# Abemaciclib Plus Fulvestrant in Participants With HR+, HER2– Advanced Breast Cancer - A Pooled Analysis of the Endocrine Therapy Naïve (EN) Participants in MONARCH 2



**Jose Luis-Gonzalez Trujillo[1], Mario Escobar Gomez[2], Joo Hyuk Sohn[3], Young Hyuck Im[4], Hwei-Chung Wang[5], Antonio Llombart-Cussac[6], Wei Zhang[7], Nadine Haddad[7], Heather Wasserstrom[7], Gertjan van Hal[7], George W. Sledge Jr.[8]**

[1]Fundacion Rodolfo Padilla AC, Leon Guanajuato, Mexico; [2]Grupo Medico Camino, SC, Mexico City, Mexico; [3]Severane Hospital, Sinchondong, Seodaemun District, South Korea; [4]Samsung Medical Center, Seoul, Korea; [5]China Medical University Hospital, Taichung City, Taiwan; [6]Hospital Arnau Villanova, Valencia, Spain; [7]Eli Lilly and Company, Indianapolis, IN, USA; [8]Stanford University, Stanford, CA, USA

## BACKGROUND

- Abemaciclib, an oral cyclin-dependent kinase 4 & 6 inhibitor, dosed on a continuous schedule, is approved for the treatment of women with hormone receptor positive (HR+), human epidermal growth factor receptor 2 negative (HER2–) advanced breast cancer (ABC), in combination with endocrine therapy (ET).
- In the Phase 3 MONARCH 2 study, abemaciclib plus fulvestrant significantly improved progression-free survival (PFS) and overall survival (OS) compared to fulvestrant alone in women with HR+, HER2– ABC with disease progression on ET.[1, 2]
- Fulvestrant monotherapy is approved for treatment of postmenopausal women with HR+, HER2– ABC who are ET naïve (EN).
  - In FIRST, fulvestrant monotherapy was associated with an unconfirmed objective response rate (ORR) of 36%, improved OS and significantly longer time-to-progression compared to anastrozole.[3, 4]
  - In FALCON, fulvestrant monotherapy was associated with an unconfirmed ORR of 46% and significantly improved PFS compared to anastrozole in EN participants.[5]
- Here we present the ORR from EN participants with measurable disease in MONARCH 2 who were treated with abemaciclib plus fulvestrant

## BASELINE CHARACTERISTICS

**Table 1. Baseline participant characteristics**

| | | Pooled EN Cohort N=110 |
|---|---|---|
| Female, n (%) | | 110 (100.0) |
| Age in years | Median (range) | 54 (31-86) |
| Race, n (%) | Asian<br>White<br>American Indian or Alaskan Native<br>Multiple | 42 (38.2)<br>41 (37.3)<br>26 (23.6)<br>1 (0.9) |
| ECOG PS, n (%) | 0<br>1<br>Missing | 61 (55.5)<br>48 (43.6)<br>1 (0.9) |
| Menopausal status, n (%) | Postmenopausal (natural or surgical)<br>Pre or perimenopausal (ovarian suppression)<br>Missing | 67 (60.9)<br>39 (35.5)<br>4 (3.6) |

Abbreviations: EN = Endocrine naïve, N = number of participants in pooled EN cohort, n = number of participants.

## KEY RESULTS

**Table 3. Summary of investigator-assessed confirmed best overall response**

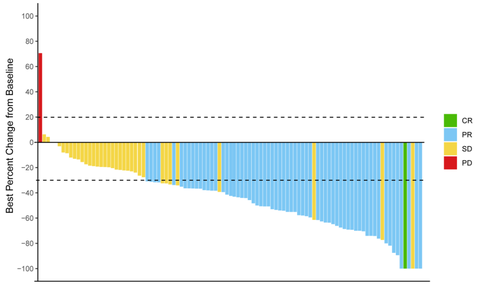
| | Pooled EN Cohort N=110 | |
|---|---|---|
| | n (%) | 95% CI |
| Best Overall Response | | |
| Complete Response, confirmed | 1 (0.9) | 0.0 – 5.0 |
| Partial Response, confirmed | 64 (58.2) | 49.0 – 67.4 |
| Stable Disease | 36 (32.7) | 24.0 – 41.5 |
| Persistent for ≥6 months | 20 (18.2) | 11.0 – 25.4 |
| Progressive disease | 1 (0.9) | 0.0 – 2.7 |
| Non evaluable | 8 (7.3) | 2.4 – 12.1 |
| Objective Response Rate[a] | 65 (59.1) | 49.9 – 68.3 |
| Clinical Benefit Rate[b] | 85 (77.3) | 69.4 – 85.1 |

