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A Comparison of Recist 1.1 and the Side Effects of Neoadjuvant Chemotherapy Based on Anthracyclines and Taxane in Patients with Advanced Local-Stage Breast Cancer at Prof. Dr. R.D. Kandou General Hospital

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Abstract

Breast cancer remains a major cause of cancer-related morbidity and mortality among women, and locally advanced disease continues to pose significant therapeutic challenges. Neoadjuvant chemotherapy is commonly administered to reduce tumor burden and improve surgical operability, with anthracycline- and taxane-based regimens being widely used. This study aimed to compare the effectiveness and adverse effects of anthracycline-based and taxane-based neoadjuvant chemotherapy in patients with locally advanced breast cancer at Prof. Dr. R. D. Kandou General Hospital. An observational analytic study with a prospective cohort design was conducted involving 27 female patients, comprising 11 patients who received anthracycline-based chemotherapy and 16 patients who received taxane-based chemotherapy. Tumor response was assessed using Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1, while adverse events were evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE). The results showed that partial response was the predominant outcome in both groups, occurring in 81.82% of patients in the anthracycline group and 75% of patients in the taxane group. The Mann–Whitney test revealed no significant difference in treatment effectiveness between the two regimens ($p = 0.708$). Most adverse effects were mild to moderate, although toxicity patterns differed between the groups. In conclusion, both regimens demonstrated comparable effectiveness, while treatment selection should consider patient characteristics, organ function, tolerability, and regimen-specific adverse-effect risks. These findings support individualized regimen selection based on therapeutic efficacy and anticipated toxicity profiles.

INTRODUCTION

Breast cancer (BC) is the most common type of cancer among women worldwide. According to Global Cancer Statistics (GLOBOCAN) 2022 data, approximately 2.5 million new cases of breast cancer were reported, accounting for 11.6% of all cancer diagnoses among women globally (Bray et al., 2024). Breast cancer ranked first among all cancer types in Indonesia, with 65,858 cases (16.6%), and caused the second-highest mortality rate after lung cancer, with 22,430 deaths (9.6%) (Rusli et al., 2021; Dwyer, 2023). Breast cancer remains a major contributor to cancer-related mortality despite advances in early detection and therapeutic approaches. According to research by Gautama (2022) over a 30-year period, data collected from several teaching hospitals in Indonesia indicated that 68–73% of breast cancer patients presented to healthcare facilities at advanced stages. This proportion has remained relatively stable despite improvements in early detection and treatment strategies. Meanwhile, data from Prof. Dr. R. D. Kandou General Hospital, Manado, between 2013 and 2014 showed that 96 of 151 cases (63.6%) were diagnosed at stage IV (Rondonuwu et al., 2016).

The principle of breast cancer management is multimodal, involving both locoregional and systemic treatment approaches. Surgery remains the primary treatment modality, particularly for patients with early-stage disease (Alkabban & Ferguson, 2023). In locally advanced breast cancer, where optimal locoregional treatment may not initially be feasible, systemic therapy becomes an important therapeutic option. One systemic treatment approach is neoadjuvant chemotherapy, which aims to reduce tumor size, improve surgical feasibility, and eradicate micrometastatic cancer cells that may have entered the circulation (Arredondo et al., 2020; Chen et al., 2023; Topalian et al., 2023; Yao et al., 2026).

According to the National Comprehensive Cancer Network (NCCN) guidelines, the primary objective of neoadjuvant chemotherapy is to reduce tumor size and increase the likelihood of complete surgical resection. However, neoadjuvant chemotherapy should not be administered for widely invasive carcinoma in situ or for tumors that are non-palpable and cannot be clinically assessed (Dwyer, 2023).

Based on NCCN and PERABOI guidelines, neoadjuvant chemotherapy options for breast cancer include anthracycline-based regimens (doxorubicin or epirubicin) and taxane-based regimens (paclitaxel or docetaxel). These two classes represent some of the most active cytotoxic agents against early-stage and advanced breast cancer and are commonly used as initial treatment strategies for patients with inflammatory breast cancer (IBC) and/or metastatic breast cancer (MBC) (Dwyer, 2023; Ntellas et al., 2019; Andreopoulou & Sparano, 2013). The selection of regimen type, including combination or sequential administration of anthracyclines and taxanes, depends on tumor characteristics, histopathological subtype, patient age, comorbidities, and other clinical considerations. Given the variation in adverse effects associated with cytotoxic agents, treatment tolerability must be considered when selecting an appropriate regimen. Furthermore, some breast cancer subtypes may develop resistance to chemotherapy, potentially reducing treatment effectiveness and patient survival outcomes (Dwyer, 2023; Tőkés et al., 2022). However, in early-stage breast cancer, anthracycline–taxane-based chemotherapy has been demonstrated to significantly improve survival outcomes compared with the absence of chemotherapy (Braybrooke et al., 2023).

Other evidence further demonstrates that differences in treatment effectiveness must be interpreted alongside variations in toxicity profiles and patient characteristics. Ntellas et al. (2019), in a pooled analysis involving 7,341 patients with HER2-negative breast cancer, found no statistically significant difference in overall survival between taxane–cyclophosphamide and anthracycline–taxane regimens. However, the anthracycline–taxane regimen demonstrated a small numerical advantage in disease-free survival, whereas the anthracycline-free regimen showed a more favorable toxicity profile. Indonesian studies have primarily focused on predictors or biomarkers of neoadjuvant chemotherapy response rather than direct comparisons between anthracycline- and taxane-based regimens. Manginstar et al. (2022), in an Indonesian prospective cohort study involving 11 patients with locally advanced breast cancer, demonstrated significant reductions in hypoxia-inducible factor-1 alpha (HIF-1α), cancer antigen 15-3 (CA15-3), and RECIST measurements after two cycles of neoadjuvant chemotherapy. The study also identified a significant association between changes in CA15-3 levels and RECIST response. Adrian et al. (2023) similarly investigated tumor necrosis factor-alpha (TNF-α) as a predictor of response to anthracycline-based neoadjuvant chemotherapy rather than directly comparing anthracycline- and taxane-based treatment strategies.

