NON-INTERVENTIONAL STUDY REPORT ABSTRACT

Title: Descriptive Analyses of Clinical Characteristics and Treatment Patterns of Breast Cancer Patients Initiating Palbociclib (Ibrance®) Treatment in the US Community Oncology Setting

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Rationale and background: The arrival of new classes of therapy on the treatment landscape warrant evaluation of real-world data regarding patient characteristics and treatment patterns to aid in the understanding of use in broad clinical practice. Pfizer is interested in gathering real-world data describing the population of patients prescribed palbociclib, concomitantly with letrozole or fulvestrant, in the community oncology setting. The purpose of this study was to assess the settings in which palbociclib was prescribed (i.e. clinical/demographic characteristics of patients, line of therapy), occurrence of neutropenia and how providers monitored and managed these events. The results of this research provide insights into these patterns during the first year of palbociclib adoption into clinical practice among community oncologists across the US.

Research question and objectives: The goals of this research were to evaluate the real-world treatment dosing patterns, line of therapy in the treatment sequence and occurrence of neutropenia (assessed through CBC laboratory test results) for female breast cancer patients prescribed palbociclib following drug approval (01 February 2015). Real-world data from patients' electronic medical records (EMR) were utilized to achieve the following research objectives:

1. Characterize the demographic and clinical characteristics of patients at the initiation of treatment with palbociclib.
2. Describe palbociclib utilization by line of therapy (LOT).
3. Assess the frequency and timing of palbociclib dose reduction.
4. Quantify the frequency of complete blood count (CBC) monitoring during treatment with palbociclib
5. Assess the incidence (by grade) and timing of neutropenia events through calculation of absolute neutrophil count (ANC) during treatment with palbociclib.

6. Describe utilization of chemotherapy and endocrine therapy prior to and following treatment with palbociclib and the use of supportive pharmacological agents concomitant with palbociclib treatment.

Study design: This was a retrospective observational study of female patients diagnosed with breast cancer and newly initiating treatment with palbociclib.

Setting: Community oncology practices treating female metastatic breast cancer patients in the United States (US).

Subjects and study size, including dropouts: All female metastatic breast cancer patients initiating therapy with palbociclib between 01 February 2015 and 31 January 2016. Patients were required to have received palbociclib concomitantly with either letrozole or fulvestrant. Patients were grouped into 6 cohorts based on the month of initiation of palbociclib (February through March 2015, April through May 2015, June through July 2015, August through September 2015, October through November 2015, and December 2015 through January 2016).

Variables and data sources: Data including demographics, clinical characteristics (ECOG-PS, stage, ER/HER2 status), laboratory assessments (complete blood counts, white blood cell counts, neutrophil percentages), treatments (oral and IV, breast cancer directed or supportive care agents) and vital status were captured for female patients receiving treatment with palbociclib from structured data fields within the EMR data system. No review of unstructured clinical progress notes was performed. No linkage to administrative claims for prescription data was available and initiation/receipt of therapies was based on treatment orders recorded in the EMR. Timing of events in terms of palbociclib cycle was approximated by using the days from palbociclib initiation where one cycle was equal to 28 days.

Results: 965 women with metastatic breast cancer were identified who had at least one treatment order for palbociclib during the study period. Of the 965 identified patients, 612 (63.4%) were treated with palbociclib concomitantly with letrozole, 151 (15.6%) concomitantly with fulvestrant, and the remaining 202 (20.9%) did not meet selection criteria. Results highlighted below are for the palbociclib + letrozole cohort only.

Mean (±SD) follow-up for palbociclib + letrozole patients was 6.4±3.9 months. The proportion of patients initiating treatment with palbociclib + letrozole in first-line was from 35.9%-42.4% of all new palbociclib + letrozole treatment starts while the proportion of new starts in fourth-line or greater declined from 40.6% (Feb/Mar 2015) to 24.3% (Dec 2015/Jan 2016). At the end of follow-up, 78.8% (n=482) were on any treatment as of last follow-up (with 296 of those receiving palbociclib + letrozole as last recorded line of therapy), 9.5% (n=58) were lost to follow-up, and 11.8% were deceased (n = 21 with last treatment received palbociclib + letrozole and n = 51 with last recorded line another therapy).

Of patients with a known palbociclib starting dose (n=417), 88.0% (n=367) initiated therapy at 125 mg, 11.0% (n=46) at 100 mg, and 1.0% (n=4) at 75 mg. Dose reductions were observed in 20.1% (n=84) of patients with a known starting dose. Mean days to first dose reduction was 48 (SD=31, median =39); 69.0% (58/84) occurred within the first two cycles (within 56 days of palbociclib initiation).

CBC laboratory data were available for 351 patients (57.4%). Of the 351 patients with CBC data available, 74.6% (n=262) had a laboratory value consistent with neutropenia (of any grade). Among patients with neutropenia, the highest grade was: grade 1 = 12.8%; grade 2 = 20.5%; grade 3 = 35.3%; and grade 4 = 6.0%.

Discussion: The entry of a novel drug such as palbociclib in the marketplace may present unique challenges for inexperienced providers who were not participants in the clinical trial development program for the agent. While randomized controlled trials (RCTs) remain the gold standard for demonstrating efficacy and safety, real-world data is important to demonstrate differences in utilization and outcomes across heterogeneous patients. In this US community oncology EMR database, patients initiating palbociclib + letrozole were a more heterogeneous patient population in terms of older, had lower performance status scores at initiation, and had more prior exposure to chemotherapy than patients in the registration trials. Over time, we noted increased initiation of palbociclib + letrozole therapy earlier in the treatment sequence. These findings suggest that early use after drug approval of palbociclib in heavily pre-treated patients has decreased over the time of observation. Next, our results demonstrated that on average two CBC tests are conducted during the first cycle of palbociclib treatment suggesting good provider compliance with monitoring guidelines in the USPI. In regard to the occurrence of neutropenia, 47.3% and 8.0% of patients in this study had laboratory findings consistent with grade 3 and grade 4 neutropenia, respectively during the treatment with palbociclib + letrozole. While results from this research cannot be directly compared to RCTs given the heterogeneity of the patient populations these findings are consistent with the 56.1% and 10.4% observed rates of grade 3 and grade 4 neutropenia, respectively, found in the PALOMA-2 trial. Further long-term follow-up of patients would allow for more direct subgroup comparisons to patients with similar disease and treatment characteristics in the RCTs to confirm these findings.

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