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Real-world Treatment Patterns of Capivasertib in Metastatic Breast Cancer in the US

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Objective

- To assess patient characteristics, treatment patterns, and clinical outcomes associated with capivasertib in combination with fulvestrant in US patients with hormone receptor–positive, human epidermal growth factor receptor 2-negative (HR+/HER2−) metastatic breast cancer (MBC) in routine clinical practice.

Conclusions

- Capivasertib plus fulvestrant treatment shows real-world effectiveness in routine U.S. practice, based on a large database analysis that includes patients with prior fulvestrant exposure before initiating the combination.
- Clinical outcomes in 2L and 3L closely match those from the pivotal CAPItello-291 trial,[1,2] which supported FDA approval of capivasertib + fulvestrant.
- Numerically improved outcomes were observed in patients who received capivasertib in earlier versus later lines of therapy.
- Further analyses are needed to assess clinical outcomes with longer follow-up time.

Plain language summary

Why did we perform this research?
Capivasertib, used together with fulvestrant, was approved to treat breast cancer when patients' initial treatment stops working for HR+/HER2- metastatic breast cancer, where one or more abnormal *PIK3CA, AKT1*, or *PTEN* genes are in the tumor. This study was conducted to better understand how this treatment regimen is used in the real world, which patients receive it, and what their treatment outcomes look like.

How did we perform this research?
We used data from a large US electronic health record database (Flatiron). Adult patients with metastatic breast cancer who received capivasertib between November 16, 2023, and July 31, 2024, were included in the study. Information on the demographic and clinical characteristics, previous treatments, and how long patients were treated with capivasertib was obtained.

What were the findings of this research?
Of 412 patients who received capivasertib, the majority (387 patients; 93.9%) also received fulvestrant. Capivasertib was commonly used as a second- or third-line treatment (56.1%). The average time before stopping treatment (time to discontinuation) or starting a new therapy (time to next treatment) was around 7 months for patients treated in the second or third line.

What are the implications of this research?
This study provides the first real-world evidence on how capivasertib is used and performs in US clinical practice. Findings observed in routine care are consistent with those from the CAPItello-291 trial[1], which supported the FDA's approval of capivasertib and fulvestrant.

Where can I access more information?
A plain language summary of previous results from the CAPItello-291 study is available. Turner NC, et al. Future Oncology 2024

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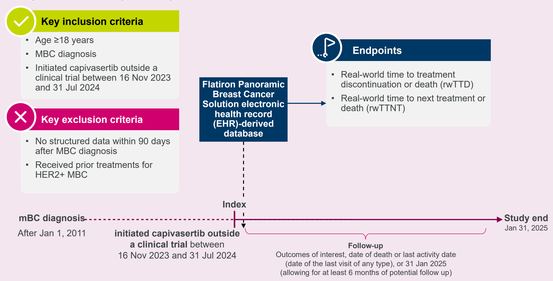
Introduction

- HR+/HER2− advanced breast cancer (aBC) represents the majority of aBC diagnoses.
- Multiple treatments are available for HR+/HER2– aBC after progression of CDK4/6i plus endocrine therapy.
- Capivasertib is an oral, first-in-class AKT inhibitor that targets all three AKT isoforms within the *PI3K/AKT* pathway and expands the set of actionable biomarkers to include *PIK3CA* mutations as well as *AKT1* and *PTEN* alterations.
- In patients with HR+/HER2− aBC who have ≥1 *PIK3CA*, *AKT1*, or *PTEN* tumor alterations, capivasertib is approved in combination with fulvestrant for those whose disease has relapsed or progressed despite at least one endocrine therapy-based treatment.

Methods

- Retrospective cohort study using data from the nationwide Flatiron Panoramic Breast Cancer Solution electronic health record (EHR)-derived database.
- This database contains longitudinal, patient-level, real-world EHR data from patients receiving care at academic and community cancer centers across the US. It includes patient records from over 280 oncology practices at 800+ unique sites of care. Approximately 75% of Flatiron Health data come from community cancer centers, and 25% come from academic medical centers.
- Index date was the date of initiation of capivasertib.
- Summary statistics were used to describe patient characteristics at baseline and treatment patterns.
- Real-world time to treatment discontinuation or death (rwTTD) and real-world time to next treatment or death (rwTTNT) were assessed from the index date and estimated using Kaplan-Meier (KM) methods. Data for patients without the event were censored at the last activity date.
- The line of therapy (LOT) was defined using an algorithm that incorporated prior treatments. The LOT start date was the date of treatment initiation, and the end date was the date of discontinuation of the last treatment within the LOT.

