Poster presented at ISPOR Europe 2023, 12–15 November 2023, Copenhagen, Denmark by Ula Nur.
Corresponding author's email address: ula.nur@astrazeneca.com

Acceptance code: PCR75

# Real-world evidence of outcomes with fulvestrant monotherapy after progression on CDK4/6 inhibitor + aromatase inhibitor in hormone receptor-positive/human epidermal growth factor receptor 2-negative metastatic breast cancer

Ula Nur[1], Gaia Schiavon[1], Lynda Grinsted[1], Sajan Khosla[1]

[1]AstraZeneca, Cambridge, UK

## Objective

- To determine real-world outcomes with fulvestrant monotherapy in patients with HR-positive/HER2-negative mBC whose disease progressed despite treatment with prior AI plus CDK4/6 inhibitor

## Conclusions

- Patients with HR-positive/HER2-negative mBC whose disease progressed on prior AI plus CDK4/6 inhibitor have poor real-world outcomes when treated with fulvestrant monotherapy, consistent with recent clinical trial findings
- Median real-world PFS was slightly longer than that reported in patients enrolled in clinical trials, possibly due to differences in scanning frequencies and patient characteristics
- Notably, the real-world patient population reported here included a higher proportion of patients with *de novo* metastatic disease and a relatively lower proportion of patients with liver metastases than typically included in recent clinical trial populations

## Plain language summary

### Why did we perform this research?

- CDK4/6 inhibitors are drugs that block the activity of proteins called CDK4 and 6, reducing the growth of cancer cells
- Aromatase inhibitors are a type of hormone therapy that blocks estrogen receptors on cancer cells or blocks tissue estrogen production, reducing their growth and spread
- These treatments are often given together to people with breast cancer that has spread from its original site (metastatic) and have a type of breast cancer where tumour cells have hormone receptors (hormone receptor-positive) but do not have a protein called HER2 (HER2-negative)
- Fulvestrant is a drug that blocks estrogen receptors on cancer cells, reducing their growth and spread, and is often given to people who are no longer responding to treatment with CDK4/6 inhibitors and hormone therapy (resistant)
- In our study, we wanted to investigate real-world outcomes in people who received fulvestrant after treatment with CDK4/6 inhibitors and hormone therapy

### How did we perform this research?

- We collected data from a patient medical records database in the US to assess real-world outcomes of patients who received fulvestrant monotherapy as a treatment after CDK4/6 inhibitors and endocrine therapy

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

- Our research showed that people with HR-positive/HER2-negative metastatic breast cancer have poor real-world outcomes when treated with fulvestrant monotherapy after treatment with CDK4/6 inhibitors and endocrine therapy
- Our findings indicate a need for improved treatments in people with this type of breast cancer

Poster

Please scan this quick response (QR) code with your smartphone camera or app to obtain a copy of these materials. Alternatively, please click on the link below

https://bit.ly/3PWdKuz



## Introduction

- First-line CDK4/6 inhibitors combined with endocrine therapy are the standard-of-care for patients with HR-positive/HER2-negative mBC,[1,2] with multiple trials demonstrating improved PFS compared to endocrine monotherapy and, in some cases, improved OS
- There is an unmet need for effective treatments in patients following first-line treatment with CDK4/6 inhibitors, with data indicating that the efficacy of fulvestrant monotherapy is low
  - Median PFS with fulvestrant monotherapy in recent trials in which patients with HR-positive/HER2-negative mBC had received a prior CDK4/6 inhibitor was 1.9 months in the phase 2 VERONICA study,[3] 1.9 months in the phase 3 EMERALD study,[4] and 2.6 months in the phase 3 CAPItello-291 study[5]
- However, there is limited real-world evidence regarding the efficacy of fulvestrant monotherapy after progression on AI plus CDK4/6 inhibitors. Understanding the real-world efficacy of fulvestrant monotherapy post-AI plus CDK4/6 inhibitor could help inform treatment decisions in the HR-positive/HER2-negative mBC setting

