Natural Resources for Human Health
eISSN: 2583-1194

Original Research

Received 09 May 2026
Revised 25 June 2026
Accepted 05 July 2026

Natural Resources for Human Health 2026, Vol. 6 (12s): 537–552

KEYWORDS:
Palbociclib; CDK4/6 inhibitor; generic; brand-name; metastatic breast cancer; HR+/HER2−; drug-acquisition cost

Clinical Outcomes, Laboratory Safety, and Drug-Acquisition Cost Analysis of Generic versus Brand-Name Palbociclib in HR+/HER2− Metastatic Breast Cancer: A Real-World Ambispective Cohort Study from Iraq

Abdullah Hussein Ali[1], Hadeel Delman Najiem[2], Nabeel Mudheher Talib[3]

[1]Department of clinical pharmacy, College of Pharmacy, Mustansiriyah University, Baghdad, Iraq, E-mail: abdallahhussain@uomustansiriyah.edu.iq, ORCID: 0009-0003-2385-9520
[2]Department of clinical pharmacy, collage of pharmacy, Mustansiriyah University, Baghdad, Iraq, E-mail: Pharm.hadeelnajjem@uomustansiriyah.edu.iq, ORCID: 0000-0003-1217-1942
[3]Medical oncology, Anbar Cancer Center, Anbar healthcare director, ministry of health, Anbar, Iraq, E-mail: drnabeelmt@gmail.com, ORCID: 0009-0002-3831-1720
Corresponding author: Abdullah Hussein Ali, E-mail: abdallahhussain@uomustansiriyah.edu.iq

ABSTRACT:

Background: The usage of Palbociclib for the treatment of HR+/HER2− breast cancer metastases is expensive, compromising its accessibility for patients in LMICs. Iraq needs evidence about generics: effectiveness, safety and price.

Objective: The aim was to compare 12-month disease control rate, overall response rate, laboratory safety, progress-free survival, and drug-acquisition cost of Ibrance® vs. IPI-Palbo® in Iraqi patients with HR+/HER2− metastatic breast cancer.

Methods: This Ambispective cohort included 57 women receiving Palbociclib plus endocrine at Anbar Cancer Center, Iraq. The patients received either brand-name (n=20) or generic (n=37) Palbociclib. CT evaluated the response of the tumor based on RECIST 1.1 at 4, 8 and 12 months. We were assessing the blood and chemical parameters in subjects. Analysis was performed of drug-acquisition costs, cost-effectiveness ratios, Kaplan-Meier progression-free survival and multivariable logistic regression for 12-month disease control.

Results: The rates of disease control were similar between the two groups at a twelve-month follow-up (60.0% vs.59.5%; p=1.000), as were the overall response rates at twelve months (15.0% versus 10.8%; p=0.687). There were no discontinuations due to (clinically) acceptable laboratory differences. Brand acquisition cost was almost four times greater (4,447,016 vs. 1,106,503 IQD; p<0.001) with IPI-Palbo® being the cost-effective option.

Conclusion: The generic version of Palbociclib showed similar efficacy in 12-month disease control with acceptable laboratory safety at lower cost. Overall, our study supports

the value of generic Palbociclib to practice in Iraq oncology, which warrants a prospective confirmation.

INTRODUCTION

Breast cancer remains the most frequently diagnosed malignancy and a leading cause of cancer-related mortality among women worldwide [1]. In Iraq, breast cancer accounts for approximately one-third of all female cancers, with a substantial proportion presenting at advanced or metastatic stages due to limitations in early detection infrastructure and screening programs [2]. The HR+/HER2− molecular subtype of (mBC) occurs in approximately 70% of patients with breast cancer, making it the most common molecular subtype encountered in clinical practice, according to the LINK study [3]. The treatment landscape for HR+/HER2− mBC has been transformed by the introduction of cyclin-dependent kinase 4/6 (CDK4/6) inhibitors, which target the cell-cycle machinery governing the G1-to-S phase transition [4]. Palbociclib (Ibrance®, Pfizer Inc.) was the first CDK4/6 inhibitor approved for clinical use following the PALOMA trials. The PALOMA-2 trial showed first-line Palbociclib plus letrozole extended median progression-free survival (PFS) to 24.8 months compared with 14.5 months for letrozole alone in postmenopausal women with HR+/HER2− mBC [5]. In a similar manner, the PALOMA-3 trial established the effectiveness of Palbociclib plus fulvestrant in patients who progressed on prior endocrine therapy, with median PFS of 9.5 months vs. 4.6 months for placebo plus fulvestrant [6]. More recently, in an Asian population PALOMA-4, confirmed the PFS benefit of Palbociclib plus letrozole [7]. These studies together demonstrated Palbociclib as a standard-of-care first-line therapy in combination with endocrine therapy for HR+/HER2− mBC. Even though CDK4/6 inhibitors have shown clinically meaningful benefits, drug costs substantially limit access to them in most low- and middle-income countries (LMICs) [8]. The yearly cost of brand Palbociclib can exceed US$100,000 in high-income settings, which is greater than per-capita healthcare expenditure in most LMICs [9]. In Iraq, the healthcare system has been interrupted by years of conflict, stressing the existing limited resources. The cost of innovative cancer drugs poses a fundamental challenge to cancer care [10]. The aforementioned economic reality necessitated the arrival on the Iraqi market of Palbociclib generic formulations; several countries, Iraq included, received IPI-Palbo® (IPHARM, Iraq) as part of the national pharmaceutical supply. The emergence of generic CDK4/6 inhibitors in LMICs could be a game changer for access to evidence-based cancer care. Nevertheless, the shift from brand to generic oncology products raises reasonable scientific inquiry concerning real-world clinical therapeutic equivalence [11]. Regulatory approval of generic formulations generally depends on demonstrating pharmaceutical equivalence and conducting bioequivalence studies in healthy volunteers. However, data on comparative effectiveness in actual cancer patients is scarce [12]. This is particularly true for oral targeted therapies such as Palbociclib, where even small changes in bioavailability could theoretically affect efficacy and toxicity over long treatment durations. So far in published literature, there are a few real-world comparative studies that have evaluated clinical outcomes between brand name and generic CDK4/6 inhibitors in patients of (mBC). Particularly, the published literature on LMIC settings is scarce where the use of generics is maximum. The evidence void leads to ambiguity for clinicians, patients, policymakers, and formulary committees characterizing therapeutic selection and resource allocation. The present study aimed to compare and assess clinical outcomes, laboratory safety parameters, drug-acquisition costs, and other effectiveness between brand-name Palbociclib (Ibrance®) and generic Palbociclib (IPI-Palbo®) in a real-world cohort of Iraqi patients with HR+/HER2− mBC. This Ambispective cohort study specifically aimed to: (1) compare 12-month disease-control rate and overall response rate between the brand and the generic formulations; (2) evaluate longitudinal laboratory safety profiles at three time points; (3) quantitate drug-acquisition cost differential and assess cost-utility; (4) examine PFS between groups; and (5) identify independent predictors of 12-month disease control through multivariable regression analysis.

