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Axillary surgery after neoadjuvant systemic therapy for early-stage breast cancer – Treatment algorithms and prognostic impact of residual micrometastases in five neoadjuvant studies of the AGO-B study group and German Breast Group (GBG)

(GeparSepto, GeparOcto, GeparNuevo, GeparX, GeparOla)

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-This is a joint study by GBG and AGO-B-

AGO-B BREAST STUDY GROUP
GBG GERMAN BREAST GROUP

Disclosure Information

Johannes Holtschmidt

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Employee of: German Breast Group (GBG) Forschungs GmbH, Neu-Isenburg, Germany.

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Background

- For patients (pts) undergoing neoadjuvant systemic therapy (NST), the axillary status before and after NST is of major importance for adjuvant systemic and locoregional treatment.
- A prior analysis in this data set of 3.199 pts suggested that micrometastases after NST (ypN1mi) may have an impact on survival with 5-year DFS and OS rates being significantly lower compared with ypN0.[1]

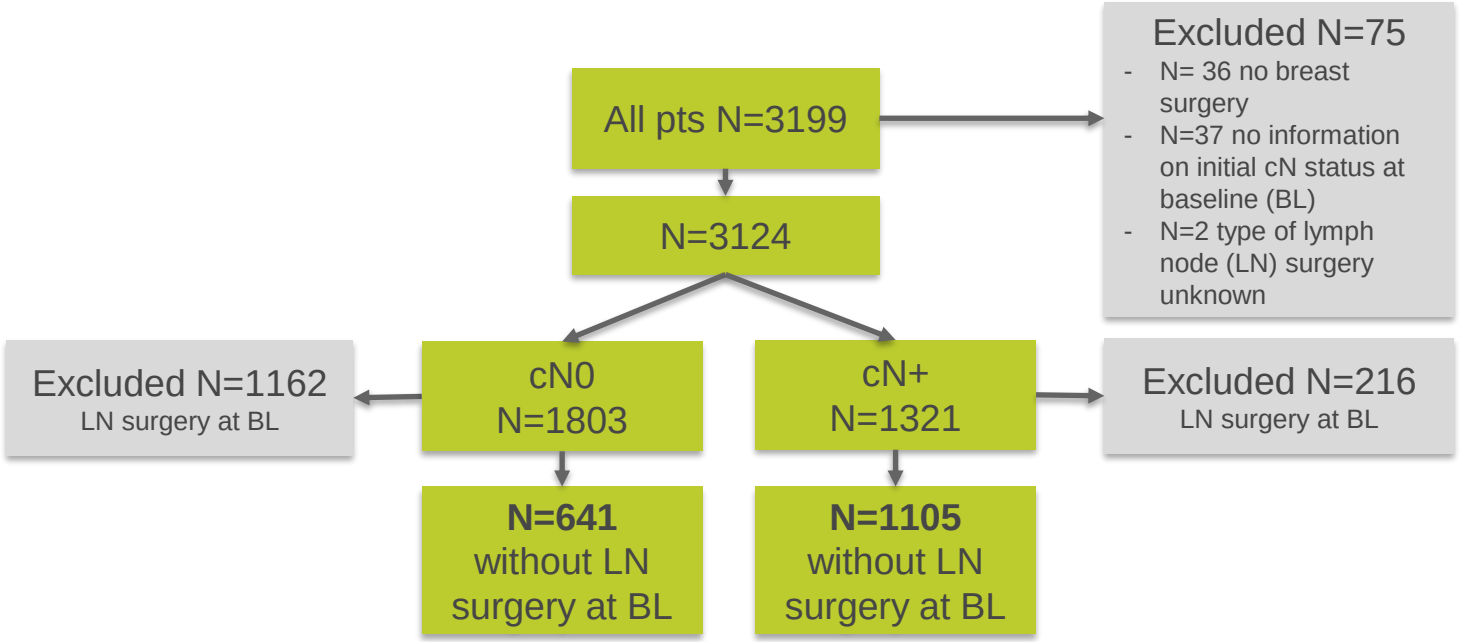
	HR	95% CI	5y survival ypN1mi	5y survival ypN0
DFS	2.53	1.63-3.91	58.5% (43.3-71.0%)	83.4% (81.8-85.0%)
OS	3.17	1.77-5.68	81.2% (66.9-89.8%)	92.7% (91.4-93.7%)

- But the results were limited because of the uncertainty concerning the clinical situation they had been detected in.
- Axillary intervention and occurrence of ypN1mi were retrospectively analyzed and correlated to outcome according to initial clinical nodal stage (cN) and to simulated contemporary surgical approaches.

