

Safety Evaluation of Cyclin-Dependent Kinase (CDK) 4/6 Inhibitors in Patients with Breast Cancer at a Community Teaching Hospital

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Purpose:

Palbociclib, abemaciclib, and ribociclib are the FDA-approved cyclin-dependent kinase (CDK) 4/6 inhibitors used in the treatment of hormone receptor (HR) positive/human epidermal growth factor receptor 2 (HER-2) negative breast cancer. They have a significant risk of neutropenia/myelosuppression, interstitial lung disease, and hepatotoxicity. CDK 4/6 inhibitors have similar activity with some differences in adverse effects that differentiate them from one another. Abemaciclib has demonstrated lower rates of neutropenia and penetrate the blood/brain barrier, compared to the other agents in the class. This study was conducted to deliver a real-world perspective of how this drug class executes safety outcomes in therapy.

Methods:

This study was performed as a retrospective chart review at Mercy Hospital in St. Louis, Missouri. Patients aged 18 years and older who have received a CDK 4/6 inhibitor (abemaciclib, palbociclib, or ribociclib) for treatment of HR (+)/HER-2 (-) advanced breast cancer through Mercy Oncology in St. Louis area within the last 2 years were eligible for this study. This study's primary objective was to describe the incidences of documented adverse effects in this patient population. Secondary objectives were to identify the incidence of documented adverse effects in patients with documented comorbidities that may escalate their risk of these adverse outcomes, the prevalence of known drug-drug interactions among patients receiving CDK 4/6 inhibitors for therapy, and the incidence of dose modifications and discontinuations due to adverse effects among patients receiving CDK 4/6 inhibitors. This study was descriptive and did not include a power of analysis. Statistics used in the study include, mean and median, to address the study endpoints.

Results:

During the eligible enrollment period, 77 patients received one of the approved CDK 4/6 inhibitors. Of this population, 71 patients were eligible for this study: 38 palbociclib, 27 abemaciclib, and 6 ribociclib. Most of the study population was Caucasian at 56 patients and the youngest mean age of 55 years old in the abemaciclib group. Patients in the palbociclib and abemaciclib groups with concurrent endocrine therapy had 89.9% and 52.6% with an aromatase inhibitor. There was a total of 79 documented adverse effects amongst all eligible patients that had taken one of the CDK 4/6 inhibitors. Neutropenia was 46.8% of adverse effects and was the most common adverse effect in the palbociclib and ribociclib groups. The abemaciclib group had 56.7% of adverse effects to be diarrhea. Significant heart disease was

present in 57.4% of QT prolongation adverse effects and 100% of VTE adverse effects that were documented. 83.3% of patients in the ribociclib group had a home medication(s) that had a possible drug-drug interaction to cause increased risk of QT prolongation. There was a total of 32 dose modifications noted with the palbociclib group being the largest at 20 compared to abemaciclib with 10 and ribociclib with 2.

Conclusion:

The study was able to support literature regarding adverse effects CDK 4/6 inhibitors can commonly cause as a class and individually. However, there were some specific adverse effects that were present in drugs that have been shown to produce a higher rate of occurrence in others. The significant co-morbidities documented throughout patients in this study showed some relevance when it came to drug of choice amongst the class and adverse effects that were more likely to occur. Any possible drug-drug interactions that were assessed in the home medication lists showed some significance but weren't noted as causes of dose modification or discontinuation. If any therapy changes were made it was due to other adverse effects or intolerance to the drug. Overall, the study was able to emphasize the prevalence of adverse effects when using these drugs and the factors that can contribute to the risk of occurrence.