METHODOLOGY

Study Design

This was an Ambispective (combined retrospective and prospective) observational cohort study. The retrospective component involved the extraction of historical clinical and laboratory data from medical records for patients who had already initiated Palbociclib therapy prior to study commencement. The prospective component involved continued follow-up of enrolled patients to complete 12 months of documented outcomes. The achievement of an appropriate sample size over a manageable time period and incorporation of their methodologies for observational data collection for part of the follow-up was made possible by this hybrid design.

Setting and Timeline

The study was done at Anbar Cancer Centre (ACC), which is a tertiary referral oncology institution in Anbar Governorate, Iraq. This center offers all cancer diagnosis and treatment services like medical oncology, radiation therapy, and surgical oncology. Initiation of patient enrollment and data collection taken place during the study period whereby eligible patients receiving Palbociclib-based therapy were identified and followed for a minimum of 12 months in treatment initiation. The study was registered prospectively on ClinicalTrials.gov (NCT07493291).

Participants

The study population included adult female patients with histologically confirmed HR+/HER2− metastatic breast cancer receiving Palbociclib with endocrine therapy.

1. **Inclusion criteria:** (1) Female patients aged ≥18 years; (2) histologically or cytological confirmed breast cancer with documented HR-positive (estrogen receptor and/or progesterone receptor positive) and HER2-negative status; (3) radiologically confirmed metastatic disease; (4) receiving Palbociclib (either brand or generic formulation) in combination with endocrine therapy (aromatase inhibitor or fulvestrant); (5) minimum 12 months of documented follow-up or documented progression prior to 12 months; (6) availability of baseline and follow-up computed tomography (CT) imaging for response assessment.

2. **Exclusion criteria:** (1) Prior exposure to any CDK4/6 inhibitor before the study observation period; (2) concurrent participation in interventional clinical trials of investigational agents; (3) incomplete medical records precluding assessment of primary outcomes; (4) switching between brand and generic formulations during the observation period.

A total of 75 patients were initially screened for eligibility, from which 57 patients met all inclusion criteria and were enrolled (Brand group, n=20; Generic group, n=37). Eighteen patients were excluded: 11 did not meet eligibility criteria and 7 had incomplete data precluding outcome assessment.

Study Groups

Patients were classified into two groups based on the Palbociclib formulation received:

1. **Brand group (n=20):** Patients receiving Ibrance® (Palbociclib capsules, Pfizer Inc., USA) at the standard approved dose of 125 mg orally once daily for 21 consecutive days followed by 7 days off treatment in 28-day cycles, administered in combination with endocrine therapy.

2. **Generic group (n=37):** Patients receiving IPI-Palbo® (Palbociclib capsules, IPHARM, Iraq) at the same dosing regimen of 125 mg orally once daily for 21 days followed by 7 days off in 28-day cycles, in combination with endocrine therapy.

Group assignment was determined by physician prescribing practice and drug availability through the institutional formulary; patients were not randomly allocated to treatment groups.

Outcome Measures

1. **Primary outcome:** Twelve-month disease control rate (DCR), defined as the proportion of patients achieving complete response (CR), partial response (PR), or stable disease (SD) at the 12-month assessment per RECIST 1.1 criteria [13].

2. **Secondary outcomes:** 1. Overall response rate (ORR), defined as the proportion achieving CR or PR, assessed at 4, 8, and 12 months. 2. DCR at 4 and 8 months. 3. Laboratory safety profile: hematological parameters (white blood cell count [WBC], hemoglobin [HGB], platelet count [PLT]) and biochemical parameters (alanine aminotransferase [ALT], aspartate aminotransferase [AST], blood urea, serum creatinine [Cr], serum calcium) at 4, 8, and 12 months. 4. Progression-free survival (PFS), defined as the time from Palbociclib initiation to documented radiological progression or death from any cause. 5. Drug-acquisition cost: monthly and 12-month total drug-acquisition costs per patient. 6. Average cost-effectiveness ratio (ACER): 12-month drug cost divided by the effectiveness measure (DCR or ORR). 7. Incremental cost-effectiveness ratio (ICER): the difference in cost divided by the difference in effectiveness between groups.

Data Collection

Clinical and laboratory data were collected at three pre-specified time points: - **Visit 1 (V1):** 4 months after Palbociclib initiation - **Visit 2 (V2):** 8 months after Palbociclib initiation - **Visit 3 (V3):** 12 months after Palbociclib initiation

At each visit, the following data were recorded:

Laboratory parameters*:* Complete blood count components (WBC, hemoglobin, platelet count), hepatic function (ALT, AST), renal function (blood urea, serum creatinine), and serum calcium. Values were obtained from routine clinical monitoring blood draws performed within ±2 weeks of each scheduled assessment time point.

Radiological response*:* CT-based tumor response assessment classified per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) [13] into: complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD). Assessments were performed by the treating oncology team as part of routine clinical practice.

Demographic and clinical data*:* Age, weight, height, body mass index (BMI), menopausal status, residence (urban/rural), monthly household income, educational level, disease presentation (de novo metastatic vs. recurrent), sites of metastasis, and concurrent endocrine therapy regimen.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent samples t-test for normally distributed data or the Mann-Whitney U test for non-normally distributed data. Normality was assessed using the Shapiro-Wilk test. Categorical variables were expressed as frequencies and percentages and compared using the chi-square test or Fisher's exact test as appropriate based on expected cell counts. Multivariable binary logistic regression was performed to identify independent predictors of 12-month disease control (DCR as the dependent variable). Covariates entered into the model included treatment group (brand vs. generic), age, liver metastasis, income category, obesity status (BMI ≥30 kg/m²), and menopausal status. Model fit was assessed using the likelihood ratio test, Akaike Information Criterion (AIC), and pseudo R^2 statistics. PFS was analyzed using the Kaplan-Meier method, and between-group comparison was performed using the log-rank test. A two-sided significance level of α=0.05 was applied for all analyses. Statistical analyses were performed using IBM SPSS Statistics (version 26.0; IBM Corp., Armonk, NY, USA) and Python (version 3.x; scipy, stats models, and lifelines libraries).

Ethical Considerations

The study was approved by the Scientific Research Ethics Committee at the College of Pharmacy, Al-Mustansiriyah University (Approval No. 97; Thesis No. 207; Administrative Decision No. 2025053). The study was conducted in accordance with the principles of the Declaration of Helsinki and applicable local regulations. Informed consent was obtained from prospectively enrolled patients. For the retrospective component, a waiver of individual consent was granted given the observational nature of the data collection and the use of de-identified clinical information. Patient confidentiality was maintained throughout the study. The study was registered on ClinicalTrials.gov (NCT07493291) prior to initiation of prospective data collection.

RESULTS

Patient Selection and Enrollment

A total of 75 patients receiving palbociclib-based therapy at Anbar Cancer Center were initially screened for study eligibility. Of these, 18 patients were excluded: 11 did not meet the pre-specified eligibility criteria (including 4 with prior CDK4/6 inhibitor exposure, 3 with concurrent investigational therapy, and 4 with HER2-positive or triple-negative reclassification), and 7 had incomplete medical records precluding assessment of the primary outcome. The final analytical cohort comprised 57 patients: 20 in the brand group (Ibrance®) and 37 in the generic group (IPI-Palbo®). The patient selection and enrollment process is depicted in **Figure 1**.

