Poster 28

Treatment Patterns and Clinical Outcomes Following Endocrine Resistance Among HER2-low Metastatic Breast Cancer Patients – Retrospective Observational Study

Sandhya Mehta,[1] Kristin M. Zimmerman Savill,[2] Peng Wang,[1] Prathamesh Pathak,[2] Clara Lam,[3] Jackie Kwong,[1] Bruce Feinberg[2]

[1] Daiichi Sankyo, Inc., [2] Cardinal Health Specialty Solution, [3] AstraZeneca.

Objective

- This study aimed to describe subsequent chemotherapy treatment patterns and clinical outcomes following endocrine resistance among patients with HR+/HER2-low (IHC 3+, IHC 2+/ISH+) mBC treated primarily in US community oncology practices

Conclusions

- In this retrospective chart review study, most patients with HR+/HER2-low mBC switched to CT after receiving 2 lines of ET-based regimens with median PFS shorter than nine months
- Results from this preliminary chart review highlight the need for more effective therapeutic alternatives to CT after development of ET resistance
- Further research using larger sample sizes and more robust clinical data is warranted to confirm this study's findings

Plain language summary

Why did we perform this research?

Generally, patients diagnosed with HR+/HER2-low mBC are initially treated with endocrine therapy (ET) with or without a CDK 4/6 inhibitor; however, many of these patients experience disease progression and subsequently receives CT.[1,2] To understand how patients with HR+/HER2-low mBC are treated after progressing on ET, we looked at the order of treatments received and the associated outcomes in patients treated in US community oncology practices.

How did we perform this research?

Oncologists within Cardinal Health OPEN Network provided information from the medical charts of adults with HR+/HER2-low mBC treated with chemotherapy and at least two different systemic therapies. The first therapy was started between February 19, 2016, and December 31, 2018. Data were analyzed for patients who received CT after their disease progressed on ET.

What were the findings of this research and what are the implications?

Most patients received CT after receiving 2 different ET-based treatments. However, responses to CT were short, with median real-world disease progression reported as approximately 8 months. These findings underscore the need for more effective therapeutic alternatives to CT administered to patients with HR+/HER2-low mBC after disease progression on ET.

Acknowledgements

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References

1. Cardoso F, et al. 4th ESO-ESMO International Consensus Guidelines for Advanced Breast Cancer (ABC 4). Ann Oncol. 2018;29(8):1634-57.
2. Hartkopf A, et al. Endocrine-resistant breast cancer: Mechanisms and treatment. Breast Care 2020;15:347–354.

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Corresponding author email address: samehta@dsi.com
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Introduction

- ET with or without a CDK 4/6 inhibitor is the preferred early treatment for HR+/HER2-low mBC; however, endocrine resistance frequently occurs, and many patients progress on an ET-based regimen and subsequently are treated with CT[1-2]
- This study examined chemotherapy treatment patterns and outcomes of patients with HR+/HER2-low mBC in US community oncology practices after developing endocrine resistance

Results and Interpretation

- A total of 173 patients with HR+/HER2-low mBC treated with an ET-based regimen in 1L were identified, of which 150 subsequently received CT after developing ET resistance (Figure 1)
- Among the 150 patients with ET resistance
  - Most (70.7%) received CT after receiving 2 lines of ET (Table 1)
  - 57.3% were White and 32.7% were Black/African American (Table 2)
  - The median duration of therapy with the prior ET-based regimen was about 30 months
  - Most patients had bone metastases (74%) and an ECOG-PS of 1 (52.0%) or 2 or higher (36.0%) prior to initiating CT
- The characteristics of patients who switched to CT after 1L ET were generally similar to those who switched to CT after 2L+ ET, except those who switched after 1L had a higher proportion of brain metastases (11.4% vs. 1.7%) and a lower proportion of bone metastases (48.6% vs. 81.7%)
- The most commonly administered 1L ET was palbociclib + letrozole (46.7%) followed by palbociclib + fulvestrant (14.0%) (Figure 2)
- The most commonly administered 2L ET was fulvestrant alone (46.1%) followed by palbociclib + fulvestrant (12%) and alpelisib + fulvestrant (11%) (Figure 3)
- The most commonly administered CT regimen was capecitabine (following 1L ET: 48.6%, 2L+ ET: 47.0%) followed by paclitaxel (1L ET: 25.7%, 2L ET: 28.7%)
- Median rwPFS on CT was 8.12 months, with slightly shorter median rwPFS among those who switched to CT after 1L ET (7.82 months) vs. 2L+ ET (8.19 months) (Table 3)