[a] ORR = CR/PR; [b] CBR = CR/PR/SD persistent for ≥6 months. Abbreviations: CBR = clinical benefit rate; CR = complete response; EN = Endocrine naïve, N = number of participants in pooled EN cohort, n = number of participants; ORR = overall response rate; PR = partial response; SD = stable disease.

- Independent review resulted in confirmed ORR of 60 (54.5%) and CBR of 87 (79.1%) which are consistent with investigator-assessed outcomes.

## RESULTS

**Figure 2. Best overall response of pooled endocrine naïve cohort participants**




Waterfall plot outlining investigator-assessed confirmed best overall response of participants in the pooled EN cohort. Percent change from baseline refers to the change in tumor size with regards to measurable disease. Summary data shown in table 3. CR = Complete response, PR = partial response, SD = stable disease, PD = progressive disease.

## CONCLUSIONS

- Primary analysis of confirmed ORR in EN participants with HR+, HER2– ABC treated with abemaciclib plus fulvestrant compares favorably with previously reported ORR in EN participants with HR+ ABC treated with fulvestrant monotherapy.
- Investigator-assessed confirmed ORR was consistent with that observed by independent review.
- PFS and DoR data are not yet mature.
- The safety profile was consistent with that previously reported in the MONARCH 2 main study.

## Study Design

### MONARCH 2 MAIN STUDY

**Women with HR+, HER2-, ABC:**
- Pre-/peri- or postmenopausal
- Only 1 prior ET for ABC and no prior chemotherapy for ABC
- ECOG PS ≤1
- Progressed on neoadjuvant or adjuvant ET, within 1 year of ET, or while receiving ET or ABC
- A small number of EN participants were initially enrolled but later excluded from the ITT population

Randomized 2:1 N=669

Placebo + fulvestrant n=233

Abemaciclib + fulvestrant n=233

EN participants (*excluded from ITT population*) n=16

MONARCH 2 ITT Population

### MONARCH 2 ENDOCRINE NAÏVE ADDENDUM

- Women with HR+ HER2– ABC who:
  - received no prior ET in any setting and no prior chemotherapy in the metastatic setting
  - had ECOG PS ≤1
  - had measurable disease at baseline
  - had postmenopausal status prior to Day 1, Cycle 1

**Pooled EN Cohort (n=110)**

MONARCH 2 EN participants with measurable disease (*excluded from ITT population*) n=20 + MONARCH 2 EN addendum n=90

**Primary endpoint:**
Investigator-assessed ORR

**Secondary endpoints:**
Investigator-assessed PFS, DoR, CBR and safety and tolerability

**Figure 1. Study design for pooled endocrine naïve cohort in MONARCH 2.**
Abbreviations: CBR = clinical benefit rate; DoR = duration or response; EN = endocrine therapy naïve; ITT = intention-to-treat; n = number of participants per treatment arm; ORR = objective response rate; PFS = progression-free survival.

## METHODS

- The pooled EN cohort (N = 110) consists of the EN participants with measurable disease enrolled to the abemaciclib plus fulvestrant arm under the MONARCH 2 main study protocol [prior to amendment that removed EN participants from ITT population] and the Addendum 7 EN cohort [designed to further explore treatment of participants who are EN]
- All participants were scheduled to receive abemaciclib (150 mg or 200 mg orally Q12H) and fulvestrant (500 mg intramuscularly on day 1 and 15 of cycle 1, then day 1 of cycle 2 and subsequent cycles)
- The efficacy analysis population consisted of all participants in the pooled EN cohort (n=110). The safety analysis population included all participants in the pooled EN cohort who received ≥1 dose of any study drug (n=108).
- ORR was defined as the proportion of participants with confirmed best overall response (BOR) of complete (CR) or partial response (PR), as defined by RECIST Version 1.1
- Safety and tolerability assessment included adverse events (AEs; using Common Terminology Criteria for Adverse Events [CTCAE] Version 4), and serious AEs (SAEs)
- Median follow-up was 9.8 (0.03 – 73.05) months