1 Warnecke et al. ESMO BC 2023

Consort Flow Diagramm

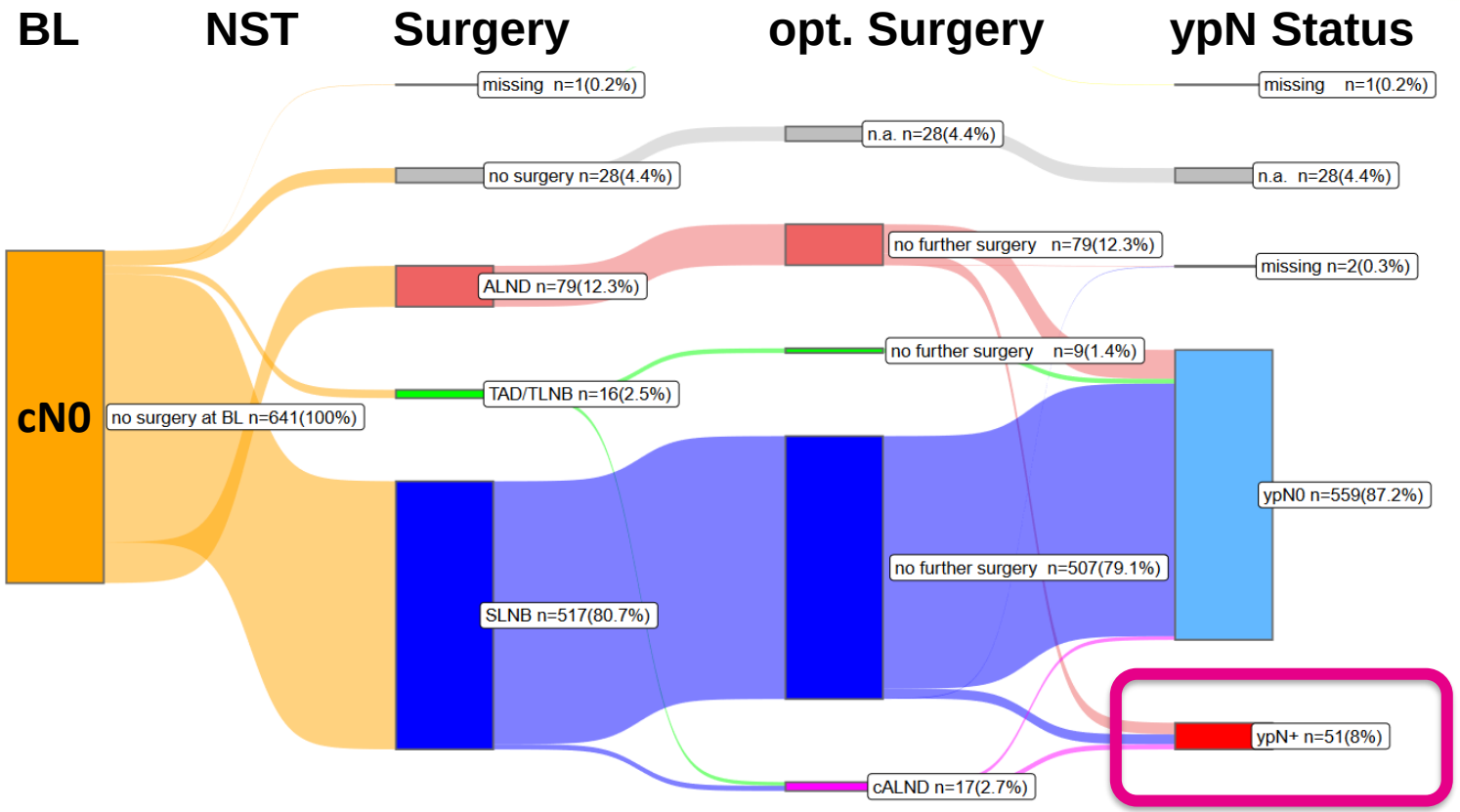
Data from 3199 pts with early BC, who were enrolled in five neoadjuvant AGO-B / GBG trials (GeparSepto, GeparOcto, GeparNuevo, GeparX, GeparOla) conducted between 2012 and 2019 were analyzed.



