Poster 1055

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Clinical Outcomes With Alpelisib Plus Fulvestrant After Prior Treatment With Fulvestrant in Patients With Advanced Breast Cancer: A Real-World Analysis

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KEY FINDINGS AND CONCLUSIONS

- This analysis of real-world data from initial years of alpelisib access in the US shows clinical benefit of alpelisib + fulvestrant use in patients with HR+/HER2− ABC with *PIK3CA* mutation who have been exposed to prior fulvestrant-containing regimens
  - The rwPFS benefit with alpelisib + fulvestrant following prior fulvestrant exposure in the overall population supports the results seen in the cohort of patients from the Phase II BYLieve trial (NCT03056755) who had prior fulvestrant exposure (cohort C)
  - Numerically longer rwPFS was observed in patients who received alpelisib + fulvestrant on earlier lines
  - Similarly, numerically longer rwPFS and OS were observed in patients who received fulvestrant + CDK4/6i immediately prior to alpelisib + fulvestrant
  - Finally, patients who did not receive any chemotherapy in the metastatic setting prior to alpelisib + fulvestrant treatment were observed to have a numerically longer rwPFS and OS
- These data are aligned with clinical trial data that support targeting the oncogenic driver *PIK3CA* mutation early in the treatment course through the use of alpelisib + fulvestrant immediately following CDK4/6i + ET, which is also the preferred sequence recommended in international guidelines

INTRODUCTION

- The α-selective PI3K inhibitor and degrader alpelisib, in combination with fulvestrant, was approved by the FDA in 2019 and included in the international guidelines for patients with HR+/HER2− ABC with *PIK3CA* mutations following progression on or after ET-based therapy[1]
  - Alpelisib + fulvestrant demonstrated significant PFS benefit compared with fulvestrant alone in these patients, as reported in the Phase III SOLAR-1 trial[2]
- The SOLAR-1 trial excluded patients with prior fulvestrant exposure,[2] and data on alpelisib + fulvestrant use following prior fulvestrant exposure are insufficient
- CDK4/6i + ET, including fulvestrant, is the SOC in the 1L or 2L setting for patients with HR+/HER2− ABC;[3] for those with *PIK3CA* mutations, alpelisib is recommended after progression on CDK4/6is; thus, more data on alpelisib + fulvestrant use are needed for patients previously exposed to fulvestrant
- Here we report treatment patterns and clinical outcomes of real-world use of alpelisib + fulvestrant in patients with HR+/HER2− ABC with *PIK3CA* mutations who have had prior fulvestrant exposure; outcomes based on the line of therapy in which patients received alpelisib + fulvestrant are also reported

METHODS

- This was a noninterventional, retrospective cohort study that used de-identified individual patient data from the ConcertAI Patient360 Breast Cancer data product
- The data were sourced from electronic health records from US oncology centers
- The data included information on the following:
  - Demographics, diagnosis, and biomarkers
  - Treatment patterns, including the line of treatment in which alpelisib + fulvestrant was received, number of prior lines of therapy, prior antineoplastic regimens, time to discontinuation, and subsequent therapy following alpelisib + fulvestrant use
- Key clinical outcomes as defined in the study:
  - rwPFS: First documented progression/death from the start date of the earliest alpelisib + fulvestrant use
  - OS: Date of death (for any reason) from the start date of earliest alpelisib + fulvestrant use
- Patients were indexed at the start date of the earliest alpelisib + fulvestrant use (index treatment) and followed up until death/last confirmed activity date
- Inclusion and exclusion criteria:
  - Adults with HR+/HER2− ABC treated with alpelisib + fulvestrant who received fulvestrant previously as a monotherapy or in combination with other therapies in the metastatic setting were included
  - Patients with a *PIK3CA* negative test result on or prior to the index date were excluded
- Limitations:
  - It should be noted that the quality of information extracted from real-world data depends on the quality of information in the available data source
  - For OS results, there was a short follow-up time and low number of events

RESULTS

Patient Characteristics and Alpelisib Treatment

- A total of 157 patients who received alpelisib + fulvestrant from 2019 to 2021 were included in this analysis
  - Data are from patients treated in community centers (80%) and academic institutions (20%)
  - The median age of the patients was 63 years (Q1-Q3, 57-71 years)
  - The majority of patients (n = 83 [52.9%]) had positive *PIK3CA* test results; the test result was not available for some patients (n = 74 [47.1%])
  - Patients received alpelisib + fulvestrant in the 1L (n = 18 [11.5%]), 2L (n = 28 [17.8%]), 3L (n = 42 [26.8%]), or 4L+ setting (n = 69 [43.9%])
    - For patients who received alpelisib + fulvestrant in 1L, prior fulvestrant exposure was in the same line, without documented progression
    - 77.7% of patients received alpelisib + fulvestrant in the 1L/2L setting in 2021 versus 27.3% in 2020 and 25.4% in 2019
    - Of patients with a documented starting dose, the majority (79.3%) started on 300 mg

