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Clinical Characteristics and Treatment Persistence in US Patients with HR+/HER2-, Node Positive Early Breast Cancer Treated with Abemaciclib: Real-World Study from First Year After Approval

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OBJECTIVES

This retrospective study describes clinical characteristics, dose modification patterns, and 3-month treatment persistence in patients with HR+/HER2-, node-positive EBC initiating abemaciclib at 150 mg BID in the first year following FDA approval.

CONCLUSIONS

- The majority of patients (88%) continued abemaciclib beyond 3 months. The low rate of adjuvant abemaciclib discontinuation in US clinical practice suggests that abemaciclib is well tolerated by most patients.
  - Among patients who discontinued, 70% did not attempt dose modifications.
- Half of the patients continued on the approved 150 mg BID dose and half had a dose reduction, with a median time to first dose reduction of 2 months.
- Patients with dose reductions had improved persistency, with 93% continuing abemaciclib beyond 3 months
- Given that the common onset of diarrhea is within the first 1-2 weeks of abemaciclib treatment and that dose reductions do not compromise efficacy, anti-diarrheal medicine and timely dose modifications should be utilized to improve tolerability and treatment persistence with abemaciclib.

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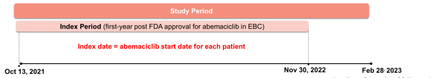
BACKGROUND

- Abemaciclib, a selective inhibitor of CDK4/6, is approved for use in combination with endocrine therapy (ET) for the adjuvant treatment of adult patients with HR+, HER2-, node-positive, early breast cancer (EBC) who are at a high risk of recurrence and is recommended by international guidelines.[1-7]
- In monarchE, adjuvant abemaciclib + ET significantly improved invasive disease-free survival (IDFS) and distant relapse-free survival (DRFS), with sustained benefit beyond the 2-year treatment period resulting in a 5-year benefit in IDFS (7.9%) and DRFS (7.1%)*.[4]
- In monarchE, 18.5% of patients discontinued abemaciclib due to adverse events (AEs), and the discontinuation rate due to AE was highest in the first month. Diarrhea occurred early on treatment (median 8 days to onset) and was the most common reason for discontinuation and/or dose reduction.[8]
- Abemaciclib is dosed at 150 mg twice daily (BID)[7] with a recommendation for dose reductions to 100 mg or 50 mg to improve tolerability. Efficacy of adjuvant abemaciclib is not compromised by dose reductions.[9]
- Understanding utilization and dose modification of abemaciclib in the real-world setting can provide insights into the treatment patterns beyond the controlled clinical trial setting and help inform AE management strategies to improve tolerability and support treatment persistence.

*5-year IDFS and DRFS rates are from the FDA-approved population from monarchE (Cohort 1).

METHODS / STUDY DESIGN

- **Study Design:** Retrospective study of patients initiating abemaciclib in the adjuvant setting.
- **Data Source:** US Flatiron Health* electronic health records-derived de-identified database comprising structured and unstructured data.



- **Patient Selection**: Included patients were aged ≥ 18 years, diagnosed with node-positive, stage I-III EBC, and initiating abemaciclib at 150 mg BID in the index period. Excluded patients with evidence of prior use of any CDK4/6 inhibitor or any other primary malignancy, except non-melanoma skin cancer and other benign in situ neoplasm while on treatment for EBC
- **Analysis**: Baseline patient demographics and clinical characteristics; dose modifications; and 3-month treatment persistence were analyzed descriptively.
  - Persistence rate is the proportion of patients on abemaciclib at 3 months, allowing for up to a 60-day medication gap.
  - Dose modification includes dose hold or a change in dose (increase or decrease) as indicated in patient's chart.

*The Flatiron Health database is a longitudinal, EHR-derived, de-identified database comprising patient-level structured and unstructured data curated via technology-enabled abstraction.[10,11] Additional data abstraction was conducted to supplement the existing database. The data presented herein originated from approximately 280 cancer clinics (~800 sites of care) from across the US, with 80% of patients from community practices and 20% from academic research hospitals.

