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Correlating time to treatment discontinuation with overall survival: real-world data on outcomes for first-line endocrine therapy + CDK4/6 inhibitor in metastatic breast cancer

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Objective

- To investigate the relationship between first-line DoT and OS in patients with HR+/HER2– mBC

Conclusions

- In this real-world dataset, longer duration of first-line treatment with CDK4/6i combination therapy prior to clinical progression was highly positively correlated with longer OS, suggesting a clinical benefit to extending first-line treatment with CDK4/6i in HR+/HER2– mBC
- Identifying ways to increase the duration of first-line CDK4/6i combination therapy may improve patient outcomes

Poster

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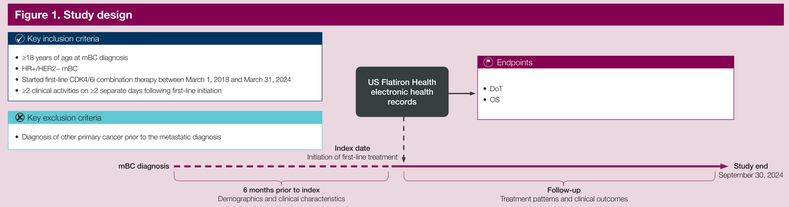
Introduction

- ET (most commonly an AI) + CDK4/6i is the standard-of-care first-line treatment for HR+/HER2– mBC[1]
  - Clinical outcomes worsen following progression to next-line therapy[2,3]
  - This may be due to several factors, including the development of treatment resistance, worsening symptoms, and limited later-line treatment options
- Understanding the relationship between duration of first-line treatment and subsequent outcomes may be an important factor for clinical decision-making

Methods

- This retrospective, observational cohort study identified adults with HR+/HER2– mBC who started first-line CDK4/6i combination therapy between March 1, 2018 and March 31, 2024 from US Flatiron Health electronic health records (**Figure 1**). Patients were followed until death, last clinical visit or September 30, 2024, whichever occurred first
- Descriptive statistics were used to summarize demographics, baseline characteristics, and treatment patterns
- First-line DoT was defined as the time from first-line initiation to the final administration of first-line therapy (whichever component was administered last) or death, whichever occurred first
- DoT and OS were assessed using Kaplan–Meier methodology
  - The relationship between first-line DoT and OS was assessed using rank correlation and a multivariate, covariate-adjusted, time-dependent Cox regression model

Figure 1. Study design



Results

Baseline characteristics

- A total of 2910 patients were included, with a mean age of 63.2 years
  - Most were White (66.2%) and postmenopausal (71.4%), with ECOG PS 0 or 1 (63.2%), and ER expression >70% (82.0%); 49.0% had *de novo* disease, 46.3% had recurrent disease, and few had liver metastases (16.1%) (**Table 1**)

Table 1. Baseline characteristics

Characteristic, n (%)	Overall (N=2910)
Age, mean ± SD, years	63.2 ± 11.9
Race	
White	1927 (66.2)
Black or African American	321 (11.0)
Asian	73 (2.5)
Other	208 (7.1)
Unknown	381 (13.1)
Insurance type	
Commercial health plan	1528 (52.5)
Medicare	233 (8.0)
Medicaid	95 (3.3)
Other	352 (12.1)
Multiple	242 (8.3)
Unknown	460 (15.8)
Follow-up time, mean ± SD, months	28.7 ± 18.4
ECOG performance score at index	
0	1052 (36.2)
1	786 (27.0)
2+	297 (10.2)
Unknown	775 (26.6)
mBC diagnosis type	
De novo	1426 (49.0)
Recurrent mBC	1346 (46.3)
Unknown	138 (4.7)
Menopausal status at initial BC diagnosis	
Postmenopausal	2,077 (71.4)
Premenopausal	659 (22.6)
Unknown/not applicable	174 (6.0)
ER expression level	
ER low-positive (1–10%)	23 (0.8)
ER-positive (11–70%)	249 (8.6)
ER-positive (>70%)	2387 (82.0)
Other or unknown	251 (8.6)
Metastasis site at baseline	
Bone	2034 (69.9)
Lung	636 (21.9)
Liver	468 (16.1)
Peritoneum	76 (2.6)
Brain	40 (1.4)

Data on type of first-line endocrine therapy was not available.

There was a strong positive correlation between DoT and OS

- With a median (interquartile range) follow-up of 24.8 (14.0–41.0) months, median first-line DoT was 20.6 (95% CI: 19.4–22.0) months (**Figure 2**)
- Median OS was not reached (**Figure 3**)
- There was a positive correlation between DoT and OS (r = 0.74, 95% CI: 0.70–0.78), indicating that patients who remained on first-line treatment for longer durations also tended to have longer overall survival

