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Abstract #4593

Long-term survival analysis of the randomized phase II trial investigating the addition of carboplatin to neoadjuvant therapy for triple-negative (TNBC) and HER2-positive early breast cancer (GeparSixto)

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Background

Patients with triple negative breast cancer (TNBC) involved in the GeparSixto study showed an improved pCR rate (ypT0 ypN0) with the addition of carboplatin (Cb) to anthracycline/taxane-based neoadjuvant chemotherapy,[1] which translated in an improved early disease-free survival (DFS).[2] No difference was observed in the HER2+ subgroup for pCR and DFS by adding Cb.[2]
Here, we present the results on the long-term survival analysis.

Patients and Methods

In the GeparSixto trial, patients were treated for 18 weeks with paclitaxel 80mg/m² q1w and non-pegylated-liposomal doxorubicin (NPLD) 20mg/m² q1w (PM), concurrently with bevacizumab 15mg/kg q3w if TNBC or trastuzumab 6(8)mg/kg q3w and lapatinib 750mg daily if HER2+. 595 patients were randomised 1:1 to receive concurrently Cb AUC 1.5-2.0 q1w (reduced to 1.5 by an amendment after 330 patients) vs no Cb, stratified by subtype (HER+ vs TNBC). 588 patients started treatment.
Primary objective was pCR (ypT0 ypN0). DFS, distant DFS (DDFS) and overall survival (OS) were secondary objectives. Analyses according to pCR (subgroups and multivariate analysis) are 6 months landmark analysis.

Figure 1. GeparSixto study design

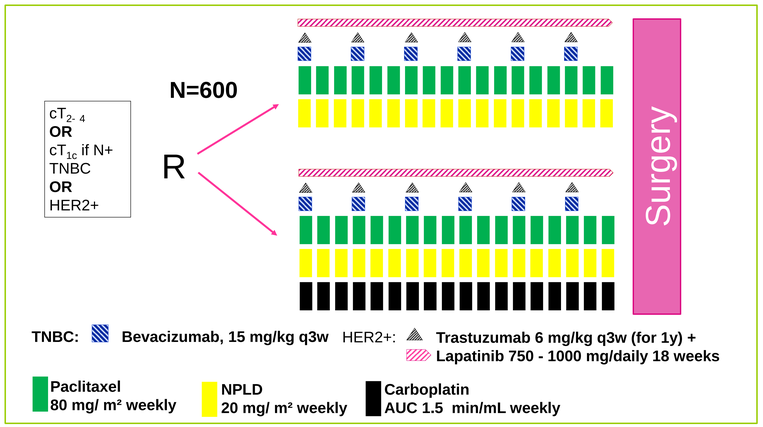


Table 1. Selected baseline characteristics

Baseline Characteristics	PM N=293 %	PMCb N=295 %
age (median yrs)	47	48
cT3-4	18.8	16.9
cN+	42.4	37.6
Grade 3	64.5	65.1
TNBC (N=315)	53.6	53.6
HER2+ (N=273)	46.4	46.4
HER2+/HR-	18.8	18.3
HER2+/HR+	27.6	28.1

Results

After a median follow-up of 47.3 months (range 1.7-62.8) overall no significant difference in DFS (Figure 2A) and in DDFS (HR=0.83 [95%CI 0.56-1.22]; p=0.336) was seen with PMCb vs PM. However, patients with TNBC had a significantly better DFS (Figure 2B) and DDFS (HR=0.50 [95%CI 0.29-0.86]; p=0.013) when treated with PMCb. No difference was seen in patients with HER2+ disease (DFS Figure 2C; interaction test p=0.022; DDFS HR=1.56 [95% CI 0.86-2.83]; p=0.145; interaction test p=0.006). A trend towards a better OS was observed in patients with TNBC when treated with PMCb (Figure 2E). OS was not different between the two arms, neither overall nor in HER2+ disease (Figure 2D-F). Multivariable analysis comfirms that pCR (pCR vs no pCR) independently predicted DFS (Figure 3A), DDFS (HR=0.23 [95%CI 0.12-0.44]; p<0.001), and OS (Figure 3B).

