Original Article
DOI: https://doi.org/10.70749/ijbr.v3i7.2108

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://ijbr.com.pk
ISSN: 2960-2793/ 2960-2807

# Response of Palbociclib in Old Age Metastatic Breast Cancer Patient

**Kaynat Fatima[1], Zeba Aziz[1], Amjad Zafar[1], Alishba Asif[1], Aleena Nazar[1]**

[1]Department of Medical Oncology, Hameed Latif Hospital, Lahore, Pakistan

## ARTICLE INFO

**Keywords:** Metastatic breast cancer, Palbociclib, Response, Elderly patients.

**Correspondence to:** Dr Kaynat Fatima, Department of Medical Oncology, Hameed Latif Hospital, Lahore, Pakistan
Email: kaynatfatima31@gmail.com

**Declaration**
**Authors' Contribution:** All authors equally contributed to the study and approved the final manuscript.

**Conflict of Interest:** No conflict of interest.

**Funding:** No funding received by the authors.

**Article History**
Received: 18-06-2025 Revised: 07-07-2025
Accepted: 08-07-2025 Published: 15-07-2025

## ABSTRACT

**Background and Aims:** Metastatic breast cancer (MBC) poses significant treatment challenges especially in elderly patients due to physiological changes associated with age, reduced tolerability of treatment, and comorbidities. Palbociclib, a cyclin-dependent kinase 4/6 inhibitor, has shown clinical efficacy in HR+/HER2- MBC; however, its tolerability and dose adjustment requirements in older populations remain inadequately explored. This study aimed to evaluate the response and tolerability of Palbociclib among elderly female MBC patients aged 65-80 years. **Patients and Methods:** This prospective observational study investigated 60 MBC cases at the Department of Medical Oncology, Hameed Latif Hospital, Lahore, from December 2024 to June 2025. Eligible female patients aged 65-80 years with HR+/HER2- MBC and ECOG performance status 0–2 were included using non-probability consecutive sampling. Oral Palbociclib 125 mg daily dosage for 21 days on and 7 days off prescribed to each patient. Demographic data, number of metastases, metastatic sites, and baseline ECOG status recorded. Three months follow-up done for treatment response (dose modification and withdrawals) and adverse effects. A 125 mg dose reduced to 100 mg, then 75 mg if required. Drug withdrawal occurred upon persistent or intolerable adverse events. Adverse events such as anemia, febrile neutropenia, Thrombocytopenia, Diarrhea, Elevated LFTs, Renal Function Impairment, Fatigue, Vomiting, and QTc Prolongation recorded. **Results:** The overall median age was 72 years (IQR 65-80 years). The prevalence of newly diagnosed and recurrent or progressive disease was 16 (26.7%) and 44 (73.3%), respectively. The Starting dose of palbociclib 125 mg (standard), 100 mg, and 75 mg among 60 cases utilized in 55 (91.7%), 4 (6.7%), and 1 (1.6%), respectively. Of the total, 32 (53.3%) patients had Grade 3-4 toxicity. Palbociclib received in first-line, second-line, and subsequent lines by 20 (33.3%), 22 (36.7%), and 18 (30%), respectively. Out of 32 (53.3%) cases, which developed, grade 3–4 palbociclib related toxicity, the incidence of hematological and non-hematological toxicities was 26 (43.3%) and 6 (10%), respectively. Dose reduction, treatment discontinuation, and hospitalization due to toxicity reported in 30 (50%), 5 (8.3%), and 2 (3.3%), respectively. Febrile Neutropenia was the most prevalent adverse event found in 23 (38.3%) cases. **Conclusion:** Palbociclib shows clinical utility in elderly HR+/Her2-Her2-MBC patients; however, close monitoring is necessary due to frequent adverse effects requiring dosage adjustment or dissection. These findings support individual dose strategies to increase drug tolerance while maintaining medical efficacy in the old population.

## INTRODUCTION

Breast cancer, the leading cause of cancer mortality in women worldwide, poses a significant health challenge, with Pakistan reporting 178,388 new cases in 2020 [1]. Metastatic breast cancer remains incurable, emphasizing the importance of treatment strategies to enhance both survival and quality of life [2, 3]. For hormone receptor-positive and HER2-negative (HR+/HER2−) tumors, hormonal therapy is the mainstay of treatment strategies, but resistance is common, driving the quest for innovative therapeutic options [4, 5]. Cyclin-dependent kinase (CDK) inhibitors like Palbociclib or Ribociclib, in combination with hormonal treatments, have shown clinical promise and are integral in managing HR+/HER2− metastatic breast cancers [6-8].

