Hematologic Toxicity Patterns and Prognostic Value of Complete Blood Count in Advanced HR-positive/HER2-negative Breast Cancer Treated with Palbociclib plus Letrozole: A Real-World Single-Center Study

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Submitted 2025/12/29
Revised 2026/4/14
Accepted 2026/4/15

Abstract

Background: The prognostic value of complete blood count (CBC) parameters in patients with advanced HR-positive/HER2-negative breast cancer receiving palbociclib plus letrozole remains unclear. This study aimed to characterize hematologic toxicity patterns associated with treatment response and survival in real-world setting.

Methods: This prospective single-center study included 80 women receiving palbociclib plus letrozole. CBC was collected at baseline and after each of six cycles. Toxicities were graded by CTCAE v5.0. Analyses were descriptive with repeated-measures ANOVA, and ROC curve analysis.

Results: Most hematologic toxicities were grade 1-2; grade 3-4 neutropenia was uncommon and no febrile events occurred. Higher mean WBC and RBC counts during treatment were significantly associated with non-response and shorter progression-free survival (PFS).

Conclusion: Palbociclib plus letrozole showed a manageable safety profile without cumulative hematologic toxicity. Higher on-treatment WBC and RBC counts are prognostic for poorer outcomes. Routine CBC monitoring may offer a low-cost tool to identify patients at risk for treatment failure.

Keywords: Palbociclib; Hematologic toxicity; Real-world evidence; Breast cancer; Prognostic biomarker

Introduction

Breast cancer is the most prevalent malignancy among women, accounting for approximately 23% of all female cancers and remaining the leading cause of cancer-related deaths worldwide, particularly in low-resource countries.[1] In Iraq, numerous studies have reported that a substantial proportion of breast cancer patients present at a younger age with more advanced and aggressive tumors compared to Western populations.[2,3] The rising prevalence of breast cancer can be attributed to population growth and aging, as well as the increasing adoption of a Western lifestyle, including sedentary behavior, tobacco use, and obesity.[3]

The side effects of systemic chemotherapy often reduce patients' quality of life and can lead to treatment noncompliance, adversely affecting therapeutic outcomes.[4]

Palbociclib, a potent and selective inhibitor of cyclin-dependent kinases 4/6 (CDK4/6), disrupts cell cycle progression by preventing phosphorylation of the retinoblastoma (Rb) protein, inducing a reversible arrest in the G1 phase. Unlike conventional chemotherapeutic agents, palbociclib does not trigger apoptosis or DNA damage, resulting in a cytostatic effect with minimal cytotoxicity.[5]

Since its approval in 2015, palbociclib has transformed the therapeutic landscape for hormone receptor-positive, HER2-negative advanced breast cancer, presenting a distinct hematological safety profile characterized by predictable, dose-dependent, and reversible myelosuppression.[6]

Mechanistic studies have shown that palbociclib induces myelosuppression through reversible G1 phase arrest without DNA damage or apoptosis. This cytostatic profile explains the prompt normalization of blood counts after dose interruption or reduction, with no evidence of cumulative myelosuppression over successive cycles.[7,8]

Among hematologic adverse events, neutropenia is the most common and clinically significant toxicity associated with palbociclib. Despite high rates of severe neutropenia, clinical effects are limited due to its rapidly reversible nature, which rarely leads to serious infectious complications.[9] This distinguishes palbociclib-induced neutropenia from chemotherapy-induced neutropenia, which carries a higher risk of febrile neutropenia and mortality.[10]

Other hematologic toxicities have also been reported. Leukopenia affects 25–45% of patients, with grade 3-4 in approximately 20 - 30%.[9] Lymphopenia occurs in about 36% of patients.[5]

Anemia has been reported in 24-29% of patients, with grade 3-4 in only 3–6%. Thrombocytopenia is less common, affecting 15–23% of patients, with grade 3-4 in 1–3%.[11] Collectively, these findings characterize palbociclib's safety profile as marked by frequent, dose-dependent

myelosuppression that is generally of low clinical risk and does not worsen cumulatively over time.

In this context, we carried out a real-world analysis of hematological toxicities in women receiving palbociclib and letrozole for advanced breast cancer. The aim of this study was to evaluate the potential utility of hematological parameters as prognostic biomarkers of therapeutic outcome, to characterize the incidence, severity, and temporal patterns of blood count abnormalities in routine clinical practice, and to compare these findings with data from controlled clinical trials.

Methods

Study design and setting

This prospective single-center observational study was carried out at the Medical City complex in Baghdad, Iraq, between February 2024 and March 2025. We evaluated hematological toxicity in a real-world cohort of patients with advanced hormone receptor–positive/HER2-negative (HR+/HER2-) breast cancer treated with palbociclib and letrozole. The study followed the STROBE guidelines for observational studies.

Participants

A total of 97 patients were initially screened. Eligible participants were women aged 35–60 years with confirmed metastatic HR+/HER2- breast cancer receiving palbociclib plus letrozole. All patients had completed at least six consecutive treatment cycles of letrozole (2.5 mg once daily) and palbociclib (125 mg once daily, 21 days on/ 7 days off, 28-day cycle).

Patients with other breast cancer subtypes (e.g., triple-negative or HER2- positive), failure to complete six cycles of the palbociclib-letrozole regimen, concurrent use of strong CYP3A inhibitors (macrolides, azole antifungals) or strong CYP3A inducers (rifampicin, carbamazepine, phenytoin), and use of granulocyte colony-stimulating factor (G-CSF) were excluded. The final cohort was ethnically homogenous (Meddle Eastern).

