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Original Article

The Real-world Experiences of Abemaciclib for Estrogen Receptor-positive Human Epidermal Growth Factor Receptor-negative-2 Metastatic Breast Cancer – Sharing from a Single Institute in Southern Taiwan

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Abstract

Background: CDK 4/6 inhibitor (CDK4/6i) is the first-line therapeutic drug to treat ER-positive (ER+) HER2-negative (HER2 -) metastatic breast cancer (MBC) now. We have three CDK4/6i: Palbociclib, Ribociclib, and Abemaciclib. In the long-term follow-up study, there are some different results among the three CDK4/6i. Some real-world reports demonstrated some patients would have clinical benefits from Abemaciclib in the ER+ HER2- metastatic BC patients who had priorly received the other CDK 4/6 inhibitor (Palbociclib). In Taiwan, Abemaciclib is the third available CDK 4/6 inhibitor behind the other two CDK4/6i. However, Abemaciclib was not reimbursed in ER+ HER2- MBC by Taiwan Health Insurance until now. Most doctors in Taiwan have the less therapeutic experiences for Abemaciclib. In this article, we would share the clinical experiences for the first thirteen patients who were prescribed with Abemaciclib to treat ER+ HER2- MBC. **Materials and Methods:** This chart review study was conducted from January 1, 2020, to May 31, 2023. We reviewed the medical charts at National Cheng Kung University Hospital (NCKUH) and identified 13 patients who had received abemaciclib treatment for ER+ HER2− MBC. The study was approved by the Institutional Review Board at NCKUH (approval number: B-ER-112-220). All of the 13 patients were treated with abemaciclib (150 mg twice daily initially), in combination with other anti-cancer medications. We recorded the clinical parameters, including sex, age, treatments in neoadjuvant/adjuvant setting, metastatic sites, other prior CDK4/6i therapy, treatment lines of abemaciclib in the metastatic setting, survival period before abemaciclib treatment, time to treatment failure for abemaciclib, causes of abemaciclib discontinuation, dose reduction, and adverse effects (AEs) related to abemaciclib. **Results:** Up to the cut-off date (May 31, 2023), four (4/13) patients were still receiving therapy and nine patients (9/13) had discontinued abemaciclib therapy. Five (5/9) patients discontinued abemaciclib due to disease progression (PD), and two (2/9) patients interrupted abemaciclib treatment due to personal reasons. Two (2/9) patients stopped abemaciclib early because of AEs, and one patient died due to PD. The time to treatment failure for abemaciclib ranged from 1 to 41 months (average: 19.2 months, median: 14 months). AEs were noted in 12 patients (no recording in one patient), of which diarrhea (10/12), anemia (4/12), and neutropenia

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(3/12) were the most common. **Conclusion:** According to our real-world data, Abemaciclib is effective and safe for the ER+ HER2- metastatic BC cancer patients who they were heavily treated.

Keywords: Abemaciclib, estrogen receptor-positive, human epidermal growth factor receptor-negative-2, metastatic breast cancer, real-world data

Introduction

CDK 4/6 inhibitors (CDK4/6i) are currently used as first-line therapeutic drugs to treat estrogen receptor-positive (ER+) human epidermal growth factor receptor-negative (HER2−) metastatic breast cancer (MBC).[1] Three CDK4/6i have been approved to date, palbociclib, ribociclib, and abemaciclib.[2] However, some review articles have mentioned pharmacological differences between abemaciclib with the other two CDK4/6i.[3,4] In the adjuvant setting, abemaciclib is the first approved CDK4/6i to improve disease-free survival for patients with early ER+ breast cancer[5,6] a benefit not seen with palbociclib.[7] A similar trial for ribociclib is ongoing.[8] In addition, some real-world reports have demonstrated that some patients who had previously received palbociclib still had clinical benefits from abemaciclib.[9] In the Monarch 1 phase II clinical trial, the use of abemaciclib as a single agent was shown to be effective and safe in heavily pretreated ER+ HER2− MBC patients.[10] In Taiwan, abemaciclib is the third available CDK4/6i after palbociclib, ribociclib. However, abemaciclib is not currently reimbursed by the Taiwan Health Insurance program for the treatment of ER+ HER2− MBC, and consequently, most doctors in Taiwan have less therapeutic experience with abemaciclib. In this chart review study, we provide our initial experiences of abemaciclib in treating 13 heavily pretreated ER+ HER2− MBC patients, including the clinical efficacy and safety of abemaciclib as a later-line treatment for these patients.

