Treatment patterns following first line CDK4/6 inhibitor progression in HR+, HER2- metastatic breast cancer

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Background

- Metastatic hormone receptor positive (HR+)/human epidermal growth factor receptor-2 negative (HER2−) breast cancer continues to be significant cause of cancer-related death [1]
- First-line treatment with a cyclin-dependent kinase 4 and 6 inhibitor (CDK4/6i) has become the standard to improve quality of care and delay time to chemotherapy [2,3]
- However, following CDK4/6i progression, prognosis is poor and optimal second line treatment is not clearly defined [2,3]
- Reviewing real world treatment patterns and understanding subsequent therapies may help guide future clinical research and decision-making

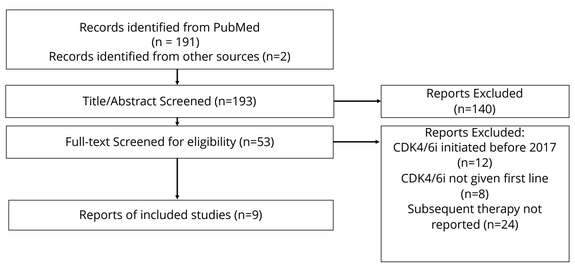
Research Objective

- Identify and assess current treatment patterns for patients with (HR+)/ HER2- metastatic breast cancer after first-line therapy CDK4/6i progression

Methods

- Targeted literature review
- PubMed was searched for articles between January 2017 – April 2024 using the following key inclusion criteria:
    - Patients with HR+, HER2- metastatic breast cancer
    - CDK4/6i initiated as first-line therapy 2017 or onward
    - Subsequent treatment following CDK4/6i progression reported
    - Patients receiving CDK4/6i in clinical trials were excluded

Figure 1: PRISMA Flow Diagram



Results

Table 1: Summary of studies included from literature review

Author (year published)	Median Age (years)	Country	Study Design	Data Source	Sample size	CDK4/6i backbone	Subsequent Therapy, N (%)	Median Subsequent Therapy PFS (months)
Li et al. (2021)[4]	55	China	Retrospective observational	EHR	35	Palbociclib	• CT:22 (63%) • ET: 13 (37%)	CT: 7.2 ET: 13.4
Gousis et al. (2022)[5]	NR	UK	Retrospective observational	EHR	38	Any CDK4/6i	• CT: 22 (58%) • ET: 12 (32%) • Clinical trials: 4 (11%)	CT: 5.4 ET: 4
Marschner et al. (2022)[6]	64	Germany	Retrospective observational	Registry (OPAL)	113	Any CDK4/6i	• CT: 79 (70%) • ET:22 (20%) • Re-challenge CDK4i: 10 (9%) • PARP-inhibitor: 2 (2%)	Overall subsequent therapy: 4.3
Wong et al. (2022)[7]	54.3 *mean	Australia	Retrospective observational	Registry (Kisqali Access Registry for Metastatic breast cancer in Australia)	65	Ribociclib	• CT: 42 (65%) • ET: 12 (19%) • Clinical Trial: 8 (12%) • Other:3 (5%)	Overall subsequent therapy: 4.5
Buller et al. (2023)[8]	61	UK	Retrospective observational	EHR	127	Any CDK4/6i	• CT: 79 (62%) • ET: 48 (38%)	NR
Karacin et al. (2023)[9]	54	Turkey	Retrospective observational	EHR	202	Any CDK4/6i	• CT: 126 (62.4%) • ET: 76 (37.6%)	CT: 5.3 ET: 9.5
Moser et al. (2023)[10]	63	Israel	Retrospective observational	EHR	144	Palbociclib	• CT: 49 (34%) • ET: 82 (57%) • Other 13 (9%)	NR
Sawaki et al. (2023)[11]	65	Japan	Retrospective observational	EHR	224	Palbociclib	• CT: 77 (34.4%) • ET: 66 (30%) • Re-challenge CDK4/6i 70 (31.2%) • Other: 11 (4.9%)	Overall subsequent therapy: 7.5
Liang et al. (2024))[12]	58	China	Retrospective observational	EHR	82	Palbociclib	• CT: 36 (43.9%) • ET: 17 (20.8%) • Re-challenge CDK4/6i: 28 (34.2%) • PARP-inhibitor: 2 (1.2%)	Overall subsequent therapy: 6.6

Abbreviations: *CT: Chemotherapy, CDK4/6i: Cyclin dependent kinase 4 & 6 inhibitor, EHR: Electronic health record, ET: Endocrine Therapy, NR: Not Reported, PFS: Progression free survival

Figure 3: Summary of chemotherapy regimens identified from literature review

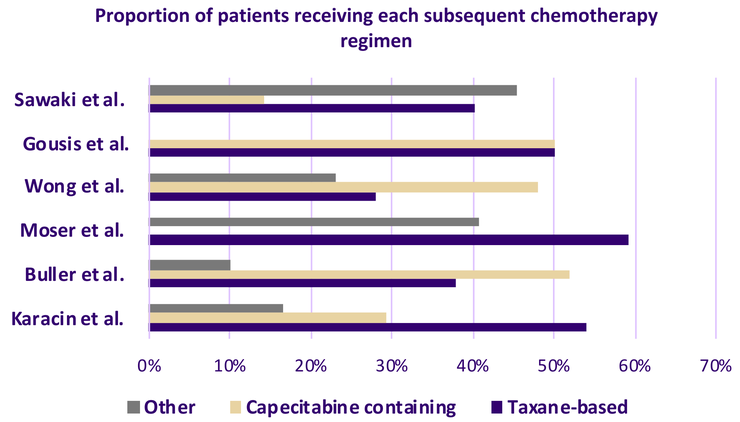


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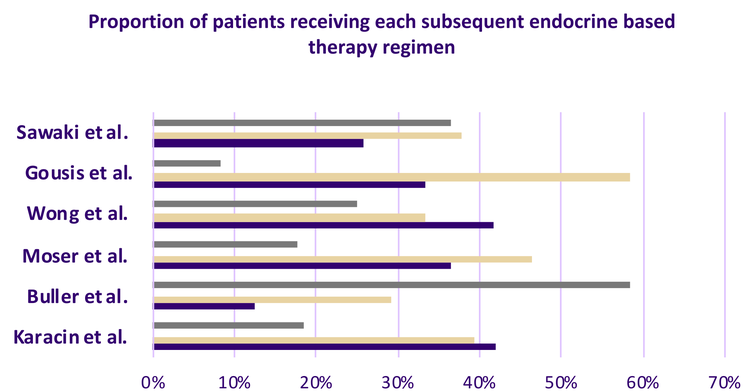
Figure 4: Summary of endocrine based therapy regimens identified from literature review



Summary of Results

- The literature review included 9 observational studies, with 7 of them reporting second- line PFS
- The most common subsequent therapy was chemotherapy (34%-70%), followed by endocrine based therapy (19%- 57%)
- Chemotherapy based regimens were mainly taxane- based (28%-59%) or capecitabine containing (23%-51%)
- For those receiving endocrine -based therapy, fulvestrant (30%-58%) and everolimus + exemestante (12%-42%) were most common

Conclusions & Implications

- Although treatment patterns after progression on a first line CDK4/6i vary, suggesting no standard of care for subsequent treatment, chemotherapy was the most common therapy after progression.
- Prognosis after second- line treatment remains a challenge, and more effective treatments options for HR+, HER2- patients are needed to help delay time to chemotherapy

Note: Li ,Marschner, and Liang did not report specific CT or ET regimens