Evidence regarding RECIST-based response evaluation further confirms that neoadjuvant chemotherapy can produce substantial tumor reduction in locally advanced breast cancer; however, existing studies have not fully addressed the comparative clinical question examined in the present study. A 2023 study evaluating neoadjuvant chemotherapy in locally advanced breast cancer reported a mean reduction in tumor diameter of approximately 74.32%, with clinical complete response observed in 35.29% of patients and partial response observed in 52.92% of patients according to RECIST 1.1 criteria. Jain (2023) also demonstrated the importance of multidisciplinary response evaluation in patients with locally advanced breast cancer, emphasizing that therapeutic response is influenced by clinicopathological and molecular characteristics. However, these studies primarily evaluated overall neoadjuvant chemotherapy responses rather than directly comparing anthracycline-based and taxane-based regimens using standardized RECIST 1.1 response categories combined with standardized CTCAE toxicity assessment. Moreover, international findings cannot be directly generalized to Indonesian populations because differences in disease stage at presentation, molecular subtype distribution, comorbidities, access to supportive care, chemotherapy adherence, and institutional treatment practices may influence both treatment effectiveness and tolerability.

Accordingly,an important research gap remains regarding the availability of prospective, institution-specific evidence that directly evaluates both therapeutic response and adverse-event profiles of anthracycline-based versus taxane-based neoadjuvant chemotherapy among Indonesian patients with locally advanced breast cancer. Existing large-scale meta-analyses provide strong evidence regarding recurrence and survival outcomes, whereas several smaller studies have focused on pathological response, biomarkers, or individual chemotherapy classes. In contrast, limited evidence simultaneously evaluates short-term objective tumor response using RECIST 1.1 and treatment toxicity using CTCAE within the same comparative framework in Indonesian tertiary referral hospitals. This gap is particularly relevant at Prof. Dr. R. D. Kandou General Hospital because previous local evidence demonstrated a high proportion of patients presenting with advanced disease. The urgency of generating contemporary local evidence is further supported by the continuing burden of breast cancer in Indonesia, with more than 93,000 estimated new cases annually. Without comparative local evidence, clinicians may have limited guidance for balancing expected tumor reduction against regimen-specific toxicity when individualizing neoadjuvant treatment.

The novelty of the present study lies not only in evaluating chemotherapy effectiveness but also in integrating two clinically complementary dimensions—objective tumor response and adverse-event burden—in a direct comparison of anthracycline-based and taxane-based neoadjuvant chemotherapy among patients with locally advanced breast cancer in an Indonesian tertiary-care setting. RECIST 1.1 provides a standardized assessment of measurable tumor response, whereas CTCAE offers a systematic approach for grading hematological and non-hematological adverse events. Combining these assessment systems enables treatment value to be interpreted through a balance between tumor control and treatment tolerability rather than tumor reduction alone. This approach is important because two regimens may demonstrate comparable response rates while producing different patterns or severities of toxicity that can influence dose intensity, treatment adherence, treatment delays, quality of life, and eligibility for subsequent definitive therapy. Therefore, this study provides a context-specific perspective that complements international clinical trials and biomarker-focused Indonesian studies by emphasizing clinically measurable outcomes relevant to daily therapeutic decision-making.

Based on this rationale, the purpose of this research is to compare the effectiveness and safety of anthracycline-based and taxane-based neoadjuvant chemotherapy in patients with locally advanced breast cancer treated at Prof. Dr. R. D. Kandou General Hospital. Specifically, this study aims to evaluate tumor response after neoadjuvant chemotherapy according to RECIST 1.1 criteria, determine the distribution and severity of chemotherapy-related adverse events according to CTCAE criteria, and assess whether significant differences exist between patients receiving anthracycline-based and taxane-based regimens. These objectives are consistent with the study protocol, which prospectively observes patients undergoing either chemotherapy approach and subsequently evaluates treatment effectiveness and adverse effects using standardized criteria. Through these objectives, this study seeks to generate empirical evidence reflecting the clinical characteristics of locally advanced breast cancer patients managed within the hospital rather than relying solely on findings derived from other populations or treatment settings.

The expected contribution of this research is both scientific and practical. Scientifically, this study may enrich the limited Indonesian comparative evidence regarding anthracycline- and taxane-based neoadjuvant chemotherapy by providing integrated data on RECIST 1.1 treatment response and CTCAE-defined toxicity. Clinically, the findings may assist oncologists, surgeons, and multidisciplinary breast cancer teams in selecting chemotherapy strategies that consider not only expected tumor reduction but also patient-specific risks of adverse events and treatment tolerance. Institutionally, the evidence may serve as a reference for evaluating and refining neoadjuvant chemotherapy practices at Prof. Dr. R. D. Kandou General Hospital and other comparable referral centers. For patients, evidence-based regimen selection may support safer treatment, appropriate monitoring, maintenance of treatment intensity, and better preparation for subsequent definitive therapy. Finally, this study may provide a foundation for future multicenter research involving larger populations, molecular subtype stratification, pathological complete response, long-term disease-free survival and overall survival outcomes, quality-of-life assessments, and pharmacoeconomic evaluations, thereby supporting a more individualized and evidence-based approach to the management of locally advanced breast cancer in Indonesia.

METHOD

Research Design

This study was an observational analytic study with a prospective cohort design. The analysis was conducted on breast cancer patients who received anthracycline- or taxane-based neoadjuvant chemotherapy. Treatment response was assessed based on changes in tumor size according to RECIST 1.1 criteria, while adverse effects were evaluated using CTCAE criteria after chemotherapy administration.