Data collection

Baseline characteristics and laboratory parameters were extracted from medical reports. Laboratory results across six treatment cycles were analyzed descriptively. Allassays were

performed in the hospital's central laboratory using standardized automated analyzers, with reference ranges based on institutional standards.

Hematological Toxicity Definitions

Hematologic adverse events were graded according to the common terminology criteria for adverse events (CTCAE) version 5.0. The grading criteria for cytopenias are summarized in Table 1.

Table 1. CTCAE grading criteria for hematologic adverse events

Toxicity	Grade 1	Grade 2	Grade 3	Grade 4
Neutropenia (ANC)	< LLN – 1.5 ×10⁹/L	1.0 – <1.5 ×10⁹/L	0.5 – <1.0 ×10⁹/L	<0.5 ×10⁹/L
Leukopenia (WBC)	< LLN – 3.0 ×10⁹/L	2.0 – <3.0 ×10⁹/L	1.0 – <2.0 ×10⁹/L	<1.0 ×10⁹/L
Anemia (Hb)	<LLN – 10 g/dL	8 – <10 g/dL	<8 g/dL	Life-threatening consequences
Thrombocytopenia (Platelets)	< LLN – 75 ×10⁹/L	50 – <75 ×10⁹/L	25 – <50 ×10⁹/L	<25 ×10⁹/L

ANC: Absolute Neutrophil Count; WBC: White Blood Cell; Hb: Hemoglobin

Assessment of disease response (RECIST version 1.1)

Tumor response was evaluated using Response Evaluation Criteria in Solid Tumors (RECIST version 1.1):

- Complete response (CR): Disappearance of all targets and non-target lesions; normalization of tumor markers.
- Partial response (PR): ≥30% decrease in sum of diameters of target lesions from baseline.
- Stable disease (SD): Neither sufficient shrinkage for PR nor sufficient increase for progressive disease, maintained 6-8 weeks.
- Progressive disease (PD): ≥20% increase in sum of target lesions, unequivocal progression of non-target disease, or appearance of new lesions.

Responders were defined as CR + RP; non-responders as SD + PD.

Statistical analysis

Statistical analysis was performed using SPSS. Continuous variables were expressed as means, and categorical variables as frequencies and percentages. Incidence and severity of hematologic toxicity were described by CTCAE grade.

To evaluate changes in hematologic parameters across the six treatment cycles, repeated-measures ANOVA was performed, with the non-parametric Friedman test applied as a confirmatory analysis due to the potential for non-normal distribution. Comparisons between responders and non-responders were conducted using the independent samples t-test for normally distributed variables and the Mann–Whitney U test as a non-parametric alternative.

Receiver operating characteristic (ROC) curve analysis was performed to assess the discriminative performance of CBC parameters for predicting non-response, the area under the curve (AUC), optimal cut-off values (Youden index), sensitivity, and specificity were calculated. Progression free survival (PFS) was estimated using the Kaplan–Meier method, differences between groups were assessed using the log-rank test, and hazard ratios (HR) were calculated to estimate relative risk. A p-value < 0.05 was considered statistically significant.

Ethical approval

The study protocol was approved by the Institutional Ethics Committee at Medical City, Baghdad (approval number: RECAUBCP0525145A). All patient data were anonymized prior to analysis to ensure confidentiality and compliance with ethical standards.

Results

Patients disposition and follow-up

During the six-cycle observation period, 17 patients were excluded due to incomplete follow-up (difficulty attending regular visits or missed doses). The final analysis included 80 patients.

Due to violations of normality and sphericity ($p < 0.05$), the non-parametric Friedman test was used for longitudinal comparisons, with repeated-measures ANOVA reported for consistency.

Neutrophil count

Neutropenia was the most frequently observed adverse event. A total of 62 patients (77.5%) experienced at least one neutropenic episode (any grade) during the six cycles. Mild to moderate neutropenia (grades 1-2) occurred in 35 patients (43.8%), while severe neutropenia was less frequent: 23 patients (28.7%) developed grade 3 neutropenia, and 4 patients (5%) developed grade 4 neutropenia (Figure 1). Neutropenia typically appeared early, with 52 of the 62 affected patients (66% of the total cohort) having developed neutropenia by the end of cycle 2.

The mean absolute neutrophil count (ANC) remained broadly stable over the six treatment cycles. Repeated-measures ANOVA showed no significant effect of cycle on ANC ($F(5, 365) = 0.27$, $p = 0.93$), indicating that neutrophil values did not change systematically over time. This finding was further confirmed by the Friedman test ($\chi^2(5) = 1.85$, $p = 0.87$), suggesting that increasing treatment cycles were not associated with progressive neutropenia at the group level.