Natural Resources for Human Health
eISSN: 2583-1194

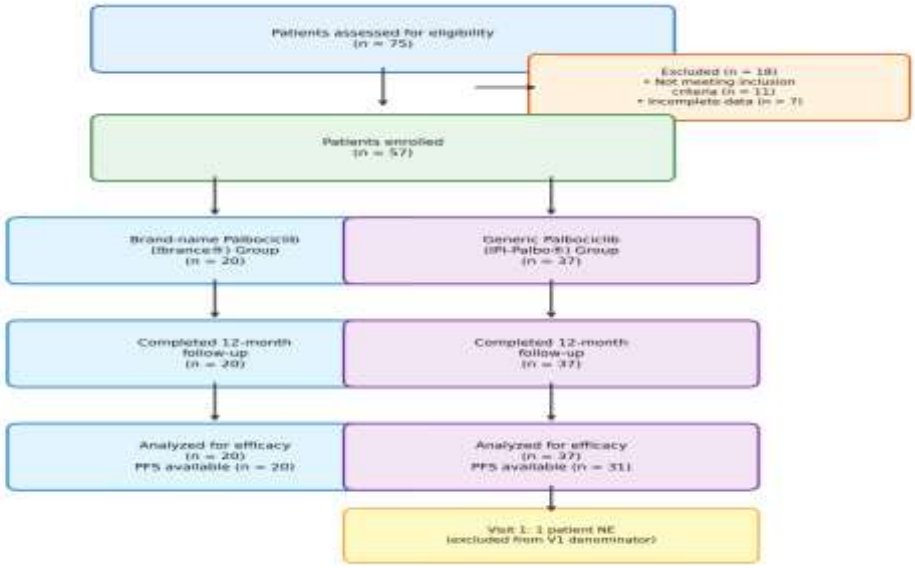

Figure 1: Patient Selection Flow Diagram

Baseline Characteristics

Baseline demographic and clinical characteristics of the two study groups are presented in **Table 1**. The groups were generally well-balanced with respect to age (brand: 56.8±10.8 years vs. generic: 55.1±10.5 years; p=0.574), BMI (brand: 31.4±5.4 kg/m² vs. generic: 29.5±6.3 kg/m²; p=0.244), menopausal status (postmenopausal: 70.0% vs. 67.6%), residence, and educational level. The distribution of metastatic sites was similar between groups, with bone being the most common site (brand: 70.0%; generic: 64.9%). The majority of patients in both groups received aromatase inhibitor-based endocrine therapy (brand: 75.0%; generic: 78.4%). The only statistically significant baseline difference was monthly household income: a higher proportion of patients in the brand group reported income below 500,000 IQD (75.0% vs. 35.1%; p=0.026). A greater proportion of liver metastases was found in the brand group (25.0% vs. 5.4%) which did not reach conventional statistical significance in the univariate comparison. The rates of disease presentation also differed, with the generic group having more de novo metastatic disease (64.9% vs. 40.0%).

Table 1. Baseline Clinical and Demographic Characteristics of Study Population.

Variable	Brand (n=20)	Generic (n=37)	p-value
Age (years), mean ± SD	56.8 ± 10.8	55.1 ± 10.5	0.574
Weight (kg), mean ± SD	80.2 ± 13.0	74.3 ± 14.5	0.136
Height (cm), mean ± SD	159.9 ± 5.8	159.1 ± 6.8	0.660
BMI (kg/m²), mean ± SD	31.4 ± 5.4	29.5 ± 6.3	0.244
BMI category, n (%)			
Normal (18.5–24.9)	3 (15.0%)	8 (21.6%)	0.138
Overweight (25.0–29.9)	4 (20.0%)	16 (43.2%)	
Obese (≥30.0)	13 (65.0%)	13 (35.1%)	
Menopausal status, n (%)			1.000
Premenopausal	6 (30.0%)	12 (32.4%)	

Postmenopausal	14 (70.0%)	25 (67.6%)	
Residence, n (%)			0.405
Urban	12 (60.0%)	17 (45.9%)	
Rural	8 (40.0%)	16 (43.2%)	
Monthly income, n (%)			0.026*
	15 (75.0%)	13 (35.1%)	
	5 (25.0%)	20 (54.1%)	
Education level, n (%)			0.455
University	3 (15.0%)	2 (5.4%)	
Secondary	3 (15.0%)	9 (24.3%)	
Primary	10 (50.0%)	14 (37.8%)	
High school	4 (20.0%)	8 (21.6%)	
Disease presentation, n (%)			0.098
De novo metastatic	8 (40.0%)	24 (64.9%)	
Recurrent	11 (55.0%)	13 (35.1%)	
Metastatic sites, n (%)			
Bone	14 (70.0%)	24 (64.9%)	0.774
Liver	5 (25.0%)	2 (5.4%)	0.074
Lung	4 (20.0%)	7 (18.9%)	1.000
Lymph node	7 (35.0%)	13 (35.1%)	1.000
Endocrine therapy, n (%)			
Aromatase inhibitor	15 (75.0%)	29 (78.4%)	0.749
Fulvestrant/SERD	5 (25.0%)	4 (10.8%)	
AI + Zoladex	0 (0.0%)	3 (8.1%)	
Zoladex alone	0 (0.0%)	1 (2.7%)	

Abbreviations: SD refers to standard deviation; while, BMI means body mass index. IQD refers to the Iraqi dinar. AI refers to aromatase inhibitors. Finally, SERD means selective estrogen receptor degrader. Results are statistically significant.

Laboratory Safety Profile

At each of the three follow-up visits, laboratory parameters have been assessed as shown in Tables 2–4. At Visit 1 (4 months), significant between-group differences were observed for ALT (brand: 11.47±3.81 vs. generic: 18.19±11.19 U/L; p=0.015), AST (brand: 16.58±3.55 vs. generic: 25.58±15.08 U/L; p=0.003), and serum calcium (brand: 8.24±0.23 vs. generic: 8.92±0.58 mg/dL; p<0.001). Hematological parameters (WBC, hemoglobin, and platelets), urea, and creatinine were similar at Visit 1. The values at Visit 2 (8 months) were significantly different for hepatic transaminases (ALT: p=0.022; AST: p=0.033) with the generic group showing greater mean values. Moreover, urea level in brand group at visit 2 was significantly higher than that of generic group (38.45±8.12 vs. 28.72±11.15 mg/dL; p=0.005). There were no important variations seen in Hematological

parameters, creatinine and calcium." At Visit 3 (12 months), there was a statistically significant increase in AST in the generic group compared to the brand-name group. The level of urea was significantly high in brand group (38.92±15.20 vs. 30.14±8.47 mg/dl; p=0.012) and the level of the creatinine was significantly high in brand group was also significant after omitting the one statistical outlier (0.84±0.12 vs. 0.73±0.20 mg/dl; p=0.020). Notably, despite the statistically significant differences, all mean laboratory values in both groups remained within normal clinical reference ranges throughout the study. During the observation period, no patient in either group had their treatment discontinued due to laboratory abnormalities.