Treatment Patterns Prior to Alpelisib + Fulvestrant Use

- Fulvestrant-containing regimens in any prior line included CDK4/6i + fulvestrant (74.5%), fulvestrant monotherapy (33.8%), and non-CDK4/6i + fulvestrant (21.0%; **Table 1**)
  - 28.0% of patients had >1 prior fulvestrant exposure
- Prior treatment in the metastatic setting included chemotherapy (72%) and/or CDK4/6i (97.5%; **Table 1**)

Table 1. Treatment Regimens Prior to Index Treatment

Prior Treatment Patterns	n (%)
Total	**157 (100)**
No. of prior regimens received before index treatment[a]	
1	9 (5.7)
2	20 (12.7)
3	24 (15.3)
4+	104 (66.2)
Prior fulvestrant treatment category[b]	
CDK4/6i + fulvestrant	117 (74.5)
Fulvestrant monotherapy	53 (33.8)
Non-CDK4/6i + fulvestrant	33 (21.0)
Patients with multiple prior exposures to fulvestrant	
CDK4/6i or non-CDK4/6i + fulvestrant / fulvestrant monotherapy	26 (16.6)
CDK4/6i + fulvestrant / fulvestrant monotherapy	23 (14.7)
No. of prior fulvestrant regimens received (categorical)	
1	113 (72.0)
2	38 (24.2)
3	4 (2.6)
4	2 (1.3)
Patients with prior exposure to chemotherapy in the metastatic setting	
Yes	113 (72.0)
No	44 (28.0)
Patients with prior exposure to CDK4/6i in the adjuvant setting	
Yes	7 (4.5)
No	150 (95.5)
Patients with prior exposure to CDK4/6i in the metastatic setting[b]	**153 (100)**
CDK4/6i + fulvestrant	108 (70.6)
CDK4/6i + aromatase inhibitor	68 (44.4)
CDK4/6i monotherapy	32 (20.9)
CDK4/6i + fulvestrant + aromatase inhibitor	16 (10.5)
CDK4/6i + other (including chemotherapy or ET)	7 (4.6)

[a] The ConcertAI line of therapy algorithm derives progression-based lines of therapy. Each line of therapy can contain multiple regimens, with the line advancing only after a progression event. Thus, patients may have received multiple regimens prior to treatment with alpelisib plus fulvestrant.
[b] Patients may have had multiple previous exposures.

Longer rwPFS and OS Were Observed in Patients Treated With Alpelisib + Fulvestrant in Earlier Lines

- The median rwPFS was 5.7 months in the overall population at 8.0 (95% CI, 5.1-9.3) months median follow-up time, with the rwPFS being 11.9 months in 1L, 6.2 months in 2L, 4.0 months in 3L, and 4.8 months in 4L+ patients (**Figure 1**)
- The median OS was 14.2 months in the overall population at 11.3 (95% CI, 9.5-12.6) months median follow-up time, with the OS being 14.6 months in 1L, 12.4 months in 2L, NR in 3L, and 11.0 months in 4L+ patients (**Figure 2**)

Figure 1. rwPFS in the Overall Population (A) and by Line of Therapy (B)

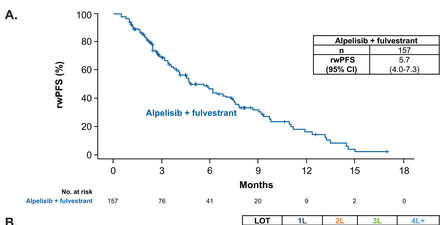
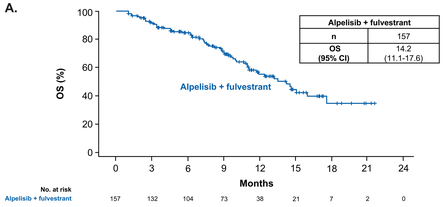