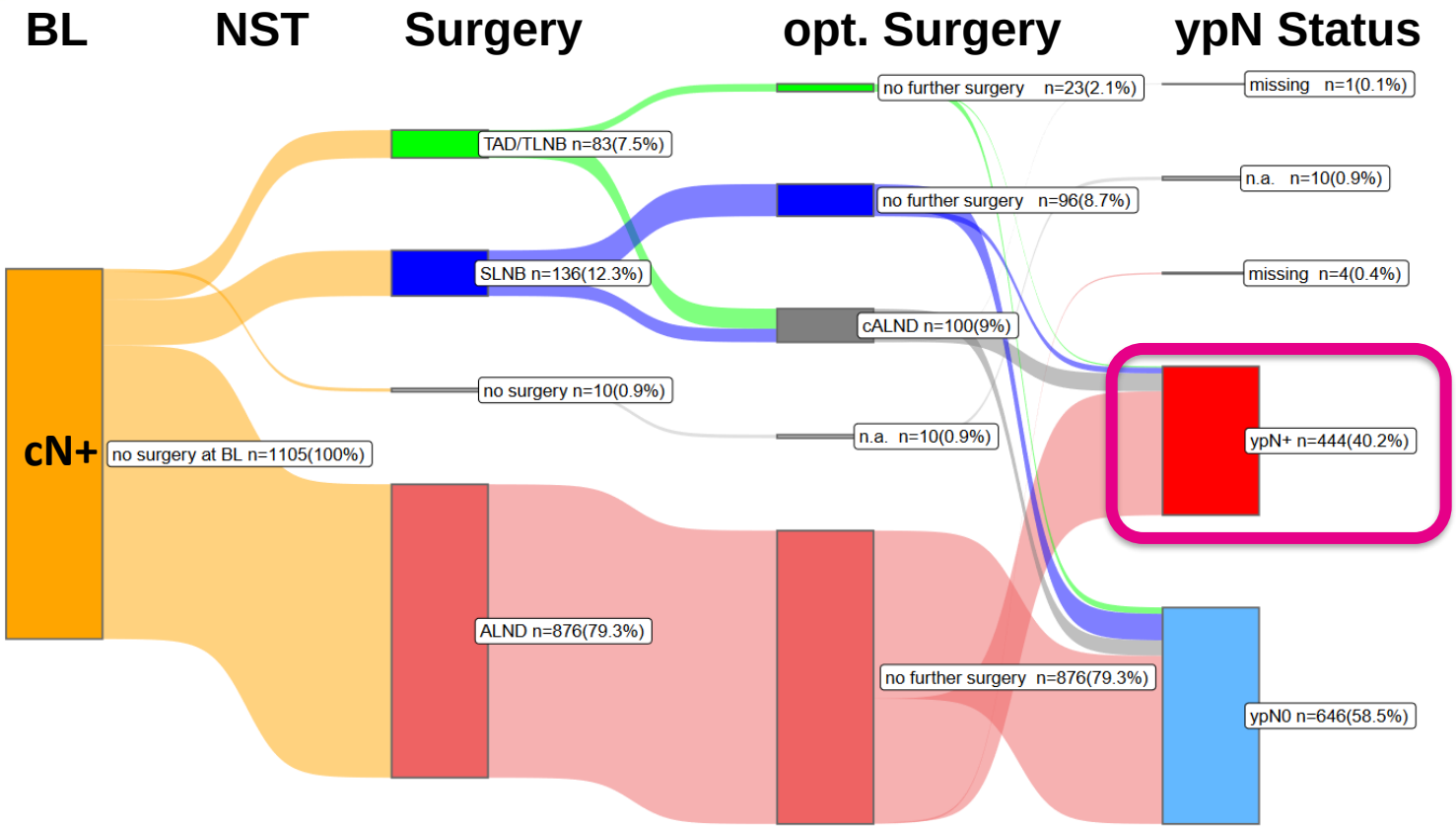
Main Baseline Characteristics

Parameter Difference to 100% is missing	cN0		cN+	
	ypN0 N=560	ypN1mi N=9	ypN0 N=646	ypN1mi N=40
Median Age (range)	49 (22-80)	48 (27-63)	49 (21-76)	50 (30-75)
cT1	269 (48.2%)	3 (33.3%)	192 (30.0%)	7 (17.5%)
cT2	261 (46.8%)	4 (44.4%)	344 (53.7%)	22 (55.0%)
cT3-4	28 (5.0%)	**2 (22.2%)**	105 (16.4%)	**11 (27.5%)**
HRpos/HER2neg	120 (21.4%)	**7 (77.8%)**	165 (25.5%)	**21 (52.5%)**
TNBC	320 (57.1%)	2 (22.2%)	211 (32.7%)	11 (27.5%)
HER2pos	120 (21.4%)	0 (0.0%)	270 (41.8%)	8 (20.0%)
G3	418 (74.6%)	**4 (44.4%)**	430 (66.6%)	**23 (57.5%)**