Methods

Data Source

- Cardinal Health OPEN; OPEN is a community of over 7000 oncologists, hematologists, and urologists from across the United States
- The OPEN Network is a geographically diverse, EMR/Group Purchasing Organization, agnostic and inclusive of multiple settings of community oncology care

Study Design

Retrospective chart review

Study Period

- Study index time was defined as initiation of 1L systemic therapy for HER2-low mBC between February 19, 2016, and December 31, 2018
- The follow-up period for outcomes assessment was variable based on index date and last date of follow-up

Inclusion Criteria

Physicians submitted data from medical charts of patients who met the following criteria:

- Age ≥18 years
- HR+ status and HER2 status of IHC1+ or IHC2+/ISH- [HER2-low]
- Received chemotherapy in the mBC setting and received ≥ 2 systemic LOT for mBC
- First-line systemic therapy for mBC initiated between February 19, 2016, and December 31, 2018

Statistical Analysis

Performed among patients who switched to CT after their last observed ET-based regimen (operationally defined as endocrine resistance)

Descriptive analysis of patient characteristics and treatment utilized overall and by line in which patients received last ET – switched to CT after (1) 1L ET, (2) 2L+ ET

Statistical Analysis (Con't)

Kaplan-Meier estimate of

- rwPFS: Time from initiation of therapy to first reported disease progression or death. Patients who DC treatment for a reason other than disease progression or death were censored at DC date and patients still on treatment at the time of data collection were censored at date of last encounter
- TTD: Time from initiation to DC of a LOT, date of death, or last encounter, whichever came first
- rwTTR: Time from initiation of a LOT to first instance of CR or PR within a given LOT or between DC of that LOT and initiation of a subsequent LOT, as reported by the managing physician/recorded in the patient's medical record; rwTTR was only reported for those patients with a documented response outcome

Table 1. No. of Prior Lines of Endocrine Therapy within Metastatic Setting

Prior lines of ET	No. of Patients (%)		
	Total N=150	≥1 prior CDK 4/6 n=131	No prior CDK 4/6 n=19
1	**35 (23.3)**	29 (82.9)	6 (17.1)
2	**106 (70.7)**	102 (88.7)	13 (11.3)
3	8 (5.3)		
4	1 (0.7)		

Table 3. Subsequent Chemotherapy Outcomes

Outcome, median months (95% CI)[a]	Total N=150	Switched to CT after	
		1L ET, n=35	2L+ ET, n=115
rwPFS	8.12 (7.36-9.24)	7.82 (7.07-9.53)	8.19 (6.97-9.99)
TTD	7.82 (7.07-8.61)	7.82 (6.38-9.01)	8.19 (6.87-9.70)
rwTTR	4.96 (4.24-5.72)	4.87 (3.22-6.51)	5.10 (3.91-5.92)
Follow-up time, median months (IQR)[b]	7.4 (10.4)	16.40 (8.90)	5.07 (6.57)

[a] Median for clinical outcomes was from KM analyses; median for follow-up time is the arithmetic median.

Table 2. Patient Characteristics

		All Patients N=150	Switched to CT after 1L ET n=35	Switched to CT after 2L+ ET n=115	*P*-value[a]
Age, years, mean (SD)	At mBC diagnosis	60 (10)	57 (11)	62 (10)	0.0059
Race, no. (%)	White	86 (57.3%)	21 (60.0%)	65 (56.5%)	0.9804
	Black/African American	49 (32.7%)	11 (31.4%)	38 (33.0%)	
	Asian	12 (8.0%)	3 (8.6%)	9 (7.8%)	
	Other/unknown	3 (2.0%)	-	3 (2.0%)	
Region, no. (%)	Northeast	29 (19.3%)	9 (25.7%)	20 (17.4%)	0.0211
	Midwest	29 (19.3%)	12 (34.3%)	17 (14.8%)	
	South	63 (42.0%)	9 (25.7%)	54 (47.0%)	
	West	29 (19.3%)	5 (14.3%)	24 (20.9%)	
Sites of metastasis, no. (%)	Brain	6 (4.0%)	4 (11.4%)	2 (1.7%)	0.0267
	Skin/soft tissue	13 (8.7%)	0	13 (11.3%)	0.0393
	Bone	111 (74.0%)	17 (48.6%)	94 (81.7%)	<0.0001
Tx duration of prior ET-based regimen, months, median (IQR)	All prior ET	30.63 (20.63-37.70)	17.90 (10.47-23.60)	33.50 (25.27-40.20)	<0.0001
	1L ET	-	17.90 (10.47-23.60)	19.97 (14.3-26.07)	
	2L ET	-	-	9.17 (6.8-14.6)	
ECOG-PS prior to CT initiation, no. (%)	0	18 (12.0%)	8 (22.9%)	10 (8.7%)	0.0542
	1	78 (52.0%)	18 (51.4%)	60 (52.2%)	
	2+	54 (36.0%)	9 (25.7%)	45 (39.1%)	