Place and Time of Research Implementation

This research will be conducted at Prof. Dr. R. D. Kandou Manado General Hospital, and will be conducted from January to December 2025, or until the sample size is met.

Research Population

Target population:

Female patients diagnosed with locally advanced breast cancer who underwent neoadjuvant chemotherapy based on anthracyclines or taxanes

Accessible population:

Patients who underwent neoadjuvant chemotherapy based on Anthracycline or Taxane at Prof. Dr. R. D. Kandou General Hospital, Manado.

Sample:

Patients who underwent neoadjuvant chemotherapy based on Anthracycline or Taxane at Prof. Dr. R. D. Kandou Manado General Hospital, who met the inclusion and exclusion criteria.

Inclusion Criteria

The inclusion criteria for this study include:

a. Patients with unilateral locally advanced breast cancer who have not received previous chemotherapy.
b. Patients with tumor conditions can be evaluated and measured according to the RECIST 1.1 criteria.
c. Patients who are willing to be research respondents.
d. Patients who will receive anthracycline-based neoadjuvant chemotherapy with a regimen of doxorubicin and cyclophosphamide or epirubicin and cyclophosphamide.
e. Patients who will receive Taxane-based chemotherapy with a regimen of docetaxel and carboplatin/cisplatin or paclitaxel and carboplatin/cisplatin.

Exclusion Criteria

Exclusion criteria in this study include:

a. Patients who did not complete at least 2 cycles of anthracycline- or taxane-based neoadjuvant chemotherapy.
b. The patient did not undergo chemotherapy according to schedule (> 1 week from the scheduled chemotherapy schedule).
c. The patient died before RECIST 1.1 re-evaluation after chemotherapy.

Samples and Sampling Methods

The sampling method used in this study was *Non-Probability sampling*, namely a sample of female patients with unilateral locally advanced breast cancer who met the inclusion and exclusion criteria.

Patients participating in the study will first be briefed on their characteristics and how they meet the inclusion criteria to become potential participants. The study procedures and follow-up after chemotherapy are explained to patients. After the briefing, patients will be asked to provide informed consent. Participants who agree to participate will be given a research questionnaire.

Sample Size

The population in this study were women with breast cancer who underwent anthracycline and taxane chemotherapy at Prof. R. D. Kandou Manado General Hospital.

The estimated sample size is calculated based on the following formula :

$$n = \frac{\left(Z_{\frac{\alpha}{2}} + Z_{\beta}\right)^2 [P_1(1-P_1) + (P_2(1-P_2)]}{(P1-P2)^2}$$

- n = Number of subjects from both sample groups
- P_1 = Proportion of effective/side effect responses of the Anthracycline-based chemotherapy sample group

- P_2 = Proportion of effective/side effect responses of the Taxane-based chemotherapy sample group
- $Z_{\alpha/2}$ = Standard alpha derivative ($Z\alpha = 1.96$) – 5% significance level with ($\alpha = 0.05$)
- $Z\beta$ = Standard beta derivative ($Z\beta = 0.84$) – Test power 80%

Based on the calculation results using the formula *"2 independent proportions"* The minimum sample size for this study was 20 samples, 10 samples in the anthracycline group and 10 samples in the taxane group.

