DATA OF THE PROSPECTIVE, INTERSECTORAL RESEARCH PLATFORM OPAL

USE OF NEWLY APPROVED DRUGS FOR PATIENTS WITH EARLY BREAST CANCER (STAGE I-III) IN GERMANY

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INTRODUCTION

In 2022, several new drugs were approved by the EMA for treatment of patients with early breast cancer (eBC) at high risk of recurrence: the CDK4/6 inhibitor abemaciclib in hormone-receptor positive, HER2-negative (HR+ HER2-), the checkpoint-inhibitor pembrolizumab in triple negative, and the PARP inhibitor olaparib in HER2-negative, gBRCA1/2 mutated eBC. How quickly are these drugs implemented in routine care? How many patients are classified as high risk of recurrence and therefore qualify to be treated with these new drugs? These questions were analyzed with data from the German OPAL registry platform.

CONCLUSIONS

The recently approved drugs abemaciclib, pembrolizumab and olaparib have demonstrated improved outcome in clinical trials with patients with eBC at high risk of recurrence and thus offer an additional target treatment option. Here, the current status in routine care is investigated. Our data show that between 8-22% (HR+HER2-) and up to 62% (TNBC) of patients can be classified as high risk for recurrence in routine care, varying depending on the criteria used. Abemaciclib and pembrolizumab were quickly implemented into the treatment of these patients. BRCA1/2 is not yet routinely tested, especially not in patients with HR+, HER2- eBC and in those younger than 70 years (data not shown). Future analyses will investigate the impact of these new drugs on the outcome of patients with high-risk eBC in their respective subgroups.

METHODS

OPAL (NCT03417115) is a prospective, observational, open, multicenter clinical registry. Patients with early and advanced breast cancer (eBC/aBC) are prospectively documented from start of their first systemic treatment. Over 200 sites (comprehensive cancer centers, clinics, and office-based gynecologic or medical oncologists) all over Germany are participating.

OPAL eBC started in April 2021 and aims to recruit 1500 patients with HR+ HER2-, 750 patients with HER2+ and 750 patients with triple-negative eBC. Detailed information is collected on neoadjuvant, post-neoadjuvant, adjuvant and extended adjuvant treatments, patient and tumor characteristics, physician-reported factors potentially influencing treatment decision, biomarker testing and local treatments (surgery, radiotherapy). Follow-up continues up to 5 years until death. There is no treatment specification. Data are collected in electronic case report forms; plausibility checks and centralized data review as well as on-site source data verification are performed to ensure data quality.

Patient-reported outcomes (PROs) are collected at start of treatment and every 3 months thereafter. Patients can also give informed consent for their tumor samples to be used in future translational research (virtual biobank).

Patients were classified by different criteria as "qualifying to receive one of the newly approved drugs" according to their labels.

For the CDK4/6 inhibitor abemaciclib: HR-positive, HER2-negative eBC at high risk of recurrence, which was defined as either (N1 and G3/T3) or N2/3 (as in the pivotal monarchE trial (NCT03155997)) and start of adjuvant endocrine therapy since 24.02.2022 (date of positive CHMP opinion for abemaciclib).

For the immune checkpoint inhibitor pembrolizumab: triple-negative eBC at high risk of recurrence, which was defined as tumor size ≥ T2 or nodal positive tumor (as in the pivotal Keynote 522 trial (NCT03036488)) and start of neoadjuvant/post-neoadjuvant therapy since 22.04.2022 (date of positive CHMP opinion for pembrolizumab).

For the PARP-inhibitor olaparib: HER2-negative, gBRCA1/2 mutated EBC at high risk of recurrence, and prior chemotherapy treatment. High risk of recurrence was defined as either residual disease after neoadjuvant chemotherapy and in case of HR-positive: GPS&EG score ≥3 OR for patients having received adjuvant chemotherapy: in case of patients with triple-negative eBC: nodal positive or tumor size ≥2 cm or in case of patients with HR+, HER2- eBC ≥4 positive lymph nodes (as in the pivotal OlympiA trial (NCT02032823)). Additionally start of adjuvant therapy since 02.08.2022 (date of EMA decision).

RESULTS

Between April 2021 and June 2023, 2975 patients with eBC were recruited at start of their first systemic treatment. At time of interim database cut on 30th June 2023, 1423 patients with HR+ HER2-, 670 patients with HER2+ and 679 patients with triple negative EBC were evaluable.

CDK4/6 inhibitor abemaciclib

Of 1423 patients with HR+ HER2- eBC, 22% (n=315) so far fulfilled the "high risk"-criteria to receive abemaciclib (N1 and T3/G3: 10% or N2/N3: 12%, **Figure 1**). 130 patients with high risk started their adjuvant endocrine therapy since 24.02.2022 and thereof 51 patients (39%) already received the drug. Of note, for 153 patients no endocrine therapy was documented at time of database cut yet, for example because they have not completed their chemotherapy yet. These patients could still receive abemaciclib. Additional 25 patients received abemaciclib without fulfilling all criteria listed above.