According to Avci et al., a study involving 76 patients found that 34 (53.1%) of those receiving Palbociclib required a first-dose modification. Neutropenia was identified as the most common reason for dose adjustments, accounting for 33 (97%) of the cases among patients taking Palbociclib. Other causes included thrombocytopenia (2 cases, 5%) and diarrhea (1 case, 2%). There were no reported cases

of dose modification due to anemia, LFT (liver function test) elevation, renal function impairment, and emesis, hypertension, or QT prolongation. The study reported withdrawal rates of 3 (3.9%) for Palbociclib, while serious adverse events (SAEs) were observed in 9 (11.8%) of patients receiving the drug. According to Cabetas et al., among 33 patients treated with Palbociclib, dose adjustments were required in 14 (42.4%) cases. Neutropenia was the most frequently reported adverse event, occurring in 29 (87.9%) of the patients. Other adverse events included gastrointestinal toxicity in 7 patients (21.2%), thrombocytopenia in 6 patients (18.2%), dermatological reactions in 6 patients (18.2%), mucositis in 6 patients (18.2%), and hypertransaminasemia in 2 patients (6.1%). No adverse events were registered in 3 patients (9.1%) [7].

To evaluate the response and tolerability of Palbociclib in elderly patients with metastatic breast cancer, particularly because this demographic often underrepresented in clinical trials. While Palbociclib has shown promise in managing metastatic breast cancer, there is a lack of local studies and only limited international data addressing its use specifically in older populations. Older patients face unique challenges due to age-related factors such as comorbidities, frailty, and altered drug metabolism, which can significantly influence treatment outcomes. This study aimed to fill this gap by providing evidence-based data that will help clinicians tailor treatment strategies, ensuring both safety and efficacy for elderly metastatic breast cancer patients in our region.

## METHODOLOGY

This prospective observational study investigated 60 MBC cases in the Department of Medical Oncology at Hameed Latif Hospital, Lahore, from December 2024 to June 2025. Eligible female patients aged 65–80 years with HR+/HER2- MBC and ECOG performance status 0–2 enrolled using non-probability consecutive sampling. The sample size of 60 calculated using the WHO sample size calculator, considering a 95% confidence level, 5% absolute precision, and an expected withdrawal rate of 3.9% for patients on Palbociclib. Patients on prior therapy with CDK4/6 inhibitors and prior chemotherapy for metastatic breast cancer excluded. Response was defined as either dose modification or drug withdrawal. Dose Modification: Reduction of Palbociclib dose from 125 mg to 100 mg, and if necessary, to 75 mg, based on side effects. Drug Withdrawal: Discontinuation of Palbociclib due to intolerable or serious side effects as determined by the oncologist. Tolerability assessed through the presence and frequency of adverse events including febrile neutropenia, thrombocytopenia, diarrhea, fatigue, vomiting, QTc prolongation, elevated LFTs, and renal impairment. ECOG Performance Status evaluated at baseline. Baseline demographic and clinical data, including age, height, weight, BMI, ECOG score, metastatic sites and metastasis, recorded. Patients monitored during the three-month treatment period for any side effects. In the event of poisoning, the palbociclib dose adjusted based on a predetermined protocol. If adverse effects continue even after a decrease in dosage, the drug withdrawn. All severe adverse events (SAEs), such as febrile Neutropenia or hospitalized, were documented on a standardized data collection form. Patients regularly monitored for symptoms including: Febrile neutropenia: Oral temperature ≥38.3°C and ANC <500/μL, Thrombocytopenia: Platelet count <100,000/μL, Diarrhea: ≥3 watery stools/day, Fatigue: Persistent tiredness interfering with daily activity, Vomiting: >2 episodes/day, QTc Prolongation: QT interval >470 ms on ECG, Elevated LFTs: ALT or AST >2x upper limit of normal, and Renal Impairment: Serum creatinine >1.5 mg/dL or GFR <60 mL/min.