## Methods

- We conducted a retrospective cohort study using electronic health record-derived data from the Flatiron Health longitudinal database[6,7] that comprises de-identified, structured, and unstructured patient-level data, curated via technology-enabled abstraction (**Figure 1**). During the study period,the de-identified data originated from approximately 800 unique sites of care, with approximately 20% from academic centres, and 80% from community practices in the United States of America
- Patients with HR-positive/HER2-negative mBC who experienced disease progression on AI plus CDK4/6 inhibitors between 1 January, 2011, and 31 January, 2021 were included in this analysis
- In patients who were initiated on fulvestrant monotherapy, electronic data were collected from the date of fulvestrant initiation (index)
- All patients were followed until the end of the study, lost to follow-up, died, or the occurrence of other outcome-specific events
- Patients were followed up from the index date until their date of death, if available, or other outcome-specific events
- Real-world PFS, OS, TTD and TFST were estimated using Kaplan-Meier methods
- In patients initiated on fulvestrant monotherapy at any time, we also investigated OS by whether disease was *de novo* or recurrent at time of diagnosis of mBC

**Figure 1. A retrospective cohort study of patient data captured in a real-world database**

### Patients

***Inclusion criteria:***

- Diagnosis of HR-positive/HER2-negative mBC
- ≥18 years of age
- Progressed on prior AI plus CDK4/6 inhibitor
- ECOG PS 0/1 within 30 days prior to or 7 days after index, or unknown ECOG PS

***Exclusion criteria:***

- ≥3 lines of endocrine therapy for advanced disease
- ≥2 lines of chemotherapy for advanced disease
- PI3K inhibitor or fulvestrant use before the index date

### Data extracted for analysis

- Demographic and clinical characteristics for patients who were initiated on fulvestrant monotherapy at any time after progression on prior AI plus CDK4/6 inhibitors
- Demographic and clinical characteristics for the subset of patients that was initiated on fulvestrant monotherapy as a next-line therapy after progression on prior AI plus CDK4/6 inhibitors

### Outcomes

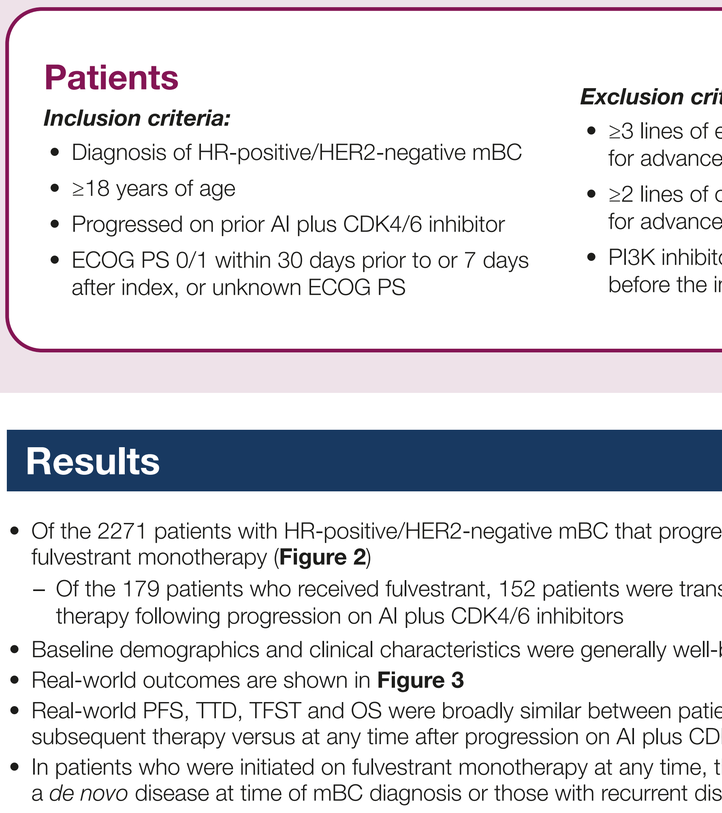
- Real-world PFS[a]
- Real-world OS[b]
- Real-world TFST[c]
- Real-world TTD[d]

[a]The time from initiation of fulvestrant after progression on AI plus CDK4/6 inhibitors for metastatic disease, until progression event, death, or censored at the last documented visit date. [b]Time from initiation of fulvestrant after progression on AI plus CDK4/6 inhibitors for metastatic disease until death or censored at the last documented visit date. [c]Time from initiation of fulvestrant after progression on AI plus CDK4/6 inhibitors for metastatic disease to start of first subsequent line of therapy or date of death. For patients with no indication of a further line of therapy or death, TFST was censored at the last documented visit date. [d]Time from initiation of fulvestrant after progression on AI plus CDK4/6 inhibitors for metastatic disease until the last drug administration date of fulvestrant or date of death. Patients who were alive and had not experienced treatment discontinuation were censored at the last documented visit date. For all assessments, the last visit was used if it preceded the end date of treatment.