Figure 1. Study design

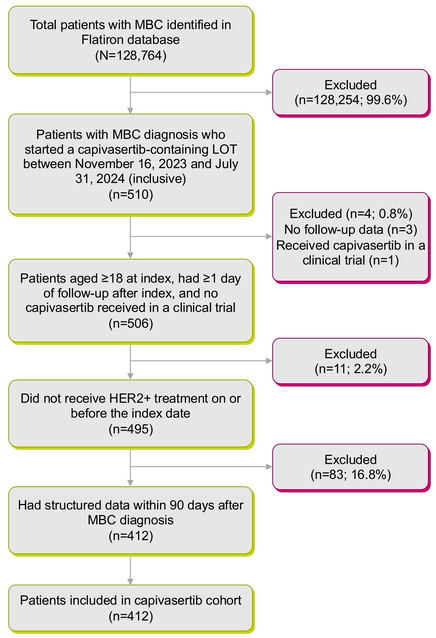


Results and interpretation

Patient characteristics

- Of 510 patients with a diagnosis of MBC who received capivasertib, 412 patients met all selection criteria (**Figure 2**).
- Median age was 67 years; the majority were female (98.8%), White (71.6%), and from community practice settings (83.0%).
- Capivasertib was prescribed as:
  - Capivasertib with fulvestrant: 387 patients (93.9%)
  - Capivasertib monotherapy: 20 patients (4.9%)
  - Capivasertib combined with other medications but without fulvestrant: 5 patients (1.2%)
- Baseline characteristics were similar in patients who received capivasertib with or without fulvestrant (**Table 1**).
- In patients who received capivasertib with fulvestrant, alterations were documented in 91.0% of patients: *PIK3CA*, 76.2%; *PTEN*, 13.7%; and *AKT1*, 9.6%. 35 patients (9.0%) had no evidence of a positive test result for *PIK3CA*, *AKT1*, or *PTEN*.

Figure 2. Patient attrition



Note: Percentage of patients excluded was calculated from the original N.

Table 1. Demographics and clinical characteristics of patients at baseline

Characteristic	Capivasertib + Fulvestrant (N=387)
Age (years) at index date	
Mean (SD)	66.5 (11.2)
Median (IQR)	67 (60 – 75)
Sex	
Male	5 (1.3%)
Female	382 (98.7%)
Race	
White	280 (72.4%)
Black or African American	28 (7.2%)
Asian	8 (2.1%)
Other	41 (10.6%)
Missing/unknown	30 (7.8%)
Practice type	
Academic	65 (16.8%)
Community	322 (83.2%)
Sites of metastases at any time before or on the index date	
Bone	355 (91.7%)
Liver	170 (43.9%)
Lung	111 (28.7%)
Brain	25 (6.5%)
Other	28 (7.2%)
Unknown	7 (1.8%)
Biomarker alteration status with a positive result before or on the index date*	
PIK3CA	295 (76.2%)
AKT1	37 (9.6%)
PTEN	53 (13.7%)
≥1 *PIK3CA, AKT1,* or *PTEN*	352 (91.0%)
ESR1 and ≥1 *PIK3CA, AKT1* or *PTEN*	101 (26.1%)

*Note: Data on sample type (tissue or liquid biopsy) are not available.

Treatment patterns

- Among 387 patients treated with capivasertib and fulvestrant:
  - Over half received capivasertib in the second line (2L) (29.7%) or third line (3L) (26.4%) (**Figure 3**).
  - Patients had a median of two prior LOTs. **Table 2** shows the types of treatments received before the index line of capivasertib and fulvestrant. 258 patients (66.7%) had received fulvestrant in one or more prior lines.
  - At the time of analysis, 180 patients (46.5%) had a subsequent LOT after capivasertib and fulvestrant: most patients received chemotherapy (44.4%) followed by hormone based-therapy (31.7%).