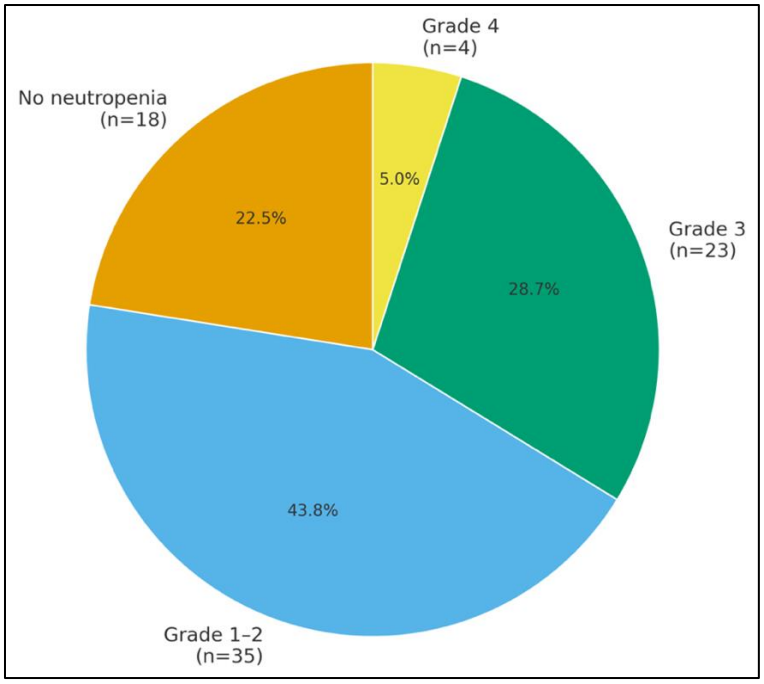

Figure 1: Distribution of Neutrophil status.

Although the mean neutrophil count was higher in the non-responders (2.41±2.07) than in responders (1.61±1.64), the independent samples t-test showed a trend toward but no statistically

significant difference (p = 0.061) (Table 2). The discriminative performance of mean neutrophil count for predicting non-response was fair (AUC = 0.6288). The optimal cut-off value (Youden index) was 1.62, achieving a sensitivity of 53.33% and specificity of 77.27%, (Figure 2). This suggests that a neutrophil count above this threshold is associated with an increased likelihood of treatment failure.

Table 2. Comparison of neutrophil counts between responders and non-responders

Group	**Mean ± SD**	**Df**	**p-value**
Responders	1.61±1.64	5, 365	0.061
Non-responders	2.41±2.07	5	

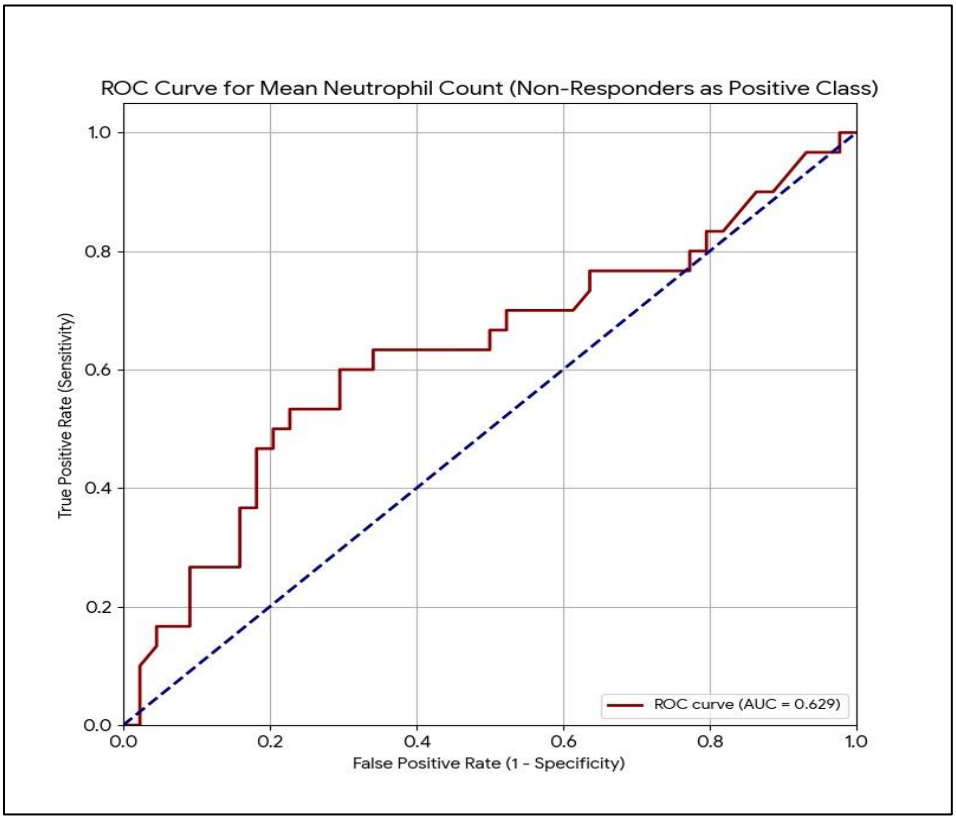

Figure 2. ROC curve for neutrophil count in no responders

Leukocytes count

Overall, 50 patients (62.5%) developed some degree of leukopenia during treatment; most cases were grade 1 or 2. Approximately 15-20% of patients developed grade ≥ 3 leukopenia, with no grade 4 leukopenia (Figure 3).