## Results

- Of the 2271 patients with HR-positive/HER2-negative mBC that progressed after AI plus CDK4/6 inhibitors, 179 received fulvestrant monotherapy (**Figure 2**)
  - Of the 179 patients who received fulvestrant, 152 patients were transitioned immediately to fulvestrant monotherapy as next-line therapy following progression on AI plus CDK4/6 inhibitors
- Baseline demographics and clinical characteristics were generally well-balanced between groups (**Table 1**)
- Real-world outcomes are shown in **Figure 3**
- Real-world PFS, TTD, TFST and OS were broadly similar between patients receiving fulvestrant monotherapy as immediate subsequent therapy versus at any time after progression on AI plus CDK4/6 inhibitor
- In patients who were initiated on fulvestrant monotherapy at any time, there were no significant differences in OS between those with a *de novo* disease at time of mBC diagnosis or those with recurrent disease at time of mBC diagnosis (**Figure 4**)

**Figure 2: Patient flow diagram**

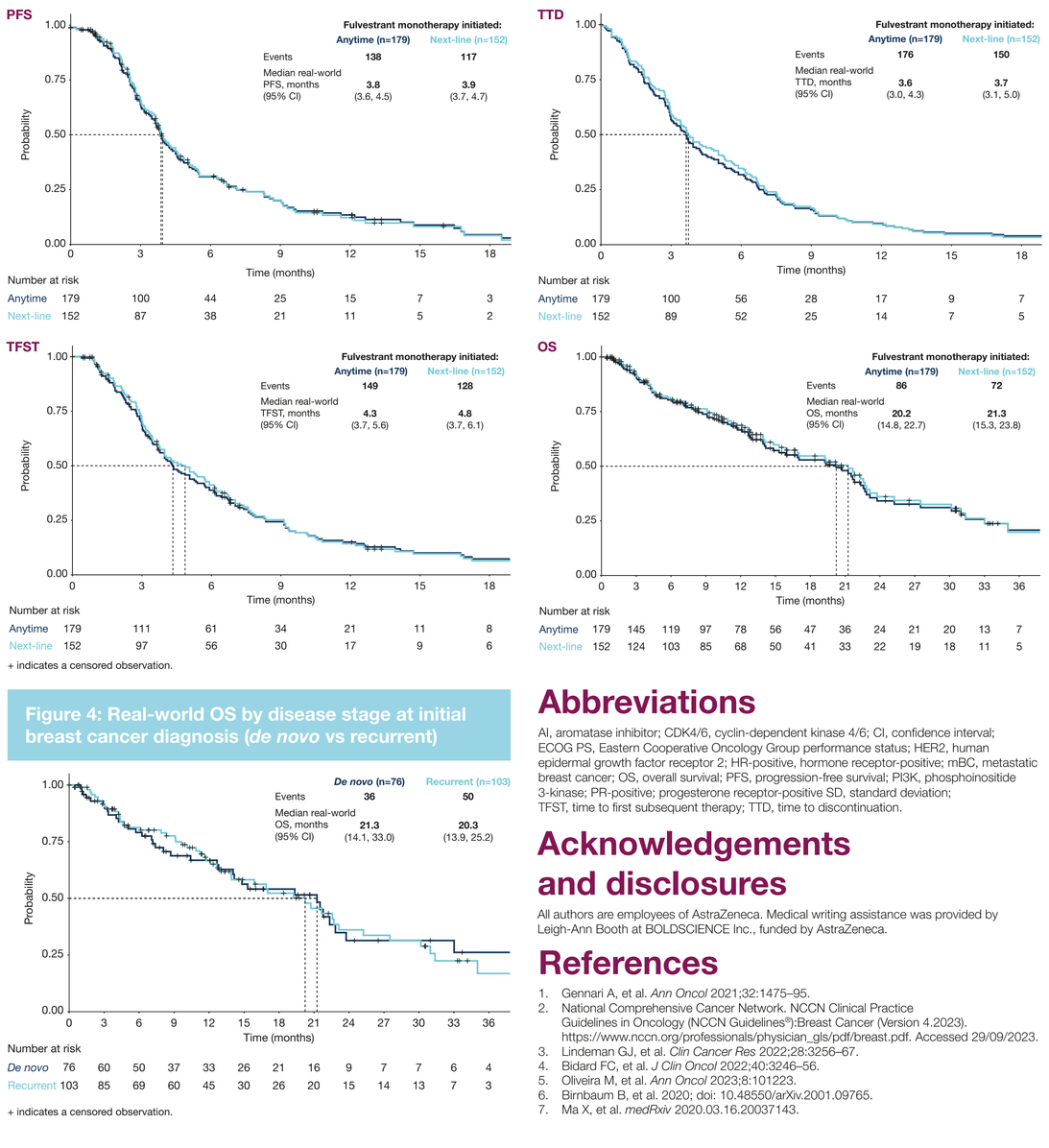



*Within 30 days prior to or up to 7 days after the index date, or unknown ECOG PS.

