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MADELINE: A Prospective Observational Study of Mobile Application Based Patient-Reported Outcomes in Advanced Breast Cancer

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Madeline
Mobile App Diary of Everyday Life and Experiences

BACKGROUND

- Ibrance® (palbociclib) is a novel cyclin-dependent kinase (CDK)4/6 inhibitor approved in the United States for hormone receptor–positive, human epidermal growth factor receptor 2–negative (HR+/ HER2–) advanced breast cancer (ABC)/metastatic breast cancer (MBC) in combination with letrozole as initial endocrine-based therapy in postmenopausal women or with fulvestrant in women with disease progression following endocrine therapy.
- It is important to understand the experiences of patients initiating ABC therapies, including the first-in-class CDK4/6 inhibitor palbociclib, in real-world settings and to document the management of these therapies to determine the needs of this patient population.
- A smartphone-based mobile application has been developed to collect patient-reported outcome (PRO) data to assess ABC, its treatment and symptoms, and patient functioning and quality of life (QoL).
- Clinical data on therapy management (eg, dose modifications, interruptions, discontinuations, adverse event management, and monitoring) will be obtained from patients' medical records to explore the association between patient-reported functioning and neutropenia.
- As an engagement program, the mobile application will provide patients initiating palbociclib access to a virtual community to connect to others enrolled in the study for peer support. As an exploratory analysis, the utility of the virtual community will be assessed at the conclusion of the observation period (outside the study protocol).

STUDY OBJECTIVES

- The primary objectives of this study are to assess and describe PROs in women with locally advanced/ unresectable or metastatic HR+/HER2– breast cancer receiving
  - Palbociclib in combination with letrozole or fulvestrant according to US labeling (group 1) OR
  - Approved therapies for ABC/MBC other than palbociclib (group 2)
- The study is not intended to compare outcomes between the 2 groups.

RESEARCH QUESTIONS

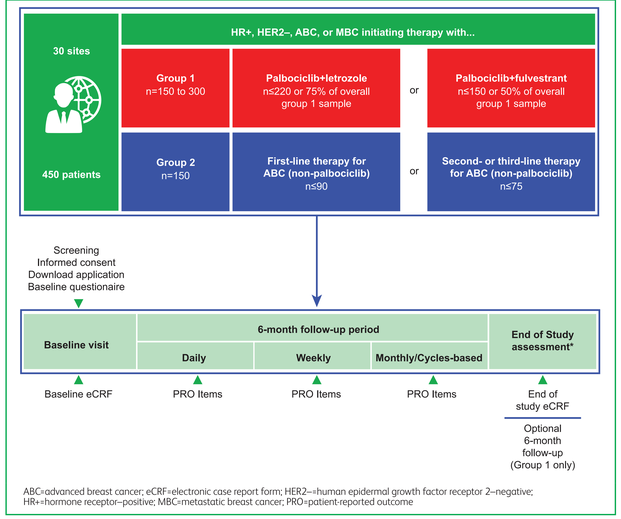
- The following research objectives will be addressed separately for both groups:
  - Characterize patients with HR+/HER2– ABC initiating treatment (eg, baseline patient demographics [eg, age, race] and clinical characteristics [eg, comorbidities, tumor stage, histology])
  - Describe changes in patients' general health status as measured by monthly (cycle-based) administration of the 12-Item Short Form Health Survey (SF-12)
  - Describe changes in patients' psychological distress as measured by monthly (cycle-based) administration of the Center for Epidemiological Studies Depression Scale (CES-D)
  - Describe the extent to which locally advanced or metastatic breast cancer and its treatment are associated with changes in patients' lives in terms of symptoms, functioning, and QoL as measured by daily and weekly administration of targeted patient-reported questions
  - For patients who are employed at baseline, quantify time lost from work in relation to locally advanced or metastatic breast cancer and its treatment
  - Assess patient's satisfaction with treatment
  - Describe dosing patterns (eg, reduction, interruptions, duration)
- The following research objectives will be addressed for group 1 only:
  - Describe the incidence, severity, and duration of neutropenia and time to first neutropenia event
  - Changes in palbociclib dose and/or schedule
  - Explore the association between patient-reported functioning and QoL and neutropenia

STUDY DESIGN

- A prospective, observational, noninterventional multicenter study
- Approximately 30 centers across the United States
- Between 300 and 450 women diagnosed with HR+/HER2– ABC or MBC will be enrolled into 2 independent patient groups for the purpose of describing the experiences of those on palbociclib and those on other treatments for ABC or MBC **(Figure 1)**.
- Group 1: Patients initiating palbociclib treatment
  - Approximately 150–300 women with HR+/HER2– ABC/MBC who are initiating palbociclib + letrozole as initial endocrine-based therapy for ABC or MBC per label

  OR
  - Palbociclib + fulvestrant for patients with disease progression following endocrine therapy for ABC or MBC per label
- Group 2: Patients with ABC/MBC initiating first-, second-, or third-line treatment with any regimen other than those containing palbociclib
  - Approximately 150 patients who are initiating treatment with any regimen other than those containing palbociclib for ABC/MBC in first, second, or third lines of treatment
- Participation in this study is not intended to change the routine treatment that patients receive as determined by their prescribing clinicians; all treatment decisions and type and timing of disease monitoring are at the discretion of the treating physician. No additional visits to the clinic will be required for the purposes of the study.

