DATA FROM THE PROSPECTIVE REGISTRY PLATFORM OPAL

SECOND-LINE THERAPIES OF PATIENTS WITH EARLY PROGRESSION UNDER CDK4/6-INHIBITOR IN FIRST-LINE

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Conflicts of Interest
N. Marschner: Employment or Leadership Position: iOMEDICO; Advisory Role or Expert Testimony: Novartis, Roche, Celgene, Lilly, Mundipharma, Mylan, Amgen, Pfizer; Stock Ownership: Shares of iOMEDICO; Financing of Scientific Research: Roche, Lilly, Pfizer, Mylan, AMGEN, Mundipharma, Celgene; **T. Decker:** Advisory Role or Expert Testimony: Novartis, iOMEDICO

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INTRODUCTION

CDK4/6-inhibitors have become standard in first-line therapy for patients with hormone receptor positive, HER2 negative advanced breast cancer. However, after disease progression on CDK4/6-inhibitor, there are few data to drive decision making for subsequent treatment strategies. Here, we present data of the German OPAL registry platform analysing the different therapy strategies used after early progression under CDK-inhibitor (less than one year from start of treatment).

METHODS

OPAL (NCT03417115) is a prospective clinical registry that continues the Tumor Registry Breast Cancer (TMK, NCT01351584, Fietz et al., 2017). Patients with early and advanced breast cancer (EBC/ABC) are prospectively recruited at start of their first systemic treatment. Follow-up continues until death or up to 5 years. There is no treatment specification. Detailed information on all (sequential) treatments, patient and tumor characteristics, physician-reported factors regarding treatment decision making, biomarker testing, outcomes (e.g. event-free survival for patients with EBC and best response, progression-free and overall survival for patients with ABC) are collected in a web-based data capture system with implemented checks for completeness and plausibility.

Data are monitored by data management and on-site. 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).

By June 30, 2022, a total of 7883 patients had been recruited, of whom 3383 since start of OPAL. Here, data were analyzed for 953 OPAL patients with hormone receptor positive, HER2-negative ABC. Recruitment for this cohort started in September 2018 and was stopped with the inclusion of the 1000th patient in July 2021. 730 patients received a CDK4/6-inhibitor first-line.

Progression-free survival (PFS) was defined as the interval between start of first-line therapy and the date of progression or death from any cause. Patients alive or lost to follow-up were censored at last contact. PFS in registries can differ from PFS in clinical trials, since the RECIST criteria are usually not applied in routine care, and method and time point of imaging is performed as per local site standard. PFS in registries represents the time to clinically relevant progression in routine care.

Figure 1

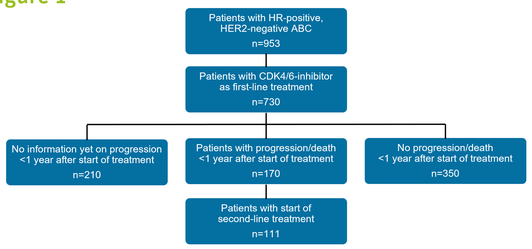

Figure 1 Flowchart
Patient with no information yet on progression within one year of start of treatment are mostly patients who had just recently started first-line treatment and some patients who were lost to follow-up within the first year of treatment.

RESULTS

Use of CDK4/6-inhibitors in first-line increased from 68% in 2018 to 79% in 2021. At time of database cut June 30th, 2022, 170 patients had an early progression/death within 12 months under CDK4/6-inhibitor (138 patients with tumor progression and 32 patients deceased). For patients with early progression, median time to early progression/death was 4.8 months.

Comparing characteristics at start of treatment of patients with vs. without progression or death within one year after start of first-line treatment, they were similar in age and comorbidities, and the tumor was equally often M1 at diagnosis. Patients with progression within one year had slightly more often an ECOG ≥ 1 and visceral metastases, for example to the lung (**Table 1**).

For 111 patients with early progression, start of second-line treatment was already documented. 74% of patients received chemotherapy as second-line treatment, mainly capecitabine +/- bevacizumab or (nab)paclitaxel +/- bevacizumab. 17% received endocrine therapy, 8% re-challenge with CDK4/6-inhibitors + endocrine therapy and 1% of patients received a PARP-inhibitor (**Figure 2**).