[a] *P*-value is for comparison between group of patients who switched to CT after 1L ET vs. 2L+ ET.

Figure 1. Patient Attrition

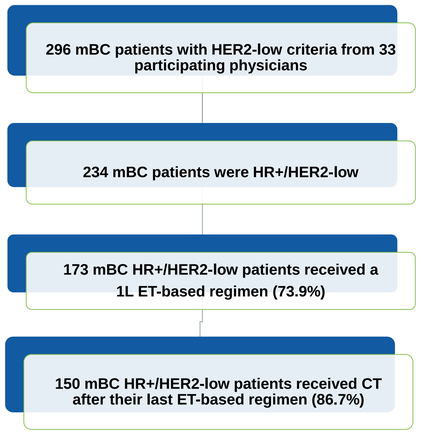


Figure 2. Utilization of Prior ET-Based Regimens

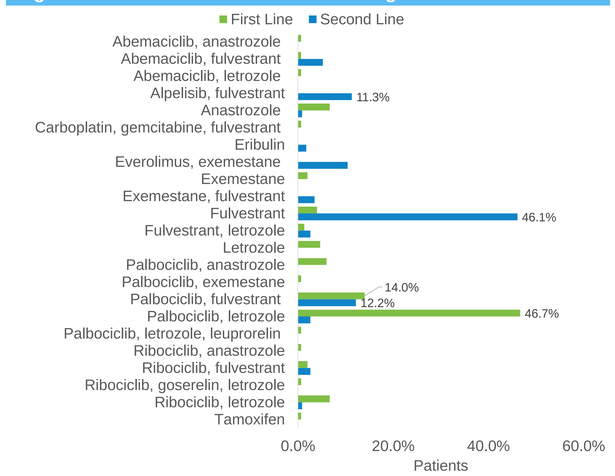
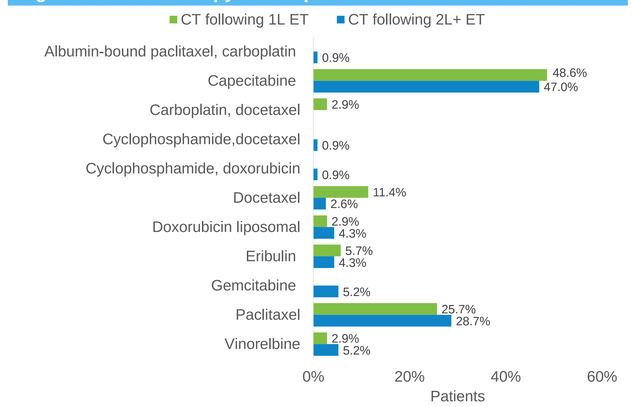


Figure 3. Chemotherapy Subsequent to Endocrine Resistance



Abbreviations

1L, first line; 2L+, second or later line; CDK, cyclin-dependent kinase; CR, complete response; CT, chemotherapy; DC, discontinuation; ECOG-PS, Eastern Cooperative Oncology Group Performance Status; EMR, electronic medical record; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; HR+, hormone-receptor positive; IHC, immunohistochemistry; ISH, in situ hybridization; KM, Kaplan-Meier; LOT, line of therapy; mBC, metastatic breast cancer; No., number; PR, partial response; rwPFS, real-world progression-free survival; rwTTR, real-world time to treatment response; TTD, time to treatment discontinuation; Tx, treatment; US, United States