Ki67 ≤20%	88 (15.7%)	**3 (33.3%)**	88 (13.6%)	**10 (25.0%)**

cN0 – Surgical Approaches



cN+ – Surgical Approaches



Axillary Status after NST according to Subtype

- For all pts without axillary surgery at baseline, axillary pCR rates varied across subtypes with high rates in case a breast pCR was also present.

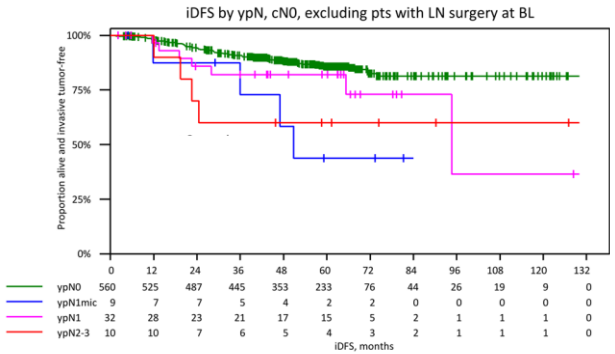
cN0

Subtype	ypN0	ypN0 if ypT0/is
HR+/HER2-	77.9%	89.6%
TNBC	96.1%	98.6%
HER2+	96.8%	98.9%

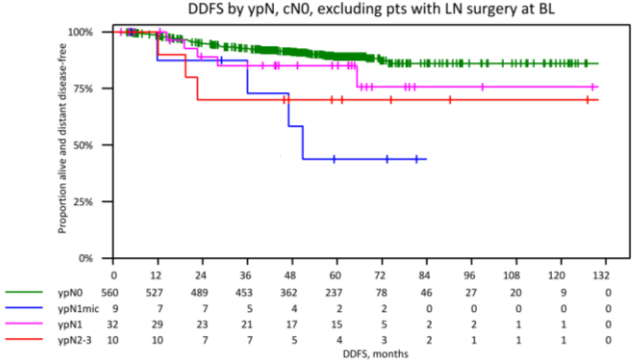
cN+

Subtype	ypN0	ypN0 if ypT0/is
HR+/HER2-	36.9%	76.5%
TNBC	65.3%	88.7%
HER2+	84.4%	95.4%

