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Dose-dense Paclitaxel with Empegfilgrastim vs weekly Paclitaxel in luminal B HER2-negative early breast cancer PULSE trial

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Background

- Luminal B HER2-negative breast cancer (BC) is an aggressive subtype with lower chemosensitivity than HER2-positive or triple-negative disease. Standard neoadjuvant chemotherapy (NCT), consisting of doxorubicin-cyclophosphamide (ACq21 or ddACq14) followed by weekly paclitaxel, yields a pathological complete response (pCR) in approximately 20% of patients, which is significantly lower than in other subtypes. Dose-dense (dd) chemotherapy has been shown to improve outcomes in high-risk BC and even in hormone receptor-positive/HER2-negative patients.
- Paclitaxel can be delivered weekly, biweekly (dose-dense) or every 3 weeks. Evidence suggests that more frequent (weekly or biweekly) paclitaxel dosing improves long term outcomes compared to 3-week schedule.
- However, no prospective studies have directly compared weekly and biweekly paclitaxel schedules in luminal B early BC. This exploratory trial aims to detect clinically meaningful differences in efficacy of a biweekly paclitaxel schedule supported by empegfilgrastim in comparison to historical weekly paclitaxel and provide early data to inform the planning of a future phase III trial.

Aim

- To determine whether a biweekly paclitaxel regimen is not inferior in efficacy (as measured by pCR rate) to the standard weekly paclitaxel regimen in patients with luminal B HER2-negative early or locally advanced BC receiving NCT.

Study Design

- Prospective, single-center, open-label, non-inferiority phase II trial using historical control.
- Patients in the intervention group will be treated prospectively and compared to a historical cohort treated with weekly paclitaxel.
- Matching will be performed in a 1:3 ratio using key clinical and pathological variables (age, clinical stage, Ki-67, tumor grade, ER and PR expression).

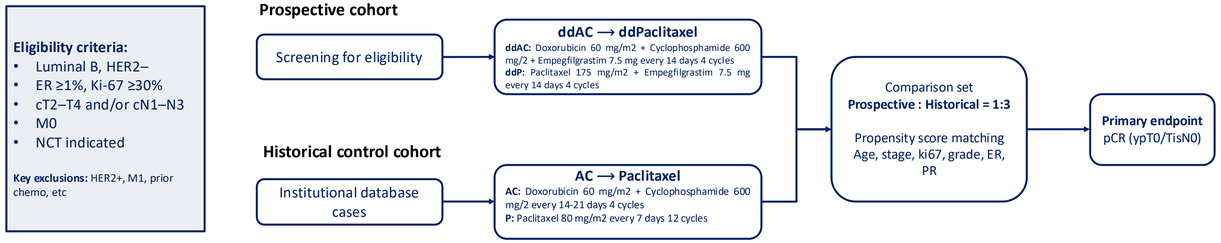


Figure 1. Trial design

Treatment

- All patients in the prospective arm will receive 4 cycles of ddAC (doxorubicin 60 mg/m² + cyclophosphamide 600 mg/m² every 14 days) with empegfilgrastim 7.5 mg as G-CSF support. This is followed by 4 cycles of biweekly paclitaxel (175 mg/m² every 14 days) with empegfilgrastim 7.5 mg support.
- The historical control arm will include patients previously treated with AC (q21 or q14) followed by weekly paclitaxel (80 mg/m² weekly ×12).

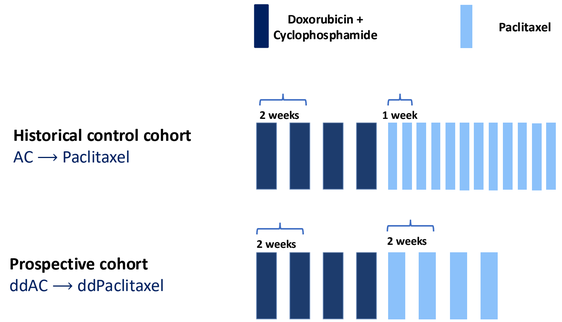


Figure 2. Treatment timeline graph.

Population

- Eligible patients are adult women (≥18 years) with histologically confirmed luminal B breast cancer, defined as estrogen receptor (ER≥1%) positive, HER2-negative tumors with Ki-67 ≥30%. Patients must have early or locally advanced disease (T2-T4 and/or N1-N3, M0) for which NCT is appropriate.
- Key exclusions include HER2-positive tumors, metastatic disease and any prior chemotherapy for the current cancer.

	Baseline	Mid-NCT	Post-NCT
Biopsy	•		
Ultrasound	•	•	•
Mammography	•		•
Breast scintigraphy	•	•	•
MRI *(optional)*	•		•
Clip placement *(breast)*	•		
I^{125} marker placement *(lymph nodes)*	•		
IHC	•		•

Table 1. Schedule of clinical procedures and tumor response assessment matrix

Endpoints

- **Primary endpoint** is pCR rate, defined as no residual invasive cancer in breast and lymph nodes (ypT0/is, ypN0) at surgery.
- **Secondary endpoints** include RCB 0-I rate, event-free survival, relative dose intensity, breast conservation rate, treatment completion rates, and safety outcomes such as neuropathy, neutropenia, and febrile neutropenia.

Statistical analysis

- Analysis will be conducted on an intention-to-treat basis. The primary endpoint will be compared between groups using a one-sided 95% confidence interval to evaluate non-inferiority, with a non-inferiority margin of 10%. Propensity score matching (1:3) will balance baseline characteristics. Logistic regression adjusted for matching strata will estimate odds ratios. Secondary endpoints will be analyzed using Kaplan-Meier estimates, log-rank tests, and Cox proportional hazards models for time-to-event outcomes.
- **Sample Size Justification.** Assuming a pCR rate of 20% in the historical weekly paclitaxel group and a non-inferiority margin of 10%, a sample size of 102 patients in the prospective biweekly arm and 307 matched historical controls (1:3 ratio) achieves 80% power with one-sided α=0.05.

Discussion

- Although dd scheduling improves outcomes in high-risk breast cancer, its specific value during the taxane phase for hormone receptor–positive disease has not been clearly established. A biweekly paclitaxel regimen supported by long-acting G-CSF may provide an optimal balance between dose intensity, treatment adherence, and toxicity control. ddPaclitaxel potentially could offer practical and clinical advantages: fewer treatment visits, simplified supportive care, and improved resource utilization, while maintaining oncologic effectiveness.
- Results of this trial may guide more precise selection of taxane schedules in HR-positive early breast cancer by clarifying whether biweekly paclitaxel with structured G-CSF support can sustain or improve treatment efficacy while reducing patient burden and optimizing neoadjuvant care pathways.

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