

nab-Paclitaxel at a dose of 125 mg/m² weekly is equally efficacious but less toxic than at 150 mg/m² - Results from the neoadjuvant randomized GeparSepto study (GBG 69)



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Background

- The GeparSepto study showed that nab-paclitaxel (nP) increased the pathological complete response (pCR) rate compared to solvent-based paclitaxel (P) as part of sequential taxane-epirubicin/cyclophosphamide (EC) neoadjuvant treatment in early breast cancer (Untch et al. Cancer Res 2015).
- After a safety analysis found higher rates of dose reductions and treatment discontinuations with nP compared to P, nP dose was reduced from 150 to 125mg/m² weekly.

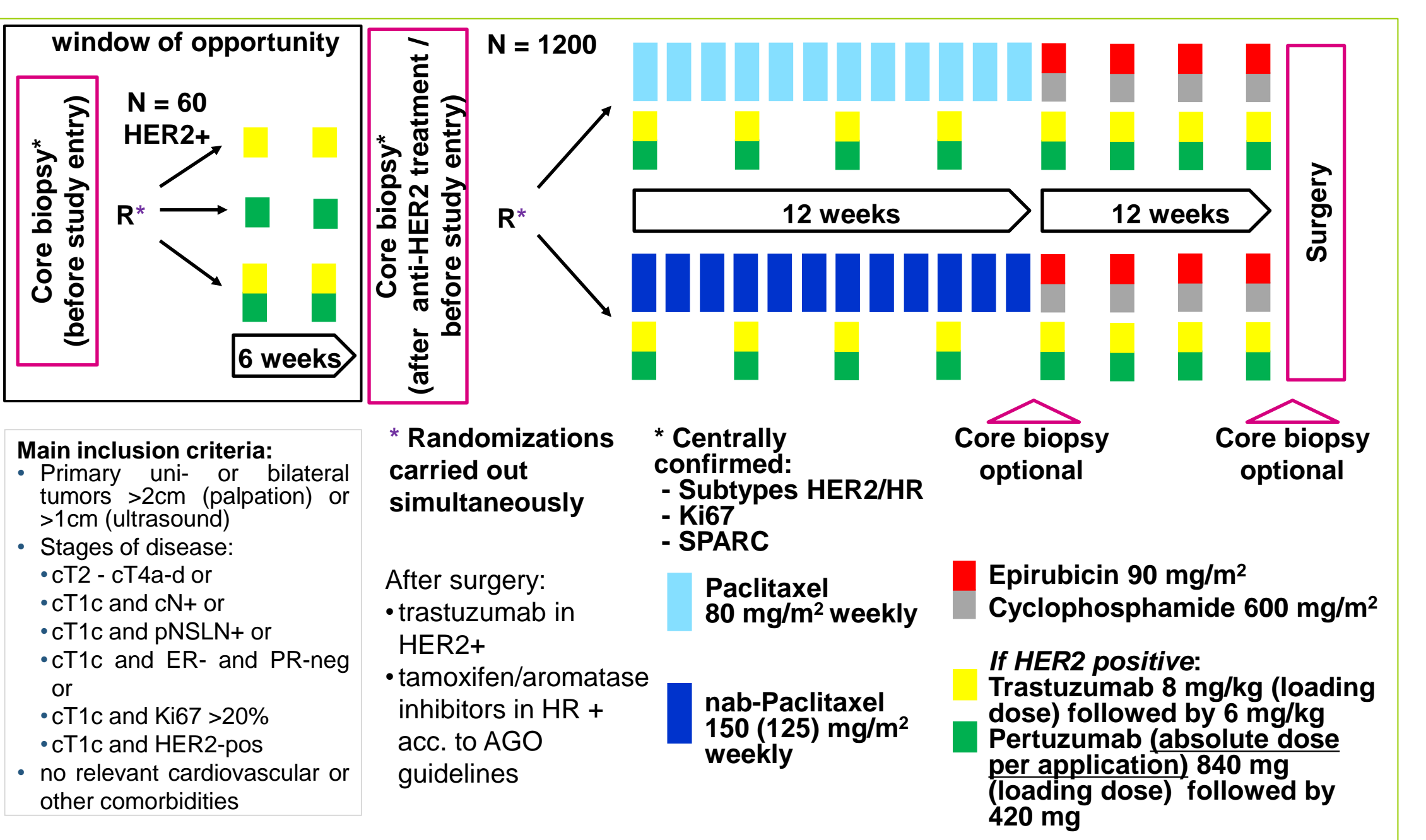
Materials and Methods

GeparSepto (NCT01583426) randomized 1206 patients to 150mg/m² nP or 80mg/m² P q1w for 12 weeks followed by 4 cycles EC q3w (Figure 1). Primary objective was pCR (ypT0 ypN0).