Figure 2. DFS and OS overall and in patients with TNBC and HER2+ disease

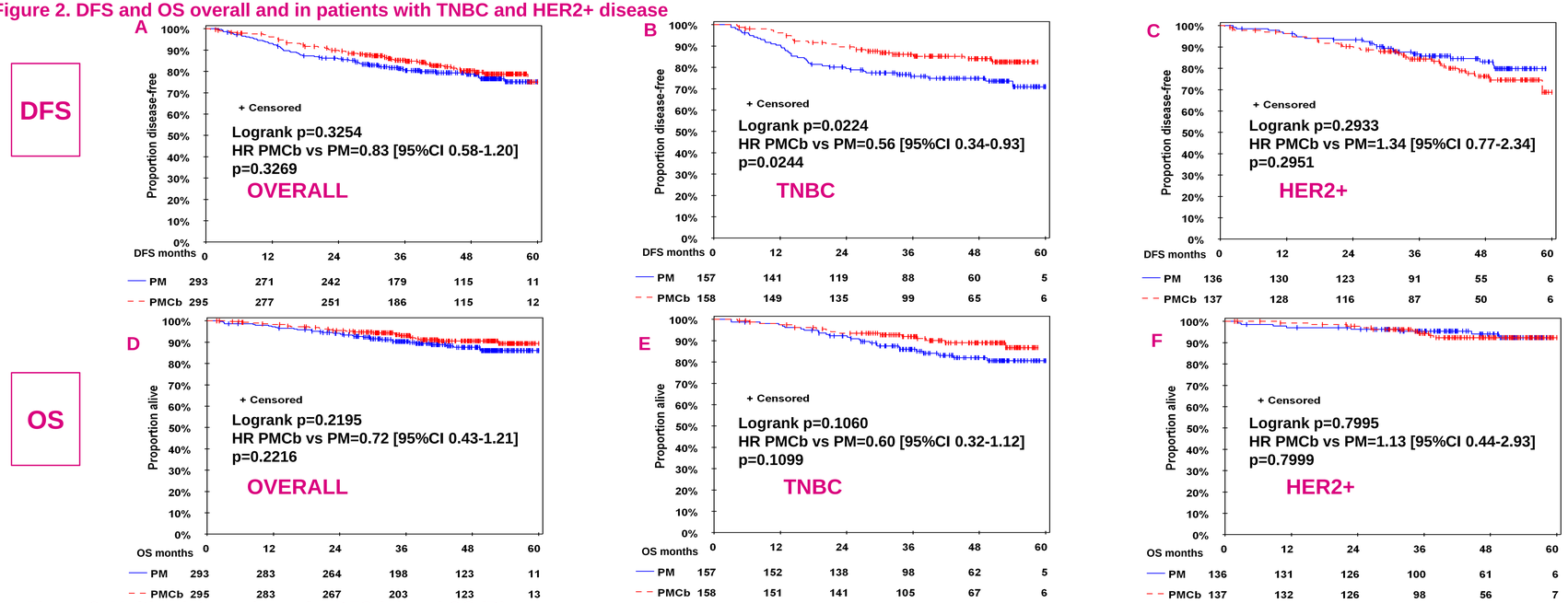
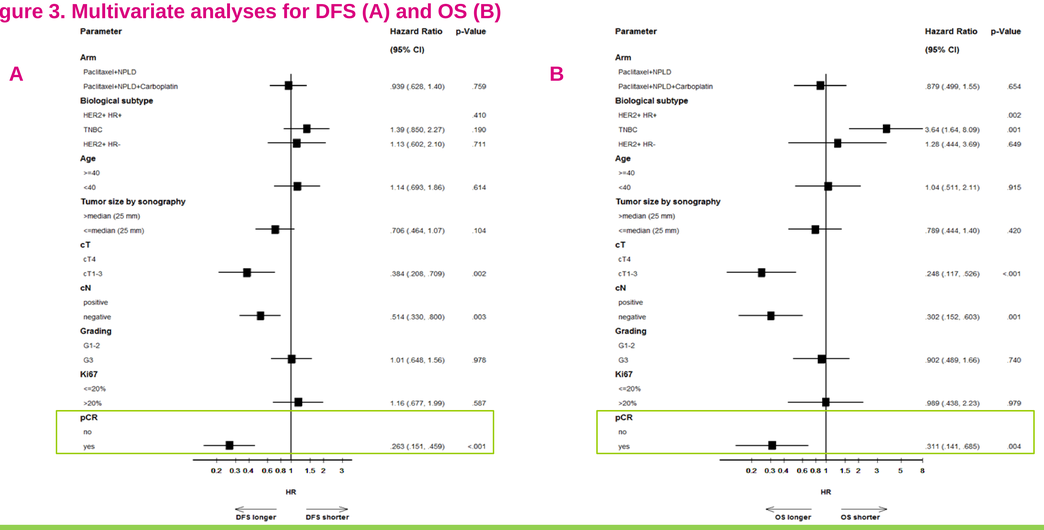


Figure 3. Multivariate analyses for DFS (A) and OS (B)



Conclusions

Long-term survival analysis supports the neoadjuvant use of Cb in TNBC. The value of pCR as a strong predictor of DFS and OS has been confirmed.

References

1. von Minckwitz G, Schneeweiss A, Loibl S et al. Neoadjuvant carboplatin in patients with triple-negative and HER2-positive early breast cancer (GeparSixto; GBG 66): a randomised phase 2 trial. Lancet Oncol. 2014;15:747-56.
2. Hahnen E, Lederer B, Hauke J, Germline Mutation Status, Pathological Complete Response, and Disease-Free Survival in Triple-Negative Breast Cancer: Secondary Analysis of the GeparSixto Randomized Clinical Trial. JAMA Oncol. 2017

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