Impact of Dose Intensity on Pathological Complete Response in Early-Stage HER2-Positive Breast Cancer

Shaheed AlHumiued, PharmD[1], Batool Albaqshi, PharmD[2], Hider Abbas, MD[3], Ahmed Alamer, PharmD, BC-ADM[4] Shareefa Alonaizi, PharmD[5], Rehab Alyousef, PharmD[6], Fatemah Alqattan, PharmD[7], Abdul Salam, PhD[8], Fatimah Almulihum, BSc health management [9]

[1, 2] Department of clinical pharmacy, KFSH-D - King Fahad Specialist Hospital, [3]Medical Oncology, KFSH-D, [4] Clinical pharmacy, Prince Sattam Bin Abdulaziz University, [5, 6] Clinical pharmacy, Imam Abdulrahman Bin Faisal University, [7] Clinical pharmacy, KFU - King Faisal University, [7] Population health management, KFSH-D - King Fahad Specialist Hospital , [8] Epidemiology and Biostatistics Administration, KFSH-D

Abstract

Chemotherapy dose intensity (DI) is a critical determinant of treatment efficacy in early-stage HER2-positive breast cancer, with reductions below 0.85 linked to poorer survival and lower pathological complete response (pCR) rates. This retrospective study evaluated the association between DI of the neoadjuvant TCHP regimen (docetaxel, carboplatin, trastuzumab, pertuzumab) and pCR outcomes in 149 patients treated at a tertiary oncology center in Saudi Arabia between 2017 and 2023.The overall pCR rate was 60.4%. Higher carboplatin DI independently predicted increased odds of achieving pCR (OR 1.01; 95% CI, 1.00–1.04; p = 0.029), while hormone receptor positivity was associated with lower odds (OR 0.23; 95% CI, 0.09–0.61; p = 0.004). No significant differences in pCR were observed for docetaxel or carboplatin when comparing DI ≥85% vs. <85%. Among all agents, Pertuzumab demonstrated the greatest dose reduction, and both Docetaxel and Pertuzumab were associated with the highest frequency of treatment delays, mainly due to drug rescheduling. Maintaining dose intensity and minimizing logistical delays are essential for optimizing pCR outcomes and improving real-world treatment delivery in early-

Introduction

- Chemotherapy dose intensity (DI), defined as the amount of drug administered per unit of time, is a critical determinant of treatment efficacy in curable malignancies.
- A reduction in **(DI) below 0.85 has been associated with inferior survival outcomes and lower rates of (pCR).** However, maintaining optimal DI throughout treatment remains a challenge in real-world practice.
- Pathological complete response is suggested as a surrogate endpoint for long-term Outcomes.
- Studies have shown variable pathological response rates in patients receiving neoadjuvant TCHP with differing dose intensities. **However, there is still limited data correlating pCR with specific agent-level DI in real-world.**

Methods and Materials

- A retrospective observational cohort single-center study.
- A total of 149 patients met the inclusion criteria between 2017 -2023 using institutional health records.
- **Criteria:**

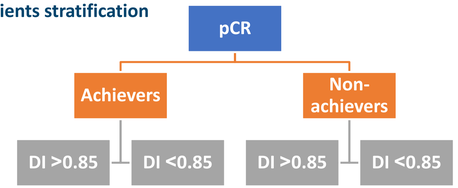
Inclusion criteria	Exclusion criteria
I. Female patient	I. Patients who received previous BC surgery due to local recurrence after curative surgery or who underwent palliative surgery were excluded.
II. ⩾18 years old	
III. Confirm diagnosis with breast stage II–III HER2 positive (IHC +3) or (IHC +2) with +ve Fish test.	
IV. Patients who received TCHP (Docetaxel, Carboplatin, Trastuzumab, Pertuzumab) neoadjuvant intravenous chemotherapy between 2017 -2023.	

- **Outcomes:**

Primary Outcome: is association between chemotherapy (DI) and (pCR) at surgery. Patients were stratified by pCR status and DI thresholds (<85% vs. ≥85%) to evaluate differences in treatment outcomes.

Secondary outcomes included analysis of factors contributing to dose reductions and treatment delays, as well as evaluation of survival outcomes such as disease-free survival (DFS) and overall survival (OS).