Median second-line progression-free survival (66% events) was 5.6 months (95%-CI 3.8 - 6.9 months) (**Figure 3**).

Abbrevations:

CCI	Charlson Comorbidity Index
ECOG	Eastern Cooperative Oncology Group
Max	Maximum
Min	Minimum
PFS	progression-free survival
StD	standard deviation

CONCLUSION

Our data show that at least a quarter of patients with hormone-receptor positive, HER2-negative advanced breast cancer in the German OPAL registry did not benefit from CDK4/6-first-line treatment but experienced progression or death within one year of start of treatment. These patients had more often visceral metastases, e.g., to the lung, compared to patients with later progression. Most patients received chemotherapy as second line treatment after early progression on CDK4/6-inhibitors, but regardless of subsequent therapy, prognosis of this subgroup remained poor. Our data emphasize the clinical need to identify prognostic markers for these patients and to find better treatment options to improve prognosis. In addition, NGS analytics are already in preparation.

Table 1

	Progression/Death < 1 year		No progression/Death < 1 year	
	N	%	N	%
Number of patients	170	100.0	350	100.0
	Median	25-75% Quantile	Median	25-75% Quantile
Median age	66.6	56.6 – 75.6	68.2	58.2 – 76.1
	N	%	N	%
ECOG Performance Status				
ECOG 0	58	34.1	136	38.9
ECOG ≥1	91	53.5	161	46.0
Unknown/missing	21	12.4	53	15.1
Comorbidities at inclusion				
At least one relevant comorbidity [a]	134	78.8	279	79.7
Comorbidity according to CCI [b]				
CCI 0	131	77.1	271	77.4
CCI ≥1	39	229	79	22.5
Metastatic breast cancer				
De novo (M1 at diagnosis)	63	37.1	130	37.1
Recurrent (M0 at diagnosis)	99	58.2	200	57.1
Status at diagnosis unknown/MX [c]	8	4.7	19	5.4
Type of metastasis [d]				
Non-visceral only [e]	48	28.2	150	42.9
Visceral only	20	11.8	40	11.4
Visceral and non-visceral	80	47.1	124	35.4
No documentation yet	22	12.9	36	10.3
Location of metastasis [d, f]				
Bone	113	66.6	229	65.4
Liver	36	21.2	78	22.3
Lung	59	34.7	66	18.9
No documentation yet	22	12.9	36	10.3

Table 1: Patient and tumor characteristics at start of first-line
Displayed are patients with hormone-receptor-positive, HER2-negative ABC with/without early progression/death (< 1 year) under CDK4/6-inhibitor.

a At least one comorbidity according to CCI or additional concomitant diseases. b Charlson Comorbidity Index (CCI) according to Quan (Quan et al., 2011). c M-Status at diagnosis not known/not evaluated/not documented. d Metastasis at start of palliative 1st-line therapy (8 weeks before to 4 weeks after start of 1st-line treatment). e Non-visceral: skin, bone and/or lymph node metastasis. f Multiple answers possible.

Figure 2

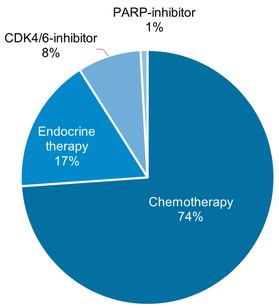

Figure 2 Second-line treatment strategies
Displayed are patients with hormone-receptor-positive, HER2-negative ABC and early progression (< 1 year) under CDK4/6-inhibitor and start of second-line (n=111).

Figure 3

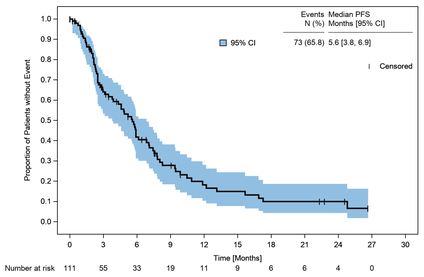

Figure 3 Progression-free survival from start of second-line
Displayed are patients with hormone-receptor-positive, HER2-negative ABC with early progression (<1 year) under CDK4/6-inhibitor in first-line treatment and start of second-line (n=111).