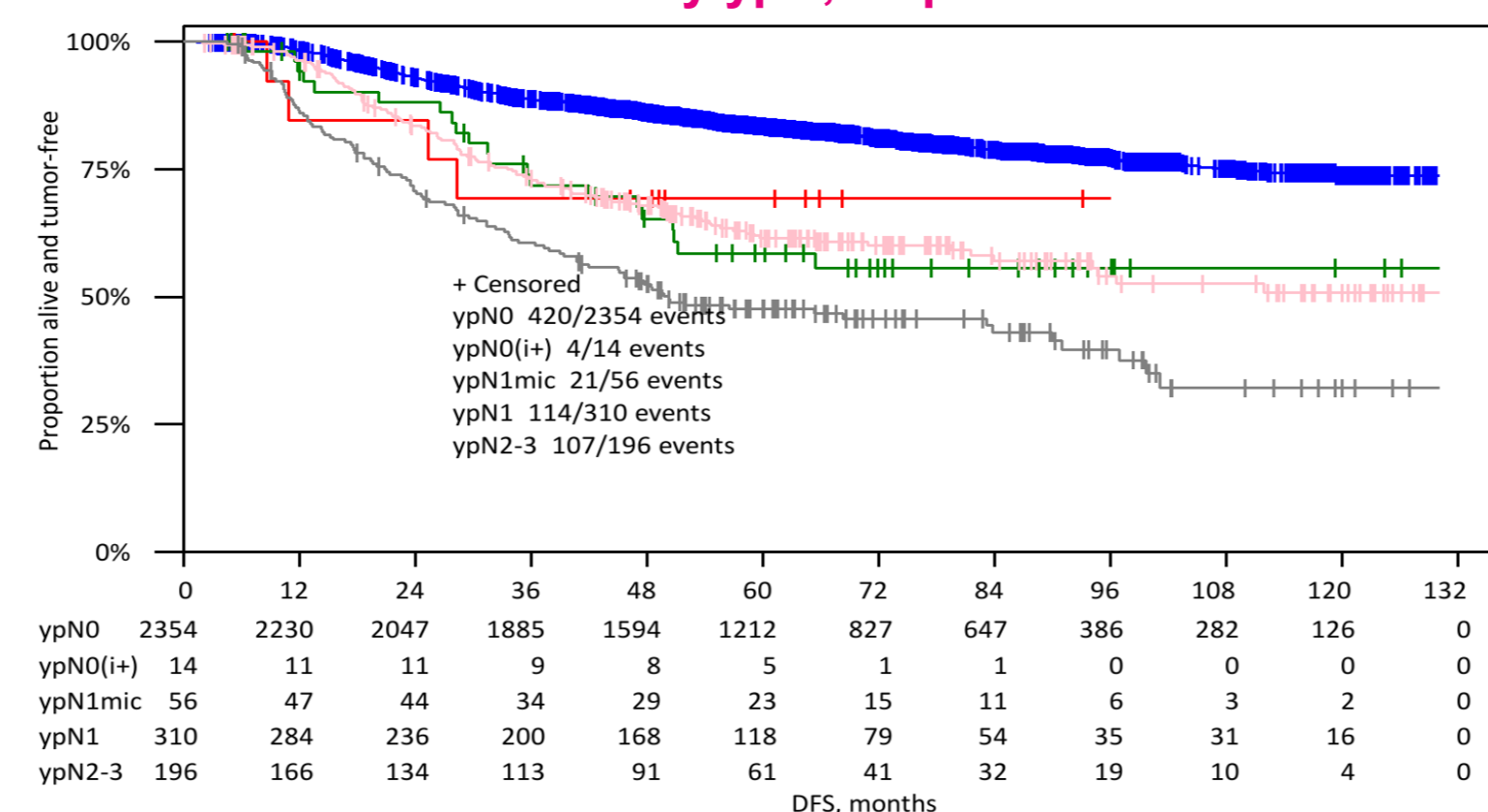
**Table 1: Baseline Characteristics**

Parameter	Parameter value	N (%)
Age	Median (yrs)	49.0
	Range (yrs)	21.0 – 80.0
cN at diagnosis	cN0	2079 (66.5)
	cN1	922 (29.5)
	cN2	85 (2.7)
	cN3	38 (1.2)
	missing	39
cT at diagnosis	cT1	1219 (38.7)
	cT2	1576 (50.0)
	cT3	228 (7.2)
	cT4	126 (4.0)
	missing	14
Biological subtype	HR+/HER2-	1013 (32.0)
	TNBC	1229 (38.9)
	HER2+	921 (29.1)
Grading	G3	2001 (63.3)