Figure 1. Patients stratification



Results

- Total patients: 149
- Median RDI <0.85 rate per patient: 3 (IQR: 2–4)
- Deviation from protocol (Paclitaxel): 43.6%
- Median Dose Intensity (25th–75th percentile):
  - Pertuzumab: 72.2 [50.0–83.3]
  - Trastuzumab: 100.0 [91.7–100.0]
  - Docetaxel: 83.4 [16.7–99.7]
  - Carboplatin: 86.0 [74.5–93.8]
- Pathologic Complete Response (pCR): Achieved in 60.4% of patients.

Table 2. Characteristics of patients achieving pCR versus non pCR achievers

Variable	pCR not achieved(n = 59)	pCR achieved (n = 90)	p-value
Age in Years Group, n (%)			0.299
18–28	0 (0.0)	4 (4.4)	
29–39	17 (28.8)	19 (21.1)	
40–59	32 (54.2)	53 (58.9)	
>59	10 (16.9)	14 (15.6)	
BMI (kg/m²), mean (SD)	31.07 (7.43)	29.14 (5.13)	0.063
Lymph Node Involvement, n (%)	43 (72.9)	66 (73.3)	1.000
ECOG, n (%)			0.721
0	23 (39.0)	45 (50.0)	
1	23 (39.0)	27 (30.0)	
2	1 (1.7)	2 (2.2)	
3	2 (3.4)	2 (2.2)	
No data	10 (16.9)	14 (15.6)	
HR Positive Status, n (%)	48 (81.4)	41 (45.6)	<0.001
AJCC Stage, n (%)			0.817
I	8 (13.6)	12 (13.3)	
II	20 (33.9)	35 (38.9)	
III	31 (52.5)	43 (47.8)	

Results

Figure 2. Median dose intensity by pCR

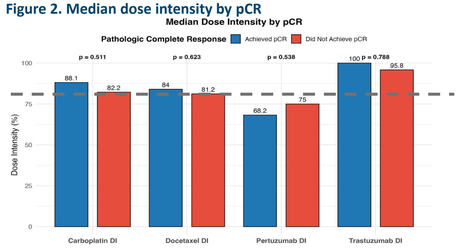
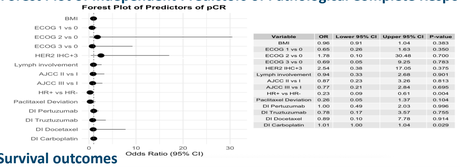


Figure 3. Forest Plot of Independent Predictors of Pathological Complete Response (pCR).



Variable	OR	Lower 95% CI	Upper 95% CI	P-value
BMI	0.96	0.91	1.04	0.383
ECOG 1 vs 0	0.65	0.26	1.63	0.360
ECOG 2 vs 0	1.78	0.10	30.48	0.700
ECOG 3 vs 0	0.69	0.05	9.25	0.783
HER2 IHC+3	2.54	0.38	17.05	0.375
Lymph involvement	0.94	0.33	2.68	0.901
AJCC II vs I	0.84	0.23	3.04	0.797
AJCC III vs I	0.77	0.21	2.84	0.695
HR+ vs HR-	0.23	0.09	0.61	0.004
Paclitaxel Deviation	0.26	0.05	1.37	0.104
DI Pertuzumab	1.00	0.49	2.03	0.996
DI Trastuzumab	0.78	0.17	3.57	0.755
DI Docetaxel	0.89	0.10	7.78	0.914
DI Carboplatin	1.01	1.00	1.04	0.029

Table 3. Survival outcomes

Outcome	No RDI (N=28)	RDI (N=121)	P value
pCR	17 (39.3%)	48 (39.7%)	1.000
Disease Free	17 (60.7%)	66 (54.5%)	0.703
Overall survival	27 (96.4%)	116 (95.8%)	1.000

Discussion

- The overall **(pCR) rate was 60.4%**. This is favorable, exceeding the rate reported in the KRISTINE trial.
- Relative Dose Intensity had no significant impact on pCR (P=1.000). Disease-free survival (54.5%, P=0.703), and overall survival (95.8%, P=1) within RDI arm.

Conclusions

In this cohort, **Carboplatin DI** was the only independent predictor of achieving pCR. **HR positivity** and **protocol deviation to paclitaxel** negatively impacted outcomes. Addressing **system barriers** causing delays (e.g., rescheduling for Docetaxel/Pertuzumab) is critical for treatment outcomes. Large studies are needed.

Contact

Shaheed AlHumiued
KFSH-D
Email: Shaheed.kh@hotmail.com
Website:
Phone: +966 54 444 7433

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