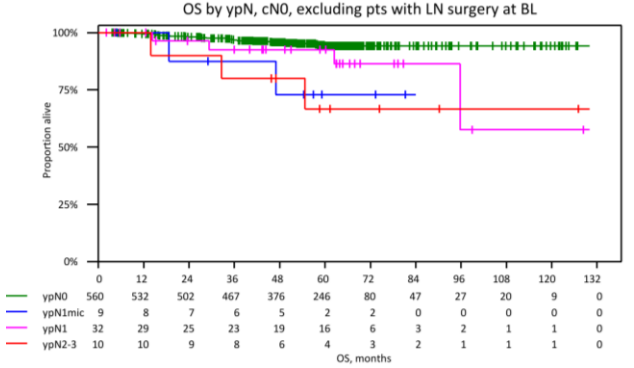
Survival in cN0 according to ypN



	ypN1mi	ypN0
iDFS events, N (%)	4 (44.4)	73 (13.0)
HR 4.03 (1.47-11.0); p=0.007		



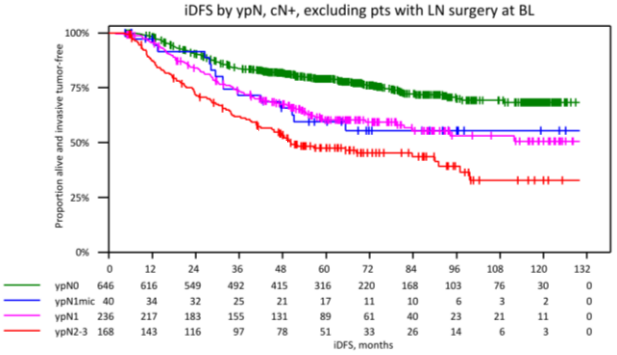
	ypN1mi	ypN0
DDFS events, N (%)	4 (44.4)	55 (9.8)
HR 5.37 (1.94-14.8); p=0.001		



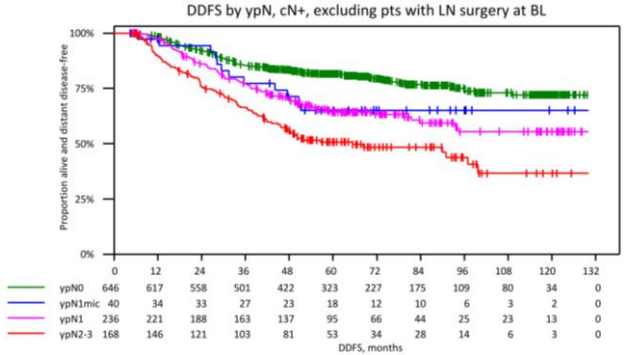
	ypN1mi	ypN0
OS events, N (%)	2 (22.2)	26 (4.6)
HR 5.76 (1.37-24.3); p=0.017		

- If cN0 at baseline, pts with ypN1mi had significantly worse iDFS, DDFS and OS compared to ypN0
- Median follow-up of 68 months

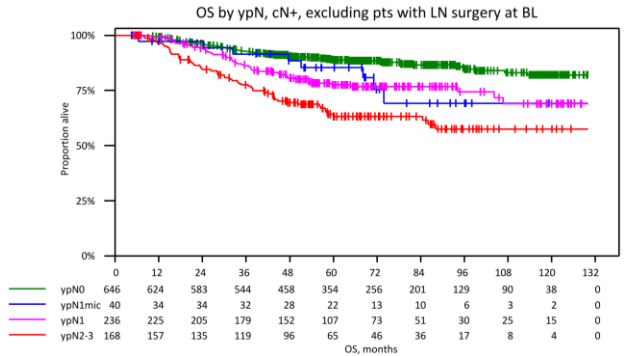
Survival in cN+ according to ypN



	ypN1mi	ypN0
iDFS events, N (%)	15 (37.5)	149 (23.1)
HR 1.85 (1.09-3.14); p=0.024		



	ypN1mi	ypN0
DDFS events, N (%)	12 (30.0)	130 (20.1)
HR 1.65 (0.96-2.98); p=0.096		



	ypN1mi	ypN0
OS events, N (%)	8 (20.0)	76 (11.8)
HR 1.85 (0.89-3.83); p=0.098		

- If cN+ at baseline, pts with ypN1mi had significantly worse iDFS, and a trend towards worse DDFS and OS compared to ypN0
- Median follow-up of 59 months

Summary and Conclusion

- In this pooled analysis of five neoadjuvant trials, pts with ypN1mi after NST had a significantly worse iDFS irrespective of initial clinical nodal status
- Impact of ypN1mi on survival was more pronounced in pts clinically node-negative at presentation (cN0)
- This observation is limited by the overall rare prevalence of this situation
  - cN0: ypN1mi accounted for 17.6% (9/51) of all ypN+ and 1.4% (9/613) of evaluable cN0 pts
  - cN+: ypN1mi accounted for 9% (40/444) of all ypN+ and 3.7% (40/1095) of evaluable cN+ pts
- Offering the same surgical approach in all subtypes can be questioned.
- Likelihood of surgical axillary staging after NST providing relevant treatment information in pts with HER2+ or TNBC tumors with initially cN0 and breast pCR was very low.
- Value of completion ALND in pts with limited axillary residuals after NST needs to be evaluated.
- Outcomes from prospective trials like EUBRAST-01 and A011202 are needed to evaluate & establish subtype specific axillary approaches.

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GBG

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