INTERIM RESULTS OF THE NON-INTERVENTIONAL STUDY PERFORM EVALUATING PALBOCICLIB IN COMBINATION WITH ENDOCRINE THERAPY FOR HR+/HER2- ADVANCED BREAST CANCER

RISK SCORE ASSESSMENT IN CLINICAL ROUTINE INCLUDING GENE EXPRESSION TESTING

BACKGROUND

Endocrine-therapy (ET) combined with CDK4/6 inhibitors is the standard of care as first-line therapy for HR+/HER2- advanced or metastatic breast cancer (mBC) patients based upon results of the pivotal phase III trials. Real-world data on treatment patterns, activity and tolerability in patients underrepresented in clinical trials, and quality of life (QoL) across different treatment lines in the ABC setting still can add valuable information. Additionally, patterns of biomarker analyses and genetic testing in clinical routine during course of disease are of interest for this patient population. In the adenocarcinoma setting of HR+/HER2- breast cancer (ABC), gene expression tests can predict benefit from adjuvant chemotherapy but there is limited data on their use in routine clinical practice. Detection of BRCA1/2 germline mutations is not only relevant for estimating the risk of developing breast cancer but can also predict response to a targeted therapy with PARPi or can be used as guidance for subsequent treatment strategies. In the metastatic setting it is known, that in HR+/HER2- ABC gBRCA1/2 mutation testing rates are low (comparing to TNBC), especially in elderly patients with unknown family history of breast/ovarian cancer, although about 5% of all unselected patients with ABC have a pathogenic BRCA1/2 mutation. As these patients are eligible for targeted therapy with PARPi, real-world data on gBRCA testing in routine clinical practice could support future strategy planning.

METHODS

Overall, 1,900 patients receiving 1st-line palbociclib/ET will be enrolled in the prospective non-interventional study PERFORM in 320 sites across Germany and Austria. Primary endpoint is progression-free survival. Secondary endpoints include treatment patterns, effectiveness (including also second- and third-line effectiveness), treatment expectation/satisfaction, potential impact of socioeconomic status and QoL as well as patterns of biomarker analyses and genetic testing. At baseline, a risk score assessment of family history of gBRCA1/2 mutation according to DXG eV as well as genetic tests and the results documented is done in clinical routine. Two years after first patient in the second interim analysis was conducted, focusing on patient/disease characteristics and genetic testing.

RESULTS

Patient characteristics

70% of 938 patients enrolled between 10/2020 and 09/2022 were followed for 6 months, and 62% patients were evaluable. Median age was 61 years (range 33-89), 93% (n=858) were postmenopausal (Table 1) and 30% of all patients were ≥75 years at inclusion. In total, 264 (39%) of patients presented with de novo ABC and 383 (61%) had relapsed after primary treatment of early-stage disease. For these patients, median time from primary diagnosis to inclusion was 8.26 years (range 0.3-64) (Table 2). No new receptor status was determined in 25.6% (n=98) of patients at inclusion.

BRCA risk assessment and testing

A risk assessment regarding gBRCA1/2 was documented for 14.2% (n=88) of patients before start of 1st-line treatment. For 2.6% (n=16) a family history of gBRCA1/2 related cancers was reported and a genetic panel test was performed in 6.6% (n=41) (Table 3).

Gene expression tests

Gene expression tests at initial diagnosis of EBC to predict benefit of adjuvant chemotherapy were documented in 3.6% (n=13/368) of the patients with relapse. In 1.3% (n=3/363) a gene expression test was documented for de novo ABC patients. If tested in the adjuvant setting (n=13) the tests used were Oncotype DX in 53.8% (n=7) and EndoPredict in 66.2% (n=6), respectively (Figure 1). 52.3% (n=47) of those patients tested with the Oncotype DX showed a low recurrence score and high risk of recurrence for most of those patients tested with EndoPredict (78.9%) (n=36) (Table 4).

CONCLUSION

The second interim analysis of the PERFORM study provides first insights into clinical routine of genetic testing prior to inclusion in 1st-line patients with HR+/HER2- ABC treated with palbociclib and ET. Gene expression analysis at initial diagnosis has rarely been documented in this patient population. This might be explained by lack of indication for testing due to early tumor stages at initial diagnosis and test availability at initial diagnosis (median time between initial EBC diagnosis and relapse of ~8 years). Although recommended by current national and international guidelines, predisposition to gBRCA-related cancers was rarely documented for patients at start of 1st-line palbociclib treatment. This could be due to insufficient documentation, as the eCRF at baseline explicitly asks for the DXG eV risk score which may not be available in all patient documents. Furthermore, targeted treatment for gBRCA mutation is limited to later HR+/HER2- ABC treatment lines. Therefore, further analyses will show if testing rates will increase during the course of disease.