Table 2. Laboratory Parameters at Visit 1 (4 Months)

Parameter	Brand (n=20)	Generic (n=37)	p-value
WBC (×10³/μL)	4.15 ± 1.53	4.41 ± 3.78	0.278
Hemoglobin (g/dL)	11.38 ± 1.12	11.18 ± 1.30	0.780
Platelets (×10³/μL)	182.77 ± 40.02	220.29 ± 126.28	0.465
ALT (U/L)	11.47 ± 3.81	18.19 ± 11.19	0.015*
AST (U/L)	16.58 ± 3.55	25.58 ± 15.08	0.003*
Urea (mg/dL)	33.97 ± 8.80	31.44 ± 9.91	0.323
Creatinine (mg/dL)	0.74 ± 0.19	0.70 ± 0.18	0.280
Calcium (mg/dL)	8.24 ± 0.23	8.92 ± 0.58	<0.001*

Abbreviations: The full form of WBC, ALT and AST are respectively. The values are expressed as mean ± SD. Mann-Whitney U test. *The value obtained from statistical hypothesis testing is lower than 0.05.

Table 3. Laboratory Parameters at Visit 2 (8 Months)

Parameter	Brand (n=20)	Generic (n=37)	p-value
WBC (×10³/μL)	4.78 ± 2.11	4.08 ± 1.78	0.375
Hemoglobin (g/dL)	11.11 ± 1.24	11.05 ± 1.16	0.968
Platelets (×10³/μL)	188.82 ± 33.64	202.44 ± 89.93	0.833
ALT (U/L)	13.09 ± 2.74	18.15 ± 8.38	0.022*
AST (U/L)	18.36 ± 3.61	24.94 ± 13.37	0.033*
Urea (mg/dL)	38.45 ± 8.12	28.72 ± 11.15	0.005*
Creatinine (mg/dL)	0.78 ± 0.18	1.32 ± 3.41	0.219
Calcium (mg/dL)	8.84 ± 0.72	8.95 ± 0.67	0.237

Abbreviations: WBC is the white blood cell count whereas ALT and AST are alanine aminotransferase and aspartate aminotransferase respectively. Mean and standard deviation (SD). Mann-Whitney U test p<0.05.

Table 4. Laboratory Parameters at Visit 3 (12 Months)

Parameter	Brand (n=20)	Generic (n=37)	p-value
WBC (×10³/μL)	5.45 ± 3.46	3.85 ± 2.21	0.168
Hemoglobin (g/dL)	10.51 ± 0.90	11.08 ± 1.08	0.149
Platelets (×10³/μL)	161.42 ± 59.67	174.71 ± 58.19	0.880
ALT (U/L)	15.17 ± 6.95	18.12 ± 5.34	0.061
AST (U/L)	19.25 ± 7.19	26.38 ± 13.22	0.030*
Urea (mg/dL)	38.92 ± 15.20	30.14 ± 8.47	0.012*

Creatinine (mg/dL)	0.84 ± 0.12	0.73 ± 0.20	0.020*
Calcium (mg/dL)	8.95 ± 0.80	8.99 ± 0.72	0.531

Abbreviations: WBC, white blood cell count; ALT, alanine aminotransferase; AST, aspartate aminotransferase. Values are mean ± SD. Mann-Whitney U test. *p<0.05. Creatinine p-value reported after exclusion of one outlier value.

Response Distribution over Follow-up

As outlined in Table 5, the radiological response category distributions at each assessment time point Visit 1 (4 months) show that the majority of patients in both groups achieved either a PR or SD, with no progressive disease seen in either group. One patient in the generic group was not evaluable at this time point. At Visit 2 (8 months), a shift in response distribution was observed: the brand group maintained 8 patients with PR and 12 with SD (no PD), while the generic group showed 5 with PR, 26 with SD, and 5 with PD. The overall response distribution differed significantly between groups at Visit 2 (p=0.033). By Visit 3 (12 months), progressive disease was observed in both groups (brand: 8/20, 40.0%; generic: 15/37, 40.5%), with the response distributions converging between groups.

Table 5. Response Distribution by RECIST 1.1 Criteria Over Follow-up

Visit	Group	CR, n	PR, n	SD, n	PD, n	NE, n	Evaluable, n
Visit 1 (4 mo)	Brand	0	11	9	0	0	20
	Generic	0	19	17	0	1	36
Visit 2 (8 mo)	Brand	0	8	12	0	0	20
	Generic	0	5	26	5	0	36
Visit 3 (12 mo)	Brand	0	3	9	8	0	20
	Generic	0	4	18	15	0	37

Abbreviations: CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease; NE, not evaluable; mo, months. Response assessed per RECIST 1.1 criteria.

3.5 ORR and DCR Trends

The trends in ORR and DCR across all three assessment time points are summarized in **Table 6** and illustrated in **Figure 2**.

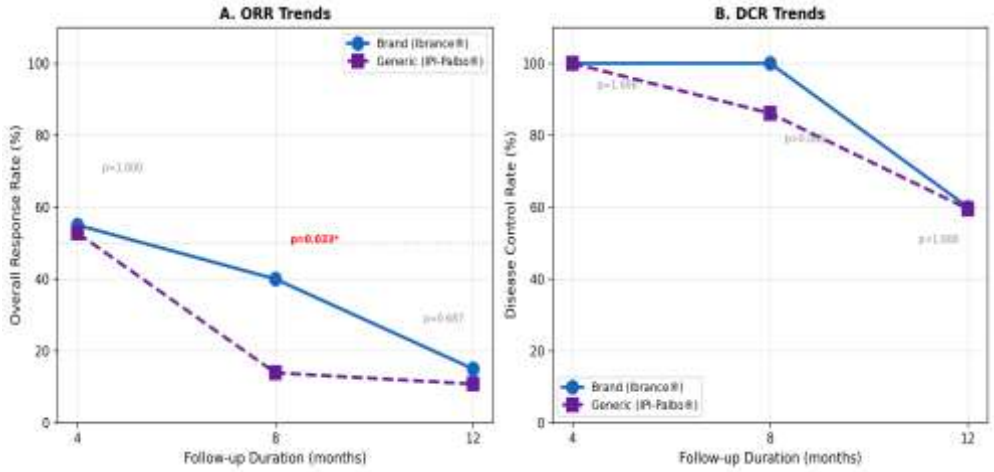

Figure 2: Overall Response Rate (ORR) and Disease Control Rate (DCR) Trends Over Follow-up Visits

At 4 months, ORR was comparable between groups (brand: 55.0% vs. generic: 52.8%; p=1.000), and DCR was 100% in both groups—indicating that all evaluable patients maintained at least disease stabilization at this early time point. At 8 months, a statistically significant difference emerged in ORR, favoring the brand group (40.0% vs. 13.9%; p=0.033). DCR also favored

the brand group numerically (100% vs. 86.1%), though this did not reach statistical significance (p=0.148). By 12 months, the ORR difference between groups had diminished and was no longer statistically significant (brand: 15.0% vs. generic: 10.8%; p=0.687). Importantly, the 12-month DCR (primary endpoint) was comparable between brand (60.0%) and generic (59.5%) (p=1.000).