Materials and Methods

Patients and methods

This chart review study was conducted from January 1, 2020, to May 31, 2023. We reviewed the medical charts at National Cheng Kung University Hospital (NCKUH) and identified 13 patients who had received abemaciclib treatment for ER+ HER2− MBC. The study was approved by the Institutional Review Board at NCKUH (approval number: B-ER-112-220) the patients' consent are obtained.

Clinical data collection and analysis

The 13 patients in this study were heavily pretreated ER+ HER2− MBC patients. All of the patients were treated with abemaciclib (150 mg twice daily initially), in combination with other anti-cancer medications. Three premenopausal patients received additional ovary function suppression. We recorded the clinical parameters, including sex, age, treatments in neoadjuvant/adjuvant setting, metastatic sites, other prior CDK4/6i therapy, treatment lines of abemaciclib in the metastatic setting, survival period before abemaciclib treatment, time to treatment failure for abemaciclib, causes of abemaciclib discontinuation, dose reduction, and adverse effects (AEs) related to abemaciclib.

Results

Patient baseline characteristics

All 13 patients were Taiwanese females, and they had all received abemaciclib treatment between January 1, 2020, and May 31, 2023, at NCKUH. Their median age was 57.9 years (range 44.0–83.0 years). Eight patients had previously received neoadjuvant adjuvant chemotherapy or hormone therapy. Five patients had only bone metastasis, and one patient presented with only lung metastasis. The remaining seven patients had more than one metastatic site. Three patients had previously received other CDK4/6i therapy. The patients had received a median of 3 (range 2–8) lines of prior systemic therapy in the metastatic setting.

The efficacy and safety of abemaciclib therapy

Up to the cut-off date (May 31, 2023), four (4/13) patients were still receiving therapy and nine patients (9/13) had discontinued abemaciclib therapy. Five (5/9) patients discontinued abemaciclib due to disease progression (PD), and two (2/9) patients interrupted abemaciclib treatment due to personal reasons. Two (2/9) patients stopped abemaciclib early because of AEs, and one patient died due to PD. The treatment lines of abemaciclib were from the 2nd to 8th (median: 4) line in a metastatic setting. The survival period for these patients before abemaciclib therapy ranged from 7 to 93 months (average: 36.2 months, median: 31 months). The time to treatment failure for abemaciclib ranged from 1 to 41 months (average: 19.2 months, median: 14 months). AEs were noted in 12 patients (no recording in one patient), of which diarrhea (10/12), anemia (4/12), and neutropenia (3/12) were the most common. The patient depositions and study results are summarized in Table 1.

Discussion

In Taiwan, this is the first study to report the real-world data of abemaciclib treatment in heavily pretreated ER+ HER2− MBC patients. Of the 13 patients included in the study, two (2/13) stopped abemaciclib treatment early due to AEs; however, the exact reasons for discontinuation were not recorded in the medical charts. One (1/13) patient died after 1 month of abemaciclib treatment due to PD. Ten patients (10/13, 77%) had satisfactory clinical benefits and received more than 8 months of abemaciclib treatment. As expected, diarrhea was the most common AE (100%). Dose reduction was needed in four (4/13)

Table 1: The patient depositions and clinical results of abemaciclib treatment in the 13 heavily pretreated estrogen receptor-positive human epidermal growth factor receptor 2-negative metastatic breast cancer patients at National Cheng Kung University Hospital

