Alpelisib + Fulvestrant in Patients With Hormone Receptor-Positive (HR+), Human Epidermal Growth Factor Receptor 2-Negative (HER2−), PIK3CA-Mutated Advanced Breast Cancer (ABC) Previously Treated With Cyclin-Dependent Kinase 4/6 Inhibitor (CDK4/6i) + Aromatase Inhibitor (AI): 18-Month Follow-up of BYLieve (NCT03056755)

**INTRODUCTION**

PIK3CA (per RECIST v1.1) or chemotherapy, or ET

**RESULTS**

**Patient Population**

- **Medians**
  - Female, n (%) 127 (100)
  - Median age (range), years 58 (33-83)
  - Disease History
    - Breast (N=127)
    - Other (N=2)
    - Prior treatment with CDK4/6is
      - Yes, n (%) 125 (98.4)
      - No, n (%) 2 (1.6)
    - Prior treatment with AI
      - Yes, n (%) 127 (100)
      - No, n (%) 0
    - Prior treatment with ET
      - Yes, n (%) 0
      - No, n (%) 127 (100)
    - Prior treatment with chemotherapy
      - Yes, n (%) 80 (63.0)
      - No, n (%) 47 (37.0)
    - Prior treatment with hormone therapy
      - Yes, n (%) 127 (100)
      - No, n (%) 0
    - Prior treatment with other therapy
      - Yes, n (%) 0
      - No, n (%) 127 (100)
  - Extent of metastatic disease, n (%) 122 (96.1)
    - Bone 108 (85.0)
    - Soft tissue 1 (0.8)
    - Central nervous system 1 (0.8)
    - Liver 3 (2.4)
    - Brain 3 (2.4)
    - Other 3 (2.4)
    - Not specified 1 (0.8)
  - Lymph node status, n (%) 33 (25.9)
    - Not specified 1 (0.8)
  - Metastatic disease (any site), n (%) 127 (100)
  - Bone 108 (85.0)
  - Soft tissue 1 (0.8)
  - Central nervous system 1 (0.8)
  - Liver 3 (2.4)
  - Brain 3 (2.4)
  - Other 3 (2.4)
  - Not specified 1 (0.8)
  - Disease activity
    - Progressive disease 126 (99.2)
    - Stable 1 (0.8)
  - Disease activity at baseline, n (%) 127 (100)
    - Stable 1 (0.8)
  - Disease activity at follow-up, n (%) 127 (100)
    - Stable 1 (0.8)
    - Progressive disease 126 (99.2)
  - Metastatic disease (any site) at baseline, n (%) 127 (100)
    - Bone 108 (85.0)
    - Soft tissue 1 (0.8)
    - Central nervous system 1 (0.8)
    - Liver 3 (2.4)
    - Brain 3 (2.4)
    - Other 3 (2.4)
    - Not specified 1 (0.8)
  - Metastatic disease (any site) at follow-up, n (%) 127 (100)
    - Bone 108 (85.0)
    - Soft tissue 1 (0.8)
    - Central nervous system 1 (0.8)
    - Liver 3 (2.4)
    - Brain 3 (2.4)
    - Other 3 (2.4)
    - Not specified 1 (0.8)

**Efficacy Outcomes, 18-Month Follow-up**

- **ORR (CR+PR), n (%) [95% CI]** 23 (19.0) [12.4-27.1]
- **PFS2 (time from first dose of study medication to documented progression on next-line therapy or death from any cause), months**
  - Cohort A (N=127)
    - M = 18 (17-18)
    - Median = 5.1 (0-43)
    - 95% CI = 2.9-7.2
  - Cohort B (N=123)
    - M = 18 (17-18)
    - Median = 8.3 (0-11)
    - 95% CI = 6.6-9.9
  - Cohort C (N=112)
    - M = 18 (17-18)
    - Median = 7.0 (0-9)
    - 95% CI = 5.6-8.5
  - Overall survival, months
    - Cohort A: 23 (17-28)
    - Cohort B: 23 (17-28)
    - Cohort C: 23 (17-28)
  - Progression-free survival; Kaplan-Meier estimates.

**Safety Outcomes, 18-Month Follow-up**

- **Number of patients with at least one event** 126 (99.2)
- **Number of patients with at least one grade ≥3 event** 88 (69.3)
- **Number of patients with at least one grade ≥3 AEs**
  - Skin rash/maculopapular 12 (9.4)
  - Hypertension 12 (9.4)
  - Fatigue 18 (14.2)
  - Weight decreased 18 (14.2)
  - Alopecia 17 (13.4)
  - Nausea 59 (46.5)
  - Muscle spasms 14 (11.0)
  - Diarrhea 14 (11.0)
  - Dyspepsia 34 (26.8)
  - Stomatitis 34 (26.8)
  - Pain 38 (29.9)
  - Dysgeusia 3 (2.4)

**CONCLUSIONS**

- The safety profile of alpelisib + fulvestrant was consistent with that in the primary analysis at 6 months of follow-up, with no new safety signals observed after prior treatment with CDK4/6i and AI.
- The median duration of response was 13.8 months (95% CI, 5.5-17.5).
- The best percentage change in tumor reduction is shown in Figure 1.
- The median duration of alpelisib monotherapy was 5.1 months (range, 0-43).
- The median duration of exposure only to alpelisib was 5.1 months (range, 0-43).
- The median duration of treatment with fulvestrant was 12.5 months (range, 0-11).