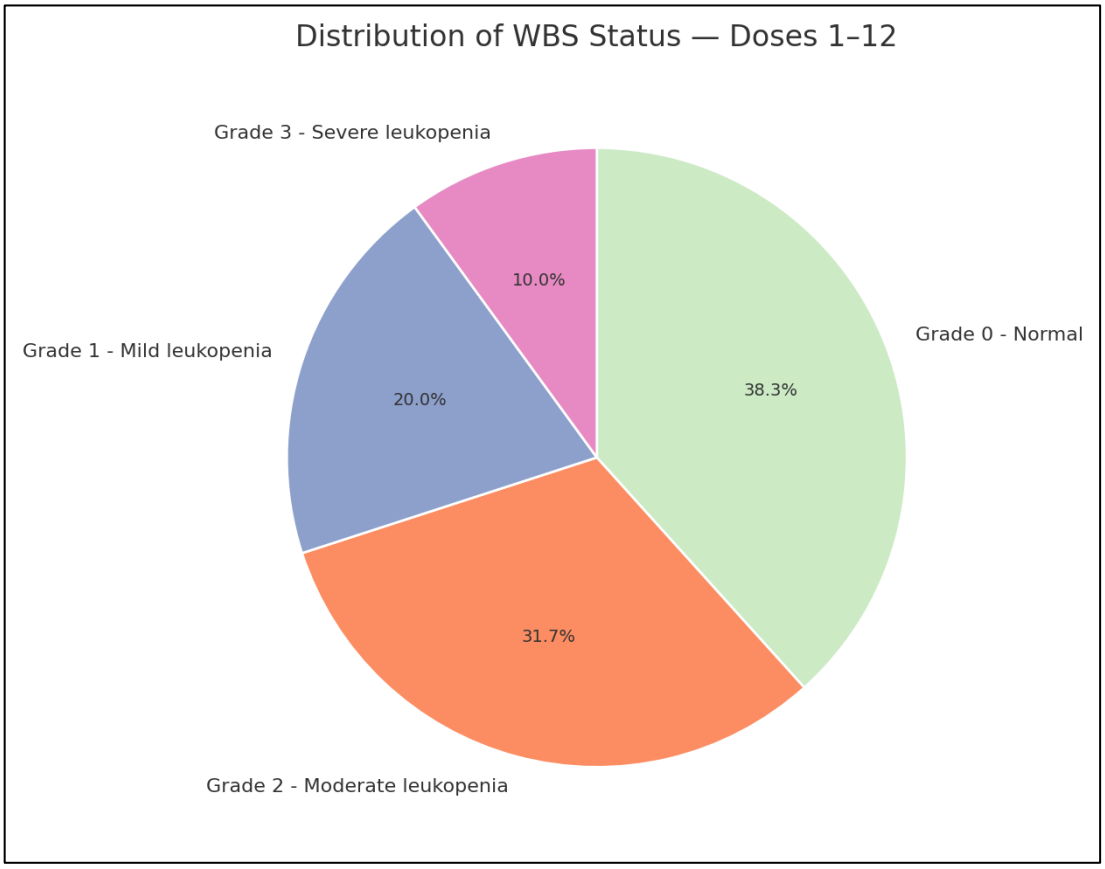

Figure 3. Distribution of WBC status

No patient required G-CSF, and WBC counts recovered during drug-free intervals in all cases. Repeated-measures ANOVA demonstrated no significant main effect of treatment cycle on WBC counts ($F(5, 365) = 1.76$, $p = 0.12$), consistent with the Friedman test (χ^2 (5) = 5.44, $p = 0.36$) (Table 3).

To assess whether cumulative treatment increased the risk of leukopenia, WBC toxicity was defined as WBC count < 4.0×10^9/L. The proportion of patients experiencing leukopenia remained relatively constant across cycles 1 to 6, and point-biserial correlation revealed no significant association between cycle number and leukopenia occurrence ($r = 0.001$, $p = 0.98$) (Table 3).

Table 3. WBC repeated-measures ANOVA and Friedman test

Test	Statistics	Df	p-value
Repeated-measures ANOVA	F = 1.76	5, 365	0.12
Friedman test (non- parametric)	$\chi^2 = 5.44$	5	0.36
Point-biserial correlation	r = 0.001	-	0.98
Mann-Whitney U	-	-	0.0271

The Mann-Whitney U test confirmed a statistically significant difference in the WBC counts between responders (mean: 3.71) and non-responders (mean: 4.49; p = 0.027) (Table 4). This finding indicates that WBC count may serve as an independent prognostic factor of treatment response.

ROC analysis for mean WBC count yielded an AUC of 0.654, with an optimal cut-off of 3.67, sensitivity of 62.07%, and specificity of 70.45% (Figure 4).