**Table 1: Baseline demographics and clinical characteristics**

| | | Fulvestrant monotherapy initiated anytime after AI + CDK4/6 inhibitor (n=179) | Fulvestrant monotherapy initiated as next-line therapy immediately after AI + CDK4/6 inhibitor (n=152) |
|---|---|---|---|
| **Age at initial breast cancer diagnosis, years** | Mean (SD) | 58.6 (12.1) | 58.6 (12.0) |
| | Median (range) | 58 (34–82) | 58 (34–82) |
| **Age at time of diagnosis of metastatic disease, years** | Mean (SD) | 63.6 (11.2) | 63.3 (11.3) |
| | Median (range) | 63 (35–82) | 63 (35–82) |
| **Female, n (%)** | | 177 (98.9) | 150 (98.7) |
| **Race, n (%)** | White | 132 (73.7) | 116 (76.3) |
| | Black or African American | 11 (6.1) | 10 (6.6) |
| | Other | 19 (10.6) | 13 (8.6) |
| | Unknown | 17 (9.5) | 13 (8.6) |
| **Practice type, n (%)** | Community | 30 (16.8) | 25 (16.5) |
| | Academic | 149 (83.2) | 127 (83.6) |
| **Stage at diagnosis, n (%)** | I | 22 (12.3) | 20 (13.2) |
| | II | 49 (27.4) | 42 (27.6) |
| | III | 22 (12.3) | 18 (11.8) |
| | IV | 76 (42.5) | 66 (43.4) |
| | Unknown | 10 (5.6) | 6 (4.0) |
| **Disease status, n (%)** | *De novo* | 76 (42.5) | 66 (43.4) |
| | Recurrent | 103 (57.5) | 86 (56.6) |
| **Liver metastases at baseline, n (%)** | | 19 (10.6) | 13 (8.6) |
| **Tumor subtype at baseline, n (%)** | ER-positive/ HER2-negative | 178 (99.4) | 151 (99.3) |
| | PR-positive/ HER2-negative | 172 (96.1) | 145 (95.4) |
| **ECOG PS, n (%)** | 0 | 45 (31.9) | 40 (34.8) |
| | 1 | 82 (58.2) | 67 (58.3) |
| | 2 | 12 (8.5) | 7 (6.1) |
| | 3 | 2 (1.4) | 1 (0.9) |

**Figure 3: Real-world outcomes in patients who received fulvestrant monotherapy after disease progression on AI plus CDK4/6 inhibitor**




+ indicates a censored observation.

**Figure 4: Real-world OS by disease stage at initial breast cancer diagnosis (*de novo* vs recurrent)**




+ indicates a censored observation.

## Abbreviations

AI, aromatase inhibitor; CDK4/6, cyclin-dependent kinase 4/6; CI, confidence interval; ECOG PS, Eastern Cooperative Oncology Group performance status; HER2, human epidermal growth factor receptor 2; HR-positive, hormone receptor-positive; mBC, metastatic breast cancer; OS, overall survival; PFS, progression-free survival; PI3K, phosphoinositide 3-kinase; PR-positive; progesterone receptor-positive SD, standard deviation; TFST, time to first subsequent therapy; TTD, time to discontinuation.

## Acknowledgements and disclosures

All authors are employees of AstraZeneca. Medical writing assistance was provided by Leigh-Ann Booth at BOLDSCIENCE Inc., funded by AstraZeneca.

## References

1. Gennari A, et al. *Ann Oncol* 2021;32:1475–95.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®):Breast Cancer (Version 4.2023). https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed 29/09/2023.
3. Lindeman GJ, et al. *Clin Cancer Res* 2022;28:3256–67.
4. Bidard FC, et al. *J Clin Oncol* 2022;40:3246–56.
5. Oliveira M, et al. *Ann Oncol* 2023;8:101223.
6. Birnbaum B, et al. 2020; doi: 10.48550/arXiv.2001.09765.
7. Ma X, et al. *medRxiv* 2020.03.16.20037143.