Table 6. Overall Response Rate and Disease Control Rate by Time point

Time point	Outcome	Brand	Generic	p-value
4 months	ORR	11/20 (55.0%)	19/36 (52.8%)	1.000
4 months	DCR	20/20 (100%)	36/36 (100%)	—
8 months	ORR	8/20 (40.0%)	5/36 (13.9%)	**0.033***
8 months	DCR	20/20 (100%)	31/36 (86.1%)	0.148
12 months	ORR	3/20 (15.0%)	4/37 (10.8%)	0.687
12 months	DCR	12/20 (60.0%)	22/37 (59.5%)	1.000

Abbreviations: ORR, overall response rate (CR + PR); DCR, disease control rate (CR + PR + SD). Fisher's exact test. *p<0.05.

Drug-Acquisition Cost Comparison

Analysis of drug-acquisition costs indicated a large and highly significant cost difference between the two formulations (Table 7; Figure 3). The mean monthly total drug-acquisition cost for was IQD 4,447,016 ± 122,939 for the brand group compared to IQD 1,106,503 ± 197,072 for the generic group (t=68.759; p< 0.001). This corresponded to a brand-to-generic cost ratio of approximately 4.02:1.

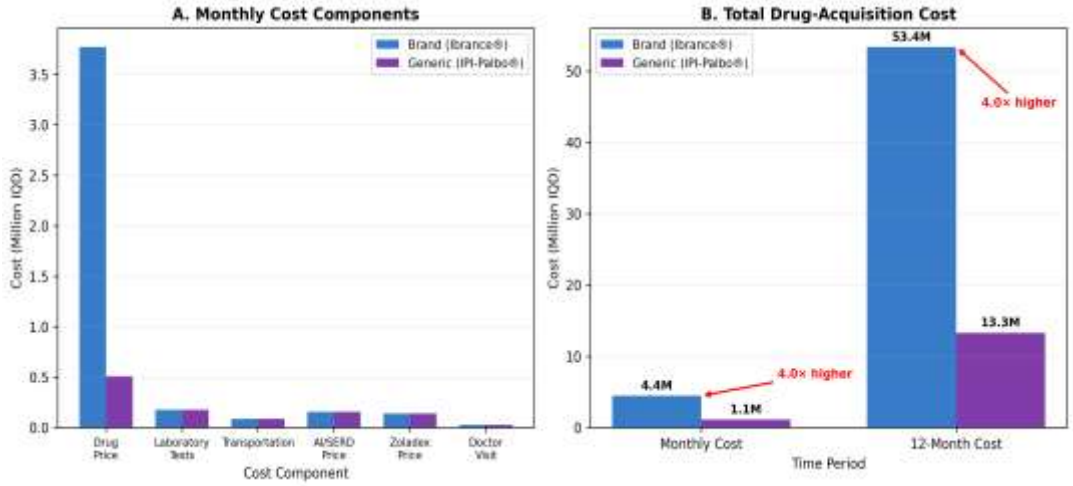

Figure 3. Monthly and Annual Drug-Acquisition Cost Comparison between Brand and Generic Palbociclib

Extrapolated to a 12-month treatment course, the mean total drug-acquisition cost per patient was 53,364,192 ± 1,475,265 IQD for brand-name Palbociclib versus 13,278,042 ± 2,364,869 IQD for generic palbociclib—a difference of approximately 40 million IQD (≈US$30,000 at prevailing exchange rates) per patient per year.

Table 7. Drug-Acquisition Cost Comparison

Parameter	Brand (Ibrance®)	Generic (IPI-Palbo®)	p-value
Drug price per cycle (IQD)	3,770,014	508,317	—
Monthly total cost (IQD), mean ± SD	4,447,016 ± 122,939	1,106,503 ± 197,072	<0.001*

12-month total cost (IQD), mean ± SD	53,364,192 ± 1,475,265	13,278,042 ± 2,364,869	<0.001*
Brand-to-Generic cost ratio	4.02: 1	—	—

Abbreviations: IQD, Iraqi dinar. Independent samples t-test. *p<0.05. Cost includes drug acquisition only; excludes consultation, monitoring, hospitalization, and adverse event management costs.

ACER and ICER Analysis

Cost-effectiveness analysis using drug-acquisition costs as the cost input is presented in Table 8. The average cost-effectiveness ratio (ACER) based on 12-month DCR was 88,940,320 IQD per disease-controlled patient for the brand formulation compared with 22,331,252 IQD per disease-controlled patient for the generic formulation—a 3.98-fold difference favoring the generic. When expressed per responder (ACER based on ORR), the brand cost 355,761,280 IQD per responder compared with 122,821,887 IQD per responder for the generic (2.90-fold difference). The incremental cost-effectiveness ratio (ICER) for the brand relative to the generic was calculated at 7,415,937,780 IQD per additional disease-controlled patient gained. This extraordinarily high ICER indicates that the marginal benefit of brand-name Palbociclib over the generic formulation (a 0.5 percentage-point difference in DCR) comes at a prohibitively disproportionate incremental cost, rendering the brand formulation not cost-effective by any conventional willingness-to-pay threshold.

Table 8. Average Cost-Effectiveness and Incremental Cost-Effectiveness Analysis

Metric	Brand (Ibrance®)	Generic (IPI-Palbo®)	Difference
12-month DCR	60.0%	59.5%	+0.5%
12-month ORR	15.0%	10.8%	+4.2%
ACER-DCR (IQD per controlled patient)	88,940,320	22,331,252	3.98×
ACER-ORR (IQD per responder)	355,761,280	122,821,887	2.90×
ICER-DCR (IQD per additional controlled patient)	—	—	7,415,937,780
ICER-ORR (IQD per additional responder)	—	—	956,895,197
Interpretation	Not cost-effective	Economically preferred	—

Abbreviations: ACER, average cost-effectiveness ratio; ICER, incremental cost-effectiveness ratio; DCR, disease control rate; ORR, overall response rate; IQD, Iraqi dinar. Drug-acquisition cost only.

Adjusted Analysis

A multivariable logistic regression analysis was performed to determine whether treatment group was an independent predictor of having control at 12 months after adjustment for confounders (Table 9). In this analysis, we included the following as covariates: treatment group, age, liver metastasis, income category, obesity status, menopausal status. The findings indicated that the type of treatment (brand versus generic) did not independently predict twelve-month DCR (odds ratio=0.973; 95% CI: 0.238–3.982; p=0.970). The only factor that proved to be an independent variable of significance was liver metastasis (OR=0.136; 95% CI: 0.020–0.941; p=0.043), which verifies that subjects with hepatic metastases had substantially lower odds of achieving disease control at 12 months, irrespective of Palbociclib formulation used. Low income came near, but did not reach, statistical significance (OR=3.646; 95% CI: 0.944–14.091; p=0.061). The overall model demonstrated modest explanatory power (pseudo R^2=0.106; AIC=82.71; likelihood ratio test p=0.226).