Research Flow

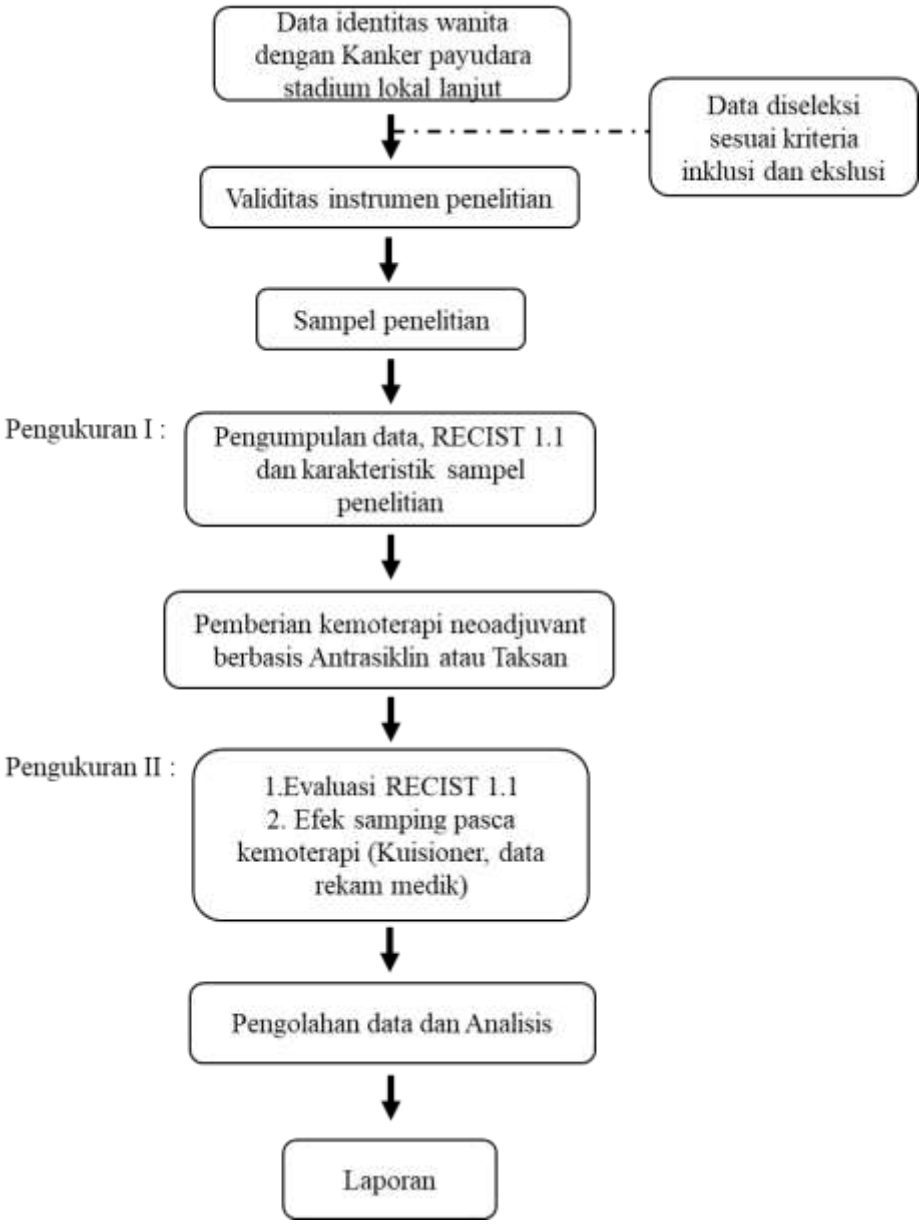

Figure 1. Research flow

Tools and materials

Tool :

- Patient Registry Data:
  Medical record data of women with breast cancer at Prof. Dr. R. D. Kandou Manado General Hospital.
- *Imaging* samples :
  - Thorax CT Scan / Thorax MRI (RECIST 1.1)
  - Chest X-ray
  - Heart ECHO
- Anatomical pathology and immunohistochemistry (IHK) data
- Questionnaire

Material :

- Anthracycline-based chemotherapy
- Taxane-based chemotherapy

Ways of working

1. The assessment was conducted on women with breast cancer who met the inclusion and exclusion criteria with lumps in the breast or were consulted from other departments to the Surgery Department of Prof. Dr. R. D. Kandou General Hospital.
2. Physical and supporting examinations were carried out to meet the inclusion and exclusion criteria.
3. Patients were evaluated based on RECIST 1.1 criteria.
4. Observations were made during the administration of neoadjuvant chemotherapy for at least 2 cycles based on Anthracycline or Taxane.
5. Patients underwent anamnesis, physical and supporting examinations, and questionnaires.
6. Data collection and analysis of the effectiveness and side effects between Anthracycline or Taxane-based neoadjuvant chemotherapy given were re-evaluated based on RECIST 1.1 criteria and side effects based on CTCAE.
7. Report writing.

Data analysis

The data obtained in this study will be processed using SPSS for Windows version 25. All data obtained will first be entered into Excel and transferred to SPSS for analysis. The data will be processed using the following steps:

1. Editing is checking for errors or incompleteness in data that has been taken from the field.
2. Coding is moving data into codes for analysis purposes.
3. Entry means entering the data obtained into a computer/data processing device so that it is ready to be processed.
4. Cleaning means checking again for errors that occur when making entries.
5. Analysis means analyzing existing data using a predetermined program.
   - Univariate analysis is performed according to the type of variable, numeric or categorical.
   - Bivariate analysis:
     - test , to evaluate the comparative effectiveness of anthracycline-based chemotherapy with taxane in advanced breast cancer patients by assessing changes in each outcome after chemotherapy.

- Chi-square test, to analyze the side effects of anthracycline-based chemotherapy with taxanes in patients with advanced breast cancer
- Significance level with P value < 0.05
- The results of the analysis will be presented in narrative and tabular form.

Research ethics

The research was conducted after being revised and approved, the proposal was submitted to the Ethics Committee to obtain approval for Health Research at Prof. Dr. R. D. Kandou Manado General Hospital. Ethical approval number, No. 117/EC/KEPK-KANDOU/VI/2025.

The entire study adhered to the ethical principles of human subject research applicable at Prof. Dr. R. D. Kandou General Hospital, Manado, which adheres to the 2008 Helsinki Declaration on medical research involving human subjects. The research itself was carried out after the researchers received ethical clearance from the Research Ethics Commission of Prof. Dr. R. D. Kandou General Hospital, Manado. The basic ethical principles in research involving human subjects are: the principle of respect for persons, the principle of benefit (beneficence), the principle of not harming research subjects (non-maleficence), and the principle of justice.

Research budget

Table 1. Research Budget

No	Activity	Price (IDR)	Quantity	Total (IDR)
1	Thesis Proposal Preparation	500000	1	500000
2	Research Implementation			
	a. Research Permission	250000	1	250000
	b. Transportation	1000000	1	1000000
3	Ethics Committee (EC) Submission Preparation	480000	1	480000
4	Questionnaire Preparation	1000	60	60000
5	Research Results Compilation	1000000	1	1000000
6	Journal Publication	1500000	1	1500000
7	Research Results Seminar	1000000	1	1000000
8	Duplication and Binding	500000	1	500000
	Total			6290000

RESULTS AND DISCUSSION

Characteristics of Research Subjects

This study involved a total of 27 patients with locally advanced breast cancer who met the inclusion and exclusion criteria. The study subjects were divided into two groups based on the type of neoadjuvant chemotherapy administered, namely the anthracycline-based chemotherapy group of 11 people and the taxane-based chemotherapy group of 16 people. All study subjects were female patients diagnosed with locally advanced breast cancer who underwent neoadjuvant chemotherapy at Prof. Dr. R. D. Kandou Manado General Hospital, as presented in Table 13 .

Age distribution: The majority of subjects were in the <45 years age group (12/27; 44.4%), with a balanced proportion between the anthracycline and taxane groups (6 patients each). Seven patients (25.9%) were in the 45–55 years age group, while eight patients (29.6%) were in the >55 years age group, with a predominance in the taxane group (7 out of 8 patients). The overall mean age was approximately 49 years.

Tumor size distribution showed that most patients presented with tumors measuring >50 mm (T3/T4), namely 24 of 27 patients (88.9%). Only one patient (3.7%) had a T1 (1–20 mm) tumor and two patients (7.4%) with T2 (21–50 mm). In both treatment groups, the proportion of tumors >50 mm dominated (anthracyclines 9/11; taxanes 15/16).