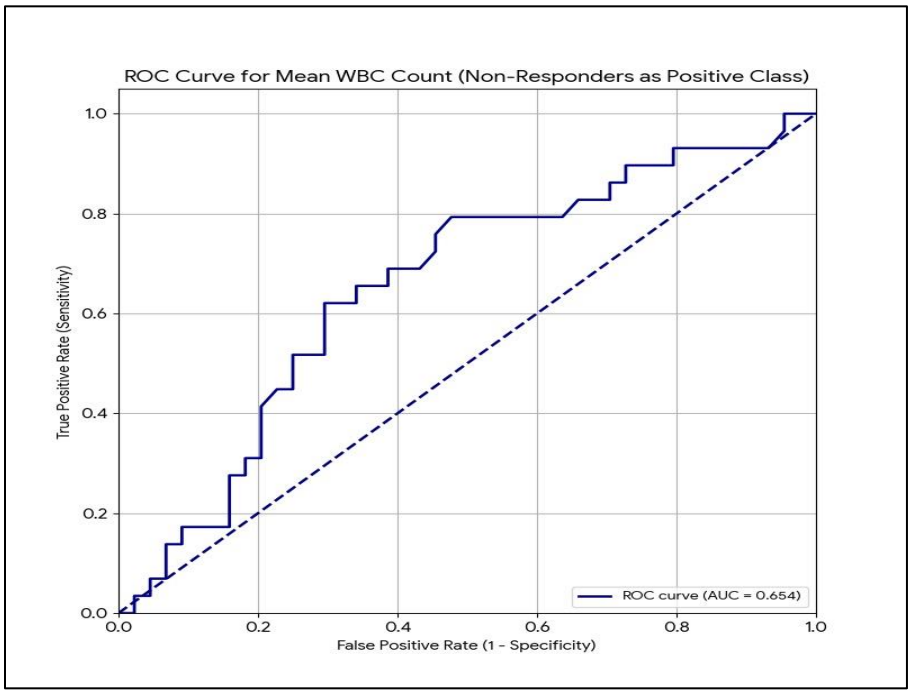

Figure 4. ROC curve for WBC.

Red blood cell count

Repeated-measures ANOVA showed no significant main effect of treatment cycle on RBC counts ($F(5, 345) = 0.23$, $p = 0.95$), confirmed by the Friedman test ($\chi^2(5) = 0.96$, $p = 0.97$) (Table 4).

Table 4. Hemoglobin repeated-measures ANOVA and Friedman test

Test	**Statistics**	**Df**	**p-value**
Repeated-measures ANOVA	$F = 0.23$	5, 345	0.95
Friedman test (non- parametric)	$\chi^2 = 0.96$	5	0.97
Point-biserial correlation	r=0.024	-	0.63
Mann-Whitney U	349.5	-	0.0271

RBC levels were significantly lower in responders (median: 3.43; IQR: 3.07-3.73) than in non-responders (median: 3.80; IQR: 3.55-4.23; Mann-Whitney U = 349.5, $p = 0.003$). Higher RBC levels were therefore associated with lack of treatment response.

ROC analysis for mean RBC level to predict non-response yielded an AUC of 0.7073. The optimal cut-off was 3.53, with sensitivity of 75.86% and specificity of 59.52% (Figure 5). High-RBC group (median RBC above 3.57) had markedly shorter 6-month PFS (55.6%) compared with the low-RBC group (88.6%; log-rank $\chi^2 = 9.31$, $p = 0.0023$; HR ≈ 4.5 for high vs. low RBC).

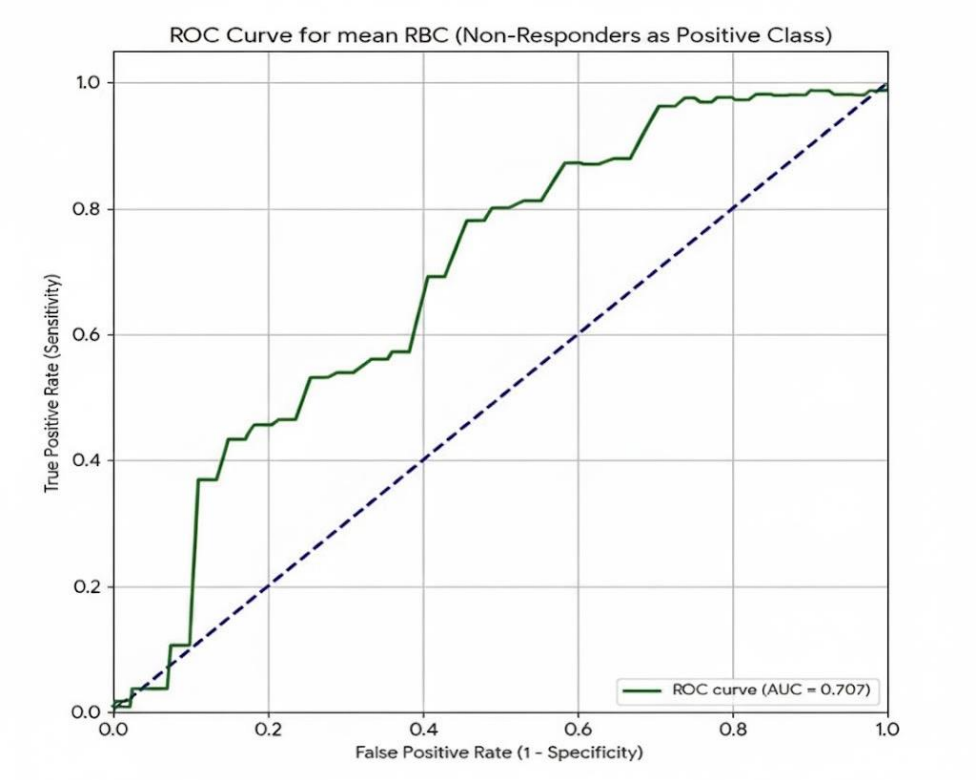

Figure 5. ROC curve for RBC

Lymphocytes and Neutrophil-to-Lymphocyte ratio (NLR)

Lymphopenia developed in 20 of 80 patients (25%). In most patients (65%), lymphocyte counts remained within normal range (Figure 6). Lymphopenia was generally grade 1 or 2, with no grade 3 or 4. A small proportion (≤ 10%) experienced transient relative lymphocytosis.