LIMITATIONS

- This is a descriptive study with a moderate sample size of patients who initiated abemaciclib during the first year after FDA approval in EBC, and hence, the results should be interpreted with caution.
- The relatively short median follow-up time (8.8 months) allowed reliable assessment of persistency only in the first 3 months, suggesting that longer follow-up is needed.
- AE grades and information on co-medication such as anti-diarrheal medications was not assessed in this study.

References: 1. FDA expands early breast cancer indication for abemaciclib with endocrine therapy. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-expands-early-breast-cancer-indication-abemaciclib-endocrine-therapy. **2**. Verzenio [package insert]. Indianapolis, IN: Eli Lilly and Company; 2023. https://uspl.lilly.com/verzenio/verzenio.html#pi. **3.** Johnston SRD, et al. J Clin Oncol. 2020;38:3987-4000. **4**. Rastogi P, et al. J Clin Oncol. 2024; 42(9), 987-993. **5**. NCCN Clinical Practice Guidelines in Oncology-Breast Cancer. Version 5. 2024. **6.** Caswell-Jin JL, et al. JCO Oncol Pract. 2024 Sep 20:OP2400663. **7**. Loibl S, et al. Ann Oncol. 2024;35(2):159-82. **8**. Rugo et al. Ann Oncol. 2022 Jun;33(6):616-627. **9**. Goetz et al. NPJ Breast Cancer 2024; 34(10). **10**. Ma X, et al. Medrxiv. doi: https://doi.org/10.1101/2020.03.16.20037143. **11**. Birnbaum B, et al. Arxiv. doi: https://doi.org/10.48550/arXiv.2001.09765

Abbreviations: AI, aromatase inhibitors; CDK, Cyclin-dependent kinase; 4/6; EBC, early breast cancer; ECOG, Eastern Cooperative Oncology Group; EHR, electronic health record; ET: endocrine treatment; HR+, hormone receptor-positive; HER2, human epidermal growth factor receptor 2-negative; IQR, interquartile range.

Disclosures: KH participated on a Data Safety Monitoring/Advisory Board of Daiichi Sankyo, AstraZeneca, and Gilead. **WGM, ZLC, BG, AML, EB, RV,** and **KM** are employees and minor shareholders of Eli Lilly and Company. **MR** and **JW** are employees of Flatiron Health. **HS** has received consulting fees from Novartis, Eli Lilly and Company, Sermonix, Pfizer, and AstraZeneca.

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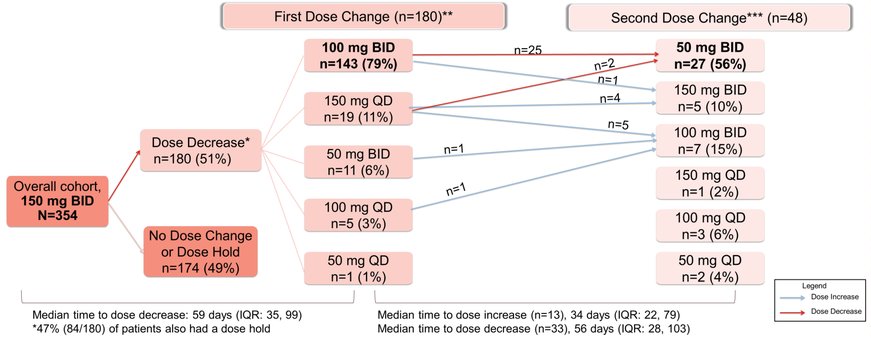
RESULTS

Dose Modification Patterns



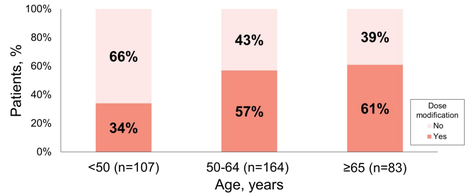
Median time to dose decrease: 59 days (IQR: 35, 99)
*47% (84/180) of patients also had a dose hold

Median time to dose increase (n=13), 34 days (IQR: 22, 79)
Median time to dose decrease (n=33), 56 days (IQR: 28, 103)

- **~50% stayed on 150 mg BID**
- **~ 50% dose reduced mostly to 100 mg BID and 50 mg BID**
- **Median time to 1st dose reduction is ~ 2 months**

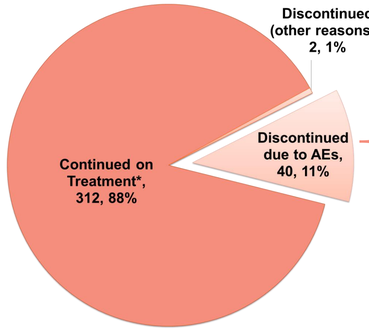
**1 patient dose unknown. ***Details on dose change from 1st dose change are included only for patients with large numbers in the 2nd dose change (see Supplemental table 1 for complete data); Dose change was unknown for 3 patients.