Nodal status indicates regional lymph node involvement. Only 5 (18.5%) patients had N0, while 10 (37.0%) and N1 and N2 patients each had N3. N3 was found in 2 patients (7.4%), all in the taxane group.

Based on molecular subtypes, the most common type was Luminal B (HER2-negative) in 7 patients (25.9%), followed by HER2-enriched in 5 patients (18.5%) and TNBC in 4 patients (14.8%). Luminal A subtype was found in 3 patients (11.1%), while Luminal B (HER2-positive) was found in 2 patients (7.4%). In the taxane group, the proportion of HER2-enriched and TNBC was relatively higher than in the anthracycline group, while the anthracycline group had more HER2-negative Luminal B subtypes.

Tumor response evaluation was performed based on the Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria after completing at least two cycles of chemotherapy.

Table 2. Table of Characteristics of Research Subjects

Variables		Anthracycline	Taxan	Total
Number of Subjects (n)		**11**	**16**	**27**
Age	**< 45 years**	6	6	**12**
	45 - 55 years old	4	3	**7**
	> 55 years	1	7	**8**
Average Age (Years)		≈47	≈50	**≈49**
Tumor Size	**1 – 2 cm (T1)**	1	0	**1**
	2 - 5 cm (T2)	1	1	**2**
	>5 cm (T3/T4)	9	15	**24**
Nodal Status	**N0**	3	2	**5**
	N1	4	6	**10**
	N2	4	6	**10**
	N3	0	2	**2**
Subtype	**Luminal A**	2	1	**3**
	Luminal B (HER2-negative)	5	2	**7**
	Luminal B (HER2-positive)	1	1	**2**
	HER2-enriched	1	4	**5**
	TNBC	0	4	**4**

The distribution of tumor responses assessed based on RECIST 1.1 criteria in all study subjects is presented in Table 14. The results of the analysis show that of the 27 patients studied, 11 patients in the anthracycline-based chemotherapy group found *Partial Response* (PR) in 9 patients (81.82%), *Stable Disease* (SD) in 1 patient (9.09%), *Progressive Disease* (PD) in 1 patient (9.09%) and obtained from 16 patients in the taxane-based chemotherapy group found *Complete Response* (CR) in 1 patient (6.25%), *Partial Response* (PR) in 12 patients (75%), and *Progressive Disease* (PD) in 3 patients (18.75%). These distribution results indicate that most

patients responded positively to neoadjuvant chemotherapy, with a dominance of *Partial Response* (PR).

Table 3. Frequency Distribution of Tumor Response Based on Recist 1.1

	anthracyclines		TAXES	
	n	**%**	**n**	**%**
Complete Response (CR)	0	0	1	6.25
Partial Response (PR)	9	81.82	12	75
Stable Disease (SD)	1	9.09	0	0
Progressive Disease (PD)	1	9.09	3	18.75
Total n	**11**		**16**	

Chemotherapy Effectiveness based on RECIST 1.1 neoadjuvant Anthracycline-based with Taxane in breast cancer after chemotherapy.

To determine the difference in the effectiveness of neoadjuvant chemotherapy between the anthracycline-based group and the taxane-based group, a non-parametric statistical test was performed using the Mann-Whitney test because the data were ordinal and not normally distributed.

The results of the comparative test of the effectiveness of anthracycline-based neoadjuvant chemotherapy based on RECIST 1.1 with taxane in breast cancer after chemotherapy are presented in Table 15. Based on the analysis results, the Mann-Whitney U value was 82,500 with a significance value (p-value) of 0.708. A p-value > 0.05 indicates that there is no statistically significant difference between the effectiveness of anthracycline-based and taxane-based neoadjuvant chemotherapy based on RECIST 1.1 criteria. And from the analysis in the anthracycline-based chemotherapy group, the mean rank was 14.50, while the taxane-based chemotherapy group had a mean rank of 13.66. Although there was a difference in the mean rank value between the two groups, the difference was not statistically significant.

Table 4. Comparison of Chemotherapy Effectiveness based on RECIST 1.1 neoadjuvant Anthracycline-based with Taxane in breast cancer after chemotherapy.

	n	**Mean Rank**	**Sum of Rank**	**Mann-Whitney University**	**Wilcoxon W**	**Z**	**Asymp. Sig. (2-tailed)**
Anthracycline	11	14.50	159.50	82,500	218,500	-.374	.708
Taxan	16	13.66	218.50				
Total	27						

Analysis of side effects of anthracycline-based neoadjuvant chemotherapy in breast cancer after chemotherapy.

In the anthracycline-based chemotherapy group, side effects assessed using *the Common Terminology Criteria for Adverse Events* (CTCAE) showed that most patients experienced both hematological and non-hematological side effects of varying degrees. These side effects were a

manifestation of the systemic toxicity of the chemotherapy drugs to tissues with high cell proliferation rates.

Most of the side effects that appear Adverse events included nausea, vomiting, anemia, leukopenia, and neutropenia, all of which were mild to moderate (grade 1–2) according to CTCAE criteria. Only a small proportion of patients experienced more severe side effects, and no life-threatening adverse events were reported.

This indicates that anthracycline-based neoadjuvant chemotherapy in this study has a toxicity profile that is still clinically acceptable, especially when accompanied by supportive therapy and adequate clinical monitoring. Distribution Analysis of side effects of anthracycline-based neoadjuvant chemotherapy in breast cancer after chemotherapy is presented in Table 5.

