Twelve Weekly Paclitaxel–Carboplatin with Trastuzumab and Pertuzumab: De-Escalation Strategy in Early HER2-Positive Breast Cancer

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Background

- Standard therapy for early HER2-positive breast cancer consists of 18 weeks of carboplatin, docetaxel, trastuzumab, and pertuzumab (TCHP)
- De-escalation strategies that maintain efficacy while improving tolerability are of interest, particularly for stage II disease or older patients.
- The outcomes of a shortened 12-week regimen of paclitaxel and carboplatin given weekly, together with trastuzumab and pertuzumab (12wTCHP), remain unknown

Method

- Retrospective cohort study.
- 12wTCHP included weekly paclitaxel (80 mg/m²) and carboplatin (AUC 1.5 or 2) for 12 weeks, in combination with HP.
- Postoperative treatment was determined by the treating physician and typically consisted of trastuzumab with or without pertuzumab in patients achieving pathological complete response (pCR), and T-DM1 in those with residual disease. Patients with estrogen receptor (ER) positive breast cancer also received adjuvant endocrine therapy.

Patients' characteristics

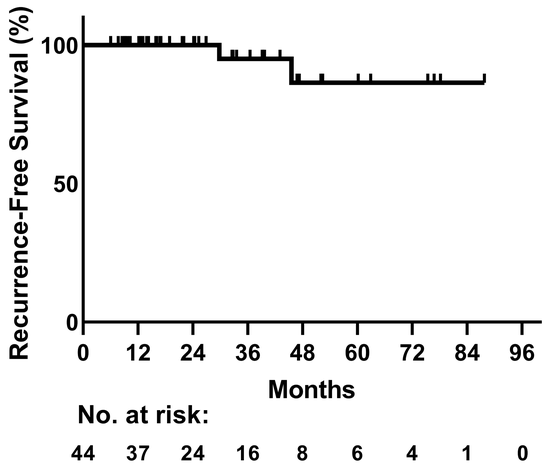
	stage IIA n=32	Stage IIB/III n=12	p	All n=44
Age, median (IQR)	59 (50-69)	77 (66-80)	**.001**	65 (52-75)
Premenopausal, n (%)	10 (32)	1 (8)	.139	11 (26)
ECOG 0, n (%)	25 (93)	6 (55)	**.014**	31 (82)
IDC, n (%)	30 (94)	11 (92)	.000	41 (93)
ER pos, n (%)	21 (66)	7 (58)	.732	28 (64)
KI67, median (IQR)	33 (20-60)	35 (22-55)	.969	33 (20-60)
Tumor size in cm. median (IQR)	2.6 (2.4-3.5)	2.9 (1.9-3.6)	.594	2.6 (2.3-3.5)

- The cohort included two distinct clinical subgroups: stage IIA patients and older or patients with comorbidities with more advanced disease, who had differing baseline characteristics, treatment tolerability.

Results

Kaplan–Meier curve for recurrence-free survival

- The median follow-up was 25 months.
- Two patients (5%) experienced a recurrence: one with stage IIA ILC, and the other with stage III IDC disease.
- **None of the 30 patients with stage IIA IDC experienced a recurrence.**



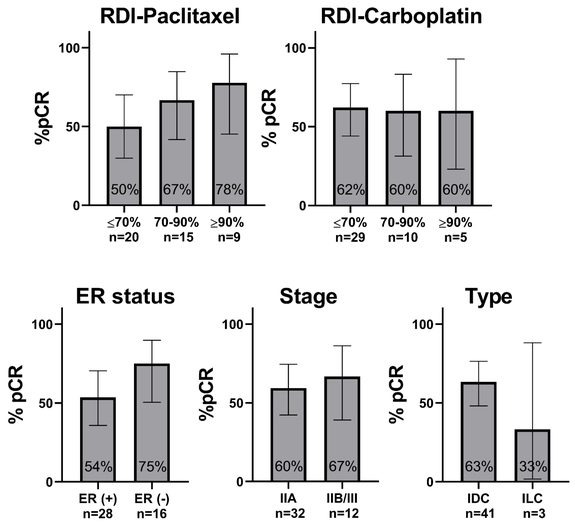
Treatment toxicity

	Grage 1-2, n (%)	Grade 3-4 n (%)
Anemia, n (%)	36 (90)	2 (5)
Thrombocytopenia, n (%)	11 (28)	2 (5)
Neutropenia, n (%)	15 (38)	8 (20)
Neutropenic fever, n (%)	---	2 (5)
Elevated liver enzymes, n (%)	19 (46)	2 (5)
Diarrhea, n (%)	25 (60)	8 (19)
Nausea, n (%)	20 (46)	0 (0)
Peripheral neuropathy, n (%)	20 (46)	4 (9)
Asthenia, n (%)	25 (66)	3 (8)
Drop in LVEF, n (%)	1 (2)	0 (0)

No treatment related death occurred

pCR rates across patient subgroups

- The overall pCR rate was 61% (95% CI: 47–74); 54% of patients with ER-positive tumors and 75% of those with ER-negative tumors (p = 0.208).
- A non-significant trend toward a higher pCR rate in patients who maintained a higher paclitaxel relative dose intensity (RDI. p = 0.314), but not higher.



Conclusions and limitations

- This is the first report evaluating a de-escalated 12-week regimen of paclitaxel and carboplatin given weekly as neoadjuvant therapy for early-stage HER2-positive breast cancer.
- Pathologic complete response rates were comparable to standard 18-week TCHP, reaching 54% in ER-positive and 75% in ER-negative tumors.
- The regimen may be a reasonable alternative for patients with small T2N0 tumors or significant comorbidities.
- The study was limited by its small cohort size and retrospective nature limits

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