We report efficacy and safety of patients treated with nP 150mg/m² (nP150) before or nP 125mg/m² (nP125) after the amendment, in comparison with P 80mg/m² (P80).

For efficacy analysis, patients randomized prior to amendment (effective 28th Mar 2013) were grouped as nP150, patients randomized thereafter as nP125. For safety analysis, patients were grouped according to their dose on day 1.

Figure 1: GeparSepto study design



Results

A total of 229 patients were grouped as nP150, 377 patients as nP125. Treatment characteristics were balanced between the two nP cohorts and compared to the P80 cohort except for HER2 status and Ki67 (Table 1). Differences in pCR rates between nP125 and P80 were greatest in the overall cohort and the TNBC subgroup (Figure 2). Hematological and non-hematological toxicities are shown in Table 2. Median time to resolve peripheral sensory neuropathy (PSN) from grade 2-4 to grade ≤1 was 6 weeks for nP125 and 12.4 weeks for nP150, and from grade 3-4 to grade ≤1 17 weeks and 20 weeks, respectively (Figure 3). Taxane treatment was discontinued in 26.8% (nP150), 16.6% (nP125) and 13.3% (P80) of patients, respectively. Median relative total dose intensity (RTDI) of taxane (based on 125mg/m² for nP) was 108 (10-123)% with nP150, 99 (17-104)% with nP125 and 100 (0-136)% with P80.

Table 1: Baseline patient and tumor characteristics

Parameter	before amendment		after amendment	
	nP150 (N=229)	P80 (N=226)	nP125 (N=377)	P80 (N=374)
Age, years, median (range)	49 (28-75)	48 (26-75)	50 (21-75)	48 (22-76)
cT1-3	209 (91.7)	209 (92.9)	356 (94.4)	354 (94.7)
cN+	101 (45.5)	103 (46.2)	174 (46.8)	162 (44.4)
ER and/or PgR positive	144 (62.9)	146 (64.6)	264 (70.0)	269 (71.9)
HER2 positive	56 (24.5)	54 (23.9)	143 (37.9)	143 (38.2)
Tumor grade 3	123 (53.7)	127 (56.2)	196 (52.0)	211 (56.4)
Ductal/ductal-lobular invasive	199 (86.9)	195 (86.3)	318 (84.4)	324 (86.6)
TNBC	64 (27.9)	62 (27.4)	75 (19.9)	75 (20.1)
HER2-/HR+	109 (47.6)	110 (48.7)	159 (42.2)	156 (41.7)
Ki67 >20%	139 (60.7)	136 (60.2)	279 (74.0)	279 (74.6)
SPARC positive (IRS6-12)	42 (18.3)	40 (17.7)	55 (14.6)	54 (14.4)

Table 2: Hematological and relevant non-hematological toxicities

Adverse Event (AE)	Grade	nP150 (N=220)	nP125 (N=385)	P80 (N=601)
Anemia	any	206 (93.6)	354 (91.9)	528 (88.1)
	3-4	5 (2.3)	8 (2.1)	4 (0.7)
Leukopenia	any	209 (95.0)	358 (93.0)	550 (91.8)
	3-4	110 (50.0)	170 (44.2)	271 (45.2)
Neutropenia	any	197 (90.0)	334 (86.8)	487 (81.3)
	3-4	140 (63.9)	228 (59.2)	371 (61.9)
Thrombocytopenia	any	51 (23.2)	93 (24.2)	145 (24.2)
	3-4	2 (0.9)	3 (0.8)	3 (0.5)
Febrile neutropenia	any	10 (4.5)	18 (4.7)	24 (4.0)
	3-4	3 (1.4)	10 (2.6)	6 (1.0)
Any non-hematological AE	any	220 (100.0)	385 (100.0)	600 (99.8)
	3-4	188 (85.5)	306 (79.5)	458 (76.2)
Peripheral sensory neuropathy	any	194 (88.2)	320 (83.1)	392 (65.2)
	3-4	32 (14.5)	31 (8.1)	16 (2.7)
Hand-foot-syndrome	any	54 (24.5)	117 (30.4)	107 (17.8)
	3-4	3 (1.4)	10 (2.6)	6 (1.0)