Table 5. Analysis of side effects of anthracycline-based neoadjuvant chemotherapy in breast cancer after chemotherapy

	Grade 1				Grade 2				Grade 3				Grade 4			
	AC	%	TC	%	AC	%	TC	%	AC	%	TC	%	AC	%	TC	%
Neutropenia	1	9.09	0	0	0	0	0	0	2	18.18	1	6.25	3	27.27	2	12.5
Anemia	2	18.18	4	25	0	0	5	31.25	0	0	0	0	0	0	1	6.25
Thrombocytopenia	0	0	1	6.25	0	0	0	0	0	0	0	0	0	0	0	0
Leucopenia	0	0	3	18.75	4	36.36	0	0	1	9.09	2	12.5	0	0	0	0
Febrile Neutropenia	0	0	0	0	0	0	0	0	0	0	1	6.25	0	0	0	0
Nausea	3	27.27	8	50	7	63.63	8	50	0	0	0	0	0	0	0	0
Vomiting	2	18.18	5	31.25	4	36.36	4	25	0	0	0	0	0	0	0	0
Diarrhea	3	27.27	4	25	0	0	2	12.5	0	0	0	0	0	0	0	0
Mucositis	4	36.36	7	43.75	0	0	1	6.25	0	0	0	0	0	0	0	0
Constipation	1	9.09	8	50	0	0	0	0	0	0	0	0	0	0	0	0
Allergy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rash	1	9.09	5	31.25	0	0	0	0	0	0	0	0	0	0	0	0
Skin toxicity	1	9.09	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nail toxicity	0	0	4	25	1	9.09	1	6.25	0	0	0	0	0	0	0	0
Fatigue	6	54.54	5	31.25	3	27.27	8	50	0	0	1	6.25	0	0	0	0
Peripheral neuropathy	0	0	4	25	0	0	0	0	0	0	0	0	0	0	0	0
Arthralgia/myalgia	8	72.72	9	56.25	0	0	1	6.25	0	0	0	0	0	0	0	0
Cardiotoxicity	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

AC : Antrasiklin	**N : 11**
TC : Taksan	**N : 16**

Analysis of side effects of Taxane-based neoadjuvant chemotherapy in breast cancer after chemotherapy.

In the taxane-based chemotherapy group, the side effects assessed by CTCAE were mostly mild to moderate (grade 1–2 according to CTCAE) hematological and non-hematological side effects. The most common hematological side effects were neutropenia, anemia, and

thrombocytopenia, reflecting bone marrow suppression due to the taxane agent's disruption of cell mitosis.

The most common non-hematological side effects include nausea and vomiting, fatigue, and some patients experience musculoskeletal complaints such as muscle and joint pain (myalgia and arthralgia), which are typical effects of taxane-based chemotherapy. Most side effects can be managed with supportive therapy and do not require chemotherapy discontinuation.

This indicates that taxane-based neoadjuvant chemotherapy in this study was within acceptable clinical tolerability limits, making this regimen relatively safe for use as neoadjuvant therapy in breast cancer with adequate clinical and laboratory monitoring. The distribution of the types and degrees of side effects in the taxane-based chemotherapy group is presented in Table 6.

Table 6. Analysis of side effects of Taxane-based neoadjuvant chemotherapy in breast cancer after chemotherapy

	Grade 1		**Grade 2**		**Grade 3**		**Grade 4**	
	TC	**%**	**TC**	**%**	**TC**	**%**	**TC**	**%**
Neutropenia	0	0	0	0	1	6.25	2	12.5
Anemia	4	25	5	31.25	0	0	1	6.25
Thrombocytopenia	1	6.25	0	0	0	0	0	0
Leucopenia	3	18.75	0	0	2	12.5	0	0
Febrile Neutropenia	0	0	0	0	1	6.25	0	0
Nausea	8	50	8	50	0	0	0	0
Vomiting	5	31.25	4	25	0	0	0	0
Diarrhea	4	25	2	12.5	0	0	0	0
Mucositis	7	43.75	1	6.25	0	0	0	0
Constipation	8	50	0	0	0	0	0	0
Allergy	0	0	0	0	0	0	0	0
Rash	5	31.25	0	0	0	0	0	0
Skin toxicity	0	0	0	0	0	0	0	0
Nail toxicity	4	25	1	6.25	0	0	0	0
Fatigue	5	31.25	8	50	1	6.25	0	0
Peripheral neuropathy	4	25	0	0	0	0	0	0
Arthralgia/myalgia	9	56.25	1	6.25	0	0	0	0
Cardiotoxicity	0	0	0	0	0	0	0	0
TC : Taksan			**N : 16**					

Comparison of side effects of Anthracycline-based neoadjuvant therapy with Taxane in breast cancer after chemotherapy.

A comparison of side effects between the anthracycline-based chemotherapy group and the taxane-based group is presented in Table 18.

The results of the analysis showed that there were differences in the distribution of types of side effects between the two chemotherapy groups, but in general, most of the side effects were still within clinically tolerable limits.

The taxane-based chemotherapy group tended to experience side effects more frequently in the form of peripheral neuropathy, anemia and neutropenia, while the anthracycline-based group experienced side effects more frequently in the form of nausea, vomiting and mild hematological disorders.

Table 7. Comparison of side effects of Anthracycline-based neoadjuvant therapy with Taxane in breast cancer after chemotherapy