No significant difference in mean lymphocyte counts was observed between responders (1.45) and non-responders (1.37; Mann-Whitney U= 621.0, p = 0.671).

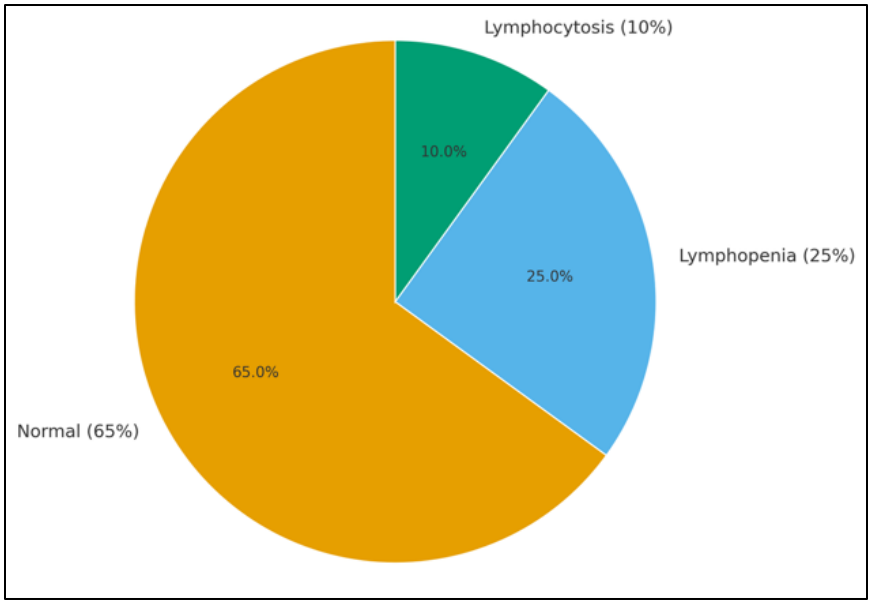

Figure 6. Distribution of Lymphocyte status

The neutrophil-to-lymphocyte ratio (NLR) was 1.25 in responders and 1.98 in non-responders, but the difference was not statistically significant ($p = 0.12$). The optimal NLR cut-off was approximately 1.59 (sensitivity: 46.7%; specificity: 70.9%) (Figure 7).

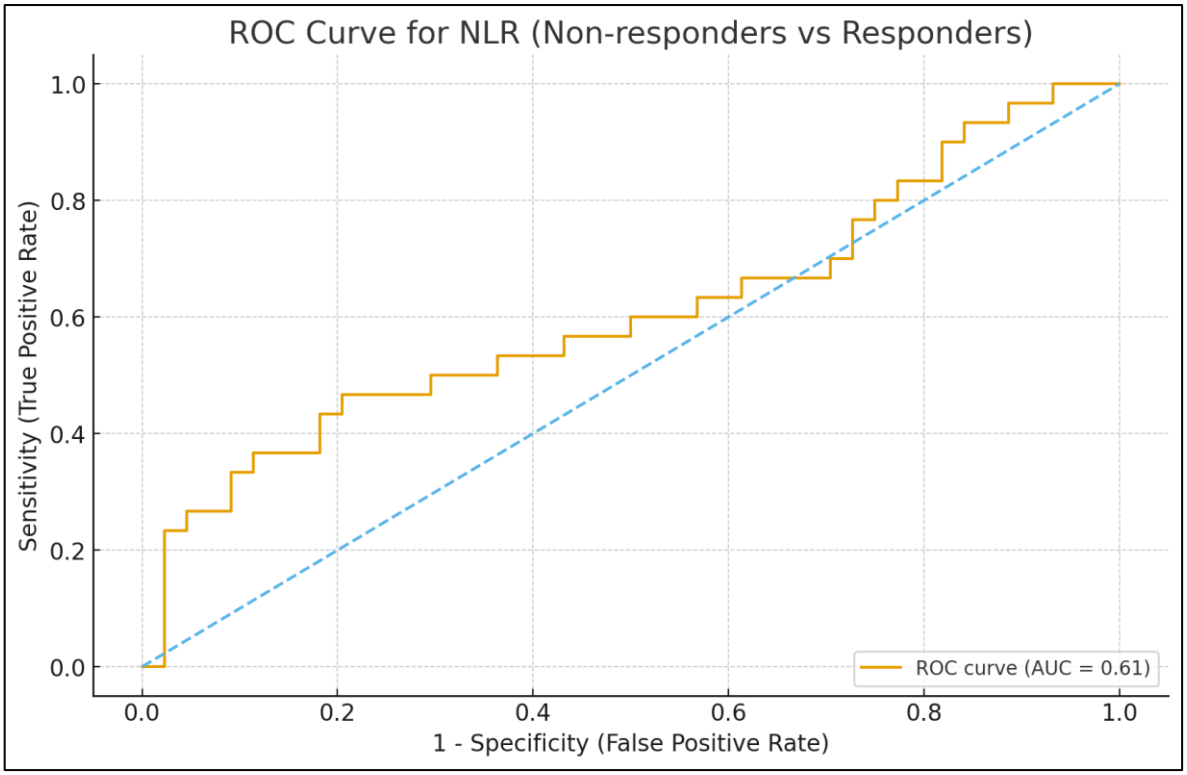

Figure 7. ROC curve for NLR

Hemoglobin (Hb)

Mean Hb demonstrated moderate discriminative performance for non-response (AUC = 0.71; z = 3.22, p = 0.001), with non-responders tending to have higher Hb values than responders. The Mann-Whitney U test confirmed a significant difference (U = 861.5, p = 0.003).