## Results

- 98.9% (3163 out of 3199) of patients underwent breast surgery, with information on axillary intervention being included in the analysis. Prior to NST, 44.1% (1395 out of 3163) of patients underwent sentinel lymph node biopsy (SLNB). 1746 patients did not undergo any axillary surgery prior to NST. Post-NST, 19.4% (612/3163) had SLNB only, 0.2% (5/3163) received targeted lymph node biopsy (TLNB) only, 0.9% (27/3163) had targeted axillary dissection (TAD), and 40.9% (1288/3163) had axilla lymph node dissection (ALND) only. Additionally, 4.0% (125/3163) patients underwent ALND following SLNB, TLNB, or TAD.
- Of all 2038 evaluable patients who had any lymph node surgery after NST, those with initial clinically node-negative status (cN0) had ypN0 in 83.4% (892/1009) of cases, whereas patients with initial cN+ had ypN+ in 39.5% (379/960) of cases. A total of 43.1% (879/2038) had a pathological complete response (pCR) in the breast (ypT0), with only 5.3% (47) of these exhibiting concurrent residual disease in the lymph nodes (ypT0, ypN+). In those ypT0 patients, axillary pCR rates according to subtype were 98.6% for patients with HER2-positive, 94.6% for triple-negative, and 84.2% for HR+/HER2-negative subtypes, respectively. Patients, who had ypT0 after NST, were analysed according to their initial clinical nodal status (cN). Patients with cN+, also displayed high rates of ypN0 when compared to those with cN0; specifically: 97.8% vs 99.4% for HER2-positive, 88.3% vs 98.0% for triple-negative, and 83.1% vs 85.1% for HR+/HER2-negative tumors.
- At axillary surgery after NST, 0.7% (14) and 2.7% (56) had ypN0i+ and ypN1mi axillary stage and 0.15% (3) and 0.64% (13) had ypN0i+ ypN1mi as sole residual disease. Five-year disease-free survival (DFS) hazard ratio (HR) showed 2.17 (CI 0.81-5.81; p=0.123) for ypN0i+, 2.53 (CI 1.63-3.91; p<0.001) for ypN1mi and 2.43 (CI 1.98-3.00; p<0.001) for ypN1 (**Table 2**). The overall survival (OS) HRs were 4.98 (CI 1.85-13.4; p=0.001) for ypN0i+, 3.17 (CI 1.77-5.68) for ypN1mi and 3.03 (CI 2.28-4.03) for ypN1 (**Table 3**).