Patient number	Age	Prior chemotherapy	Prior hormone therapy	Metastatic sites	Prior CDK4/6i use	Treatment line of abemaciclib	Period of metastasis before abemaciclib administration (months)	Treatment period for abemaciclib (months)	Treatment continuation or reasons for discontinuation	Combination drugs with abemaciclib	Dose reduction (only one level)	AEs
1	44	Yes	Yes	Bone	No	3rd	7	41	Continuation	Abemacicliab Letrozole OFS	Yes	Diarrhea, vomiting, anemia, thrombocytopenia
2	58	Yes	Yes	Bone	No	7th	31	4	Discontinuation (disease progression)	Abemaciclib Exemestane	No	Diarrhea, neutropenia, anemia
3	48	NA	NA	Lung, bone	No	8th	55	11	Discontinuation (personal reason)	Abemaciclib Fulvestrant	No	Diarrhea
4	68	Yes	Yes	Bone	Yes	3rd	45	24	Discontinuation (personal reason)	Abemaciclib Fulvestrant	Yes	Skin rash, diarrhea
5	52	Yes	Yes	Lung, bone	No	4th	40	1	Discontinuation (AE)	Amebaciclib Letrozole	No	Diarrhea
6	50	Yes	Yes	Lung, bone, liver	No	4th	70	2	Discontinuation (AE)	Abemacicliab Letrozole Capecitabine Navelbine	No	Neutropenia
7	73	NA	NA	Bone	No	3rd	31	21	Discontinuation (disease progression)	Abemaciclib Letrozole	No	Vomiting
8	56	NA	NA	Lung, bone	No	6th	93	38	Continuation	Abemaciclib Exemestane	Yes	Diarrhea, renal functional impairment, liver function injury
9	50	Yes	Yes	Lung	Yes	2nd	20	40	Continuation	Abemacicliab Letrozole OFS	No	Diarrhea, neutropenia
10	83	No	Yes	Lung, bone, liver	Yes	2nd	7	12	Discontinuation (disease progression)	Abemaciclib Letrozole	Yes	Diarrhea, anemia
11	62	Yes	Yes	Bone, liver	No	2nd	31	14	Discontinuation (disease progression)	Abemaciclib Letrozole	No	Diarrhea, anemia
12	64	NA	NA	Lung, bone	No	2nd	10	8	Discontinuation (disease progression)	Abemaciclib Letrozole	No	No report
13	45	NA	NA	Bone	No	2nd	31	34	Continuation	Abemaciclib Letrozole OFS	No	Diarrhea

NA: Not available, OFS: Ovary function suppression, CDK4/6i: CDK 4/6 inhibitor, AE: Adverse effect

patients (only one level), three (3/13) patients developed new anemia, and three (3/13) patients developed neutropenia. The other AEs included vomiting, thrombocytopenia, skin rash, and renal and liver function impairments. Four patients received more than 30 months of abemaciclib treatment. These results demonstrate that abemaciclib is effective and safe even in heavily treated ER+ HER2− MBC patients. In the Monarch 1 phase 2 clinical trial, abemaciclib was used as a single agent to treat heavily pretreated ER+ HER2− MBC patients. At the 12-month final analysis, the primary objective response rate was 19.7%, the clinical benefit rate (CR + PR + SD) was 42.4%, the median progression-free survival was 6.0 months, and the median overall survival was 17.7 months. The most common treatment-emergent AEs of any grade were diarrhea, fatigue, and nausea. Discontinuation due to AEs was infrequently (7.6%). In our study, eight patients received more than 12 months of abemaciclib treatment. The objective response rate was 61.5% (8/13), the clinical benefit rate (6 months) was 76.9% (10/13), the median progression-free survival was 14 months, and the median overall survival was 24 months. The most common AEs were diarrhea, anemia, and neutropenia. The discontinuation rate due to AEs was 15.3% (2/11). Our study showed a better treatment results than the Monarch 1 trial.

There were three limitations to this study. First, the study was retrospective and based on a chart review. We could not provide the exact and detailed medical records for these study subjects. In addition, we did not have information on AEs in one patient. Second, the included MBC patients were all heavily treated (two or more treatment lines after metastasis), and they had heterogeneous and complex therapeutic journeys. Consequently, we cannot conclude which ER+ HER2− MBC patients would benefit more from abemaciclib treatment. Finally, only 13 patients were included in the study, and the small number of patients makes precludes making definitive conclusions on abemaciclib treatment in his patient group. The results of this real-world study suggest that abemaciclib treatment is effective and safe as a later-line treatment for ER+ HER2− MBC patients.

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Data availability statement

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

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Conflicts of interest

There are no conflicts of interest.

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