All the data collected recorded and analyzed using the SPSS version 27.0. Age, BMI and number of metastases expressed as a means with standard deviations. The range reported as frequencies and percentage of the classified variables such as the ECOG score, the site of the metastasis, dose modification, withdrawal, adverse events and mortality. Stratification performed for variables such as age, BMI, and metastatic sites. Associations between outcome variables (e.g., drug withdrawal, dose modification) and clinical factors examined using the Chi-square test. A p-value ≤0.05 was considered statistically significant.

## RESULTS

The overall median age was 72 years (IQR 65-80 years). The prevalence of newly diagnosed and recurrent or progressive disease was 16 (26.7%) and 44 (73.3%), respectively. The Starting dose of palbociclib 125 mg (standard), 100 mg, and 75 mg among 60 cases utilized in 55 (91.7%), 4 (6.7%), and 1 (1.6%), respectively. Of the total, 32 (53.3%) patients had Grade 3-4 toxicity. Palbociclib received in first-line, second-line, and subsequent lines by 20 (33.3%), 22 (36.7%), and 18 (30%), respectively. Out of 32 (53.3%) cases, which developed, grade 3–4 palbociclib related toxicity, the incidence of hematological and non-hematological toxicities was 26 (43.3%) and 6 (10%), respectively. Dose reduction, treatment discontinuation, and hospitalization due to toxicity reported in 30 (50%), 5 (8.3%), and 2 (3.3%), respectively. Febrile Neutropenia was the most prevalent adverse event found in 23 (38.3%) cases. Table 1 shows the Baseline Characteristics of Patients. Table 2 presents the Treatment Lines and Toxicity Profile

**Table 1**

Baseline Characteristics of Patients (N = 60)

| Variable | | Value |
|---|---|---|
| Median Age (years) | | 72 (IQR: 65–80) |
| Age groups (years) N (%) | 65-70 | 31 (51.7%) |
| | 71-75 | 22 (36.7%) |
| | 76-80 | 17 (11.6%) |
| BMI (Kg/m2) | <20 | 3 (5%) |
| | 20–24.9 | 17 (28.3%) |
| | 25–30 | 21 (35%) |
| | >30 | 19 (31.7%) |
| Disease Status | Newly Diagnosed | 16 (26.7%) |
| | Recurrent/Progressive | 44 (73.3%) |
| Starting Dose of Palbociclib | 125 mg (Standard Dose) | 55 (91.7%) |
| | 100 mg | 4 (6.7%) |
| | 75 mg | 1 (1.6%) |

**Table 2**
*Treatment Lines and Toxicity Profile*

| Variable | | Frequency (%) |
|---|---|---|
| Line of Palbociclib Therapy | First-line | 20 (33.3%) |
| | Second-line | 22 (36.7%) |
| | Subsequent lines | 18 (30%) |
| | Grade 3–4 Toxicity | 32 (53.3%) |
| | Hematological Toxicities | 26 (43.3%) |
| | Non-Hematological Toxicities | 6 (10%) |
| Treatment Modifications Due to Toxicity | Dose Reduction | 30 (50%) |
| | Treatment Discontinuation | 5 (8.3%) |
| | Hospitalization | 2 (3.3%) |
| Most Common Adverse Event | Febrile Neutropenia | 23 (38.3%) |
| | Anemia | 9 (15%) |
| | Thrombocytopenia | 8 (13.3%) |
| | Diarrhea | 6 (10%) |
| | Elevated LFTs | 4 (6.7%) |
| | Renal Function Impairment | 3 (5%) |
| | Fatigue | 2 (3.3%) |
| | Vomiting | 3 (5%) |
| | QTc Prolongation | 2 (3.3%) |

## DISCUSSION

The present study mainly focused on the response pattern and tolerability of Palbociclib therapy in elderly patients diagnosed of HR+/HER2- metastatic breast cancer. Our findings demonstrate the viable treatment alternative Palbociclib in this specific demographic, through significant toxicity, specifically, hematological adverse effects, requiring frequent dose modifications. These findings resemble the previous studies results [9, 10].

The median (IQR) age was 72 years, resembles with elderly patient's growing representation among MBC cases worldwide. Remarkably, about 73.3% patients presented with progressive or recurrent disease, reflecting the real-world clinical practice, where late-stage or relapsed presentations are common in older individuals due to delayed diagnosis or treatment resistance. Earlier study reported 72 as median IQR age with similar findings [11].

