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# Updated monarchE Trial Data Shows Abemaciclib Continues to Benefit Patients With High-risk, HR-positive, HER2-negative, Early-stage Breast Cancer

SAN ANTONIO – Extended follow-up data from the phase III monarchE trial showed that adding the cyclin-dependent kinase (CDK) inhibitor abemaciclib (Verzenio) to standard adjuvant endocrine therapy continued to improve invasive disease-free survival (IDFS) among patients with high-risk, node-positive, early-stage, HR-positive, HER2-negative breast cancer, according to data presented at the 2020 San Antonio Breast Cancer Symposium, held Dec. 8-11.

"While many patients with HR-positive early breast cancer will not experience recurrence on endocrine therapy alone, approximately 20 percent may experience disease recurrence in the first 10 years, often in the form of incurable metastatic breast cancer," said Priya Rastogi, MD, associate professor at the University of Pittsburgh Department of Medicine and medical director of the National Surgical Adjuvant Breast and Bowel Project (NSABP) Foundation.

"The risk of recurrence is higher among patients whose cancer has certain clinical and/or pathological risk factors such as a high number of positive lymph nodes, large tumor size, or a high cellular proliferation as measured by tumor grade or biomarkers," Rastogi continued. "There is a significant unmet need for this patient population, and research must be done to find new treatment options to help prevent early breast cancer from returning for these patients."

Earlier results from an interim analysis of the monarchE trial, which is comparing abemaciclib plus adjuvant endocrine therapy with endocrine therapy alone in 5,637 patients with high-risk, node-positive, early-stage, HR-positive, HER2-negative breast cancer, have been previously reported. After a median follow-up of 15.5 months and 323 invasive disease-free events, it was found that the addition of abemaciclib to endocrine therapy reduced the risk of invasive disease by 25 percent. The two-year IDFS rates in the combination arm and the endocrine therapy alone arm were 92.2 percent and 88.7 percent, respectively.

The current study describes an extended follow-up of this trial, capturing results from 395 invasive disease-free events with a median follow-up time of 19 months.

Following surgery, and radiotherapy and/or chemotherapy as indicated, patients were randomly assigned to receive standard of care adjuvant endocrine therapy with or without abemaciclib (150 mg twice per day for two years). Eligibility criteria included having at least four positive nodes, or having one to three positive nodes in combination with either grade 3 disease, a tumor of at least 5 cm, or centrally assessed high Ki-67 status (where "high" is defined as at least 20 percent positivity in tumor cells). Higher levels of Ki-67 protein are indicative of a fast-growing, aggressive tumor with increased probability of recurrence.

At the time of this analysis, 1,437 patients (25.5 percent) had completed the two-year treatment period and 3,281 patients (58.2 percent) were in the two-year treatment period. Compared with patients who received endocrine therapy alone, those who also received abemaciclib had a 28.7 percent reduced risk

of invasive disease. The two-year IDFS rate in the combination arm and the endocrine therapy alone arm was 92.3 percent and 89.3 percent, respectively. Further, the researchers observed an improvement in the two-year distant relapse-free survival (DRFS) rate among patients who received the combinatorial treatment compared with those who received endocrine therapy alone (93.8 percent versus 90.8 percent, respectively).

The researchers also evaluated outcomes among 2,498 patients with centrally assessed high Ki-67 status. Among patients in this cohort, those who received the combination treatment had a 30.9 percent decreased risk of invasive disease compared with those who received endocrine therapy alone. The two-year IDFS rates in the combination arm and the endocrine therapy alone arm were 91.6 percent and 87.1 percent, respectively.

“Across the spectrum of data for abemaciclib, we have observed a consistent benefit, in all subgroups,” said Rastogi. Safety data from this trial were consistent with the known safety profile of abemaciclib and no new safety signals were observed.

“These results may mark a notable treatment advance in the last two decades for people living with high-risk, node-positive, HR-positive, HER2-negative early breast cancer,” Rastogi continued. “These clinically meaningful results have the potential to change how high-risk, HR-positive, HER2-negative early breast cancer is treated.”

Rastogi noted that overall survival data are immature at this time, and additional follow-up is warranted.

This study was sponsored by Eli Lilly and Co.

Rastogi has received reimbursement for travel and accommodation expenses from AstraZeneca, Genentech/Roche, and Eli Lilly and Co.