Figure 2. Time to first-line treatment discontinuation in the overall population

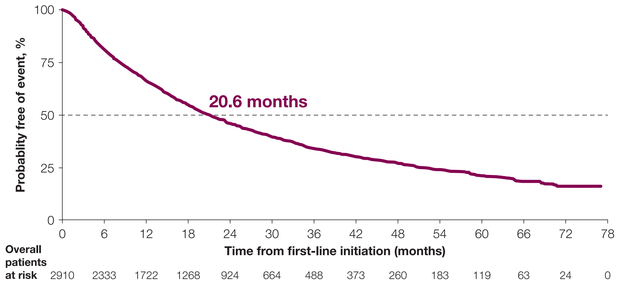


Figure 3. Time from first-line treatment initiation to death in the overall population

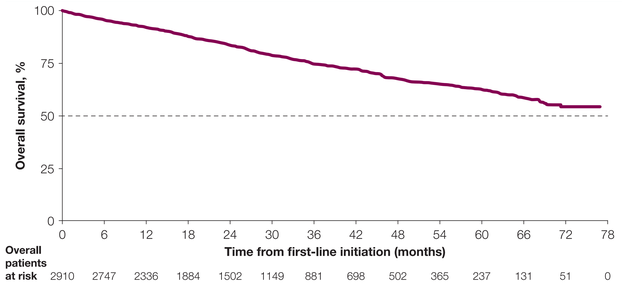
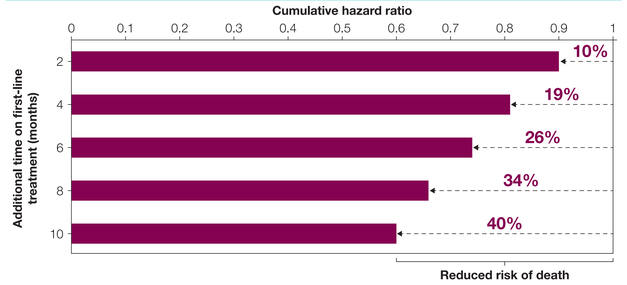


Figure 4. Reduced risk of death with each additional month on first-line treatment



Each additional month on first-line treatment lowered the risk of death by ~5%

- For each additional month on first-line treatment, the adjusted hazard ratio for OS was 0.95 (95% CI: 0.94–0.96; p<0.001)
  - In real-world terms, this means that an additional 2, 4, 6, 8, and 10 months on first-line treatment would result in cumulative hazard ratios (calculated as 0.95^number of months) of 0.90, 0.81, 0.74, 0.66, and 0.60, respectively, and so a 10%, 19%, 26%, 34%, and 40% lower risk of death, respectively (**Figure 4**)
  - This cumulative effect suggests that there is a meaningful survival benefit from extended first-line treatment over time
- Lower ECOG PS, *de novo* disease, and ER expression >70% were also associated with better survival outcomes (**Figure 5**)
  - Age, region, menopausal status, and practice type were not associated with survival outcomes

Figure 5. Association between different factors and OS

	Adjusted hazard ratio (95% CI)	p-value
Treatment duration on first-line therapy (per additional month)		
Time on treatment	0.95 (0.94–0.96)	**< 0.001***
Age at index		
50–64 years vs. <50 years	0.96 (0.72–1.28)	0.783
≥65 years vs. <50 years	0.92 (0.66–1.28)	0.619
Race		
Black or African American vs. White	1.34 (1.04–1.71)	**< 0.05***
Asian vs. White	0.77 (0.43–1.37)	0.374
Other vs. White	1.37 (1.03–1.81)	**< 0.05***
Unknown vs. White	1.07 (0.81–1.42)	0.614
Region		
West vs. South	1.09 (0.84–1.41)	0.520
Northwest vs. South	1.03 (0.80–1.34)	0.817
Midwest vs. South	1.21 (0.94–1.54)	0.132
Other or unknown vs. South	1.13 (0.74–1.73)	0.559
Practice setting at index		
Academic vs. community	1.08 (0.69–1.68)	0.744
Unknown vs. community	1.21 (0.72–2.03)	0.469
ECOG performance score at index		
1 vs. 0	1.77 (1.45–2.15)	**< 0.001***
2+ vs. 0	2.23 (1.71–2.89)	**< 0.001***
Unknown vs. 0	1.09 (0.86–1.37)	0.475
mBC diagnosis type		
Recurrent mBC vs. *De novo*	1.34 (1.13–1.59)	**< 0.001***
Unknown vs. *De novo*	0.96 (0.65–1.40)	0.828
Menopausal status at initial BC diagnosis		
Premenopausal vs. postmenopausal	0.8 (0.62–1.03)	0.082
Unknown or not applicable vs. postmenopausal	1.17 (0.84–1.64)	0.347
Metastasis site		
Liver	2.01 (1.67–2.41)	**< 0.001***
ER expression level		
>70% vs. ≤70%	0.7 (0.54–0.90)	**< 0.01***
Other or unknown vs. ≤70%	0.77 (0.54–1.09)	0.142



Abbreviations

AI, aromatase inhibitor; BC, breast cancer; CI, confidence interval; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; DoT, duration of treatment; ECOG PS, Eastern Cooperative Oncology Group performance status; ER, endocrine receptor; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR, hormone receptor; mBC, metastatic breast cancer; OS, overall survival; SD, standard deviation.

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