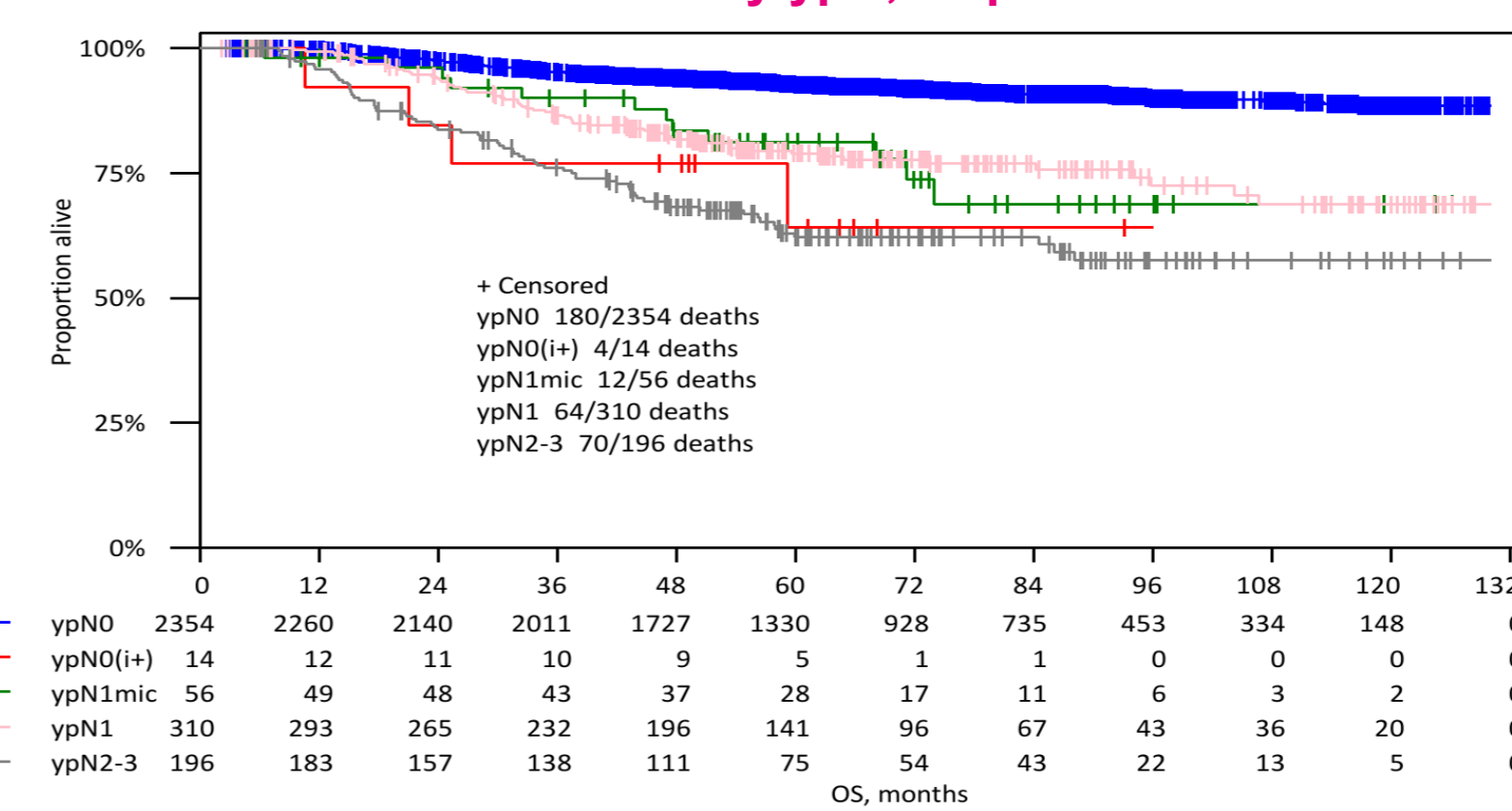
**DFS by ypN, all patients**



**Table 2: 5-year DFS rate (95% CI) by ypN**

ypN0	83.4% (81.8%, 85.0%)
ypN0i+	69.2% (37.3%, 87.2%)
ypN1mi	58.5% (43.3%, 71.0%)
ypN1	61.4% (55.2%, 67.0%)
ypN2-3	47.6% (40.2%, 54.6%)

**OS by ypN, all patients**



**Table 3: 5-year OS rate (95% CI) by ypN**

ypN0	92.7% (91.4%, 93.7%)
ypN0i+	64.1% (28.2%, 85.5%)
ypN1mi	81.2% (66.9%, 89.8%)
ypN1	79.0% (73.5%, 83.4%)
ypN2-3	62.2% (54.4%, 69.0%)

## Conclusions

- During our retrospective study period, surgical standards changed to preferring SLNB in cN0 and allowing TAD in cN+ patients both after NST starting 2017 and 2019 respectively. Of all pts with any surgery after NST 69.3% (1413 of 2038) had ALND with only 27.9% (568 of 2038) having at least ypN0i+.
- Regarding patients with pCR in the breast after NST, axillary pCR rates varied with subtype and according to initial cN status. Identifying patient groups not deriving benefit from axillary staging after NST seems desirable, but further analyses of the data according to type, setting and era of the axillary intervention is required, to draw such clinical conclusions.
- Our data suggest that minimal axillary residuals after NST may have an impact on DFS and OS, but further analyses are essential to evaluate the impact of other variables.