Real-World Evidence on Adherence to the First CDK 4/6 Inhibitor (Palbociclib) in Breast Cancer Patients From Romania

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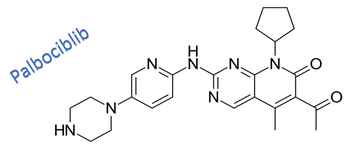
OBJECTIVES: Breast cancer is the second most common cancer in women after skin cancer with a percentage of 15.2% from all new cancer cases and 7.1% from all cancer deaths in 2023.

The aim of our study was to evaluate medication adherence and identify influencing factors in patients undergoing palbociclib for advanced or metastatic breast cancer.



The identification of cyclin-dependent kinases (CDK) and their regulatory mechanisms in cell cycle processes marked a pivotal advancement in cancer therapy. Among these, cyclin-dependent kinase 4 and 6 (CDK4/6) are enzymes crucially involved in cell cycle regulation.

The global market for CDK 4/6i drugs is segmented across various categories, including drug types such as palbociclib(@Ibrance), ribociclib (@Kisqali), and abemaciclib (@Verzenio). The first CDK4/6 inhibitor drug approved by the FDA was ***palbociclib*** in February 2015.

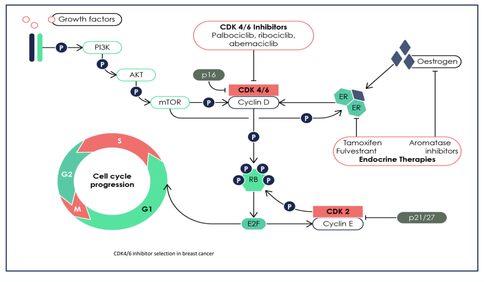
Palbociclib is taken daily orally with food in a cycle of 21 days of active medication followed by 7 without. Currently palbociclib is prescribed as a combination therapy with either *letrozole* or *fulvestrant*. Patients should also not consume CYP3A inhibitors or inducers while taking palbociclib. FDA information also cautions against consuming grapefruit products while taking palbociclib.

Treatment nonadherence is associated with disease progression and mortality among patients with breast cancer. The existing research on adherence to CDK4/6i anticancer agents is limited.

METHODS: Palbociclib, the first CDK4/6 inhibitor approved by the FDA, received unconditional approval from the National Agency for Medicines and Medical Devices in Romania for inclusion in the Positive Drug List in November 2017.

Our study included patients diagnosed with breast cancer who had received electronic prescriptions from their oncologists. Medication adherence was assessed using the Proportion of Days Covered (PDC) method.

To explore potential correlations between medication adherence and patient age and gender, Spearman's coefficients were calculated. Statistical analysis was performed using GraphPad Prism 10.1, with a significance level set at $p < 0.05$ (two-tailed).



CONCLUSIONS: While high adherence rates were observed among patients treated with palbociclib, it is important to note that the collected data from the Romanian National Health Insurance House were limited, lacking information on potential adverse reactions that might lead to treatment discontinuation.

References

1. Finn RS, Martin M, Rugo HS, Jones S, Im SA, Gelmon K, et al. (November 2016). "Palbociclib and Letrozole in Advanced Breast Cancer". The New England Journal of Medicine. 375 (20): 1925–1936. doi:10.1056/NEJMoa1607303. PMID 27959613.
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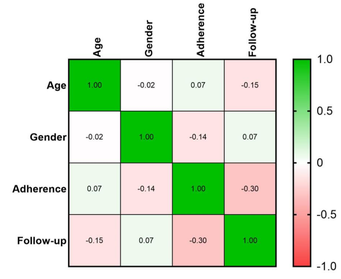
3. Finn RS, Martin M, Rugo HS, Jones S, Im SA, Gelmon K, et al. (November 2016). "Palbociclib and Letrozole in Advanced Breast Cancer". The New England Journal of Medicine. 375 (20): 1925–1936. doi:10.1056/NEJMoa1607303

RESULTS: Between January 2018 and December 2022, a total of 330 patients were prescribed CDK4/6 inhibitors, of which 55% (180 patients) received palbociclib.

The eligible patients included in our study had an average follow-up period of 14.6 ± 12.5 months. Among patients treated with palbociclib, no significant correlation was found between adherence and age (rho = 0.07, p = 0.35) or gender (rho = -0.144, p = 0.054). However, a significant correlation was observed with the duration of follow-up (rho = -0.304, $p < 0.0001$). The absence of adherence barriers related to costs was noted, as the drugs were provided free of charge and fully covered by the Romanian National Oncology Program, reimbursed by the National Health Insurance House.



The adherence rates for palbociclib were 92.5% ± 13.7%. Most patients received combination therapy with letrozole (46%) and exemestane (13%).