Table 9. Multivariable Logistic Regression for 12-Month Disease Control

Predictor	Odds Ratio	95% CI	p-value
Treatment group (Brand vs. Generic)	0.973	0.238–3.982	0.970
Age (per year)	1.027	0.945–1.117	0.529
Liver metastasis (present vs. absent)	0.136	0.020–0.941	**0.043***
Low income (<500,000 IQD)	3.646	0.944–14.091	0.061

Obesity (BMI ≥30 kg/m²)	0.752	0.216–2.619	0.654
Postmenopausal status	0.330	0.047–2.303	0.263

Abbreviations: CI, confidence interval; IQD, Iraqi dinar; BMI, body mass index. Model statistics: Pseudo R^2=0.106; AIC=82.71; LLR p-value=0.226. *p<0.05.

3.9 Progression-Free Survival

Progression-free survival analysis was conducted for all patients with available progression or censoring dates (**Table 10**; **Figure 4**). Median PFS was numerically longer in the brand group (13.6 months) compared with the generic group (12.4 months); however, this difference did not reach statistical significance (log-rank p=0.151). Mean PFS was 15.6 ± 6.7 months in the brand group versus 12.3 ± 4.7 months in the generic group. The range of PFS values was 6.0–32.0 months for brand and 4.0–25.0 months for generic.

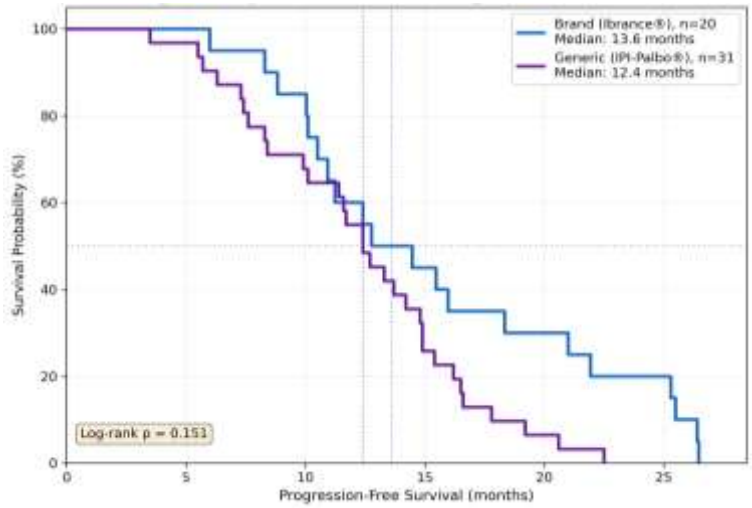

Figure 4. Kaplan-Meier Curve for Progression-Free Survival

Table 10. Progression-Free Survival Analysis

Parameter	Brand (n=20)	Generic (n=31)	p-value
Median PFS (months)	13.6	12.4	0.151
Mean PFS (months) ± SD	15.6 ± 6.7	12.3 ± 4.7	—
Range (months)	6.0–32.0	4.0–25.0	—

Abbreviations: PFS, progression-free survival; SD, standard deviation. Log-rank test. PFS defined as time from Palbociclib initiation to radiological progression or death.

DISCUSSION

Summary of Principal Findings

This Ambispective cohort study compared clinical outcomes, laboratory safety, and drug-acquisition costs between brand-name Palbociclib (Ibrance®) and generic Palbociclib (IPI-Palbo®) in 57 Iraqi patients with HR+/HER2− mBC. The principal findings were: (1) the primary endpoint of 12-month DCR was comparable between groups (60.0% vs. 59.5%; p=1.000); (2) while a significant difference in 8-month ORR favored the brand group, this discrepancy resolved by 12 months; (3) laboratory safety profiles showed statistical differences in select parameters without clinical significance; (4) median PFS did not differ significantly; (5) the generic formulation was approximately 4-fold less expensive; (6) cost-effectiveness analysis strongly favored the generic; and (7) multivariable regression confirmed that treatment group was not an independent predictor of disease control.

Comparison with Previous CDK4/6 Inhibitor Generic Studies

The present findings are consistent with the limited emerging literature on generic CDK4/6 inhibitor performance in LMICs. The 12-month DCR of approximately 60% observed in both groups in our study is broadly consistent with the disease control rates reported in real-world registries of palbociclib-treated patients, which typically range from 55% to 75% depending on the line of therapy and patient selection criteria [14]. Our ORR findings at 4 months (approximately 53–55%) are similarly aligned with real-world data from the PALOMA trials' long-term follow-up and post-marketing registries [5], [6]. Bioequivalence studies of generic Palbociclib formulations have demonstrated comparable pharmacokinetic parameters to the reference product in healthy volunteer studies, meeting regulatory standards for area under the curve and peak concentration within the 80–125% confidence interval required for approval [12]. However, pharmacokinetic equivalence in healthy volunteers does not necessarily translate to clinical equivalence in cancer patients, who may have altered drug absorption, metabolism, and elimination due to disease burden, hepatic involvement, concurrent medications, and nutritional status [15]. The present study provides preliminary real-world clinical evidence suggesting that observed outcomes with the generic formulation are comparable at the most clinically meaningful time point (12 months).

Interpretation of the Visit 2 Discrepancy

The statistically significant difference in ORR at 8 months (brand: 40.0% vs. generic: 13.9%; p=0.033) merits careful interpretation. Several non-causal explanations should be considered. To begin with, this finding may represent a Type I error given multiple comparisons across three time points without correction for multiplicity. Moreover, the small sample sizes heighten the effect of individual patient courses on group-level proportions; the 8-month difference of about 26 percentage points translates into a difference of just 3 additional patients achieving PR in the brand group. Thirdly, the fracture in liver metastases, 25.0% for the brand and 5.4% for the generic, might paradoxically contribute, which our regression showed, liver metastases predict a worse long-term outcome, but measurable hepatic lesions may show more dramatic response per RECIST criteria, potentially inflating early PR rates. The outcomes by 12 months were virtually identical, with the DCR being the same and the ORR not statistically significant. Therefore, the authors suggest that the difference at 8 months likely reflects differences in the kinetics of response classification, not a difference in the efficacy sustained over time. The importance of maintaining PR versus SD at an intermediate time point is debatable if long-term disease control is the same. These findings need to be carefully monitored along with larger sample sizes.

Laboratory Safety in Context

The laboratory safety evaluation indicated various statistically significant intergroup differences over the three assessment time points. The mean hepatic transaminase (ALT and AST) levels were higher for the generic group, but the brand group's means were higher for urea and creatinine. It is essential to note that statistical significance is not clinical significance [16]. Throughout the study period, the mean values for both groups remained within normal reference range limits, and no patient required discontinuation of treatment or dose adjustment in response to an abnormality in the laboratory. A limitation of the present analysis is the lack of CTCAE grading which does not allow a systematic assessment of whether individual patients experienced clinically relevant grade ≥3 toxicities [17]. The variances seen in transaminases may be a result of individual differences, excipient differences which can change liver metabolism, or unobserved confounding. The slightly higher urea and creatinine levels observed in the brand cohort may be attributed to that group's distribution of older ages or greater frequency of confounding illnesses, although not at baseline.

