PERFORM

HR+/HER2- ADVANCED BREAST CANCER TREATED 1ST-LINE

AN EPIDEMIOLOGICAL, PROSPECTIVE COHORT STUDY FOR PATIENTS WITH AN ENDOCRINE-BASED PALBOCICLIB COMBINATION THERAPY IN REAL WORLD IN GERMANY AND AUSTRIA

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BACKGROUND

CDK4/6 inhibitors, e.g. palbociclib, combined with endocrine therapy (ET) are approved and recommended 1st-line standard of care for patients (pts.) with hormone receptor-positive (HR+) and human-epidermal-growth-factor-receptor 2-negative (HER2-) advanced breast cancer (ABC). Randomized clinical trials as well as a current meta-analysis[1,2,3,4] have presented high efficacy and a consistent safety profile. The overall goal of the non-interventional study PERFORM is to complement clinical evidence of palbociclib in combination with ET with new real-world insights into routine clinical decision making including genetic testing patterns over the time, effectiveness, and patient-reported health-related quality of life (HRQoL).

CONCLUSION

PERFORM will provide real-world data on palbociclib treatment patterns, clinical outcomes, tolerability and safety, patient-reported HRQoL as well as treatment expectation and satisfaction and patient management during the COVID-19 pandemic. Focus will be on longitudinal patient follow-up including treatment sequences and strategies in the post-CDK4/6 inhibitor setting, long-term impact on patient outcomes, and HRQoL beyond progression, evaluated in the overall patient population with HR+/HER2- ABC and across different patient subgroups. In addition, a broad range of data on routinely used genetic tests/ predictors during course of disease will be evaluated, giving insights into the development and changes of testing patterns. Furthermore, with the increasing impact of real-world evidence, PERFORM will provide important insights into the daily care and expand the real-world body of evidence of palbociclib as used in routine clinical practice in Germany and Austria.

TRIAL DESIGN

The ongoing non-interventional, prospective, multicenter study PERFORM seeks to enroll 1,900 female and male patients scheduled to receive 1st-line palbociclib in combination with ET from 300 sites across Germany and 20 sites across Austria (**Figure 1**). The targeted recruitment period is 4 years and the total study duration 7.5 years (**Figure 2**). PERFORM will complement clinical evidence of palbociclib in combination with ET. Primary endpoint is the 1st-line progression-free survival (PFS). Furthermore, subsequent therapy sequences including analysis of post-palbociclib treatment strategies and effectiveness (e.g., response rates, 2nd-/3rd-line PFS) in total and in different treatment cohorts (**Figure 3**) will be described. PERFORM also focuses on a broader collection of data on patient-relevant factors including HRQoL beyond progression using the FACT-B questionnaire, socioeconomic factors, treatment expectation and satisfaction as well as patient management in times of COVID-19 pandemic. HRQoL will be analyzed for time to deterioration and change over time in the total population and in different subgroups. Additionally, the goal of PERFORM is to collect information about biomarkers and routinely used tests over time in real world. Descriptive statistics will be used to analyze data. In total five interim analysis are planned with an annually presentation of results. Overall, several important knowledge gaps of palbociclib in the real-world management of HR+/HER2- ABC will be addressed in PERFORM, including information on patient subgroups not well represented in clinical trials to date[1,2,3] such as elderly, male patients and patients with ECOG score ≥2 (**Figure 4**).

ELIGIBILITY CRITERIA

Inclusion criteria

Patients must meet all of the following inclusion criteria to be eligible for inclusion in the study:

a. Diagnosis of HR+/HER2- locally advanced, inoperable or metastatic breast cancer.

b. Age of 18 years or older.

c. Physician has determined that first-line treatment with palbociclib is indicated
   - in combination with an aromatase inhibitor, or
   - in combination with fulvestrant in women who received prior endocrine therapy

   as per current local product label.

   In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinizing hormone-releasing hormone (LHRH) agonist.

d. Patients who in the opinion of the investigator are willing and able to comply with regular clinic visits as per local standard of care practice at the study site.

e. Signed and dated informed consent.

Exclusion criteria

Patients meet any of the following criteria will not be included in the study:

a. Any contraindication as per current local product label.

b. Prior systemic antineoplastic treatment for advanced disease.
   - Exception: Start of first line treatment with palbociclib in combination with aromatase inhibitor or fulvestrant as per current local product label is allowed up to 4 weeks prior to inclusion.

c. Patients currently participating in any interventional clinical trial that includes investigational or marketed products at the time of enrollment.
   - Note: A concomitant participation in other non-interventional/observational studies, registries and translational research networks (e.g., PRAEGNANT, OPAL) or chart reviews is allowed.

d. Patients who are unable to understand the nature of the study or are unwilling to sign an informed consent.

CURRENT STATUS

The first patient (first-patient-in, FPI) was enrolled in October 2020. Currently, 130 patients have been included from 130 sites across Germany (**Figure 5**). In Austria, the FPI is awaited for June 2021. The first interim analysis is planned for the end of 2021.

Figure 1

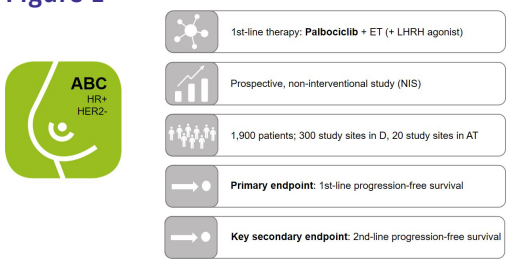

Figure 1 - Benchmarks

Figure 2

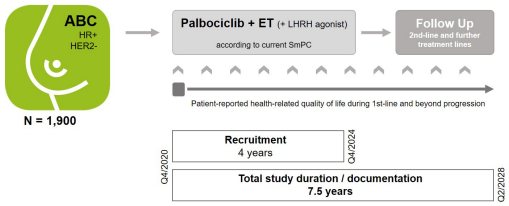

Figure 2 - Trial design

Figure 3

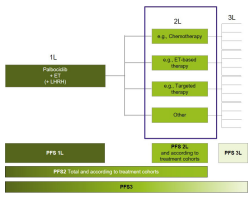

Figure 3 - Key Objectives

Figure 5

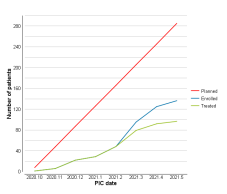

Figure 5 - Recruiting curve

Figure 4

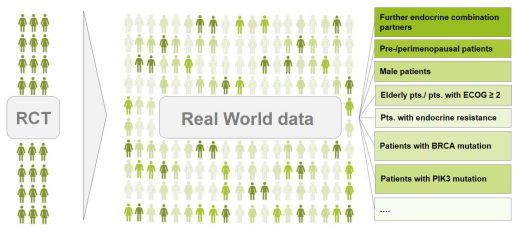

Figure 4 - Potential Subgroups

Abbreviations:
ABC: Advanced breast cancer | AI: Aromatase inhibitor | CDK4/6: Cyclin-dependent-kinase 4/6 | ET: Endocrine therapy | ECOG: Eastern Cooperative Oncology Group | FACT-B: Functional Assessment of Cancer Therapy - Breast | FPI: First-patient-in | HER2: Human-epidermal-growth-factor-receptor 2 | HR: Hormone receptor | HRQoL: Health-related quality of life | LHRH: Luteinizing hormone-releasing hormone | PFS: Progression-free survival | PS: Propensity-score

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