Figure 3. Capivasertib LOT in patients treated with capivasertib and fulvestrant

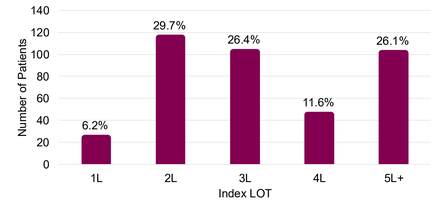


Table 2. Most common treatments in prior and immediate subsequent LOTs in patients treated with capivasertib and fulvestrant

Treatment	Prior treatments irrespective of LOT (n=387)	Immediate subsequent treatments (n=180)
Hormone therapy	356 (92.0%)	57 (31.7%)
CDK4/6 inhibitors	338 (87.3%)	8 (4.4%)
Fulvestrant	258 (66.7%)	30 (16.7%)
Chemotherapy	125 (32.3%)	80 (44.4%)
Alpelisib	84 (21.7%)	8 (4.4%)
Antibody-drug conjugate	55 (14.2%)	50 (27.8%)
Elacestrant	28 (7.2%)	18 (10.0%)

Clinical outcomes

- The median follow-up time was 7.9 months.
- 2L and 3L median rwTTNT was 7.1 and 6.9 months, respectively (**Table 3** and **Figure 4a**).
- 2L and 3L median rwTTD was 6.9 and 6.6 months, respectively (**Table 3** and **Figure 4b**).
- Time to each of these outcomes appeared to decline with increasing LOT of capivasertib initiation.

Table 3. rwTTN and rwTTD by LOT among patients treated with capivasertib and fulvestrant

Capivasertib + fulvestrant (n=387)	rwTTNT[a] Median (95% CI), months	rwTTD[a] Median (95% CI), months
1L (n=24)	10.0 (6.5 – NE)	9.5 (5.6 – NE)
2L (n=115)	7.1 (5.8 – NE)	6.9 (5.3 – NE)
3L (n=102)	6.9 (6.1 – 7.8)	6.6 (5.2 – 7.1)
4L (n=45)	6.2 (4.8 – 9.9)	5.5 (4.3 – 7.4)
5L+ (n=101)	5.0 (3.9 – 6.7)	4.6 (3.5 – 5.9)

*The sensitivity analysis showed similar mTTNT and mTTD for patients who received capivasertib + fulvestrant only compared with those who had a record of receiving capivasertib + fulvestrant (with or without other treatment)

Figure 4a. KM analysis for rwTTNT of patients treated with capivasertib and fulvestrant by LOT

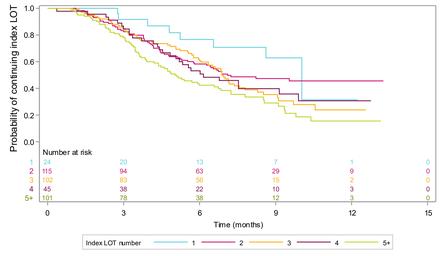
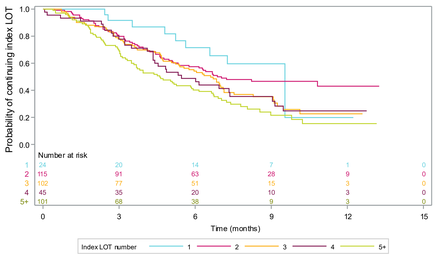


Figure 4b. KM Analysis for rwTTD of Patients Treated with Capivasertib and Fulvestrant by LOT



Limitations

- A small number of patients (9%) who received capivasertib had no documented positive test result for *PIK3CA, AKT1*, or *PTEN* alterations, which may be due to incomplete documentation.
- Some patients had chart evidence of receiving capivasertib monotherapy or capivasertib with another endocrine therapy, but these could be due to limitations in the data used to define LOT.
- rwTTNT and rwTTD were used as proxies for progression; while they may not precisely capture true progression, both are well-established and commonly used endpoints in real-world studies.[3]

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Reference: 1. Turner NC, et al. *N Engl J Med*. 2023;388(22):2058-2070; **2.** Rugo HS, et al. *Ann Oncol*. 2025;36:S422-S3. **3.** Blumenthal GM, et al. *Ann Oncol*. 2019;30(5):830-838.

Abbreviations: 1L = first line; 2L = second line; 3L = third line; 4L = fourth line; 5L = fifth line; aBC = advanced breast cancer; CDK = cyclin-dependent kinase; HR+/HER2− = hormone receptor-positive/human epidermal growth factor receptor 2-negative; IQR = interquartile range; KM = Kaplan-Meier; LOT = line of therapy; MBC = metastatic breast cancer; PI3K = phosphoinositide 3-kinase; rw = real-world; TTD = time to treatment discontinuation; TTNT = time to next treatment; SD = standard deviation.