Prognostic stratification of breast cancer after neoadjuvant systemic therapy by application of a modified Sinn regression grade

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Background

Despite its importance for prognosis and treatment decisions, no universal tumor regression grading (TRG) for pathological response evaluation after neoadjuvant systemic therapy (NST) in breast cancer (BC) exists. The TRG by Sinn et al.[1] is based on a semiquantitative scoring system, ranging from 0 to 4 (0 = no effect, 4 = no tumor detectable) but is restricted to the breast. Therefore, we combined the TRG with post-treatment nodal stage to explore whether the combination increases prognostic accuracy.

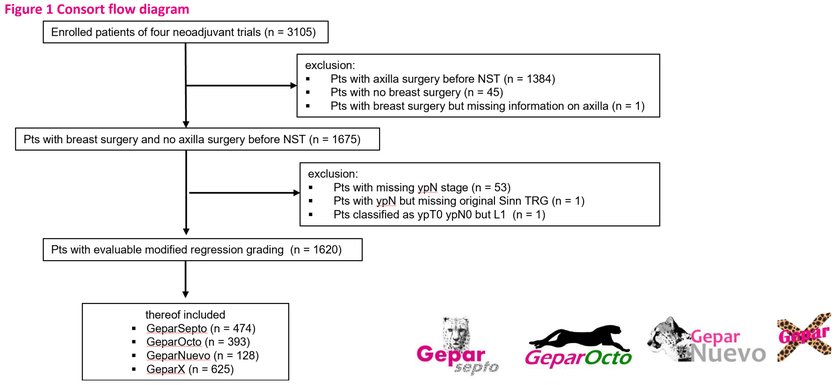
Patients and Methods

We investigated the modified TRG (**Table 1**) in a set of four neoadjuvant GBG/AGO-B trials (GeparSepto, GeparOcto, GeparNuevo, GeparX[2-5]) carried out between 2012-2019. Only patients (pts) without axillary surgery prior to NST and who underwent surgery after NST were included (**Figure 1**). The impact of modified TRG on distant disease-free survival (DDFS) and overall survival (OS) was explored. Time-to-event (TTE) outcomes DDFS and OS start from time of surgery date since regression grading is determined at surgery and were compared using log-rank test. Uni- and multivariate Cox regression models were used for calculation of hazard ratio (HR) together with its 95% confidence interval (CI).

Table 1 Original and modified Sinn tumor regression grading

Original Sinn regression grading		Modified Sinn regression grading	
RG0	No effect	RG0 ypN0	RG0 ypN+
RG1	Resorption and tumor sclerosis	RG1 ypN0	RG1 ypN+
RG2	Minimal residual invasive tumor (<0.5cm)	RG2 ypN0	RG2 ypN+
RG3	Residual noninvasive tumor only	RG3 (ypTis) ypN0	RG3 (ypTis) ypN+
RG4	No tumor detectable	RG4 (ypT0) ypN0	RG4 (ypT0) ypN+

Figure 1 Consort flow diagram



Results

Of all pts enrolled (n=3105), 1620 were evaluable. Median follow-up was 61 months (IQR, 47.4-93.8). Pts mostly had cT1+2 stage (84.7%), cN+ (65.1%), and G3 tumors (64%). The most prevalent subtype was triple negative breast cancer (TNBC, 36.9%), followed by HR+/HER2- (35.7%), and HER2+ (27.3%). Baseline characteristics are given in **Table 2**. Most pts had axillary dissection (+/- prior SLNB/TAD; 64.3%) according to cN status and guidelines at that time. The 5-year DDFS rates for the modified TRG are summarized in **Table 3** and show marked differences between ypN0 and ypN+. The difference between modified TRG levels was significant for DDFS (log-rank p<0.001) with numerically worse DDFS for all TRG levels compared to ypN0 RG4 (e.g. ypN+ RG4 vs. ypN0 RG4 HR 1.83 95% CI 0.922-3.62). The modified TRG remained prognostic for DDFS in multivariate analysis adjusted for other prognostic factors like age, grading, and receptor status (p<0.001). For OS, the results were comparable to DDFS (**Figure 2 and 3**).

