Long-term survival of a randomised, open-label, phase II study comparing the efficacy and safety of cabazitaxel versus weekly paclitaxel given as neoadjuvant treatment in patients with operable triple-negative or luminal B/HER2-negative breast cancer (GENEVIEVE)

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Background

The GENEVIEVE study compared the pathological complete response (pCR) rate in patients with operable triple-negative (TNBC) or luminal B/human epidermal growth factor receptor 2 (HER2)-negative breast cancer (BC) treated with either cabazitaxel or weekly paclitaxel. Primary analyses showed no short-term effect of cabazitaxel in TNBC or luminal B/HER2-negative primary BC, while there seemed to be no differences in drug exposure and patient compliance between the two arms[1]. Here, we report long-term survival data.

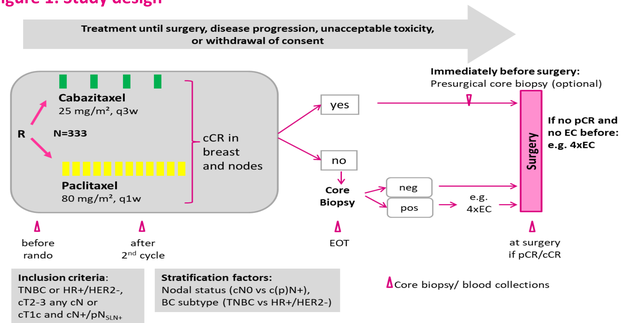
Patients and Methods

Study design: GENEVIEVE (NCT01779479) study randomised patients with cT2-3 any cN or cT1, cN+/pN_{SLN+} and centrally confirmed TNBC or luminal B/HER2-negative BC to receive either cabazitaxel 25 mg/m^2 q3w for 4 cycles or paclitaxel 80 mg/m^2 weekly for 12 weeks. All patients had the opportunity to receive anthracycline-containing chemotherapy before (if core biopsy detected invasive tumour residuals after end of study treatment) or after surgery (Figure 1).

Endpoints: Primary endpoint was pCR (ypT0/is ypN0/+) rate. Secondary time-to-event endpoints included invasive disease-free survival (iDFS), distant disease-free survival (DDFS) and overall survival (OS). Long-term endpoints were defined as the time in months between randomization and first event.[2]

Statistical considerations: Time-to-event endpoint analyses were planned with mature follow-up of at least 5 years after a follow-up completeness of at least 70%. Differences in iDFS, DDFS and OS between treatment arms were analyzed by the log-rank-test and depicted by Kaplan-Maier curves. Cox proportional hazard model was used to estimate hazard ratio of cabazitaxel arm to paclitaxel arm with 95% CI. The significance level was set to a two-sided α=0.05.

Figure 1: Study design



Results

Figure 2: Consort flow

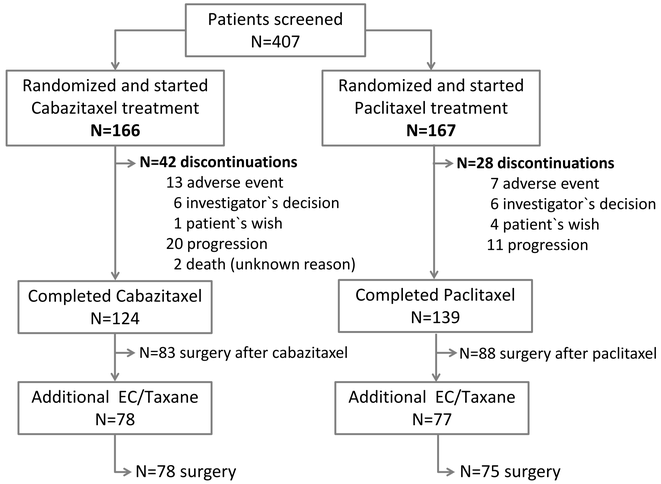
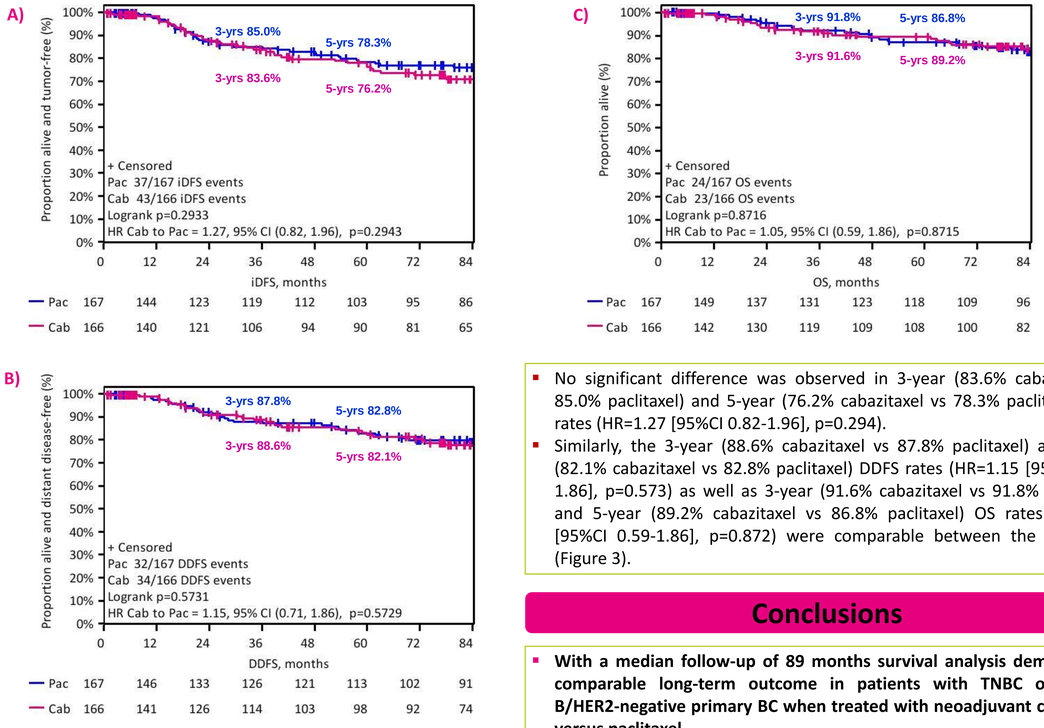