A second ROC analysis for mean Hb showed modest but significant discrmination (AUC = 0.65, z = 2.23, p = 0.026), supported by the Mann-Whitney U test (U= 767.1, p = 0.032). When stratified by median Hb (10.84 g/dL), 6-month PFS was 80% in the low-Hb group and 65.7% in the high-Hb group, but this difference was not statistically significant (log-rank $\chi^2 = 1.82$, p = 0.18; HR = 1.85).

Univariate survival analysis

In univariate time-to-event analyses, mean WBC count was the only CBC-derived index with a statistically significant association with PFS. Patients with WBC above the median (3.4×10^9/L) had markedly shorter PFS (6-month PFS: 62.2% vs 86.1%; log-rank $\chi^2 = 5.40$, p = 0.020; HR = 3.1 for high vs. low WBC). Higher mean neutrophil counts and elevated NLR were associated with numerically worse PFS (HR ≈ 1.8 and 1.5, respectively), whereas higher LNR showed a modest trend toward improved PFS (HR ≈ 0.65). However, none of these associations reached statistical significance (Table 5). Mean lymphocyte count showed no meaningful association with PFS.

Table 5. PFS according to CBC parameters

Marker	Cut-off	n (low/high)	6-month PFS (low/high)	HR (high vs. low)	p-value
Mean Neutrophil ($\times 10^9$/L)	1.14	36 / 37	0.81 / 0.68	1.82	0.190
Mean WBC ($\times 10^9$/L)	3.40	36 / 37	0.86 / 0.62	3.06	0.020
Mean lymphocytes ($\times 10^9$/L)	1.29	36 / 37	0.81 / 0.68	1.78	0.204
NLR	1.04	36 / 37	0.78 / 0.70	1.45	0.406
LNR	0.96	36 / 37	0.69 / 0.78	0.65	0.332

WBC, White Blood Cell; NLR, neutrophil-to-lymphocyte ratio; LNR, lymphocyte-to-neutrophil ratio; PFS, Progression-Free Survival; HR, Hazard Ratio.

Data available for 73 of 80 patients (7 excluded due to incomplete CBC records).

Discussion

In this real-world study of 80 Iraqi women with advanced HR+/ HER2- breast cancer treated with palbociclib plus letrozole, we observed a distinct pattern of hematologic toxicities. Our findings confirm the manageable safety profile of palbociclib while highlighting differences in incidence compared to pivotal clinical trials. Notably, 62.5% of patients developed leukopenia, while 28.7% experienced grade 3 and 5% experienced grade 4 neutropenia. No febrile neutropenia events occurred, and no patient required G-CSF support.

This rate of high-grade neutropenia in our cohort is substantially lower than the 60–66% reported in the registration PALOMA trials[12] and the 60.9% incidence (95% CI: 57.8–63.8%) documented in a systematic review of eight clinical trials encompassing 1515 patients.[13]

However, our results align with real-world evidence, where grade 3-4 neutropenia has been reported in approximately 30–47% of patients.[14] The disparity between clinical trial and real-world data can be attributed to multiple factors. Trial populations are highly selected and undergo intensive laboratory monitoring, which may lead to more frequent detection of asymptomatic neutropenia.[15] Importantly, the grade 4 neutropenia rate in our cohort (5%) was similar to or lower than that reported in other studies; a pooled analysis of PALOMA trials reported approximately 10%, while a recent Asian real-world study observed around 5%.[16]

The absence of progressive decline in ANC across multiple cycles indicates that prolonged treatment does not exacerbate neutropenia at the population level. This finding supports the safety of continued palbociclib administration without cumulative hematologic deterioration.[17] This stable ANC pattern contrasts with chemotherapy-induced myelosuppression and reflects the predictable pharmacodynamic profile of CDK 4/6 inhibition, in which the one-week off-treatment interval allows consistent neutrophil recovery between cycles.[18] Our cohort corroborates these findings, as confirmed by repeated-measures ANOVA and Friedman tests, indicating no systematic decline in neutrophil values over time.

Early reductions in neutrophil counts appeared associated with favorable treatment response, whereas higher counts were observed among non-responders, although these differences did not reach statistical significance. Moreover, lower ANC values were numerically associated with improved PFS. These observations are consistent with previous reports indicating that a reduction in ANC during the first two cycles of single-agent palbociclib, as neutropenia of any grade, are independently associated with prolonged PFS.[19]

Mean neutrophil count exhibited only modest discriminatory capacity between responders and non-responders, with ROC analysis suggesting fair performance at best. Nevertheless, this analysis identified a clinical threshold above which patients appeared were more likely to experience treatment failure, with moderate sensitivity and relatively high specificity. To our knowledge, no prior palbociclib study has applied ROC methodology to neutrophil counts.

Although treatment cycles had no significant effect on WBC count, significant differences were observed between responders and non-responders. Higher WBC values ($> 3.4 \times 10^9$/L) were significantly associated with shorter PFS. In contrast, lymphocyte counts showed no significant association with treatment response. Elevated leukocyte counts in cancer patients have been linked to pro-tumorigenic inflammatory signaling, including increased levels of cytokines such as IL-6 and G-CSF, which may promote tumor proliferation, immune evasion, and resistance to endocrine-based therapies.[20]

The NLR ratio was evaluated as a predictor of treatment response and did not differ significantly between response groups. ROC analysis demonstrated a sensitivity of 46.7% and specificity of 70.9%, indicating modest discriminatory performance. Elevated NLR was associated with numerically worse PFS, whereas a higher LNR showed a modest trend toward improved PFS.