Table 2 Baseline and clinical characteristics by study

Category	GeparSepto N=474 n (%)	GeparOcto N=393 n (%)	GeparNuevo** N=128 n (%)	GeparX N=625 n (%)	Overall N=1620 n (%)
cT					
cT1+2	354 (75.4)	319 (81.1)	119 (93.0)	574 (92.3)	1366 (84.7)
cT3+4	116 (24.6)	74 (18.9)	9 (7.0)	48 (7.7)	247 (15.3)
missing	4	0	0	3	7
cN					
cN0	72 (15.3)	55 (14.0)	81 (63.3)	356 (57.1)	564 (34.9)
cN+	399 (84.7)	337 (86.0)	47 (36.7)	268 (42.9)	1051 (65.1)
missing	3	1	0	1	5
Grading					
G1+2	216 (45.6)	134 (34.1)	23 (18.0)	210 (33.6)	583 (36.0)
G3	258 (54.4)	259 (65.9)	105 (82.0)	415 (66.4)	1037 (64.0)
Tumor biology					
HR+/HER2-	221 (46.6)	109 (27.7)	0	249 (39.8)	579 (35.7)
HRany/HER2+	162 (34.2)	149 (37.9)	128 (100)	132 (21.1)	443 (27.3)
TNBC	91 (19.2)	135 (34.4)	0	244 (39.0)	598 (36.9)
Type of surgery					
BCT	289 (61.0)	228 (58.0)	94 (73.4)	462 (73.9)	1073 (66.2)
Mastectomy	185 (39.0)	165 (42.0)	34 (26.6)	163 (26.1)	547 (33.8)
Axilla surgery					
SLN/TAD only	34 (7.2)	69 (17.6)	85 (66.4)	390 (62.4)	578 (35.7)
ALND*	439 (92.8)	324 (82.4)	43 (33.6)	235 (37.6)	1041 (64.3)
missing	1	0	0	0	1

*with or without prior SLN/TAD
**GeparNuevo enrolled TNBC patients only.

Table 3 Five-year DDFS rates for modified Sinn tumor regression grading

	ypN0 [%] (95% CI)	ypN+ [%] (95% CI)
RG0	62.5% (34.9%, 81.1%)	47.2% (31.3%, 61.6%)
RG1	79.7% (73.2%, 84.8%)	59.9% (53.8%, 65.5%)
RG2	80.3% (72.3%, 86.2%)	54.9% (40.7%, 67.1%)
RG3 (ypTis)	83.5% (72.7%, 90.4%)	71.8% (44.3%, 87.4%)
RG4 (ypT0)	87.1% (84.1%, 89.6%)	72.2% (52.9%, 84.7%)

Figure 2 Kaplan Meier curve for DDFS by modified regression grade

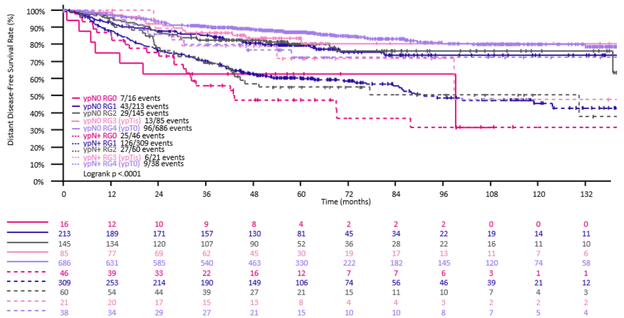
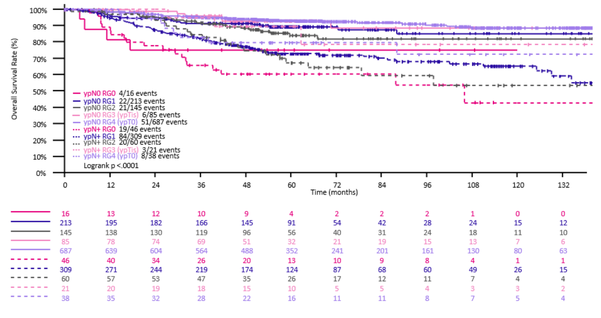


Figure 3 Kaplan Meier curve for OS by modified regression grade



Conclusion

- This modified regression grading showed clear prognostic stratification in BC after NST and the importance of including posttreatment nodal status (ypN).
- Validation in further studies is needed.

References

1. Sinn et al. Histological Regression of Breast Cancer after primary (neoadjuvant) chemotherapy. Geburtsh u Frauenheilk 1994
2. Untch et al. Nab-paclitaxel versus solvent-based paclitaxel in neoadjuvant chemotherapy for early breast cancer (GeparSepto-GBG69): a randomized, phase 3 trial. Lancet Oncol 2016
3. Schneeweiss et al. Survival analysis of the randomised phase III GeparOcto trial comparing neoadjuvant chemotherapy of intense dose-dense epirubicin, paclitaxel, cyclophosphamide versus weekly paclitaxel, liposomal doxorubicin (plus carboplatin in triple-negative breast cancer) for patients with high-risk early breast cancer. Eur J Cancer 2022
4. Loibl et al. Neoadjuvant durvalumab improves survival in early triple-negative breast cancer independent of pathological complete response. Ann Oncol 2022
5. Blohmer et al. Effect of denosumab added to 2 different nab-paclitaxel regimens as neoadjuvant therapy in patients with primary breast cancer the GeparX 2 × 2 randomized clinical trial. JAMA Oncol 2022

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