Figure 1. Study Design



ABC=advanced breast cancer; eCRF=electronic case report form; HER2–=human epidermal growth factor receptor 2–negative; HR+=hormone receptor–positive; MBC=metastatic breast cancer; PRO=patient-reported outcome

STUDY POPULATION

Inclusion Criteria

- Patients must meet all of the following inclusion criteria to be eligible for the study:
  - Owns or has regular access to an Apple iPhone (version 5.0 or higher with latest software: iOS 9.0 or higher) or Android phone (eg, Nexus or Galaxy with latest software: version 4.4.2 or higher)
  - Postmenopausal adult women (≥18 years of age) with diagnosis of adenocarcinoma of the breast with evidence of metastatic disease or locoregionally advanced disease not amenable to resection or radiation therapy with curative intent
  - Documented evidence of HR+ tumor based on the patient's most recent tumor biopsy
  - Documented evidence of an HER2– tumor based on the patient's most recent tumor biopsy; HER2– is determined as an immunohistochemistry score of 0/1+ or negative by *in situ* hybridization (fluorescence *in situ* hybridization/chromogenic *in situ* hybridization/silver enhanced *in situ* hybridization [FISH/CISH/SISH]), defined as an HER2/CEP17 ratio <2 or, for single probe assessment, an HER2 copy number <4)
  - Initiating on-label treatment with one of the following therapies: (1) palbociclib and letrozole as initial endocrine-based therapy for advanced or metastatic disease or (2) palbociclib with fulvestrant if the patient has experienced disease progression following endocrine therapy

    OR
    - Other approved therapy as the first treatment for advanced or metastatic breast cancer or initiating other approved therapy as the second or third treatment for ABC or MBC
  - Evidence of a personally signed and dated informed consent document indicating that the patient has been informed of all pertinent aspects of the study
  - Able to read and understand English
  - Willing and able to complete collection of data via mobile application

Exclusion Criteria

- Patients meeting any of the following criteria will not be included in the study:
  - Patient is initiating neoadjuvant systemic therapy.
  - In the judgment of the investigator, the patient's life expectancy is <3 months at the time of diagnosis of ABC or MBC.
  - The patient is participating in any interventional clinical trial that includes investigational or marketed products. Patients participating in other investigator-initiated research or noninterventional studies can be included as long as their standard of care is not altered by the study.
  - The patient is on active treatment for other malignancies other than ABC or MBC.
- Patient eligibility will be reviewed, documented, and confirmed by an appropriately qualified member of the investigator's study team before patients are enrolled in the study.

Figure 2. PRO Items to Be Collected via Mobile Application

Baseline
- Age
- Race/ethnicity
- Education
- Employment
- Insurance
- SF-12
- CES-D-10
- Mood (7-point scale)
- Pain (0-to-10 NRS)
- Fatigue (0-to-10 NRS)

Weekly
- Impact on mood or emotions
- Interference with family life
- Interference with social life or activities
- Physical activity
- Energy or stamina
- Productivity
- Missed work time (number of hours)
- Overall health rating
- Overall quality of life
- Awareness of neutropenia diagnosis and resolution
- Changes in treatment*

Daily
- Mood (7-point scale)
- Pain (0-to-10 NRS)
- Fatigue (0-to-10 NRS)
- Palbociclib use*
- Use of pain medication

Monthly (or at the Start of Cycle)
- CES-D-10
- SF-12

End of Study
- CES-D-10
- SF-12
- Overall satisfaction with treatment
- Utility of virtual community†

CES-D-10=10-Item Center for Epidemiological Studies Depression Scale; NRS=numerical rating scale; PRO=patient-reported outcome; SF-12=12-Item Short Form Health Survey.
*Group 1 only; †These exploratory measures are outside the primary study objectives (and study protocol) and will be assessed within the application itself. Additional information will be collected about the patients' usage patterns of these tools and used to explore associations with specific PROs.

STUDY DURATION

- It is anticipated that all data collection for this study **(Figure 2)** will occur over a 12-month period (from the first patient's first visit to the last patient's end of follow-up assessment), assuming a 6-month enrollment period with a 6-month follow-up period.
- The duration of data collection for an individual patient will be approximately 6 months, although this period may be truncated because of treatment switching, patient withdrawal from the study, or death.
- Specifically, follow-up for patients in group 1 will end if they discontinue the palbociclib combination initiated at the start of the study, and follow-up for patients in group 2 will end if they begin a treatment regimen that includes palbociclib.
- Patients in group 1 may be given the option to continue with the study for an additional 6 months, leading to a total study duration of 18 months.

STATISTICAL METHODS

- The enrollment target for this noninterventional prospective study is between 300 and 450 women across multiple centers in the United States, with a minimum of 150 to a maximum of 300 patients enrolled in group 1 and 150 patients enrolled in group 2.
- This is an observational study designed to provide descriptive summary information and is not designed for hypothesis testing; as such, no formal power calculation has been performed.
- The number of patients was chosen on a practical basis in conjunction with the ability to have reasonable precision around key estimates.

SITE AND PATIENT ENROLLMENT

- Approximately 450 patients from up to 30 US centers will be enrolled.
- Study duration will be approximately 12 months, assuming 6 months of recruitment.
- As of November 15, 2016, 4 centers had been enrolled and were awaiting site initiation.
- No patients have been enrolled yet. Patient enrollment is expected to begin in December 2016.

SPONSOR

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