	Grade 1				Grade 2				Grade 3				Grade 4			
	AC	%	TC	%	AC	%	TC	%	AC	%	TC	%	AC	%	TC	%
Neutropenia	1	9.09	0	0	0	0	0	0	2	18.18	1	6.25	3	27.27	2	12.5
Anemia	2	18.18	4	25	0	0	5	31.25	0	0	0	0	0	0	1	6.25
Thrombocytopenia	0	0	1	6.25	0	0	0	0	0	0	0	0	0	0	0	0
Leucopenia	0	0	3	18.75	4	36.36	0	0	1	9.09	2	12.5	0	0	0	0
Febrile Neutropenia	0	0	0	0	0	0	0	0	0	0	1	6.25	0	0	0	0
Nausea	3	27.27	8	50	7	63.63	8	50	0	0	0	0	0	0	0	0
Vomiting	2	18.18	5	31.25	4	36.36	4	25	0	0	0	0	0	0	0	0
Diarrhea	3	27.27	4	25	0	0	2	12.5	0	0	0	0	0	0	0	0
Mucositis	4	36.36	7	43.75	0	0	1	6.25	0	0	0	0	0	0	0	0
Constipation	1	9.09	8	50	0	0	0	0	0	0	0	0	0	0	0	0
Allergy	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Rash	1	9.09	5	31.25	0	0	0	0	0	0	0	0	0	0	0	0
Skin toxicity	1	9.09	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Nail toxicity	0	0	4	25	1	9.09	1	6.25	0	0	0	0	0	0	0	0
Fatigue	6	54.54	5	31.25	3	27.27	8	50	0	0	1	6.25	0	0	0	0
Peripheral neuropathy	0	0	4	25	0	0	0	0	0	0	0	0	0	0	0	0
Arthralgia/ myalgia	8	72.72	9	56.25	0	0	1	6.25	0	0	0	0	0	0	0	0
Cardiotoxicity	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

AC : Antrasiklin	N : 11
TC : Taksan	N : 16

Breast cancer is a leading cause of cancer morbidity and mortality in women worldwide. GLOBOCAN data from 2022 shows that breast cancer has the highest incidence globally (Bray et al., 2024). In Indonesia, breast cancer remains a major health problem, with incidence rates continuing to rise.

Tumor size in breast cancer is not only a reflection of disease duration, but also the result of a complex interaction between cell proliferation, apoptosis, angiogenesis, genomic instability, and the tumor environment. Mutations in suppressor genes such as BRCA1 and BRCA2 disrupt DNA repair through homologous recombination, thus increasing the accumulation of genetic damage and uncontrolled cell proliferation (Baselga & Norton, 2002; Sharma et al., 2010). Loss of cell cycle control accelerates the initiation and promotion phases of carcinogenesis. In the

progression phase, tumor cells undergo oncogene activation, suppressor gene inactivation, increased invasiveness, and angiogenesis, all of which contribute to tumor growth. High genomic instability accelerates the tumor doubling time, which has direct implications for tumor size (Alkabban & Ferguson, 2023).

Molecular classification based on ER, PR, HER2, and Ki-67 expression has direct implications for tumor size and therapeutic response. Breast cancer subtypes are divided into Luminal A, Luminal B, Luminal/HER2, HER2-enriched, and Triple Negative Breast Cancer (TNBC) (GENG et al., 2015). Subtypes with high cell proliferation have larger (Andreopoulou & Sparano, 2013; GENG et al., 2015) initial tumor sizes but can show higher rates of pathologic complete response (pCR) to neoadjuvant chemotherapy. With a high initial tumor burden, *a partial response* (PR) is more likely than a *complete response* (CR) due to the mathematical factors of the RECIST definition, tumor biological heterogeneity, limited drug penetration, and the presence of resistant subclones. However, achieving a PR remains clinically significant because it indicates tumor sensitivity to chemotherapy and can often allow definitive surgery with tumor-free margins (Martin et al., 2011; Rašić et al., 2019).

Neoadjuvant chemotherapy is one of the primary therapeutic approaches for locally advanced breast cancer. It aims to reduce tumor size, increase the likelihood of surgery with tumor-free margins, and evaluate tumor sensitivity to cytotoxic agents. The NCCN Breast Cancer Guidelines recommend anthracycline- and taxane-based regimens as standard therapy. However, neoadjuvant chemotherapy should not be administered to widely invasive carcinoma *in situ*, or to carcinomas where the tumor is non-palpable or clinically inappreciable (Dwyer, 2023).

Evaluation of chemotherapy response uses the RECIST 1.1 criteria as an internationally recognized standard for assessing tumor response, and has good reliability and reproducibility (Gouel et al., 2023).

This study involved 27 patients with locally advanced breast cancer with a mean age of 47-50 years who met the inclusion criteria. The results of this study showed that most patients provided a significant clinical response to neoadjuvant chemotherapy based on RECIST 1.1 criteria, with a predominance of *Partial Responses* (PR) of 77.8%. The absence of significant differences between anthracycline- and taxane-based regimens indicates that both regimens have relatively equal effectiveness in reducing tumor size. The results of the Mann-Whitney statistical test in this study showed no statistically significant difference between the anthracycline-based chemotherapy group and the taxane-based group ($p = 0.708$). These findings are in line with the meta-analysis of Braybrooke et al. (2023) involving more than 100,000 patients, which stated that both anthracycline- and taxane-based regimens have significant clinical benefits in the treatment of early-stage and locally advanced breast cancer, and the report of Ntellas et al. (2019), which also reported that the difference in effectiveness between the two regimens is not always significant, especially when used as part of a neoadjuvant protocol.

Anthracyclines (doxorubicin and epirubicin) work primarily by inhibiting topoisomerase II, an enzyme involved in DNA replication and transcription. Topoisomerase II inhibition causes double-strand breaks in DNA, disrupting the stability of the cancer cell genome and triggering tumor cell apoptosis. Anthracyclines also generate free radicals (reactive oxygen species/ROS) through intracellular redox processes. This ROS production causes membrane lipid peroxidation, protein damage, and mitochondrial damage, leading to cancer cell death. However, the effects of free radical formation also contribute to toxicity to normal tissues, particularly the myocardium. Therefore, the use of anthracyclines is limited by the risk of cumulative cardiotoxicity due to

myocardial oxidative stress. This risk is a clinical consideration in selecting a chemotherapy regimen for patients with risk factors for heart disease (Andreopoulou & Sparano, 2013; Sharma et al., 2010). This toxicity can limit the dose administration and affect *the Relative Dose Intensity* (RDI), thus indirectly affecting tumor size reduction.