## Abstract

**GS1-01**

**Primary outcome analysis of invasive disease-free survival for monarchE: abemaciclib combined with adjuvant endocrine therapy for high risk early breast cancer**

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**Background** monarchE is a phase 3, open-label study evaluating abemaciclib combined with endocrine therapy (ET) compared to ET alone in patients with node positive, HR+, HER2-, high risk early breast cancer (EBC) that resulted in a statistically significant improvement in invasive disease-free survival

(IDFS) at a pre-planned interim analysis. Following the positive interim analysis, patients continued to be followed for IDFS, distant recurrence, and overall survival. **Methods** After surgery and, as indicated, radiotherapy and/or chemotherapy, 5,637 patients with HR+, HER2-, high risk EBC were randomized (1:1) to standard of care adjuvant ET with or without abemaciclib (150 mg BD for 2 years). Patients with ≥4 positive nodes, or 1-3 nodes and either grade 3 disease, tumor size ≥5 cm, or central Ki-67 ≥20% were eligible. Here we present results of the primary outcome IDFS analysis which was planned after approximately 390 IDFS events. **Results** At the primary outcome analysis, median follow-up was approximately 19 months in both arms (an increase of 3.5 months from the interim analysis). A total of 1437 (25.5%) patients had completed the 2-year treatment period; 3281 (58.2%) were still in the 2-year treatment period. With 395 IDFS events observed in the intent-to-treat population, abemaciclib plus ET continued to demonstrate superior IDFS versus ET alone, with a 28.7% reduction in the risk of developing invasive disease (p=.0009; HR = 0.713; 95% CI = 0.583, 0.871). Two-year IDFS rates were 92.3% in the abemaciclib plus ET arm and 89.3% in the ET alone arm. There was a consistent benefit of abemaciclib in all prespecified subgroups. The addition of abemaciclib to ET also resulted in an improvement in distant relapse-free survival (DRFS). Overall survival was immature at the time of analysis. A key secondary endpoint was efficacy in patients with centrally assessed high Ki-67 (≥20%) (Ki-67H) (n=2498). Disease characteristics were well balanced between the arms of this population. Abemaciclib plus ET demonstrated superior IDFS vs ET alone, with a 30.9% reduction in risk of developing invasive disease (p=.0111; HR = 0.691; 95% CI = 0.519, 0.920) and 2-year IDFS rates of 91.6% and 87.1%, respectively. An improvement in DRFS treatment effect was also observed in the Ki-67H population. At the time of data cutoff, the median treatment duration of abemaciclib was 17.3 months and the median duration of ET was balanced between the arms (18.3 months in the abemaciclib arm and 18.7 months in the ET alone arm). Safety was consistent with the results at the interim IDFS analysis and with the known safety profile of abemaciclib. **Conclusions** At the primary outcome analysis, with a median follow-up of approximately 19 months, abemaciclib combined with ET continued to demonstrate a clinically meaningful improvement in IDFS in patients with HR+, HER2-, node-positive, high risk, EBC with a statistically significant improvement in IDFS in patients with central Ki-67 ≥20%. ClinicalTrials.gov: NCT03155997

Table 1: Primary Outcome Efficacy

| | **Intent-to-Treat Population** | | **Ki-67 high Population** | |
|---|---|---|---|---|
| **Endpoint** | Abemaciclib + ET<br>N = 2808 | ET alone<br>N = 2829 | Abemaciclib + ET<br>N = 1262 | ET alone<br>N = 1236 |
| IDFS<br># events, n (%) | 163 (5.8) | 232 (8.2) | 82 (6.5) | 115 (9.3) |
| log rank p-value,<br>HR (95% CI) | | p=0.009, 0.713<br>(0.583, 0.871) | | p=0.0111, 0.691<br>(0.519, 0.920) |
| Rate % at 2 years<br>(95% CI) | 92.3 (90.9, 93.5) | 89.3 (87.7, 90.7) | 91.6 (89.4, 93.4) | 87.1 (84.3, 89.5) |
| Difference (%) in<br>2-year rates (95%<br>CI) | | 3 (1.1, 5.0) | | 4.5 (1.2, 7.7) |
| DRFS<br># events, n (%) | 131 (4.7) | 193 (6.8) | 65 (5.2) | 102 (8.3) |
| log rank p-value,<br>HR (95% CI) | | p=0.0009, 0.687<br>(0.551, 0.858) | | p=0.0018, 0.609<br>(0.445, 0.833) |
| Rate % at 2 years<br>(95% CI) | 93.8 (92.6, 94.9) | 90.8 (89.3, 92.1) | 93.6 (91.6, 95.1) | 88.5 (85.7, 90.7) |
| Difference (%) in<br>2-year rates (95%<br>CI) | | 3 (1.2, 4.8) | | 5.1 (2.1, 8.1) |

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