Immune checkpoint inhibitor pembrolizumab

Of 679 patients with triple-negative eBC, 62% (n=419) fulfilled the high risk criteria to receive pembrolizumab **(Figure 2)**. Most patients (89%, n=372) started their treatment with a neoadjuvant therapy. Of these patients, 62% (n=229) started their treatment after 22.04.2022 and were therefore classified as eligible to receive pembrolizumab. Thereof, 86% of patients (n=197) were treated with pembrolizumab. Additionally, 67 patients received pembrolizumab without fulfilling all criteria above, for example because patients started their chemotherapy before 22/04/2022 and switched to pembrolizumab later.

PARP-inhibitor olaparib

Patients with HR+, HER2- eBC

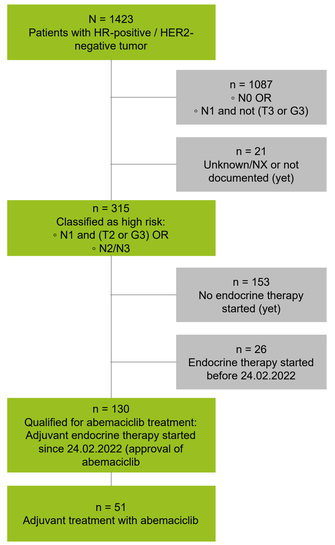
Of 1423 patients with HR-positive, HER2-negative eBC, 8% (n=116) of patients were classified as high risk (**Figure 3A**; either neoadjuvant chemotherapy, non-pCR and CPS&EG score ≥ 3: 1%, or initial adjuvant chemotherapy and pN ≥ 2: 7%). 2% (n=2) of these patients had documented tests for BRCA1/2 but no BRCA1/2 mutation was detected, and therefore, no patients qualified for treatment with olaparib. Of note, BRCA1/2 tests have also been performed in patients not fulfilling all high-risk criteria. 45 additional patients with HR-positive, HER2-negative tumors and BRCA1/2 tests were documented, resulting in 11 BRCA1/2 mutations, of which 2 patients were treated with olaparib. Of note, some BRCA1/2 tests were performed before olaparib was approved.

Patients with triple-negative eBC

Of 679 patients with triple-negative eBC, 27% (n=185) of patients were classified as high risk (**Figure 3B**; either neoadjuvant chemotherapy and non-pCR: 21%, or initial adjuvant chemotherapy and nodal positive OR nodal negative and T2/T3: 6%). For 22% (n = 40) of these patients, a BRCA1/2 test was documented. 15 patients had the test result BRCA1/2 mutation, and seven patients thereof completed their chemotherapy since 02/08/2022 and already started their adjuvant therapy and therefore qualified for the treatment with olaparib. Thereof, two patients received olaparib so far.

71 additional patients with triple-negative tumors and BRCA1/2 test were documented with 33 BRCA1/2 mutations being detected, of which 4 received olaparib. The number of patients receiving olaparib can still rise, e. g. because some patients have not started their adjuvant therapy yet.

Figure 1: Flowchart of patients with HR+ HER2- eBC qualifying for and receiving abemaciclib



HR: Hormone receptor | HER2: HER2 receptor

Figure 2 : Flowchart of patients with triple-negative eBC qualifying for and receiving

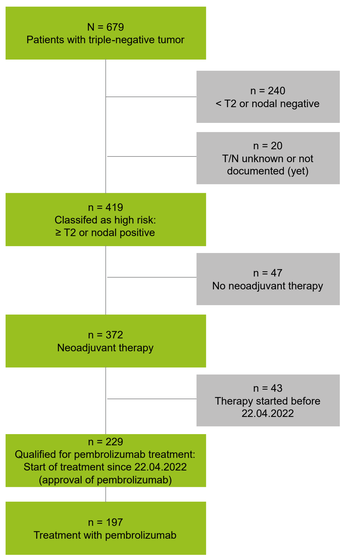


Figure 3A: Flowchart of patients with HR+, HER2- eBC qualifying for or being treated with olaparib

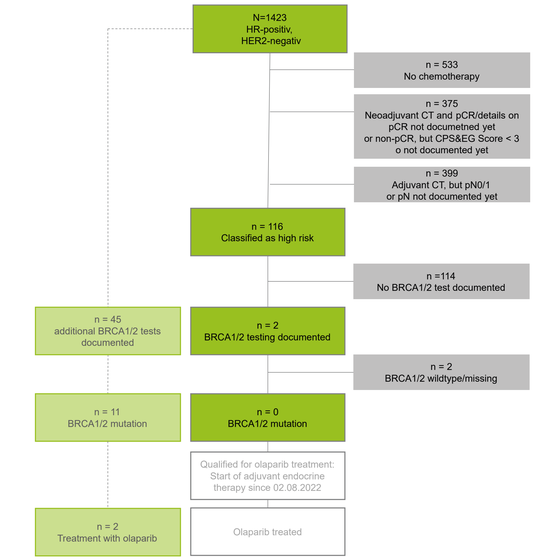


Figure 3B: Flowchart of patients with triple-negative eBC qualifying for and receiving olaparib