Taxanes (paclitaxel and docetaxel) work by stabilizing microtubules and preventing the depolymerization of these structures during mitosis. As a result, cancer cells arrest in the G2/M phase of the cell cycle and are unable to complete cell division, ultimately undergoing apoptosis (Andreopoulou & Sparano, 2013; Sharma et al., 2010). This mechanism is highly specific to actively dividing cells, making taxanes effective in tumors with a high proliferation index. Furthermore, taxanes also influence cellular signaling pathways that regulate apoptosis and tumor angiogenesis, thus having additional antitumor effects beyond mitosis inhibition (Tőkés et al., 2022). However, because microtubules also play a crucial role in peripheral neuron function, microtubule stabilization by taxanes can lead to impaired peripheral nerve function that manifests clinically as peripheral neuropathy. This explains why peripheral neuropathy side effects are more common in patients receiving taxane-based chemotherapy compared to anthracyclines (Andreopoulou & Sparano, 2013). Tőkés et al. (2022) stated that these differences in mechanisms of action affect glucose and fatty acid metabolism in tumor cells, which in turn affects tumor sensitivity to therapy. Muley et al. (2020) explained that chemotherapy resistance can occur due to decreased drug uptake into cancer cells, increased activity of drug efflux pumps (such as P-glycoprotein), and changes in the expression of drug target proteins (see also Andreopoulou & Sparano, 2013). These differences in mechanisms of action explain why clinical efficacy can be relatively comparable, but the side effect profiles between the two regimens differ.

Chemotherapy side effects in this study were assessed using CTCAE, according to standards established by the US Department of Health and Human Services. The results showed that both the anthracycline-based chemotherapy group and the taxane group experienced side effects. Most side effects were mild to moderate (grade 1–2) and were clinically manageable. In the anthracycline group, the dominant side effects were nausea, vomiting, and hematological disorders such as anemia and leukopenia. This is consistent with the mechanism of action of anthracyclines, which are cytotoxic to rapidly dividing cells, including bone marrow cells and gastrointestinal mucosal cells. Furthermore, in the taxane group, the more common side effects were neutropenia and peripheral neuropathy. Peripheral neuropathy is a typical side effect of taxanes due to disruption of the microtubules of peripheral nerve cells. The differences in side effect profiles between the two groups are consistent with the pharmacological characteristics of each drug, so the choice of chemotherapy regimen needs to consider the patient's clinical condition and the potential risk of side effects. These differences in side effect profiles are consistent with the pharmacological characteristics of each chemotherapy regimen, so the choice of regimen needs to consider the patient's clinical condition and the potential risk of side effects that may arise.

The use and monitoring of side effects using CTCAE helps clinicians identify toxicity objectively and consistently, allowing rational and standardized dose modification decisions. Without a standardized assessment system, dose reduction decisions can be subjective and potentially lead to unnecessary reductions in *the Relative Dose Intensity* (RDI). Chemotherapy doses that are reduced or intervals extended due to uncontrolled toxicity can lead to decreased cumulative cytotoxic efficacy and increased risk of resistance. This is in line with the principle

of Gompertzian tumor growth, where the remaining tumor cells after reduction, the mass can grow faster due to reduced nutrient competition and hypoxia (Muley et al., 2020).

Limitations of this study include the relatively small sample size, resulting in variations in therapeutic response that were not fully identified. A study by Martin et al. (2011) showed that response to anthracycline and taxane chemotherapy is strongly influenced by tumor genomic factors. In addition, compliance with the chemotherapy schedule, the patient's general clinical condition, and the presence of comorbidities can also affect the effectiveness of therapy.

The results of this study indicate that both anthracycline- and taxane-based chemotherapy can be used as neoadjuvant therapy with comparable efficacy. The NCCN and ASCO recommend that chemotherapy regimen selection should consider the patient's clinical condition, organ function, and risk of side effects. With no significant differences in efficacy found, tolerability and safety are the primary considerations in clinical practice. The differing side effect profiles between the two regimens provide a basis for clinicians to individualize therapy.

CONCLUSION

This study concluded that anthracycline-based and taxane-based neoadjuvant chemotherapy demonstrated comparable effectiveness among patients with locally advanced breast cancer treated at Prof. Dr. R. D. Kandou General Hospital. Among the 27 patients included in the study, partial response was the predominant RECIST 1.1 outcome, occurring in 81.82% of patients receiving anthracycline-based chemotherapy and 75% of patients receiving taxane-based chemotherapy. The Mann–Whitney test revealed no statistically significant difference in therapeutic effectiveness between the two regimens ($p = 0.708$), indicating that both treatment approaches resulted in relatively similar tumor-response outcomes. However, the toxicity profiles differed between regimens. Anthracycline-based therapy was more frequently associated with nausea, vomiting, and hematological abnormalities, whereas taxane-based therapy was more commonly associated with neutropenia and peripheral neuropathy. Most adverse events were clinically manageable, suggesting that regimen selection should not be based solely on tumor response but should also consider patient characteristics, organ function, treatment tolerance, and the potential risk of regimen-specific adverse effects.

Future research should include larger patient populations and multicenter study designs to improve statistical power and enhance the generalizability of findings, particularly because the relatively small sample size in this study may have limited the detection of differences in therapeutic response. Future studies should also incorporate stratified or adjusted analyses based on molecular breast cancer subtypes, genomic characteristics, comorbidities, clinical status, chemotherapy adherence, and treatment intensity, as these factors may influence responses to anthracycline- and taxane-based chemotherapy. Furthermore, longer follow-up periods are recommended to evaluate pathological complete response, disease-free survival, overall survival, treatment-related quality of life, and pharmacoeconomic outcomes. Such investigations would provide more comprehensive evidence regarding not only short-term tumor response and treatment toxicity but also the long-term clinical value of each regimen, thereby supporting more individualized and evidence-based neoadjuvant treatment strategies for locally advanced breast cancer.

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