A study published in 2021 demonstrated that CDK6 is a key regulator of erythropoiesis, with CDK6-deficient mice exhibiting reduced RBC and Hb levels, establishing that effective CDK6 inhibition directly suppresses erythrocytes production.[14] These findings support our results, as mean RBC levels were significantly lower in responders than non-responders ($p = 0.003$). Ma et al. (2025)[21] recently developed an RBC-balanced immune-inflammatory signature that predicted response to CDK4/6 inhibitors with an AUC of 0.854 when combined with metabolic markers, further validating erythrocyte parameters as clinically relevant biomarkers. Consistently, our ROC analysis indicated that an RBC level above 3.53×10^{12}/L was associated with a markedly higher likelihood of non-response, supporting mean RBC as a potential prognostic marker of therapeutic failure.

Although RBC count is traditionally not considered a prognostic biomarker in breast cancer, the substantial survival differences between low- and high-RBC groups align with emerging evidence suggesting that erythrocyte parameters may serve as pharmacodynamic biomarkers of CDK4/6 inhibitor efficacy. Anampa et al. (2018)[22] reported that greater erythroid changes during palbociclib

treatment were observed, and MCV increase was proposed as a potential pharmacodynamic biomarker of CDK4/6 inhibition.

ROC analysis demonstrated that mean Hb had moderate discriminatory performance (AUC = 0.65, p = 0.026) in distinguishing responders from non-responders. This exceeds the composite HALP score (AUC = 0.56) reported by 23. Belen Gülbağci et al. (2024),[23] which incorporated Hb, albumin, lymphocyte, and platelet values but failed to predict early progression in CDK4/6 inhibitor-treated patients (p = 0.334). Anampa et al.[22] reported that macrocytic anemia may serve as a pharmacodynamic indicator of CDK4/6 inhibition and is associated with improved PFS. Similarly, in our study, patients with lower Hb achieved numerically higher 6-month PFS (80%) compared with those in the high-Hb group (65.7%), although this difference did not reach statistical significance.

These patterns are consistent with palbociclib's cytostatic mechanism, which induces reversible G1 arrest in hematopoietic precursors without causing DNA damage or apoptosis.[14] This explains both the predictable dose-response relationship and rapid hematologic recovery distinguishing CDK4/6 inhibitor-induced neutropenia from chemotherapy-induced myelosuppression. Population pharmacokinetic modeling has shown that targeting an AUC_{0-24} below 2900 ng.h/mL limits the risk of grade 4 neutropenia to approximately 10%,[24] indicating that higher drug exposure increases the likelihood of severe neutropenia.

Overall, these findings provide real-world evidence supporting individualized monitoring and population-specific dosing, particularly given ethnic variations in baseline hematological parameters and CDK4/6 inhibitor sensitivity.[25] Meta-analysis have demonstrated greater PFS benefit in Asian populations,[26] alongside higher rates of dose reductions (58.0%) and treatment interruptions (75.0%) due to adverse events.[27]

This single-center prospective observational study has a relatively small sample size. Follow-up was limited to the initial six cycles for all patients, with extended data available for only a subset. Despite these limitations, our study provides valuable real-world evidence reinforcing the manageable hematologic safety of palbociclib.

Conclusion

In conclusion, palbociclib plus letrozole was associated with frequent but predominantly low-grade hematologic toxicities, with no febrile neutropenia or life-threatening thrombocytopenia,

and recovery observed during off-treatment intervals. The incidence of grade 3–4 neutropenia was lower than that reported in PALOMA trials, confirming a predictable and manageable safety profile. Notably, higher mean white blood cell (WBC) counts linked to poorer clinical outcomes may reflect tumor-driven systemic inflammation rather than a direct causal effect, given the established association of elevated WBC with pro-tumorigenic inflammatory signaling, cytokine activation (e.g., IL-6, G-CSF), and paraneoplastic leukocytosis, which may promote tumor progression and therapy resistance. Collectively, routine monitoring of WBC and red blood cell (RBC) dynamics could serve as a low-cost tool to anticipate treatment failure and guide early optimization of palbociclib-based therapy in HR+/HER2- advanced breast cancer.

Authors' Contribution

Conceptualization: Eman Saadi Saleh, Ahmed Zuhair Alsammarraie
Data curation: Adnan Mustafa Isamail
Formal analysis: Eman Saadi Saleh, Ahmed Zuhair Alsammarraie
Investigation: Adnan Mustafa Isamail
Methodology: Eman Saadi Saleh, Ahmed Zuhair Alsammarraie
Writing–original draft: Adnan Mustafa Isamail
Writing–review & editing: Eman Saadi Saleh, Ahmed Zuhair Alsammarraie

Competing Interests

The authors state no conflict of interest.

Ethical Approval

The study protocol was approved by the Institutional Ethics Committee at Medical City, Baghdad (approval number: RECAUBCP0525145A). All patient data were anonymized prior to analysis to ensure confidentiality and compliance with ethical standards.

Funding

Not applicable

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