Table 1: Recurrence events

First event of the patient	Cabazitaxel N=166 N(%)	Paclitaxel N=167 N(%)	Overall N=333 N(%)
Patient with events	43 (25.9)	37 (22.2)	80 (24.0)
Site of first invasive disease event			
Distant recurrence	14 (8.4)	14 (8.4)	28 (8.4)
Invasive locoregional relapse	15 (9.0)	13 (7.8)	28 (8.4)
Invasive contralateral breast cancer	2 (1.2)	1 (0.6)	3 (0.9)
Secondary malignancy	5 (3.0)	5 (3.0)	10 (3.0)
Death without previous event	7 (4.2)	4 (2.4)	11 (3.3)

Figure 3: Kaplan-Meier estimates for iDFS (A), DDFS (B) and OS (C) according to treatment arm



Abbreviations: Cab, cabazitaxel, Pac, paclitaxel; HR, hazard ratio

- Between April 2013 and June 2015, 333 patients were randomised and started treatment with 74.7% and 83.2% of patients completing treatment in the cabazitaxel and paclitaxel arms, respectively (Figure 2). Baseline characteristics were well balanced. Patients in cabazitaxel arm had a significantly lower pCR rate compared to the paclitaxel arm (1.2% vs 10.8%; p=0.001).[1]
- After a median follow-up of 89.3 months (range 87.2-90.6), overall 80 iDFS events (43 after cabazitaxel and 37 after paclitaxel) and 47 deaths (23 after cabazitaxel and 24 after paclitaxel) were reported.
- Recurrence events which occurred as first iDFS event are listed in Table 1.
- No significant difference was observed in 3-year (83.6% cabazitaxel vs 85.0% paclitaxel) and 5-year (76.2% cabazitaxel vs 78.3% paclitaxel) iDFS rates (HR=1.27 [95%CI 0.82-1.96], p=0.294).
- Similarly, the 3-year (88.6% cabazitaxel vs 87.8% paclitaxel) and 5-year (82.1% cabazitaxel vs 82.8% paclitaxel) DDFS rates (HR=1.15 [95%CI 0.71-1.86], p=0.573) as well as 3-year (91.6% cabazitaxel vs 91.8% paclitaxel) and 5-year (89.2% cabazitaxel vs 86.8% paclitaxel) OS rates (HR=1.05 [95%CI 0.59-1.86], p=0.872) were comparable between the two arms (Figure 3).

Conclusions

- **With a median follow-up of 89 months survival analysis demonstrated comparable long-term outcome in patients with TNBC or luminal B/HER2-negative primary BC when treated with neoadjuvant cabazitaxel versus paclitaxel.**
- **The significantly lower pCR rate in patients treated with cabazitaxel did not negatively impact survival rates.**

References

1. Kümmel et al. Eur J Cancer 2017
2. Hudis et al. J Clin Oncol. 2007

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