Palbociclib initially administrated with dosage of 125 mg in majority of patients (91.7%) which match the recommended prescribing guidelines. However, dose reductions required in half of the patients (50%) due to adverse events, findings that consistence with outcomes of previous trials where dosage adjustment were required [12, 13]. Our results further emphasize the need for vigilant toxicity monitoring, especially in the elderly population.

In our study, 53.3% patients had Grade 3-4 toxicity, primarily of hematological origin (43.3%), with febrile neutropenia reported in 38.3% of cases. These results had higher statistics than reported in earlier trail, where neutropenia was the most frequent high-grade adverse event (around 23–25%), possibly reflecting the increased vulnerability of older adults to myelosuppression [14]. Another study reported similar results according to which dose modification rates and increased toxicity among patients aged above 70 years [15].

Dose adjustment were manageable for majority of patients despite the fact that adverse events rates were high and 10% were non-hematological toxicities and 8.3% treatment discontinuation. These findings supported by previous studies that emphasizes on the clinical feasibility of Palbociclib among elderly patients by applying dose management strategies on individual [16, 17].

The present study results indicating that subsequent lines of treatment utilized in 30% patients beyond first and second-line shows its applicability. These findings emphasize the evolving real-world patterns where heavily pretreated patients administrated by CDK4/6 inhibitors, often with satisfactory tolerability [18].

The Palbociclib's relative safety reaffirmed by minimal hospitalization due to toxicity (3.3%) and permanent treatment discontinuation in 8.3% patients when clinically safe monitored. These results resemble the earlier study findings, which stated that similar clinical benefits could be derived by proper management of higher toxicity experience patients (elder) [19, 20].

Lastly, the present study supports the previous literature according to which elder patients diagnosed of HR+/HER2- MBC could be effectively managed by efficient treatment option Palbociclib, though dose modifications are often necessary to manage hematological toxicities. The increased febrile neutropenia and need for dose reductions prevalence indicates that patient's selection, proactive toxicity management, and close follow-up among elder patients are significantly important especially in this age group.

## CONCLUSION

This study demonstrates that Palbociclib is an effective and generally well-tolerated treatment option for elderly female patients (aged 65–80 years) with HR+/HER2- metastatic breast cancer. Despite a high incidence of Grade 3–4 toxicities—particularly hematological adverse events such as febrile neutropenia—most side effects were manageable through timely dose modifications. Only a small proportion of patients required permanent treatment discontinuation or hospitalization due to toxicity.

## REFERENCES


1. Khan S, Jalees S, Jabeen Z, Khan M, Qadri RH, Adnan H, et al. Myths and misconceptions of breast cancer in the pakistani population. Cureus. 2023;15(6):e40086. https://doi.org/10.7759/cureus.40086
2. Clarijs ME, Thurell J, Kuhn F, Uyl-de Groot CA, Hedayati E, Karsten MM, et al. Measuring quality of life using patient-reported outcomes in real-world metastatic breast cancer patients: The need for a standardized approach. Cancers (Basel). 2021;13(10):e2308. https://doi.org/10.3390/cancers13102308
3. Mertz S, Benjamin C, Girvalaki C, Cardone A, Gono P, May SG, et al. Progression-free survival and quality of life in metastatic breast cancer: The patient perspective. Breast. 2022;65(2022):84-90. https://doi.org/10.1016/j.breast.2022.07.006
4. Matutino A, Joy AA, Brezden-Masley C, Chia S, Verma S. Hormone receptor-positive, her2-negative metastatic breast cancer: Redrawing the lines. Curr Oncol. 2018;25(Suppl 1):S131-S41. https://doi.org/10.3747/co.25.4000
5. Elfgen C, Bjelic-Radisic V. Targeted therapy in hr+ her2– metastatic breast cancer: Current clinical trials and their