Health-Economic Implications for Iraq

The healthy-economic analysis indicated that brand-name Palbociclib is roughly 4 times more expensive than the generic in Iraq, which equals an extra 40 million IQD (around US$30,000) for each patient each year of treatment. In a country where per capita health spending is estimated to be around US$ 200–300 per annum [10], this level of cost differential has serious implications for drug access, formulary inclusion, and health system sustainability. The ICER of 7.4 billion IQD per additional disease-controlled patient is extraordinarily high by any standard. Even applying the World Health Organization's recommendation that interventions costing less than three times the gross domestic product per capita per quality-adjusted life-year may be considered cost-effective [18], the brand formulation cannot be justified on economic grounds given the near-identical 12-month DCR between groups. The ACER analysis further demonstrates that the generic achieves comparable disease control at approximately one-quarter of the cost per controlled patient. It is important to note that this analysis captures drug-acquisition costs only and does not constitute a comprehensive pharmacoeconomic evaluation. A full economic analysis

would additionally incorporate costs of adverse event management, hospitalization, monitoring, quality-of-life adjustments, and indirect costs [19]. Nevertheless, given the dominance of drug-acquisition costs in the total treatment cost for oral targeted therapies administered in the outpatient setting, the present findings provide a meaningful estimate of the relative economic efficiency of generic versus brand formulations.

Adjusted Analysis Implications

The multivariable logistic regression analysis provided exploratory evidence suggesting that the comparable 12-month DCR between groups was not confounded by baseline imbalances. After adjustment for age, liver metastasis, income, obesity, and menopausal status, treatment group demonstrated an odds ratio of 0.973 (p=0.970)—indicating virtually no association between formulation type and disease control. This near-null effect size is particularly informative given that the baseline income imbalance (the only significant demographic difference) was explicitly controlled for in the model. Liver metastasis, as the only important variable significantly associated with 12-month DCR (OR=0.136; p=0.043), is plausible, given that visceral metastases, and in particular liver metastasis, are well known to be associated with poor outcome with CDK4/6 inhibitors [20]. As site of metastasis is a more relevant prognostic factor than formulation type, disease control outcomes were favorably comparable. The pseudo-R^2 equal to 0.106 is modest, indicating that there is an important unobserved variable that contributes significantly to variation in outcomes. This is as expected given the complexity of cancer biology and response to treatment.

PFS Findings

The median PFS associated with the brand was 13.6 months versus 12.4 months for the generic, p=0.151. Clinical trial (PFS) estimates of palbociclib-based regimens (12 to 20 months depending on line of therapy and patient characteristics) were similar to those from observational studies [14], [21]. The post-marketing surveillance 101 expected PFS of Palbociclib was consistent 102 with other published studies. The PFS figures found in the current study are lesser than the 24.8 months sustained in PALOMA-2 trial. The differences in PFS values maybe due to strict eligibility in clinical trial with real world heterogeneity, line of therapy and our cohort's high burden of visceral metastases [5]. The Advantage Should Be Interpreted with Caution. Benefit of 1.2 Months PFS Non-Statistically Significant in Real World Data Base. The 1.2 Mo PFS advantage for the brand group deserves some caution in interpretation for a number of reasons. A small sample size means only modest power to detect modest PFS differences; PFS date was extracted retrospectively from patient records introducing imprecision over event timing; and the design of the study not being randomized means there is still residual confounding that may explain the benefit. PFS values were more heterogeneous in the brand group (6.0–32.0 months vs. 4.0–25.0 months), possibly as a result of the outlier patients with long responses.

Clinical Implications

As this study's results have many implications for practice in resource-poor settings. First, the comparable 12-month DCR and non-significant PFS difference suggest that generic Palbociclib may represent an acceptable therapeutic alternative for patients who would otherwise have no access to CDK4/6 inhibitor therapy due to cost barriers. In the Iraqi context, where out-of-pocket pharmaceutical expenditure represents a significant portion of household income, the 4-fold cost reduction enables broader patient access to guideline-concordant first-line therapy for HR+/HER2− mBC. Moreover, the observed 8-month ORR gap, possibly reflecting methodological artefacts, raises the question of closer imaging surveillance during the first months of therapy when generics are used. Clinicians might gauge response assessment at 8 months as SOP to identify patients with early progression that might benefit from a therapeutic switch. Third, the discovery that liver metastasis, rather than formulation type, is the principal determinant of disease control, reinforces the need for prognostic assessment tailored to the individual, rather than a formulation-based approach.

Limitations

This article showed that the study had several important limitations that affected the analysis:

1. Single-center design: The fact that all the patients were taken from a single institution (Anbar Cancer Center) limits generalizability to other geographic and institutional settings within Iraq and other LMICs.
2. Small sample size: Due to an inadequate sample size, the study was not sufficiently powerful to detect even slightly important differences in either efficacy or safety. The sample sizes greater than 10 000 patients would be necessary to achieve statistical significance for DCR.

3. Non-randomized design: The treatment group allocation in this observational study was not randomly assigned but rather as a result of physician preference, drug availability and patient financial capacity which may lead to selection bias.
4. Absence of blinding: Both the patients and the treating physician knew about the formulation received by the patients. So, there are chances of performance and detection bias regarding which trial formulations were better.
5. Baseline income imbalance: The substantial contrast in household income among groups (p=0.026) could be beneficial as a proxy for other socioeconomic determinants of health outcomes, such as nutritional status, adherence capacity, and access to supportive care, which were not evaluated.
6. No CTCAE adverse event grading: The laboratory parameters were reported as continuous values without any systematic grading according to the CTCAE criteria, which does not allow standardized assessment of clinically significant toxicities or comparison with safety data from regulatory trials.
7. Retrospective component: The Ambispective design uses data retrospective to the study, which involves an analysis of medical records. Such an analysis does have limitations. Medical record review is limited by missing data, documentation inconsistencies, and an inability to confirm whether the patient adhered to treatment or not.
8. Drug-acquisition cost only: The economic assessment incorporated costs of acquiring pharmaceuticals but failed to account for monitoring, adverse effect treatment, hospitalization, lost productivity, and quality of life drop costs.
9. PFS dates extracted from medical records: They determined progression dates based on clinical notations rather than mandated protocol imaging dates, injecting variability for event timing accuracy.
10. No quality-of-life assessment: The treatment tolerability or patient experience could not be evaluated as patient-reported outcomes and health-related quality of life were not assessed.
11. Single generic manufacturer: The findings can't be applied to other generic Palbociclib products that may differ in formulation, manufacturing processes, or quality control standards. Only one generic formulation (IPI-Palbo® by IPHARM) was evaluated.

CONCLUSION

In this single-center Ambispective cohort study, generic Palbociclib (IPI-Palbo®) demonstrated comparable observed 12-month disease-control rates to brand-name Palbociclib (Ibrance®) in HR+/HER2− metastatic breast cancer patients, at a substantially lower drug-acquisition cost. The ICER analysis indicated that the brand-name formulation is not cost-effective relative to the generic alternative. However, the observed differences in intermediate (8-month) response rates and certain laboratory parameters warrant further investigation. Larger, multicenter, randomized, adequately powered prospective studies are required to confirm these findings and confirm comparative real-world effectiveness and safety in real-world clinical practice.

