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Case Study

To Determine the Cost Effectiveness and Efficacy of Generic Palbociclib in Resource-Limited Countries

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Abstract

CDK4/6 inhibitors with hormonal therapy have become the standard of care for first and second-line therapy for hormone receptor-positive HER2-negative metastatic BC. Unfortunately, the long-term treatment cost of CDK4/6 inhibitors is prohibitive leading to non-compliance and loss of follow-up. To increase access and compliance for patients with breast cancer we used generic palbociclib in our patients. Here, we report the data on 33 patients using generic palbociclib. For generic Palbociclib progression-free survival was 14 months.

Keywords: Metastatic Breast Cancer (MBC); CDK4/6; Toxicity

Introduction

The development of CDK4/6 has changed the therapeutic management in patients with hormone receptor-positive metastatic breast cancer (MBC) [1]. Three highly active oral selective reversible inhibitors of CDK4/6 are currently being used in combination with endocrine therapy. The drugs approved by the FDA include palbociclib, ribociclib, and Abemaciclib as first- and second-line therapies. In the first-line setting, median PFS with CDK4/6 inhibitors plus endocrine therapy increased approximately to 25 months compared to 15 months with endocrine therapy. While in second-line therapy PFS improves by 9-16 months compared to 5-9 months. OS has also been improved in pre-, peri-and post-menopausal women and the risk of death was reduced by 28% compared with endocrine therapy alone [2,3]. The drugs are mostly associated with manageable toxicities and easily managed with supportive care and dose adjustments if needed.

Long-term adherence to oral therapy is average to poor even with drugs that are not expensive. The high cost of CDK/4/6 inhibitors reduces oral compliance, including dose reduction and dose discontinuation. This is true especially in patients from low-middle income countries due to out-of-pocket payments. There are no studies on CDK4/6 compliance rates and survival (nurses' perspective). Quite a few patients in LMICs refuse/stop treatment with CDK4/6 inhibitors due to economic constraints and prefer capecitabine or IV chemotherapy despite more side effects. Even in high-income countries high out-of-pocket costs may reduce medication adherence and limit the benefit of guidelines-recommended treatment while increasing the burden of therapy among patients with chronic conditions [4].

Pakistan is a low-middle-income country with a GDP of $1505 [5]. The government allocates 3% of GDP to health of which minimal allocation is provided for cancer drugs. Out-of-pocket expenditure is approximately 58-60%, especially for chronic diseases. The cost of long-term use of CDK4/6 inhibitors for hormone receptor-positive patients is a major challenge to the patients and healthcare systems.

To improve access, availability, and compliance of CDK4/6 inhibitors to more patients with HR+ MBC, we used a generic version of the CDK4/6 inhibitor of palbociclib.

We report a case series of 33 women with HR+ MBC who were put on generic palbociclib produced in Bangladesh. We sought to determine tolerability, efficacy, toxicity, progression-free survival, and discontinuation due to financial constraints.

Methods

33 patients with metastatic breast cancer hormone receptor-positive and HER2-negative were evaluated. The median duration of follow-up was 26 months.

As seen in Table 1, patients were stratified according to menopausal status, relapsed versus denovo disease, performance status, organ involvement, and first or second-line treatment.

Side effects and median progression-free survival were determined.

Patient Demographics	Number (%)
Menopausal Status	
Premenopausal Status	8 (23.5%)
Postmenopausal Status	26 (76.5%)
Receptor Status	
ER+, PR+, HER2-ve	30 (80.2%)
ER+, PR+, HER2+ve	3 (8.8%)
Disease Status	
Relapsed	13 (38.2%)
Denovo	21 (61.8%)
Performance Status	
0	9 (26.5%)
1	21 (61.8%)
2	4 (11.8%)
Visceral Crisis	
Yes	14 (41.2%)
No	20 (58.8%)
Treatment Setting	
1st Line Treatment	4 (11.8%)
2nd Line Treatment	28 (82.5%)
Current Status	
Alive	30 (88.2%)
Dead	4 (11.8%)
Progression Free Survival	14 months (1-31 months)
Neutropenia	5(15.5%)
Fatigue	4(12.1%)
Diarrhea	3(0.9%)

Table 1

Discussion

Our results indicate that generic palbociclib is effective in both first and second-line treatment of metastatic ER/PR+ MBC. Three patients with Her2 +ve disease were included as they refused chemotherapy. The median PFS is 14 months.

Palbociclib was chosen as it is the only generic CDK4/6 inhibitor available in Pakistan. The cost of the drug is approx. 50% lower than the original, the toxicities are fewer with less utilization of health systems. We used a utilitarian approach of near equivalence so we could reach a larger number of patients and reduce financial toxicities [6] for our patients and resultant non-compliance. The generic version of palbociclib increased the access in 30-35% more patients. The use of the generic palbociclib led to less discontinuation, improved compliance, and decreased financial stress on patients, families, and public health systems.

Most of the women were post-menopausal (76.5%) and 68% had *denovo* disease. Palbociclib was used in visceral crises (41%) when either the patients refused chemotherapy or had poor PS and were not able to tolerate chemotherapy. Palbociclib was used in more than 80% of patients in second-line treatment. and our results did not show any differences in terms of PFS between first and second-line therapy. The Sonia trial [7] has confirmed that CDK4/6 inhibitors are equally effective in first and second-line therapy. In the third world, it saves patients and the health system from excessive financial burden, fewer toxicities, and utilization of health care resources.

PFS was 14 months, slightly less than reported by Miron., *et al*. of 17 months (REAL world`). Since 42% of patients were in visceral crisis this may have contributed to lower PFS [8].

The toxicity profile was mild with only 5 patients having grade 2 neutropenia, 4 patients complained of fatigue, and grade 1 diarrhoea was reported by 3 patients.

In conclusion, based on our experience of increased access, adherence, and manageable toxicity profile we continue to use generic palbociclib in our indigent patients.

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