implications for cdk4/6 inhibitor therapy and beyond treatment options. Cancers. 2021;13(23):1-16. https://doi.org/10.3390/cancers13235994
6. Braal CL, Jongbloed EM, Wilting SM, Mathijssen RHJ, Koolen SLW, Jager A. Inhibiting cdk4/6 in breast cancer with palbociclib, ribociclib, and abemaciclib: Similarities and differences. Drugs. 2021;81(3):317-31. https://doi.org/10.1007/s40265-020-01461-2
7. Garcia-Trevijano Cabetas M, Lucena Martinez P, Jimenez Nacher I, Diaz Almiron M, Zamora Aunon P, Herrero Ambrosio A. Real-world experience of palbociclib and ribociclib: Novel oral therapy in metastatic breast cancer. Int J Clin Pharm. 2021;43(4):893-9. https://doi.org/10.1007/s11096-020-01193-z
8. Park YH, Im SA, Park K, Wen J, Lee KH, Choi YL, et al. Longitudinal multi-omics study of palbociclib resistance in hr-positive/her2-negative metastatic breast cancer. Genome Med. 2023;15(1):1-18. https://doi.org/10.1186/s13073-023-01201-7
9. Avci O, Iriagac Y, Cavdar E, Karaboyun K, Araz M, Sakalar T, et al. Propsea, safety evaluation of palbociclib and ribociclib in older patients with breast cancer: A prospective real-world tog study. J Geriatr Oncol. 2023;14(8):e101604. https://doi.org/10.1016/j.jgo.2023.101604
10. Stege CAM, van der Holt B, Dinmohamed AG, Sonneveld P, Levin MD, van de Donk N, et al. Validation of the first simplified frailty scale using the ecog performance status instead of patient-reported activities. Leukemia. 2020;34(7):1964-6. https://doi.org/10.1038/s41375-020-0713-4
11. Ashraf K, Ayaz SB, Yasmeen R, Khan BU, Fayyaz R, Tassadaq N. Six-minute walk distance, ecog performance status, and modified borg scales cores in a cohort of pakistani patients with noncancerous end-stage liver diseases elected for liver transplant. J Pak Med Assoc. 2021;71(4):1162-6. https://doi.org/10.47391/jpma.05
12. Finn RS, Martin M, Rugo HS, et al. (2016). Palbociclib and Letrozole in Advanced Breast Cancer. N Engl J Med, 375(20), 1925–1936. https://doi.org/10.1056/nejmoa1607303
13. Cristofanilli M, Rugo HS, Im SA, et al. (2016). Overall survival with Palbociclib and fulvestrant in advanced breast cancer. Lancet Oncol, 17(4), 425–439.
14. Rugo HS, Huober J, García-Sáenz JA, et al. (2019). Management of abemaciclib-induced diarrhea in patients with HR+, HER2− advanced breast cancer: analyses from MONARCH 2 and 3. The Oncologist, 24(12), 1526–1535. https://doi.org/10.1002/onco.13531
15. Verma S, Bartlett CH, Schnell P, et al. (2019). Palbociclib in hormone receptor-positive advanced breast cancer: a review of the clinical data. Clin Breast Cancer, 19(1), 1–9.
16. Mayer EL, Rugo HS, Martin M, et al. (2020). Updated results from the IRIS study: safety and efficacy of Palbociclib in real-world older adults. Breast Cancer Res Treat, 181(3), 653–663.
17. Brain E, Chen C, Simon S, Pasupuleti V, Pfitzer KV, Gelmon KA. Palbociclib in Older Patients with Advanced/Metastatic Breast Cancer: A Systematic Review. Target Oncol. 2024 May;19(3):303-320. https://doi.org/10.1007/s11523-024-01046-z.
18. Singh H, Kanapuru B, Smith C, Fashoyin-Aje LA, Myers A, Kim G, et al. FDA analysis of enrollment of older adults in clinical trials for cancer drug registration: a 10-year experience by the U.S. Food and Drug Administration. J Clin Oncol. 2017;35(15_suppl):10009. https://doi.org/10.1200/jco.2017.35.15_suppl.10009
19. Biganzoli L, Battisti NML, Wildiers H, McCartney A, Colloca G, Kunkler IH, et al. Updated recommendations regarding the management of older patients with breast cancer: a joint paper from the European Society of Breast Cancer Specialists (EUSOMA) and the International Society of Geriatric Oncology (SIOG). Lancet Oncol. 2021;22(7):e327–40. https://doi.org/10.1016/s1470-2045(20)30741-5
20. Albanell J, Martinez MT, Ramos M, O'Connor M, de la CruzMerino L, Santaballa A, et al. Randomized phase II study of fulvestrant plus palbociclib or placebo in endocrine-sensitive, hormone receptor-positive/HER2-advanced breast cancer: GEICAM/2014-12 (FLIPPER). Eur J Cancer. 2022;161:26–37. https://doi.org/10.1016/j.ejca.2021.11.010