Conflict of Interest: The authors declare no conflicts of interest.

Funding*:* This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data Availability: The datasets generated and analyzed during the current study are available from the corresponding author upon reasonable request.

Registration: *ClinicalTrials.gov Identifier: NCT07493291*

Ethics Approval: Scientific Research Ethics Committee, College of Pharmacy, Al-Mustansiriyah University (Approval No. 97; Thesis No. 207), dated October 1, 2025. Administrative approval from Al-Anbar Health Directorate / Training and Human Development Center (Decision No. 2025053), dated August 3, 2025.

REFERENCES

[1] H. Sung, J. Ferlay, R. L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, and F. Bray, "Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries," *CA Cancer J. Clin.*, vol. 71, no. 3, pp. 209–249, 2021. https://doi.org/10.3322/caac.21660

[2] Iraqi Cancer Board, "Results of the Iraqi Cancer Registry 2019," Ministry of Health, Republic of Iraq, Baghdad, 2020.

[3] A. G. Waks and E. P. Winer, "Breast cancer treatment: A review," *JAMA*, vol. 321, no. 3, pp. 288–300, 2019. https://doi.org/10.1001/jama.2018.19323

[4] S. Goel, M. J. Seidel, and P. Sicinski, "CDK4/6 inhibition in cancer: Beyond cell cycle arrest," *Trends Cell Biol.*, vol. 28, no. 11, pp. 911–925, 2018. https://doi.org/10.1016/j.tcb.2018.07.002

[5] R. S. Finn, M. Martin, H. S. Rugo, S. Jones, S. A. Im, K. Gelmon, N. Harbeck, O. N. Lipatov, J. M. Walshe, S. Mouber, et al., "Palbociclib and letrozole in advanced breast cancer," *N. Engl. J. Med.*, vol. 375, no. 20, pp. 1925–1936, 2016. https://doi.org/10.1056/NEJMoa1607303

[6] N. C. Turner, J. Ro, F. André, S. Loi, S. Verma, H. Iwata, N. Harbeck, S. Loibl, C. Huang Bartlett, K. Zhang, et al., "Palbociclib in hormone-receptor-positive advanced breast cancer," *N. Engl. J. Med.*, vol. 373, no. 3, pp. 209–219, 2015. https://doi.org/10.1056/NEJMoa1505270

[7] H. S. Rugo, R. S. Finn, C. S. Diéras, S. A. Im, K. Gelmon, et al., "Palbociclib plus letrozole as first-line therapy in estrogen receptor-positive/human epidermal growth factor receptor 2-negative advanced breast cancer: Efficacy and safety updates with longer follow-up across subgroups from PALOMA-4," *J. Clin. Oncol.*, vol. 39, no. 15, suppl., 2021.

[8] Z. Cherny, R. Sullivan, U. Dafni, J. M. Kerst, A. Sobrero, C. Zielinski, E. G. E. de Vries, and M. J. Piccart, "A standardised, generic, validated approach to stratify the magnitude of clinical benefit that can be anticipated from anti-cancer therapies: The European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS)," *Ann. Oncol.*, vol. 28, no. 5, pp. 1149–1166, 2017. https://doi.org/10.1093/annonc/mdx045

[9] A. T. Bui, T. N. Tran, and B. T. Nguyen, "Access to targeted cancer therapies in low- and middle-income countries: Challenges and potential solutions," *Lancet Oncol.*, vol. 23, no. 1, pp. e52–e62, 2022. https://doi.org/10.1016/S1470-2045(21)00656-2

[10] World Health Organization, "Global Health Expenditure Database: Iraq Country Profile," WHO, Geneva, 2023. [Online]. Available: https://apps.who.int/nha/database

[11] A. Rizzo, A. D. Ricci, and G. Brandi, "The use of generic drugs in oncology: A systematic review," *Expert Opin. Drug Saf.*, vol. 20, no. 10, pp. 1205–1213, 2021. https://doi.org/10.1080/14740338.2021.1945032

[12] U.S. Food and Drug Administration, "Bioequivalence studies with pharmacokinetic endpoints for drugs submitted under an ANDA: Guidance for industry," Center for Drug Evaluation and Research, Silver Spring, MD, 2021.

[13] E. A. Eisenhauer, P. Therasse, J. Bogaerts, L. H. Schwartz, D. Sargent, R. Ford, J. Dancey, S. Arbuck, S. Gwyther, M. Mooney, et al., "New response evaluation criteria in solid tumours: Revised RECIST guideline (version 1.1)," *Eur. J. Cancer*, vol. 45, no. 2, pp. 228–247, 2009. https://doi.org/10.1016/j.ejca.2008.10.026

[14] A. DeMichele, S. Cristofanilli, K. Brufsky, J. Liu, J. Mardekian, L. McRoy, and M. Rubin, "Real-world outcomes with palbociclib plus letrozole versus letrozole alone in HR+/HER2− metastatic breast cancer: A retrospective database analysis," *Breast Cancer Res. Treat.*, vol. 184, no. 2, pp. 559–568, 2020. https://doi.org/10.1007/s10549-020-05873-w

[15] L. Z. Benet, "The role of BCS (Biopharmaceutics Classification System) and BDDCS (Biopharmaceutics Drug Disposition Classification System) in drug development," *J. Pharm. Sci.*, vol. 102, no. 1, pp. 34–42, 2013. https://doi.org/10.1002/jps.23359

[16] G. M. Sullivan and R. Feinn, "Using effect size—or why the P value is not enough," *J. Grad. Med. Educ.*, vol. 4, no. 3, pp. 279–282, 2012. https://doi.org/10.4300/JGME-D-12-00156.1

[17] U.S. Department of Health and Human Services, "Common Terminology Criteria for Adverse Events (CTCAE) version 5.0," National Cancer Institute, Bethesda, MD, 2017.

[18] World Health Organization, "Making choices in health: WHO guide to cost-effectiveness analysis," WHO, Geneva, 2003.

[19] M. F. Drummond, M. J. Sculpher, K. Claxton, G. L. Stoddart, and G. W. Torrance, *Methods for the Economic Evaluation of Health Care Programmes*, 4th ed. Oxford, UK: Oxford University Press, 2015.

[20] N. Turner, S. Ro, F. André, and S. Loi, "PALOMA-3: Updated overall survival analysis of fulvestrant + palbociclib vs fulvestrant + placebo in HR+/HER2− metastatic breast cancer," *J. Clin. Oncol.*, vol. 36, no. 15, suppl., 2018.

[21] A. Brufsky, S. Sridhar, and M. Engel-Nitz, "Real-world effectiveness of palbociclib plus an aromatase inhibitor or fulvestrant in HR+/HER2− metastatic breast cancer: A US community oncology network study," *Oncologist*, vol. 26, no. 1, pp. e37–e48, 2021. https://doi.org/10.1002/onco.13545