Figure 3: Time to resolve PSN of grade 2-4 (A) or grade 3-4 (B) to grade ≤1

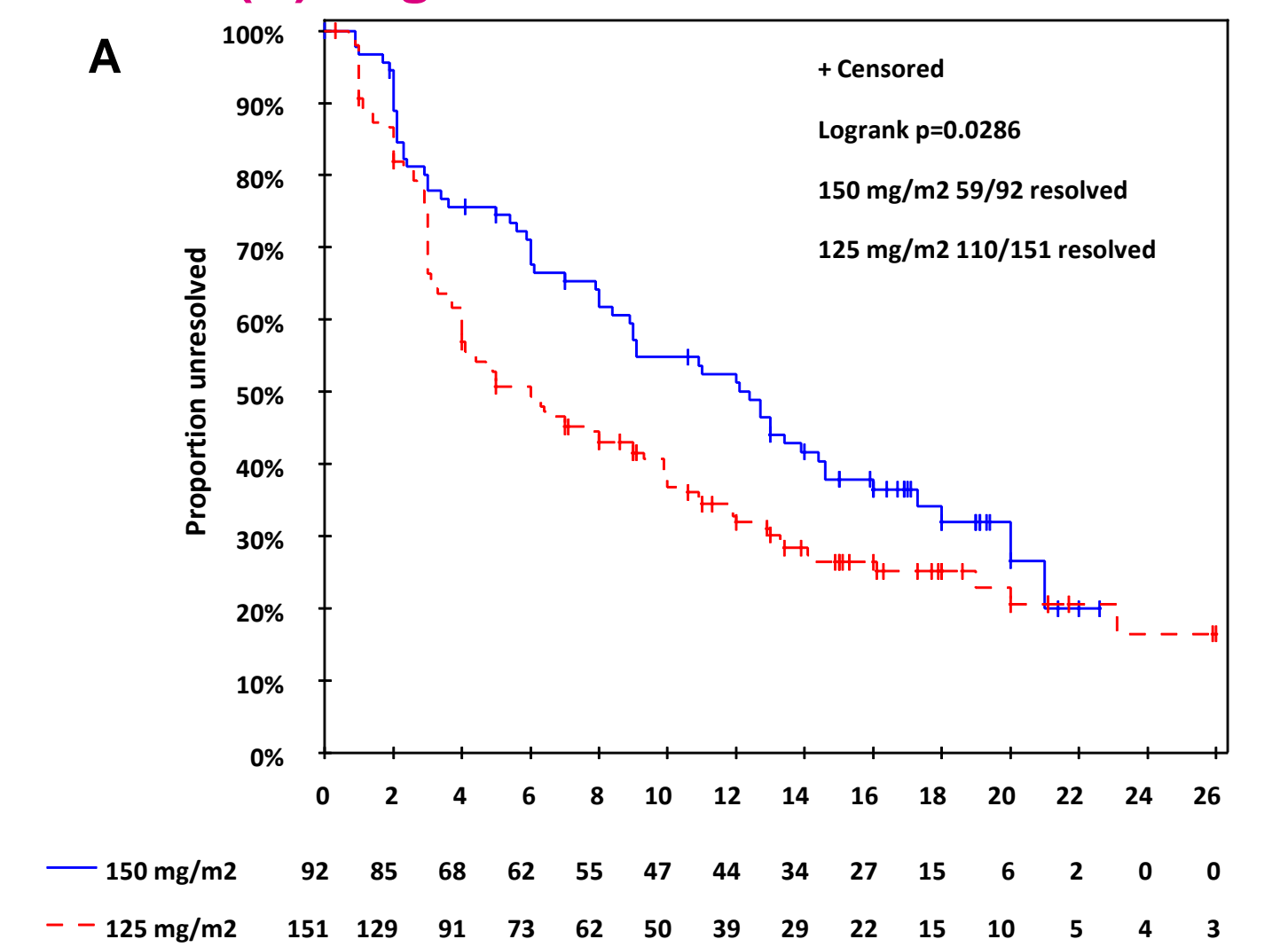
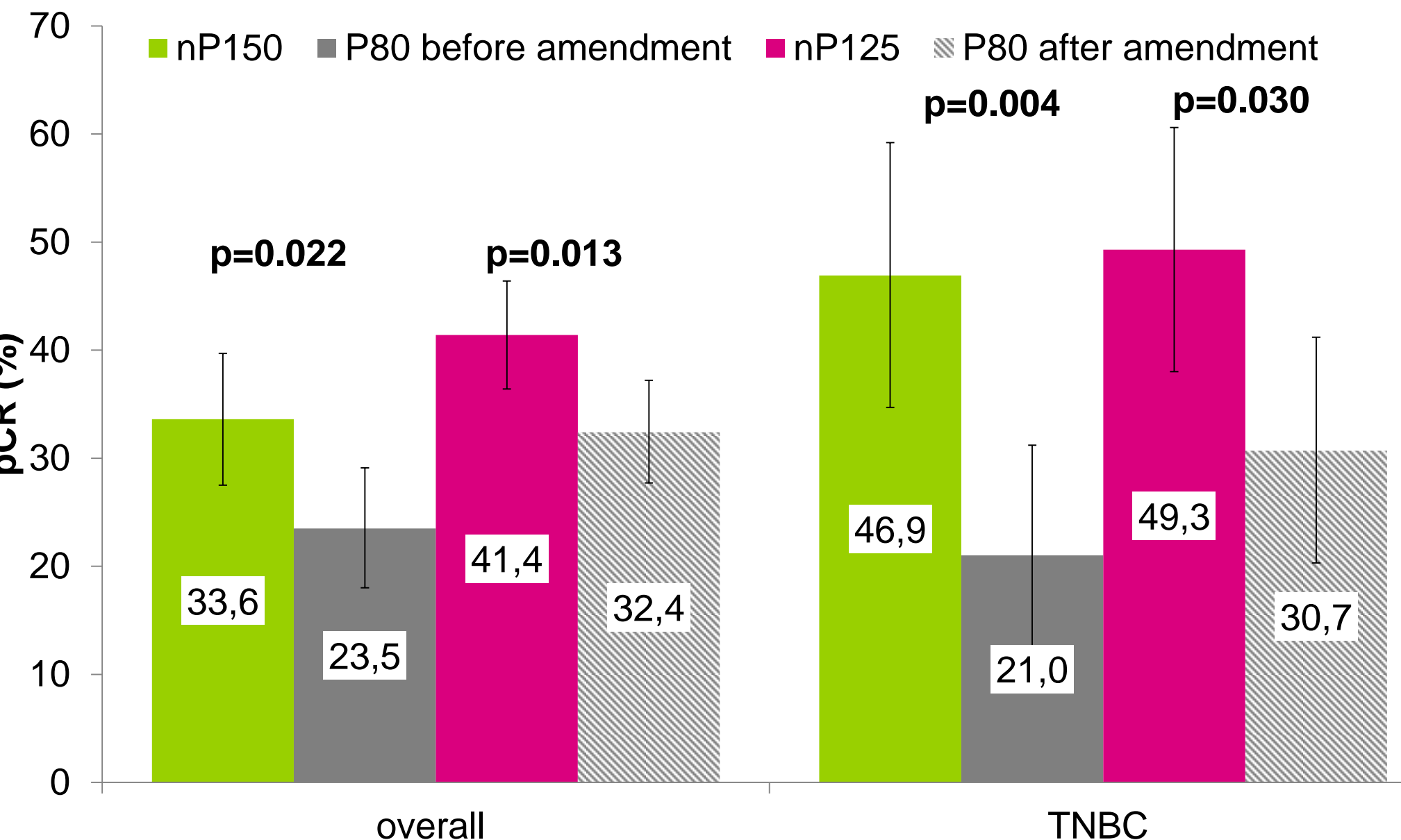


Figure 2: pCR rates according to nP dose overall and in TNBC



Conclusions

Risk-benefit ratio of nP125 was improved over nP150 with better drug adherence and RTDI, lower frequency of PSN and comparable pCR. The increased pCR rate after the amendment was observed in both arms and is probably due to differences in baseline characteristics in the two cohorts. nP125 should therefore be considered instead of nP150. Whether or not the regimen can be further improved by including a break will be investigated in the GeparX study.