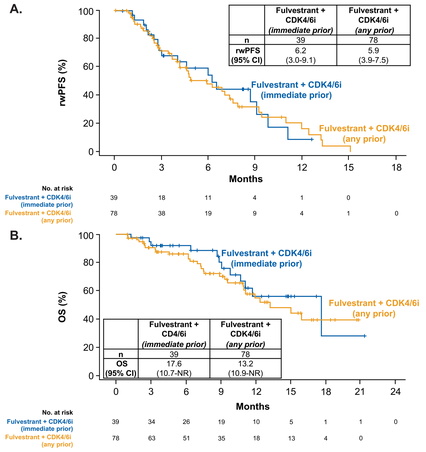
Figure 2. OS in the Overall Population (A) and by Line of Therapy (B)



Longer rwPFS and OS Observed in Patients Who Received Fulvestrant + CDK4/6i as Immediate Prior Line of Therapy

- The median rwPFS and OS were 6.2 and 17.6 months, respectively, in patients with CDK4/6i + fulvestrant as immediate prior therapy (n = 39) compared with 5.9 and 13.2 months in those who received CDK4/6i + fulvestrant not immediately prior to index treatment (n = 78) (**Figure 3**)
- The majority of the patients (n = 31 [79.5%]) exposed to CDK4/6i + fulvestrant as immediate prior therapy received the treatment in the 1L, 2L, or 3L setting

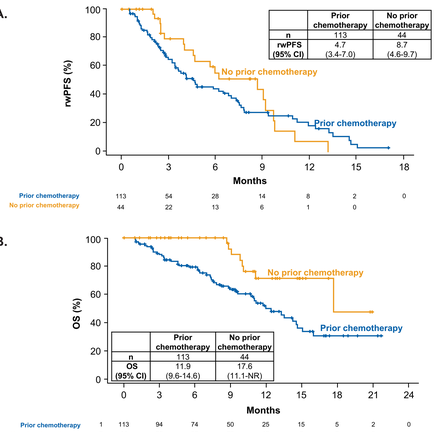
Figure 3. CDK4/6i as Immediate Versus Any Prior Line of Therapy: rwPFS (A) and OS (B)



Longer rwPFS and OS Observed in Patients Who Had No Prior Chemotherapy

- The median rwPFS and OS were 4.7 and 11.9 months, respectively, in patients who received chemotherapy prior to alpelisib + fulvestrant compared with 8.7 and 17.6 months in those who did not receive chemotherapy prior to index treatment (**Figure 4**)

Figure 4. Prior Chemotherapy Versus No Prior Chemotherapy: rwPFS (A) and OS (B)



Median Time to Discontinuation of Alpelisib + Fulvestrant Was 4.7 Months

- At the time of analysis, 107 patients (68.2%) had discontinued alpelisib + fulvestrant; the median time to discontinuation was 4.7 (95% CI, 3.7-6.1) months

Chemotherapy Was the Most Common Subsequent Treatment

- In patients who received a subsequent therapy, chemotherapy alone was the most common (81.5%; **Table 2**)

Table 2. Subsequent Therapy Category Following Index Treatment

Subsequent Therapy	n (%)
All patients	**157 (100)**
Received subsequent therapy	65 (41.4)
Chemotherapy	53 (81.5)
Chemotherapy + aromatase inhibitor	6 (9.2)
CDK4/6i + aromatase inhibitor	1 (1.5)
CDK4/6i monotherapy	1 (1.5)
Other	4 (6.1)
No subsequent therapy	92 (58.6)
Death	40 (43.5)
Censoring	52 (56.5)

[a] The high proportion of patients with no subsequent therapy may be due to either continued treatment with alpelisib + fulvestrant or lack of follow-up, especially for patients who were censored.

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Abbreviations

ABC, advanced breast cancer; CDK4/6i, cyclin-dependent kinase 4/6 inhibitor; ET, endocrine-based therapy; FDA, US Food and Drug Administration; HER2−, human epidermal growth factor receptor 2 negative; HR+, hormone receptor positive; LOT, line of therapy; NCCN, National Comprehensive Cancer Network; NR; not reached; OS, overall survival; PI3K, phosphoinositide 3-kinases; *PIK3CA*, phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit α; PFS, progression free survival; rwPFS, real-world progression free survival; SOC; standard of care; 1L, first line; 2L, second line; 3L, third line; 4L+, fourth line and beyond

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1. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer. 2. André F, et al. *N Engl J Med*. 2019;380:1929-1940. 3. Pernas S, et al. *Ther Adv Med Oncol*. 2018;10:1758835918786451.

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