Dose Modifications by Age



- **A higher proportion of patients ≥50 years old changed dose vs <50 years.**

Majority of patients continued on treatment beyond 3 months



In those who discontinued due to AEs:

- Most common AEs were diarrhea (n=24), fatigue (n=16), and nausea/vomiting (n=12)
- Dose modifications not attempted in majority of patients (70%)
- Characteristics of those who discontinued#:
  - Median age of 64.0 years (IQR 52.5, 71.0)
  - 55.0% had ≥1 comorbidities

- **Discontinuations occurred in the first two months, median 39 days (IQR 20, 54)**
- **High treatment continuation (93%) and low discontinuation rate (7%) in patients who experienced dose reductions**

*1 financial and 1 non-cancer related medical issue. *Includes 20 patients who had dose hold >60 days and resumed treatment within the follow-up period; and 3 patients on dose hold whose follow-up time did not allow for assessment of resumption of treatment. #Additional characteristics are included in supplemental table 2.

Baseline Demographics and Clinical Characteristics

	Patients, N =354
Follow up time (months), median (IQR)	8.8 (5.9, 12.1)
Age (years) at index date, median (IQR)	56.0 (48.0, 64.0)
Female, n (%)	353 (99.7%)
Race[a], n (%)	
White	204 (57.6)
Black or African American	45 (12.7)
Asian	14 (4.0)
Other Race	44 (12.4)
ECOG Performance Status[a,b] at Index Date, n (%)	
0	205 (57.9)
1	89 (25.1)
2	9 (2.5)
No. of Comorbidities, n (%)	
0	234 (66.1)
1	77 (21.8)
2+	43 (12.1)
Practice Type, n (%)	
Academic	53 (15.0)
Community	286 (80.8)
Academic & Community	15 (4.2)
Menopausal Status[a] at Index Date, n (%)	
Pre and perimenopausal	137 (38.7)
Postmenopausal	196 (55.4)
Stage at Diagnosis[a,c], n (%)	
Stage I	59 (16.7)
Stage II	148 (41.8)
Stage III	136 (38.4)
Pathologic Node Status at Diagnosis[a,c,d], n (%)	
N1	160 (45.2)
N2	125 (35.3)
N3	50 (14.1)
Tumor grade at Diagnosis[a], n (%)	
Grade 1	31 (8.8)
Grade 2	185 (52.3)
Grade 3	136 (38.4)
Treatments received prior to initiating abemaciclib	
Neoadjuvant therapy, n (%)	164 (46.3)
Chemotherapy n (%)	294 (83.1)
Adjuvant ET, n (%)	262 (74.0)
Time on prior adjuvant ET (months), median (IQR)	1.6 (0.0, 5.0)
Endocrine Therapy Choice[e], n (%)	
Abemaciclib + AI (anastrozole, exemestane or letrozole)	322 (91.0)
Abemaciclib+ tamoxifen	32 (9.0)

- **With a median follow-up of 8.8 months this cohort of patients was more racially diverse and older than in monarchE.[3]**
- **The majority of patients have Stage II or Stage III disease.**
- **>90% of patients were treated with abemaciclib+AI.**

[a]Race, ECOG PS and menopausal status at index date and stage, node status, and tumor grade at diagnosis data was unknown/not documented for 47, 51, 21, 11, 4, and 2 patients, respectively; [b]ECOG performance status closest to the index date (30 days prior to 7 days after the index date); [c]Stage and node status at diagnosis were derived from clinician notes for patients who received neoadjuvant therapy and pathologic reports for patients who did not receive neoadjuvant therapy; [d]Nodal status was determined from clinician notes in 19 patients; [e]Regimens may also include ovarian suppression.