## Baseline Disease Characteristics

**Table 2. Baseline disease characteristics**

| | | Pooled EN Cohort N=110 |
|---|---|---|
| Initial pathological diagnosis, n (%) | Carcinoma, ductal breast<br>Carcinoma, lobular, breast<br>Other<br>Missing | 83 (75.5)<br>9 (8.2)<br>17 (15.5)<br>1 (0.9) |
| Initial diagnosis disease stage, n (%) | Stage I<br>Stage II<br>Stage III<br>Stage IV<br>Missing | 4 (3.6)<br>9 (8.2)<br>20 (18.2)<br>76 (69.1)<br>1 (0.9) |
| Initial diagnosis histopathological grade, n (%) | GX<br>G1<br>G2<br>G3<br>Missing | 24 (21.8)<br>3 (2.7)<br>65 (59.1)<br>17 (15.5)<br>1 (0.9) |
| Hormone receptor status | ER+ PR+<br>ER+ PR-<br>ER- PR+<br>Missing | 86 (78.2)<br>20 (18.2)<br>3 (2.7)<br>1 (0.9) |
| Disease setting at baseline, n (%) | Recurrent locally advanced<br>Metastatic<br>Unknown | 6 (5.5)<br>103 (93.6)<br>1 (0.9) |
| Numbers of organs involved at baseline, n (%) | 1<br>2<br>3+<br>Missing | 5 (4.5)<br>29 (26.4)<br>75 (68.2)<br>1 (0.9) |
| Disease site, n (%) | Breast<br>Nodal<br>Bone<br>Lung<br>Liver<br>Other[a]<br>Missing | 84 (76.4)<br>83 (75.5)<br>61 (55.5)<br>46 (41.8)<br>21 (19.1)<br>40 (36.4)<br>1 (0.9) |

[a] Other summarizes disease sites detected below 18% including pleura, soft tissue, other viscera, skin and peritoneum. Abbreviations: EN = Endocrine naïve; ER = estrogen receptor; HR = hormone receptor; N = number of participants in pooled EN cohort; n = number of participants; PR = progesterone receptor.

## Adverse Events

**Table 4. Overview of adverse events**

| | Pooled EN Cohort N=110 | |
|---|---|---|
| | Total, n (%) | Related to study treatment, n (%) |
| Subjects with ≥1 TEAE | 107 (99.1) | 103 (95.4) |
| Subjects with ≥1 Grade ≥3 TEAE | 60 (55.6) | 45 (41.7) |
| Subjects with ≥1 SAE | 13 (12.0) | 4 (3.7) |
| Subjects who discontinued study treatment due to AE | 8 (7.4) | 4 (3.7) |
| Subjects who discontinued study treatment due to SAE | 4 (3.7) | 1 (0.9) |
| Subjects who died due to AE[a] | 1 (0.9) | 0 (0.0) |
| Subjects who died due to AE within 30 days of discontinuation | 0 (0.0) | 0 (0.0) |

[a] One patient on study treatment died due to grade 5 embolism deemed unrelated to study treatment. Abbreviations: AE = adverse event; EN = Endocrine naïve; N = number of subjects in treatment group; n = number of subjects; SAE = serious adverse event; TEAE = treatment emergent adverse event.

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## Treatment Emergent AEs

**Table 5. Treatment emergent adverse events (occurring ≥20%)**

| | Pooled EN Cohort N=110 | |
|---|---|---|
| | Total, n (%) | Grade ≥3 TEAE, n (%) |
| **Participants with ≥1 TEAE** | 107 (99.1) | 60 (55.6) |
| Diarrhoea | 93 (86.1) | 15 (13.9) |
| Neutropenia | 46 (42.6) | 25 (23.1) |
| Nausea | 42 (38.9) | 2 (1.9) |
| Fatigue | 41 (38.0) | 1 (0.9) |
| Anaemia | 37 (34.3) | 7 (6.5) |
| Decreased appetite | 32 (29.6) | 0 (0.0) |
| Abdominal pain | 24 (22.2) | 0 (0.0) |
| Leukopenia | 22 (20.4) | 2 (1.9) |
| Vomiting | 22 (20.4) | 1 (0.9) |

Abbreviations: EN = Endocrine naïve; N = number of participants in treatment group; n = number of participants; TEAE = treatment emergent adverse event.

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